# Journal of Pharmacology and Toxicology

ISSN 1816-496X

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## Saponins from *Eugenia jambolana* with Antibacterial Activity Against Beta-Lactamase Producing Methicillin Resistant *Staphylococcus aureus*

R. Jasmine, B.N. Selvakumar and P. Daisy

The present study was carried out to investigate the role of *Eugenia jambolana* against the beta-lactamase producing *Staphylococcus aureus* and to isolate and identify the putative antibacterial compound based on bioassay-guided fractionation. The test bacteria were resistant to several antibiotics, including several beta-lactams. The crude plant extracts demonstrated zones of inhibition in the range of 18 mm against the chosen test bacteria. On the basis of promising activity, methanol extract was subjected to fractionation, which yielded five fractions. The effective fractions had MIC of 31.75-62.5 μg $mL^{-1}$. Phytochemical analyses and Thin Layer Chromatography (TLC) of the most promising fraction showed the presence of saponins as the active phytoconstituent. The active fraction was further tested for its *in vitro* haemolytic activity to sheep and human erythrocytes and demonstrated no haemolysis at recommended and higher doses. Further studies are needed to elucidate the structure of the compound and establish the mode of action of the compound against these multi drug-resistant bacteria. (*Research Journal of Medicinal Plant 1 (1): 1-6, 2007;* ***doi:*** *10.3923/rjmp.2007.1.6)*

## Antibacterial Activity of Isolated Constituents and Extract of Roots of *Inula racemosa*

P.D. Lokhande, K.R. Gawai, K.M. Kodam, B.S. Kuchekar, A.R. Chabukswar and S.C. Jagdale

The resistance of different bacteria to the current antibacterial agents, toxicity of the antibacterial agents and the cost of the treatment has led to the development of new active molecules against the bacteria. Since ancient times medicinal plants have been used for the treatment of bacterial infections. The roots of the plant *Inula racemosa* has been used as folk medicine in East Asia and Europe. However, no systematic data is available on the antibacterial activity profile of the different constituents of *Inula racemosa*. In the present studies, attempt has been made for isolation of root constituents of *Inula racemosa* (Compositae) and evaluation of its antibacterial activity. The constituents were isolated and purified by column chromatography. The structure of the isolated constituents were confirmed by spectral analysis and were used for the determination of the

antibacterial activity of *Inula racemosa* against various microorganisms. The constituent alantolactone showed maximum antibacterial activity as compared to other constituents and ethyl acetate extract of the roots. *(Research Journal of Medicinal Plant 1 (1): 7-12, 2007;* ***doi:*** *10.3923/rjmp.2007.7.12)*

## *In vitro* Antioxidant Activity of Ethanolic Extracts of *Centella asiatica, Punica granatum, Glycyrrhiza glabra* and *Areca catechu*

M.S. Ashawat, Saraf Shailendra and Saraf Swarnlata

The present investigation deals with antioxidant activities of the ethanolic extract of *C. asiatica* fresh leaves, *P. granatum* seeds, *G. glabra* dry root and *A. catechu* nuts. The effects of all ethanolic extracts of the herbs were studied via reducing power estimation method. The antioxidant activities of the extracts were compared with standard i.e., of ascorbic acid. The equal amount of extract and ascorbic acid combination antioxidant activity was also studied to know the synergistic effect of chemical and extract in any pharmaceutical and cosmetic formulations. The individual antioxidant activity of *C. asiatica*, *P. granatum*, *G. glabra* and *A. catechu* were found to be 8.23±0.12, 24.35±0.25, 24.25±0.52, 31.31±1.80%, respectively to the standard indicating antioxidant activity to all ethanolic extracts, but catechu showed highest activity ($p<0.05$). The combined antioxidant activity (ascorbic acid with extracts) showed additive synergistic effect as compared to standard i.e., 110.51±0.422, 127.51±0.745, 128.09±0.235, 134.73±0.60, respectively with each extract. These studies may suggest that the combination of chemical with extract as antioxidant can be utilized in pharmaceutical and cosmetic formulation or chemical antioxidant replaced by herbal natural antioxidants. *(Research Journal of Medicinal Plant 1 (1): 13-16, 2007;* ***doi:*** *10.3923/rjmp.2007.13.16)*

## Increase Insulin Activity by *Phyllanthus amarus* Linn on Liver Cell Regeneration in Partially Hepatectomised Albino Rats

P. Chattopadhyay, A. Garg, V.P. Varshey, A.K. Sharma and S.S. Agrawal

The hydroalcoholic extract of whole plant of *Phyllanthus amarus* Linn showed significant increase in activity of insulin at 200 mg $kg^{-1}$ dose in regenerative hepatocytes against alcohol induced liver cell injury in partially hepatectomised albino rats. The blood sample were collected from the abdominal aorta and the serum insulin estimated by radio immuno assay and regenerative capacity measured by thymidine kinase assay by $^{3}H$ thymidine incorporation into hepatic

DNA which showed that *Phyllanthus amarus* Linn has a potential role in insulin action during liver cell regeneration. *(Research Journal of Medicinal Plant 1 (1): 17-20, 2007; **doi:** 10.3923/rjmp.2007.17.20)*

## Antimicrobial Properties of *Osmanthus fragrans* (Lour)

Ashok Kumar and Deepak Ganjewala

The ethanol extract and essential oil of *Osmanthus fragrans* (Lour.) family (Oleaccae) were evaluated for antimicrobial action on *Staphylococcus aureus*, *Bacillus cereus*, *Salmonella typhi* and *Shigella dysentery* by using agar disc diffusion method. Essential oil have shown strongest inhibitory effect against *Staphylococcus aureus*, *Bacillus cereus* and *Salmonella typhi*. Ethanol extract had less antimicrobial activity against the microorganisms tested. However, both essential oil and ethanol extract had no inhibitory effect against *Escherichia coli* and *Pseudomonas*. *Shigella dysentery* in particular was more susceptible for essential oil. Results have shown that essential oil had two fold more antibacterial activities as compared to that of ethanol extract. The minimum concentration of ethanol extract and essential oil used was 0.0625 mg $mL^{-1}$. *(Research Journal of Medicinal Plant 1 (1): 21-24, 2007; **doi:** 10.3923/rjmp.2007.21.24)*

## Anti-microbial Activity of *Acacia nilotica* Extracts Against Some Bacteria Isolated from Clinical Specimens

Abeer M. Haj Ali and Sanaa O. Yagoub

The comparative antimicrobial activity of ethanol and chloroform extracts from *Acacia nilotica* fruit was studied. The bacteria isolated from abscesses or wounds of hospitalized patients were *Staphylococcus aureus*, *Escherichia coli*, *Proteus vulgaris*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*. The susceptibility of isolated bacteria against ethanol extract (13, 6.7, 5, 3 and 1%) was higher than chlorform extract used in similar concentrations especially *S. aureus* (30-4 mm), *E. coli* (25-9 mm), *Kl. pneumonia* (18-0 mm), *P. vulgaris* (10-1 mm) and *Ps. aeruginosa* (20-4 mm). The inhibitory effects of the extracts on bacteria were compared with those of selected antibiotics. The ethanol extract of *A. nilotica* fruit was either equally or more effective than the test antibiotics. *(Research Journal of Medicinal Plant 1 (1): 25-28, 2007; **doi:** 10.3923/rjmp.2007.25.28)*

## Some Medicinal Flora of Okomu Forest Reserve in Southern Nigeria

M. Idu and O.O. Osemwegie

A survey of useful medicinal plants of Okomu Forest Reserve was undertaken and a total of 60 species of plants comprising of 50 leafy plants and 10 mushrooms were identified and recognized to be useful in native health care services by inhabitants of various communities in the South-South of Nigeria. Different southern Nigerian communities show not only individual characteristic dialect, culture and therapeutic practices involving the application of ethnomedicinal plants but also share common indigenous folk knowledge of what plant is used for the treatment of which ailment. Studies also show that 75% of men in most rural communities visited have inherited ethnobotanical knowledge from their fathers. *(Research Journal of Medicinal Plant 1 (1): 29-31, 2007;* ***doi:*** *10.3923/rjmp.2007.29.31)*

## Medicinal Plants of Edo State, Nigeria

M. Idu and H.I. Onyibe

An ethno-medical field survey was carried in communities spanning the three vegetation (Fresh Water Swamp, Lowland Rain Forest and Derived Savanna) zones of Edo State, Nigeria. 300 plant species distributed in 247 genera, belonging to 77 families, used in the treatment of various diseases were enumerated, identified and their ethnomedical value documented. The most used species include: *Ageratum conyzoides*, *Asystasia gangetica*, *Azadirachta indica*, *Calopogonium muconoides*, *Carica papaya*, *Chromolaena odorata*, *Citrus aurantifolia*, *Citrus sinensis*, *Cocos nucifera*, *Colocasia esculenta*, *Commelina erecta*, *Elaeis guineensis*, *Eleusine indica*, *Ficus benghalensis*, *Gmelina arborea*, *Hura crepitans*, *Irvingia gabonensis*, *Mangifera indica*, *Manihot esculenta*, *Musa paradisiaca*, *Musa sapientum*, *Nauclea pobeguinii*, *Newbouldia laevis*, *Phyllanthus amarus*, *Psidium guajava*, *Sida acuta*, *Spondias mombin* and *Synedrella nodiflora*. Leaves and roots were the most frequently used plant parts while malaria fever, muscular pains, gastrointestinal problems, cardiovascular problems, bronchial problems and skin infections are amongst the frequently managed conditions malaria fever, muscular pains, gastrointestinal problems, cardiovascular problems, bronchial problems and skin infections among others. *(Research Journal of Medicinal Plant 1 (2): 32-41, 2007;* ***doi:*** *10.3923/rjmp.2007.1.6)*

## Regeneration of Plantlets from Embryo Explants of *Bunium Persicum* (Boiss.) B. Fedtsch

M. Valizadeh, S.K. Kazemi Tabar and G.A. Nematzadeh

A new simple method was developed for regeneration of Parsi Zira. This method yielded a large number of shoots within short period of time (30-40 days) without any sub culturing. The effect of various combinations of Plant Growth Regulators (PGRs) on callus formation and shoot regeneration were investigated on MS medium. Simultaneous callus and root formation and shoot regeneration were obtained. The experiment was conducted in a completely randomized design with 30 treatments and 10 replications per treatment. The best treatment for regeneration was the medium supplemented with 0.1 mg $L^{-1}$ α-Naphthalene Acetic Acid (NAA) and 2 mg $L^{-1}$ kinetin (Kin). The highest somatic embryogenesis was obtained in the treatment containing 0.1 mg $L^{-1}$ NAA and 0.5 mg $L^{-1}$ Kin. The medium containing 2 mg $L^{-1}$ NAA and 2 mg $L^{-1}$ Kin was the best treatment for callus and root induction and regeneration simultaneously. *(Research Journal of Medicinal Plant 1 (2): 42-47, 2007;* ***doi:*** *10.3923/rjmp.2007.42.47)*

## Effect of Plant Growth Regulators on Callus Induction and Regeneration of *Bunium persicum* (Boiss.) B. Fedtsch

M. Valizadeh, S.K. Kazemi Tabar and G.A. Nematzadeh

The effect of various media and combinations of Plant Growth Regulators (PGRs) on callus induction and shoot regeneration from hypocotyl explant were investigated. Simultaneous callus and shoot regeneration were obtained. The experiment was conducted as a completely randomized design. The highest callus frequency was observed on MS medium containing 0.1 mg $L^{-1}$ 2,4-dichlorophenoxyacetic acid (2,4-D) or 1 mg $L^{-1}$ 2,4-D as well as 2 mg $L^{-1}$ 2,4-D and 0.5 mg $L^{-1}$ Kinetin (Kin). The best response for shoot regeneration was observed on MS medium containing 1 mg $L^{-1}$ 2,4-D. MS medium supplemented with 1 mg $L^{-1}$ 2,4-D was the best for callus induction and shoot regeneration simultaneously. The regenerated plantlets were transferred to basal medium to be rooted. However suitable combination of auxins and cytokinins are important for embryogenesis and organogenesis. For the exploitation of *in vitro* techniques it is essential to optimize the conditions for whole plant regeneration. *(Research Journal of Medicinal Plant 1 (2): 48-53, 2007;* ***doi:*** *10.3923/rjmp.2007.48.53)*

## Analgesic, Antipyretic and Ulcerogenic Effects of Indian Ayurvedic Herbal Formulation Triphala

E.P. Sabina and M. Rasool

An Indian ayurvedic herbal formulation, Triphala (500/1000 $kg^{-1}$ $b.wt^{-1}$) was assessed for analgesic, antipyretic and ulcerogenic activities on the experimental models in mice. For comparison purpose, non-steroidal anti-inflammatory drug Indomethacin (10 mg $kg^{-1}$ $b.wt^{-1}$) was used as a standard. It was found that Triphala at both the dose levels produced excellent analgesic and antipyretic effect, with the absence of gastric damage. The results obtained clearly show that Triphala possesses potent analgesic, antipyretic and gastroprotective effect. *(Research Journal of Medicinal Plant 1(2): 54-59, 2007;* ***doi:*** *10.3923/rjmp.2007.54.59)*

## Antimicrobial Activity of Cassava Seed Oil on Skin Pathogenic Microorganisms

T.O.S. Popoola, O.D. Yangomodou and A.K. Akintokun

An assessment of the antimicrobial activity of oil extracted from cassava (*Manihot esculenta*. Crantz) seeds was investigated using agar-well diffusion method against clinical isolates of *Staphylococcus aureus*, *Propionibacterium acnes*, *Escherichia coli*, *Pityrosporium ovale* and *Candida albicans* which were isolated from skin infections. The results of the investigation showed that cassava seed oil had inhibitory effect on the growth of all the test isolates. Significant differences ($p<0.05$) were observed in the degree of inhibition of the isolates, but non-significant variations were observed in inhibition among strains of the same species. The most pronounced inhibition as confirmed by the zones of inhibition around growing colonies was on *S. aureus*; *P. acnes* was moderately inhibited, while inhibition of growth of *E. coli* was mild. Growth inhibition by the oil was not significant ($p>0.05$) between *P. ovale* and *C. albicans*. The inhibitory ability of the oil decreases with a decrease in concentration of oil in the solvent, resulting in marked variation in the minimum inhibitory concentration. The implication of this observation is that the oil may be of medical and particularly dermatological importance. *(Research Journal of Medicinal Plant 1 (2): 60-64, 2007;* ***doi:*** *10.3923/rjmp.2007.60.64)*

## An Antisalmonellal Agent and a New Dihydroanthracenone from *Cassia petersiana*

Pierre C. Djemgou, Donatien Gatsing, Marguerite Kenmogne, Dieudonné Ngamga, Roseline Aliyu, Abiodun H. Adebayo, Pierre Tane, Bonaventure T. Ngadjui, Elisabeth Seguin and Godwin I. Adoga

Phytochemical and biological investigation of the leaves of *Cassia petersiana* afforded four compounds including a new dihydroanthracenone (1), two known chromones (2,3), in addition to stigmasterol glucoside (4). The work was guided by the antisalmonellal activity of the extract and fractions. Compound 4 was found to be the active principle. The structures of the compounds were determined by combination of spectroscopic techniques, including $^{1}H$, $^{13}C$, DEPT, COSY, HMQC, HMBC, MS and IR. *(Research Journal of Medicinal Plant 1 (2): 65-71, 2007; **doi**: 10.3923/rjmp.2007.65.71)*

## Isolation of Bactericidal Constituents from the Stem Bark Extract of *Grewia tiliaefolia* Vahl.

B. Mohamed Khadeer Ahamed, V. Krishna, Harish B. Gowdru, H. Rajanaika, H.M. Kumaraswamy, Sharath Rajshekarappa, Chethan J. Dandin and K.M. Mahadevan

*Grewia tiliaefolia* (Tiliaceae) is a subtropical medicinal tree, the stem bark is widely used in traditional Indian medicines to cure pneumonia, bronchitis and urinary infectious disorders. Antibacterial activity of sequential extracts of the stem bark and constituents isolated from petroleum ether extract were screened against eighteen clinical strains belonging to *Pseudomonas aeruginosa* and *Klebsiella pneumonia* collected from hospitalized patients suffering from different kinds of infectious ailments. Two steroids β-sitosterol, stigmasterol and a triterpenoid lupeol were isolated from petroleum ether extract. The compounds were characterized by UV, IR, $^{1}H$ NMR, $^{13}C$ NMR and mass spectral studies. Minimum inhibitory concentrations of petroleum ether, chloroform and methanolic extracts were 120, 150 and 210 μg per 100 μL, respectively. Minimum inhibitory concentrations for isolated constituents β-sitosterol, stigmasterol and lupeol were 80, 70 and 30 μg per 100 μL, respectively. Among the three crude extracts and the three bioactive constituents tested, petroleum ether extract and the lupeol showed significant zones of inhibition in the cultures of both bacterial strains. The activity was moderate in steroids loaded wells. Results of this investigation provide a supportive scientific evidence for the medicinal use of *Grewia tiliaefolia*. *(Research Journal of Medicinal Plant 1 (3): 72-82, 2007; **doi**: 10.3923/rjmp.2007.72.82)*

## Effect of a Herbal Drug, Cogent db on Plasma and Tissue Glycoproteins in Alloxan-Induced Diabetic Rats

G. Saravanan and L. Pari

Cogent db, a poly herbal drug, was investigated for its beneficial effect in diabetic rats on derangement in glycoprotein components. Diabetes was induced in male albino Wistar rats by a single intraperitoneal injection of alloxan (150 mg $kg^{-1}$) and the animals were divided into 5 groups as follows: Group 1: Normal untreated rats, Group 2: Normal rats treated with Cogent db (450 mg $kg^{-1}$), Group 3: Diabetic control rats, Group 4: Diabetic rats treated with Cogent db (450 mg $kg^{-1}$) and Group 5: Diabetic rats treated with glibenclamide (600 μg $kg^{-1}$). The effect of Cogent db on blood glucose, plasma insulin, urine sugar, plasma and tissue glycoproteins studied was in comparison to glibenclamide, a standard reference drug. The levels of blood glucose, urine sugar, plasma glycoproteins were increased significantly whereas the level of plasma insulin was significantly decreased in diabetic rats. There was a significant decrease in the level of sialic acid and elevated levels of hexose, hexosamine, fucose in the liver and kidney of diabetic rats. Oral administration of Cogent db to diabetic rats for 45 days significantly decreased levels of blood glucose, urine sugar and plasma glycoproteins. On the other hand, the levels of plasma insulin and tissue sialic acid were increased while the levels of tissue hexose, hexosamine and fucose were near normal. Cogent db was more effective than glibenclamide in restoring the values of these parameters. It is likely that the changes in glycoprotein metabolism induced by hyperglycaemia will have biological and possibly pathological importance in the development of diabetic complications. The present investigation indicates that Cogent db treatment possesses a significant beneficial effect on glycoproteins in addition to its antidiabetic action. *(Research Journal of Medicinal Plant 1 (3): 83-91, 2007;* ***doi:*** *10.3923/rjmp.2007.83.91)*

## *In vitro* Biological Activities of *Carica papaya*

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The present study was designed with the aim of confirming or otherwise the ethno-medicinal claims of *C. papaya* in the treatment and or management of ailments such as ringworm, digestive disorders, fevers and tumors. Hence, the anti-microbial, larvicidal and brine-shrimp lethality studies on leaves, stem and roots extracts were carried out. The extracts and fractions of roots elicited good anti-microbial activity against *B. subtilis*, *S. aureus* but gave minimal activity against

*E. coli*, *S. typhi* and *K. pneumoniae* and none against fungal isolates (*A. niger* and *C. albicans*). Both the leaves and stem, however afforded lesser activities. The larvicidal activity determined in terms of percentage mortality showed that the roots gave moderate larvicidal activity (LA%) of 40 and 55% (at 5%w/v) while the activity was potent at 70 and 80% (at 10% w/v) both at 12 and 24 h incubation respectively. However, the activity displayed by both the leaves and stem was insignificant. Interestingly, the brine-shrimp lethality assay; analyzed using the Finney probit method, showed the leaves displayed a significant $LD_{50}$ value at 2.7 ppm, while the stem and roots gave moderate $LD_{50}$ values at 384 and 272 ppm respectively compared with literature values below the 200 ppm which are generally considered significant. These findings indicate a potential of the plant to serve as panacea for infectious diseases and also lend scientific justification to some of the folkloric uses. *(Research Journal of Medicinal Plant 1 (3): 92-99, 2007; **doi:** 10.3923/rjmp.2007.92.99)*

## Anticancerous Effect of *Hibiscus sabdariffa* Leaves on Hepatocellular Carcinoma Cell Line Hep 3B

A. Umamaheswari and Nivedita Govindan

*Hibiscus sabdariffa* L. (Malvaceae) is a natural plant containing a lot of pigments that was found to possess anti-oxidant activity. Therefore, the present study was aimed to evaluate the anticancer potential of *Hibiscus sabdariffa* (*H. sabdariffa*) leaves on Hep 3B. Different extracts of methanol, ethanol, ethyl acetate and chloroform were prepared and tested for their cytotoxic effect by MTT assay in a dose and time dependent manner. Among the different organic solvent extracts tested, methanolic extract showed a greater cytotoxic effect (i.e.,) IC 50 value of 50% reduction when compared to others. The time required to show 75% decrease in cell number was found to be 24 h. *(Research Journal of Medicinal Plant 1 (3): 100-105, 2007; **doi:** 10.3923/rjmp.2007.100.105)*

## A New Steroid and α-glucosidase Inhibitors from *Anthocleista schweinfurthii*

R.N. Mbouangouere, P. Tane, D. Ngamga, S.N. Khan, M.I. Choudhary and B.T. Ngadjui

The dichloomethane/methanol extract of the roots of *Anthocleista schweinfurthii* Gilg. has provided a new steroid, schweinfurthiin 1, two known compounds, bauerenone 2 and bauerenol 3 which were found to be highly promising α-glucosidase inhibitors. Along with these, two known xanthones, 1-hydroxy-3, 7,

8-trimethoxyxanthone 4 and 1, 8-dihydroxy-3, 7-dimethoxyxanthone 5 were also isolated. *(Research Journal of Medicinal Plant 1 (3): 106-111, 2007; **doi:** 10.3923/rjmp.2007.106.111)*

## Role of Terpenoids From *Elephantopus scaber* Against a Few Extended Spectrum β-Lactamase Producers

R. Jasmine, P. Daisy and B.N. Selvakumar

The extended spectrum β-lactamase producers are highly resistant to several conventional antibiotics. Hence efforts are now taken to screen few medicinal plants against the ESBL producers. Among the several plants screened, we have chosen to screen the alcohol extracts of a traditional medicinal plant, *Elephantopus scaber* (Asteraceae) against ESBL producers. ESBL producers were screened by double disc synergy test. Methanol, hexane and acetone extracts of *Elephantopus scaber* were investigated for their ability to inhibit the growth of extended spectrum β-lactamases (ESBL) producing multidrug-resistant enteric bacteria by the disc diffusion method. MICs were determined by micro broth dilution method. The crude plant extracts demonstrated zones of inhibition in the range of 5-16 mm against the chosen test bacteria. On the basis of promising activity, acetone extracts were selected to determine their efficacy in terms of Minimal Inhibitory Concentration (MIC), which ranged from 1.6-25 mg $mL^{-1}$. The acetone extract was subjected to activity-guided fractionation. The most effective fraction had a MIC of 62.5-250 μg $mL^{-1}$. Phytochemical analysis showed the presence of terpenoids, proteins and traces of steroids. TLC bioautography of the fraction showed the active compound to be terpenoids. The fraction was further tested for their *in vivo* cytotoxic activity to mammalian system using rats. No marked manifestations were observed. Normal liver and kidney functioning were also observed. The strong *in vitro* antibacterial activity of terpenoid derivatives against ESβL-producing Gram-negative bacteria suggests the compounds might find wide pharmaceutical use. *(Research Journal of Medicinal Plant 1 (4): 112-120, 2007; **doi:** 10.3923/rjmp.2007.112.120)*

## Effects of Ethanolic Fruit Extract of *Parinari polyandra* (Rosaceae) on Serum Lipid Profile and Some Electrolytes in Pregnant Rabbits

A.O. Abolaji, A.H. Adebayo and O.S. Odesanmi

The effects of the ethanolic fruit extract of *Parinari polyandra* on lipid profile and electrolyte levels in pregnant rabbits were investigated. Graded concentrations of

0, 10, 50 and 250 mg $kg^{-1}$ body weight of the extracts were administered by gastric intubations for a period of 14 days from the 12th -25th day of gestation after which they were fasted for 18 h. The following lipid profiles were examined in the serum. Triglyceride, Total Cholesterol, High Density Lipoprotein (HDL) and Low Density Lipoprotein (LDL) cholesterol. Serum electrolytes also examined were: Sodium ($Na^+$), Potassium ($K^+$), Calcium($Ca^{2+}$), Chloride ($Cl^-$), Bicarbonate($HCO_3^-$) and Phosphorus (P). After these durations of treatment, there was significant elevation in triglycerides ($p<0.01$). The LDL/HDL Cholesterol ratio was greater than 0.3 in all the treated groups. Also, there were significant elevations in $Na^+$ ($p<0.05$), Cl-($p<0.05$), P ($p<0.05$) and $Ca^{2+}$ ($p<0.05$). The result therefore suggests that the ethanolic fruit extract of *Parinari polyandra* may predispose to hyperlipidemia and electrolytes imbalance leading to hypercalcaemia and high risk of raised blood pressure in pregnant rabbits. *(Research Journal of Medicinal Plant 1 (4): 121-127, 2007;* ***doi:*** *10.3923/rjmp.2007.121.127)*

## Ethnobotanical Studies on Medicinal Plants Used by the Chenchus of Nallamalais in Kurnool District, Andhra Pradesh, India

C. Sudhakar Reddy, K.N. Reddy, K. Thulsi Rao and Chiranjibi Pattanaik

Ethnobotanical studies were carried out to collect information on the use of medicinal plants by the Chenchus who live in forests of Nallamalais in Kurnool district, Andhra Pradesh, India. Ethnomedicinal uses of 51 plant species along with local name, botanical name, family, part used, ailments for which the drug is administrated, mode of administration are presented. They belong to 48 genera and 33 angiospermous families. These plants use to cure 26 ailments. Most remedies were taken orally, accounting for 62% of medicinal use. Most of the remedies were reported to have been from herbs (37.3%) and tree (33.3%) species. The most widely sought after plant parts in the preparation of remedies in the areas are the root (14) and stem bark (12). Chenchus have high number of medicinal plant species for the treatment of fever and skin diseases. *(Research Journal of Medicinal Plant 1 (4): 128-133, 2007;* ***doi:*** *10.3923/rjmp.2007.128.133)*

## Antidiabetic Effects of *Homalium letestui* (Flacourtiaceae) in Streptozotocin Induced Diabetic Rats

Jude E. Okokon, Bassey S. Antia and Basil N. Ita

Evaluation of antidiabetic activity of ethanolic root extract of *Homalium letestui* in rats was carried out. Antidiabetic potentials of the plant *Homalium letestui*

extract (500-1000 mg $kg^{-1}$) was investigated in streptozotocin induced diabetes in rats. Treatment of streptozotocin diabetic rats with the extract caused a significant ($p<0.01$) reduction in fasting Blood Glucose Levels (BGL) of the diabetic rats both in acute study and prolonged treatment (2 weeks). The activity of the extract was comparable to that of the reference drug, glibenclamide. This results suggest that the root extract of *Homalium letestui* possesses antidiabetic effect on streptozotocin induced diabetic rat. *(Research Journal of Medicinal Plant 1 (4): 134-138, 2007;* ***doi:*** *10.3923/rjmp.2007.134.138)*

## Effect of Aqueous *Nauclea pobeguinii* Leaf Extract on Rats Induced with Hepatic Injury

Helen Kadiri, Ese Adegor and Samuel Ogheneovo Asagba

Forty male albino rats (Wistar strain) weighing between 150 and 170 g were used to study the antioxidant property of *Nauclea pobeguinii* extract. The rats were divided into four groups, each group consisting of 10 animals. The antioxidant activity of the extract was evaluated using $CCl_4$-induced lipid peroxidation model. Group one was kept on normal diet and served as control, the second group received the extract alone three times daily for 10 days by oral route, the third received only $CCl_4$ in olive oil by subcutaneous injection, while the fourth group received the extract at the same dose and duration as group two before exposure to $CCl_4$. Eighteen hours after $CCl_4$ administration, the animals were sacrificed, blood was collected and serum separated for analysis. Biochemical analysis of serum indicate increased activities of L-alanine aminotransferase (L-ALT), L-aspartate aminotransferase (L-AST) and alkaline phosphatase (ALP) in $CCl_4$ administered rats which is an indication of liver damage occassioned by lipid peroxidation. Prior treatment of $CCl_4$ exposed rats with the plant extract lowered the serum activities of these enzymes to levels that were comparable to control. The study indicates that aqueous extract of *N. pobeguinii* possess antioxidant property since it improves recovery or reduces the toxic effects of $CCl_4$ in liver cells of male rats. *(Research Journal of Medicinal Plant 1 (4): 139-143, 2007;* ***doi:*** *10.3923/rjmp.2007.139.143)*

## Enumeration of Antidiabetic Herbal Flora of Tamil Nadu

R. Jeyachandran and A. Mahesh

This study showed the first had information on 57 interesting medicinal herbal plants used by tribal people, Vaidyas, Siddha and Ayurveda for diabetes mellitus.

Present enumeration of antidiabetic herbal flora of Tamil Nadu includes information regarding previous findings. This information's were gathered at the time of field study from various local inhabitants, viz., vaidyas. Medicinal plant seller, healers, priests, hakims and local elderly people. Furthermore, information's regarding antidiabetic nature of plants were confirmed by previous findings reported in various national and international journals. *(Research Journal of Medicinal Plant 1 (4): 144-148, 2007;* ***doi:*** *10.3923/rjmp.2007.144.148)*

## Preliminary Phytochemistry and Antimicrobial Properties of *Stachytarpheta jamaicensis* (Linn.) Vahl. Stem

M. Idu, E.K.I. Omogbai, G.E. Aghimien, F. Amaechina, O. Timothy and S.E. Omonigho

The phytochemical analysis on stems of *Stachytarpheta jamaicensis* proved the presence of secondary metabolites, including; tannins, saponins and flavonoids Crude concentrations of aqueous extract of stem showed antimicrobial activity on *Bacillus subtilis*, *Escherichia coli*, *Candida albicans*, *Staphylococcus aureus*, *Pseudomonas aureginosa* and slight activity on *Proteus vulgaris* while the alcoholic extract had almost similar activity, but lesser activity was observed on *Escherichia coli. (Research Journal of Medicinal Plant 1 (4): 149-153, 2007;* ***doi:*** *10.3923/rjmp.2007.149.153)*

## Hypolipidaemic and Cardioprotective Activity of *Mammea africana*

Jude E. Okokon and Bassey S. Antia

The effect of ethanolic stembark extract of *Mammea africana* Sabine on total cholesterol, triglyceride and lipoproteins levels was studied on normal rats. The extract (30-90 mg $kg^{-1}$) was orally administered to rats for 21 days after which they were sacrificed and blood taken for analysis. The extract produced a significant ($p<0.05$) dose-dependent decrease in the levels of total cholesterol, triglyceride, LDL-cholesterol and VLDL cholesterol, with a significant ($p<0.05$) increase in the level of HDL-cholesterol. The stembark extract has the potential to produce hypolipidaemia as well as preventing the development of atherosclerosis. *(Research Journal of Medicinal Plant 1 (4): 154-157, 2007;* ***doi:*** *10.3923/rjmp.2007.154.157)*

## Micropropagation, Isolation and Characterization of Berberine from Leaves of *Naravelia zeylanica* (L.) DC.

H. Raja Naika and V. Krishna

An *in vitro* regeneration protocol was standardized using leaf explants of *Naravelia zeylanica* (Ranunculaceae) a rare medicinal plant of the Western Ghats, India. The adventitious shoot buds were organized directly from mid veins and margin of the excised leaf explants cultured on MS-medium fortified with a range of 2.0 to 3.0 mg $L^{-1}$ BAP and 0.3 to 0.7 mg $L^{-1}$ IBA. The frequency of shoot bud organogenesis was the highest (14.9±0.27 shoots per explants) at the concentration of 2.5 mg $L^{-1}$ BAP and 0.5 mg $L^{-1}$ IBA. The excised micro shoots were pretreated in 0.5 mg $L^{-1}$ IBA and transferred to MS half strength semisolid medium induced root initials from the cut ends. A mean of 13.5±0.30 root intact plantlets was recovered per explants showed morphological similarity with the *in vivo* plants. Two hundred and fifty gram of the powdered leaves from *in vivo* plants of *N. zeylanica* was subjected to Soxhlet extraction using methanol. Ten gram of each of the extracts were used for total alkaloid isolation and the yield was 270 mg. An alkaloid berberine was isolated by preparative TLC method using the solvent system methanol, water and ammonium hydroxide in the ratio 8: 1: 1 v/v. The characterization of the constituent was confirmed by IR, $^1$HNMR and Mass spectral studies. *(Research Journal of Medicinal Plant 2 (1): 1-9, 2008;* ***doi:*** *10.3923/rjmp.2008.1.6)*

## Comparative Evaluation of Antihyperglycaemic and Hypoglycaemic Activity of Various Parts of *Catharanthus roseus* Linn.

E. Edwin Jarald, E. Sheeja, S. Motwani, K.R. Dutt and R.K. Goel

Hydroalcoholic extracts of flowers, leaves, stems and roots of *Catharanthus roseus* Linn. (Apocynaceae) were tested for antihyperglycaemic and hypoglycaemic activities. Antihyperglycaemic activity was tested in glucose over loaded hyperglycemic rats and hypoglycaemic activity in fasted normal rats at two dose levels, 100 and 200 mg $kg^{-1}$, respectively. Glimepride 0.1 mg $kg^{-1}$ was used as the reference drug for both the activities. Results showed that the hydroalcoholic extracts of every part tested, exhibited significant antihyperglycaemic and hypoglycaemic activity. Comparatively the hydroalcoholic extract of leaves exhibited better activity, next to this stems and flowers were equally effective followed by roots. This study gives an indication to traditional

healers those who use different parts of this plant to use the active part that has the ability to manage the complications of diabetes. *(Research Journal of Medicinal Plant 2 (1): 10-15, 2008;* ***doi:*** *10.3923/rjmp.2008.10.15)*

## Checklist and Conservation of Botanicals Used for Natality by the Okpe-Speaking People of Delta State, Nigeria

J. Kayode, E.S. Christmas and G.M. Kayode

A combination of social survey and direct field observation was used to identify and determine the conservation status of botanicals used by the indigenous okpe-speaking people of Delta State, Nigeria during natality periods. While a total of 11 botanicals belonging to 11 different families were found to be widely utilized during the pre-natal periods, another 10 botanicals, belonging to 10 different families were widely utilized during the post-natal periods. Only 7 of these botanicals were cultivated. Among the uncultivated botanicals, only 4 were regularly preserved in the study area. Over 40% of the botanicals were sourced from the forest and some of the botanicals were harvested by annihilative extraction methods. Over 40% of the botanicals were presently rare on the abundance scale. Sustainable strategies that could enhance the conservation of these species were proposed. *(Research Journal of Medicinal Plant 2 (1): 16-21, 2008;* ***doi:*** *10.3923/rjmp.2008.16.21)*

## Role of *Elephantopus scaber* on the Glucose Oxidation in Liver and Skeletal Muscles of Streptozotocin (STZ) Induced Diabetic Adult Male Rats

P. Daisy and R. Jasmine

In type-II diabetic individuals, there is an increase in hepatic glucose production impaired insulin signaling, decreased glucose transport and phosphorylation and diminished glycogen synthesis contribute to insulin resistance in target tissues. Liver and skeletal muscles are major target sites for insulin-mediated glucose uptake, metabolism and utilization in humans. Indeed, impaired insulin action in liver and skeletal muscles is responsible for the majority of the decreased levels of non-oxidative glucose disposal observed in type II diabetes. The influences of *Elephantopus scaber* (ES) (roots and leaves) on glucose oxidation in liver and skeletal muscles were studied. The present study shows that *E. scaber* extracts have a positive role in glucose oxidation and corrects the metabolic alterations caused by diabetes effectively. A significant reduction in the blood glucose levels

and a corresponding increase in the serum insulin levels further proves the hypoglycemic activity of the plant by oxidation of glucose. These observed effects of *E. scaber* on glucose oxidation in liver and skeletal muscles are comparable to the effects of insulin and suggest a possible therapeutic effect of *E. scaber* on glucose oxidation in diabetes. Further studies on the isolation of active compounds and determining their mode of action would be of great interest. *(Research Journal of Medicinal Plant 2 (1): 22-27, 2008;* ***doi:*** *10.3923/rjmp.2008.22.27)*

## Antiperoxidative Effect of *Withania somnifera* Root Powder on Liver Lipid Peroxidation and Antioxidant Status in Adjuvant-induced Arthritic Rats

M. Rasool and P. Varalakshmi

The present study was carried out to evaluate the antiperoxidative effect of *Withania somnifera* Linn. Dunal (family-Solanaceae) on liver lipid peroxidation and antioxidant status in adjuvant induced arthritic rats. Results were compared with those for Indomethacin, a non steroidal anti-inflammatory drug. Arthritis was induced by intra dermal injection of complete freund's adjuvant (0.1 mL) in to the right hind paw of Wistar albino rats. *Withania somnifera* root powder (1000 mg $kg^{-1}$ b.wt.) and indomethacin (3 mg $kg^{-}$ b!wt.) were orally administered for 8 days beginning 11 days after adjuvant injection. The antiperoxidative effect of *Withania somnifera* root powder was investigated by measuring changes in lipid peroxidation and antioxidant status of liver in arthritic animals. Results of the present investigation showed significant decrease in the level of lipid peroxides, constituents with the increased enzymic antioxidants and depleted non-enzymic anti-oxidant status in arthritic animals. The oral administration of *Withania somnifera* root powder (1000 mg $kg^{-1}$ b.wt.) modulated the above altered lipid peroxidation and antioxidant status to near normal levels in arthritic animals. *(Research Journal of Medicinal Plant 2 (1): 28-33, 2008;* ***doi:*** *10.3923/rjmp.2008.28.33)*

## The Phytochemical Screening and Antimicrobial Activity of Leaf Extracts of *Eucalyptus camaldulensis* and *Eucalyptus torelliana* (Myrtaceae)

B.A. Adeniyi and O.O. Ayepola

Extracts of leaves of *Eucalyptus camaldulensis* and *Eucalyptus torelliana* were screened phytochemically for the presence of secondary metabolites and for

*in vitro* antibacterial properties. Methanol and dichloromethane extracts of leaves of *Eucalyptus camaldulensis* and *Eucalyptus torelliana* were studied for their antibacterial activity against 8 clinically isolated organisms of gastrointestinal origin viz., *Klebsiella species* UCH 2101, *Proteus mirabilis* UCH 2102, *Proteus mirabilis* UCH 2204, *Salmonella typhi* UCH 2201, *Escherichia coli* CHO 3101, *Escherichia coli* UCH 2103, *Pseudomonas aeruginosa* CHO 3102 and *Pseudomonas aeruginosa* UCH 2203. The result of the phytochemical screening showed that both extracts contained tannins, saponins, cardiac glycosides but in addition to these, *E. torelliana* was found to contain anthraquinones. Both extracts were also found to inhibit all the isolates at 10 mg $mL^{-1}$ concentration. The diameter of zones of inhibition exhibited by the extracts was between 10 and 22 mm. The methanol extracts compared favorably with gentamycin used as a standard control. The minimum inhibitory concentrations determined by the agar dilution method were between 0.04 and 10 mg $mL^{-1}$. The results obtained from this study reveals that extracts of *Eucalyptus camaldulensis* and *Eucalyptus torelliana* possess antibacterial activities against enteric pathogens and the extracts may be a potential source of new antimicrobials against enteric organisms. *(Research Journal of Medicinal Plant 2 (1): 34-38, 2008;* ***doi:*** *10.3923/rjmp.2008.34.38)*

## Antimicrobial Activity of Saponin Fraction from the Roots of *Hemidesmus indicus*

Venkatesan Gopiesh Khanna and Krishnan Kannabiran

The antimicrobial activity of saponin fraction from the roots of *Hemidesmus indicus* was evaluated against pathogenic bacteria and fungi in an *in vitro* condition by agar diffusion assay. Pure saponin extract exhibited remarkable antimicrobial activity against *Staphylococcus aureus*, *Salmonella typhi*, *Klebsiella pneumoniae*, *Aspergillus flavus*, *Aspergillus fumigatus* and *Aspergillus niger*. The present study suggests that the saponin fraction possesses significant antibacterial activity. It can be concluded from this study, saponin may be a phytochemical of choice to develop as a potential antimicrobics against pathogenic microorganisms. *(Research Journal of Medicinal Plant 2 (1): 39-42, 2008;* ***doi:*** *10.3923/rjmp.2008.39.42)*

## The Effectiveness of *Nigella sativa* Against Liver Damage in Rats

Afaf I. Abuelgasim, E.A. Omer and B. Elmahdi

The role of *Nigella sativa* (*N. sativa*) in the prevention of liver damage induced by carbon tetrachloride ($CCl_4$)was investigated. Twenty five Wister albino rats

were allocated into 5 groups named as A, B, C, D and E. Group (A) was given paraffin oil, group (B) was given dimethylsulfoxide, group (C) was given $CCl_4$ to induced hepatotoxicity, group (D) and (E) were administered with $CCl_4$ together with 250 and 500 mg $kg^{-1}$ body weight (b.wt.) methanolic extract of *N. sativa* which was dissolved in dimethylsulfoxide, respectively. Rats were scarified after 10 days. There was an increase in the body weights of the control groups A and B at a rate of 2%. However, the body weights in group C, D and E were reduced by 10.3, 9.3 and 10.3%, respectively. There were no significant changes in the blood picture between the control groups and the treated ones on day 10. The mean plasma ALT, AST and ALP were found to be significantly higher in both $CCl_4$ and *N. sativa* treated groups compared to the controls, but the increase was less in the groups which were treated with *N. sativa* methanolic extract with $CCl_4$. The bilibrubin concentration was raised from 0.2 to 0.7 in the group treated with $CCl_4$ and to 0.6 and 0.4 in those treated with 250 and 500 mg $kg^{-1}$ b.wt. of *N. sativa* methanolic extract. The histopathological changes in the livers of the group treated with $CCl_4$ exhibited severe centrilobular vacuolation and congestion but in the groups treated with 250 and 500 mg $kg^{-1}$ b.wt., these changes were to a lesser extent. *(Research Journal of Medicinal Plant 2 (1): 43-47, 2008;* ***doi:*** *10.3923/rjmp.2008.43.47)*

## A Study of the Seasonal Variation in the Antimicrobial Constituents of the Leaves of *Loranthus micranthus* Sourced from *Percia americana*

P.O. Osadebe, C.A. Dieke and F.B.C. Okoye

A comparative study of the antimicrobial constituents of the leaves of *Loranthus micranthus* (parasitic on *Percia americana*) harvested at different seasons of the year, namely, January, April, July and November, was carried out. The air-dried and pulverized leaves harvested at the stated periods were extracted with petroleum ether and the extract subjected to antimicrobial screening and phytochemical investigation. Using various solvent treatments the powdered leaves harvested in April was fractionated into four fractions, A, B, C and D; each fraction was screened for antimicrobial activity and phytochemical constituents. Phytochemical analysis of the extracts showed presence of tannins, flavonoids, alkaloids, terpenoids and saponins with some of these constituents showing variations across the seasons. Broad spectrum

antibacterial activity was observed for all the extracts. However, the activity against *Bacillus subtillis* and *Salmonella kapemba* was significantly ($p<0.001$) lower for the extracts of the leaves harvested in January when compared with the extracts of the leaves harvested in the other months. Only the extracts of the leaves harvested in April showed antifungal activity. Fractions A, B and D showed antimicrobial activity comparable ($p<0.05$) to standard antibiotic, chloramphenicol. Fraction A is rich in alkaloids, B in terpenoids, A and D in tannins. The presence of alkaloids only in April and July may explain the higher antimicrobial activity observed in these months. In conclusion, mistletoe used for herbal remedy of nonspecific infections may be preferentially harvested in April and July. *(Research Journal of Medicinal Plant 2 (1): 48-52, 2008;* ***doi:*** *10.3923/rjmp.2008.48.52)*

## Chemical and Pharmacological Study of *Cymbopogon proximus* Volatile Oil

Kamal E.H. El Tahir and Maged S. Abdel-Kader

The volatile oil of *Cymbopogon proximus* was prepared by hydrodistillation method and analyzed chemically by GC/MS. The chromatogram showed 8 peaks corresponding to eight components with piperitone representing 72.44% of the oil's composition. Oral and intraperitoneal (i.p.) administration of the volatile oil to male, female rats and mice resulted in $LD_{50}$ values in the range of 1.9-2.6 mL $kg^{-1}$ with an oral absorption of 80-90%. I.p. administration of the oil to anaesthetized rats (0.2-1.6 mL $kg^{-1}$) decreased the arterial blood pressure in a dose-dependent manner without significant changes in the heart rate except in the largest dose tested where a 16% decrease was observed. The induced decreases were not antagonized by atropine or mepyramine but were significantly reduced by indomethacin. The oil did not induce significant changes in the ECG. I.p. administration of the oil (1.2 mL $kg^{-1}$) to mice before induction of convulsions with electric shock, pentylenetetrazole, picrotoxin and strychnine resulted in complete protection only against the electrically induced convulsions. I.p. administration of the oil to pigeons in doses of 0.4 and 0.8 mL $kg^{-1}$ significantly protected against ouabain-induced vomiting. The results of these studies pointed to the involvement of prostaglandins in the oil-induced cardiovascular depressant effects and a probable antidopaminergic and antiglutamic-aspartic acids in the antiemetic and anticonvulsant effects, respectively. *(Research Journal of Medicinal Plant 2 (2): 53-60, 2008;* ***doi:*** *10.3923/rjmp.2008.53.60)*

## Antimicrobial and Antioxidant Potentials of *Verbesina encelioides* (Cav.) Benth. and Hook. Fil ex Gray

Satish C. Jain, Renu Singh and Renuka Jain

Methanol, cold water and hot water extracts from fresh roots of *V. encelioides*, a weed, were studied for their putative antimicrobial activities against select microorganisms (Bacteria: *Bacillus subtilis, Enterobacter aerogenes, Escherichia coli*, *Pseudomonas aeruginosa* and Fungi: *Aspergillus niger*, *Candida albicans*, *Penicillium crysogenum*, *Tricophyton rubrum*) by disc diffusion method at different concentrations (2.5, 5 and 10 mg disc$^{-1}$) and for antioxidant potential by DPPH method. All the test extracts exhibited potential antimicrobial activity but hot water extract showed appreciable activity (IZ 23 mm) against *P. aeruginosa* and *P. crysogenum.* Hot water extract demonstrated 20.04% inhibition of DPPH at 80 µg concentration. *(Research Journal of Medicinal Plant 2 (2): 61-65, 2008;* ***doi:*** *10.3923/rjmp.2008.61.65)*

## Alterations in Serum Lipid Profile of Male Rats by Oral Administration of Aqueous Extract of *Fadogia agrestis* Stem

Yakubu Musa Toyin, Akanji Musbau Adewumi and Oladiji Adenike Temidayo

The effects of repeated administration of aqueous extract of *Fadogia agrestis* (Schweinf. Ex Hiern) stem on serum lipid profile of male rats and their recovery tendencies for 10 days post-administration were investigated. Graded doses of 18, 50 and 100 mg kg$^{-1}$ body weight of the extracts were administered orally on daily basis for 28 days. Rats were sacrificed 24 h after their daily doses of 1, 14 and 28 while those for the recovery test were sacrificed 10 days after terminating their 28 daily administration. The serum lipid profile investigated included Total Cholesterol (TC), triacylglycerol (TG), high-density lipoprotein-cholesterol (HDL-C) and low-density lipoprotein-cholesterol (LDL-C). The administration of the plant extract to the animals at all the doses produced significant increase ($p<0.05$) in the serum concentration of total cholesterol, triacylglycerols, high-density lipoprotein-cholesterol and low-density lipoprotein-cholesterol with no reversal towards their control by the end of 10 days post-treatment. The computed atherogenic index did not portend predisposition to atherosclerosis. The results indicated alterations in the serum lipid profile of the animals but these alterations are not sufficient enough to predispose the animals to atherosclerosis. *(Research Journal of Medicinal Plant 2 (2): 66-73, 2008;* ***doi:*** *10.3923/rjmp.2008.66.73)*

## Phytochemical and Antimicrobial Screening of *Indigofera conferta* GILLETT (Papilionaceae)

A.M. Musa, G. Abbas, A.B. Aliyu, M.S. Abdullahi and I.N. Akpulu

Antimicrobial activities of the crude methanol extract as well as the n-butanol and residual aqueous fractions from the aerial part of *Indigofera conferta* used in traditional medicine to treat infected wound were investigated using disc diffusion and broth dilution techniques. The extract and the fractions were tested against *Staphylococcus aureus*, *Bacillus subtilis*, *Pseudomonas aeruginosa*, *Escherichia coli* and *Candida albicans* using Ampiclox as standard antibiotic. The crude methanol extract and the aqueous fraction exhibited activity against all the organisms tested (zones of inhibition 16-34 and 14-31 mm, respectively). The n-butanol fraction showed activity on *Staphylococcus aureus*, *Bacillus subtilis* and *Pseudomonas aeruginosa* only (zones of inhibition 14-25 mm). Phytochemical screening on crude extract revealed the presence of tannins, flavonoids and steroids. This study showed that the leaves of *Indigofera conferta* contains active compounds and its antimicrobial activity justifies its use in traditional medicine. *(Research Journal of Medicinal Plant 2 (2): 74-78, 2008; **doi:** 10.3923/rjmp.2008.74.78)*

## Cellular Effects of Garlic (*Allium sativum*) Extract on *Pseudomonas aeruginosa* and *Staphylococcus aureus*

B.E. Boboye and A.J. Alli

Effects of garlic extract at 67, 134 and 201 mg $mL^{-1}$ on *Pseudomonas aeruginosa* and *Staphylococcus aureus* were studied. In the absence of the extract, the cells grew to high densities within 11/2 h at 37°C. Garlic extract-treated cells reduced in number and died. Percentage living cells at 201 mg $mL^{-1}$ was 0% for both bacteria. Sucrose and $MgSO_4$ stabilized and protected the cells. At 67, 134 and 201 mg $mL^{-1}$ of the extract in the presence of this sugar and the compound, 47, 4 and 0% of *Ps. aeruginosa* cells were viable. Microscopic examination of carbol fuschin and Giemsa stained cells showed that the garlic treated cells were bigger in size than those of untreated ones; and intact and definite nuclei were lacking. The cell wall was the target of attack and the extract was bacteriolytic in action. *(Research Journal of Medicinal Plant 2 (2): 79-85, 2008; **doi:** 10.3923/rjmp.2008.79.85)*

## Antimicrobial Activities of *Coula edulis*

Bukola C. Adebayo-Tayo and Kola K. Ajibesin

Crude ethanolic extracts of leaves, stem bark, roots and fruits of *Coula edulis* were analyzed phytochemically and evaluated for their antibacterial and antifungal activities against five clinically isolated pathogenic microorganisms namely: *Staphylococcus aureus*, *Escherichia coli*, *Salmonella typhi*, *Pseudomonas aeruginosa* and *Candida albicans*. Flavonoids, saponins, tannins, alkaloids, anthraquinones, terpenes and cardiac glycosides were detected in the ethanolic extracts of the leaves, stem bark, roots and fruits of *C. edulis*. The highest antimicrobial activity of the ethanolic extract of *C. edulis* was recorded by stem bark against *Ps. aeruginosa* and *S. aureus*. *Candida albicans* was sensitive only to the leaf and stem bark extracts of *C. edulis*. The minimum inhibitory concentration of the extracts ranged between 6.25 and 200 μg $mL^{-1}$. These results suggest that ethanolic extracts of the leaves, stem bark, roots and fruits can be used in the treatment of infectious diseases. The results revealed that the leaves, stem bark, roots and fruits of *C. edulis* exhibited varying degrees of antimicrobial activity. *(Research Journal of Medicinal Plant 2 (2): 86-91, 2008; **doi:** 10.3923/rjmp.2008.86.91)*

## Accelerative Effect of Fenugreek Seeds on the Healing of Mandibular Fracture in Male Dromedary Camels and Monitoring of the Healing by Bone Biomarkers

F.A. Al-Sobayil

The present study was designed to determine the possible effect of fenugreek (*Trigonella foenum graecum*) seeds on acceleration of healing of mandibular fracture in male dromedary camels. The mandibular fracture healing was monitored by determining the concentrations of serum bone resorption {pyridinoline (PYD) cross-links} and formation {Bone Alkaline Phosphatase (BAP) and osteocalcin} biomarkers. Twenty adult male camels with recent bilateral mandibular fractures were used in this study. Interdental wiring technique using stainless steel wire was adopted to immobilize the fractured horizontal rami. The camels were randomly divided into two groups: Treatment group and control group. The results showed that feeding camels in the treatment group with fenugreek (100 g/camel/day for 2 weeks) accelerated mandibular fracture healing. It was concluded that serial determination of the concentrations of serum PYD, BAP and osteocalcin during mandibular fracture could be a useful tool in predicting fracture healing in male dromedary camels. *(Research Journal of Medicinal Plant 2 (2): 92-99, 2008; **doi:** 10.3923/rjmp.2008.92.99)*

## Role of Anserine and/or Zinc in Modulating Nucleic Acid and Protein Disorders in Rats Exposed to Gamma Irradiation

Hanan F. Ali, Laila M. Faddah, Maha Z. Rizk and Hisham El-Ebiary

In view of radiation injuries to tissues, the present study was carried out to provide information on the deteriorative effects induced by γ-irradiation (5.7Gy) after 24 h and 14 days and to determine both the prophylactic and curative influences of intraperitoneally administered anserine and/or zinc on liver nucleic acids and on total serum total protein, albumin and also different serum protein fractions, namely, prealbumin, α- and β-lipoproteins, α-1 antitrypsin, α-1 acidic glycoprotein, α-1 macroglobulin, cholinesterase, transferrin, ceruloplasmin, haptoglobin and haemopexin. The data obtained revealed that all liver and serum parameters measured significantly declined in rats exposed to whole body irradiation in the two time phases except for the lipoprotein fractions. Administration of anserine and/or zinc either pre or post radiation dose induced a significant improvement in all parameters. It could be concluded that either anserine or zinc has a pronounced effect in overcoming the disturbances induced by γ-irradiation especially when administered post irradiation and the action of each can be potentiated by supplementation of the other. It is thus recommended to use a collective combination of both anserine and zinc as radioprotectors as well as for treatment of radiation hazards. *(Journal of Pharmacology and Toxicology 2 (1): 1-19, 2007;* ***doi:*** *10.3923/jpt.2007.1.19)*

## Molecular Modelling Analysis of the Metabolism of Toluene

Fazlul Huq

Toluene has been widely used as an organic solvent, ingredient of thinners, as a coating in the leather industry and in the synthesis of a number of chemicals. It is a common cause of neurotoxicity in people that intentionally and repetitively breather high concentrations of toluene over a long period of time. Recent investigations have shown that toluene may induce reproductive dysfunctions and cancer. However, little is known about the molecular mechanisms by which toluene elicits its toxic effects on male reproductive organs and carcinogenicity. Following exposure in humans, toluene is readily transformed into several metabolites including benzyl alcohol, ortho-, meta- and para-cresols. The main metabolic pathway involves its oxidation to benzyl alcohol which is further oxidised to benzoic acid via benzaldehyde and excreted in the urine as hippuric acid. Ortho-, meta- and para-cresols are formed as minor metabolites through the

formation of epoxides although there is evidence for direct hydroxylation of aromatic ring. Ortho-cresol is further hydroxylated to form MHQ which on oxidation produces MBQ. Molecular modelling analyses based on molecular mechanics, semi-empirical and DFT calculations show that the most toxic metabolite of toluene namely MBQ has the smallest LUMO-HOMO energy difference and hence it will be most reactive kinetically. The presence of electron-rich and electron-deficient sites indicates that the metabolite may undergo both electrophilic and nucleophilic attacks, the latter providing an explanation as to why it can cause oxidative damage to DNA. *(Journal of Pharmacology and Toxicology 2 (1): 20-32, 2007;* ***doi:*** *10.3923/jpt.2007.20.32)*

## Molecular Modelling Analysis of the Metabolism of Naphthalene

Fazlul Huq

Naphthalene is a bicyclic aromatic hydrocarbon widely used as an intermediate in chemical and plastics industry and in the manufacture of insecticides and fungicides. It is metabolized by microsomal enzymes to naphthols and dihydrodiols via the formation of an epoxide which has a very short half-life. Reactive metabolites of naphthalene can deplete glutathione and in the absence of sufficient glutathione, get covalently bound to tissue macromolecules. In this study, molecular modelling analyses based on molecular mechanics, semi-empirical and DFT calculations have been carried out to provide information on the relative stability of naphthalene and its metabolites, deemed to be useful in the understanding of naphthalene induced toxicity. The analyses show that although naphthalene has a low thermodynamic stability, the larger LUMO-HOMO energy difference makes it less labile kinetically and hence less toxic than its more labile metabolites. Although naphthalene-1,2-epoxide has the lowest thermodynamic stability, the larger LUMO-HOMO energy difference makes the epoxide also labile. Much lower LUMO-HOMO energy differences make the naphthoquinones more reactive and hence more toxic. *(Journal of Pharmacology and Toxicology 2 (1): 33-43, 2007;* ***doi:*** *10.3923/jpt.2007.33.43)*

## Evaluation of Anti-inflammatory Activity of *Cleome gynandra* L. Leaf Extract on Acute and Chronic Inflammatory Arthritis Studied in Rats

R.T. Narendhirakannan, S. Subramanian and M. Kandaswamy

The present study was aimed to evaluate the anti-inflammatory potential of *Cleome gynandra* leaf extract on both acute (carrageenan induced paw edema)

and chronic (cotton pellet granuloma) experimental inflammatory models induced in rats. The effect of *C. gynandra* on adjuvant induced arthritis was also evaluated. The extract at a dose of 150 mg $kg^{-1}$ body weight was found to possess significant anti-inflammatory activity in all the experimental models and the results were comparable with indomethacin, a standard reference drug. The extract significantly decreased the carrageenan induced paw edema and cotton pellet granuloma. The increased activities of acid and alkaline phosphatase activity and decreased serum level albumin in cotton pellet granulomatous rats were reverted back to near normal levels after treatment with the extract. The extract significantly decreased the lipid peroxide (LPO) content of exudates, liver and spleen and the activity of γ-glutamyl transpeptidase in the exudates of cotton pellet granuloma. Moreover, *C. gynandra* also significantly suppressed the development of chronic arthritis induced by Freund's complete adjuvant. These results demonstrated that the ethanolic extract of *Cleome gynandra* possess anti-inflammatory activity on both acute and chronic inflammation. *(Journal of Pharmacology and Toxicology 2 (1): 44-53, 2007;* ***doi:*** *10.3923/jpt.2007.44.53)*

## Molecular Modelling Analysis of the Metabolic Activation of Ethylene Glycol

Fazlul Huq and Deena Ababneh

Molecular modelling analyses based on molecular mechanics, semi-empirical (PM3) and DFT (at B3LYP/6-31G* level) calculations using the programs Spartan '02 and HyperChem 7.0 show that glycolic acid has high thermodynamic stability and low kinetic lability so that the reaction in which glycolic acid is converted to glyoxylic acid is indeed rate-determining. The metabolite glyoxal has the lowest LUMO-HOMO energy difference that makes it most kinetically labile. The high kinetic lability and the presence of electron-deficient region on the molecular surface may make glyoxal the most toxic metabolite as it can cause depletion of cellular glutathione, thus compromising antioxidant status of the cell. *(Journal of Pharmacology and Toxicology 2 (1): 54-62, 2007;* ***doi:*** *10.3923/jpt.2007.54.62)*

## Molecular Modelling Analysis of the Metabolism of Phenytoin

Fazlul Huq

Phenytoin (PHT, also known as Dilantin) is a broad-spectrum anticonvulsant that is widely used for the prevention and treatment of seizure disorders. However, it

provokes skin rash in 5 to 10% patients and has been found to be teratogenic in various experimental animal species. Epidemiological and clinical studies indicate that women who have taken PHT during pregnancy have an increased risk of bearing a child with a congenital anomaly. The toxic side effects of PHT may result from its primary and secondary metabolites, rather than the parent drug. PHT is metabolised by cytochrome P450 enzymes (CYP2C9 and CYP2C19) primarily to inactive metabolite 5-(4-hydroxyphenyl)-5-phenylhydantoin (4HPPH, in both *R*- and *S*-forms, accounting for about 80% of all metabolites). 4HPPH may be further metabolized to catechol that spontaneously oxidizes to semiquinone and quinone species that bind covalently with proteins. Other minor metabolites in man are: 5-(3-hydroxyphenyl)-5-phenylhydantoin (3HPPH) and 5-(3,4-dihydroxy-1, 5-cyclohexadiene-1-yl)-5-phenylhydantoin (DHD). Molecular modelling analyses show that PHT and most of its metabolites do not differ widely in their kinetic lability except Q and SQ which have much lower values. Q has the lowest HOMO-LUMO energy difference and is therefore considered to be most toxic. The differences in heats of formation suggest that Q may be thermodynamically unstable as well that may be subject to both electrophilic and nucleophilic attack. *(Journal of Pharmacology and Toxicology 2 (1): 63-71, 2007;* ***doi:*** *10.3923/jpt.2007.63.71)*

## Molecular Modelling Analysis of the Metabolism of Mefenamic Acid

Fazlul Huq

Mefenamic acid is a NSAID that is widely used in analgesia. However, its use has been implicated in several cases of nephrotoxicity including acute renal failure and tubulointestinal nephritis. Molecular modelling analyses based on molecular mechanics, semi-empirical (PM3) and DFT (at B3LYP/6-31G* level) calculations show that MFA and its metabolites have similar LUMO-HOMO energy differences except MFA-Glu which has a much smaller value. This means that MFA and its metabolites have similar kinetic lability except MFA-Glu which is much more labile. The high kinetic lability of MFA-Glu suggests that it may react with biomolecules such as intra- and extracellular proteins more readily. However, whether this binding manifests itself as being a cause of MFA-induced toxicity remains unclear and may be confusing since the acyl glucuronides are considered to be less toxic. It may be that the formation of acyl glucuronide reduces toxicity associated with the carboxylic group but introduces new ones due to its high reactivity. It is found that the metabolites if MFA have higher solvation energies than MFA so that they may be more readily excreted in the urine. *(Journal of Pharmacology and Toxicology 2 (1): 72-79, 2007;* ***doi:*** *10.3923/jpt.2007.72.79)*

## Indian Melghat Honey: A Prospective Antibiotic

D.H. Tambekar and G.N. Rathod

Honey is acceptable in the medical profession as an antibacterial agent for the treatment of some diseases and infections resulting from wounds and burns. Antibacterial and antifungal properties of honey are well documented against a number of Gram positive and Gram-negative bacteria and vary with origin and processing. In this study, we attempted to assess the Melghat honey as therapeutic agent and recorded high quality broad-spectrum antimicrobial properties. The bacterial pathogens, *Staphylococcus epidermidis*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Escherichia coli*, *Salmonella typhimurium*, *Salmonella typhi* and *Proteus vulgaris* were highly sensitive to Melghat honey. Thus, the Melghat honey can be used as an alternative to antibiotics as well as a dressing for burns and other wounds. *(Journal of Pharmacology and Toxicology 2 (1): 80-84, 2007;* ***doi:*** *10.3923/jpt.2007.80.84)*

## Evaluation of Anti-ulcerogenic Potential of *Aloe vera* Leaf Gel Extract Studied in Experimental Rats

S. Subramanian, D. Sathish Kumar, P. Arulselvan, G.P. Senthilkumar and U.S. Mahadeva Rao

In the present study, anti-ulcerogenic potential of *Aloe vera* leaf gel was evaluated using two different models of gastric lesions induced in experimental rats; 1) Indomethacin-induced gastric lesions and 2) Ethanol-induced gastric lesions. Pretreatment with oral administration of the extract of *Aloe vera* gel (150 mg $kg^{-1}$) prevented the formation of acute gastric lesions induced by both the experimental models. Further, treatment with the ethanolic extract of *Aloe vera* leaf gel for a period of 15 days significantly reduced the ulcer index, ulcerated surface and significantly elevated the levels of glycoprotein contents in gastric juice. The histological observations made on the stomach tissue provided further evidence on the anti-ulcerogenic potential of the *Aloe vera* leaf gel extract. *(Journal of Pharmacology and Toxicology 2 (1): 85-97, 2007;* ***doi:*** *10.3923/jpt.2007.85.97)*

## Adverse Effects of Abuse Potential by Ritalin among Iranian Medical Students

Vahid Ziaee, Lila Tabatabaee, Zohreh Baniyaghoob, Ehsan Akbari Hamed and Reza Rostami

Methylphenidate (Ritalin) is a CNS stimulant that inhibits dopamine and norepinephrine reuptake into presynaptic neurons. It has potential for abuse and diversion. This case-series study has been performed in Tehran University of Medical Sciences. Thirty six medical students of 4 medical schools participated in this study in spring 2004. A questionnaire has been designed for this study for collecting data. This questionnaire was certificated by psychiatric professors of Tehran University of Medical Sciences. Thirty three male and three female students participated in this study. The mean age was 25.1 and 94.4% of the students retried Ritalin for more than one time. Two third of the students had history of other illicit drugs abuse (42.5% alcohol, 28.6% Cannabis). The most common adverse effects after the last time of abusing were increasing in concentration (97.2%), tachycardia (61.1%), restlessness (41.7%), decreasing the appetite (38.4%), anxity (35.7%), diaphoresis (32.5%) this case series shows, unfortunately the average illicit drug abusers was high in participants. Ritalin abuse in medical students is a potentially serious health threat. *(Journal of Pharmacology and Toxicology 2 (1): 98-102, 2007;* ***doi:*** *10.3923/jpt.2007.98.102)*

## Small RNA Molecules as Therapeutic Agents for Viral Infectious Diseases

Jing Zhang and Toshio Hattori

The potential of using small RNA molecules as therapeutic agents has been extensively explored, antisense RNA, ribozyme, aptamer, decoy and more recently siRNA have been demonstrated to be highly efficient in inhibiting a number of pathogenic viruses including human immunodeficiency virus, hepatitis B and C virus, poliovirus and influenza virus. The specificity and potency of the sequence-specific agents such as antisense, ribozyme and siRNA in particular, imply that these strategies will prove to be promising therapeutics for treating viral infections, although the antiviral efficacy may be limited by emergence of escape variants. Distinct from the reagents targeting viral RNA, decoy and aptamer inhibit viral replication by binding and thus inactivating the viral component such as regulatory gene product and viral enzyme. This review provides an up-to-date overview of the progress and problems in small RNA-based antiviral approaches, with a focus on their therapeutic utility, delivery and unwanted side effects. *(Journal of Pharmacology and Toxicology 2 (2): 103-113, 2007;* ***doi:*** *10.3923/jpt.2007.103.113)*

## Molecular Modelling Analysis of the Metabolism of Cocaine

Fazlul Huq

Cocaine is one of the main alkaloids of Erythroxylum coca that has a long history of human use and abuse. Cocaine acts as a local anaesthetic and stimulant causing increased alertness and a sense of euphoria. Sustained abuse of cocaine as a recreational drug is widespread around the world. Cocaine abuse during pregnancy is of major concern in certain countries where pregnant women take several drugs along with cocaine because it is known that cocaine can cross placenta. Cocaine has been reported to cause toxicity mainly to cardiovascular system and to a lesser extent to the liver. Cocaine is extensively metabolised in humans so that only a small percentage is excreted unaltered in urine. Cocaine is metabolized in vivo to pharmacologically inactive metabolites ecgonine methyl ester (ECG), benzoylecgonine (BE) and ecgonine (ECG). Among the metabolites BE has six times longer half-life than cocaine. Norcocaine is a relatively minor metabolite in humans. Molecular modelling analyses show that among cocaine and its metabolites, the metabolite cocaine N-oxide has the lowest LUMO-HOMO energy difference indicating that it has the greatest kinetic lability. The surface of the metabolite is also found to abound in electron-deficient regions so that it can cause oxidation of reduced form of glutathione and that of nucleobases in DNA, thus compromising the antioxidant status of the cell and inducing damage to DNA. *(Journal of Pharmacology and Toxicology 2 (2): 114-130, 2007;* ***doi:*** *10.3923/jpt.2007.114.130)*

## Electrometric Determination of Erythrocyte, Plasma and Whole Blood Cholinesterase Activities in Sheep, Goats and Cattle and Their *in vitro* Inhibition by Anticholinesterase Insecticides

F.K. Mohammad, M.H.I. Al-Zubaidy and A.S. Alias

Determination of blood cholinesterase activity in animals is used for diagnosis and monitoring poisoning induced by organophosphate and carbamate insecticides. An electrometric method was applied in one step single incubation period (30 min) for measurement of normal reference range values of erythrocyte, plasma and whole blood cholinesterase activities in sheep, goats and cattle, of both sexes. The reaction mixture contained 3 mL distilled water, 3 mL barbital-phosphate buffer (pH 8.1), 0.2 mL erythrocytes, plasma or the whole blood and 0.1 mL acetylcholine iodide (7.5%) as a substrate. The mixture was incubated at 37°C for 30 min in the three animal species. This step avoided variations in enzyme activity

across animal species due to differences in the incubation periods found in previous studies. The pH of the reaction mixture was determined by a pH meter before and after the incubation. The initial pH was measured before the substrate addition. The unit of enzyme activity was expressed as Δ pH/30 min. The mean normal reference range values of erythrocytes, plasma and whole blood cholinesterase activities (Δ pH/30 min) in males of the three animal species were as follows, respectively: Sheep (0.306, 0.133 and 0.249), goats (0.366, 0.135 and 0.234) and cattle (0.469, 0.135 and 0.374) whereas those of the females were as follows, respectively: Sheep (0.436, 0.121 and 0.257), goats (0.338, 0.175 and 0.252) and cattle (0.645, 0.137 and 0.450). The method of inhibitor-cholinesterase incubation was used to measure the *in vitro* inhibition of plasma, erythrocyte and whole blood cholinesterase activities by the organophosphate insecticides chlorpyrifos and methidathion and by the carbamate insecticide carbaryl. Chlorpyrifos in concentrations of 0.5 and 1 μM inhibited plasma, erythrocyte and whole blood cholinesterase activities by 5-30% in sheep, 10-55% in goats and 5-61% in cattle. Methidathion in concentrations of 0.5 and 1 μM inhibited plasma, erythrocyte and whole blood cholinesterase activities by 3-70% in sheep, 8-53% in goats and 6-65% in cattle. Carbaryl in concentrations of 4 and 8 μM inhibited them by 8-54% in sheep, 8-53% in goats and 14-74% in cattle. The study establishes for the first time by using the described electrometric method in a unified way across the three ruminant species sheep, goats and cattle, normal reference range values of erythrocytes, plasma and whole blood cholinesterase activities. The results also suggest that the described electrometric method could be efficiently used for detecting cholinesterase inhibition by organophosphate and carbamate insecticides. Further, the experimental protocol of *in vitro* cholinesterase inhibition is of value in preliminary toxicological examinations of anticholinesterase pesticides. *(Journal of Pharmacology and Toxicology 2 (2): 131-141, 2007;* ***doi:*** *10.3923/jpt.2007.131.141)*

## Molecular Modelling Analysis of the Metabolism of Paracetamol

Fazlul Huq

Paracetamol is probably the most versatile and widely used analgesic and antipyretic drug all over the world and is also one of the commonest means of committing suicide. In humans, high doses of paracetamol can cause hepatotoxicity and sometimes nephrotoxicity. The drug is metabolized by different hepatic pathways to produce metabolites paracetamol sulfate, paracetamol glucuronide, NAPQI, PLCC and PNALCC. of these paracetamol sulfate and paracetamol

glucuronide form the largest proportion. The metabolic activation of aspirin is associated with the formation of NAPQI which is highly toxic but is normally detoxified by reaction with glutathione. Molecular modelling analyses based on molecular mechanics, semi-empirical (PM3) and DFT (at B3LYP/6-31G* level) show that among paracetamol and its metabolites, NAPQI has the highest kinetic lability, lower solubility in water and possibly lower thermodynamic stability. *(Journal of Pharmacology and Toxicology 2 (2): 142-150, 2007;* ***doi:*** *10.3923/jpt.2007.142.150)*

## Time Course of Urinary Metallothionein Excretion in Rats Exposed to Cadmium

Yong Ning, Liang Chen, Lijian Lei, Yihuai Liang, Ming Sheng and Taiyi Jin

Cadmium chloride was administered to the rats, subcutaneously, at the doses of 0, 0.5, 1.0 and 2.0 mg Cd $kg^{-1}$ body weight, 5 times/week up to 3 weeks. The levels of cadmium, metallothionein and N-acetyl-β-D-glucosaminidase were determined in urine within the exposed period. Both urinary cadmium and metallothionein increased dose-time-dependently upon cadmium exposure. The continuously mild increasing excretion of urinary metallothionein was observed in the rats exposed to 1.0 mg Cd $kg^{-1}$, starting from the 10th day after cadmium exposure. The excretion of urinary metallothionein started increasing from one week after cadmium exposure and further significant more excretion after two weeks, when NAGuria appeared, in the group exposed to 2.0 mg Cd $kg^{-1}$. There was a similar pattern for urinary metallothionein excretion in both genders of rats. In this study it has been well demonstrated that there are two phases of increasing excretion of urinary metallothionein, i.e., the first phase, which could be related to overflow of new synthesized metallothionein in kidney and the second phase, which was the result of cadmium induced renal tubular dysfunction. *(Journal of Pharmacology and Toxicology 2 (2): 151-159, 2007;* ***doi:*** *10.3923/jpt.2007.151.2007)*

## Antioxidant Activity of Two Steroid Alkaloids Extracted from *Solanum aculeastrum*

Srinivas Koduru, F.O. Jimoh, D.S. Grierson and A.J. Afolayan

In this study two steroid glycosides were isolated from the berries of this plant, which were identified as tomatidine and solasodine by spectroscopic techniques.

Antioxidant activities of these compounds were investigated using DPPH, ABTS and reducing power assays. The $IC_{50}$ confirmed the antioxidant potentials of tomatidine and solasodine. DPPH free radical activity was examined at 30 and 60 min. The highest inhibition was observed when the two compounds were combined, followed by solasodine while tomatidine showed the least inhibition. On the other hand, the activity of ABTS was greater than the DPPH and the activity of the combined compounds was faintly less than solasodine. The activity observed in the reducing power assay was higher in the combined compounds and followed by solasodine and tomatidine. This study has revealed strong antioxidant activity and synergistic effect of the isolated compounds from *S. aculeastrum* berries. *(Journal of Pharmacology and Toxicology 2 (2): 160-167, 2007;* ***doi:*** *10.3923/jpt.2007.160.167)*

## Antibacterial, Phytochemical and Toxicity Studies of *Pteridium aquilinum* L. (Dennstaedtiaceae) in Rabbits

S.W. Hassan, R.A. Umar, Y.U. Dabai, A.A. Ebbo and U.Z. Faruk

The aqueous and organic solvent leaves extracts of *Pteridium aquilinum* were screened for antibacterial activity by hole-in-plate bioassay procedure. The effect of aqueous leaves extract of the plant on hepatorenal functions in rabbits was also studied. Hexane (HX) fraction at 10 to 120 mg $mL^{-1}$ did not show activity against *Escherichia coli* and *Pseudomonas aeruginosa*. However, it was significantly ($p<0.05$) active against *Staphylococcus aureus* at 90 and 120 mg $mL^{-1}$. The chloroform (CHL) extract fraction at concentrations of 50-120 mg $mL^{-1}$ was significantly ($p<0.05$) active on all the bacterial species. Petroleum ether (PE) at 10-120 mg $mL^{-1}$ showed significant ($p<0.05$) inhibition of *S. aureus* and *E. coli*. Aqueous (W) extract exhibited significant inhibitory activity at 50-120 mg $mL^{-1}$ on *S. aureus* and *P. aeruginosa*. Tannins, anthraquinone glycosides, cardiac glycosides, cyanogenic glycosides and volatile oils were detected in the extracts. The lethal dose ($LD_{50}$) of the aqueous leaves extracts was found to be greater than 3000 mg $kg^{-1}$ (p.o.) in rabbits. Non significant ($p>0.05$) and significant ($p<0.05$) changes in renal and liver indices, respectively were observed. Aqueous leaves extract of *Pteridium aquilinum* is toxic to the liver of rabbits only at 1500-3000 mg $kg^{-1}$. These results have provided scientific evidence to justify the indigenous use of the plant against infectious diseases. *(Journal of Pharmacology and Toxicology 2 (2): 168-175, 2007;* ***doi:*** *10.3923/jpt.2007.168.175)*

## Molecular Modelling Analysis of the Metabolism of Fentanyl

Fazlul Huq

Fentanyl (FT) is a synthetic μ-opioid receptor agonist, widely used for surgical analgesia and sedation. FT undergoes rapid and extensive hepatic biotransformation to metabolites that result from hydrolysis, N-delalkylation and hydroxylation reactions. The major metabolite is norfentanyl (NFT) formed from N-delakylation. CYP3A4 is responsible for the oxidative dealkylation of FT in the human liver suggesting that FT may be subject to drug interactions *in vivo* as numerous other therapeutic agents including nifedipine, lidocaine and paracetamol are metabolized by the same enzyme. The toxicity of FT may be in part due to CYP3A4*1B and CYP3A5*3 variant alleles, resulting into variation in FT metabolism. Molecular modelling analyses based on molecular mechanics, semi-empirical (PM3) and DFT (at B3LYP/6-31G* level) calculations show that FT and all its metabolites have large LUMO-HOMO energy differences so that they would be kinetically inert. However, the molecular surfaces of FT, PAL and NFT are found to abound in electron-deficient regions so that they may be subject to nucleophilic attack by glutathione and nucleobases in DNA resulting into glutathione depletion and DNA damage, respectively. The kinetic inertness of the molecules means that the rates of such adverse reactions would be low unless the reactions are speeded up enzymatically. *(Journal of Pharmacology and Toxicology 2 (2): 176-182, 2007;* ***doi:*** *10.3923/jpt.2007.176.182)*

## Effect of Feeding Pearl Millet (*Pennisetum typhoides*), Potassium Iodate or Their Mixture to Nubian Goats

Warda S. Abdel Gadir and S.E.I. Adam

Pearl millet 1 g/kg day, potassium iodate 50 ppm, and the two combined were fed to male Nubian goats for periods up to 111 days. There was no evidence of any carcinogenic effect of Pearl millet on the thyroid gland or other vital organs, but the main features were goiter and entero-hepatonephropathy. In male goats, dietary potassium iodate was neither toxic nor protective against goiter. Severe damage to the thyroid follicles associated with prominent alopecia, nervous signs and exophthalmia were correlated with changes in serum AST, GGT and ALP activities and total protein, albumin, globulin, total lipid, cholesterol, creatinine, calcium, inorganic phosphate, magnesium, iodine and selenium concentrations and with alteration in thyroid, liver, kidneys, heart, spleen and semi-membranous muscles iodine and selenium levels and in hematology. *(Journal of Pharmacology and Toxicology 2 (2): 183-189, 2007;* ***doi:*** *10.3923/jpt.2007.183.189)*

## Immune Boosting Herbs: Lipid Peroxidation in Liver Homogenate as Index of Activity

O.A. Odukoya, S.I. Inya-Agha and O.O. Ilori

*In vitro* antioxidant activity of aqueous extracts of *Phyllantus amarus* (Schum and Thonn.) Euphorbiaceae, *Sida acuta* Burman f. (Malvaceae), *Sida cordifolia* Linn. (Malvaceae) and *Xylopia aethiopica* (Dunal) A. Rich (Annonaceae) was assessed by lipid peroxidation (LPO) and reduced glutathione content (GSH). Inhibition of peroxidation and GSH oxidation in all concentrations was dose-dependent. % inhibition at 1 mg $mL^{-1}$ concentration activity for lipid peroxidation was mixture of all plant extracts with *S. cordifolia* (86.83±1.23) > mixture with *S. acuta* (72.92±0.96) >*P. amarus* (72.03±0.39) > *S. cordifolia* (56.82±0.54) > *S. acuta (*42.77±1.76) > *X. eathiopica* (39.48±2.07). Inhibition of GSH oxidation was 97.47±0.42, 83.56±0.39, 78.33±0.09, 61.69±0.87, 56.48±0.19 and 49.44±1.13, respectively in the same order.The extracts inhibited lipid peroxidation and GSH oxidation and thus could slow down aging process and improve immune responses. *(Journal of Pharmacology and Toxicology 2 (2): 190-195, 2007;* ***doi:*** *10.3923/jpt.2007.190.195)*

## Antianaemic and Antimicrobial Activity of *Eremomastax speciosa*

J.E. Okokon, B.S. Antia, A.E. Udoh and M.M. Akpan

The ethanolic leaf extract of *Eremomastax speciosa* was evaluated for antimicrobial and antianaemic activities. The crude ethanolic extract, as well as n-hexane and acqueous fractions were tested against pure clinical cultures of *Staphylococcus aureus*, *E. coli*, *Candida albicans* and *Aspergillus niger*. The acqueous fraction showed a higher activity against all tested organisms except *A. niger*. This was followed by n-hexane fraction which showed a broad activity against all tested organisms. The crude extract was only active against *E. coli* and *Staph. aureus*. The ethanolic crude extract (500-2000 mg $kg^{-1}$) also demonstrated antianaemic property by significantly ($p<0.01$) elevating Red blood cell counts, packed cell volume, Haemoglobin concentration and white blood cell counts of rats treated with it. These findings justify the ethnomedical use of this plant. *(Journal of Pharmacology and Toxicology 2 (2): 196-199, 2007;* ***doi:*** *10.3923/jpt.2007.196.199)*

## The Immunostimulatory Effects of Ethanolic Extract of *Cassia alata* on Immune System of Albino Rats Dosed with *Staphylococcus aureus* (NCIB 8588)

M.K. Oladunmoye

The immunostimulatory effect of the ethanolic extract of *Cassia alata* was tested on Swiss albino rats infected with *Staphylococcus aureus* by evaluating the White Blood Cells (WBC), Packed Cell Volume and total differential WBC count. The rats were in 6 groups of 2 animals per cage. The first group was given the standard inoculum but not treated. The second group was given the standard inoculum and treated with the extract. The third group was given *Cassia alata* ethanolic extract only while the control was given normal saline. Increase in White Blood Count (WBC) from 5000 to 7600 $mm^3$, decrease in Packed Cell Volume (PCV) from 51 to 21% and increase in neutrophil-lymphocyte ratio indicates active infection in the infected-untreated group. In the group treated with extract there was lower White Blood Count (WBC) of 5000 and 2900 $mm^3$ before and during infection, respectively. Decrease in neutrophil-lymphocyte ratio indicates suppression of infection/inhibition of proliferation of *Staphylococcus aureus* infection. The group given extract only showed WBC, PCV, Neutrophil and Lymphocyte value of 5200 $mm^3$, 45, 44 and 55% before infection; 2300 $mm^3$. 32, 50 and 50% during infection and 3100 $mm^3$, 32, 72 and 28% after infection, respectively. There is a boosting of the immune system as compared to the control. The result of the urinalysis showed a pH of 5, negative to glucose, Ascorbic acid, Ketone, Nitrite, Bilirubin, Protein and Blood, normal for Urobilinogen for all the groups before infection. The untreated rats showed a pH of 7 positive for nitrite and Bilirubin, negative for other parameters. The infected/untreated rats showed 6-8 pus cells/HPF, 2-4 casts/HPF, 6-8 crystals/HPF and 4-6 bacterial cells/HPF indicating active infection. The result of this study is significant for the development of *Cassia alata* to be utilized as an augment for the current antimicrobial therapy that is becoming less efficacious against *Staphylococcus aureus.* *(Journal of Pharmacology and Toxicology 2 (2): 200-204, 2007;* ***doi:*** *10.3923/jpt.2007.200.204)*

## Peroxisome Proliferator Activated Receptor Agonists: Emerging Therapy for Cardiovascular Complications

Pitchai Balakumar, Madhankumar Rose and Manjeet Singh

Peroxisome Proliferator Activated Receptors (PPARs) are ligand-activated transcription factors of nuclear hormone receptor superfamily. The PPAR

subfamily comprises of three members such as PPARα, PPARγ and PPARδ. Activation of PPARα induces gene expressions that promote fatty acid oxidation. Fibrates, which are currently used as hypolipidemic agents are PPARα ligands. PPARγ regulates gene expressions that promote insulin sensitization followed by glucose metabolism. Thiazolidinediones, which are presently employed as insulin-sensitizing anti-diabetic agents are PPARγ agonists. On the other hand, PPARδ also known as PPARβ is expressed ubiquitously and involved in fatty acid oxidation in tissues, which lack PPARα. But no selective PPARδ agonists are currently available for therapeutic use. Evidences from ongoing pre-clinical and clinical studies suggest that PPAR ligands exert broad spectrum of cardioprotective activities in addition to their above-mentioned properties. Agonists of PPARs are shown to inhibit the pathogenesis of atherosclerosis, endothelial dysfunction, heart failure and myocardial infarction. In this review, we discussed various recently developed PPAR ligands and their potential role in the prevention of pathogenesis of cardiovascular complications. Moreover, the novel class of currently developed PPAR dual agonists such as PPARα/γ and PPARα/δ agonists and pan agonists such as PPARα/γ/δ agonists have also been discussed, which may be novel emerging therapeutic agents for cardiovascular complications. *(Journal of Pharmacology and Toxicology 2 (3): 205-219, 2007; **doi:** 10.3923/jpt.2007.205.219)*

## Phytochemical and Toxicological Studies of *Zygophyllum album* L.f.

Amal M.Y. Moustafa, Ahmed I. Khodair, Faiza M. Hammouda and Husseiny A. Husseiny

Investigation of the chemical constituents of *Zygophyllum album* L.f. (Zygophyllaceae family) let to isolate three flavonoids via Kaempferol, Isorhamnetin and Quercetin-3-O-glucoside, one β-carboline alkaloids; Harmine, 16 n-alkanes ($C_{12}$-$C_{32}$), β-amyrin, stigmasterol and β-sitosterol and nine fatty acids. The stucctures of these compounds were established by Mass spectrometry (MS), Gas-liquid chromatography (GLC) and spectroscopic techniques, including Ultra-violet (UV), Infra-red (IR) and Nuclear Magnetic Resonance spectroscopic analysis ($^1$H NMR). The oral $LD_{50}$±standard error and their 95% fiducial limits of the total alcoholic extract were 5.9±0.25 and (5.59-6.23) g $kg^{-1}$ bw, respectively. While, the intra peritoneal $LD_{50}$±standard error and their 95% fiducial limits of the extract were 2.60±0.15 and (2.44-2.77) g $kg^{-1}$ bw, respectively. The total alcoholic extract of the plant could be highly toxic for rats. The extrapolated calculation to human revealed that, this plant could be considered as slightly toxic

for man. *(Journal of Pharmacology and Toxicology 2 (3): 220-237, 2007; **doi:** 10.3923/jpt.2007.220.237)*

## Molecular Modelling Analysis of the Metabolism of Irbesartan

Fazlul Huq

Irbesartan (IS) is a potent, long-acting receptor antagonist for the octapeptide angiotensin II (AII), having high selectivity for the $AT_1$ subtype. AII accelerates the development of atherosclerosis by activating AII subtype 1 receptors that promote generation superoxide anion and cause oxidative stress, leading to activation of nuclear transcription factor and endothelial dysfunction. IS is used in the treatment of hypertension, diabetic nephropathy and heart failure. The drug is metabolized in animals and humans to give at least seven urinary metabolites (denoted as M1, M2, M3, M4, M5, M6 and M7) although it does not rely on biotransformation for its pharmacological effect. IS shows minimal potential for drug or food interactions. Molecular modelling analyses based on molecular mechanics, semi-empirical (PM3) and DFT (at B3LYP/6-31G* level) calculations show that IS and its metabolites have moderately large LUMO-HOMO energy differences ranging from 5.0 to 5.2 eV from DFT calculations, indicating that IS and all its metabolites will be kinetically inert. Thus, although the molecules have some electron-deficient regions on their surface so that they could potentially react with glutathione and nucleobases in DNA, the high kinetic inertness of the molecules is believed to provide protection against such adverse reactions. *(Journal of Pharmacology and Toxicology 2 (3): 238-247, 2007; **doi:** 10.3923/jpt.2007.238.247)*

## Synthesis and Pharmacological Study of Some Novel Schiff Bases of 4-Hydroxy 6-Carboxhydrazino Benzothiophene Analogs

K.N. Venugopala, Gopal Krishna Rao and P.N. Sanjay Pai

A versatile method for the synthesis of novel schiff bases of 4-hydroxy 6-carboxhydrazino benzothiophene derivative was described. The title compounds were characterized on the basis of spectroscopic techniques and evaluated for their qualitative and quantitative antibacterial activity by agar cup plate method and micro titration method, respectively. From the biological activity it was possible to observe that some of the substituents on the phenyl ring of the benzothiophene analogs influenced the biological activity. *(Journal of Pharmacology and Toxicology 2 (3): 248-255, 2007; **doi:** 10.3923/jpt.2007.248.255)*

## Convenient Synthesis of Some Triazolothiadiazoles and Triazolothiadiazines Carrying 4-Methylthiobenzyl Moiety as Possible Antimicrobial Agents

Mithun Ashok and B. Shivarama Holla

4-Amino-3-(4-methylthiobenzyl)-5-mercapto-1,2,4-triazole 5 reacts with various substituted acids (aryl/aryloxy) in presence of phosphorus oxychloride and with various substituted phenacyl bromides in presence of anhydrous sodium acetate to give two series of fused heterocycles namely, 6-(substituted aryl/aryloxymethyl)-3-(4-methylthiobenzyl)-1,2,4-triazolo[3,4-*b*]-1,3,4-thiadiazoles 6 and 7*H*-6-(substituted aryl)-3-(4-methylthiobenzyl)-1,2,4-triazolo[3,4-*b*]-1,3,4-thiadiazines 7, respectively. The structures of the newly synthesized compounds were confirmed on the basis of elemental analysis, IR, $^1$H NMR and mass spectral studies. All the newly synthesized compounds were tested for their antibacterial and antifungal activity against a variety of microorganisms. *(Journal of Pharmacology and Toxicology 2 (3): 256-263, 2007; **doi:** 10.3923/jpt.2007.256.263)*

## Zinc Oxide (ZnO): An Efficient Catalyst for the Synthesis of 4-arylmethylidene-2-phenyl 5(4*H*)-oxazolones Having Antimicrobial Activity

M.A. Päsha, V.P. Jayäshankara, K.N. Venugopala and Gopal Krishna Rao

A straightforward and a general method has been developed for the synthesis of some important functionalized 4-arylmethylidene-2-phenyl-5(4*H*)-oxazolone derivatives by combining araldehydes and hippuric acid in the presence of catalytic amount of zinc oxide at room temperature in ethyl alcohol is reported. The method was very easy, rapid and products obtained were in excellent yields. The compounds were purified, characterized and were subjected for *in vitro* antibacterial activity (determination of *Minimum Inhibitory Concentration* (MIC) by micro titration method) using two standard drugs Streptomycin and Ampicillin against *Bacillus subtilis* and *Escherichia coli*. Five of the synthesized compounds showed remarkable antibacterial activity when compared to that of standards. *(Journal of Pharmacology and Toxicology 2 (3): 264-270, 2007; **doi:** 10.3923/jpt.2007.264.270)*

## Synthesis, Biological Evaluation and QSPR Studies of Amino Acid Conjugates of Cinmetacin

C.M. Lucksha, D. Agarwal, N.S.H.N. Moorthy, C. Karthikeyan and P. Trivedi

Synthesis and biological evaluation of amino acid conjugates of cinmetacin was carried out to improve some pharmacokinetic properties and to minimize some undesirable side effects (especially ulcerogenic effect). Dissolution studies and hydrolysis studies on simulated intestinal fluid (pH 7.4) follow the first order kinetics. The quantitative structure property relationship studies reveals that rate of hydrolysis of the compounds is inversely related to partition coefficient values. The study of acute and chronic anti-inflammatory and ulcerogenic activity gave statistically significant results and it concluded that the compounds minimize the gastric side effects of cinmetacin remarkably. *(Journal of Pharmacology and Toxicology 2 (3): 271-277, 2007;* ***doi:*** *10.3923/jpt.2007.271.277)*

## Antidiabetic and Hypolipidemic Effects of *Mammea africana* (Guttiferae) in Streptozotocin Induced Diabetic Rats

Jude E. Okokon, Bassey S. Antia, L.C. Osuji and Pius M. Udia

Evaluation of antidiabetic and hypolipidaemic activities of ethanolic stembark extract of *Mammea africana* in rats was carried out. Treatment of streptozotocin diabetic rats with the extract caused a significant ($p<0.01$) reduction in fasting Blood Glucose Levels (BGL) of the diabetic rats both in acute study and prolonged treatment (2 weeks). The activity of the extract was comparable to that of the reference drug, glibenclamide. *M. africana* treatment showed considerable lowering of serum total cholesterol, triglycerides, LDL cholesterol, VLDL cholesterol and an increase in HDL cholesterol in the treated diabetic group. This results suggest that the stembark extract of *M. africana* possesses antidiabetic and hypolipidaemic effect on streptozotocin induced diabetic rats. *(Journal of Pharmacology and Toxicology 2 (3): 278-283, 2007;* ***doi:*** *10.3923/jpt.2007.278.283)*

## Molecular Modelling Analysis of the Metabolism of Enoxacin

Fazlul Huq

Enoxacin (ENX) is an orally active fluorinated quinolone antimicrobial agent that has strong activity against both gram-positive and gram-negative bacteria.

Molecular modelling analyses based on molecular mechanics, semi-empirical (PM3) and DFT (at B3LYP/6-31G* level) calculations show that ENX and its metabolites have moderately large LUMO-HOMO energy differences so that neither ENX nor any its metabolites is expected to be extremely inert and highly labile. The molecular surfaces of the compounds are found to possess neutral (green) and negative (yellow and red) and electron-deficient (blue) regions so that they may be subject to lyophilic, electrophilic and nucleophilic interactions. Nucleophilic attack may be due to glutathione and nucleobases in DNA resulting into glutathione depletion and oxidation of nucleobases. Depletion of glutathione depletion would induce oxidative stress and hence cellular toxicity whereas oxidation of nucleobases in DNA would cause DNA damage. Some what higher reactivity of ENX coupled with the presence of a larger amount of electron-deficient regions may mean that the consequences of such adverse reactions would be greater in the case of the parent drug than in any of the metabolites. *(Journal of Pharmacology and Toxicology 2 (3): 284-289, 2007;* ***doi:*** *10.3923/jpt.2007.284.289)*

## Assessment of the Role of the μ Opioid Receptor in Ethanol-Induced Hyperprolactinemia in Mice

Richard Stripp and Kelly Brinsko

The purpose of this study was to examine the role of the endogenous opiate system, specifically the opiate receptor subtypes, in response to ethanol induced prolactin secretion in male Swiss-Webster mice. In order to determine the role of μ opiate receptors in ethanol induced hyperprolactinemia, animals were treated with ethanol with and without pretreatment with the opiate receptor antagonist β-Funaltrexamine. Additional animals were also treated with β-Endorphin under similar conditions as a positive control of opiate receptor activity and prolactin secretion. Opiate receptor antagonists successfully ameliorated ethanol induced hyperprolactinemia. This research could provide insight into ethanol's role in prolactin secretion and indirectly monitor changes in reproductive and immunological functions. *(Journal of Pharmacology and Toxicology 2 (3): 290-294, 2007;* ***doi:*** *10.3923/jpt.2007.290.294)*

## Molecular Modelling Analysis of the Metabolism of Meropenem

Fazlul Huq

Meropenem (MER) is a new carbapenum antibiotic that is highly active in the treatment of a broad range of pathogenic infections including gram-positive and

gram-negative bacteria. It is water-soluble and eliminated mainly by renal excretion, through both glomerular filtration and tubular secretion. MER is metabolized into open ring metabolite UK-1a which is also microbiologically active. In healthy volunteers, 70% of the administered dose is excreted as the unchanged drug and 20% as the metabolite UK-1a, in the urine. There is a significant reduction in renal excretory capacity for MER and its metabolite UK-1a in elderly subjects. Molecular modelling analyses based on molecular mechanics, semi-empirical and DFT calculations show that both MER and UK-1a have large LUMO-HOMO energy differences so that they would be kinetically inert. Also, neither MER nor UK-1a is found to abound in electron-deficient regions so that they would not readily react with glutathione and nucleobases in DNA. This may explain why the side-effects from MER-therapy are low. *(Journal of Pharmacology and Toxicology 2 (3): 295-299, 2007;* ***doi:*** *10.3923/jpt.2007.295.299)*

## Studies on the Biochemical Effects of *Talinum triangulare* in Rat

Arit Ekpo, Olorunfemi Eseyin, Ndukwe Kalu, Obot Jackson and E.J. Edoho

Ethanol extract of *Talinum triangulare* was administered parenterally to Wistar albino rats weighing 144-179 g daily for a period of twenty eight days at four dose levels: 100, 250, 500 and 1000 mg $kg^{-1}$. Control group received saline water only in place of the extract. The rats were fasted overnight after extract administration on the 28th day. On the 29th day the rats were dissected under chloroform anaesthesia and blood collected by cardiac puncture. Serum was obtained from the blood by centrifugation after clotting. The concentration of the following enzymes and biomolecules were determined from the serum using appropriatre commercial kit (Randox R, United Kingdom): Alanine and aspartate aminotransferases, alkaline phosphatases, total cholesterol, high density lipoproteins, triglycerides, creatinine, total proteins, total and conjugated bilirubin and glucose. The extract significantly reduced the concentration of creatinine to 105.0, 94.20, 100.20 and 82.00 mmol $L^{-1}$ from control level of 134.44 mmol $L^{-1}$ and increased glucose concentration to 81.0, 76.8, 82.0 and 72.8 mg $dL^{-1}$ compared to control at all dose levels (100, 250, 500 and 1000 mg $kg^{-1}$, respectively). Changes in concentration of all the other biomolecules were insignificant at $p<0.05$. The results showed that Talinum triangulare possesses hemolytic and hyperglycemic effect and should therefore be consumed with caution by diabetic patients. *(Journal of Pharmacology and Toxicology 2 (3): 300-303, 2007;* ***doi:*** *10.3923/jpt.2007.300.303)*

## Genotoxicity of Gasterolan (An Herbal Product) on Chromosomes of Cultured Human Lymphocytes and Rat Bone Marrow

Mostafa Saadat, Mohammad Masoudi and Zahra Zendehboody

It is well known that many components of herbal products are mutagens. Because of increasing use of medical herbs, in the present study the genotoxicity of Gasterolan was investigated using cultured human lymphocytes and rat bone marrow. Gasterolan (Goldaru Company, Esfahan, Iran) is used as an antispasmodic, carminative and for spastic disorders of the gastrointestinal tract. The drug contains hydroalcoholic extracts of *Foeniculum vulgare* fruits, *Matricaria chamomilla* flowers and *Mentha piperita*. The cultured human lymphocytes were treated with 0.5 and 0.75% (v/v) of Gasterolan and 0.75% of ethanol for 14 h. Chromatid break was used as a marker for damage. Ethanol did not increase the frequency of chromatid break ($Z = 0.0068$, $p = 0.948$). The frequency of chromatid break is significantly increased in 0.5 ($Z = 2.75$, $p = 0.006$) and 0.75 ($Z = 7.47$, $p<0.001$) percent of Gasterolan. Considering that ethanol does not increase the frequency of chromatid break, the observed effect is probably due to some components present in the herbal product. Investigation of rat bone marrow metaphases show that chromatid breaks increased as a function of harvest time (from 2-8 days after beginning the treatment) ($r = 0.998$, $df = 2$, $p = 0.002$). More studies are necessary to find components that increased chromosomal aberrations. *(Journal of Pharmacology and Toxicology 2 (3): 304-306, 2007;* ***doi:*** *10.3923/jpt.2007.304.306)*

## Histopathological Changes Induced in Mice after Inramuscular and Intra Peritoneal Injections of Venom from Spine-bellied Sea Snake, *Lapemis curtus* (Shaw, 1802)

R. Karthikeyan, S. Karthigayan, M. Sri Balasubashini, S. Vijayalakshmi and T. Balasubramanian

The venom of the *Lapemis curtus* was tested for its ability to induce histopathological changes in mice intraperitoneal injection of the venom ($LD_{50}$ of 0.65 mg $kg^{-1}$), by light microscopic examination of some organs (liver, kidney and spleen). *L. curtus* venom induces changes including necrosis and edematous appearance with cellular infiltration and vacuolation. The injury of kidneys includes significant changes of the glomerular apparatus. Venom treated mice liver shows congestion, micro vesicular fatty changes and infiltration of inflammatory cells

around the portal vein. Where as, spleen showed hemorrhage, congested and inflammation were observed. Areas of hemorrhage, vascular congestion and cloudy swelling in renal tubules were observed in the kidney. No myoglobinuria was noted in any group of animals. The crude venom was also administered intraperitoneally into the experimental animals and tissue samples were taken at several time intervals. The venom of the sea snake *L. curtus*, was tested for its ability to induce myonecrosis changes in albino mice. Induction of myonecrosis was demonstrated by their ability to release Creatine Kinase (CK) from damaged muscle fibers and direct histopathological examination of the injected muscles (i.m.). Crude venom exhibits intense myonecrosis characterized by the changes including, necrosis and edematous appearance with cellular infiltrate, vacuolation and degenerated muscle cells with delta lesions and heavy edema in between the cells. *(Journal of Pharmacology and Toxicology 2 (4): 307-318, 2007; **doi:** 10.3923/jpt.2007.307.318)*

## Molecular Modelling Analysis of the Metabolism of Tolterodine

Fazlul Huq

Tolterodine is a new antimuscarinic drug used for the treatment of patients with overactive bladder presenting urinary frequency, urgency and urge incontinence. *In vitro*, TTD has high affinity and specificity for muscarinic receptors and shows selectivity for the urinary bladder over salivary glands *in vivo*. It is a weak base that is rapidly absorbed in humans and eliminated mainly by metabolism. Two oxidative metabolic pathways of TTD involve hydroxylation and N-dealkylation. Hydroxylation produces 5-HM-TTD and is catalysed by CYP2D6 while the N-dealkylation to produce ND-TTD from tolterodine and ND-5-HM-TTD from 5-HM-TTD is catalysed by CYP3A. Oxidation of 5-HM-TTD produces TTDA. Delakylation of TTDA produces ND-TTDA. The major portion of administered dose is excreted as TTDA and ND-TTDA. Molecular modelling analyses based on molecular mechanics, semi-empirical (PM3) and DFT (at B3LYP/6-31G* level) calculations show that TTD and its primary metabolite M1 have moderately large to large LUMO-HOMO energy differences so that they would be kinetically inert. Thus, although TTD and its metabolites have some electron-deficient regions on their molecular surfaces so that they could react with glutathione and nucleobases in DNA, the rates of such adverse reactions are expected to be low. *(Journal of Pharmacology and Toxicology 2 (4): 319-329, 2007; **doi:** 10.3923/jpt.2007.319.329)*

## Effect of Calcitonin on Acute Hepatic Damage in Rats *in vivo*

Omar M.E. Abdel Salam, Amany A. Sleem and Nermeen M. Shaffie

This study aimed to investigate the effect of salmon calcitonin on the acute hepatic injury in rats. Hepatotoxicity was induced by $CCl_4$ orally (2.8 mL $kg^{-1}$ followed by 1.4 mL $kg^{-1}$ after one week). Calcitonin at three dose levels (2.25, 4.5 or 9 mg $kg^{-1}$, s.c.) or silymarin (25 mg $kg^{-1}$, p.o.) was given daily for 14 days, starting at time of administration of $CCl_4$. Liver damage was assessed by determining liver serum enzyme activities and by hepatic histopathology. Calcitonin administration decreased the elevations in serum alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP) and also prevented the development of hepatic necrosis caused by $CCl_4$. The effect of calcitonin was dose-dependent one. Calcitonin given to $Ccl_4$-treated rats at 2.25 mg $kg^{-1}$ reduced the elevated plasma ALT by 25.5%. Calcitonin administered at doses of 4.5 or 9 mg $kg^{-1}$ significantly decreased the raised plasma ALT by 49.3 and 72.4%, AST by 51.3 and 61%, ALP by 29.1 and 48.3%, respectively. Silymarin, in comparison, decreased elevated ALT, AST and ALP levels by 72.6, 67.4 and 64.4%, respectively Histopathologic examination of the livers of rats treated with $CCl_4$ + calcitonin showed marked restoration of the normal architecture of the liver tissue. It is concluded that administration of calcitonin in liver injury induced by $CCl_4$results in less liver damage. *(Journal of Pharmacology and Toxicology 2 (4): 330-339, 2007;* ***doi:*** *10.3923/jpt.2007.330.339)*

## Molecular Modelling Analysis of the Metabolism of Ceftiofur

Fazlul Huq

Ceftiofur sodium (CF) is a third generation broad-spectrum cephalosphorin, that is active against both Gram-positive and Gram-negative pathogenic bacteria of veterinary importance and has been approved for subcutaneous treatment of certain respiratory diseases in cattle, horses, pigs, poultry and dogs. CF is rapidly metabolized to its active metabolite desfuroylceftiofur (DFC) and furoic acid (FA) after parenteral administration. DFC is further metabolized to disulfides such as desfuroylceftiofur dimer (DFC-D), desfuroylceftiofur cysteine disulfide (DFC-CYS) and desfuroylceftiofur glutathione (DFC-GS) and desfuroylcetiofur protein conjugate that may be playing a role in the activity and efficacy of CF. Molecular modelling analyses based on molecular mechanics, semi-empirical (PM3) and DFT (at B3LYP/6-31G* level) calculations show that metabolite DFC-D has the

lowest LUMO-HOMO energy difference so that it would be most reactive kinetically. CF and DFC are also expected to be significantly more labile than FA and DFC-CYS. The higher kinetic lability and the presence of electron-deficient regions on the molecular surfaces of DFC-D, CF and DFC mean that the compounds would react more readily with reduced form of glutathione and nucleobases in DNA. The depletion of glutathione level will induce cellular toxicity resulting from oxidative stress and oxidation of nucleobases in DNA will cause DNA damage. In actual fact, the effects of such adverse reactions may be lower in the case of most reactive metabolite DFC-D because of its much greater ease in excretion. *(Journal of Pharmacology and Toxicology 2 (4): 340-349, 2007;* ***doi:*** *10.3923/jpt.2007.340.349)*

## Trends of Fatal Poisoning in Northern India: A Ten-year Autopsy Analysis

B.R. Sharma, Nidhi Relhan, Neha Gupta and Harshabad Singh

Knowledge of poisons, their clinical manifestations, remedial measures, etc. and the causing of death by poisoning, has been prevalent all over the world since time immemorial. But the present day poisoning scenario is altogether different due to rapid development in the field of science and technology and vast growth in the industrial and agricultural sectors. The ups and downs in the incidence of poisoning have been reported from time to time both in the developed and the developing world. Toxicology became a specialized branch of medicine in early 1950s in the developed countries in response to the proliferation and use of chemicals in every day life. The first Poison Information Center started functioning in America in the mid fifties and by the early eighties there were nearly 400 such centers in USA. Many countries of Europe and Asia Pacific Region have established poison information center facilities. In India, a Toxicology Laboratory was setup at the Medicolegal Institute Bhopal, in 1984, following Bhopal Gas Tragedy. In 1994, National Poison Information Center was setup at All India Institute of Medical Sciences New Delhi followed by the establishment of Poison Information Centers at National Institute of Occupational Health at Ahmedabad and Mahatma Gandhi Institute of Medical Sciences Sevagram in 1996. However, the spurt in the number of intentional as well as unintentional poisoning and poisoning deaths continues to be a cause for concern. *(Journal of Pharmacology and Toxicology 2 (4): 350-358, 2007;* ***doi:*** *10.3923/jpt.2007.350.358)*

## Molecular Modelling Analysis of the Metabolism of Latanoprost

Fazlul Huq

Latanoprost (LP) is a synthetic derivative of the natural prostaglandin PGF2α, used as an anti-glaucoma agent that is effective in various types of glaucoma and ocular hypertension. It reduces intraocular pressure mainly by increasing outflow of aqueous humor. Ocular side effects of LP include increase in length, number, colorization and thickness of eyelashes and hypertrichosis. LP also appears to aggravate epithelial herpes and increases the risk of recurrences of herpetic keratitis. Increased iris pigmentation occurs in at least 10% of hazel-eyed patients after treatment with LP. Molecular modelling analyses based on molecular mechanics, semi-empirical (PM3) and DFT (at B3LYP/6-31G* level) calculations show that LP and its metabolites have large LUMO-HOMO energy differences so that the compounds would be kinetically inert. This means that although there are some electron-deficient regions on the molecular surfaces of LP and its metabolites so that they can be subject to nucleophilic attacks by glutathione and nucleobases in DNA, in actual fact, the rates of such adverse reactions may be low. Thus, LP and its metabolites may not cause oxidative stress and DNA damage resulting from their reactions with glutathione and nucleobases in DNA unless such reactions are speeded up enzymatically. *(Journal of Pharmacology and Toxicology 2 (4): 359-365, 2007;* ***doi:*** *10.3923/jpt.2007.359.365)*

## Isolation and Identification of Bioactive Antibacterial Component(s) in Root Extracts of *Boscia angustifolia* (Capparidaceae)

S.W. Hassan, M. Lawal, B.Y. Muhammad, R.A. Umar, L.S. Bilbis, A.A. Ebbo and Y.U. Dabai

The column chromatographic fractions of chloroform (CHL1, CHL2 and CHL3) root extracts of *Boscia angustifolia* were screened for antibacterial activity and phytochemical properties. CHL1 fraction was significantly active ($p<0.05$) at 5 to 60 mg $L^{-1}$ on *Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli* and *Streptococcus pneumoniae* with Minimum Inhibitory Concentration (MIC) of 0.63 to 1.25 mg $L^{-1}$. The active fraction (CHL1) revealed the presence of only alkaloids with Retention factor ($R_f$) value of 0.36. The active antibacterial agent in the most potent fraction (CHL1) was isolated and identified by thin layer chromatography (TLC) and phytochemistry. The CHL2 and CHL3 fractions did

not show inhibitory activity at 5 to 60 mg $L^{-1}$. The antibacterial activity of root extract of *Boscia angustifolia* is due to a chloroform-extractable compound. The results support the ethnomedicinal use of root of *Boscia angustifolia* for the treatment of bacterial diseases. *(Journal of Pharmacology and Toxicology 2 (4): 366-372, 2007;* ***doi:*** *10.3923/jpt.2007.366.372)*

## The Effects of Ethanolic Leaf Extract of *Commiphora africana* (Burseraceae) on Rat Liver and Kidney Functions

R. Aliyu, A.H. Adebayo, D. Gatsing and I.H. Garba

The effects of *Commiphora africana* ethanolic leaf extract on some biochemical markers of liver and kidney functions were investigated in rats. The results showed a significant ($p<0.05$) decrease in serum albumin after 10 days of treatment for the group administered 100 mg $kg^{-1}$ body weight of the extract. There was no significant ($p>0.05$) change in alkaline phosphatase activity, while groups administered 100 and 150 mg $kg^{-1}$ showed significant ($p<0.05$) increases in serum total bilirubin, after 10 days of treatment. Also, aspartate aminotransferase activity was significantly increased in groups administered 100 mg $kg^{-1}$ ($p<0.01$) and 150 mg $kg^{-1}$ ($p<0.05$), while alanine aminotransferase showed no significant ($p>0.05$) increase. The group administered 25 mg $kg^{-1}$ showed significant ($p<0.05$) increase in serum creatinine after 24 h of treatment. The results of the liver and kidney histology showed that there was no noticeable damage to the liver tissues of rats administered the extract. However, hydropic degeneration of the cortical-tubular epithelium and glomerulus was seen with the group administered 100 mg $kg^{-1}$. Similarly, the group treated with 150 mg $kg^{-1}$ showed acute glomerulonephritis and proliferation of the mesangial cells. These results suggest that *C. africana* extract may enhance liver function at low doses and may cause adverse effects at high doses. *(Journal of Pharmacology and Toxicology 2 (4): 373-379, 2007;* ***doi:*** *10.3923/jpt.2007.373.379)*

## Therapeutic Evaluation of *Aloe vera* Leaf Gel Extract on Glycoprotein Components in Rats with Streptozotocin Diabetes

S. Rajasekaran and D. Sathishsekar

Generalized abnormalities in glycoprotein metabolism are reported in both naturally occurring and experimental diabetes. The effect of *Aloe vera*, a traditionally used plant for the treatment of diabetes mellitus, was examined in Streptozotocin (STZ)-induced diabetic rats on derangement in glycoprotein's levels. STZ injection

(55 mg $kg^{-1}$ body weight) caused massive alterations of glycoprotein components such as hexose, hexosamine and sialic acid in plasma and tissues (liver and kidney) of diabetic control and experimental groups of rats. Oral administration ethanolic extract of *Aloe vera* leaf gel extract (300 mg $kg^{-1}$ body weight) for 21 days significantly restored the levels of hexose, hexosamine and sialic acid to near normalcy. These effects were compared with glibenclamide, a reference drug. Thus, the present study confirms that *Aloe vera* gel extract possesses a significant beneficial effect on glycoprotein components in STZ-induced diabetic rats, thereby preventing glycoprotein's mediated secondary diabetic complications. *(Journal of Pharmacology and Toxicology 2 (4): 380-385, 2007;* ***doi:*** *10.3923/jpt.2007.380.385)*

## Phytochemical and Pharmacological Screening of *Senna tora* Roxb.

G.M.M. Murshid, M. Moniruzzaman, A.A. Rahman, M. Saifuzzaman and Sarder Nasir Uddin

Phytochemical analysis of the dried aerial part of *Senna tora* (L.) Roxb. (Family-Fabaceae) indicated the presence of reducing sugars, tannins, steroids, saponins and gums. The pharmacological interest of these compounds, coupled with the use of this plant in traditional medicine prompted the authors to check *Senna tora* (L.) Roxb. for its probable antibacterial and analgesic activities. The dried aerial part of the plant was subjected to successive extraction with ethanol and the extract was used to investigate the activities. The extract showed mild antibacterial activity against tested microorganisms in agar diffusion method. The extract, however exhibited significant ($p<0.001$) inhibition of writhing reflex at the dose of 500 mg $kg^{-1}$ body weight compared with the standard drug Diclofenac Sodium at the dose of 25 mg $kg^{-1}$ body weight. The obtained result provided a support for the use of this plant in traditional medicine and its further investigation. *(Journal of Pharmacology and Toxicology 2 (4): 386-390, 2007;* ***doi:*** *10.3923/jpt.2007.386.390)*

## Pharmacological Evaluation of Different Extract of *Asclepias daemia* Leaves

C. Karthikeyan, S. Siva kumar, P. Chandrasekar, A. Heber, S.J.H. Robert and N.S.H.N. Moorthy

Antisecretory, gastric transit time and wound healing activity of various extract of the shade-dried powder of *Asclepias daemia* leaves was studied in albino rat and

mice respectively. Concentration of gastric hydrogen ions was determined for antisecretory activity by titration with 0.01 N sodium hydroxide using Tofer's reagent as an indicator. The gastric transit activity was determined by using charcoal meal. The results showed that chloroform and aqueous extract produced significant action on antisecretory, gastric transit time and wound healing activities, while petroleum ether extract have no remarkable activity. Aqueous extract showed highly significant ($p<0.01$) antisecretory and gastric transit activities. *(Journal of Pharmacology and Toxicology 2 (4): 391-395, 2007; **doi:** 10.3923/jpt.2007.391.395)*

## Some Toxic Effects of Aqeous Leaf Extract of *Anogeissus leiocarpus* in Rats

B.M. Agaie, P.A. Onyeyili, B.Y. Muhammad and M.J. Ladan

Some toxic effects of the aqeous leaf extract of *Anogeissus leiocarpus* was evaluated in rats using changes in haematological and biochemical parameters as well as body weight changes. The results indicate that the extract had no significant effect ($p>0.05$) on haematological parameters except the packed cell volume and lymphocytes. Significant ($p<0.05$) dose-dependent increase were observed in serum levels of aspartate aminotransferase, alanine aminotransferase and alkaline phosphatase. Serum sodium and potassium were not affected by extract administration. However, total protein, bilirubin, urea and cholesterol as well as body weight values were significantly lower than in the control especially in groups that received higher doses. The results of this study therefore suggest that the leaf extract of this plant could affect feed intake and utilization and also elicit some changes in biochemical parameters of rats. *(Journal of Pharmacology and Toxicology 2 (4): 396-401, 2007; **doi:** 10.3923/jpt.2007.396.401)*

## Effects of Dietary Chromium Supplementation on the Performance and Some Serum Parameters in Bovans-type Chicks

A.O. Bakhiet and S.M.A. Elbadwi

This study was conducted to investigate the effect of increasing dietary levels of inorganic chromium ($CrCl_3 \cdot 6H_2O$) on the performance and some serum parameters of chicks. One hundred 1-day-old Bovans-type chicks were randomly distributed to four groups. The control group received no supplemental chromium. 0.2, 0.3 and 0.4 mg chromium (Cr) $kg^{-1}$ diet from chromium chloride were added

to other three groups. Each experimental group consisted of five replicates each of five birds and the supplementation was continued for 35 days. Blood samples were collected for the determination of serum concentration of proteins, albumin, glucose, total cholesterol, High Density Lipoprotein (HDL) and Low Density Lipoprotein (LDL) cholesterol, triglycerides and the activities of spartate aminotransferase (AST) and Alkaline Phosphatase (ALP). Chromium by the doses used had no effect on weight gain. Supplementation with Cr decreased the serum total cholesterol, LDL cholesterol ($p<0.05$), triglycerides ($p<0.05$) and glucose ($p<0.05$) concentrations whereas serum HDL and cholesterol were increased. Serum total protein concentration, AST and ALP activities slightly but not significantly increased in all Cr. treated groups. *(Journal of Pharmacology and Toxicology 2 (4): 402-406, 2007;* ***doi:*** *10.3923/jpt.2007.402.406)*

## Comparative Studies of the Phytochemical and Antimicrobial Properties of the Leaf, Stem and Tuber of *Anchomanes difformis*

V.O. Oyetayo

Ethanolic extracts of the stem, leaf and tuber of *Anchomanes difformis* were screened for the presence of phytochemicals. The extracts of these three parts of the plant were found to contain saponin, tannins and alkaloids. Antibacterial assay of the extract against indicator bacteria reveal zones of inhibition ranging between 2 to 35 mm. The extract of the tuber was found to be more effective in inhibiting *Salmonnella species* and *Bacillus subtilis*. The result of this study confirms the local use of the extract of tubers soaked in water in the treatment of dysentery by herbal practitioners. *(Journal of Pharmacology and Toxicology 2 (4): 407-410, 2007;* ***doi:*** *10.3923/jpt.2007.407.410)*

## Modelling Vasorelaxant Activity of Some Drugs/Drug Candidates Using Artificial Neural Networks

S. Soltani, H. Babaei, K. Asadpour Zeynali and A. Jouyban

Cardiovascular diseases are the most common health problems in developed and developing societies and the vasodilating agents are one of the medicinal groups to improve the life style of the patients suffering from the cardiovascular diseases. To study the quantitative structure-activity relationship of a number of pharmacological agents, the published data sets containing more than 10 vasodilating agents assessed on rat thoracic aorta, were collected from the

literature. Different physico-chemical and structural descriptors of the compounds were computed using HyperChem® (12 descriptors) and Dragon software (1479 descriptors). The more suitable descriptors (Jhetv, Lop, SP20, RDF020u, RDF030m and R6m) were selected using a combination of linear regression and genetic algorithm methods. The artificial neural networks method was used for modelling -log of vasodilating activity (pEC50) using selected descriptors. The statistical analyses were performed using SPSS software and the average percentage deviation between calculated and observed values for predicted data points studied in this work was 15.0 (±18.8). *(Journal of Pharmacology and Toxicology 2 (5): 411-426, 2007;* ***doi:*** *10.3923/jpt.2007.411.426)*

## Hypoglycemic, Hypolipidemic, Antioxidant and Male Sexual Improvement Potentials of Olive Oil in Alloxan Treated Rats

I.M. Alhazza and Samir A.E. Bashandy

*Diabetes mellitus* is a degenerative disease that has deleterious effects on male reproductive function, possibly through an increase in oxidative stress by free radicals. The protection against such deleterious effects can be offerd by antioxidant supplementation. This study aimed to evaluate the significance of treatment of diabetic rats with olive oil in reducing oxidative stress, hyperglycemia, hyperlipidemia and testicular dysfunction induced by alloxan. The diabetic rats exhibited an increase in blood glucose, cholesterol, hydroperoxide levels and sperm abnormalities. Moreover, a significant decrease in the weights of sex organs, plasma testosterone, LH, sperm motility and sperm count was noticed in diabetic animals. Administration of olive oil to diabetic rats exhibited hypoglycemic and hypocholesterolemic effects associated with an improvement of sexual organ weights, hormone levels, sperm quality and sperm count. Furthermore, olive oil reduced the elevation of hydroperoxide level induced by alloxan. Administration of olive oil to normal rats showed hypocholesterolemic effect, a decrease in hydroperoxide level and increase in plasma testosterone level after eight weeks. On the other hand, olive oil has no significant influence on blood glucose, luteinizing hormone (LH) level, weight of sex organs, sperm quality and sperm count of normal rats. These results demonstrate that olive oil may be of advantage in lowering hyperglycemia, hypercholesterolemia, oxidative stress and deleterious effects on male reproductive functions induced by diabetes. It is suggested that the administration of olive oil may be helpful in alleviation of diabetic complications associated with oxidative stress and male reproductive dysfunction. *(Journal of Pharmacology and Toxicology 2 (5): 427-436, 2007;* ***doi:*** *10.3923/jpt.2007.427.436)*

## Novel Use of Uric Acid and Sodium Arsenite to Induce Vascular Endothelial Dysfunction in Rats

Pitchai Balakumar, Seema Jindal and Manjeet Singh

The present study has been designed to investigate the potential of *in-vivo* administration of uric acid and sodium arsenite in the development of vascular endothelial dysfunction (VED) in rats. The uric acid (100, 150, 200 mg $kg^{-1}$ $day^{-1}$, i.p., 3 weeks) and sodium arsenite (1, 1.5, 2 mg $kg^{-1}$ $day^{-1}$, i.p., 2 weeks) were administered to rats. Vascular endothelial dysfunction was assessed by employing isolated aortic ring preparation, electron microscopy of thoracic aorta and estimating serum concentration of nitrite/nitrate. Further, serum thiobarbituric acid reactive substances (TBARS) and aortic production of superoxide anion were estimated to assess oxidative stress. High dose of uric acid (200 mg $kg^{-1}$ $day^{-1}$, i.p., 3 weeks) and sodium arsenite (2 mg $kg^{-1}$ $day^{-1}$, i.p., 2 weeks) were noted to produce high mortality rate (>85%) in animals. On the other hand, less mortality rate (<5%) was observed in animals treated with uric acid (100, 150 mg $kg^{-1}$ $day^{-1}$, i.p., 3 weeks) and sodium arsenite (1, 1.5 mg $kg^{-1}$ $day^{-1}$, i.p., 2 weeks). Moreover, uric acid (100, 150 mg $kg^{-1}$ $day^{-1}$, i.p., 3 weeks) and sodium arsenite (1, 1.5 mg $kg^{-1}$ $day^{-1}$, i.p., 2 weeks) were noted to produce vascular endothelial dysfunction by attenuating acetylcholine-induced endothelium dependent relaxation, impairing the integrity of vascular endothelial lining, decreasing serum nitrite/nitrate concentration and increasing serum TBARS and aortic superoxide anion generation. Hence, it may be concluded that uric acid (100 to 150 mg $kg^{-1}$ $day^{-1}$, i.p., 3 weeks) and sodium arsenite (1 to 1.5 mg $kg^{-1}$ $day^{-1}$, i.p., 2 weeks) may be employed as potential chemically-induced models to produce vascular endothelial dysfunction in rats. *(Journal of Pharmacology and Toxicology 2 (5): 437-446, 2007;* ***doi:*** *10.3923/jpt.2007.437.446)*

## Molecular Modelling Analysis of the Metabolism of Tegaserod

Fazlul Huq

Molecular modelling analyses based on molecular mechanics, semi-empirical (PM3) and DFT (at B3LYP/6-31G* level) calculations show that TGS and its major metabolites MIM, MIMA, MIMAG, ODMTGS, TGSG1, TGSG2 and TGSG3 have LUMO-HOMO energy differences ranging from 4.4 to 5.0 eV from DFT calculations so that they all would be moderately inert kinetically. The molecular surfaces of TGS and its metabolites are found to abound in neutral (green) and electron-rich (red and yellow) regions so that the compounds may

undergo lyophilic and electrophilic attacks. The molecular surface of none of the compounds is found to abound in electron-deficient (blue) regions so that the compounds may not react readily with cellular nucleophiles such as glutathione and nucleobases in DNA. This means that none of the compounds may cause significant oxidative stress associated with glutathione depletion or DNA damage associated with oxidation of nucleobases. *(Journal of Pharmacology and Toxicology 2 (5): 447-455, 2007;* ***doi:*** *10.3923/jpt.2007.447.455)*

## Piperine Inhibits Visceral Pain Caused by Acetic Acid in Mice

Omar M.E. Abdel Salam, Siham EL-Shenawy, Salwa M. Nofal and Mózsik Gy

Piperine administered orally at increasing concentrations of 0.5-4 mg $mL^{-1}$ (5-40 mg $kg^{-1}$; 0.3 mL) caused dose-dependent inhibition of the number of abdominal constrictions induced 60 min later by i.p. injection of 0.6% acetic acid in mice by 14.5-66.2%. Higher concentrations of 8 or 16 mg $mL^{-1}$ (80-160 mg $kg^{-1}$; 0.3 mL) did not produce further inhibition of the nociceptive behavior (-49.5 and -33.9% inhibition, respectively). The inhibition of visceral pain by piperine was evident 15 min after its oral administration. The antinociceptive effect of orally administered piperine (4 mg $mL^{-1}$; 40 mg $kg^{-1}$) was unaffected by atropine (2 mg $kg^{-1}$, s.c.) or theophylline (20 mg $kg^{-1}$, s.c.), but increased by co-treatment with propranolol (2 mg $kg^{-1}$, s.c.), prazosin (2 mg $kg^{-1}$, s.c.), guanethidine (16 mg $kg^{-1}$, s.c.), glibenclamide (5 mg $kg^{-1}$, s.c.) or yohimbine (10 mg $kg^{-1}$, s.c.). Lidocaine administered orally just prior to piperine enhanced the antinociceptive effect of the latter. The antinociceptive effect of piperine (2 mg $mL^{-1}$) and dexamethasone (0.1 mg $kg^{-1}$, s.c.) or indomethacin (10 mg $kg^{-1}$, s.c.) was additive. The present study indicates that the oral administration of piperine exerts antinociceptive properties in a model of visceral inflammatory pain in mice. It is suggested that stimulation of sensory afferent by piperine and transmission of nociceptive information centrally leads to the activation of descending antinociceptive mechanism interfering with the noxious visceral stimulus. *(Journal of Pharmacology and Toxicology 2 (5): 456-464, 2007;* ***doi:*** *10.3923/jpt.2007.456.464)*

## Effect of *Bauhinia variegata* on Complete Freund's Adjuvant Induced Arthritis in Rats

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Effect of ethanol extract of *Bauhinia variegata* (EBV) was evaluated for antiarthritic activity on complete Freund's adjuvant (CFA) induced arthritis in rat.

The EBV was administered orally at the dose level of 250 mg $kg^{-1}$ for 15 days. The paw volume was measured at 3rd, 5th, 10th and 15th days. At the end of these 15 day, the animals were sacrificed and various biochemical parameters such as serum aspartate transaminase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), total cholesterol and triglycerides were estimated. Antioxidant enzymes such as superoxide dismutase (SOD), catalase, glutathione peroxidase (GPx) and lipid peroxide (LPO) in liver and kidney of normal, arthritic control and EBV treated rats were studied. Oral administration of EBV effectively inhibits rat paw edema volume. EBV significantly ($p<0.01$) altered the biochemical parameters which got affected in arthritic rats. There was a significant alteration in LPO, SOD, catalase and GPx levels when compared to arthritic control rats. Our finding showed a significant antiarthritic effect of EBV against CFA induced arthritis in rats. *(Journal of Pharmacology and Toxicology 2 (5): 465-472, 2007;* ***doi:*** *10.3923/jpt.2007.465.472)*

## *In vitro* Evaluation of Uranium Induced Immunotoxicity in Chicken Lymphocytes

G. Shukla, P. Chattopadhyay, L.K. Singhal, P. Chaudhury and R.S. Chuahan

In this present investigation *in vitro* Uranyl Nitrate (UN) induced immonotoxicity in chicken spleens lymphocytes was evaluated. At dose levels $15\times10^{-4}$ $mL^{-1}$ UN induced maximum DNA toxicity with in 90 min. It was observed shrunken cells, migration of chromatin, karyorehxis, budding and phagocytic apoptotic bodies were observed after by transmission electron microscopy analysis (TEM). Abortive DNA detected by agarose gel electrophoresis and damaged lymphoid cells was observed by immunoperoxidase assay. Hence, it was concluded that low concentration uranium can produce in immunotoxicity. *(Journal of Pharmacology and Toxicology 2 (5): 473-480, 2007;* ***doi:*** *10.3923/jpt.2007.473.480)*

## Novel Schiff Bases of 4-Hydroxy 6-Carboxhydrazino Benzofuran Analogs: Synthesis and Pharmacological Study

Gopal Krishna Rao, K.N. Venugopala and P.N. Sanjay Pai

The present investigation was aimed to study the effect of bioisosteric replacement of sulfur with oxygen with regard to antibacterial activity. Hence some new bioisosteric analogues of benzothiophen derivatives namely schiff bases of 4-hydroxy 6-carboxhydrazino benzofuran for antibacterial activity were carried out. The title compounds were characterized on the basis of spectroscopic techniques viz. IR, $^1$H-NMR, Mass spectral studies and evaluated for their qualitative and quantitative antibacterial activity by agar cup plate method and micro titration

method, respectively. From the biological activity it was possible to observe that some of the substituents such as chloro, dimethylamino, hydroxy and methyl on the phenyl ring of the benzofuran analogs influenced the biological activity. *(Journal of Pharmacology and Toxicology 2 (5): 481-488, 2007; **doi:** 10.3923/jpt.2007.481.488)*

## A Molecular Modelling Analysis of Toxicity of Fosamax and Risedronate

Fazlul Huq

Fosamax (FSM) and risedronate (RDT) are a second and a third generation aminobisphosphonate respectively that are approved for the prevention and treatment of osteoporosis in post-menopausal women and elderly men. Molecular modelling analyses based on molecular mechanics, semi-empirical (PM3) and DFT (at B3LYP/6-31G* level) calculations show that RDT has a much larger LUMO-HOME energy difference than FMX so that it would be more inert kinetically than FMX. The molecular surface of FSM is found to abound more in electron-rich red and yellow regions than that of RDT so that FSM may be subject to electrophilic attack. This means that FSM can compete better than RDT, with phospholipids for the binding sites on the surface of the mucus gel layer, thus causing a much greater reduction in the protective hydrophobic barrier. The lower gastric irritating action of FSM and RDT at low pH may be explained as being due to partial neutralization of surface charge on the molecules as a result of association with readily available hydrogen ions. Also at low pH, hydrogen ion may displace sodium ion from FSM producing the acid form of the molecule that is found to have much lower negative charge on its molecular surface. *(Journal of Pharmacology and Toxicology 2 (5): 489-495, 2007; **doi:** 10.3923/jpt.2007.489.495)*

## Toxicologic Interaction of Potassium Bromate and *Allium cepa*, *Allium sativum* or Sodium Selenite in Wistar Rats

E.H. Abdel Gadir, W.S. Abdel Gadir and S.E.I. Adam

Although diets containing mixtures of 600 mg $kg^{-1}$ of $KBrO_3$ plus 2% *Allium sativum*, 600 mg $kg^{-1}$ $KBrO_3$ plus 2% *Allium cepa* and 600 mg $kg^{-1}$ of $KbrO_3$ plus 1 mg $kg^{-1}$ sodium selenite did not adversely affect the growth of Wistar rats, a significant decrease in body weight gain, hepatonephropathy, desquamation of the intestinal epithelium into the lumen and lymphocytic accumulation in vital organs were observed in the rats fed a diet consisting of 600 mg $kg^{-1}$ of $KBrO_3$ singly for

4 weeks. These changes associated with macrocytic normochromic anemia were correlated with alterations in serum aspartate transaminase (AST), alanine transaminase (ALT) and alkaline phosphatase (ALP) activities and concentrations of cholesterol, urea and other serum constituents. However, none of the rats died during the 4-week period. *(Journal of Pharmacology and Toxicology 2 (5): 496-501, 2007; **doi**: 10.3923/jpt.2007.496.501)*

## Genotoxicological Evaluation for the Hepanox Drug and its Major Components

M.S. Hassanane, K.B. Abdel Aziz, M. Amer and A. Hamdy

Hepanox is widely used as an anti-oxidant drug for treating some liver problems additional to its two main components: selenium and silymarin were evaluated for possible genotoxicity on laboratory albino mice. The evaluation was performed on somatic and germ cells as well as sperm morphology. The mice were orally administrated with the therapeutic dose and its double of Hepanox up to three successive months. The animals were also orally received selenium and silymarin. Their doses were chosen according to their percentages in the Hepanox drug. The results showed that selenium induced a significant reduction in the mitotic and meiotic activity. It also induced chromosomal abnormalities in both somatic and germ cells, but the induced chromosomal abnormalities in the spermatocytes were shown only after the third month of treatment. Silymarin didn't affect the mitotic and meiotic activity, it is also didn't induce chromosomal abnormalities in somatic and germ cells. The hepanox drug didn't affect the mitotic and meiotic activity, it induced some chromosomal abnormalities such as gaps and deletions after the third month of treatment, similarly for spermatocytes the induced abnormalities were X-Y univalents and fragments. Regarding sperm morphology assay, it was found that only selenium which affects the sperm count. All treatments showed significant levels of sperm abnormalities after selenium treatment. Hepanox reduced the rate of sperm shape abnormalities. *(Journal of Pharmacology and Toxicology 2 (6): 502-512, 2007; **doi**: 10.3923/jpt.2007.502.512)*

## Partial Purification and Elucidation of Mechanism of Hypoglycaemic Agent of Aqueous Leaf Extract of *Albizzia chevalieri* Harms (Leguminosae)

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This research studied the hypoglycaemic effect of aqueous leaf extract of *Albizzia chevalieri* in alloxan-induced diabetic albino rats, using activity-guided fractionation. Preliminary elucidation of the mechanism of hypoglycaemic activity

was also studied. The crude aqueous leaf extract of the plant (100 mg $kg^{-1}$ body weight) reduced blood glucose levels of both the diabetic and normal rats by about 30%. The hypoglycaemic agent(s) were fractionated in the hexane fraction of the aqueous extract and partitioned in the second elution fraction ($H_2$) by column chromatography. Thin layer chromatography of $H_2$ gave a single spot with water as the mobile phase. The preliminary results of the mechanism of action indicated that the extract did not affect the *in vivo* digestion of carbohydrate or intestinal absorption of glucose. It however caused significant ($p<0.05$) increase in the hepatic and extrahepatic glycogen store. Phytochemical screening of the crude extract indicated the presence of saponins, flavonoids, tannins, terpenes, steroids, balsams, glycosides and alkaloids. UV/visible spectral studies of $H_2$ indicated a $\lambda_{max}$ of 320 nm. These results suggest that the hypoglycaemic effect of the extract is as a result of induction of glycogenesis. *(Journal of Pharmacology and Toxicology 2 (6): 513-523, 2007; **doi:** 10.3923/jpt.2007.513.523)*

## Molecular Modelling Analysis of the Metabolism of Thiabendazole

Fazlul Huq

Thiabendazole (TBZ) is a broad-spectrum anthelmintic that is effective against gastrointestinal nematodes in ruminants and lungworms in sheep. Molecular modelling analyses based on molecular mechanics, semi-empirical (PM3) and DFT (at B3LYP/6-31G* level) calculations show that TBZ and its metabolites have moderately large LUMO-HOMO energy differences except 5K-TBZ which has a much smaller value. The results indicate that generally TBZ and its metabolites would be fairly inert kinetically except 5K-TBZ which would be highly labile. The molecular surfaces of TBZ and its metabolites are found to possess neutral (green) and negative (yellow and red) and some electron-deficient (blue) regions so that they may be subject to lyophilic, electrophilic and nucleophilic interactions. Terminal metabolite TBZ-5S is found to abound most in electron-rich negative regions so that it may be most subject to electrophilic attack whereas the most reactive metabolite 5K-TBZ is found to abound most in electron-deficient regions so that it can be most subject to nucleophilic attack. Nucleophilic attack to the electron-deficient sites may be due to glutathione and nucleobases in DNA resulting into glutathione depletion and oxidation of nucleobases. Depletion of glutathione depletion would induce oxidative stress and hence cellular toxicity whereas oxidation of nucleobases in DNA would cause DNA damage. *(Journal of Pharmacology and Toxicology 2 (6): 524-532, 2007; **doi:** 10.3923/jpt.2007.524.532)*

## Effect of Ramipril, Valsartan and Candesartan on Thermal and Visceral Pain in Mice

Omar M.E. Abdel Salam, Siham El-Shenawy and Salwa M. Nofal

The effect of the angiotensin converting enzyme inhibitor ramipril and the angiotensin II receptor blockers valsartan and candesartan on thermal and visceral pain was studied using the hot plate and abdominal stretching assays in mice. In both tests, ramipril (0.22 and 0.44 mg $kg^{-1}$, s.c.) and valsartan (6.9 and 13.8 mg $kg^{-1}$, s.c.), but not candesartan (0.69 and 1.38 mg $kg^{-1}$, s.c.) produced a dose-related reduction in nociceptive responses. The analgesic effect of ramipril (0.22 mg $kg^{-1}$, s.c.) in the writhing test was slightly reduced by co-treatment with atropine (1 mg $kg^{-1}$, s.c.), but almost reversed by propranolol (1 mg $kg^{-1}$, s.c.) or naloxone (5 mg $kg^{-1}$, i.p.). Meanwhile, the analgesic effect of valsartan (13.8 mg $kg^{-1}$, s.c.) was reversed by co-treatment with propranolol or atropine. These results suggest the involvement of beta adrenoceptor mediated mechanism in the visceral analgesic effect of ramipril and valsartan. In addition, results suggest that the visceral antinociceptive effect of ramipril is likely to involve an opioid sensitive mechanism; whilst that of valsartan involves a muscarinic acetylcholine receptor mediated mechanism. *(Journal of Pharmacology and Toxicology 2 (6): 533-541, 2007;* ***doi:*** *10.3923/jpt.2007.533.541)*

## Analgesic and Anti-inflammatory Effects of the Leaf Extracts of *Pseudocedrella kotschyii* Harms (Meliaceae)

Y.M. Musa, A.K. Haruna, M. Ilyas, A.H. Yaro, A.A. Ahmadu and H. Usman

The n-butanol soluble portion of the ethanolic extract of the leaves of *Pseudocedrella kotschyii* Harms, was evaluated for anti-nociceptive and anti-inflammatory activities in mice and rats, respectively. The n-butanol portion of the ethanolic extract (50 and 100 mg $kg^{-1}$ body weight i.p.) exhibited a significant analgesic (acetic acid-induced writhes) and anti-inflammatory (raw egg albumin and formalin induced-oedema) effects. The analgesic and anti-inflammatory effects of the n-butanol portion of the ethanolic extract was comparable to piroxicam (20 mg $kg^{-1}$ body weight i.p.), an analgesic and non-steroidal anti-inflammatory drug. The extract had an intraperitoneal $LD_{50}$ of 1131 mg $kg^{-1}$ body weight in mice. Preliminary phytochemical screening of the extract revealed the presence of carbohydrates, glycosides, steroids, tannins, saponins, flavonoids and terpenoids Present results make the n-butanol portion of the ethanol extract worthy of further investigation. *(Journal of Pharmacology and Toxicology 2 (6): 542-550, 2007;* ***doi:*** *10.3923/jpt.2007.542.550)*

## Effects of Losartan Potassium on Central Dopaminergic System in Mice

Vijay Pandi, Anantha Naik Nagappa and Prasad A. Thakurdesai

The present study was designed to evaluate the effect of Losartan Potassium (LP) pretreatment at various time intervals against apomorphine (APM) induced stereotyped behavior and haloperidol (HP) induced catalepsy in mice. LP (100 mg $kg^{-1}$, p.o.) reduced the intensity of the APM induced stereotyped behavior at when administrated 3 h and 6 h. prior to APM. However, such reversal was not observed when LP pretreatment time was 1, 12 or 24 h. LP (100 mg $kg^{-1}$) was also found to potentiate HP-induced catalepsy both pretreated (2 h prior) and co-administrated with LP. However, onset of catalepsy in co-administrated LP group was 240 min which as drastically different when LP was administrated 2 h prior to HP (30 min). These results suggests that effects of LP induced modulation of dopaminergic functions are not because of LP *per se* ($t_{1/2}$ = 2.12 h) but because of its active metabolite, EXP 3174 ($t_{1/2}$ = 6-9 h). *(Journal of Pharmacology and Toxicology 2 (6): 551-558, 2007;* ***doi:*** *10.3923/jpt.2007.551.558)*

## Effect of *Sesbania grandiflora* on Membrane-bound ATPases in Cigarette Smoke Exposed Rats

T. Ramesh, R. Mahesh and V. Hazeena Begum

The aim of present study to assesse the harmful effects of chronic cigarette smoking on membrane-bound ATPases and the protective effect of *S. grandiflora* in rat lung, liver, kidney and heart. Adult male WKY rats were exposed to cigarette smoke for a period of 90 days and consecutively treated with aqueous suspension of *S. grandiflora* (1000 mg $kg^{-1}$ b.w/day, p.o) for a period of 3 weeks. The levels of lipid peroxides as marker for evaluating the extent of membrane damage, the activities of $Na^+$-$K^+$-ATPase, $Ca^{2+}$-ATPase and $Mg^{2+}$-ATPase and associated cations sodium ($Na^+$), potassium ($K^+$), calcium ($Ca^{2+}$) and magnesium ($Mg^{2+}$) were investigated in rat lung, liver, kidney and heart. Membrane damage was evident from the increased levels of lipid peroxides, decreased activities of membrane-bound ATPases and alterations in the levels of inorganic cations were observed in cigarette smoke exposed rats. Administration of aqueous suspension of *S. grandiflora* (ASSG) inhibited the levels of lipid peroxides, ameliorated the activities of membrane-bound ATPases and maintained the ionic equilibrium in rats exposed to cigarette smoke. The results of our study indicate that ASSG protects the membrane-bound ATPases from cigarette smoking induced membrane damage. *(Journal of Pharmacology and Toxicology 2 (6): 559-566, 2007;* ***doi:*** *10.3923/jpt.2007.559.566)*

## A Molecular Modelling Analysis of Luliconazole, Lanconazole and Bifonazole

Fazlul Huq

In this study, molecular modelling analyses based on molecular mechanics, semi-empirical (PM3) and DFT (at B3LYP/6-31G* level) calculations have been carried out to obtain insight into their toxicity. The results of the analyses show that LLZ, LCZ and BFZ have LUMO-HOMO energy differences ranging from 4.5 to 4.9 eV, indicating that the compounds would be moderately inert with BFZ being the most inert one. The molecular surfaces of all the compounds are found to possess significant amounts of positively charged electron-deficient regions so that they may be subject to nucleophilic attacks by glutathione and nucleobases in DNA, thus causing cellular toxicity due to glutathione depletion and DNA damage due to oxidation of nucleobases. However, because of kinetic inertness of the molecules, the rates of such adverse reactions are expected to be low. *(Journal of Pharmacology and Toxicology 2 (6): 567-573, 2007;* ***doi:*** *10.3923/jpt.2007.567.573)*

## Antibacterial Activity of Extracts of *Piper longum*

P.D. Lokhande, K.R. Gawai, K.M. Kodam, B.S. Kuchekar, A.R. Chabukswar and S.C. Jagdale

Dry roots of the plant *Piper longum* were extracted with n-hexane. The constituents were isolated and purified by column chromatography. The structures of the isolated constituents were confirmed by spectral analysis. The isolated constituents and n-hexane extract were found to show varying degree of antibacterial activity against all the tested bacteria. However, the aqueous extract did not show antibacterial activity against the tested bacteria. The isolated constituents were found to show better activity profile than the n-hexane extract, which indicates that the isolated constituents might be responsible for the antibacterial activity. The Minimum Inhibitory Concentration (MIC) value of piperine against *Bacillus cereus* and *Escherichia coli* was found to be 12.5 mg $mL^{-1}$. *(Journal of Pharmacology and Toxicology 2 (6): 574-579, 2007; doi: 10.3923/jpt.2007.574.579)*

## Anti-oxidant and Anti-inflammatory Activity of *Centrosema pulmieri* Benth (Leguminosea-papilionaceae)

H.O. Oladimeji, R. Nia and E. Oforah

The aim of present study was designed to investigate the anti-oxidant activity and as well as to confirm or otherwise the anti-inflammatory activity of the *Centrosema pulmieri* Benth (Leguminosae-papilionaceae). Hence the DPPH (2-2-diphenyl-1-picrylhydrazyl hydrate) and HET-CAM(Hen's Eggs Chorioallanthoic Membrane) assays were, respectively carried out. The crude extract and ethyl-acetate fraction gave significant anti-oxidant activity ($IC_{50}$) at 2.10 and 1.56 μg $mL^{-1}$ ($p<0.05$), respectively compared with 0.66 μg $mL^{-1}$ displayed by ascorbic acid. Interestingly, the anti-inflammatory assay showed that the crude extract and ethyl-acetate fraction had a 100% inhibition while the hexane and chloroform fractions demonstrated a below 50% response. The ethyl-acetate fraction when serially diluted exhibited a concentration-dependent anti-inflammatory activity. These findings have revealed a correlation between the anti-oxidant and anti-inflammatory activities, hence scientific justification to the uses of the plant in folkloric medicine. *(Journal of Pharmacology and Toxicology 2 (6): 580-585, 2007; doi: 10.3923/jpt.2007.580.585)*

## Phytochemical Profile and Antibacterial Properties of the Seed and Leaf of the Luffa Plant (*Luffa cylindrica*)

F.L. Oyetayo, V.O. Oyetayo and V. Ajewole

This study aims at determination of the antimicrobial activity of the seeds extracts of *Luffa cylindria* on certain pathogenic microbes and screening for substances that may be responsible for these actions. *Luffa cylindrica* seeds and Leaves were extracted with ethanol, choloroform and methanol and screened for secondary metabolites. Extracts were found to contain alkaloids, saponnins and cardiac glycosides. The extracts also showed antimicrobial activities against *Escherichia. coli*, *Staphylococcus aureus*, *Salmonella typhi* and *Bacillus subtilis*. The zones of inhibition ranged between 6.00 to 10.00 mm. The inhibitory potentials of the extracts might be ascribed to their content of secondary metabolites. The ability of the extracts to inhibit the pathogens used as indicator organisms holds promise for potential application in the pharmaceutical industry. *(Journal of Pharmacology and Toxicology 2 (6): 586-589, 2007; **doi:** 10.3923/jpt.2007.586.589)*

## Probiotic Toxicity, Any Evidence?

Kingsley C. Anukam

Probiotics defined as 'live microorganisms, which when administered in adequate amounts, confer a health benefit on the host' is now more relevant than ever

before, with few concerns raised on toxicity potential. This review examined the safe use of probiotics in chronically ill patients and cases of adverse effects. Safety assessment for the selection of probiotics and toxicological related animal/human studies were evaluated based on Pubmed search for allied articles. There were conflicting reports on the safety use of probiotics in immunocompromized patients, with few isolated cases of bacteraemia in patients with underlying co-morbidities. Probiotic strains are less likely to participate in the pathogenesis of infections in healthy individuals. This is based on the fact that each year, >20 billion doses of probiotics are used by healthy people and by those diagnosed with a range of medical conditions. Conventional toxicology and safety evaluation employed for pharmaceutical products may be of limited value in assessing the safety of probiotics. If probiotic toxicology is to be developed, then a threshold defined as a dose at or below which a response is not seen in an experimental setting will have to be evaluated. Establishing proof of absence of an effect at such a dose in absolute terms is scientifically and practically demanding. There is no evidence or documentation that lactic acid bacteria used as probiotics do synthesize any toxins detrimental to humans. However, as probiotics is safe in healthy people, immuno-compromised individuals should consult their health care providers before using probiotics. *(Journal of Pharmacology and Toxicology 2 (7): 590-598, 2007;* ***doi:*** *10.3923/jpt.2007.590.598)*

## Molecular Modelling Analyses of the Metabolism of Clofarabine

Fazlul Huq

Clofarabine (CLF) is a new purine nucleoside antimetabolite developed for the treatment of solid and hematologic tumours. In this study molecular modelling analyses based on molecular mechanics, semi-empirical (PM3) and DFT (at B3LYP/6-31G* level) calculations have been carried out to gain information on the relative toxicity of CLF and its metabolites. The study shows that CLF and its metabolites have large LUMO-HOMO energy differences of the order 5.3 eV from DFT calculations, indicating that CLF and all its metabolites would be kinetically inert. The molecular surfaces of CLF and all its metabolites are found to possess significant amounts of electron-rich (yellow and red) and neutral (green) regions so that the compounds may be subject to electrophilic and lyophilic attacks. However, the molecular surfaces do not appear to abound in electron-deficient (blue) regions (although the presence may be significant in the case of CLF, 2CAD and CLFDP) so that the compounds generally may not react to any significant extent with cellular nucleophiles such as the reduced form of glutathione and nucleobases in DNA. This means that other factors besides glutathione

depletion and DNA damage may be playing key role in toxicity of CLF and its metabolites. *(Journal of Pharmacology and Toxicology 2 (7): 599-609, 2007; **doi**: 10.3923/jpt.2007.599.609)*

## The Effect of Amlodipine, Diltiazem and Enalapril on Hepatic Injury Caused in Rats by the Administration of $CCl_4$

Omar M.E. Abdel Salam, Nabila S. Hassan, Ayman R. Baiuomy and Sawsan H. Karam

The present study compared the effect of the calcium channel blockers amlodipine and diltiazem with the ACE inhibitor enalapril on $CCl_4$-induced acute hepatic injury in rats. Amlodipine (0.9 or 1.8 mg $kg^{-1}$), diltiazem (10.8 or 21.6 mg $kg^{-1}$) and enalapril (0.9 or 1.8 mg $kg^{-1}$) were administered per os daily for 7 days, then acute hepatic injury was induced by treating rats using a gavage with a single dose of $CCl_4$-olive oil (1:1, 0.2 mL/100 g). Drug administration continued after $CCl_4$ and the treated animals were killed on day 3 after $CCl_4$ administration. Results indicated that whereas a reduction in serum enzyme levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP) was obtained with amlodipine and enalapril, no protective effect was observed for diltiazem in this model of hepatic injury. Thus, compared with the $CCl_4$ control group, serum ALT decreased by 56.2-61.4 and AST by 16-25.1%, after the administration of amlodipine at 0.9 and 1.8 mg $kg^{-1}$, respectively. Serum ALP was significantly reduced by 40% by 1.8 mg $kg^{-1}$ amlodipine. Enalapril administered at 0.9 and 1.8 mg $kg^{-1}$ significantly decreased ALT by 22.8-61.4%, while AST and ALP were significantly reduced by 37.3 and 54.5%, respectively by 1.8 mg $kg^{-1}$ enalapril. In contrast, diltiazem administered at 20.4 mg $kg^{-1}$ increased ALT and AST levels by 43 and 16%, respectively. Histologic examination of haematoxylin and eosin stained sections from the livers of rats treated with $CCl_4$ and amlodipine showed prominent improvement in liver architecture, a decrease in inflammatory cells and necrotic area. Electron microscopic examination of hepatocytes of $CCl_4$-treated rat showed disorganization of the cytoplasmic structure and degeneration of cytoplasmic organelles. Electron microscopy of hepatocytes from the rats treated with $CCl_4$ + amlodipine revealed healthy cytoplasmic content with healthy nuclei and normal mitochondria. Similar findings were observed after enalapril treatment. In contrast, intensive necrosis and degeneration was seen in livers of rats treated with diltiazem. On electron microscopy in most of hepatocytes, the cytoplasm became lytic with distorted mitochondrial cristae and highly dilated endoplasmic reticulum. Thus two calcium channel blockers behaved differently as regards to hepatic injury in the model of $CCl_4$-induced hepatic injury. It is suggested that profound haemodynamic

effects of diltiazem which undergoes extensive hepatic metabolism and the resultant decrease in hepatic blood flow account for the observed effect of the drug. *(Journal of Pharmacology and Toxicology 2 (7): 610-620, 2007; **doi:** 10.3923/jpt.2007.610.620)*

## Antihyperglycemic Effect of *Solanum surattense* Leaf-Extract in Streptozotocin Induced Diabetic Rats

M. Sridevi, S. Senthil and K.V. Pugalendi

In the present study, we have evaluated the validity of traditional usage of *Solanum surattense* as an antidiabetic agent. Adult male albino rats of Wistar strain, weighing 180-200 g, were made diabetic by administration of streptozotocin (STZ) (40 mg $kg^{-1}$ body weight) intraperitoneally. In a dose determination study, alcoholic leaf extract of *S. surattense* at 100, 200 and 300 mg $kg^{-1}$ body weight was orally administrated for 15 days and the extract at 100 mg dose significantly reduced blood glucose and also found to reduce the increased lipid peroxidation marker in diabetic rats. Extending oral administration of 100 mg $kg^{-1}$ bw to diabetic rats, for 45 days, resulted in a significant decrease in blood glucose and an increase in plasma insulin level. In addition, diabetic rats showed significant reduction in the glycogen content and in the activities of glucose metabolizing enzymes such as glucokinase, glucose 6-phosphate dehydrogenase and an elevation in the activities of gluconeogeneic enzymes such as glucose-6-phosphatase and fructose-1, 6-bisphosphatase. *S. surattense* extract administration to diabetic rats reversed these changes in a significant manner. Thus, the results show that *S. surattense* possesses antihyperglycemic activity and provide evidence for its traditional usage in the control of diabetes. *(Journal of Pharmacology and Toxicology 2 (7): 621-629, 2007; **doi:** 10.3923/jpt.2007.621.629)*

## Inhibitory Effect of Methanolic Extract of *Asparagus pubescens* Bak Root in Rats and Guinea Pigs Uterine Muscle

Paul A. Nwafor and F.K. Okwuasaba

The inhibitory effect of methanolic extract of *Asparagus pubescens* Bak root was studied in rat and guinea pig uterine muscles, respectively. The extract caused a concentration dependent decrease in frequency and amplitude of spontaneous activity in rat uterine muscle. It also caused a significant ($p<0.05$-$0.001$) dose-dependent decrease in acetylcholine-induced contraction in guinea pig uterine muscle. The sensitization of the tissue caused by $8.0\times10^{-6}$ g $mL^{-1}$ of extract

accentuated with $1.6\times10^{-5}$ g $mL^{-1}$ was blocked by verapamil, an extracellular calcium antagonist. The extract dose-dependently also inhibited Ach-induced contraction in $Ca^{2+}$ free Physiological Salt Solution (PSS). This inhibition which was statistically significant ($p<0.05$-0.001) was substantially reversed by addition of extracellular calcium. This inhibitory effect may in part involve the interference with intracellular/extracellular calcium mobilization. *(Journal of Pharmacology and Toxicology 2 (7): 630-637, 2007;* ***doi:*** *10.3923/jpt.2007.630.637)*

## A Molecular Modelling Analysis of the Metabolism of Mexiletine

Fazlul Huq

In this study, molecular modelling analyses based on molecular mechanics, semi-empirical (PM3) and DFT (at B3LYP/6-31G* level) calculations have been carried out to obtain information on the toxicity of mexiletine (MEX) and its metabolites. The results of the analyses show that MEX and its metabolites have moderately large to large LUMO-HOMO energy differences ranging from 5.4 to 6.4 eV indicating that the compounds would be inert kinetically, with the parent drug being most inert. The molecular surface of one of the metabolites namely HMMEX is found to possess significant amount of positively charged electron-deficient regions so that it may be subject to nucleophilic attacks by glutathione and nucleobases in DNA, thus causing cellular toxicity due to glutathione depletion and DNA damage due to oxidation of nucleobases. However, because of kinetic inertness of the molecule, the rate of such adverse reactions is expected to be low. *(Journal of Pharmacology and Toxicology 2 (7): 638-645, 2007;* ***doi:*** *10.3923/jpt.2007.638.645)*

## Evaluation of Gellan Gum as a Mini-Matrix for Sustained Release of Ephedrine Hydrochloride Granules

Patricia I. Franklin-Ude, Martins O. Emeje and Sabinus I. Ofoefule

Gellan gum was evaluated for its swelling capacity and sustained release properties in varying pH media; 0.1 N hydrochloric acid (pH 1.2), simulated gastric juice (pH 1.5) and simulated intestinal fluid (pH 7.5). Granules were prepared by the conventional wet granulation method of massing and screening. Results obtained showed that the time for 50 ($t_{50\%}$) and 70% drug release ($t_{70\%}$) were higher for gellan gum than sodium carboxymethylcellulose. *In vitro* sustained release of ephedrine hydrochloride from granules in hard gelatin capsules was achieved over

eight hours in all dissolution media. The matrix forming capacity of the polymer was concentration dependent and comparable to that of sodium carboxymethylcellulose. Maximum sustaining effect of gellan gum was achieved in the acidic media. The release kinetics of ephedrine hydrochloride from granules containing gellan gum was generally a mixture of first order and fickian diffusion. Gellan gum is suitable for the sustained-release formulation of ephedrine granules without the additional step of tablet formation. *(Journal of Pharmacology and Toxicology 2 (7): 646-652, 2007;* ***doi:*** *10.3923/jpt.2007.646.652)*

## Effect of Combined Paracetamol and *Cuminum cyminum* or *Nigella sativa* Use in Wistar Rats

Einas M. Elhabib, M.M.A. Homeida and S.E.I. Adam

*Cuminum cyminum* fruit or *Nigella sativa* seed, a traditional medicine for treatment of various disorders, was fed to male Wistar rats at 6% of standard rat diet for 4 weeks. A 6% *C. cyminum* fruit or 6% *N. sativa* seed diet was not toxic to rats. Depression in growth, hepatotoxicity and nephrotoxicity were observed in rats that had been given paracetamol at 500 mg $kg^{-1}$ per os for 4 weeks. These findings were accompanied by leucopenia, macrocytic normochromic anemia and alterations of serum aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP) activities and concentrations of cholesterol, urea and other serum constituents. Serum bilirubin did not change. In rats given the mixture of paracetamol 500 mg $kg^{-1}$ plus 6% *C. cyminum* fruit or 6% *N. sativa* seed for 4 weeks, the recovery of paracetamol hepatotoxicity was evidenced by increase in body weight, absence of hepatocellular fatty vacuolation and significant improvement of serbiochemical and hematological parameters. There was no evidence of any antinephrotoxic activity of plants used. *(Journal of Pharmacology and Toxicology 2 (7): 653-659, 2007;* ***doi:*** *10.3923/jpt.2007.653.659)*

## Anti-Mitotic and Cytotoxic Effect of *Mussaenda queensirkit*

K.S. Vidyalakshmi, A.I. Charles Dorni and Hannah R. Vasanthi

*Mussaenda queensirkit* (MQ), an ornamental plant grown in tropical countries is shown to exhibit cytotoxic property. The 70% methanolic extract of fresh flowers of *Mussaenda queensirkit* (MQF) was studied for its cytotoxic and anti-mitotic activity with Brine Shrimp Lethality assay and *Allium cepa* Root Tip mitosis experiment, respectively. The $LC_{50}$ value for MQF was found to be 83.33 μg $mL^{-1}$ in Brine Shrimp Lethality Assay. The extract showed maximum

anti-mitotic activity at the highest concentration studied (2000 μg $mL^{-1}$) with a mitotic index of 9.0. In the MTT Assay for cytotoxic activity, MQF at 500 μg $mL^{-1}$, showed a maximum of 71.44% inhibition against fibroblast cultured from skin compared to control whereas the standard, quercetin (50 μg $mL^{-1}$) exhibited a maximum of 92.7% inhibition. The HPLC profile obtained had characteristic peaks due to flavonol glycosides which might be responsible for the observed cytotoxic and anti-mitotic activity of MQF. The observed cytotoxic and anti-mitotic activity of the extract shows the potential of the plant in the exploration of anti-cancer molecules. *(Journal of Pharmacology and Toxicology 2 (7): 660-665, 2007;* ***doi:*** *10.3923/jpt.2007.660.665)*

## A 9-week Feeding Study of *Cuminum cyminum* and *Hibiscus sabdariffa* in Bovans Chicks

I.A. Ibrahim, S.M.A. El Badwi, A.O. Bakhiet, W.S. Abdel Gadir and S.E.I. Adam

The objective of the present study was to investigate the effects of low levels of dietary *Cuminum cyminum* seeds and *Hibiscus sabdariffa* calyces on the growth, organ pathology, haematological and serobiochemical parameters of Bovans chicks. *C. cyminum* seeds and *H. sabdariffa* calyces were fed to 7-day-old Bovans chicks at 2 and 10% of the diet for 9 weeks. The 10% *H. sabdariffa* calyx was toxic but not fatal to chicks and caused reduced body weight gain, inefficient feed utilization, enterohepatotoxicity, anaemia and alterations in serum aspartate aminotransferase and creatine kinase activities and cholesterol, total lipid and uric acid concentrations. These changes were also observed in the chicks fed *C. cyminum* seed at 10% of the diet and *H. sabdariffa* calyx at 2% of the diet but were less marked. *(Journal of Pharmacology and Toxicology 2 (7): 666-671, 2007;* ***doi:*** *10.3923/jpt.2007.666.671)*

## Effects of Various Levels of Dietary Potassium Bromate on Wistar Rats

E.H. Abdel Gadir, W.S. Abdel Gadir and S.E.I. Adam

The toxicity to male Wistar rats of potassium bromate ($KBrO_3$) was investigated. $KBrO_3$ was fed to rats at 75, 150, 600 and 1200 mg $kg^{-1}$ diet for 4 weeks. The rats fed diets containing 600 and 1200 mg $kg^{-1}$ of $KBrO_3$ had the lowest growth rate but none of the rats died during the 4 week period. Depression in growth, nephropathy, hepatopathy and lymphocytic infiltration in vital organs were

accompanied by anemia, leukopenia and alterations in serum alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP) activities with changes in concentration of urea, cholesterol and other serum constituents. Diet consisting of 150 mg $kg^{-1}$ of $KBrO_3$ was less toxic to rats. *(Journal of Pharmacology and Toxicology 2 (7): 672-676, 2007; **doi:** 10.3923/jpt.2007.672.676)*

## Cytotoxicity and Antimicrobial Activity of Harman Alkaloids

Verdian Rizi Mohammad Reza and Hadjiakhoondi Abbas

The cytotoxicity and antimicrobial activities of harman alkaloids including harmane, harmine, harmalol and harmaline were investigated. The cytotoxicity was monitored by the brine shrimp lethality test and microdilution method was used to determine MIC and MBC of the compounds. Harmane showed the most cytotoxicity and the most antimicrobial activity. *(Journal of Pharmacology and Toxicology 2 (7): 677-680, 2007; **doi:** 10.3923/jpt.2007.677.680)*

## Phytochemical Investigation and Toxicological Studies of Lipid Constituents Isolated from *Leptadenia pyrotechnica*

Amal M. Youssef Moustafa, Ahmed I. Khodair and Mahmoud A. Saleh

Investigation of the chemical constituents of *Leptadenia pyrotechnica* (Asclepiadaceace family) let to isolate three terpenes; phytol, squalene and taraxerol, five sterols; cholesterol, campasterol, stigmasterol, β-sitosterol and fucosterol. Fifteen fatty acids were isolated ($C_{14}$-$C_{25}$), eleven n-alkanol ($C_{29}$-$C_{39}$), series of n-alkanes ($C_{12}$-$C_{36}$), one n-alkene; 3-tetradecene. Also, for the first time eighteen aromatic hydrocarbons were isolated. 5-phenyl-undecane and 6-phenyl-tridecane are the major constituents. The structures of these compounds were established by gas chromatography; GC-FID and GC-MS, spectroscopic techniques; Infra-red (IR) and comparison with the published data. The unsaponifiable matter was divided into two parts: The first part was directly subjected to GC/FID and GC/MS chromatographic analysis. While the second part, was subjected to column chromatographic fractionation. The isolated fractions were identified as fatty alcohols, hydrocarbons, terpenes and sterols. Adduction method was used to separate the straight-chain fatty acids. The acute toxicity study of the total lipid extract was examined on brine shrimp, the $LC_{50}$ was 35.48 ppm. The extract is highly toxic. *(Journal of Pharmacology and Toxicology 2 (8): 681-697, 2007; **doi:** 10.3923/jpt.2007.681.697)*

## *In vitro* Effect of *Terminalia arjuna* Bark Extract on Antioxidant Enzyme Catalase

T.N. Padma Sree, S. Krishna Kumar, A. Senthilkumar, Gopala Krishna Aradhyam and Sathyanarayana N. Gummadi

The bark extract of *Terminalia arjuna* is an age old Ayurvedic prescription for cardiac ailments and has been reported to be particularly beneficial in improving cardiac muscle function. However the specific biological activity of individual components of *T. arjuna* bark is not yet clearly understood. In this study, bark extract of *Terminalia arjuna* in six different solvents i.e., ethanol, acetone, water, ethyl acetate, chloroform and hexane were evaluated for free radical scavenging property, total phenols and reducing properties. Among all the extracts of *T. arjuna*, crude ethanolic bark extract had high phenolics, high reducing power and high free radical scavenging activity indicating that it is the best extract to isolate antioxidant compounds which could be used for further studies. Maximum phenol content (894.95 GAE/mg extract) and radical scavenging property (~88%) was observed for ethanol extract. *In vitro* studies on the effect of the bark extract of *T. arjuna* on endogenous antioxidant enzyme catalase showed inhibition of catalase activity. Among all the extracts used, ethanolic extract showed significantly higher levels of inhibition of catalase activity. Dose dependent studies showed a concentration dependent linear increase in inhibition of catalase activity and further assessment of the kinetic parameters showed a specific and rare competitive-non competitive" kind of inhibition. Although it has been shown in earlier studies on animal models that the bark extract increases the catalase expression levels, in this study we observed that the bark extract does not enhance the catalase activity *in vitro*. This suggests the possible role of compounds in ethanolic bark extract of *T. arjuna* in catalase gene expression. *(Journal of Pharmacology and Toxicology 2 (8): 698-708, 2007;* ***doi:*** *10.3923/jpt.2007.698.708)*

## Modulatory Role of *Terminalia chebula* on Erythrocyte Defenses in Young and Aged Rats

R. Mahesh and V. Hazeena Begum

The present study was aimed to evaluate the oxidants, enzymatic and nonenzymatic antioxidants, glycoproteins and membrane adenosine triphosphatases (ATPases). The increased levels of oxidants and decreased levels of enzymatic, nonenzymatic antioxidants, glycoproteins and ATPases were

observed in erythrocytes of aged rats. After administration of *Terminalia chebula*, the levels were reverted to normal in aged rats. These results indicate that the administration of *T. chebula* acts as a free radical scavenger with potential antioxidant effects in erythrocytes of aged rats. *(Journal of Pharmacology and Toxicology 2 (8): 709-717, 2007; **doi:** 10.3923/jpt.2007.709.717)*

## Some Commercial Azo Dyes as Inhibitors of Mushroom Tyrosinase DOPA Oxidase Activity

Shiv Kumar Dubey, Archana Pandey, Ashok Kumar Bajaj and Krishna Misra

The colour of mammalian skin is determined by many factors and mainly by the degree and distribution of melanin pigmentation. Tyrosinase is the key enzyme for melanin biosynthesis. Contact with different azo dyes is well known to produce contact dermatitis and some times depigmentation of the skin. In the present study we have reported the effect of known depigmenting dyes as well as some food, cosmetic and drug dyes on the activity of tyrosinase enzyme. The activity of the enzyme has been assessed in terms of oxidation of DOPA. The inhibitory effect of PPD was found to be maximum i.e., 85% while solvent yellow 3 and Brilliant crocin showed inhibition of 70 and 60%, respectively. The PPD and solvent yellow 3 were identified as noncompetitive inhibitors of tyrosinase by Linweaver Burk plot. *(Journal of Pharmacology and Toxicology 2 (8): 718-724, 2007; **doi:** 10.3923/jpt.2007.718.724)*

## Therapeutic Effect of Indian Ayurvedic Herbal Formulation Triphala on Acetaminophen-Induced Hepatotoxicity in Mice

Mahaboob Khan Rasool, Evan Prince Sabina, Kumar Lavanya and Pichandi Nithya

Triphala, an Indian ayurvedic formulation used widely in ayurveda, is believed to promote health, immunity and longevity. The present study evaluates its hepatoprotective role. Triphala extract (100 mg $kg^{-1}$ $b.wt.^{-1}$, i.p.) inhibited acetaminophen (900 mg $kg^{-1}$ $b.wt.^{-1}$, i.p.) -induced hepatotoxicity in mice as indicated by the decrease of serum aminotransferases, alkaline phosphatase, inflammatory mediator TNF-α and hepatic lipid peroxidation. Triphala extract also protected acetaminophen-induced hepatic enzymic anti-oxidants and glutathione depletion. These observations demonstrate that Triphala treatment may attenuate acetaminophen-induced hepatoxicity in mice. *(Journal of Pharmacology and Toxicology 2 (8): 725-731, 2007; **doi:** 10.3923/jpt.2007.725.731)*

## Molecular Modelling Analysis of the Metabolism of Eszopiclone

Fazlul Huq

Eszopiclone (ESZ) is a recently introduced drug to treat insomnia. In this study, molecular modelling analyses based on molecular mechanics, semi-empirical (PM3) and DFT (at B3LYP/6-31G* level) calculations have been carried out to obtain insight into toxicity of ESZ and its metabolites. The results of the study show that both ESZ and its metabolites NDMESZ and ESZNO have small LUMO-HOMO energy differences, indicating that the compounds would be kinetically labile with ESZNO being most reactive. The molecular surfaces of ESZ, NDMESZ and ESZNO are found to posses significant amounts of electron-deficient regions so that the compounds, especially ESZNO, can react readily with cellular nucleophiles such as glutathione and nucleobases in DNA thus causing depletion of glutathione and oxidation of nucleobases. The former would induce cellular toxicity due to oxidative stress and the latter would cause DNA damage associated with oxidation of nucleobases. *(Journal of Pharmacology and Toxicology 2 (8): 732-736, 2007;* ***doi:*** *10.3923/jpt.2007.732.736)*

## Hepatoprotective Effect of Methanolic Leaves Extracts of *Tylophora asthmatica* Against Paracetamol-Induced Liver Damage in Rats

R. Malathi and M. Patrick Gomez

The aim of the present study was to evaluate the hepatoprotective and antioxidant properties of methanolic leaves extracts of *Tylophora asthmatica* (META) on paracetamol-induced (1 g $kg^{-1}$ body weight, i.p.,) hepatotoxicity in wistar strain of rats. The extract produced significant hepatoprotective effects as evidenced by decreased ($p<0.05$) serum enzyme activities, ALT, AST, ALP, LDH and serum bilirubin (200 mg $kg^{-1}$ body weight orally for 21 days) compared with control group. For antioxidant activity, META exhibited significant ($p<0.05$) hepatoprotective effect by increasing the levels of superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx) and reducing lipid peroxidation (LPO). These results suggest that META may have hepatoprotective potential, probably by its antioxidant properties on hepatocytes and also support the use of the plant as a hepatoprotective agent. *(Journal of Pharmacology and Toxicology 2 (8): 737-742, 2007;* ***doi:*** *10.3923/jpt.2007.737.742)*

## Studies on the Toxicity of *Ageratum conyzoides*

A.C. Igboasoiyi, O.A. Eseyin, N.K. Ezenwa and H.O. Oladimeji

The mean lethal dose of ethanolic extract of *Ageratum conyzoides* was evaluated. Serum levels of some enzymes and biomolecules were also evaluated after a daily oral administration of 500 and 1000 mg $kg^{-1}$ of the extract for 28 days. The enzymes and biomolecules evaluated were: Alanine and Aspartate aminotransferases, alkaline phosphatase, amylose, glucose, total proteins, creatinine, cholesterol, high density, low density-and very low density-lipoproteins. The result showed that the LD50 of *Ageratum conyzoides* was 10,100 mg $kg^{-1}$. the extract did not significantly affect serum levels of alanine and aspartate transaminases, alkaline phosphatase, amylase, creatinine, glucose and total proteins at any of the two dose levels. the extract however reduced significantly the serum level of cholesterol and high density lipoproteins. One thousand milligram per kilogram of the extract also enhanced growth of the animals as observed in the weight increase of the rats. The results of this work showed that the extract of *A. conyzoides* at the dose of 500 and 1000 mg $kg^{-1}$ administered orally and daily for a one month period did not show any toxic effect in rats. This, coupled with the high LD50 value confirm that *A. conyzoides* is safe for use in ethnomedicine. *(Journal of Pharmacology and Toxicology 2 (8): 743-747, 2007;* ***doi:*** *10.3923/jpt.2007.743.747)*

## Molecular Modelling Analysis of the Metabolism of Clotrimazole

Fazlul Huq

Clotrimazole (CTZ; bispheny l(2-chlorophenyl)-methan)) is an N-substituted imidazole drug that is used therapeutically as a topical antifungal agent. Molecular modelling analyses based on molecular mechanics, semi-empirical (PM3) and DFT (at B3LYP/6-31G* level) calculations show that both CTZ and its major metabolite 2-chlorophenybiphenylmethanol (2CLBPM) have LUMO-HOMO energy differences so that they would be kinetically inert. The molecular surface CTZ is found to abound in electron-deficient regions so that it can react with cellular nucleophiles such as glutathione and nucleobases in DNA thus causing depletion of glutathione and oxidation of nucleobases. The former would induce cellular toxicity due to oxidative stress and the latter would cause DNA damage. However, because of kinetic inertness of CTZ, the rates of such adverse reaction are expected to be low unless speeded up enzymatically. *(Journal of Pharmacology and Toxicology 2 (8): 748-752, 2007;* ***doi:*** *10.3923/jpt.2007.748.752)*

## Phytochemical, Antibacterial and Antinociceptive Studies of *Hoya parasitica*

M.S.H. Reza, C. Mandal, K.A. Alam, A. Salam, M.A. Rahman, M.R. Amin, M.N. Huda, N.C. Ghosh, M.R. Ali and F. Ahmed

The ethanol extract of leaves of *Hoya parasitica* was tested for its phytochemical groups, antibacterial and antinociceptive activities. The ethanol extract showed the presence of flavonoids, reducing sugars, tannins, gums and saponins. The extract showed moderate antibacterial activity against both gram-positive and gram-negative bacteria. It also produced significant ($p<0.01$) writhing inhibition in Swiss albino mice at oral dose of 500 mg $kg^{-1}$ body weight comparable to the standard drug diclofenac sodium. *(Journal of Pharmacology and Toxicology 2 (8): 753-756, 2007; **doi**: 10.3923/jpt.2007.753.756)*

## Hypoglycaemic and Antihyperglycaemic Effect of *Syzygium cumini* Bark in Streptozotocin-Induced Diabetic Rats

G. Saravanan and L. Pari

The aim of the present study was to investigate the hypoglycaemic and antihyperglycaemic effect of *Syzygium cumini* (*S. cumini*) bark in diabetic rats. Diabetes was induced in male albino Wistar rats by a single intraperitoneal injection of streptozotocin (45 mg $kg^{-1}$ body weight). An aqueous extract of *S. cumini* bark (SBEt) was administered orally (75, 150 and 300 mg $kg^{-1}$ body weight) for 45 days and changes in blood glucose, urine sugar, food and fluid intakes and body weight were examined in diabetic rats. Glibenclamide was used as a standard reference drug. The levels of blood glucose and urine sugar were increased significantly in diabetic rats. Oral administration of SBEt to diabetic rats led to significantly decreased levels of blood glucose and urine sugar. The effect exerted by the extract at a dose of 300 mg $kg^{-1}$ body weightwas greater than that of doses 75 and 150 mg $kg^{-1}$ body weight. The daily food and fluid intakes were significantly increased while the body weights were significantly reduced in diabetic rats when compared to normal rats. Treatment with SBEt significantly restored the above physiological parameters to near normal in streptozotocin diabetic rats. During oral glucose tolerance test (OGGT), long-term administration of SBEt was able to significantly decrease the blood glucose concentrations at 30, 60, 90 and 120 min when compared to the OGTT pattern of diabetic rats. The effect of SBEt at 300 mg $kg^{-1}$ body weight was better than glibenclamide (600 μg $kg^{-1}$ body weight). These results suggest that SBEt possesses a significant antidiabetic effect

by attenuating the above biochemical and physiological alterations in streptozotocin diabetes. Further, our findings revealed the possible therapeutic value of *S. cumini* bark for the better control, management and prevention of diabetes mellitus progression. *(Journal of Pharmacology and Toxicology 3 (1): 1-10, 2008;* ***doi:*** *10.3923/jpt.2008.1.10)*

## Molecular Modelling Analysis of the Metabolism of Methimazole

Fazlul Huq

Molecular modelling analyses based on molecular mechanics, semi-empirical (PM3) and DFT (at B3LYP/6-31G* level) calculations show that MET and its major metabolites have LUMO-HOMO energy differences ranging from 4.1 to 6.7 eV from DFT calculations, indicating that they would vary significantly in their kinetic inertness. The molecular surfaces of MET, MTU, MET-EPO and GLX are found to possess significant amounts of electron-deficient regions so that they can react with cellular nucleophiles such as glutathione and nucleobases in DNA, thus causing depletion of glutathione and oxidation of nucleobases. The former would induce cellular toxicity due to oxidative stress and the latter would cause DNA damage. The rates of such adverse reactions are expected to be significant for GLX which would be moderately labile kinetically. This means that the toxicity due to MET may be mediated via the formation of GLX although the parent drug itself may also be responsible for toxicity if the rates of its reactions with glutathione and nucleobases in DNA are speeded up enzymatically. *(Journal of Pharmacology and Toxicology 3 (1): 11-19, 2008;* ***doi:*** *10.3923/jpt.2008.11.19)*

## Hepatoprotecive Effect of *Pongamia pinnata* Leaves in Ammonium Chloride Induced Hyperammonemic Rats

M. Mohamed Essa and P. Subramanian

Effect of *Pongamia pinnata* (an indigenous plant used in Ayurvedic Medicine in India) leaf extract (PPEt) on the levels of circulatory ammonia, urea, lipid peroxidation products such as TBARS (thio barbituric acid reactive substances), HP (hydroperoxides) and liver markers such as bilirubin, AST (aspartate transaminase), ALT (alanine transaminase), ALP (alkaline phosphatase), LDH (Lactate dehydrogenase), Gamma glutamyl-S-transferase (GGT) were studied for its hepatoprotective effect during ammonium chloride induced

hyperammonemia. Ammonium chloride treated rats showed a significant increase in the levels of circulatory ammonia, urea, bilirubin, AST, ALT, ALP, LDH, GGT, TBARS and HP. These changes were significantly decreased in PPEt and ammonium chloride treated rats. Our *in vitro* studies have shown that PPEt effectively scavenge reactive oxygen species including superoxide anion, hydroxyl and 1,1-diphenyl-2-picrylhydrazyl (DPPH) radicals. Our results indicate that PPEt offers hepatoprotection by influencing the levels of lipid peroxidation products and liver markers in experimental hyperammonemia and this could be due to its ability to detoxify excess ammonia, urea and creatinine and free radical scavenging property (both *in vitro* and *in vivo*) by means of reducing lipid peroxidation and the presence of natural antioxidants. *(Journal of Pharmacology and Toxicology 3 (1): 20-26, 2008;* ***doi:*** *10.3923/jpt.2008.20.26)*

## Molecular Modelling Analysis of the Metabolism of Venlafaxine

Fazlul Huq

Venlafaxine (VEN) is a new phenylethylamine bicyclic antidepressant whose activity is due to inhibition of neuronal uptake of norepinephrine, serotonin and dopamine. Molecular modelling analyses based on molecular mechanics, semi-empirical (PM3) and DFT (at B3LYP/6-31G* level) calculations show that VEN and its major metabolites have high LUMO-HOMO energy differences ranging from 5.0 to 5.7 eV, indicating that the compounds would all be kinetically inert. The molecular surface of neither VEN nor any of its metabolites is found to abound in electron-deficient regions so that the compounds may not react with cellular nucleophiles such as glutathione and nucleobases in DNA. This means the compounds may not induce cellular toxicity associated with glutathione depletion and DNA damage associated with oxidation of nucleobases. *(Journal of Pharmacology and Toxicology 3 (1): 27-33, 2008;* ***doi:*** *10.3923/jpt.2008.27.33)*

## Evaluation of Preliminary Toxicity Studies on the Methanolic Leaves Extract of *Tylophora asthmatica* in Experimental Rats

R. Malathi and Patric Gomaz

The methanolic leaves extract of *Tylophora asthmatica* was screened for its toxicological and biochemical effects on rats, because of the traditional healers of

India uses this plant as an anti-inflammatory and anti-anaphylactic. The extract was safe in the smaller doses needed to produce a therapeutic effect, ($LD_{50}$ = 223.6 mg $kg^{-1}$ body weight) and had significant toxic effect on the liver at extremely high doses leading to death of the animal. In acute toxicity study (72 h), single dose of the methanolic extract of *Tylophora asthmatica* (META) leaves (50, 100, 200, 500 and 1000 mg $kg^{-1}$ body weight) were given to male rats. Smaller doses of META (50, 100 and 200 mg $kg^{-1}$ body weight) produced no signs of poisonous or death in animals while 500 mg $kg^{-1}$ body weight caused death of two animal and 1000 mg $kg^{-1}$ body weight caused death of four animals within 72 h. The degree of protection was also measured by evaluating biochemical indices like serum AST, ALT, ALP, total protein, albumin, globulin and bilirubin. In addition, sub-chronic administration for 15 days showed a significant ($p<0.05$) increase in the serum ALT, ALP and reduction in total protein, albumin and globulin showing that the plant leaves extract i.e. META has hepatoprotective effects after prolonged use. These studies demonstrated that the META is (50-200 mg $kg^{-1}$ body weight) safe and did not cause any detrimental effects *in vivo* under the conditions investigated in this study. *(Journal of Pharmacology and Toxicology 3 (1): 34-40, 2008;* ***doi:*** *10.3923/jpt.2008.34.40)*

## Molecular Modelling Analysis of the Metabolism of Entecavir

Fazlul Huq

In this study, molecular modelling analyses based on molecular mechanics, semi-empirical (PM3) and DFT (at B3LYP/6-31G* level) calculations have been carried out to investigate the relative stability of ETV and its metabolites with the aim of providing a better understanding of their relative toxicity. The results of the analyses show that both ETV and its major metabolites have LUMO-HOMO energy differences so that they would be kinetically inert. The molecular surface of ETV is found to posses neutral, electron-rich and electron-deficient regions so that the compounds may be subjected to lyophilic, electrophilic and nucelephilic attacks. Nucleophilic attacks can be due to cellular nucleophiles such as glutathione and nucleobases in DNA. However, because of the kinetic inertness of the molecules the rates of such adverse reactions are expected to be low so that ETV and its metabolites may not cause high toxicity. *(Journal of Pharmacology and Toxicology 3 (1): 41-46, 2008;* ***doi:*** *10.3923/jpt.2008.41.46)*

## Studies on the Analgesic, Antipyretic and Ulcerogenic Properties of *Spirulina fusiformis* in Mice

M. Rasool, E.P. Sabina, P. Nithya and K. Lavanya

This study was intended to evaluate the analgesic, antipyretic and ulcerogenic properties of aqueous suspension of *Spirulina fusiformis* (400/800 mg $kg^{-1}$ b.wt.$^{-1}$) in different experimental standard models in mice. For comparison purpose, non-steroidal anti-inflammatory drug Indomethacin (10 mg $kg^{-1}$ b.wt.$^{-1}$) was used as a standard. The results showed that *Spirulina fusiformis* possesses significant analgesic and antipyretic effect with the absence of gastric damage at different dose levels in mice. *(Journal of Pharmacology and Toxicology 3 (1): 47-52, 2008; **doi:** 10.3923/jpt.2008.47.52)*

## Evaluation of Gellan Gum as a Granulating Agent for Chloroquine Phosphate Tablets

P.I. Franklin-Ude, M.O. Emeje and S.I. Ofoefule

Gellan gum was evaluated as a granulating agent in chloroquine phosphate tablet formulations at varying concentrations of 2.5 to 7.5% w/w. Granules were prepared using the wet granulation method. Maize starch and gelatin were employed as reference granulating agents. Prepared granules were evaluated for their micromeritic properties, while the compressed tablets were evaluated for mechanical, disintegration and dissolution properties. The effect of varying concentrations of calcium ion on the mechanical properties of the compressed tablets was also investigated. Results obtained showed that gellan gum exhibited higher binding capacity than maize starch or gelatin. The presence of calcium ions reduced the mechanical properties of the chloroquine phosphate tablets. At 0.4% w/w calcium chloride concentration, tablets with marked reduction in disintegration time and fast dissolution rate without appreciable reduction in mechanical properties were obtained. This concentration was considered to be the optimum for use of calcium chloride as an additive in chloroqinue phosphate tablets containing gellan gum. *(Journal of Pharmacology and Toxicology 3 (2): 53-63, 2008; **doi:** 10.3923/jpt.2008.53.63)*

## Molecular Modelling Analysis of the Metabolism of Terbinafine

Fazlul Huq

Terbinafine (TBN) is an orally active allylamine derivative that has fungicidal activity against dermatocytes and many pathogenic fungi. The drug is extensively

metabolized in humans with systemic clearance being dependent primarily on its biotransformation. The five most prominent metabolites found in plasma are N-desmethylterbinafine (DTBN), hydroxyterbinafine (HTBN), N-desmethylhydroxy- terbinafine (DHTBN), carboxyterbinafine (CTBN) and N-desmethylcarboxyterbinafine (DCTBN) that together account for 25% of the total urinary excretion. Four other metabolites are 1-naphthaldehyde (NAL), 1-naphthalenemethanol (NM), 1-naphthanoic acid (NA) and N-desmethylterbinafine aldehyde (DATBN). Molecular modelling analyses based on molecular mechanics, semi-empirical (PM3) and DFT (at B3LYP/6-31G* level) calculations show that TBN and its metabolites have LUMO-HOMO energy differences ranging from 4.22 to 4.73 eV based on from DFT calculations. The values suggest neither TBN nor any of its metabolites would be highly reactive or extremely inert. The molecular surface of TBN and the metabolites DATBN, NAL and DTBN are found to have significant electron-deficient regions so that they may be subject to nucleophilic attack by glutathione and nucleobases in DNA. DATBN that has been implicated as a possible cause for toxicity of TBN is found to abound most in electron-deficient regions although it has a slightly higher LUMO-HOMO energy difference than NAL. Reaction with glutathione would cause glutathione depletion resulting into oxidative stress and therefore cellular toxicity whereas the oxidation of nucleobases in DNA would cause DNA damage. *(Journal of Pharmacology and Toxicology 3 (2): 64-74, 2008;* ***doi:*** *10.3923/jpt.2008.64.74)*

## Antihepatotoxic Effects of *Boerhaavia diffusa* L. on Antituberculosis Drug, Rifampicin Induced Liver Injury in Rats

M. Muthulingam

The aim of the present study was to investigate the antihepatotoxic effect of aqueous leaf extract of *Boerhaavia diffusa* (BDEx) on rifampicin induced liver injury. The activities of serum hepatic marker enzymes viz., aspartate aminotransferase (AST, 95.30±2.96), alanine aminotransferase (ALT, 51.27±2.52) and alkaline phosphatase (ALP, 167.04±2.59), levels of bilirubin (0.96±0.01), cholesterol (95.88±3.29) and protein (8.43±0.10) were estimated in control rats. Significant elevation of serum hepatic marker enzymes (AST, 254.59±3.10; ALT, 181.95±2.45; ALP, 316.57±2.35), bilirubin (3.46±0.28) and cholesterol (151.09±1.15) whereas protein (5.28±0.07) level decreased in rats treated with rifampicin (1 g $kg^{-1}$ b. wt. orally one day only). Oral administration of BDEx (250 and 500 mg $kg^{-1}$ b. wt. once daily for 28 days) and silymarin to rifampicin induced liver injury rats caused significantly ($p<0.05$) attenuated the aforementioned parameters. The maximum antihepatotoxic effect

against rifampicin induced liver injury was achieved with BDEx 500 mg $kg^{-1}$ b. wt. but doses higher than 500 mg $kg^{-1}$ b. wt. were less effective. These results are compared to the reference hepatoprotective agent silymarin. These results suggest that BDEx possess the antihepatotoxic activity against rifampicin induced liver injury. *(Journal of Pharmacology and Toxicology 3 (2): 75-83, 2008; **doi:** 10.3923/jpt.2008.75.83)*

## Hydro-Alcoholic Media: An Emerging *in vitro* Tool for Predicting Dose Dumping from Controlled Release Matrices

M.O. Emeje, P.I. Nwabunike, C.Y. Isimi, O.O. Kunle and S.I. Ofoefule

In present study, the release profiles of hydrochlorothiazide from polyacrylic acid polymer (carbopol 71G) matrices in hydro-ethanolic media were done. Percent drug released increased with increasing levels of ethanol in the dissolution media, but there was no direct correlation with the drug's solubility in the media. Although, the result showed that an initial rapid release was observed in the media containing 30% ethanol, this could not be regarded as dose dumping of hydrochlorothiazide. Release in this medium was considered to be both erosion and diffusion-mediated, in contrast to the release in 0, 10, 20, 40 and 50% ethanol media, where erosion-controlled release dominated. Image analysis of matrix swelling and swelling kinetics suggests a complex interaction between ethanol, hydrochlorothiazide and Carbopol 71 G accounting for the suppressed drug release in the ethanolic-media. *(Journal of Pharmacology and Toxicology 3 (2): 84-92, 2008; **doi:** 10.3923/jpt.2008.84.92)*

## Molecular Modelling Analysis of the Metabolism of Zolpidem

Fazlul Huq

Zolpidem (ZP) is a new orally active sleep inducer belonging to the class of compounds known as imidazopyridine. Molecular modelling analyses based on molecular mechanics, semi-empirical (PM3) and DFT (at B3LYP/6-31G* level) calculations show that parent drug and all its metabolites have moderately large LUMO-HOMO energy differences so that none is expected to be highly labile kinetically. The molecular surface of ZP is found to abound in electron-deficient regions so that it can react with cellular nucleophiles such as glutathione and nucleobases in DNA, thus inducing cellular toxicity and causing DNA damage respectively. However, because of kinetic inertness, the rates of such adverse reaction may be low unless speeded up enzymatically. Increased incidence of nausea and vomiting associated with higher doses of ZP may be due to the parent drug rather than any of its metabolites. *(Journal of Pharmacology and Toxicology 3 (2): 93-101, 2008; **doi:** 10.3923/jpt.2008.93.101)*

## Synthesis and Studies on Some New Fluorine Containing Hydroxypyrazolines and 1H Pyrazoles-as Possible Antiproliferative Agents

B. Sooryanarayana Rao, P.M. Akberali, B. Shivarama Holla and B.K. Sarojini

A series of twenty four newly synthesized 1-aroyl-3-aryl-5-hydroxy-5-(2,4-dichloro-5-fluorophenyl) pyrazolines (3) and 1H-3-aryl-5-hydroxy-5-(2,4-dichloro-5-fluorophenyl)-pyrazoles (6) were tested for cytostatic and cytotoxic effects on in a primary three cell line-one dose anticancer assay against NCI-H 460 (Lung), MCF 7(Breast) and SF 268 (CNS). Proliferation of these cancer cell lines was strongly inhibited by eleven compounds. These eleven compounds were then passed on for evaluation in the full panel of 60 cell lines derived from seven cancer types namely, Lung, Colon, Melanoma, Renal, Ovarian, CNS and Leukemia. These compounds showed antiproliferative activity on the whole cell panel. Compound 1H-pyrazole, 6d [3,4-methylenedioxy at C 3] showed highest activity with Growth Inhibition ($GI_{50}$) value <10 μM against all tested 60 cell lines except for Leukamia CCRF-CEM, HL-60TB, K-562 cell lines. Whereas hydroxypyrazolines 3i, 3k 3m, 3o, 3p and 3q showed moderate activity with $GI_{50}$ value <50 μM against all tested 60 cell lines. Compounds 3h, 3c, 6c appear to be less active with $GI_{50}$ value >100 μM for some of the tested cell lines. Compound 6a appears to be least active with $GI_{50}$ value >100 μM for almost all the tested cell lines. The Total Growth Inhibition (TGI) and Lethal Concentration ($LC_{50}$) values for the most active compound [6d] found to be >100 μM for Leukemia cell lines and for the other cell lines these values remain <20 μM and hence prove to be a cytostatic and cytotoxic for these lines. Hence these newly synthesized pyrazole and pyrazoline derivatives showed promising antiproliferative property. *(Journal of Pharmacology and Toxicology 3 (2): 102-110, 2008;* ***doi:*** *10.3923/jpt.2008.102.110)*

## An Evaluation of the Toxic Effects of *Tamarindus indica* Pulp Extract in Albino Rats

M.G. Abukakar, A.N. Ukwuani and R.A. Shehu

The effects of graded doses of *Tamarindus indica* pulp extract on the haematological, toxicological and histopathological indices in rats were evaluated. Hematological parameter was determined using micro-hematocrit method and

Neubauer hemocytometer counting chamber. The haematological parameters (PCV, WBC, Lymphocytes and Monocytes) of the treated groups showed no significant difference ($p<0.05$) when compared with the control. Although there was a significant increase ($p<0.05$) ($p<0.01$) in the nuetrophils in group 3 and 4 and decrease ($p<0.05$) ($p<0.01$) in eosinophils at group 4 and 5, respectively. There was no fatality recorded in the acute toxicity tests when the animals received 900-4500 mg $kg^{-1}$ body weight of the extract, however the higher doses of the extract (2700-4500 mg $kg^{-1}$ body weight) exhibited some behavioral changes in the rats such as aggressive scratching of the body and mouth part, anorexia, mild restlessness and sensitive to slight sound. There was no significant difference ($p<0.05$) in the toxicological parameters investigated when compared with the control. The gastro intestinal tract revealed no apparent congestion or hemorrhage while the histopathological examination of liver and kidney showed no visible lesions indicating its non toxic effect to these organs. These results have provided scientific evidence to justify the safety of this plant in tradition medicine. *(Journal of Pharmacology and Toxicology 3 (2): 111-118, 2008;* ***doi:*** *10.3923/jpt.2008.111.118)*

## Molecular Modelling Analysis of the Metabolism of Ramelteon

Fazlul Huq

Ramelteon (RMT) is an agonist of the melatonin receptor, used for treatment of insomnia. Molecular modelling analyses based on molecular mechanics, semi-empirical (PM3) and DFT (at B3LYP/6-31G* level) calculations show that RMT and its metabolites RMTM1, RMTM2, RMTM3 and RMTM4 have moderately large to large LUMO-HOMO energy differences so that the compounds would be moderate to highly inert kinetically. In spite of its kinetic inertness, the metabolism of RMT takes place rapidly because of the involvement of enzymes. The molecular surfaces RMT and its metabolites are found to abound in neutral (green) and electron-rich (red and yellow) regions so that the compounds may be subject to both lyophilic and electrophilic attacks. The absence of any significant amounts of electron-deficient (blue) regions on the molecular surface means that the compounds may not react with cellular glutathione and nucleobases in DNA. This means that RMT and its metabolites may not induce cellular toxicity (associated with glutathione depletion) and may not also cause DNA damage (associated with oxidation of nucleobases in DNA). Rather, the compounds may act more like antioxidants. *(Journal of Pharmacology and Toxicology 3 (2): 119-126, 2008;* ***doi:*** *10.3923/jpt.2008.119.126)*

## Phytochemical and Anticonvulsant Screening of the Ethanolic Flower Extracts of *Newbouldia laevis* (Bignoniaceae) in Mice

H. Usman, A.H. Yaro and M.M. Garba

The anticonvulsant effects of the ethanolic flower extract of *Newbouldia leavis* (Bignoniaceae) were studied in mice. Preliminary phytochemical analysis of ethanolic flower extract revealed the presence of cardiac and saponins glycosides, flavonoids, steroids and tannins. The ethanolic flower extract had an intraperitoneal (i.p.) $LD_{50}$ of 1264.9 mg $kg^{-1}$ body weight in mice. Anticonvulsant studies were carried out on pentylenetetrazole (PTZ)-induced and 4-amino pyridine (4-AP)-induced seizures in mice. The results showed that the extract under study possesses slight dose-dependent anticonvulsant activities between 40-60% (50-200 mg $kg^{-1}$ body weight) protection against PTZ-induced convulsion; and also a dose-dependent delay on the onset of convulsion was observed in 4-AP-induced convulsion in mice ranging from 8.0±0.45 to 11.2±1.31 min (50-200 mg $kg^{-1}$ body weight). The data obtained correlate to the traditional claim of this plant in the treatment of convulsion due to petit mal seizure. *(Journal of Pharmacology and Toxicology 3 (2): 127-133, 2008;* ***doi:*** *10.3923/jpt.2008.127.133)*

## Evaluation of Toxicity of *Rhanterium epapposum* in Wistar Rats

Shama I. Younis and S.E.I. Adam

We present the first reported study of the effects of feeding *Rhanterium epapposum* aerial parts at 20, 50, 100 and 200 g $kg^{-1}$ of standard diet to male Wistar rats for 12 weeks. The criteria of assessment of the plant toxicity were the effects on growth, organs of the body, hematological and serobiochemical parameters of rats. Depression in growth and hepatonephropathy were severe in rats fed diets containing 100 and 200 g $kg^{-1}$ of *R. epapposum* aerial parts. These findings were accompanied by macrocytic hypochromic anemia, leukocytosis due to lymphocytosis and alterations of serum concentrations of urea, total protein, globulin and other serum constituents. Toxicity may be frequent in animals that ingest this plant in a dry year. While this plant has traditionally been used in Sudan and other Afro-Asian countries it may show toxic effects in human that result from over-dosage because, in general, there is no standardized dosage system in traditional medical practice. *(Journal of Pharmacology and Toxicology 3 (2): 134-140, 2008;* ***doi:*** *10.3923/jpt.2008.134.140)*

## Alloxan-Induced Diabetes in Rats and the Effects of Black Caraway (*Carum carvi* L.) Oil on Their Body Weights

A.C. Ene, E.A. Nwankwo and L.M. Samdi

The effect of different doses of Black caraway (*Carum carvi* L.) oil on the body weights of alloxan-induced diabetic rats was studied. Forty white male albino rats of the Winster strain weighing between 145-240 g were used for this study. Diabetes was induced in the experimental rats with alloxan (70 mg $kg^{-1}$ body weight). Group 1 rats served as the normal control, group 2 served as the caraway control, whereas group 3 rats served as the diabetic control. Groups 4, 5, 6, 7 and 8 were the test groups. All the test groups were administered various doses of the black caraway oil ranging from 5, 10, 20, 40 and 80 mg $kg^{-1}$ body weights, respectively. Group 2 (the caraway control) rats were administered 10 mg $kg^{-1}$ body weight of black caraway oil. The duration of the experiment was 10 weeks. The weights of the animals in each group were recorded daily throughout the duration of the experiment. The blood glucose levels in the different groups were assayed. The results show that the normal control, the caraway control and the diabetic rats treated with 10 mg $kg^{-1}$ body weight of black caraway oil showed progressive and steady increase in the % mean weekly body weights, while the diabetic untreated rats and the other test groups showed decreasing and alternating increments, respectively in the % mean weekly body weights. The blood glucose level in the 10 mg caraway treatment group was significantly reduced ($p<0.01$) compared to the diabetic control and the other treatment groups. This shows that the black caraway oil increases the % mean weekly body weights of the diabetic/non-diabetic rats at a dose not more than 10 mg $kg^{-1}$ body weight. It can also be inferred that the 10 mg $kg^{-1}$ body weight of caraway oil is the safe dose that can be used in managing Diabetes mellitus. The information obtained from this study would be used in the management of diabetic patients. *(Journal of Pharmacology and Toxicology 3 (2): 141-146, 2008;* ***doi:*** *10.3923/jpt.2008.141.146)*

## Molecular Modelling Analysis of the Metabolism of Ambroxol

Fazlul Huq

Ambroxol (AMB) is used to treat acute and chronic bronchitis, bronchiectasia and lung tuberculosis and possesses antioxidant properties. Molecular modelling analyses based on molecular mechanics, semi-empirical (PM3) and

DFT (at B3LYP/6-31G* level) calculations show that AMB and its metabolites DHTQ and DBABA have LUMO-HOMO energy differences of 5.11, 5.01 and 4.28 eV, respectively from DFT calculations. The values indicate that AMB and DHTQ would be significantly more inert kinetically than DBABA. The molecular surfaces of AMB, DHTQ and DBABA are found to abound in neutral green regions so that the compounds can undergo lyophilic attack. The molecular surfaces of the three compounds are also found to possess significant amounts of electron-rich (red and yellow) regions so that they may be subject to electrophilic attacks as well. However, the compounds may not undergo significant nucleophilic attacks as their molecular surfaces do not abound in electron-deficient regions. The presence of neutral and electron-rich regions may impart antioxidant properties to AMB and its metabolites. *(Journal of Pharmacology and Toxicology 3 (2): 147-152, 2008; **doi:** 10.3923/jpt.2008.147.152)*

## Histopathological, Hematobiochemical and Urinalysis Changes in Experimental Consumption of Oak (*Quercus brantii*) in Sheep

A. Derakhshanfar, M. Pourjafar, K. Badiei, H. Talebanfard and M. Shakhse-Niaie

Acorn contains variable amounts of tannins, so that causes occasional livestock toxicity. Because of its cheapness, accessibility and bad economic condition of many farms, oak ration is used in many parts of Iran. The 20 day period experiment was conducted on 9 female sheep (one-year-old and 40±3 kg weight) of the Karakul breed. Sheep were randomly divided into treatment group (n = 6) and control group (n = 3). In the treatment group, the mean amount of acorn powder added to control ration was 2.2 kg $day^{-1}$. Venous Blood and urine samples were taken on 0, 10th and 20th days of experiment. At the end of experiment all the animals were slaughtered and histopathological samples were taken after necropsy. Then hematocrit and hemoglobin, serum glucose, total protein, albumin, fibrinogen, blood urea nitrogen, aspartate aminotransferase, Urine glucose and protein were measured. The results indicated that serum fibrinogen of treatment group increased significantly ($p<0.05$) on 10th day. Other parameters didn't show significant changes. Only mild hepatic fibrosis, lymphocytic hepatitis and interstitial nephritis were observed in one case of treatment group. It was concluded that the gradual increase of acorn powder in diet cause no overt clinical signs of oak poisoning in sheep. *(Journal of Pharmacology and Toxicology 3 (2): 153-157, 2008; **doi:** 10.3923/jpt.2008.153.157)*

## Effect of Ethanol Extract of *Cansjera rheedii* J. Gmelin (Opiliaceae) on Hepatotoxicity

V.M. Mounnissamy, S. Kavimani, V. Balu and S. Darlin Quine

The hepatoprotective activity of ethanol (95%) extract of (250 mg $kg^{-1}$) *Cansjera rheedii* J. Gmelin whole plant was evaluated against paracetamol induced hepatotoxicity by evaluating biochemical parameters such as Serum Glutamate Pyruvate Transaminase (SGPT), Serum Glutamate Oxaloacetate Transaminase (SGOT), Alkaline Phosphatase (ALP), Total bilirubin, Total Protein and Gamma Glutamate Transpeptidase (GGTP). A 10% of liver homogenate was used for estimation of enzyme such as Superoxide Dismutase (SOD), Glutathione S-Transferase (GST), Lipid Peroxidase (LPO) and Glutathione Peroxidase (GPx) for antioxidant study. Treatment of rats with ethanol extract significantly ($p<0.001$) altered serum marker enzymes and antioxidants level near to normal against paracetamol intoxicated rats. Silymarin (50 mg $kg^{-1}$, p.o.) used as control. *(Journal of Pharmacology and Toxicology 3 (2): 158-162, 2008; **doi:** 10.3923/jpt.2008.158.162)*

## Study of Aspartate Aminotransferase Activity in Intoxified Rat by Cadmium

M. Najafi, A.A. Moshtaghie M. Ani and M. Shabani

The current study was designed to investigate the effects of cadmium administration on the AST (Aspartate aminotransferase) and its isoenzyme activities in the serum and liver for durations of 15 and 60 days, respectively. AST isoenzymes were separated by gel filtration chromatography technique and evaluated kinetically. Results showed significant increases in the serum AST activities up to 47 and 38.35% upon Cd administrations of 0.25 and 0.5 mg $kg^{-1}$, respectively. This increase was not time and dose dependent in the long period. At the end of each period, the specific activity both isoenzymes in the serum increased significantly ($p<0.05$) while in the liver, mitochondrial AST activity increased as compared to cytosolic AST activity. We concluded that the total serum AST activity was not dose and time dependent. However, the changes of liver AST isoenzymes in the short and long periods might be due to hepatotoxicity following oxidative stress and delayed synthesis of AST isoenzymes, respectively. *(Journal of Pharmacology and Toxicology 3 (2): 163-167, 2008; **doi:** 10.3923/jpt.2008.163.167)*

## Molecular Modelling Analysis of the Metabolism of Rasagiline

Fazlul Huq

Rasagiline (RSG) is a second-generation, selective and irreversible inhibitor of monoamine oxidase type B (MAO-B) developed for the treatment of Parkinson's diseases. Molecular modelling analyses based on molecular mechanics, semi-empirical (PM3) and DFT (at B3LYP/6-31G* level) calculations show that both RSG and its metabolite ADN have large LUMO-HOMO energy differences so that they would be kinetically inert. The molecular surfaces RSG and ADN are found to possess neutral, electron-deficient and negatively charged regions so that they may be subject to lyophilic, nucleophilic and electrophilic attacks. However, because of kinetic inertness of the molecules, the rates of the reactions including any adverse reactions with glutathione and nucleobases in DNA are expected to be low. This may explain why RSG and ADN have little side effects. *(Journal of Pharmacology and Toxicology 3 (2): 168-172, 2008;* ***doi:*** *10.3923/jpt.2008.168.172)*

## Neuroimmune Responses to Toxic Agents: Comparison of Organometal Electrophiles Using Detection of Antibodies to Neural Cytoskeleton and Myelin as Biomarkers

Geetha Surendran and Hassan A.N. El-Fawal

Chemicals, including heavy metals, are of health and ecological concern due to environment release from industrial and agricultural activity. Neurotoxicity is of particular concern because of effects on the developing Nervous System (NS) and contribution to neurodegeneration in later life. A pressing need exists to develop and validate biomarkers of neurotoxicity to monitor those at risk and implement successful intervention strategies. Fischer 344 rats were given one of three documented neurotoxic organometals: trimethyltin (TMT), methylmercury (MeHg) or trimethyl lead (TML) at 16 ppm in the drinking water and compared to water-only controls (n = 8/group). Detection of serum antibodies, IgM and IgG isotypes, against neurofilaments (NF), astrocytic Glial Fibrillary Acidic Protein (GFAP) and Myelin Basic Proteins (MBP) were used as biomarkers of neurotoxicity confirmed by measurement of brain GFAP, a marker of astrogliosis, in rats on day 12 of exposure. While sera from control rats did not have detectable levels of antibodies against neural proteins, sera from rats exposed to all three metals had antibodies, both IgM and IgG, against all neural antigens, with the exception of IgM against

MBP which was not detected in sera of MeHg-exposed rats. Serum IgM titers against NF-L and MBP were significantly ($p \leq 0.001$) higher with TML exposure. Serum IgG titers against NF and GFAP were more prevalent and significantly ($p \leq 0.001$) higher in TMT-exposed rats, compared to the other two organometals. This suggests that neurotoxicity was more advanced with TMT, an observation substantiated by greater generalized toxicity indicated by reduced body weight and hyperexcitability after the first week of exposure. Furthermore, anti-GFAP, IgM and IgG, were consistently higher in this group, the only metal of the three, reported to be gliotoxic. Brain GFAP was significantly ($p \leq 0.001$) elevated in hippocampus of rats exposed to TMT or TML and in the cerebellum for those exposed to MeHg. This regional vulnerability of the brain is consistent with the neurotoxicity of these agents. Despite treatment of rats with equivalent levels of oragnaometals in the drinking water and similarities as electrophiles that complex with nucleophilic molecules, other mechanisms underlie their differential neurotoxicity. Proposed mechanism of neurotoxicity and immune activation are reviewed and discussed. This study further supports the utility of neuroantibody detection as a biomarker of neurotoxicity. *(Journal of Pharmacology and Toxicology 3 (3): 173-189, 2008;* ***doi:*** *10.3923/jpt.2008.173.189)*

## Ultrastructural and Biochemical Abnormalities in the Liver of Streptozotocin-Diabetic Rats: Protective Effects of *Murraya koenigii*

P. Arulselvan and S. Subramanian

The objective of the present study is to evaluate the antioxidant potential of ethanolic extract of *Murraya koenigii* leaf on enzymatic, non enzymatic antioxidants and ultrastructural changes in liver of streptozotocin (STZ) induced diabetic rats. Effect of oral administration of *M. koenigii* leaves extract (200 mg $kg^{-1}$ body weight) on the levels of blood glucose, plasma insulin, glycosylated hemoglobin, Thiobarbituric Acid Reactive Substances (TBARS), hydroperoxides, enzymatic and non-enzymatic antioxidants were estimated in STZ induced diabetic rats. Ultrastructural changes in the liver were also examined. Glibenclamide was used as a standard drug. The elevated levels of blood glucose, glycosylated hemoglobin, TBARS, hydroperoxides and decreased level of insulin observed in diabetic rats were significantly altered after treatment with the *M. koenigii*. The altered enzymatic and non-enzymatic antioxidants in the liver of streptozotocin induced diabetic rats, were restored to near normal levels by treatment with the *M. koenigii* leaves extract. Ultrastructure analysis of the liver

of diabetic rat revealed a reduction in the Rough Endoplasmic Reticulum (RER) and swelling of mitochondria in the hepatocytes and these abnormalities were restored to near normal morphology by the treatment of rats with *M. koenigii* leaf extract. Our results suggested that the ethanolic extract of *M. koenigii* possess potent antioxidant properties which may be due to the presence of biologically active ingredients such as carbazole alkaloids, glycosides, triterpenoids and phenolic compounds. Thus the hepatoprotective and antidiabetic properties of *M. koenigii* leaves were probably of its antioxidant property. *(Journal of Pharmacology and Toxicology 3 (3): 190-202, 2008;* ***doi:*** *10.3923/jpt.2008.190.202)*

## Histomorphological Assessments of the Female Reproductive Organs of Rats under Indomethacin and Aspirin Treatments

A.U. Ekanem, S.H. Garba and A.G. Jankada

The effect of Aspirin (ASA) and indomethacin (Indocin) on the histomorphology of the female reproductive organs was investigated. A total of 60 female albino rats of the Wister Strain were randomly divided into 12 groups of 5 rats each (group's 1-12). Groups 1 and 2 served as the control groups and were administered normal saline and dimethylsulfoxide (DMSO 5 mg $kg^{-1}$ body weight), respectively for 14 days. Groups 3-7 were administered 10, 25, 50, 75 and 100 mg $kg^{-1}$ body weight of aspirin respectively for 14 days while groups 8-12 received 2.0, 2.5, 3.0, 3.5 and 4.0 mg $kg^{-1}$ body weight of indomethacin respectively for 14 days. At the end of the 14 day, the animals were sacrificed and the ovary, uterine tubes and uterus obtained for routine histological processing and subsequent histopathological assessment. Results from this study showed normal histological profiles of all organs obtained from the rats in the control groups while the experimental groups treated with aspirin and indomethacin presented with vasoconstriction in the ovary and atrophy of smooth muscles of the uterine tubes and uterus. This study has establish to some extent, the vasoconstrictive potency of aspirin and indomethacin and thus providing an experimental basis for the use of these drugs to reduce and if possible stop ovarian and uterine hemorrhage but further investigation to elucidate the vasoconstrictory effect, smooth muscle atrophy and the reversibility of some of the toxic effect of these drugs on the female reproductive organs and the mechanism involved is recommended in further studies. *(Journal of Pharmacology and Toxicology 3 (3): 203-212, 2008;* ***doi:*** *10.3923/jpt.2008.203.212)*

## Pharmacological Actions of *Cassia auriculata* L. and *Cissus quadrangularis* Wall.: A Short Review

M. Ayyanar and S. Ignacimuthu

Nature has been a source of medicinal agents for thousands of years and an impressive number of modern drugs have been isolated from natural sources, many based on their use in traditional medicine. Therapeutically interesting and important drugs can be developed from plant sources which are used in traditional systems of medicines. Indian traditional system of medicine is based on empirical knowledge of the observations and the experience over millennia and more than 5000 plants are used by different ethnic communities in India. The present communication constitutes a review on the medicinal properties and pharmacological actions of *Cassia auriculata* L. and *Cissus quadrangularis* Wall. used in Indian traditional medicine. These plants are known to contain various active principles of therapeutic value and to possess biological activity against a number of diseases. *(Journal of Pharmacology and Toxicology 3 (3): 213-221, 2008;* ***doi:*** *10.3923/jpt.2008.213.221)*

## Pharmacological Properties of the Venom of a Marine Gastropod *Babylonia spirata* (L.)

A. Shanmugam, T. Bhuvaneswari, R.A. Nazeer, S. Sambasivam, S. Vairamani, S. Ravindrand and S. Babuji and G. Devanathan

Mid Gut Gland (MGG) and Salivary Gland (SG) of *B. spirata* were collected separately and extracts were prepared in three volumes of 1% Acetic Acid in Methanol, centrifuged and lyophilised. The lyophilised powder was dissolved with 0.9% saline solution in a required amount and used for further assays. The assays were done in perfused isolated frog heart, isolated frog rectus abdominis muscle, frog sciatic nerve-muscle preparation, lumbar plexus of frog and in albino mice. Both MGG and SG extracts showed dose dependent effect and cholinergic principle in the perfused frog heart preparation. They didn't alter the acetylcholine-produced contraction in the rectus abdominis muscle and they affected the sciatic nerve much than the muscle in nerve-muscle preparation which showed that they contain neurotoxins like TTX. The MGG extract proves that it has the local anaesthetic effect in the lumbar plexus experiment. *(Journal of Pharmacology and Toxicology 3 (3): 222-229, 2008;* ***doi:*** *10.3923/jpt.2008.222.229)*

## Monitoring Ames Assay on Urine of Clinical Pathology

## Laboratories Technicians

M. Rezai-Basiri, M. Samini, M. Ghazi-Khansari, M. Rezayat, M. Sahebgharani and A. Partoazar

Forty urine samples of clinical pathology laboratory technicians were examined for the presence of mutagenic substance in urine. Mutagenic substance in this study was formaldehyde, formaline, hematoxyline-eosin, Xylole and Xyline which are used for smear fixation and staining in clinical pathology laboratories. We used Ames test to determine the mutagenic potential of above mentioned substances. Mutagenicity was evaluated by TA100 strain of *S. typhimurium*. Urine extracts were prepared using XAD-2 resin in column. The resin was then rinsed with Milli-Q water. This procedure eliminates traces of water soluble growth factors (especially histidine) from the resin. Residual water was removed by vacuum aspiration and adsorbed substance were eluted with a mixture of methanol/acetonitrile v/v. After evaporation to dryness with $N_2$ gas, the residue was dissolved in DMSO to reach 100 to 250 fold concentration and then urine extraction were kept frozen in liquid nitrogen gas until use. Mutagenicity was evaluated in TA100 *Salmonella thyphimurium* tester stain (overnight cultures) with and without addition of S-9 mix. The results of this study has been shown that 20% of urine samples from technicians of clinical pathology laboratories in Tehran (Iran) were contained mutagen materials. The staff with working history in clinical pathology laboratories may excrete mutagenic compounds in urine. *(Journal of Pharmacology and Toxicology 3 (3): 230-235, 2008;* ***doi:*** *10.3923/jpt.2008.230.235)*

## Effect of Chloroquine Sensitive *Plasmodium berghei* in Pregnant Mice

A.C. Ene, T.M. Adisa, E.A. Nwankwo and P.U. Agomo

Pregnant mice were examined to determine whether or not they transmitted *Plasmodium berghei* to their fetuses. On the 14th day of pregnancy, mice were inoculated with approximately $3\times10^6$ *P. berghei* infected red blood cells by intraperitoneal injection. The parasitemia in 20 adult females and 145 neonates was assessed using thin blood films fixed with methanol and stained with 10% giemsa solution. The average parasitemia of females at delivery was 7.5%. Malaria parasites were microscopically confirmed in 8 of the 145 neonates. Maternal parasitemia at the time of delivery was not correlated with the incidence of vertical infection (8.71%). Present study showed that this model may be used to examine

vertical transmission of malaria. *(Journal of Pharmacology and Toxicology 3 (3): 236-240, 2008; **doi:** 10.3923/jpt.2008.236.240)*

## Curative and Protective Effects of Penicillin G on Experimental *Chlorophyllum molybdites* Poisoning in Mice

S.F. Ambali, M. Mamman, A.O. Adaudi, K.A.N. Esievo, J.O. Ayo and M.S. Abubakar

The aim of this study is evaluate the curative and protective effects of penicillin G in mice poisoned with the lyophilized extract of *Chlorophyllum molybdites*. Fifty Swiss albino mice were divided into 5 groups of 10 mice each. Mice in group 1 were pretreated with penicillin G at 38, 280 IU $kg^{-1}$, i.p. and then dosed with $LD_{99}$ of *C. molybdites* (741 mg $kg^{-1}$) i.p., mice in group 2 were dosed with the extract and then treated with penicillin G, while mice in group 3 were dosed with the extract only. Mice in groups 4 and 5 were dosed with penicillin G and physiological saline solution, respectively. The mice were monitored for clinical signs of toxicity, pathological lesions and death over a period of 72 h. The mean time of death in mice from penicillin-treated groups 1 and 2 were compared with those in the extract-treated group using one-way analysis of variance (ANOVA) and values of $p<0.05$ were considered significant. The result showed a significant reduction in the severity of clinical signs and mortality in penicillin-treated groups 1 and 2 compared to the group dosed with only the extract. There was a significant difference in the mean time of death in mice from groups 1, 2 and 3. However, there was no reduction in the severity of lesions in mice from groups 1 and 2 treated with penicillin G compared with extract-treated group. Therefore, this study has shown that penicillin G has significant curative and protective effects in mice poisoned with the lyophilized extract of *C. molybdites*. This result may prove useful in the treatment of humans and animals suffering from *C. molybdites* poisoning. *(Journal of Pharmacology and Toxicology 3 (3): 241-245, 2008; **doi:** 10.3923/jpt.2008.241.245)*

## Elimination of Arsenic Toxicity in Some Tissues and Organs by Supplementing Methionine and Methionine-Betaine in Laying Hens

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An experiment was conducted to find out the effect of excess methionine and methionine-betaine supplementation on deposition of arsenic in different tissues,

organs and eggs of hen and contribution of hen egg and meat to human health hazard along with the arsenic contaminated drinking water. One hundred twenty Rhode Island Red, 16 week-old, were allocated into four groups having three replicates with nine hens and one cock in each replicate. The experimental groups were C (control group fed with basal diet only), $T_1$ (fed control diet with 5.5 ppm arsenic through water), $T_2$ (fed control diet with 5.5 ppm arsenic through water + 50 g methionine per 100 kg of feed) and $T_3$ (fed same as $T_2$ but 50% of the excess methionine supplement was replaced with betaine). The birds were maintained in deep litter system of housing. Statistical analysis confirmed that the concentration of arsenic in different organs, tissues and eggs were varied significantly ($p<0.01$) due to dietary treatments. The long term intake of such arsenic contaminated hen eggs and meat by human being may act as some contributory factor to suffer from the serious health hazard. Statistical analysis confirmed that the concentration of arsenic (As) in various organs, tissues and eggs was significantly ($p<0.01$) reduced due to supplementation of methionine and methionine-betaine in $T_2$ and $T_3$ groups, respectively as significantly ($p<0.01$) larger amount of arsenic was voided through faeces in $T_2$ and $T_3$ groups than $T_1$ group where no excess methionine or betaine was added in diet. So it may be concluded that supplementation of either methionine or methionine-betaine combination may able to protect the chronic arsenic toxicity during exposure of As in laying hen. *(Journal of Pharmacology and Toxicology 3 (4): 246-253, 2008;* ***doi:*** *10.3923/jpt.2008.246.253)*

## Preliminary *in vivo* Antimalarial Screening of Petroleum Ether, Chloroform and Methanol Extracts of Fifteen Plants Grown in Nigeria

A.C. Ene, D.A. Ameh, H.O. Kwanashie, P.U. Agomo and S.E. Atawodi

Fifteen plants were screened for *in vivo* antimalarial activity in albino mice. The plants are *Mormodica balsamina*, *Artemisia maciverae*, *Xylopia aethiopica*, *Cyperus articulatus*, *Guiera senegalensis*. *Syzygium aromaticum*, *Zingiber officinale*, *Thonningea sanguinea*, *Sorghum* sp., *Securinega virosa* B, *Chrozophora senegalensis*, *Feretia apodanthera*, *Diospyrous mespiliformis*, *Centaurea perrottetti* and *Acacia nilotica* Del. The petroleum ether, chloroform and methanol extracts from the various parts of the plants were screened for *in vivo* antimalarial activity in mice experimentally infected with *Plasmodium berghei*. Three days after inducing the malaria, the plant extracts were administered intraperitoneally to the mice daily for four days, while chloroquine was used as a standard drug control. Parasitaemia was monitored microscopically

in all the groups for four days using thick and thin blood films obtained from tail vein of each mouse. At the end of this study, it was observed that the chloroform extracts of *Artemisia maciverae* (whole plant), *Xylopia aethiopica* (fruits) and *Acacia nilotica* Del (Leaves) have antimalarial activity. The methanol extracts of *Syzygium aromaticum* (cloves) and *Zingiber officinale* (tuber stem) showed slight antimalarial activity, while the rest of the plant extracts earlier listed showed no noticeable activity. These results suggest that many plants used as recipes in ethnomedical preparation for malaria, have no direct antimalarial activity. *(Journal of Pharmacology and Toxicology 3 (4): 254-260, 2008;* ***doi:*** *10.3923/jpt.2008.254.260)*

## Sedative and Anticonvulsant Effects of Ethyl Acetate Fraction of *Waltheria indica* in Mice

L.J. Hamidu, J.O. Ayo, A.B. Adelaiye and M.S. Abubakar

This study evaluated the central action of *Waltheria indica* extract. Aqueous ethanolic extract of the plant showed bioactivity in acetic-acid induced stretches in animal model. The central effects of the most biologically active fraction (ethyl acetate) of extract of *Waltheria indica* was evaluated in mice using the elevated plus maze paradigm and the strychnine and leptazol-induced convulsions. Sedative effect was studied using the amylobarbitone-induced sleeping time. The extract fraction significantly ($p<0.05$) increased the amylobarbitone sleeping time and protected (100%) mice from death due to pentylenetetrazole convulsion. The extract failed to protect mice against strychnine convulsion, even though it delayed the time of onset of death. The exploratory activity was also significantly ($p<0.05$) decreased in the extract treated mice. The extract blocked leptazole-induced convulsion, potentiated amylobarbitone sleeping time and decreased exploratory activity, indicating anticonvulsant and sedative actions. *(Journal of Pharmacology and Toxicology 3 (4): 261-266, 2008;* ***doi:*** *10.3923/jpt.2008.261.266)*

## Antimicrobial Spectrum and Phytochemical Study of *Walsura trifoliata* (A. Juss.) Harms. (Meliaceae) Bark Extracts

K. Sri Rama Murthy and Nagamani Kandimalla

Indigenous uses of *Walsura trifoliata* (A. Juss.) Harms. (Meliaceae) bark in different parts of Eastern Ghats of Southern Peninsular India, curing skin allergies, astringency and diarrhoeia is wide spread. The objective of the present study was to evaluate the antimicrobial and phytochemical activity of bark extract against

pathogenic microorganisms. Successive petroleum ether, methanol, benzene and aqueous extracts of *Walsura trifoliata* bark were tested for their phytochemical constituents, antibacterial and antifungal activity. The methanol and aqueous extracts were found to be most effective against most of the tested organisms. The present findings significantly conform the uses of *Walsura trifoliata* in the indigenous systems of medicine to treat various diseases like skin allergies, astringency and diarrhoea. *(Journal of Pharmacology and Toxicology 3 (4): 267-271, 2008;* ***doi:*** *10.3923/jpt.2008.267.271)*

## Protective Effect of *Raphanus sativus* Against Carbon Tetrachloride Induced Hepatotoxicity In Wistar Albino Rats

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The present study aimed to investigate for a possible hepatoprotective activity of *Raphanus sativus* against carbon tetrachloride induced hepatotoxicity beside its toxicity and phytochemistry of the plant. Thirty albino rats were divided into 6 groups. The first served as a control, the second was injected with $CCl_4$ and the four other groups were injected with $CCl_4$ and treated orally and simultaneously with either methanolic or water extract at doses of 200 and 400 mg $kg^{-1}$ (b.wt.). The animals were scarified after 10 days. The same doses were tested for toxicity. The phytochemical tests revealed presence of triterpenes, alkaloids, flavanoids, tannins, saponin and coumarins but negative for cyanogenic glycosides and anthraquinone glycosides. Biochemical results showed that $CCl_4$ induced hepatotoxicity which was reduced by the use of the plant as indicated by inhibition of the increased serum AST, ALT and ALP activities and bilirubin concentration beside histopathological changes. Toxicity study indicated that *Raphanus sativus* had no adverse effect on livers. *(Journal of Pharmacology and Toxicology 3 (4): 272-278, 2008;* ***doi:*** *10.3923/jpt.2008.272.278)*

## Combinational Effect of Green Tea, Phytic Acid and Inositol on Bone Mineralization and Mineral Balance in with Azoxymethane-Induced Colon Carcinogenesis Induced Fisher 344 Male Rats

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The aim of the study was to determine the combinational effect of dietary Phytic Acid (PA), Green Tea (GT) and Inositol (I) at 1 and 2% level (in drinking water)

on bone mineralization in rats with azoxymethane (AOM)-induced colon carcinogenesis. After one week period of acclimatization, 9 groups of rats (6 rats each) were fed AIN 93G (till 20 week) and later switched to AIN 93 M diets (till 45 weeks age). All rats received AOM s/c at the rate of 16 mg $kg^{-1}$ body weight at 7 and 8 weeks of age. Urine and fecal samples were collected for a 12 day period. Rats were killed by $CO_2$ asphyxiation at 46 week of age and samples (cecum, blood, tibia and femur) were collected and analyzed by ICP for selected minerals (Ca, P, Mg, Fe and Zn). Physical parameters (weight, length, circumference and volume) of tibia and femur were examined. There were no significant differences in apparent absorption, retention and serum concentrations of macro minerals (Ca, P and Mg), although apparent absorption, bone and serum levels of Fe and Zn were significantly lower in 2% combinations. Results of this study showed that combination of treatments at lower levels may be beneficial in reducing the negative effects on bone mineralization. *(Journal of Pharmacology and Toxicology 3 (4): 279-290, 2008;* ***doi:*** *10.3923/jpt.2008.279.290)*

**The Mechanism of Cryptolepine-Induced Cell Death**

C. Ansah, H. Zhu and N.J. Gooderham

The objective of the present study was to use morphological and biochemical approaches to characterize the mode of CLP-induced cell death. Using a differential staining technique, a Chinese Hamster fibroblast cell line (V79 cells) and a human lymphoblastoid cell line (MCL-5) showed morphology consistent with apoptosis after treatment with CLP. In contrast, HepG2, a human hepatoma cell line showed morphology that was more like necrosis after treatment with CLP. Using annexin V staining for apoptotic cells, MCL-5 cells showed a three fold increase in apoptosis within 6 h. Although we observed only a marginal increase in BAX protein expression, cytochrome c was released into the cytosol of CLP-treated MCL-5 cells. Furthermore, procaspase-3 was processed into the active caspase-3 (17 kDa). Consistent with the caspase-3 activation, PARP was cleaved to the typical 85 kDa fragment confirming apoptosis as the mode of cell death in CLP-treated MCL-5 cells. However, there was no evidence of increased BAX expression, cytochrome c release, caspase activation or PARP cleavage in CLP-treated HepG2 cells. This observation together with the morphology of CLP-treated HepG2 cells indicates that in contrast to MCL-5 cells, the CLP-mediated demise of HepG2 cells is not apoptotic. *(Journal of Pharmacology and Toxicology 3 (4): 291-301, 2008;* ***doi:*** *10.3923/jpt.2008.291.301)*

## BacoMind®: A Cognitive Enhancer in Children Requiring Individual Education Programme

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*Bacopa monnieri* belonging to family Scrophulariaceae has been used since time immemorial by Ayurvedic medical practitioners in India as brain tonic. In the present clinical trial, efficacy of BacoMind®, an enriched phytochemical composition from *Bacopa monnieri* on cognitive function in children requiring individual education programme was evaluated. Twenty-eight volunteers with Intelligent Quotient between 70-90 were enrolled in the clinical trial. The study was conducted as outpatient procedure in hospital settings with close monitoring. BacoMind® at 225 mg as single oral dose for a duration of four months showed significant change in the baseline value of working memory and short term verbal memory from 5.21±0.32 to 6.38±0.25 ($p \leq 0.05$) and 5.33±0.44 to 6.54±0.35 ($p \leq 0.05$), respectively in 70.83% of study population. Significant improvement ($p \leq 0.05$) was also seen in logical memory, memory related to personal life and also in visual as well as auditory memory. BacoMind® was also found to be well tolerable with no major side effects. The findings of the current study revealed the cognitive enhancing effect of the BacoMind® in children requiring individual education programme. *(Journal of Pharmacology and Toxicology 3 (4): 302-310, 2008; **doi:** 10.3923/jpt.2008.302.310)*

## Protective Effects of *Andrographis paniculata* Against Endothelial Dysfunction in Diabetic Wistar Rats

Anilkumar M. Dandu and Naseeruddin M. Inamdar

The aim of the present study was to elicit the therapeutic effect of *Andrographis* extract on oxidative stress in aorta as well as liver and kidney of streptozotocin diabetic rats. Aqueous leaf extract of *Andrographis paniculata* (*Andrographis*) [400 mg (kg body weight)$^{-1}$ day$^{-1}$] was administered to the animals 30 days before diabetes induction and continued for next 6 months after the diabetes induction. There was a significant decrease in the activity of superoxide dismutase (SOD), catalase and glutathione (GSH) in liver and kidney of the diabetic rats. *Andrographis* administration to diabetic rats resulted in increase in the activity of SOD, catalase and GSH both in liver as well as kidneys. The diabetic rats exhibited endothelial dysfunction as it was evident from the loss of vasodilatory response to the acetyl choline (Ach). This vasodilatory response was restored in

the diabetic animals treated with *Andrographis*. Based on these observations, we conclude that *Andrographis* reverses the endothelial dysfunction associated with diabetes. This effect appears to be due to its antioxidant properties. *(Journal of Pharmacology and Toxicology 3 (4): 311-317, 2008; **doi:** 10.3923/jpt.2008.311.317)*

## Antimycotic Effect of the Aqueous Leaf Extract of *Pterocarpus erinaceus* in Rats

E.U. Etuk, H.A. Suberu, I.G. Ameh and K. Abubakar

The aqueous leaf extract of *Pterocarpus erinaceus* (Leguminoceae) was investigated for possible antimycotic effect in Sprague dawley rats. The extract was tested against moulds (*Aspergillus niger* and *Aspergillus flavus*) and dermatophytes (*Trichophyton rubrum* and *Microsporum gypseum*). The extract at 20-40 mg $kg^{-1}$ body weight significantly ($p<0.05$) and dose dependently inhibited the growth rate of the moulds and dermatophytes by over 60 and 97%, respectively. In the *in vivo* study, there was also a significant reduction in the number of dermatophyte spores recovered from the infected sites treated with the extract as compared with the non treated sites. The extract produced no sign of acute toxicity or death when a limit dose of 2 g $kg^{-1}$ body weight was administered orally in rats. Collectively, these results suggest that the extract possess antimycotic effect and appears to be safe when given orally at a limit dose of 2 g $kg^{-1}$ body weight of the rats. This therefore supports the use of *Pterocarpus erinaceus* leaf extract traditionally for the treatment of fungal skin diseases. *(Journal of Pharmacology and Toxicology 3 (4): 318-323, 2008; **doi:** 10.3923/jpt.2008.318.323)*

## *In vivo* Antiplasmodial Activity and Acute Toxicity of the Fraction of the *Garcinia parvifolia* Miq. Stem Bark

Syamsudin, Soesanto Tjokrosonto, Subagus Wahyuono and Mustofa

The study of *in vivo* antiplasmodial activity and acute toxicity of the active fraction of *Garcinia parvifolia* Miq. has been conducted. The fraction was obtained by maceration of n-hexane extract with methanol. A standard 4-day test on *P. berghei* infected Swiss mice was used to evaluate the *in vivo* antiplasmodial activity after an oral administration of the fraction in series dose of 25 to 200 mg $kg^{-1}$ b.wt. once daily for 4 consecutive days. The *in vivo* antiplasmodial activity was expressed by the dose inhibiting 50% of parasite growth ($ED_{50}$).

Acute toxicity was evaluated in Swiss mice after oral administration of the active fraction in series dose of 2000 to 8000 mg $kg^{-1}$ b.wt. The acute toxicity was expressed by the dose leading 50% deaths ($LD_{50}$). The results showed that the active fraction of *G. parvifolia* Miq. was active against *P. berghei* in mice with an $ED_{50}$ of 74.45 mg $kg^{-1}$ b.wt. $day^{-1}$. In addition, the active fraction was also relatively safe as expressed by the $LD_{50}$ of 8000 mg $kg^{-1}$ b.wt. *(Journal of Pharmacology and Toxicology 3 (4): 324-329, 2008;* ***doi:*** *10.3923/jpt.2008.324.329)*

## Effects of Aqueous Suspension of the Root of *Hyphaene thebaica* (L.) Mart on Some Indicators of Liver and Kidney Function in Rats

H. Zanna, S. Adeniji, B.B. Shehu, S. Modu and G.M. Ishaq

The effect of crude aqueous suspension of the root of *Hyphaene thebaica* (L.) mart on some indices of liver and kidney function in rats were studied. Sixteen white albino rats of wistar strain were divided into 4 groups of 4 rats each. Groups 1, 2 and 3 were administered daily orally by intubation, 0.25, 0.5 and 1.0 g $kg^{-1}$ body weight of the aqueous suspension of the root respectively while group 4 served as control and was given 0.0 $kg^{-1}$ body weight. All the rats were kept under normal breeding condition and fed with normal diet (sanders seepc Nig. Ltd., Nigeria) and water *ad libitum* for 4 weeks. Results revealed a dose-dependent increase in body weight compared to the control. There was also no statistically significant ($p<0.05$) change in the levels of alanine aminotransferase (ALT), Total protein, urea, potassium and chloride ions in the treatment groups while aspartate aminotraferase (AST), globulins and triglyceride levels showed a significant ($p<0.05$) increase in the groups administered 0.5 and 1.0 g $kg^{-1}$ body weight. However, levels of cholesterol, albumin and sodium ions decreased and that of creatinine increased significantly ($p<0.05$) in all the groups compared to the control. Levels of total lipids showed no alteration. Hence, results revealed that aqueous root suspension of the plant could be hyponatremic, hypocholesterolemic, hepato and nephrotoxic. *(Journal of Pharmacology and Toxicology 3 (4): 330-334, 2008;* ***doi:*** *10.3923/jpt.2008.330.334)*

## Toxicological Evaluation of the Anti-Malarial Herb *Cryptolepis sanguinolenta* in Rodents

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In this study, we evaluated the aqueous extract of the roots of *Cryptolepis sanguinolenta* (Periplocaceae), an anti-malarial herb in the West African sub-region for possible toxicity in rodents. Administration of cryptolepis (10-1000 mg $kg^{-1}$) daily for two weeks did not cause significant changes in most of the haematological parameters assessed. However, the MCV reduced from a vehicle-treated value of 63.1±0.6 to 58.1±0.9 g $dL^{-1}$ at a dose of 10 mg $kg^{-1}$, which reflected in an increased MCHC (27.8±0.3 to 30.5±0.3 g $dL^{-1}$), since the Hb concentration remained unchanged. Serum transaminase levels did not change significantly suggesting a limited effect on the liver. Administration of the extract (50-1000 mg $kg^{-1}$, p.o.) 30 min before pentobarbitone (50 mg $kg^{-1}$, i.p.) caused a dose-dependent prolongation of the rat sleeping time from 66.6±8.1 min (vehicle-treated control) to 266.5±7.0 min (1000 mg $kg^{-1}$). Similarly, daily treatment with the extract (50-1000 mg $kg^{-1}$) for 2 weeks prolonged the sleeping time from 155±28.4 to 292.8±28.7 min. This effect appeared to be CNS-related rather than an enzymatic as reflected in a decreased locomotor activity (19.4±1.5 to 1.8±0.8 $min^{-1}$) at a dose of 500 mg $kg^{-1}$ body weight. All together, our results suggest that *Cryptolepis* could synergize with hypno-sedatives or other CNS depressants and therefore caution needs to be taken in the concomitant administration of *Cryptolepis* and other CNS depressants. *(Journal of Pharmacology and Toxicology 3 (5): 335-343, 2008;* ***doi:*** *10.3923/jpt.2008.335.343)*

## Antioxidant and Hepatoprotective Activity of Ethanol Extract of *Indigofera trita* Linn. on $CCl_4$ Induced Hepatotoxicity in Rats

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The ethanol extract of *Indigofera trita* (EIT) was studied for its antioxidant and hepatoprotective properties. The ethanol extract exhibited potent *in vitro* antioxidant activity as evidenced by the low $IC_{50}$ values in the scavenging of ABTS, DPPH and hydroxyl radical methods. The $IC_{50}$ values obtained were 9.50±0.50 and 19.91±1.73 μg $mL^{-1}$, respectively for ABTS and DPPH methods. The $IC_{50}$ values obtained for hydroxyl radical scavenging by p-NDA and deoxyribose methods were found to be 104.50±4.50 and 99.00±0.28 μg $mL^{-1}$, respectively. The treatment with the EIT at 200 and 400 mg $kg^{-1}$ body weight showed a significant and dose dependent decrease in the levels of SGOT, SGPT, ALP and TBARS and significant increase in the levels of albumin, total protein, SOD and catalase, when compared to $CCl_4$ treated rats. The treatment with EIT exhibited better results than the standard vitamin-E treatment in some of these

parameters. Thus, the EIT showed significant antioxidant and hepatoprotective activity. These results were also confirmed by the histological observation. *(Journal of Pharmacology and Toxicology 3 (5): 344-350, 2008;* ***doi:*** *10.3923/jpt.2008.344.350)*

## Anticonvulsant Activities of Crude Flavonoid Fraction of the Stem Bark of *Ficus sycomorus* (Moraceae)

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The anticonvulsant effects of the crude flavonoid fraction of the stem bark of *Ficus sycomorus* were studied using the subcutaneous Pentylenetetrazole (PTZ) and Maximal Electroshock Test (MEST) models in mice and chicks respectively. The crude flavonoid fraction exhibited a significant ($p<0.05$) latency in mean onset and mean time of death of convulsed animal with a 20% protection at a dose of 10 mg $kg^{-1}$ body weight i.p. (comparable to Valproic acid at 200 mg $kg^{-1}$) while it showed a significant ($p<0.05$) and dose dependent maximal protection (83.3%) in the Maximal Electroshock Test (MEST) at an optimal dose of 20 mg $kg^{-1}$ body weight i.p. (comparable to Phenytoin at 20 mg $kg^{-1}$). The results obtained supported the claim in the traditional use of the stem bark of the plant in the management of epilepsy. *(Journal of Pharmacology and Toxicology 3 (5): 351-356, 2008;* ***doi:*** *10.3923/jpt.2008.351.356)*

## Larvicidal and Anti-Microbial Potentials of *Nymphaea odorata*

H.O. Oladimeji, P.M. Ubulom, E.I. Akpabio, I.E. Etim and E. Nyong

*Nymphaea odorata* (Nymphaeaceae) is an old herbal recipe used in the treatment and or management of ocular, skin, gastrointestinal and urino-genital ailments amongst many others. However, its use in malaria control at the larval stage is yet to be investigated. Hence the larvicidal and anti-microbial studies were undertaken. The larvicidal assay determined in terms of percentage mortality showed that the crude leaf extract gave weak larvicidal activity (LA %) of 10 and 20% (at 5% w/v) and 20 and 30% (at 10% w/v) both at 12 and 24 h incubation, respectively. Surprisingly, the crude extract and fractions were inactive against the bacterial and fungal isolates tested. These results in particular render untenable claims in ethno-medicine of the uses of the plant in treating infections especially those of microbial origin. *(Journal of Pharmacology and Toxicology 3 (5): 357-362, 2008;* ***doi:*** *10.3923/jpt.2008.357.362)*

## Ameliorative Effect of *Ficus hispida* Linn. Leaf Extract on Cyclophosphamide-Induced Oxidative Hepatic Injury in Rats

T.S. Shanmugarajan, M. Arunsundar, I. Somasundaram, D. Sivaraman, E. Krishnakumar and V. Ravichandran

The current study was designed to scrutinize the putative hepatoprotective potential of the methanolic leaf extract of *Ficus hispida* Linn. (FH) (400 mg $kg^{-1}$ body weight) on cyclophosphamide (CP) elicited oxidative injury in rat liver. CP administration (150 mg $kg^{-1}$ body weight, i.p., twice, in 2 consecutive days) caused liver injury, featuring substantial increase in serum aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), lactate dehydrogenase (LDH), gamma-glutamyl transpeptidase (GGT) and bilirubin levels. In contrast, treatment with FH significantly precluded all these alterations. CP intoxicated rats depicted a remarkable oxidative stress, as evidenced by a significant elevation in lipid peroxidation (LPO) with a concomitant decrease in the GSH activity. These changes were coupled with a marked decline in the activities of enzymic antioxidants [superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), glutathione-S-transferase (GST) and glutathione reductase (GR)] in the liver tissue of CP-administered rats. FH treated rats displayed a significant inhibition of lipid peroxidation (LPO) and augmentation of endogenous antioxidants. Taken together, these findings emphasize the hepatoprotective effect of *F. hispida* leaf extract against CP-induced oxidative liver injury. Hence, *F. hispida* might serve as a promising medicinal herb in complementary chemotherapeutic modalities. *(Journal of Pharmacology and Toxicology 3 (5): 363-372, 2008; **doi**: 10.3923/jpt.2008.363.372)*

## Comparison of Smooth Muscle Contractility in Rat Vas Deferens (Tube) and Rat Stomach Strip (Sheet) in Various Physiological Salt Solutions

Peter I. Aziba

Prototype agents such as Acetylcholine ($1.0\times10^{-9}$ to $5.0\times10^{-9}$ M), Nor-adrenalin ($2.5\times10^{-8}$ to $4.2\times10^{-7}$ M) and Potassium (50 mM) which stimulate different receptor populations in smooth muscle contraction have been examined on the contractility in Rat Vas Deferens (RVD) and Rat Stomach Strip (RSS) in various Physiological Salt Solution (PSS), varying the extra- cellular calcium in the medium

shows a reversed sigmoidal curve in both tissues. In $Ca^{2+}$-free medium, the rat vas deferens contractility diminished rapidly <10 min, but the rat stomach strip, maintained successively diminished and remained stable after 1 h of this treatment. The contractile heights diminished as extracellular $Ca^{2+}$ decreases in the bathing PSS from 1.8 mM $Ca^{2+}$ to 0.9 mM $Ca^{2+}$ and 0.45 mM $Ca^{2+}$ and $Ca^{2+}$-free medium, (64, 81 and 98.2% in RVD and 31, 68 and 87% in RSS. In Depolarising medium, both tissues looses contractility rapidly less than five minutes in RVS and RSS maintained diminished contractions for over 1 h. The results in this study suggest that the rat stomach strip under the experimental conditions has more intra cellular calcium storage when compared to contractility in rat vas deferens. *(Journal of Pharmacology and Toxicology 3 (5): 373-377, 2008;* ***doi:*** *10.3923/jpt.2008.373.377)*

## Antipyretic Activity of Ethanol Extract of *Cansjera rheedii* J. Gmelin (Opiliaceae)

V.M. Mounnissamy, S. Kavimani, V. Balu and S. Darlin Quine

The antipyretic activity of ethanol (95%) extracts of *Cansjera rheedii* J. Gmelin aerial parts of the plant was evaluated against brewer's yeast-induced pyrexia in rats to assess their antipyretic activity. Rectal temperatures were recorded before and after inducing pyrexia at interval of one hour to five hours. At the same time parallel experiments were run with a standard antipyretic paracetamol (100 mg $kg^{-1}$) and control (Normal Saline 5 mL $kg^{-1}$). Ethanol extract of *Cansjera rheedii* J. Gmelin at dose of 250 mg and 500 mg $kg^{-1}$ body weight showed the antipyretic activity significantly ($p<0.001$) compared to that of control. *(Journal of Pharmacology and Toxicology 3 (5): 378-381, 2008;* ***doi:*** *10.3923/jpt.2008.378.381)*

## Effects of Selected Antimuscarinic Agents on the Intra-Ocular Pressure in Healthy Rabbits

Goudarz Sadeghi-Hashjin and Hovig Manokzadeh

This study was designed to challenge this important issue in healthy animals. The effects of atropine, cyclopentolate and tropicamide was studied on IOP in the rabbit. For this, 12 healthy and adult white New Zealand rabbits were used. Drugs were applied topically once daily for 14 days. IOP was measured using Schiötz

tonometer 5 min after surface anesthesia before the instillation of the next dose of the antimuscarinics. Three drops of a 1% concentration was applied on one eye and the other eye served as control and received saline solution only. IOP was increased during the treatment period with a peak value up to 39, 29 and 39% with atropine, cyclopentolate and tropicamide, respectively ($p<0.001$). The IOP was still high one day after cessation of the treatment and returned to the baseline levels 7 days after termination of the treatment. In conclusion, chronic administration of antimuscarinics may lead to a critically increased IOP of normotensive eyes. These agents should be considered serious risks not only for patients with glaucoma, but also for subjects with no ophthalmologic problems. *(Journal of Pharmacology and Toxicology 3 (5): 382-385, 2008;* ***doi:*** *10.3923/jpt.2008.382.385)*

## *In vivo* Biocompatibility and Toxicity Assessment of a Gentamicin-Loaded Monoolein Gel Intended to Treat Chronic Osteomyelitis

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Biocompatibility and preliminary toxicity of a novel gentamicin-loaded monoolein gel (implant) intended for the local treatment of chronic osteomyelitis were investigated in mice. The mice, randomly allotted in 3 groups of 10, received respectively a single dose (0.05 mL) of normal saline, monoolein and the gel by subplantar injection. Clinical monitoring and assessment of induced oedema were carried out during 52 days after implantation. A histologic examination of the implantation site was performed at the end of the experiment. Renal and hepatic functions of the implant were also assessed on 52 days post-implantation by using biochemical and histological methods. In mice, no adverse reaction occurred after implantation. Only, a transitional foreign body reaction was observed in mice implanted by the monoolein and the implant. The paw volume of the mice increased within 3 h post-implantation and returned to baseline by 52 days. The liver and kidneys histology at light microscopy and biochemical parameters were similar for all mice. Further investigation is undertaken to detect eventual early damages which could have been resolved with time. Nevertheless, the novel gel is biocompatible and doesn't show sub-chronic toxicity. *(Journal of Pharmacology and Toxicology 3 (5): 386-393, 2008;* ***doi:*** *10.3923/jpt.2008.386.393)*

## *In vitro* Biocompatibility and Genotoxicity Assessment of a Gentamicin-Loaded Monoolein Gel Intended to Treat of Chronic Osteomyelitis

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The aim of the study was to assess *in vitro* the biocompatibility and the genotoxicity of a gentamicin-loaded monoolein gel intended to treat of chronic osteomyelitis. Indeed, we are developing biodegradable implants based on monoolein and gentamicin. The results of formulations, physico-chemical characterization of the formulated implants and *in vitro* release kinetic of gentamicin from implants were encouraging. As biocompatibility and absence of genotoxicity are the prerequisites for safe use of implants, we performed *in vitro* hemolysis, cytotoxicity and, genotoxicity tests. Hemolysis was evaluated by incubating human erythrocytes in direct contact with the implant whereas cytotoxicity was evaluated by 3-[4, 5-dimethylthiazol-2-yl]-2, 5-diphenyltetrazolium bromide (MTT) assay using fibroblasts and macrophages. Alkaline comet Assay was used to evaluate genotoxic potential of the implants. From these *in vitro* assays, the implant based on monoolein and gentamicin showed no genotoxic potential and has satisfactory biocompatibility. *(Journal of Pharmacology and Toxicology 3 (5): 394-401, 2008;* ***doi:*** *10.3923/jpt.2008.394.401)*

## Protective Effects of Propolis Against the Amitraz Hepatotoxicity in Mice

Attalla Farag El-Kott and Ayman Ahmed Owayss

The present study was aimed to study the protective effects of honeybee propolis against the amitraz hepatotoxicity in mice. Forty-eight male Swiss albino mice of 8 weeks of age, 22 to 25 g body weight was divided into four groups. The 1st was control, the 2nd treated orally with 150 mg $kg^{-1}$ propolis extract, the 3rd treated with 160 mg $kg^{-1}$ amitraz and the 4th one had 160 mg $kg^{-1}$ amitraz +150 mg $kg^{-1}$ propolis extract. These daily treatments lasted for 8 weeks and laboratory assays were measured weekly. Results, after mice sacrificed, histopathology and immunohistology tests were carried out. The obtained results revealed that amitraz had affected liver biochemicals concentrations, whereas propolis led to a

significant decrease in these levels in treated group. But, hepatocytes of mice treated with amitraz + propolis demonstrated positive stained nuclei, by using Ki67 immunostaining, less than those of amitraz treated only. The study suggests that propolis ameliorated the recovery of hepatotoxicity of amitraz in the tested mice. *(Journal of Pharmacology and Toxicology 3 (5): 402-408, 2008;* ***doi:*** *10.3923/jpt.2008.402.408)*

## Pharmacodynamic Drug Interaction of Metformin with Statins in Rats

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The present study is aimed to explore the pharmacodynamic interaction of metformin with statins like atorvastatin and rosuvastatin in rats. Wistar albino rats of either sex (150-200 g) were induced diabetes by administering alloxan and they were divided into six groups, each consisting of six rats. Normal control group (1) is treated with 1%w/v carboxy methyl cellulose (CMC) suspension. Group 2 served as diabetic control. To the diabetic 3rd, 4th and 5th group metformin, atorvastatin and rosuvastatin were administered orally respectively for 7 days. The combination of metformin + atorvastatin and metformin + rosuvastatin were administered to the 6th and 7th group of diabetic rats for 7 days. On the last day blood samples were collected, serum was isolated and subjected to glucose, triglycerides (TG), total cholesterol (TC), low density lipoprotein (LDL) and high density lipoprotein (HDL) estimation. Body weight was also calculated. Metformin significantly reduced the serum glucose level in diabetic rats. Atorvastatin and rosuvastatin produced mild hypoglycemia. On the other hand the combination of metformin + atorvastatin and metformin + rosuvastatin significantly reduced the serum glucose level when compared to metformin alone. Atorvastatin and rosuvastatin significantly reduced the serum TG, TC and LDL and increased HDL level. Metformin also altered the lipid profile of diabetic rats. Whereas the combination of metformin + atorvastatin and metformin + rosuvastatin significantly reduced the lipid profile when compared to atorvastatin and rosuvastatin alone. The combination of drugs also increased the body weight of diabetic animals. The antidiabetic drug metformin enhanced the hypolipidemic activity of atorvastatin and rosuvastatin. Similarly atorvastatin and rosuvastatin enhanced the hypoglycemic activity of metformin due to pharmacodynamic interactions. *(Journal of Pharmacology and Toxicology 3 (5): 409-413, 2008;* ***doi:*** *10.3923/jpt.2008.409.413)*

## Interaction of Propranolol with Garlic in Isoproterenol Induced Myocardial Infarction in Rat

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The current study dealt with the interaction of Garlic Homogenate (GH) with propranolol (PRO) on isoproterenol (ISO)-induced Myocardial Infarction (MI) in rats. Albino rats were treated either with GH at three different doses of 125 mg $kg^{-1}$, (GH-125), 250 mg $kg^{-1}$ (GH-250) and 500 mg $kg^{-1}$ (GH-500) orally for 30 days or different doses of GH along with PRO (10 mg $kg^{-1}$, p.o.) during the last 7 days of GH treatment. Myocardial damage was induced by administration of ISO (150 mg $kg^{-1}$ body weight s.c.) for 2 consecutive days. The PRO, moderate dose of GH alone or in combination with PRO was found to ameliorate the effect of ISO on superoxide dismutase (SOD), catalase and retained the activities of the diagnostic marker enzymes such as lactate dehydrogenase (LDH) and creatine phosphokinase isoenzyme (CK-MB). Incorporation of PRO during GH treatment provided further protection to myocardium from injury. However, higher dose of GH alone or in presence of PRO failed to prevent ISO induced myocardial injury. The results of the present study indicate that mild to moderate doses of GH exerts a protective effect, whereas, high dose of GH shows toxic effect against ISO-induced MI either alone or with PRO. *(Journal of Pharmacology and Toxicology 3 (6): 414-424, 2008;* ***doi:*** *10.3923/jpt.2008.414.424)*

## Efficacy and Tolerability of BacoMind® on Memory Improvement in Elderly Participants - A Double Blind Placebo Controlled Study

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A randomized double blind placebo controlled study was designed to evaluate the efficacy and tolerability of BacoMind®, an enriched phytochemical composition from *Bacopa monnieri* on memory improvement upon chronic administration in elderly subjects as memory loss in elderly people is one of the leading health problems worldwide and its uncertain recovery with conventional therapies has paved way to elucidate the use of complementary and alternative system of medicine. Elderly individuals with mini mental state examination score of twenty four and above were enrolled. BacoMind® or placebo was given as a single oral dose of 450 mg daily for the duration of 12 weeks. The combination of well

established battery of neuropsychological tests revealed that BacoMind® improved performance in tests associated with attention and verbal memory in elderly participants. Significant interaction effects between group and time were observed in digit span backward test ($p = 0.008$), list learning delayed recall test ($p = 0.014$), paired associates dissimilar delayed recall test ($p = 0.047$) and in visual retention-I test ($p = 0.035$). In conclusion, the study findings suggested that BacoMind® improved the cognitive functions such as attention and verbal memory in elderly individuals and was also found to be well tolerated. *(Journal of Pharmacology and Toxicology 3 (6): 425-434, 2008;* ***doi:*** *10.3923/jpt.2008.425.434)*

## Antihypertensive Effects and Antioxidant Action of a Hydro-Alcoholic Extract Obtained from Fruits of *Euterpe oleracea* Mart. (Açaí)

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Earlier, we have demonstrated that a hydro-alcoholic extract of the stone of *Euterpe oleracea* Mart., commonly known as Açaí, exerts a significant endothelium-dependent vasodilator action *in vitro*. The present study has evaluated potential antihypertensive proprieties of Açai Stone Extract (ASE) in four established models of experimental hypertension in the rat; spontaneously hypertensive rats (adult and young 21 days of age SHR), Goldblatt (2 kidney, 1-clip; 2K-1C), l-NAME and DOCA-salt-induced hypertension. Blood pressure was measured non-invasively using the tail-cuff method. A significant antihypertensive effect of ASE (200 mg/kg/day) was observed in adult SHR, Goldblatt, l-NAME and DOCA-salt models of hypertension. Administration of ASE just after weaning prevented the development of hypertension in SHR. Interestingly, expression of eNOS (endothelial nitric oxide synthase), which was elevated in SHRs compared to normontensive rats, was reduced in SHRs by ASE treatment. In addition, a significant antioxidant action of ASE, evaluated by TBARS measured in the bronchoalveolar lavage of rats exposed to cigarette smoke, was observed. In conclusion, the present study has demonstrated an antihypertensive action of ASE that is probably mediated via its vasodilator and antioxidant actions and the current preclinical data suggest a potential therapeutic use of ASE in hypertensive patients. *(Journal of Pharmacology and Toxicology 3 (6): 435-448, 2008;* ***doi:*** *10.3923/jpt.2008.435.448)*