Journal of Pharmacology and Toxicology

ISSN 1816-496X

Academic Journals Inc.

www.academicjournals.com

Spermicidal Action of Styrene Maleic Anhydride Polyelectrolyte in Combination with Magnetic and Electrically Conductive Particles

Rakhi K. Jha, Pradeep K. Jha, Suresh V.S. Rana and Sujoy K. Guha

The aim of this study is to evaluate impact of a new polymeric contraceptive SMA-Fe_3O_4-Cu-DMSO called Smart RISUG (acronym for Smart Reversible Inhibition of Sperm under Guidance), a colloidal suspension of styrene maleic anhydride co-polymer (SMA), nano-micro iron oxide (Fe_3O_4) and copper powder (Cu) (one milligram) dissolved in dimethylsulphoxide (DMSO) (1:30); on Albino rat's sperm solution (one milliliter). Experiments to assess the morphology and viability of control as well as treated sperm cells were performed by using microscopic techniques like High Resolution Transmission Electron Microscopy (HRTEM), Field Emission Scanning Electron Microscopy (FESEM), Atomic Force Microscopy (AFM), Scanning Electron Microscopy (SEM)-X ray microanalysis, phase contrast microscopy and Fluorescent Activated Cell Sorting (FACS). Treated cells indicate uniform adhesion of Smart RISUG particles to the sperm cell membrane, topological alteration, decrease in the cell count, reduced cell motility and viability, increased sperm abnormality and complete cell inactivation in about 72 h. This study suggests use of smart RISUG as a potential non-invasively reversible male/female contraceptive in future. (*International Journal of Pharmacology 5 (1): 1-12, 2009; **doi:** 10.3923/ijp.2009.1.12*)

Anticancer and Biochemical Effects of Calcium Chloride on Ehrlich Carcinoma Cell-Bearing Swiss Albino Mice

Yousif A. Asiri

The anticancer activity of calcium chloride was evaluated from the total count and viability of Ehrlich Ascites Carcinoma (EAC) cells and their proteins, nucleic acid, malondialdehyde (MDA) and Nonprotein sulfhydryl (NP-SH) groups in addition to observations on survival and the body weight changes. The tumors at site of injection were investigated for histopathological changes. The treatment with calcium chloride (50, 100 and 200 mg/kg/day) caused cytotoxic activity. These data are substantiated by biochemical and histopathological changes and are attributed to calcium ions, which are known to disrupt calcium homeostasis, produce ROS, damage mitochondria and cause DNA breaks. Nevertheless, these data were not in agreement with the results on survival and body weight of the

same animals. Treatment at the higher doses of calcium chloride increased the body weight and restricted the life span much earlier than the lower dose of calcium chloride and ADM. The discrepancy between these results might be due to the difference in the time of observation. While the experiments on cytotoxic activity, biochemical investigation and histopathology were conducted 10 and 5 days after the implantation of EAC cells and treatment, respectively, the observations on body weight and mortality were continued until death of all the animals or up to a maximum of 50 days. Data obtained in the present study demonstrate that treatment of calcium chloride at the higher doses had no influence on body weight and cause mortality as a long term effect, which might be due to co-morbidity of several diseases, caused by hypercalcemia and impairment of mitochondria. Further experiments are warranted on the use of a sufficient number of lower doses of calcium chloride to determine a pharmacologically effective and non-toxic dose. (*International Journal of Pharmacology 5 (1): 13-21, 2009;* ***doi:*** *10.3923/ijp.2009.13.21*)

Antidepressant-Like Effects of an Ethanolic Extract of *Sphenocentrum jollyanum* Pierre Roots in Mice

E. Woode, N. Amidu, W.K.B.A. Owiredu, E. Boakye-Gyasi, C. Ansah and M. Duwiejua

In the present study, the effect of an ethanolic extract of the roots of the plant in two animal models of depression the Forced Swimming Test (FST) and Tail Suspension Test (TST) has been reported. The extract (100-1000 mg kg^{-1}; p.o.), dose-dependently reduced the duration of immobility in both the FST (ED_{50}: 296.20±53.97 mg kg^{-1}) and TST (203.90±39.01 mg kg^{-1}).The effect of the extract was 20-50 times less potent than imipramime and fluoxetine which were used as standards. Pretreatment with α-methydopa (400 mg kg^{-1}; 3 h; p.o.) attenuated the anti-immobility effects of imipramime but not SJE and fluoxetine. Similarly, pretreatment with reserpine (1 mg kg^{-1}; 24 h; s.c.) abolished the effect of imipramime and partially the effects of SJE but not fluoxetine. A concomitant treatment with α-methyldopa and reserpine attenuated the effects of all but fluoxetine. The extract, imipramime and fluoxetine did not modify motor performance on the rotarod test at all doses tested. Putting all together, present results suggest that SJE has antidepressant-like effects in the model employed and may possibly exert its effects by modifying monoamine transport and/or metabolism. (*International Journal of Pharmacology 5 (1): 22-29, 2009;* ***doi:*** *10.3923/ijp.2009.22.29*)

Quantification of Acute Renal Denervation Diuresis and Natriuresis in Sprague Dawley and Spontaneously Hypertensive Rats

I.M. Salman, M.A. Sattar, N.A. Abdullah, O.Z. Ameer, M.H. Abdulla, Md. A.H. Khan and E.J. Johns

The present study was undertaken to quantify the renal salt and water excretory functions in response to acute unilateral renal denervation in Sprague Dawley (SD) and spontaneously hypertensive (SHR) rats in an attempt to characterize the relative contribution of renal sympathetic nerve activity (RSNA) to renal functional excretory responses in normotensive and hypertensive conditions. Adult male SD and SHR rats were fasted overnight, anesthetized with pentobarbitone sodium (60 mg kg^{-1} i.p.), denervated by application of phenol to the left renal artery and maintained on an intravenous (i.v.) infusion of normal saline for 2 h. Throughout this period, six urine and plasma samples were collected at 20 min intervals to study kidney function parameters. The data showed that there was a significantly higher ($p<0.05$) amount of sodium and water excretions in the urine of denervated SD and SHR rats as compared to their innervated counterparts. No significant difference in the renal salt and water excretions was seen between innervated SD and SHR rats; however, the difference was significant ($p<0.05$) following removal of renal sympathetic input. No appreciable changes in the mean arterial blood pressure (MAP) and plasma sodium (P_{Na}) were observed in denervated SD and SHR rats as compared to the innervated ones; yet, MAP values were significantly higher ($p<0.05$) in denervated and innervated SHR rats in comparison to the denervated and innervated SD rats. Moreover, P_{Na} in denervated SHR rats, which was significantly higher ($p<0.05$) in SHR rats as compared to SD rats prior to renal denervation, tended to approximate the one in denervated SD rats. In conclusion, this study confirmed the significant role played by the renal nerves in the control of renal functions. Diuresis and natriuresis are typical responses to acute renal denervation (ARD) in SD and SHR rats. Enhanced salt and water excretion following ARD in SHR rats suggests high renal sympathetic nerve discharge in these animals and highlights the significant contribution of renal nerves to the genetic model of essential hypertension. (*International Journal of Pharmacology 5 (1): 30-36, 2009; **doi:** 10.3923/ijp.2009.30.36*)

Torreya nucifera Essential Oil Inhibits Skin Pathogen Growth and Lipopolysaccharide-Induced Inflammatory Effects

W.J. Yoon, S.S. Kim, T.H. Oh, N.H. Lee and C.G. Hyun

In this study, the chemical composition of *Torreya nucifera* essential oil (TEO) and its biological activities were analyzed. TEO was obtained by steam distillation

from leaves collected from Jeju Island and analyzed using gas chromatography (GC)-flame ionization detection (FID) and GC-MS. dl-Limonene (30.1%), δ-3-carene (15.37%) and α-pinene (11.5%) were the major components in TEO. The antibacterial and anti-inflammatory activities of TEO against skin pathogens have not previously been reported. Thus, we assessed the antibacterial activities of TEO using the disk diffusion method. TEO showed excellent antibacterial activities against *Propionibacterium acnes*, *Propionibacterium granulosum*, *Malassezia furfur*, *Staphylococcus epidermidis* and *Candida albicans*. The minimum inhibitory concentration (MIC) of TEO against these skin pathogens ranged from 2.5 to 20.0 μL mL^{-1}. In addition, TEO reduced the LPS-induced secretion of interleukin-1β (IL-1β), IL-6, NO and PGE_2 in RAW 264.7 cells, indicating that it has anti-inflammatory effects. Therefore, we suggest that TEO may be an attractive candidate for promoting skin health. (*International Journal of Pharmacology 5 (1): 37-43, 2009;* ***doi:*** *10.3923/ijp.2009.37.43*)

Vasorelaxant Properties of *Loranthus ferrugineus* Roxb. Methanolic Extract

O.Z. Ameer, I.M. Salman, M.F. Yam, H.H. Abd Allah, M.H. Abdulla, A.M. Shah, A. Sadikun and M.Z. Asmawi

In the present study, *Loranthus ferrugineus* was evaluated for blood pressure lowering activity using *in vitro* and *in vivo* animal experimental approaches. The fresh aerial parts of the plant were dried, pulverized into powder and successively extracted with petroleum ether, chloroform, ethyl acetate, methanol and water using hot extraction methods. Each of the extracts was dried under reduced pressure using rotary evaporator and subsequently freeze-dried. The effects of three different concentrations (0.5, 1 and 2 mg mL^{-1} of each extract were examined on isolated rat aortic ring preparations and responses to cumulative doses of noradrenaline (NA) were measured. It was found that the relatively polar methanol extract was the most potent to produce a significant ($p<0.05$) dose-dependent inhibition in the maximum response and to shift the dose-response curve of NA to the right which suggests that *Loranthus ferrugineus* methanolic extract (LFME) contains compound(s) with non-competitive inhibitory activity. In another set of experiments, LFME was found to be the most active in blood pressure lowering activity in anaesthetized normotensive Sprague Dawley (SD) rat model. Moreover, LFME produced a dose-dependent blood pressure lowering effect. Chemical analysis of LFME showed the presence of significant amounts of polyphenolic and flavoniod constituents. The data suggests that LFME contains some biologically active substances that produce a significant dose-dependent blood pressure lowering effect and vasodilatation is one of the possible

mechanisms which may explain its use in the management of hypertension. Furthermore, LFME effects can possibly be attributed to the high polyphenolic contents of this plant. (*International Journal of Pharmacology 5 (1): 44-50, 2009; **doi:** 10.3923/ijp.2009.44.50*)

Evaluation of the Reproductive Toxicity of Chlorpyrifos Methyl, Diazinon and Profenofos Pesticides in Male Rats

Nour El-Hoda A. Zidan

The toxic effects of organophosphorus pesticides (i.e., chlorpyrifos methyl, diazinon and profenofos) on male reproductive system of rats were evaluated. Rats received pesticides mixed with powdered feed at concentrations of 5 and 50 ppm of each pesticide for 65 successive days. Sex organs weight, semen picture, concentrations of the hormones [i.e., testosterone, Luteinizing Hormone (LH) and Follicle Stimulating Hormone (FSH)], activities of acetylcholinesterase (AChE) and histopathological changes in testes were the criteria used to evaluate the reproductive toxicity of the treated rats. Results showed that the effect of all tested pesticides on testes and seminal vesicles weights was dose-dependent since all tested pesticides at 50 ppm significantly decreased their weights. Serum AChE activity was inhibited with all tested pesticides. Both the concentrations of the tested pesticides decreased sperm count associated with increase in the number of morphologically abnormal spermatozoa of treated rats; however sperm motility was significantly decreased with the highest concentration of the tested pesticides. A decrease in the serum testosterone was observed in all treated groups; however LH and FSH levels were decreased with the highest concentration of the tested pesticides. Tissues of treated rat's testes showed slight alterations when histopathologically examined especially with the higher concentrations. (*International Journal of Pharmacology 5 (1): 51-57, 2009; **doi:** 10.3923/ijp.2009.51.57*)

Modulation of Restraint Induced Gastric Oxidative Changes in Rats by Tocotrienol and Tocopherol

M.F. Nur Azlina, K. Rubaizah, M. Siti Muliana and M.I. Nafeeza

The present study compares the effect of tocotrienol mixture and α-tocopherol on gastric malondialdehyde (MDA), glutathione peroxidase (GPx), superoxide dismutase (SOD), reduced and oxidized glutathione (GSH and GSSG) content and prostaglandin E_2 level in rats exposed to restraint stress. Twenty-four male *Sprague dawley* rats were randomly assigned into 4 equal sized groups; two

control groups and two treated groups which were supplemented with either tocotrienol (TT) or α-tocopherol (TF) orally at a dose of 60 mg kg^{-1} body weight. After 28 days of treatment, one control group, the TT and TF groups were subjected to restraint stress, 2 h daily for 4 consecutive days. After the last exposure to stress, the stomach was excised for the evaluation of the parameters. Present findings showed that TT was better in preventing the formation of gastric lesion compared to TF while both TT and TF significantly reduces the gastric MDA content compared to stress control. We also found that both TT and TF have the ability to reduce prostaglandin E_2 loss which was apparent with stress exposure. The endogenous content of antioxidant enzyme GPx activity and GSH content was maintained towards the normal levels in rats receiving TT but not in the TF treated group. The SOD level however was not altered in stressed rats. As a conclusion, tocotrienol posses a better protective effect against stress-induced gastric lesions compared to α-tocopherol. The protective effect was associated with decreased lipid peroxidation, increased prostaglandin E_2 (PGE_2) and restoration of GPx activity and GSH content which was altered by stress. (*International Journal of Pharmacology 5 (1): 58-64, 2009;* ***doi:*** *10.3923/ijp.2009.58.64*)

Antisickling Activity and Thermostability of Anthocyanins Extract from a Congolese Plant, *Hymenocardia acida* Tul. (Hymenocardiaceae)

P.T. Mpiana, V. Mudogo, Y.F. Kabangu, D.S.T. Tshibangu, K.N. Ngbolua, E.K. Atibu, K.P. Mangwala, M.B. Mbala, L.K. Makelele and M.T. Bokota

Antisickling activity of anthocyanins extract from a Congolese plant (*Hymenocardia acida* Tul.) was evaluated using Emmel test. Chromatographic separations using chloroform-benzene (2:1) provided three fractions A_1, A_2 and A_3 with the most polar [A_1 (TLC, R_f = 0.21)] exhibiting the highest activity. Thermal kinetic degradation of this fraction at 100 and 120°C produced a first order rate constants $k = 2.64\times10^{-4}$ and 4.08×10^{-4}, respectively. Structural elucidation of isolated compounds is in progress. (*International Journal of Pharmacology 5 (1): 65-70, 2009;* ***doi:*** *10.3923/ijp.2009.65.70*)

Biological Activities of *Pereskia bleo* Extracts

S.I.A. Wahab, A.B. Abdul, S.M. Mohan, A.S. Al-Zubairi, M.M. Elhassan and M.Y. Ibrahim

The aim of this study is to screen the hexane, dichloromethane, ethyl acetate and methanol extracts of *Pereskia bleo* (PB) for their antibacterial, anti-oxidant and

anti-cancer properties using disc diffusion method, DPPH assay and MTT cytotoxicity test, respectively. It is found that hexane and methanol extracts showed highly and moderately, respectively, considerable antibacterial activity towards two Gram-negative bacteria, *P. aeruginosa* 60690 and *S. choleraesuis*. Ethyl acetate extract showed a week narrow spectrum activity (≈35% of streptomycin activity). The highest antibacterial activity on MRSA is obtained by DCM extract. Hexane extract was the most effective DPPH radical scavenger (37.55%). Ethyl acetate and DCM extracts were less effective free radical scavenger (16.1%). None of the extracts were cytotoxic significantly towards MCF-7, HT-29 and CEM-SS cell lines after 72 h incubation time (IC_{50} > 30 μg mL^{-1}). It could be concluded that antibacterial activity of *P. bleo* is the most promising biological activity attributed to this plant. (*International Journal of Pharmacology 5 (1): 71-75, 2009;* ***doi:*** *10.3923/ijp.2009.71.75*)

Effect of Xylazine Sedation on Some Haematological Indices after Chloramphenicol Pre-Treatment in Sokoto Red Goats

M. Gweba, K.I. Onifade and O.O. Faleke

The effect of a single dose pre-treatment with chloramphenicol at 50 mg kg^{-1} given intramuscularly on xylazine sedation was evaluated on 6 Sokoto Red goats weighing 11-14 kg. The duration of xylazine sedation after xylazine administration at 0.2 mg kg^{-1} IM alone was 83.16±10.95 min (control), as against 129±1.78 and 157.83±4.99 min for the other two pre-treatments with chloramphenicol, respectively. There was a significant ($p<0.05$) decrease in the haemoglobin concentration for all treatments while a significant increase in the white blood cells count was observed for all treatments. Irrespective of weight variation, the goats in all exhibited the same clinical signs. It can be deduced from this research that chloramphenicol pre-treatment may prolong the duration of action of xylazine sedation. (*International Journal of Pharmacology 5 (1): 76-80, 2009;* ***doi:*** *10.3923/ijp.2009.76.80*)

Antibacterial, Antifungal and Toxicity of Rare Iranian Plants

K. Keymanesh, J. Hamedi, S. Moradi, F. Mohammadipanah and S. Sardari

As a part of our drug discovery program, an effort to introduce new effective medicinal plants, with antibacterial, antifungal and cytotoxic properties was made. The extracts of aerial part of 8 plants, collected in southeastern Iran, were investigated against standard strains of *Bacillus subtilis*, *Enterococcus faecalis*,

Pseudomonas aeruginosa, *Salmonella entrica* subsp. *entrica* ser. Typhi, *Escherichia coli*, meticillin resistant *Staphylococcus aureus* (isolated from patients), *Fusarium oxyosporum*, *Aspergilus niger*, and *Aspergilus fumigatus*. We used brine shrimp (*Artemia salina*) cytotoxicity bioassay in order to provide a better base for introducing the extracts as the new therapeutic candidates. *Capparis deciduas* (Forsk.) Edjw. and *Cleome oxypetala* Boiss. (both from Capparidaceae family) were recognized as having the potential for development of new antibiotics. On the other hand, *Cistanche tubulosa* (Schrenk) R.Wight, could be worthy of attention for finding anticancer phytochemicals. (*International Journal of Pharmacology 5 (1): 81-85, 2009;* ***doi:*** *10.3923/ijp.2009.81.85*)

Dual Effects of Interaction Between Meloxicam, Diclofenac Sodium or Tramadol and Nitrogen Species Radicals: *In vitro* Comparative Study

M.S.M. Al-Nimer and E.A. Ali

This study aimed to investigate the interaction between synthetic peroxynitrite or sodium nitroprusside (nitric oxide donor) and meloxicam, diclofenac sodium or tramadol HCl. Meloxicam, diclofenac sodium or tramadol HCl (100-500 μg) were incubated in phosphate buffer saline in presence or absence of synthetic peroxynitrite (180 μM) or sodium nitroprusside as nitric oxide donor (10 mM). The level of peroxynitrite and nitric acid in solution were measured using UV-visible spectrophotometer. The results showed that meloxicam scavenged synthetic peroxynitrite and involved in peroxynitrite mediated phenol nitration when it incubated alone in phosphate buffer. All tested compounds, *in vitro*, behaved like sodium nitroprusside in releasing nitric oxide. Both meloxicam and diclofenac sodium reduced the activity of sodium nitroprusside-releasing nitric oxide. Tramadol HCl was not interacted with sodium nitroprusside at any concentration. We concluded that selective or non selective nonsteroidal anti-inflammatory drugs reduced the activity of nitric oxide donor while tramadol HCl is free from this effect. (*International Journal of Pharmacology 5 (1): 86-89, 2009;* ***doi:*** *10.3923/ijp.2009.86.89*)

Solid Lipid Nanoparticles Preparation and Characterization

N. AL-Haj and A. Rasedee

The presents study aimed to prepare and characterize Solid Lipid Nanoparticles (SLNs) from palm oil materials. Hydrogenated palm oil and lecithin incorporated

with surfactant were mixed and formed by High Pressure Homogenization (HPH) at elevated temperature. Appropriate analytical methods are needed for the characterization of SLN. The use of several analytical techniques is a necessity such as particle size which determined using Photon Correlation Spectroscopy (PCS). The change of particle charge was studied by Zeta Potential (ZP) measurements, while the melting and recrystallization behavior characterized by Differential Scanning Calorimetry (DSC). Data showed physical stability of the formulation. In conclusion, the SLN presented here are well suited for several applications including drug delivery. (*International Journal of Pharmacology 5 (1): 90-93, 2009;* ***doi:*** *10.3923/ijp.2009.90.93*)

Evaluation of the Proposed Inhibitory Effect of the Aqueous Stem-Bark Extract of *Ficus exasperata* on Uterine Preparations *in vitro*

E.E. Bafor, M. Nwiko, E.K.I. Omogbai, R.I. Ozolua and Z.A.M. Nworgu

The effect of the aqueous stem-bark extract of *Ficus exasperata* (ASE) was studied on oxytocin- and acetylcholine-induced uterine contractions in uterine preparations isolated from non-pregnant Sprague-Dawley rats in oestrus. Preliminary phytochemical analysis was also performed. There were no statistically significant increases in the concentrations of oxytocin and acetylcholine required to elicit 30 and 50% of maximum response (EC_{30} and EC_{50}, respectively) in the presence of the extract. Salbutamol and atropine, however, significantly inhibited the effects of oxytocin and acetylcholine, respectively. Phytochemical analysis revealed the presence of alkaloids, tannins and saponin glycosides. These results indicate that ASE possesses no inhibitory effect on the non-pregnant rat uterus as claimed by traditional healers. (*International Journal of Pharmacology 5 (1): 94-97, 2009;* ***doi:*** *10.3923/ijp.2009.94.97*)

Antimicrobial Activity of Essential Oil from *Nelumbo nucifera* Gaertn. Pollen

Chaiyasit Sittiwet

The *Nelumbo nucifera* Gaertn. pollen essential oil was extracted by using vapor distillation. Antimicrobial activity of *Nelumbo nucifera* Gaertn. pollen essential oil has been investigated using agar diffusion susceptibility test and broth macro-

dilution. The essential oil were tested against both gram positive (*S. aureus* ATCC 25923, *S. epidermidis* ATCC 12228, *M. luteus* A TCC 9341, *B. subtillis* ATCC 6633 and *L. plantarum* ATCC 14917) and gram negative (*E. coli* ATCC25922, *S. typhimurium* ATCC 14028, *K. pneumoniae* ATCC 10031, *P. vulgaris* ATCC 13315, *Ps. aeruginosa* ATCC 9721) bacteria using agar diffusion susceptibility test. Significant zone of inhibition were observed for *S. typhimurium* ATCC14028 and *E. coli* ATCC25922). The MICs and MBCs are 10-40 and 20-80 ml L^{-1}, respectively. *Nelumbo nucifera* pollen essential oil show inhibitory effect on growth of food born pathogen bacteria in low concentration which indicated the possibility of used as food preservation additive. (*International Journal of Pharmacology 5 (1): 98-100, 2009;* ***doi:*** *10.3923/ijp.2009.98.100*)

Anti-Nociceptive Effects and the Mechanism of *Palisota hirsuta* K. Schum. Leaf Extract in Murine Models

E. Woode, E. Boakye-Gyasi, G.K. Ainooson, C. Ansah and M. Duwiejua

The anti-nociceptive effect of an ethanolic leaf extract of *Palisota hirsuta*, a plant used locally in Ghana for various painful conditions was assessed, using various pain models. *Palisota hirsuta* extract (PHE) together with morphine and diclofenac (positive controls), all showed significant dose-dependent anti-nociceptive activity in all the models used, that is the tail withdrawal test, the inflammatory-induced mechanical hyperalgesia test, the acetic acid induced writhing test and the formalin test. The anti-nociceptive effect exhibited by PHE in the formalin test was reversed by the systemic administration of the non-selective opioid antagonist, naloxone, the NO synthase inhibitor, N_{ω}-nitro-arginine methyl ester (L-NAME) and the ATP-sensitive K^+ channel inhibitor, glibenclamide. However, theophyline, a non-selective adenosine receptor antagonist did not reverse this effect. PHE, unlike morphine, did not induce tolerance to its anti-nociceptive effect in the formalin test after chronic administration and also morphine tolerance did not cross-generalize to PHE. Overall, the present results demonstrate that the anti-nociceptive effects of PHE might partially or wholly be due to the stimulation of peripheral opioid receptors through the activation of the nitric oxide-cyclic GMP-ATP-sensitive K^+ (NO/cGMP/K^+ATP)-channel pathway without tolerance induction after chronic administration. (*International Journal of Pharmacology 5 (2): 101-113, 2009;* ***doi:*** *10.3923/ijp.2009.101.113*)

Safety Evaluation of Long Term Treatment of Methanol Sub-Fraction of Seeds of *Carica papaya* as a Male Contraceptive with Particular Emphasis on Carcinogenicity in Albino Rats

S. Goyal, B. Manivannan, A.S. Ansari and N.K. Lohiya

A preliminary study to evaluate if long term treatment of Methanol Sub-Fraction (MSF) of the seeds of *Carica papaya* as a male contraceptive would develop neoplastic lesions in vital organs was carried out in albino rats at 50, 250 and 500 mg kg^{-1} b.wt. day^{-1} for a period of 24 months, with a minimum dose being one therapeutic dose. Pre-terminal deaths, 45% in males and 48% in females, well within the acceptance limit, were reported to be age related and not treatment related, resulted due to general/respiratory/gastrointestinal/ urogenital disorders in both males and females of control and treated animals. Skin peeling, withering of fur leaving skin patches were observed in few of the animals after 18 months of treatment. Absence of spermatozoa in the cauda epididymis was evident in all the treated animals. No major structural changes compared to control were evident in the vital organs. Serum testosterone, serum electrolytes, tissue biochemical, hematology and clinical chemistry were comparable to those of control animals, suggesting no adverse effect of the test substance following long term treatment. The results provided evidence that the methanol sub-fraction of the seeds of *Carica papaya* does not lead any development of neoplastic lesion following life term treatment for 24 months in rats and is safe enough to be permitted for further trials as a male contraceptive. (*International Journal of Pharmacology 5 (2): 114-125, 2009;* ***doi:*** *10.3923/ijp.2009.114.125*)

Selenomethionine Induced Changes on the Binding of Spermine with DNA: A Study by Fourier Transform Raman and Fourier Transform Infra Red Spectroscopy

N. Iyandurai and R. Sarojini

In this research, FT Raman and FTIR spectroscopy had been used to extend our knowledge about spermine-DNA and selenomethionine-spermine-DNA interaction at different volume ratios. The analysis of FT Raman and FTIR data supported the existence of structural specificities in the interaction. From the observed results, the effect of spermine on DNA is reversed when selenomethionine is added with spermine-DNA complexation. For example, band at 1511 cm^{-1} is assigned to an adenine carbon-carbon stretching vibration. This band shifts downward by 3 cm^{-1} in the spectra of spermine-DNA of all the

complexes studied. Similarly this band shifts upward by 2 cm^{-1} in the spectra of selenomethionine-spermine-DNA of all the complexes studied. (*International Journal of Pharmacology 5 (2): 126-136, 2009; **doi:** 10.3923/ijp.2009.126.136*)

Effect of Green and Black Teas on Immobilization Induced Stress in Male Wistar Albino Rats

Salim S. Al-Rejaie

The present study was undertaken to investigate the potential of green and black teas to modulate restraint stress-induced oxidative changes in male Wistar albino rats. Repeated immobilization for 4 h daily for five consecutive days per week (for 2 and 4 weeks) was used as a test model. Repeated immobilization stress significantly decreased glutathione (GSH), RNA and total protein levels, while malondialdehyde (MDA) levels were elevated in brain and liver tissues. Daily drinking of green or black tea only attenuated the RNA decrease and the MDA increase in stressed groups in liver tissues. Green tea group attenuated the decrease in GSH and RNA and the increase in MDA induced by immobilization stress in brain tissues. However, black tea only attenuated the increase in brain MDA in stressed animals. The effect of green tea on restraint stress was higher in brain than liver. In conclusion, the present results revealed that the antioxidative effect of green tea during immobilization stress was higher, possibly attributed to the presence of relatively higher concentrations of flavonoids than in black tea. (*International Journal of Pharmacology 5 (2): 137-145, 2009; **doi:** 10.3923/ijp.2009.137.145*)

Inhibition of Ethanol-Induced Gastric Mucosal Damage by Carvedilol in Male Wistar Albino Rats: Possible Biochemical Changes

Salim S. Al-Rejaie

The effect of acute carvedilol (a third-generation nonselective β-blocker) pretreatment on gastric mucosal injury induced by 80% ethanol was investigated in male Wistar albino rats. The effects caused by pylorous ligation, accumulated gastric acid secretions and ethanol-induced changes in gastric mucus secretions, levels of proteins, nucleic acid, malondialdehyde (MDA) and non-protein sulfhydryl groups (NP-SH) in the stomach wall were investigated. The gastric

ulcers were induced by administration of 1 mL of 80% ethanol, as a necrotizing agent into the stomach. Carvedilol pretreatment at two oral doses of 30 and 60 mg kg^{-1} body weight were found to protect against the ulcerogenic effects of ethanol. Same dose regimen of carvedilol offered significant protection against ethanol-induced damage on the parameters evaluated for histopathology. Furthermore, the pretreatment afforded a significant inhibition of pylorous ligated accumulation of gastric acid secretions and ethanol-induced depletion of stomach wall mucus, nucleic acids, proteins and NP-SH contents. Only higher dose of carvedilol provided inhibition of ethanol-induced increase in MDA concentration. The protective effects of carvedilol against gastric secretion or damage to the gastric-wall mucosa may be mediated through its effects on mucus production and NP-SH concentrations, possible free-radical scavenging ability and/or cytoprotective properties. (*International Journal of Pharmacology 5 (2): 146-154, 2009;* ***doi:*** *10.3923/ijp.2009.146.154*)

A Preliminary Study of Dexamethasone Against Ischemia/Reperfusion Liver Injury in Rats

Amr A. Fouad, Mahmoud H. El-Bidawy, Arif Mohy Uddin and Mohamed T. Yacoubi

The hepatoprotective effect of dexamethasone was investigated in rats exposed to ischemia/ reperfusion liver injury. Ischemia was induced by clamping the pedicle of the left hepatic lobe for 1 h followed by 3 h of reperfusion. Dexamethasone was administered 24 h before the ischemic insult in two i.p., doses (10 mg kg^{-1}, each) with 12 h interval. Dexamethasone significantly attenuated the ischemia/reperfusion-induced elevations in serum aminotransferase and hepatic levels of tumor necrosis factor-α and nitric oxide. Dexamethasone also significantly compensated deficits in hepatic antioxidant defense mechanisms (reduced glutathione and catalase and superoxide dismutase activities) and suppressed lipid peroxidation observed with liver hypoxia-reoxygenation. This was associated with significant restoration of the ischemia/reperfusion-induced increase in hepatic caspase-3 activity. Neutrophil infiltration and hepatocellular necrosis and apoptosis detected by histopathological examination of liver tissue were markedly ameliorated by pre-ischemic dexamethasone treatment. In conclusion, dexamethasone can be considered a potential therapeutic agent to protect against the major clinical challenge of liver injury resulting from ischemia/reperfusion. (*International Journal of Pharmacology 5 (2): 155-161, 2009;* ***doi:*** *10.3923/ijp.2009.155.161*)

Anti-Angiogenic and Anti Oxidant Properties of *Orthosiphon stamineus* Benth. Methanolic Leaves Extract

H.B. Sahib, A.F. Aisha, M.F. Yam, M.Z. Asmawi, Z. Ismail, S.M. Salhimi, N.H. Othman and A.M.S. Abdul Majid

Angiogenesis is a process by which new blood vessels are formed from the pre-existing blood vessel. *Orthosiphon stamineus* Benth. OS has been used as a medicinal herb for many centuries. Due to the presence of high level of anti-oxidants and phenolic content compounds in OS and the effect of anti-oxidants and phenolic compounds being anti-angiogenic, the perturbation of new blood vessels ability of OS was tested. Dry powdered leaves of the OS plant were extracted with Petroleum Ether (PE), chloroform (CE), methanol (ME) and water (WE) by using sequential cold maceration method. The ME of OS has the highest anti-angiogenic activity (93.28±1.24%) in the rat aortic assay followed by CE (85.55±1.64%), PE (51.54±4.12%) and WE (50.22±1.23%) in descending order of reactivity. The methanol extract was also found to have potent anti-oxidant activity in the 1, 1-diphenyl-2-picrylhydrazyl (DPPH) free radical scavenging activity assay. The IC_{50} value was measured to be 0.286 mg mL^{-1}. The total phenolic content of 1 mg mL^{-1} of methanol extract was equal to 38.27%. (*International Journal of Pharmacology 5 (2): 162-167, 2009;* ***doi:*** *10.3923/ijp.2009.162.167*)

The Decoction of Leaves of *Phyllanthus discoideus* Possesses Anticonvulsant and Sedative Properties in Mice

E. Ngo Bum, M.M. Pelanken, N. Njikam, E. Talla, G.S. Taiwe, G.C.N. Nkantchoua and G.T. Ngoupaye

The aim of this study is to scientifically look for sedative and anticonvulsant properties of the decoction of *Phyllanthus discoideus* Baill (*P. discoideus*) in mice. The *in vivo* models of epilepsy were used to evaluate the anticonvulsant properties of the plant. These models were maximal electroshock-, N-methyl-D-aspartate-, pentylenetetrazol-, isonicotinic hydrazide- acid and strychnine- induced convulsions or turning behavior in mice. The potentiation of sleep induced by diazepam in mice was used for the determination of the sedative properties. Four doses of the plant in the decoction were used: 17.1, 42.7, 85.5 and 171 mg kg^{-1}. The decoction of the leaves of *P. discoideus* strongly increased the total sleep time

($p<0.001$) induced by diazepam and precipitated its onset ($p<0.001$). The decoction also protected mice against maximal electroshock- ($p<0.001$), pentylenetetrazol- ($p<0.001$), strychnine- ($p<0.001$) and N-methyl-D-aspartate-induced seizures or turning behavior ($p<0.001$). Finally, the decoction increased the latency to the onset of seizure in isonicotinic hydrazide acid test ($p<0.001$). In conclusion the decoction of *P. discoideus* posses anticonvulsant and sedative properties in mice. The presence of these properties could explain its use in traditional medicine in Cameroon in the treatment of insomnia and epilepsy. (*International Journal of Pharmacology 5 (2): 168-172, 2009;* ***doi:*** *10.3923/ijp.2009.168.172*)

Effect of Protein Depletion on Host and Tumor Response to Paclitaxel in Experimental Animals

Abdel-Moneim M. Osman, Azza A. Abdel-Fatah, Basent B. Hassan, Mahmoud M. El-Merzebani and Zoheir A. Damanhouri

The present study is aimed to examine the possible effects of Protein Malnutrition (PM) on the therapeutic activity and toxicity of paclitaxel in mice implanted with Ehrlich carcinoma cells. Mice that were fed either with standard or low protein diets were treated with a single dose of paclitaxel (10 mg kg^{-1}, i.p.). Paclitaxel administration increased the tumor growth delay of Ehrlich carcinoma from 2.8 days in protein deficient animals to 4.9 days in normal feeding mice and this represented about 43% increase in tumor growth delay. Furthermore, protein deficiency also interfered with the antitumor activity of paclitaxel. The percent survival of tumor-bearing mice after paclitaxel treatment were 56 and 19% in normal fed and protein deficient animals, respectively. Moreover, Paclitaxel administration increased the serum level of creatine phosphokinase isoenzyme (CPK-MB) in both groups, with maximum effect appeared after 48 h. Seventy two hours later, the levels was reduced to the normal values in normal fed animals while in protein malnourished mice, the activity was found to be high. In addition, paclitaxel administration significantly increased the plasma histamine concentration after 10 min and persisted for 120 min in animals on protein malnourished diet, however, in animals on a normal fed diet, histamine concentration reached the normal level after 120 min of paclitaxel administration. In conclusion, Paclitaxel administration exerts its toxic effects on both protein malnourished and normal feeding animals, however, its toxicity is enhanced and therapeutic activity is reduced in the protein deficient animals. (*International Journal of Pharmacology 5 (2): 173-177, 2009;* ***doi:*** *10.3923/ijp.2009.173.177*)

The Effect of Oxamate on Fertilization Capacity of Mouse Sperm *in vitro*

F. Rahim, G. Saki, B. Ghavamizadeh, A. Jafaee and M. Kadkhodaee

This study was conducted *in vitro* to show the effect of oxamate on motility and fertility of the mouse. The spermatozoa were extracted from the caudal part of epididymis. The study animals divided into four groups: (1) control group in TYH medium+5 mg m L^{-1} BSA; (2) test groups in TYH medium in which contain 10 Mm oxamate; (3) test groups in TYH medium in which contain 20 Mm oxamate and (4) test groups in TYH medium in which contain 30 Mm oxamate. All four groups were incubated for 90 min to obtain capacitation. Further their motility was checked after incubation time. The mice were super ovulated with PMSG and HCG hormones to obtain oocytes. Total of 600 oocytes were collected and cultured in drops of KSOM medium+5 mg mL^{-1} BSA, then for fertilization process received spermatozoa from different groups of mentioned above. After 24-26 h, the rate of fertilization was checked. The results of this research indicated that oxamate at the concentration of 20 and 30 Mm significantly reduce ($p<0.05$) the progress of motility and fertility. Statistical analysis showed that percentage of the sperm progress motility in both concentration of 20 and 30 Mm was significantly differ ($p<0.05$) in compare with control group and in concentration of 10 Mm, respectively. The same results were obtained in the case of fertility. These findings suggested that oxamate has an inhibitory role on motility and fertility of mouse sperm. (*International Journal of Pharmacology 5 (2): 178-180, 2009;* ***doi:*** *10.3923/ijp.2009.178.180*)

Anti-Arthritic Effects of *Palisota hirsuta* K. Schum. Leaf Extract in Freund's Adjuvant-Induced Arthritis in Rats

E. Woode, E. Boakye-Gyasi, C.A. Danquah, C. Ansah and M. Duwiejua

The anti-arthritic effect of an ethanolic leaf extract of *Palisota hirsuta*, a plant used locally in Ghana for v arious painful inflammatory conditions was assessed, using the Freund's adjuvant induced-arthritis model in rats. *Palisota hirsuta* Extract (PHE) as well as dexamethasone and methotrexate, used as positive controls, showed significant dose-dependent anti-arthritic properties prophylactically, curatively and also in combination therapy. PHE (30-300 mg kg^{-1}) significantly reduced the arthritic edema in the ipsilateral paw with the highest

dose used giving a maximum inhibition of 13.02±8.77%. PHE 300 mg kg^{-1} also significantly prevented the spread of the edema from the ipsilateral to the contralateral paw indicating inhibition of systemic spread. Dexamethasone (0.3-3 mg kg^{-1}) and methotrexate (0.1-1.0 mg kg^{-1}) significantly and in a dose dependent manner also inhibited polyarthritis edema as well as completely preventing the spread of the arthritis from the ipsilateral to the contralateral paws of the treated animals. PHE in combination with methotrexate did not show any significant effect, however, there was a significant inhibition of arthritis in both the acute and the polyarthritis phases when PHE was combined with dexamethasone. Dexamethasone in combination with methotrexate gave the greatest inhibition of both phases with an extreme level of significance as expected. Overall, the present results demonstrate that PHE has anti-arthritic effect which could be similar to that exhibited by methotrexate. (*International Journal of Pharmacology 5 (3): 181-190, 2009;* ***doi:*** *10.3923/ijp.2009.181.190*)

Vascular Responsiveness to *Macrosolen cochinchinensis* Extracts in Isolated Rat Thoracic Aorta

O.Z. Ameer, I.M. Salman, Md. J.A. Siddiqui, M.F. Yam, R.N. Sriramaneni, A.F. Mutee, A. Sadikun, Z. Ismail and M.Z. Asmawi

The aim of the current investigation was to examine the vascular responsiveness to different extracts obtained from *M. cochinchinensis* using isolated Sprague Dawley (SD) rat aortic rings preparations. The fresh aerial parts of the plant were dried, pulverized into powder and sequentially extracted with petroleum ether, chloroform, methanol and water using hot extraction method. The effects of three concentrations (0.5, 1 and 2 mg mL^{-1}) of each extract on rat thoracic aorta were tested using cumulative concentrations of noradrenaline (NA). The data showed that all the extracts had the ability to relax vascular smooth muscle; however, high concentrations of the methanol and water extracts caused the most significant ($p<0.05$) reduction in NA-induced vasoconstriction as compared to petroleum ether and chloroform extracts. Polyphenolic content, HPLC profiling and IR spectra were indicative of the presence of diterpenoid constituents. The results collectively suggested the presence of some biologically active ingredients of possible diterpenoid nature that have the ability to modulate the action of naturally occurring vasoactive agents such as NA on vascular smooth muscle responses *in vitro*. (*International Journal of Pharmacology 5 (3): 191-199, 2009;* ***doi:*** *10.3923/ijp.2009.191.199*)

Antihyperglycemic, Hypolipidemic and Antioxidant Enzymes Effect of *Strobilanthes crispus* Juice in Normal and Streptozotocin-Induced Diabetic Male and Female Rats

N.A. Norfarizan-Hanoon, R. Asmah, M.Y. Rokiah, O. Fauziah and H. Faridah

The aim of the present study was to investigate the effect of *Strobilanthes crispus* juice on glucose, lipid profile, glutathione peroxidase and superoxide dismutase in normal and streptozotocin-induced diabetic male and female albino Sprague-Dawley rats. This study was conducted on normal and streptozotocin-induced diabetic male and female Sprague-Dawley rats fed with basal diet and *S. crispus* juice with different doses 1.0, 1.5 and 2.0 mL kg^{-1} b.wt. for 30 days. The results showed that significant ($p<0.05$) decrease in serum glucose levels in male and female diabetic and normal rats with treated *S. crispus* juice (1.0, 1.5 and 2.0 mL kg^{-1} b.wt.). Cholesterol and triglyceride level significantly ($p<0.05$) decreased in diabetic rats treated with 1.0, 1.5 and 2.0 mL kg^{-1} b.wt. of *S. crispus* juice. Cholesterol, triglyceride and LDL-cholesterol level showed reduction in treated male and female normal rats. HDL-cholesterol showed the increasing but not significant ($p<0.05$) difference in treated diabetic and normal male and female rats. Glutathione peroxidase and superoxide dismutase activities significantly ($p<0.05$) increased in treated diabetic and normal male and female rats. In conclusion, *S. crispus* juice possesses antihyperglycemic, hypolipidemic and antioxidant effect in streptozotocin-induced diabetic rats. Thus, *S. crispus* juice could be the alternative treatment for lowering glucose, cholesterol and triglyceride for diabetic patients in the future. (*International Journal of Pharmacology 5 (3): 200-207, 2009;* ***doi:*** *10.3923/ijp.2009.200.207*)

Efficacy and Safety of Folic Acid During Toxic Hepatitis Induced by Acute Overdose of Paracetamol

N.S. AL-Sowyan

Paracetamol, a major cause of acute liver failure represents a significant clinical problem. Intake of a large dose of paracetamol (APAP) may result in severe hepatic necrosis. Oxidative stress mediated by oxidative capacities of the APAP metabolite (N-acetyl-P-benzoquinon-imine (NAPQI)) is considered as the main cause of hepatotoxicity of APAP. This labor therefore seeks to induce liver damage in rats using single dose of APAP and to evaluate the possible protective effects of administration of folic acid on APAP induced liver damage in rats. Serum transaminases and lactic dehydrogenase levels were assessed as markers

of hepatic damage. Also, bilirubin, total protein, albumin, globulin and A/G ratio were analyzed. Equally, comparative effects of folic acid on the markers were also evaluated. Paracetamol caused liver damage as evident by statistically significant increased in the activities of alanine aminotransferase, aspartate aminotransferase and alkaline phosphates. There were general statistically significant losses in the activities of lactic dehydrogenase and an increase in total bilirubin and protein with significant decrease in A/G ratio in paracetamol treated group compared with the control group. Also, the histopathological examination of liver showed marked degeneration of hepatic cells and necrosis with congested portal vein and dilated hepatic sinusoid. However, folic acid was able to counteract the effect of APAP. The present results suggest that folic acid can act as hepatoprotective against paracetamol toxicity and that the mechanism by which they do this is by acting as antioxidants. (*International Journal of Pharmacology 5 (3): 208-214, 2009;* ***doi:*** *10.3923/ijp.2009.208.214*)

Comparative Effect of Vitamins A and E on Gasoline Vapours-Induced Haematotoxicity and Weight-Loss in Male Rats

F.E. Uboh, M.I. Akpanabiatu, Y. Alozie, E.E. Edet, J.I. Ndem and P.E. Ebong

Comparative effect of vitamins A and E on gasoline vapours haematotoxicity, growth-depression and weight-loss was assessed in male Wistar albino rats. The rats were exposed to gasoline vapours (17.8±2.6 $cm^3/h/m^3$/day), 6 h/day, 6 days/week for 20 weeks. Vitamins A (retinol) and E(α-tocopherol) at prophylactic dosage (400 and 200 IU/kg/day, respectively) were orally administered to the rats separately, in the last 2 weeks of exposure. The levels of haemoglobin (Hb), haematocrit or Packed Cell Volume (PCV), Red Blood Cells (RBC), growth-rate and weight-gain in the rats exposed to the vapours were significantly lower ($p<0.05$) compared, respectively to the levels obtained for control rats. On the other hand, the levels of White Blood Cells (WBC) in the test rats were significantly higher ($p<0.05$) compared, respectively with the level obtained for male control rats. These observations indicate that exposure to gasoline vapours may cause haematotoxicity, growth-depression and weight-loss in male rats. However, administration of vitamins A and E was observed to produce a significant recovery ($p<0.05$) in haematotoxicity, growth-depression and weight-loss observed to be associated with exposure to gasoline vapours, although, the rats administered with vitamin E were noted to respond more favourably than those administered with vitamin A. This suggests that although retinol and α-tocopherol may be used to reverse or prevent haematotoxicity, growth-depression and weight-loss in subjects exposed to gasoline vapours, the reversal potency of

α-tocopherol is higher than that of retinol. (*International Journal of Pharmacology 5 (3): 215-221, 2009;* ***doi:*** *10.3923/ijp.2009.215.221*)

Hepatoprotective Activity of *Coccinia grandis* Leaves Against Carbon Tetrachloride Induced Hepatic Injury in Rats

J. Anbu Jeba Sunilson, M. Muthappan, Amitava Das, R. Suraj, R. Varatharajan and P. Promwichit

Coccinia grandis Linn. (Cucurbitaceae) is a perennial branched handsome tendril climber, distributed through out India. It has been used in folk medicine for the treatment of jaundice. The aim of this work was to study the hepatoprotective effect of crude ethanolic and aqueous extracts from the leaves of *C. grandis* against liver damage induced by CCl_4 in rats. The ethanolic extract at an oral dose of 200 mg kg^{-1} exhibited a significant ($p<0.05$) protective effect as shown by lowering serum levels of glutamic oxaloacetic transaminase, glutamic pyruvic transaminase, alkaline phosphatase, total bilirubin and total cholesterol and increasing levels of total protein and albumin levels as compared to silymarin, the positive control. These biochemical observations were supported by histopathological examination of liver sections. The activity may be due to the presence of flavonoid compounds. The extracts showed no signs of acute toxicity up to a dose level of 2000 mg kg^{-1}. Thus it could be concluded that ethanolic extract of *C. grandis* leaves possesses significant hepatoprotective activity. (*International Journal of Pharmacology 5 (3): 222-227, 2009;* ***doi:*** *10.3923/ijp.2009.222.227*)

Evaluating the Antibacterial Activity and *in vivo* Assay of Methanolic Extract of *Stichopus badionotus*

N.S. Mariana, M.A. Norfarrah, K.A.N.I. Nik, F.M. Yusoff and A. Arshad

This study investigated the antibacterial activity of the methanolic extract of the animal to justify its use in traditional medicine. Antimicrobial activity was assayed by disc diffusion method and broth macro dilution method. From the result it appeared that the methanolic extract of *Stichopus badionotus* displayed antibacterial activities against *Staphylococcus aureus*, three non resistant strains and three multiple resistant strains. The Minimum Inhibitory Concentration (MIC) of the extract against non resistant strain values were 3.75 mg mL^{-1} and for resistant strain values 7.50 mg mL^{-1}. Further more, this extract tested on rats in wound infection model justified faster healing rates compared to antibiotics. These

results indicate that the traditional use of these holothurians for the treatment of *S. aureus* infection mainly on resistant strains should be elucidate to bring out the potential antibacterial agent. (*International Journal of Pharmacology 5 (3): 228-231, 2009;* ***doi:*** *10.3923/ijp.2009.228.231*)

Assessment of Inhaler Technique in Patients Attending a Chest Hospital in Riyadh City

M.I. Al-Hassan

The study population consisted of patients diagnosed with Chronic Obstructive Pulmonary Disease (COPD), who were maintained on MDIs. The data was collected through structured questionnaire on demographic data, patient information characteristics and possible factors that might affect proper MDI utilization and scoring system to assess the technique. The results obtained demonstrated defective use of MDIs, which warrants education of the society and public awareness. Health professionals, including pharmacists should be well prepared to train the patients for their correct use. The present study concludes that most patients use the inhalers incorrectly. Thus, education of the society is an important factor that may increase public awareness about medication and therefore improve patient compliance. More studies are needed to assess health professionals' knowledge about use of inhalers and role of pharmacists in teaching patients their proper use. (*International Journal of Pharmacology 5 (3): 232-235, 2009;* ***doi:*** *10.3923/ijp.2009.232.235*)

Anti-Nociceptive Assets of Coral Associated Gastropod, *Drupa margariticola*

C. Chellaram and J.K. Patterson Edward

The extract of gastropod, *Drupa margariticola* tested for their analgesic assets using chemical (acetic acid) induced and hot plate method on Swiss mice model showed promising results. One hundred percent column purified extracts of the *D. margariticola* (25 and 100 mg kg^{-1} p.o.) exhibited significant ($p<0.001$) writhing inhibition of 65 and 78.57%, respectively against acetic acid induced abdominal constrictions. The result of hot plate study, in the difference between the mean reaction time and increased percentage of jump response of test animals in the treated groups, control and standard groups were statistically significant ($p<0.001$). At 30 min, the mean reaction time for extracts (50 mg kg^{-1} p.o.) group was 6.67±1 sec, when compared to control group (2.67±0.52 sec) and

pentazocine treated groups (11.5±1.22 sec) for 100 mg kg^{-1} p.o. These facts suggest that the 100% acetone fraction of the *D. margariticola* was shown the strongest analgesic action. The important results obtained in present study were central and peripheral analgesic activities demonstrated by the inhibitory action on the acetic acid induced writhings and hot plate models. The hot plate method was found to be suitable in the evaluation of centrally acting analgesic action but not for peripherally acting analgesic action. (*International Journal of Pharmacology 5 (3): 236-239, 2009;* ***doi:*** *10.3923/ijp.2009.236.239*)

In vitro Antimicrobial Activity of *Schefflera leucantha*: The Potential of Respiratory Tract and Urinary Tract Infection Treatment

C. Sittiwet, D. Puangpronpitag and N. Niamsa

The antimicrobial activity testing to evaluated the possibility of *S. leucantha* for treatment of nosocomial infection such as respiratory tract and urinary tract infections. The aerial part of *S. leucantha* was extracted using aqueous system with yield of 0.7-1.3% of dried weight of dried plant's powder. The antibacterial activity of *S. leucantha* aqueous extract has been screened using agar diffusion method. The *S. leucantha* aqueous extract showed inhibitory effect on growth of *L. plantarum* ATCC 14917, *E. coli* ATCC 25922, *K. pneumoniae* ATCC 10031 and *P. vulgaris* ATCC 13315. The MICs of *S. leucantha* are in the rage of 8-16 g L^{-1} while MBCs are in the rage of 16-32 g L^{-1}. In conclusion, the aqueous extract of *S. leucantha* showed inhibitory effect on growth of respiratory tract and urinary tract infection bacteria at low concentration. This result may give supporting data of used *S. leucantha* as nosocomial infection treatment. (*International Journal of Pharmacology 5 (3): 240-243, 2009;* ***doi:*** *10.3923/ijp.2009.240.243*)

Fatty Acid Profile, α-Tocopherol Content and Total Antioxidant Activity of Oil Extracted from *Nigella sativa* Seeds

Ghanya Al-Naqeeb, Maznah Ismail and Adel S. Al-Zubairi

Nigella sativa (*N. sativa*) is popularly known as the black seed, a herb that has traditionally been used for centuries in many parts of the world. It has gained popularity due to its potential health benefits. However, more scientific data is needed to support the various health claims. This study was carried out to determine the fatty acid profile, α-tocopherol content and to evaluate the

antioxidant activity of seed oil samples from three different regions in Yemen namely Marib, Sadah and Taiz. *N. sativa* seeds oil was extracted using three different solvents (n-hexane, petroleum ether and chloroform: methanol 2:1 v/v) and the fatty acids composition was analyzed using gas chromatography, while the α-tocopherol was determined using HPLC. Ferric thiocyanate (FTC) and thiobarbituric acid (TBA) methods were used to evaluate the antioxidant activity of the seeds oil. Results indicated that *N. sativa* seeds contain high amount of oil (30-48%) and the major unsaturated fatty acids were linoleic acid (57.96, 58.04 and 57.04%) followed by oleic acid (21.49, 20.87 and 20.60%), while the main saturated fatty acids were palmitic (11.56, 11.23 and 11.22%), followed by stearic and myristic acids in Marib, Taiz and Sadah samples respectively. Oil extracts exhibited strong antioxidant properties when compared to α-tocopherol with 78-82% inhibition in the FTC method and 70-80% in the TBA assays. The oil extracts were found to be rich in α-tocopherol content 290±1.5, 170±0.40 and 120±0.15 mg/100 g, in Marib, Sadah and Taiz samples, respectively. Present results suggest that *N. sativa* seeds contain high amount of antioxidants that are essential for health and preventing numerous diseases. (*International Journal of Pharmacology 5 (4): 244-250, 2009;* ***doi:*** *10.3923/ijp.2009.244.250*)

Studies on the Anti-Inflammatory, Analgesic and Antipyretic Properties of *Andrographis echioides* Nees

S.K. Basu, M. Rupeshkumar and K. Kavitha

The purpose of this investigation was to study the anti-inflammatory, analgesic and anti-pyretic properties of total extract and three fractions (ether, chloroform and ethyl acetate) from *Andrographis echioides* (Acanthaceae) in rats and mice. The plant material was extracted with methanol. In order to estimate the polarity of the active compounds, the total extract was successively partitioned between ether, chloroform and ethyl acetate. Dose of 200 and 400 mg kg^{-1} of each extracts were used in carrageenan-induced paw edema, cotton-pellet granuloma in rats, writhing nociception in mice and yeast induced hyperpyrexia in rats. All compounds reduced paw edema in comparison to the control group at 5 h post carrageenan injection. The total, ether and ethyl acetate extracts were similar to phenylbutazone ($p<0.001$), while the chloroform extract was weaker than phenyl butazone in reduction of paw edema and cotton-pellet granuloma. All extracts as well as Paracetamol induced antinociception in writhing test in comparison to control. Positive results for flavanoids and phenolic compounds were investigated by phytochemical analysis of total extract. Phenolic compounds were found in three fractions. The higher antinociception effects of total and ether extracts among

different extracts tested, might back to the presence of flavanoids and phenolic compounds. The total, ether, ethyl acetate extract produced a significant dose dependent inhibition of temperature elevation. These data suggest that different extracts of *A. echioides* produce antinociceptive, anti-inflammatory and anti-pyretic activities that could be due to the effect of one or a combination of the bio active components in each extract. (*International Journal of Pharmacology 5 (4): 251-256, 2009;* ***doi:*** *10.3923/ijp.2009.251.256*)

Preventive Effect of Grape Seed Hydroalcholic Extract on Dementia Type of Alzheimer's Disease in Aged Male Rats

Y. Farbood, A. Sarkaki and M. Badavi

Aim of this study was to investigate the effects of Grape Seed Extract (GSE), as a potent antioxidant on spatial memory in rats with Alzheimer's Disease (AD). Alzheimer's disease is a progressive neurodegenerative disease clinically characterized by dementia and neurobehavioral deterioration. Forty five aged male wistar rats were divided randomly into three equal number groups (n = 15). Control; AD and GSE+AD. The rat model of Alzheimer's disease was induced by local injection of Ibotenic acid (Ibo) into brain Nucleus Basalis Magnocellularis (NBM) or meynert bilaterally (Ibo, 6 μg μL^{-1} each site) under stereotaxic surgery. The spatial memory performance was evaluated by Morris Water Maze task. The results show that injection of Ibo into NBM of rats could impair spatial memory capacity. The GSE supplementation (100 mg kg^{-1}, by gavages) for 30 days before NBM lesion could be alleviating pre-lesion memory impairment. Present results showed that GSE could be a useful agent to prevent neurodegenerative disorders such as AD. *(International Journal of Pharmacology 5 (4): 257-262, 2009;* ***doi:*** *10.3923/ijp.2009.257.262)*

Antitumoral Effect of *L. inermis* in Mice with EAC

Mehmet Ozaslan, Mehmet Emin Zümrütdal, Kenan Daglıoglu, Ibrahim Halil Kılıc, Işık Didem Karagoz, M.E. Kalender, Muhittin Tuzcu, Omer Colak and Beyhan Cengiz

In recent years, prophylactic usage of natural products and tendency to resort to alternative medicine has increased rapidly. Henna (*Lawsonia* sp.) has been used not only cosmetically but also medicinally in Turkish population. Among the studies of henna's antifungal, anti-microbial, tuberculostatic and antitumoral effects come on the science. In this study, we planned to research the effect of *Lawsonia*

inermis that is an oxidant agent against development of cancer, by constituting peritonitis carcinomatous with Ehrlich ascites cells. The animals were divided to three groups and *Lawsonia inermis* extract and tap water were given to mice for 5 days. After 5 days, all of animals were decapitated by cervical dislocation and their liver tissues were sampled to measure reduced glutathione (GSH) level. Mean Survival Time (MST) and Average Survival Time (AST) were calculated; peritoneal liquid pH was measured; Ehrlich Ascites Carcinoma (EAC) cells were counted with hemocytometer. At the result, the longest life period was detected on the group which was given 10 mg/kg/day *Lawsonia inermis*. In group 2 and 3 which were given *Lawsonia inermis* following to forming Ehrlich ascites carcinoma, total number of cancer cell decreased. The scaled pH levels belonging to group 2 and 3 changed into alkaline compared to that of group1 (pH = 6.2). Glutathione levels of liver tissue were determined to decrease in group 2 and 3 in comparison with group1. In conclusion, *Lawsonia inermis* may lead cells to apoptosis related to deficiency in detoxification of intracellular radicals. (*International Journal of Pharmacology 5 (4): 263-267, 2009;* ***doi:*** *10.3923/ijp.2009.263.267*)

Hepatoprotective Effect of *Enicostemma littorale blume* and *Eclipta alba* During Ethanol Induced Oxidative Stress in Albino Rats

P. Baranisrinivasan, E.K. Elumalai, C. Sivakumar, S. Viviyan Therasa and E. David

The leaves of *Enicostemma littorale blume* (Ens) and *Eclipta alba* (Ecl) have been used for skin infection, antiviral and antibacterial activity in traditional medicine. The present study is aimed at to evaluate the hepato-protective effect of the aqueous leaf extracts of the above two plants during ethanol induced oxidative stress in albino rats. The aqueous leaf extracts of *Enicostemma littorale* and *Eclipta alba* combine (1:1) at dose level of 250 mg kg^{-1} b.wt. were tested for hepato-protective and antioxidant effects during ethanol induced oxidative stress in liver tissue of wistar male albino rats. The degree of hepatoprotection was assessed by measuring the activity levels of the marker enzymes such as serum aspartate transaminase (AST), alanine transaminase (ALT) and alkaline phosphatase (ALP). Free radicals generated lipid peroxidation was assessed by measuring the tissue levels of thiobarbituric acid reacting substances (TBARS) and the activity levels of the tissue antioxidant enzymes such as catalase (CAT), superoxide dismutase (SOD). The ethanol supplemented rats recorded elevated activity levels of serum AST, ALT and ALP revealing ethanol induced hepatotoxicity. The increased levels of TBARS in liver and decreased activity

levels of SOD and CAT in ethanol fed animal's revealed oxidative stress. The aqueous leaf extracts supplementation of Ens+Ecl in 1:1 produced significant hepatoprotection and antioxidative effect during ethanol induced hepatotoxicity. The study can be concluded that the therapeutic effect of aqueous leaf extracts of Ens+Ecl in 1:1 is not only hepatoprotective but also possess significant antioxidant property. (*International Journal of Pharmacology 5 (4): 268-272, 2009;* ***doi:*** *10.3923/ijp.2009.268.272*)

Orthosiphon stamineus Benth. Methanolic Extract Enhances the Anti-Proliferative Effects of Tamoxifen on Human Hormone Dependent Breast Cancer

H.B. Sahib, Z. Ismail, N.H. Othman and A.M.S. Abdul Majid

Estrogen Receptor (ER+) antagonist, Tamoxifen (TMX), is widely used in the treatment of the hormone responsive breast cancer. However, the common occurrence of resistance after prolonged treatment of TMX hampers its effectiveness. *Orthosiphon stamineus* Benth. (OS) is a common herb found in South East Asia and is used traditionally to treat various types of ailments. The aim of this study was to determine whether the methanolic extract of *Orthosiphon stamineus* Benth. (MEOS), that had been proven in previous study to act as anti-angiogenic agents, enhance the anticancer efficacy of ER+ antagonists. In this study methanolic extract of (MEOS) was treated to MCF-7 hormone sensitive breast cancer cell line with the addition of TMX. MEOS showed no significant cytotoxic effect towards MCF-7 when used alone, however when combined with TMX, the anti proliferative activity of the combination increased five fold higher when compared to the anti-proliferative activity of singly treated TMX. The result suggests that MEOS synergistically enhance the activity of TMX against hormone responsive breast cancer cells *in vitro* and may prove to be useful for the treatment of metastatic breast cancer. (*International Journal of Pharmacology 5 (4): 273-276, 2009;* ***doi:*** *10.3923/ijp.2009.273.276*)

α-Glucosidase Inhibitor Activity of *Terminalia* Species

K. Anam, R.M. Widharna and D. Kusrini

Terminalia arjuna, *Terminalia ballerica*, *Terminalia chebula*, *Terminalia catappa*, *Terminalia kaerbachii* and *Terminalia microcarpa* leaves were tested for their α-glucosidase inhibitory activity *in vitro*. The α-glucosidase activity was determined by measuring the p-nitrophenol release from pNPG at 400 nm. *Terminalia kaerbachii* has the highest α-glucosidase inhibitor activity with IC_{50}

value of 0.27±0.17 μg mL^{-1} and is a promising antidiabetic herbal medicine candidate. However, most of the *Terminalia* species are also potential as antidiabetic medicine candidates as the IC_{50} values are approximately 5 μg mL^{-1}, which is near the IC_{50} value of 1-deoxynojirimycin, the reference compound, except for *Terminalia microcarpa*, which has IC_{50} value of 25.15±0.04 μg mL^{-1} (above 21 μg mL^{-1}). From the phytochemical screening, *Terminalia kaerbacchi* contains alkaloids, flavonoids and cathechic tannins, but does not contain saponin, quinon, steroid/terpenoids and gallic tannins. It is estimated that there is a correlation between α-glucosidase inhibitory activity and its phytochemical content. (*International Journal of Pharmacology 5 (4): 277-280, 2009;* ***doi:*** *10.3923/ijp.2009.277.280*)

Anti-Microbial Properties of Clove (*Eugenia caryophyllum* Bullock and Harrison) Aqueous Extract Against Food-Borne Pathogen Bacteria

D. Puangpronpitag, N. Niamsa and C. Sittiwet

Anti-microbial activity of *Eugenia caryophyllum* Bullock and Harrison aqueous extract has been tested against food-borne pathogen bacteria (*S. aureus* ATCC 25923, *S. typhimurium* ATCC 14028 and *E. coli* ATCC 25922), normal flora (*S. epidermidis* ATCC 12228 and *L. plantarum* ATCC 14917) and other pathogen bacteria (*P. vulgaris* ATCC 13315). The agar diffusion susceptibility test revealed inhibition zone of *Eugenia caryophyllum* Bullock and Harrison aqueous extract against *S. aureus* ATCC 25923, *S. typhimurium* ATCC 14028, *E. coli* ATCC 25922, *S. epidermidis* ATCC 12228, *L. plantarum* ATCC 14917 and *P. vulgaris* ATCC 13315. The Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC) were determined by using agar dilution and broth macro-dilution methods. The MIC and MBC of clove against all tested bacteria were in the range of 1 to 4 g L^{-1} and 2 to 8 g L^{-1}, respectively. In conclusion, the aqueous extract of *E. caryophyllum* showed good inhibitory effect on tested food-borne pathogen bacteria. (*International Journal of Pharmacology 5 (4): 281-284, 2009;* ***doi:*** *10.3923/ijp.2009.281.284*)

Antioxidative and Antibacterial Activities of *Pangium edule* Seed Extracts

Fook Yee Chye and Kheng Yuen Sim

Phenolic and alkaloid extracts of *Pangium edule* Reinw (Flacourtiaceae) seed were investigated for their antioxidative activities using DPPH radical scavenging

and β-carotene bleaching assays. The extracts were evaluated for antibacterial activity against *Salmonella typhimurium* and *Listeria monocytogenes*. The acetone extract with higher phenolic content (22.22±0.05 mg GAE g^{-1}) showed the most potent antioxidative activity in both DPPH radical scavenging and β-carotene bleaching assays as compared to other extracts. The phenolic extract seems to have stronger inhibitory against *L. monocytogenes* than *S. typhimurium*. The free phenolic acid extract was found to have the highest Minimum Inhibition Concentration (MIC) among the seed extracts, indicates its weak antibacterial activity against both bacteria. Nevertheless, both tested pathogens were killed at the Minimum Bactericidal Concentration (MBC) of 30.3 and 55.5 mg mL^{-1}, respectively, for the phenolic extracts. Significant correlation ($p<0.05$) was observed between the total phenolic content and its antioxidative activity ($r = 0.878$) as well as antibacterial ($r = 0.840$) activity suggesting that phenolics of the seed extract could be potential sources of natural antioxidant and antibacterial. (*International Journal of Pharmacology 5 (5): 285-297, 2009;* ***doi:*** *10.3923/ijp.2009.285.297*)

In vitro Cytotoxic Activity of *Sargassum thunbergii* and *Dictyopteris divaricata* (Jeju Seaweeds) on the HL-60 Tumour Cell Line

K.N. Kim, Y.M. Ham, J.Y. Moon, M.J. Kim, D.S. Kim, W.J. Lee, N.H. Lee and C.G. Hyun

The cytotoxic activity of a variety of Jeju coastal seaweeds against a panel of tumour cell lines was tested *in vitro* using a calorimetric 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay. Twenty-three extracts were screened against HL-60 (human promyelocytic leukaemia cell line), HT-29 (human colon carcinoma cell line), B16F10 (murine melanoma cell line) and A549 (human lung cancer cell line). The ethyl acetate (EtOAc) extracts of *Sargassum thunbergii* and *Dictyopteris divaricata* showed excellent cytotoxic activity against the HL-60 cell line. Furthermore, the *S. thunbergii* extract also exhibited good cytotoxic activity against the HT-29 and B16F10 cell lines. To explore the mechanisms of cytotoxicity of *S. thunbergii* and *D. divaricata*, we used several measures of apoptosis to determine whether these processes were involved in EtOAc fraction-induced HL-60 cell death. We found that EtOAc fractions induced cell shrinkage, cell membrane blebbing and formation of apoptotic bodies. In addition, HPLC fingerprinting of the *S. thunbergii* extract revealed that fucosterol was a standard component of these fractions. These results suggest that *S. thunbergii* and *D. divaricata* have great potential value as food additives,

medicinal supplements for patients with chronic diseases and preventive agents against cancer. (*International Journal of Pharmacology 5 (5): 298-306, 2009; **doi**: 10.3923/ijp.2009.298.306*)

Diffusion of Sulbactomax and Ceftriaxone into Cerebrospinal Fluid of Meningitis Induced Rat Model

V.K. Dwivedi, M. Chaudhary, A. Soni, J. Yadav, A. Tariq, M.R. Siddiqui, A. Ahmad and P.S. Negi

The present study was to investigate the comparative efficacy of ceftriaxone and a fixed dose combination of ceftriaxone plus sulbactam along with VRP1034 (Sulbactomax) in cerebrospinal fluid (CSF) of meningitis induced rat model. Eighteen rats were divided into three groups of six rats each. Meningitis were induced by MRSA strain (log 10^6cfu mL^{-1}). Group I was infected group; whereas group II and III were ceftriaxone and sulbactomax treated groups. Drugs were analyzed in CSF by high performance liquid chromatography. Some biochemical parameters were studied in infected and treated groups. Present results showed that the mean level of ceftriaxone drug concentration was increased significantly in sulbactomax treated group in comparison to ceftriaxone alone treated group. Glucose level was increased in sulbactomax treated group as compared to ceftriaxone alone treated group. The levels of protein, calcium and phosphorus were significantly lowered in both treated group as compared to infected group. These biochemical parameters were decreased along with increased glucose level in sulbactomax treated group in comparison to ceftriaxone alone treated group. Present findings concluded that sulbactomax enhanced the penetration rate in CSF than ceftriaxone alone due to VRP1034. It plays a therapeutic role in crossing blood brain barrier and helps in prevention of bacterial meningitis infection. (*International Journal of Pharmacology 5 (5): 307-312, 2009; **doi**: 10.3923/ijp.2009.307.312*)

A Randomized Open-Label Comparison of Lamotrigine and Valproate in Patients with Juvenile Myoclonic Epilepsy

S.E.M. Nejad, M.R.A. Nikpour, F. Rahim, S.N. Naghibi and M.A. Bahrammi

The aim of this study was to evaluate the efficacy and tolerability of lamotrigine and valproate in patients with different types of generalized epilepsy characterized by myoclonic seizures as well as compare the efficacy of those two drugs. A pilot, randomized controlled trial analysis of 46 female patients (age 8-30 years) in a

large university hospital. All patients underwent several interictal EEG including routine awake and sleep EEGs. Lamotrigine was started at the dose of 500 mg day^{-1} and was progressively increased to a mean dose of 1500-2000 mg day^{-1} in a time course of 8 weeks. The target maintenance dose for valproate was 800 mg day^{-1} after starting valproate at the dose of 200 mg/12 h. The mean dose was reached within 4 weeks. Out of total 46 patients, 46 (100%) had juvenile myoclonic epilepsy; 43 (93.48%) had tonic-clonic; 5 (11%) had myoclonic absences. In the valproate and lamotrigine groups, there was significant reduction ($p<0.001$, $p<0.001$) in myoclonic seizure and tonic-clonic seizure frequencies. There was no clinically significant difference ($p>0.05$) between the effect of those two drugs that means the lamotrigine and valproate have similar effect in reducing the myoclonic seizure and tonic-clonic seizure frequencies. There was statistically significant effect ($p<0.05$) of those two drugs that means the lamotrigine and valproate also have significant effect in reducing the absences seizure frequency. The results suggest that lamotrigine monotherapy is a possible alternative for valproate among patients with juvenile myoclonic epilepsy who experienced unaccepted side effects or inadequate seizure control with valproate monotherapy. (*International Journal of Pharmacology 5 (5): 313-318, 2009;* ***doi:*** *10.3923/ijp.2009.313.318*)

Evaluation of Preserving Efficacy for Different Cough Syrups Manufactured by Different Pharmaceutical Companies

M. Khanfar, R. Khalil and A. AbuJafal

The aim of the current investigation is to assess the efficacy of different preservatives ingredients of different expectorant cough syrups manufactured by different pharmaceutical companies by comparing the growth of five microorganisms of known quanta of *S. aureus*, *E. coli*, *P. aeruginosa* and *C. albicans*. The microorganisms were inoculated into syrup A (glycerol and propylene glycol), syrup B (propylene glycol and glycerin), syrup C (glycerin, propylene glycol and butyl paraben), syrup D (methyl paraben and probylparaben) and normal saline as a control. All microorganisms were taken from standard stock cultures and incubated for 24 h. Growth of microorganisms into syrup was compared by counting the CFUs from a subculture of inoculated syrup at zero, 3, 6, 12, 24 and 48 h intervals. The data showed that all the combinations of the preservatives in the four studied cough syrups behaved similarly in term of antimicrobial efficiency. The findings suggested that the preservatives mixtures of propylene glycol with glycerol or with glycerin or with butyl paraben preservatives as well as methyl paraben with probylparaben are acceptable clinically and have

considerably antimicrobial activity against infectious bacteria during the 48 h studied period. (*International Journal of Pharmacology 5 (5): 319-322, 2009; **doi:** 10.3923/ijp.2009.319.322*)

Hypoglycaemic and Hypolipidemic Activities of *Rauwolfia serpentina* in Alloxan-Induced Diabetic Rats

S.A. Qureshi, A. Nawaz, S.K. Udani and B. Azmi

The prevalence of diabetes is increasing worldwide. Changes in lipid metabolism are secondary to diabetes, which may become the cause of hypertension, atherosclerosis and other cardiovascular diseases. The present study was designed to investigate the effect of methanolic root extract of *Rauwolfia serpentina* (a known antihypertensive herb) on glucose, total cholesterol (TC), triglycerides (TG) and alanine aminotransferase (ALT). Alloxan-induced diabetic rats were divided in to 3 groups viz., group I: diabetic control treated with 5% dimethyl sulfoxide (DMSO) in distilled water (1 mL kg^{-1}), group II (positive control): diabetic rats treated with known anti-diabetic drug chlorpropamide (20 mg kg^{-1}) and group III (diabetic test): treated with methanolic root extract (30 mg kg^{-1}). Glucose was estimated from each group at 0, 1, 2 and 4 h after intra-peritoneal injection of each treatment by using glucometer. Rats were decapitated at 4 h, blood was collected to separate the serum that used to analyze TC, TG and ALT. There was a significant decrease ($p<0.0001$) found in glucose level from 0 to 4 h (94-106 mg dL^{-1}) in test rats as compared to diabetic control. Similarly, TG ($p<0.01$), TC and ALT ($p<0.05$) were also significantly decrease in test group. The methanolic root extract of *R. serpentina* was found hypoglycaemic, hypolipidemic and hepato-protective in alloxan-induced diabetic rats. (*International Journal of Pharmacology 5 (5): 323-326, 2009; **doi:** 10.3923/ijp.2009.323.326*)

Dextromethorphan Attenuates Ethanol Withdrawal Induced Hyperalgesia in Rats

U.S. Rao Chakradhara and K.S. Karanth

Ethanol withdrawal increases sensitivity to painful stimuli. N-methyl-D-aspartate glutamate receptors may have a role in alcohol dependence and the development of withdrawal signs and symptoms. This study examined the effect of oral administration of dextromethorphan on the hyperalgesia induced by ethanol

withdrawal, using hot plate assay and chemical induced writhing in rats. Wistar albino rats (250-300 g) were divided into three groups of six animals each. All the groups received 7.5% v/v alcohol and food *ad libitum*, for 10 days and were given saline (10 mL kg^{-1}) or dextromethorphan dissolved in saline (32 and 64 mg kg^{-1}) orally once daily for 10 days. Ethanol was withdrawn on day 10. The reaction times on the hot plate were measured on Day 0, at 6, 12 h after ethanol withdrawal. The ethanol withdrawal signs were rated immediately before testing. Chemical assay using acetic acid (1% v/v) was done on day 0 and at 12 h after ethanol withdrawal. Chronic exposure to ethanol produced antinociception while withdrawal produced hyperalgesia. Repeated administration of dextromethorphan prevented ethanol withdrawal induced hyperalgesia and significantly reduced total ethanol withdrawal scores at both the doses tested. This study demonstrated that dextromethorphan can attenuate hyperalgesia during ethanol withdrawal and suggests the role of N-methyl-D-aspartate receptors in ethanol withdrawal induced hyperalgesia. (*International Journal of Pharmacology 5 (5): 327-332, 2009;* ***doi:*** *10.3923/ijp.2009.327.332*)

Comparison of Efficacy of Turmeric and Commercial Curcumin in Immunological Functions and Gene Regulation

A.K. Chakravarty, S.N. Chatterjee, H. Yasmin and T. Mazumder

Curcumin, the active constituent of turmeric possesses anti-cancer, anti-inflammatory and other properties. Earlier we have shown ethanolic extract of turmeric rhizome (ETE) activates murine lymphocytes and induces apoptosis in tumor cells. The present investigation is intended to study comparative efficacy of ETE as used by us and others and commercially available curcumin. The efficacy of these two substances was tested for immunostimulatory, anti-inflammatory and anti-oxidant properties in murine model. The expression of a few genes such as perforin, IL-2, IL-6, TNF-αand iNOS related with these events have also been studied at transcriptional level in T-cells. The ETE promoted cell division and functions of murine lymphocytes like production of NO^{-}, up regulation of perforin, IL-2 and IL-6 genes in course of functional differentiation much better than curcumin. The ETE acts better as anti-inflammatory agent in DTH reaction than curcumin. The better efficacy of ETE over curcumin could be due to presence of other compounds in the total extract than only diferuloylmethane as curcumin. The present study intends to recommend use of turmeric over curcumin whenever possible. (*International Journal of Pharmacology 5 (6): 333-345, 2009;* ***doi:*** *10.3923/ijp.2009.333.345*)

A Study on the Effects of IL-10 in Anti-Thy 1-Induced Glomerulonephritis in Rats

H. Rachmawati, L. Beljaars, C. Reker-Smit, H.I. Bakker, A.M. Van Loenen-Weemaes and K. Poelstra

In the present study, we examined the effects of IL-10 after 24 h in a model of acute glomerulonephritis (GN). One hour after the anti-Thy 1 antibody administration, a single i.v. dose of IL-10 was administered to rats. Normal rats, control nephritic rats and nephritic rats treated with IL-10, were sacrificed 24 h after administration of antibody. Samples of urine, blood and organs were subsequently collected. The effects of IL-10 were studied by quantification of various inflammatory parameters at the protein level after immunohistochemical staining and at the mRNA level by a quantitative real time PCR technique. Nitric oxide and protein content were determined in serum and in 24 h-excreted urine, respectively. The inflammatory parameters were reduced in the IL-10-treated group: in increment in glomerular CD14, ICAM-1 and MMP-13 staining induced by anti-Thy 1 injection was significantly attenuated by IL-10. In contrast, mRNA levels for CD14, IL-1β, TNF-α and MCP-1 were not different between IL-10-treated and control GN groups. In conclusion, a single i.v. dose of IL-10 suppresses the expression of several inflammatory parameters, 24 h after inducing of acute GN but at this time point mRNA levels of all parameters examined were not affected. Although its therapeutic efficacy needs further evaluation, anti-inflammatory effects of this short-lived cytokine can be found one day after its administration. (*International Journal of Pharmacology 5 (6): 346-353, 2009;* ***doi:*** *10.3923/ijp.2009.346.353*)

Antinociceptive Effects of an Ethanolic Extract of *Capparis erythrocarpos* Isert Roots in the Mice Formalin Test

E. Woode, C.A. Danquah, E. Boakye-Gyasi, C. Ansah and G. Ainooson

Antinociceptive effect of an ethanolic extract of *Capparis erythrocarpos* Isert roots (10-300 mg kg^{-1}; p.o.) was evaluated in the mouse formalin test. Morphine (1-10 mg kg^{-1}; i.p.) was used as positive control. The extract dose-dependently reduced pain scores in both phases of formalin-induced nociception with the 100 mg kg^{-1} dose significantly reducing formalin-induced pain by 47.54±5.65 and 80.01±3.77% in the first and second phases, respectively. Naloxone (an opioid antagonist) did not block the antinociceptive effect of the extract in both the neurogenic phase and the inflammatory phase; however, theophylline (an adenosine antagonist) completely blocked the effect in the neurogenic phase and significantly inhibited the effect in the inflammatory phase. These findings

demonstrate that the ethanolic extract of *C. erythrocarpos* roots has both central and peripheral antinociceptive effect with possible involvement of adenosinergic mechanism. (*International Journal of Pharmacology 5 (6): 354-361, 2009; **doi**: 10.3923/ijp.2009.354.361*)

Effects of *Piper sarmentosum* Water Extract on 11-β Hydroxysteroid Dehydrogenase Type 1 Bioactivity in Ovariectomy-Induced Obese Rats

A. Aida Azlina, H.S. Farihah, H.M.S. Qodriyah and M.F. Nur Azlina

The 11β-hydroxysteroid dehydrogenase type 1 (11β-HSD1) convert inactive circulating 11-keto steroids into active glucocorticoids, amplifying local glucocorticoidaction. It is elevated in adipose tissue inobese humans and rodents, suggesting that adipose tissue glucocorticoidexcess may be the causative factor for obesity. This study was conducted to evaluate the effects of *Piper sarmentosum* (PS) water extract and glycyrrhizic acid (GCA) on 11β-HSD1 bioactivity in ovariectomized induced obese rats. Forty-two female *Sprague-Dawley* rats were randomly divided into six groups; four treatments (PS, GCA, CTRL and SHM) and two basal (B-CTRL and B-SHM). All groups underwent ovariectomy excluding SHM and B-SHM which underwent sham operation. Basal groups were sacrificed on the first day of treatment, while ovariectomized groups were given PS extract (0.125 g kg^{-1}), GCA (0.120 g kg^{-1}) and water (CTRL), respectively, while SHM received only water. Blood pressure was measured monthly while body weight weekly. After five months, rats were sacrificed and liver, heart and visceral adipose tissues were taken for analysis. *Piper sarmentosum* (PS) and GCA group showed a significant reduction in enzyme activity but no difference in body weight compared to CTRL group. Meanwhile only the blood pressure in GCA group was significantly higher after three months of treatment as compared to CTRL group but no difference after five months. In conclusion, both PS water extract and GCA have the ability to reduce 11β-HSD1 enzyme activity but only GCA cause an increased in blood pressure. (*International Journal of Pharmacology 5 (6): 362-369, 2009; **doi**: 10.3923/ijp.2009.362.369*)

Screening of Antiangiogenic Activity of Some Tropical Plants by Rat Aorta Ring Assay

A.F.A. Aisha, K.M. Abu-Salah, Y. Darwis and A.M.S. Abdul Majid

Angiogenesis is essential for the growth and metastasis of most solid malignancies. Accordingly, tumor angiogenesis is an important pharmacological target for cancer prevention and treatment. This study was conducted to study antiangiogenic

activity of some tropical plants. Seven plants were extracted successively with n-hexane and methanol to prepare 18 extracts and antiangiogenic properties of the extracts were studied by rat aorta ring assay. Nine extracts showed more than 50% inhibition of the blood vessels outgrowth from the primary tissue explants. The MTT assay was used to study the cytotoxic activities of extracts with more than 50% inhibition. The Human Umbilical Vein Endothelial Cells was used as a test cell line versus two human colon cancer cell lines HCT-116 and HT-29, two human breast cancer cell lines MCF-7 and T47D and one hepatocarcinoma cell line HepG-2. The selectivity index on Human Umbilical Vein Endothelial Cells was calculated. The selectivity index results indicated antiangiogenic activities of three plants *Parkia speciosa*, *Syzygium campanulatum* and *Sandoricum koetjape*. The results presented in this research article make these plants good candidates for further studies to purify the active compounds and to study *in vivo* antiangiogenic activity. (*International Journal of Pharmacology 5 (6): 370-376, 2009;* ***doi:*** *10.3923/ijp.2009.370.376*)

Evaluation of Free Radical Scavenging Activity of *Pandanus odoratissimus*

R. Londonkar and A. Kamble

Pandanus odoratissimus is used in traditional medicinal and it is also famous for its fragency. The present study was performed to evaluate the methanolic effect of *Pandanus odoratissimus* (MEPO) against free radical damage. The antioxidant activity of has MEPO been studied using its ability to scavenging DPPH, Nitric acid, superoxide radicals and hydroxyl radicals. The MEPO shows antioxidant activity by 87.52% reducing the DPPH and 73.55% inhibition of nitric acid. The result also indicates maximum inhibition of superoxide radical's inhibition 74.12 and 78.14% inhibition of hydroxyl radicals. The BHT was used as standard. (*International Journal of Pharmacology 5 (6): 377-380, 2009;* ***doi:*** *10.3923/ijp.2009.377.380*)

Effect of Administration of Fungal Mycotoxin (Gliotoxin) on Clinical and Serobiochemical Parameters in Camels

M.S. Shathele

The main objective of this study was to determine the effect of administration of fungal mycotoxin (Gliotoxin) on clinical and serobiochemical parameters in camels. A bolus of 0.1 μg kg^{-1} b.wt. of gliotoxin was administered intravenously to camels.

The treated camels were lethargic and decreased their appetite from day 3 onwards. The toxin administration decreased the protein and glucose concentration of serum. The increased activity of aspartate amino transferase, gamma glutamyl-transferase, sorbitol dehydrogenase and alkaline phosphatase due to mycotoxin administration was indicative of liver damage. High concentration of urea nitrogen and creatinine in treated animals was a characteristic of renal injury. In conclusion, the gliotoxin is acutely toxic to camels affecting liver and kidney function. (*International Journal of Pharmacology 5 (6): 381-383, 2009;* ***doi:*** *10.3923/ijp.2009.381.383*)

Antiaflatoxigenic Activities of Some Plant Aqueous Extracts Against Aflatoxin-B1 Induced Renal and Cardiac Damage

Azza M. Mohamed and Nadia S. Metwally

The present investigation aims at assessing the antiaflatoxigenic effect of aqueous extracts of some traditional medicinal plants (namely, *Zingiber officinale* Roscoe rhizome, *Cinnamomum zeylanicum* bark, *Trigonella foenum graecum* seeds, *Camellia sinensis* leaves and *Salvia officinalis* leaves) compared to the anticancer drug, methotrexate (MTX) against aflatoxin-B1 (AFB1) induced renal and cardiac damage in rats. The results revealed that administration of AFB1 induces oxidative stress in kidneys of AFB1-treated rats through elevating the level of malondialdehyde (MDA) and depleting the levels of tissue antioxidants, glutathione reductase (GR), glucose-6-phosphate dehydrogenase (G-6-PDH) and vitamin C. The results also showed that aflatoxicosis interfere with the cellular energy supply of rat hearts through its inhibitory action on some markers of energy metabolism indicated by a decrease in glucose and glycogen contents of heart and a reduction in the activities of some glycolytic enzymes, phosphogluco-isomerase (PGI), glyceraldehyde-3-phosphate dehydrogenase (GAPDH) and lactate dehydrogenase (LDH) compared to normal healthy animals. Supplementation of the aqueous extracts of the above mentioned plants, effectively ameliorated the deviation induced in both kidneys and hearts of animals in response to AFB1 administration. This effect was evident through reducing MDA level and releasing the inhibitory effect of AFB1 on the levels of antioxidants in kidneys as well as on the energetic biomarkers in hearts. However, administration of MTX to AFB1-treated rats dramatically amplified the toxic effect of aflatoxicosis induced in both kidneys and hearts, indicated by marked increment in MDA level and decrease in the levels of antioxidants in kidneys of AFB1- MTX group in relation to AFB1-group, also a marked decrease in the bioenergetic markers in hearts of AFB1-MTX treated animals versus AFB1-treated ones was documented. From the

current investigation, it can be concluded that supplementation of the extracts of the different plants presented in this study was beneficial in modulating the alterations induced in kidneys and hearts of rats under the effect of AFB1. (*Journal of Pharmacology and Toxicology 4 (1): 1-16, 2009; **doi:** 10.3923/jpt.2009.1.16*)

Anti-Nociceptive Effects of an Ethanolic Extract of the Whole Plant of *Synedrella nodiflora* (L.) Gaertn in Mice: Involvement of Adenosinergic Mechanisms

E. Woode, P. Amoateng, C. Ansah and M. Duwiejua

This study presents the effect of an ethanolic extract of the whole plant of *Synedrella nodiflora*, a plant used in Ghana for the treatment of epilepsy and pain, in formalin-induced pain and acetic acid-induced writhing assay and the possible mode(s) of action of its analgesic action. For comparison, morphine and diclofenac were used as standard opioid and NSAID respectively. The ethanolic extract (100-1000 mg kg^{-1}; p.o.) and morphine (1-10 mg kg^{-1}; i.p.) dose-dependently decreased both phases of the formalin-induced nociceptive behavior. The antinociceptive effect of *S. nodiflora* (300 mg kg^{-1} p.o.) on the first and second phases of formalin induced pain was significantly blocked by caffeine but not by naloxone. In the acetic acid-induced writhing test, diclofenac and *S. nodiflora* significantly reduced the number of writhes dose dependently. Also, the effect of *S. nodiflora* (300 mg kg^{-1} p.o.) was blocked by caffeine (3 mg kg^{-1} i.p.) but the analgesic effect of diclofenac was enhanced significantly. The observed effects of caffeine on the central and peripheral analgesic effects of *S. nodiflora* in the formalin and acetic acid induced writhing suggest the possible involvement of adenosinergic mechanism(s). (*Journal of Pharmacology and Toxicology 4 (1): 17-29, 2009; **doi:** 10.3923/jpt.2009.17.29*)

Immunotherapy of 347 Volunteer Outpatient Morphine Addicts by Human Therapeutic Morphine Vaccine in Kermanshah Province of Iran

A. Akbarzadeh, D. Norouzian, A. Farhangi, M. Mehrabi, M. Chiani, D. Zare, Z. Saffari, M. Mortazavi and A. Nikdel

The effective constituent of human therapeutic morphine vaccine is morphine-6-succinate-BSA which would be produced by mixed anhydride method. By

injection of 3 doses of vaccine at the interval of 0-30-60 days, humoral immunity would be caused in addicts. In this study 347 morphine addicted volunteers were vaccinated with therapeutic morphine vaccine according to WHO and national vaccination protocol. The variables were doses of vaccine, concentration of anti-morphine antibody, total protein and gamaglobuline. Volunteers were bled and then injected at the interval of 0-30-60 days. All subjects were bled at day 90 and after 1 year, 10% of them were bled randomly. Total protein and gamaglobuline were determined by serum electrophoresis and anti-morphine antibody level was estimated by ELISA. Considered variables were directly correlated with number of injections that were detected on 30 days after the first injection reaching their peak by three months after first injections and were not declined to the baseline by 1 year. All subjects were followed up and monitored for 1 year. The vaccine was well tolerated by addicted volunteers and had no serious drug-related adverse events. Only 1% at the first dose experienced brief post injection twitching and all subjects were immunized. *(Journal of Pharmacology and Toxicology 4 (1): 30-35, 2009; **doi**: 10.3923/jpt.2009.30.35)*

Selective Digestive Decontamination can be an Infection-Prevention Regimen for the Intoxicated Patients

Aysun Yılmazlar, Gürayten Özyurt, Ferda Kahveci and Güher Göral

Selective Digestive Decontamination (SDD) the risk factors for the respiratory tract of the intoxicated patients receiving have never been investigated. Thirty intoxicated patients who were admitted to the intensive care unit are included in this study. The three different methods of SDD were randomly studied: SDD, SDD with systemic Antibiotic Therapy (AT) and only systemic AT were applied to groups of ten patients each. On admission, samples were taken from the oropharynx and trachea before the first administration of SDD and then every three days. In cultures, Gram-negative bacilli (*Pseudomonas aeruginosa*, *Klebsiella pneumoniae*) and Gram-positive cocci (*Staphylococcus aureus*) colonizations were significantly higher in Group SDD+AT and Group AT than Group SDD ($p<0.005$, $p<0.05$). The pulmonary infection and pulmonary consolidation on chest X-rays were significantly more visible in Group SDD+AT and Group AT ($p<0.05$). As a conclusion, SDD is an effective method to prevent intoxicated patients from respiratory system infection. Moreover, SDD can be an infection-prevention regimen in a biological event. *(Journal of Pharmacology and Toxicology 4 (1): 36-40, 2009; **doi**: 10.3923/jpt.2009.36.40)*

Anti-Microbial Activities of *Millingtonia hortensis* Linn. Flowers Essential Oil

Chaiyasit Sittiwet

Millingtonia hortensis Linn. flowers have been extracted for essential oil using vapor distillation with 0.5-2% yield. The essential oil of *M. hortensis* Linn. was tested against various species of bacteria. The agar diffusion susceptibility test showed an inhibitory effect on 6 out of 10 tested strains. The growth of 4 of gram-positive bacteria (*S. aureus* ATCC 25923, *S. epidermidis* ATCC12228, *B. subtilis* ATCC6633 and *L. plantarum* ATCC14917) and 2 of gram negative bacteria (*E. coli* ATCC25922 and *P. vulgaris* ATCC13315) were inhibited by *M. hortensis* Linn. flower essential oil. The MICs (minimal inhibitory concentration) of *M. hortensis* Linn. flower essential oil are 0.5-2 and 1-4 ml L^{-1}, respectively. In this study *M. hortensis* Linn. flower essential oil showed broad spectrum for the anti-microbial activity at low concentration. (*Journal of Pharmacology and Toxicology 4 (1): 41-44, 2009;* ***doi:*** *10.3923/jpt.2009.41.44*)

Glycemic Control and Therapeutic Effect of *Nigella sativa* and *Curcuma longa* on Rats with Streptozotocin-induced Diabetic Hepatopathy

A.M. Mohamed, F.Z. EL-Sharkawy, S.A.A. Ahmed, W.M. Aziz and O.A. Badary

This study investigated the possible antidiabetic role and therapeutic crucial action of two medicinal plants namely *Curcuma longa* L. (Zingiberaceae) rhizome and *Nigella sativa* L. (Ranunculaceae) seeds compared to the currently available antidiabetic drug gliclazide (diamicron) against diabetic complication induced liver injury in rats. Experimental diabetes was induced by a single-dose (40 mg kg^{-1}, intraperitoneally, i.p.) streptozotocin (STZ)-injection and the two studied plants were administered orally (300 mg kg^{-1} b.wt. either each alone or in their synergistic combination) for 30 days commenced 2 weeks after induction of diabetes. The following parameters were measured: blood glucose (marker of hyperglycemia), blood fructosamine, hemoglobin (Hb) and albumin (indices of diabetic protein glycation), hepatic glycolytic enzymes, hexokinase (HK), pyruvate kinase (PK) and lactate dehdrogenase (LDH) as well as hepatic gluconeogenic enzyme, phophoenolpyruvate carboxykinase (PEPCK) (to assess the mechanism (s) of hypoglycemic action of the used plants), hepatic oxidative stress markers,

Nitric Oxide (NO) and malondialdehyde (MDA, marker of lipid peroxidation), hepatic antioxidant markers including superoxide dismutase (SOD), catalase (CAT), glutathione reductase (GR) and reduced glutathione (GSH). Blood alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were also measured as markers of liver function. The results revealed that induction of diabetes induces metabolic disorder and oxidative hepatopathy indicated by the deviation in the above markers in both blood and livers of diabetic rats. Oral administration of either *C. longa* rhizome or *N. sativa* seeds or their synergistic combination successfully modulated the diabetic increase in blood glucose and fructosamine to their normal levels as well as the consequence diabetic decrease in the Hb and albumin levels, indicating their potential antidiabetic and antiglycating abilities. The plants also effectively have beneficial action in up-regulating of hepatic glycolytic enzymes and down regulating the gluconeogenic enzyme which have the major role in diabetic hyperglycemia and this may demonstrate the mechanisms of glycemic control of these plants. Furthermore, ingestion of the current plants effectively modulated hepatic oxidative tissue damage indicated by amelioration of the deterioration occurred in oxidative stress and antioxidants markers in hepatic of diabetic animals and ensured by normalization of liver function blood enzymes activities, confirming their potential antioxidant activity. Supplementation of diabetic animals with gliclazide modulated diabetic induced alteration in most of the above studied markers. These results suggest that either *C. longa* rhizome or *N. sativa* seeds or their synergistic combination have multi-beneficial actions in controlling diabetes and consequence complication induced in liver and may candidate as natural antidiabetic drugs. (*Journal of Pharmacology and Toxicology 4 (2): 45-57, 2009;* ***doi:*** *10.3923/jpt.2009.45.57*)

Dibutylnitrosamine Induces Histopathological Changes in Rat: Possible Protective Effects of Cinnamon Flavonoid Extract

Y.A. Elhassaneen, S.A. Saleh, S.F. El-Abd, M.M. El-Sayed and N.N. El-Nashar

The aim of this study was to investigate the protective role of Cinnamon Flavonoid Extract (CFE) against histopathological changes in albino rats of Wistar strain treated with Dibutylnitrosamine (DBNA) for 12 weeks. The results indicated that rats treated with DBNA recorded decreasing in the total body and liver weights and increasing in spleen and kidney weights with significant values when compared with the control group all over the experiment period 4, 8 and 12 weeks. Addition of CFE by 150 and 300 mg kg^{-1} b.wt./day in the presence of nitrosamine induced significant improvements in all organs weights. Also, DBNA treated group had

histopathological changes on liver through degeneration hyperemia, inflammatory reaction, kidney through hemorrhages renal casts hyperemia, inflammatory reaction and also urinary bladder through papillary hyperplasia with papillary projection formation in the cell layer of the lining epithelium. The co-treatment of CFE with DBNA leads to prevent some of the previous histopathological changes mainly on liver and urinary bladder and secondary on the kidney. It could be concluded that CFE was effective in protecting against DBNA-induced histopathological changes. These results supported present hypothesis that CFE contains several compounds that are able to prevent or inhibit DBNA toxicity. (*Journal of Pharmacology and Toxicology 4 (2): 58-69, 2009;* ***doi:*** *10.3923/jpt.2009.58.69*)

Assessment of Tonica, an Aqueous Herbal Haematinic, in the Modulation of Rat Hepatic Microsomal CYP-Mediated Drug Metabolizing Enzymes: Implications for Drug Interactions

O.N.K. Martey, A. Ocloo, E. Koomson and L.K.N. Okine

The effects of Tonica (TN), an herbal haematinic prepared from the stem barks of *Khaya senegalensis*, *Mitragyna stipulosa* and *Kigelia africana*, on the activities of hepatic microsomal cytochrome P450 (CYP) enzymes were investigated in Sprague-Dawley rats. TN was administered to rats, by oral gavage, at the normal human dose (28 mg/kg/day), 10x and 20x that dose for 6 weeks. Activities of certain hepatic CYP drug-metabolizing enzymes and pentobarbital-induced sleeping time were determined in control and TN-treated animals. There were insignificant ($p>0.05$) increases in the microsomal protein content (3.25-31%) at all doses of TN in a non-dose-dependent fashion. However, there was a general insignificant attenuation of NADPH cytochrome c (P_{450}) reductase activity in TN-treated animals compared to control (8.9-26.1%). p-Nitrophenol hydroxylase (pNPH) activity was insignificantly ($p>0.05$) elevated (14.8-23%) in the TN-treated rats compared to control. The activities of aminopyrine-N-demethylase (AmD) and nitroanisole-O-demethylase (NOD) at the normal and 10x the normal dose of TN were not significantly different from controls, but at 20x the normal dose these enzyme activities were insignificantly ($p>0.05$) elevated above controls (11.7 and 39.8% for AmD and NOD, respectively). Pentobarbital-induced sleeping time in TN pre-treated animals were insignificantly ($p>0.05$) inhibited compared to control (3.7-9.5%). These results suggest that TN by insignificantly elevating certain CYP isozymes may have the potential of modulating the metabolism of substances other than pentobarbital. (*Journal of Pharmacology and Toxicology 4 (2): 70-78, 2009*; ***doi:*** *10.3923/jpt.2009.70.78*)

CNS Activity of Methanol and Acetone Extracts of *Acorus calamus* Leaves in Mice

V. Pandy, N. Jose and H. Subhash

The present study was designed to evaluate CNS depression or analeptic activity of acute oral administration of methanol (ACME) and acetone (ACAE) extracts of *Acorus calamus* leaves in mice. Spontaneous locomotor activity, immobility time using forced swim test, diazepam-induced sleeping time and motor impairment assessment using rotarod were used to assess CNS depression/analeptic activity of ACME and ACAE in mice. The extracts ACME (5, 20 and 50 mg kg^{-1}, p.o.) and ACAE (20 and 50 mg kg^{-1}, p.o.) significantly decreased the spontaneous locomotor activity in dose dependent manner. The acute treatment of ACME and ACAE (5, 20 and 50 mg kg^{-1}, p.o.) significantly increased the immobility time and decreased the swimming behavior. Administration [6 h prior] of ACME (50 mg kg^{-1}, p.o.) and ACAE (20 and 50 mg kg^{-1}, p.o.) significantly potentiated the diazepam (25 mg kg^{-1}, i.p.)-induced sleeping time in mice. These extracts did not induce disturbance in motor coordination. The results of the present research provided evidences that ACME and ACAE may contain psychoactive substances that are CNS depressant in nature. The CNS depression property of these extracts can be utilized for further anticonvulsant research. (*Journal of Pharmacology and Toxicology 4 (2): 79-86, 2009;* ***doi:*** *10.3923/jpt.2009.79.86*)

In vitro Antimicrobial Activity of *Pluchea indica* Aqueous Extract: The Potential for Urinary Tract Infection Treatment

Chaiyasit Sittiwet

The *P. indica* aqueous extract was tested against both gram positive bacteria (*S. aureus* ATCC 25923, *S. epidermidis* ATCC 12228, *M. luteus* ATCC 9341, *B. subtillis* ATCC 6633 and *L. plantarum* ATCC 14917) and gram negative (*E. coli* ATCC25922, *S. typhimurium* ATCC 14028, *K. pneumonia* ATCC 10031, *P. vulgaris* ATCC 13315, *Ps. aeruginosa* ATCC 9721) using agar diffusion susceptibility test. The result showed zone of inhibition against *E. coli* and *K. pneumoniae*. The Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC) are between 1-2 and 4-8 mg L^{-1} respectively. This result show the possibility of using *P. indica* as an alternative therapy in the treatment of urinary tract infections. (*Journal of Pharmacology and Toxicology 4 (2): 87-90, 2009;* ***doi:*** *10.3923/jpt.2009.87.90*)

Anxiogenic-like Effects of a Root Extract of *Sphenocentrum jollyanum* Pierre in Murine Behavioural Models

E. Woode, N. Amidu, William K.B.A. Owiredu, E. Boakye-Gyasi, E.F. Laing, C. Ansah and M. Duwiejua

This study has characterized the effect of an ethanolic extract of roots of *Sphenocentrum jollyanum* (SJE) which are chewed or taken in alcoholic bitters in Ghana for its stimulant effect on the CNS and as an aphrodisiac agent. Four widely used animal models of anxiety: the open field test, elevated plus maze, hole-board and light/dark box were employed. Results were compared qualitatively to those obtained for diazepam and caffeine which served as anxiolytic and anxiogenic drugs, respectively. Acute administration of SJE (100-1000 mg kg^{-1}, p.o.) exhibited anxiety-like effects dose-dependently, which were qualitatively similar to those induced by caffeine (10-100 mg kg^{-1}). Both drugs decreased the number of entries and time spent on the open arms of the elevated-plus maze and increased the number of visits to the corners of the open field. In addition, SJE decreased the number and duration of head dips compared to vehicle-treated mice. Also, the extract exhibited anxiogenic properties in hole-board and light/dark box by significantly decreasing the number of head-dips and the time spent in the dark portion of the light/dark box, respectively. In contrast, diazepam (0.1-1 mg kg^{-1}) exhibited a typical profile of an anxiolytic drug. At all doses tested, SJE produced no motor deficits in animals using the rotarod test but decreased spontaneous locomotor activity in the activity cage apparatus. In conclusion, the results indicate that the root extract of *S. jollyanum* has anxiogenic like effects in mice and thus supports the use of the plant in traditional medicine. (*Journal of Pharmacology and Toxicology 4 (3): 91-106, 2009;* ***doi:*** *10.3923/jpt.2009.91.106*)

Nephrotoxicity Reduction by Ceftriaxone plus Vancomycin (Vancoplus) Reconstituted with VRP 1020 in Blood *of Mus musculus* Mice

Arvind Soni, Manu Chaudhary and Vivek Kumar Dwivedi

The aim of the present study was to evaluated the effect of the VRP 1020 in reconstitution with fixed dose combination of ceftriaxone-vancomycin (Vancoplus). The mice were fed standard pelleted diet and water *ad libitum*. The test room was air conditioned with temperature 23±20°C, humidity 65±5% and with artificial fluorescent light (10-14 h) of light and dark, respectively. Thirty

Mus musculus mice (weighing 30±5 g) were divided into 5 groups containing 6 mice in each group. Group I: control (normal saline), group II: ceftriaxone (28.57 mg kg^{-1} body weight/day) group III: vancomycin (14.2 mg kg^{-1} body weight/day), group IV: ceftriaxone-vancomycin (42.8 mg kg^{-1} body weight/day) and group V: ceftriaxone-vancomycin+VRP 1020 (42.8 mg kg^{-1} body weight/day). Present finding showed that activities of antioxidant enzymes (superoxide dismutase and catalase) and pyridoxal-5-phosphate level (biologically most active co-enzyme of vitamin B_6) were significantly increased along with decreased in lipid peroxidation (malonaldialdehyde) level in vancoplus treated group as compared to ceftriaxone and vancomycin alone and combination of ceftriaxone-vancomycin treated group. Similarly, the levels of extracellular antioxidant (creatinine and uric acid) were found to be significant lowered in vancoplus treated group when compared to ceftriaxone, vancomycin and ceftriaxone-vancomycin treated group. These results indicated that reconstitution of VRP 1020 with fixed dose combination of ceftriaxone-vancomycin protects against ceftriaxone and vancomycin induced nephrotoxicity that improved the activities of free radical scavenging enzymes. (*Journal of Pharmacology and Toxicology 4 (3): 107-116, 2009*; ***doi**: 10.3923/jpt.2009.107.116*)

Anti-Diarrhoeal Activity of *Blighia sapida* (Sapindaceae) in Rats and Mice

S. Antwi, O.N.K. Martey, K. Donkor and L.K. Nii-Ayitey Okine

The anti-diarrhoeal activity of the ethanolic and aqueous extracts of *Blighia sapida* (Sapindaceae) stem bark on castor oil-induced diarrhoea and enteropooling and gastrointestinal motility in rats and mice were investigated. Doses of the ethanolic and aqueous extracts of *B. sapida* (265, 530 and 1060 mg kg^{-1} body weight) or loperamide (3 mg kg^{-1}) were administered (p.o.) to rats and mice 4 h before castor oil challenge and the numbers of diarrheoal defaecations or weight of feacal matter in intestines noted. In another study, animals were administered with charcoal meal or tragacanth and similar doses of extracts (p.o.) or 0.1 mg kg^{-1} atropine (i.p.) or tragacanth administered immediately thereafter and the distance moved by the charcoal meal from the pylorus measured. The results indicate that both extracts of *B. sapida* caused significant ($p<0.001$) dose-dependent inhibitions of the castor oil-induced diarrhoea (39.7-93.2%) and intestinal motility (31.9-77.5%) with the highest dose (1060 mg kg^{-1}) showing inhibitions (70.4-93.2%) comparable to loperamide (89-100%) and atropine (72.8-100%), respectively. However, castor oil-induced enteropooling was significantly ($p<0.05$) inhibited by the ethanolic and aqueous extracts in rats (23.8-25.9 %) and mice (58.4-59.0%) at the highest dose compared to 41.6-46.8% for loperamide. These results

indicate that there were no significant differences between the ethanolic and aqueous extracts of *B. sapida* in the reduction or prevention of castor oil-induced diarrhoea and that *B. sapida* may act through the inhibitions of intestinal motility and enteropooling. (*Journal of Pharmacology and Toxicology 4 (3): 117-125, 2009*; ***doi**: 10.3923/jpt.2009.117.125*)

Effects of Mercury Exposure on Blood Chemistry and Liver Histopathology of Male Rats

Mohammad A.M. Wadaan

The present investigation aimed at evaluating blood chemistry and histological changes in liver of male rats exposed to mercury (20 ppm) in their drinking water for 8 weeks. Body weight was recorded at weekly interval during the exposure period and after 8 weeks, blood was collected for serum analysis and thereafter the animals were sacrificed by cervical dislocation and their liver was collected for histopathological studies. For light microscopy the liver tissue was stained with haematoxylin and eosin. The body weight gain in the mercury exposed animals lagged behind the controls. Almost all blood parameters analyzed in the present study were altered significantly in the mercury exposed animals as compared to the control. The liver tissue was conspicuously damaged and degenerative and necrotic changes were observed in almost every areas of the mercury exposed liver tissue. The blood parameters studied herein may serve as potential serum enzyme biomarkers for mercury-induced hepatotoxicosis which ultimately affects the general health of the animals by inducing alterations in the integrity of the vital organ liver. (*Journal of Pharmacology and Toxicology 4 (3): 126-131, 2009*; ***doi**: 10.3923/jpt.2009.126.131*)

In vitro Evaluation of Lozenges Containing Extracts of Roots of *Zapoteca portoricensis* (FAM: Fabaceae)

C.O. Esimone, P.U. Onuh, N.C. Obitte, M.K. Egege and K.C. Ugoeze

The aim of this research was to formulate *Zapoteca portoricensis* root extract as Lozenges and to evaluate some of their antimicrobial and tablet properties. The root extracts were formulated into Lozenges using either Sodium Carboxy Methyl Cellulose (SCMC) or Carboxy Methyl Cellulose (CMC) as binders. Uniformity of weight, crushing strength, microbial sensitivity and pre-extinction time studies (using *E. coli*, *S. aureus* and *Candida albicans*) were conducted on three Lozenges formulated with either SCMC (Batch A), CMC (Batch B) and a reference standard, Dequadin^{R}, containing dequalinium hydrochloride (Batch C).

Results showed that Batches B and C passed the weight uniformity test. The three batches had mean crushing strengths of 4.86±0.043, 3.9±0.03 and 13.1±0.43 KgF, respectively for A, B and C. *S. aureus* and *Candida albicans* were sensitive to the test lozenges whereas *Escherichia coli* was not. *Candida albicans* was minimally sensitive to the standard lozenge, while *S. aureus* was not. Both the test and the standard samples showed extinction times greater than 30 min. (*Journal of Pharmacology and Toxicology 4 (3): 132-137, 2009*; ***doi:*** *10.3923/jpt.2009.132.137*)

An Evaluation of the Anti-inflammatory, Antipyretic and Antinociceptive Effects of Ficus exasperata (Vahl) Leaf Extract

E. Woode, R.A. Poku, G.K. Ainooson, E. Boakye-Gyasi, W.K.M. Abotsi, T.L. Mensah and A.K. Amoh-Barimah

The hydro alcoholic leaf extract of Ficus exasperata (Vahl) (family Moraceae) (FEE) was evaluated for its antinociceptive, anti-inflammatory and anti-pyretic properties in animal models. The leaf extract (10-300 mg kg^{-1}) showed a dose-dependent anti-inflammatory activity in carrageenan-induced foot oedema in chicks, with an IC_{50} of 46.05±12.3 mg kg^{-1} which was approximately 3.5 times less potent than diclofenac (IC_{50}:13.01±5.28 mg kg^{-1}) and about 130 times less potent than dexamethasone (0.36±0.45 mg kg^{-1}). In the formalin test, the extract showed dose dependent antinociceptive effects in both phases of the formalin test. The role of adenosinergic and opioidergic involvement in the antinociceptive effects was also investigated. While theophylline, a non-selective adenosine receptor antagonist, completely inhibited the antinociceptive effect of the extract, naloxone, an opioid antagonist had very little effect. The extract also showed weak activity in pyrexia induced by baker's yeast. These results suggest antinociceptive as well as anti-inflammatory activities a confirmation of its traditional use. Also, the results show the involvement of adenosinergic pathway in the antinociceptive effects of FEE. (*Journal of Pharmacology and Toxicology 4 (4): 138-151, 2009*; ***doi:*** *10.3923/jpt.2009.138.151*)

Anti Inflammatory, Antinociceptive and Central Nervous System Depressant Activities of Marine Bacterial Extracts

M. Santhana Ramasamy and S. Senthil Kumar

The main objective of this study is to isolate the bacterial strains which are producing biomedicinally relevant secondary metabolites. To achieve this, the ethyl acetate extracts of four marine bacterial strains BR1, PC4, EM13 and EM14 which were isolated from *Balanus amphitrite* (barnacle), *Polyclinum*

constellatum (ascidian) and *Enteromorpha compressa* (Seaweed), respectively subjected to study the anti inflammatory, analgesic and central nervous system depressant activities. Anti inflammatory activity was studied by carragennan induced rat paw edema model. Though the results were significant ($p<0.05$) for all the four bacterial extracts the more effective anti-inflammatory activity was exhibited by EM13 and EM14 (range between 20-59% of inhibition). Interestingly EM13 inhibited early phases, whereas EM14 inhibited the later phases of inflammation. These two extracts produced the same effect on analgesic activity which was studied by using hotplate test. However, the ethyl acetate extracts of EM13 and BR1 showed remarkable reduction in locomotor activity and prolongation of phenobarbitone sodium induced sleeping time that demonstrated the significant CNS depressant activity. The experimental data identified that the strains EM13, EM14 and BR1 contain potential pharmacologically active compounds and suggested that to further isolation and characterization of active principles and phylogenetic identification of the epibiotic bacterial strains. The present study evidenced that the bacteria associated with marine organisms are the potential sources of pharmacologically active natural products. (*Journal of Pharmacology and Toxicology 4 (4): 152-159, 2009*; ***doi:*** *10.3923/jpt.2009.152.159*)

Protective Effect of *Moringa oleifera* Lam. and *Lannea kerstingii* Extracts Against Cadmium and Ethanol-induced Lipid Peroxidation

A. Diallo, K. Eklu-Gadegkeku, T. Mobio, S. Moukha, A. Agbonon, K. Aklikokou, E.E. Creppy and M. Gbeassor

The present study had evaluated the protective effect of hydroalcoholic (50-50: v/v) and aqueous extracts of *L. kerstingii* and *M. oleifera* against lipid peroxidation induced *in vivo* and *in vitro* by either cadmium or ethanol. In a first series of experiments, lipid peroxidation induced *in vitro* by cadmium (5 $\mu g\ mL^{-1}$) is decreased by hydroalcoholic extracts of *M. oleifera* and *L. kerstingii* (100 $\mu g\ mL^{-1}$) by 94% and 50% ($p<0.001$) respectively whereas their aqueous extracts (100 $\mu g\ mL^{-1}$) reduced the cadmium induced lipid peroxidation by 94% ($p<0.001$) and 44% ($p<0.001$) respectively. *In vivo*, the pretreatment with hydroalcoholic extracts of *M. oleifera* and *L. kerstingii* at 1 $g\ kg^{-1}$ b.wt. reduced significantly ethanol-induced lipid peroxidation, in liver, by 53 and 50% ($p<0.001$), respectively. Similar results were found in the kidney even though lipid peroxidation is slightly increased by ethanol in this organ. (*Journal of Pharmacology and Toxicology 4 (4): 160-166, 2009*; ***doi:*** *10.3923/jpt.2009.160.166*)

Hepatoprotective Activity of Aqueous and Methanolic Extracts of *Capparis decidua* Stems Against Carbon Tetrachloride Induced Liver Damage in Rats

S.A. Ali, T.H. Al-Amin, A.H. Mohamed and A.A. Gameel

The aqueous and methanolic extracts of *Capparis decidua* stems locally known as Altoundob were screened for their hepatoprotective activity against CCl_4-induced hepatotoxicity in rats. This plant is used in traditional system medicine in the treatment of jaundice. Yet, no systematic studies on its hepatoprotective activity have been reported. The hepatotoxicity produced by administration of CCl_4 in paraffin oil (1:9 v/v) at a dose of 0.2 mL kg^{-1} for 10 days, was found to be inhibited by simultaneous oral administration of aqueous and methanolic extracts of *C. decidua* stems (200, 400 mg kg^{-1} b.wt.) for 10 days, with evidence of decreased level of serum aspartate amino transferase, alanine amino transferase, alkaline phosphatase and bilirubin. In addition, the concurrent administration of both extracts with CCl_4 for 10 days masked the liver fatty changes induced by the hepatotoxic compound observed in the intoxicated control rats. The results were compared with the hepatoprotective effect of the standard drug silymarin. The preliminary phytochemical screening of the powdered plant showed the presence of alkaloids, flavonoids, tannins, sterols, saponins, cyanogenic glycosides and cumarins as major conistituents of the studied extracts. The results of this study indicated that aqueous and methanolic extracts of *C. decidua* stems could afford a significant protection against Ccl_4-induced hepatotoxicity in rats. (*Journal of Pharmacology and Toxicology 4 (4): 167-172, 2009*; ***doi:*** *10.3923/jpt.2009.167.172*)

Antimicrobial Activity of *Curcuma longa* Aqueous Extract

N. Niamsa and C. Sittiwet

Ethnopharmacological relevance of *Curcuma longa* (Zingiberaceae) is known in many countries. The root of it was widely used as food ingredient and remedy. The present study aim to evaluate the antimicrobial activity of *C. longa* aqueous extract. The antimicrobial test was screened using agar diffusion method. The Minimum Inhibitory Concentration (MIC) were determined using agar dilution and confirm with broth macrodilution methods, while the Minimum Bactericidal Concentration (MBC). The aqueous extract of *C. longa* exhibited antimicrobial activity against *Escherichia coli* ATCC 25922, *Staphylococcus aureus* ATCC25923, *Krebsilla pneumoniae* ATCC 10031 and *Staphylococcus*

epidermidis ATCC 12228 (MIC = 4-16 g L^{-1}; MBC = 16-32 g L^{-1}). In conclusion, the *C. longa* aqueous extract exhibited good antimicrobial activity against some of tested bacteria at low concentration. The results provide promising information for the potential use of *C. longa* aqueous extract in the treatment of infection. (*Journal of Pharmacology and Toxicology 4 (4): 173-177, 2009;* ***doi:*** *10.3923/jpt.2009.173.177*)

Protective Effect of N-acetyl Cysteine and/or Pro Vitamin A against Monosodium Glutamate-Induced Cardiopathy in Rats

Nayira A. Abdel Baky, Azza M. Mohamed and L.M. Faddah

In the present study the prophylactic effects of the antioxidants, β-carotene and/or N-acetyl cysteine (NAC) in ameliorating the metabolic abnormalities and oxidative damage induced cardiopathy under the effect of the flavor enhancers, monosodium glutamate (MSG) toxicity were studied. Animals were divided into 5 groups; G1: normal control, G2: MSG-treated group, Gs 3,4 and 5: animals pretreated with either NAC or β-carotene or their combination prior MSG administration, respectively. The present results revealed that, chronic administration of MSG caused metabolic dysfunction characterized by significant increases in the levels of serum glucose, total lipids, triglycerides (TG), total cholesterol (TCh) and Low Density Lipoprotein (LDL) and a decrease in the high density lipoprotein (HDL), parameters have important role in MSG induced cardiovascular disorders. The adverse effects of MSG may be related to an imbalance between the oxidant and antioxidant systems. This was indicated by marked increased levels of serum nitric oxide (NO) accompanied by pronounced increased level of thiobarbituric acid reactive substances (TBARS, marker of lipid peroxidation) and decreased levels of the antioxidants, L-ascorbic acid, glutathione (GSH), superoxide dismutase (SOD) and catalase (CAT) in cardiac tissue versus normal animals. Significant inhibition in cardiac Na^+/K^+ ATPase with increase in serum activities of creatine phophokinase (CPK) and aspartate aminotransferase (AST) were also observed in MSG treated animals as biomarker enzymes of cardiac tissue damage. This result was supported by myocardial infarction (necrotic lesion) observed by histopathological examination. Administration of either β-carotene or NAC prior MSG injection significantly modulated the alteration in most of the previously mentioned parameters to near their normal levels. Administration of synergistic combination of the these antioxidants showed the most significant effect as it has the ability to restore all of the studied parameters to their normal levels. The biochemical results were supported by the improvement in histological architecture of heart tissue, implicating that these antioxidants either alone or

their combination may protect heart from the harmful effects of cardio-toxic agents. (*Journal of Pharmacology and Toxicology 4 (5): 178-193, 2009*; ***doi:*** *10.3923/jpt.2009.178.193*)

In vitro Study on the Interaction of Caffeine with Gliclazide and Metformin in the Aqueous Media

Mohammad Mohiuddin, A.T.M. Zafrul Azam, Md. Shah Amran and Md. Amjad Hossain

An *in vitro* study of interaction of caffeine with gliclazide and metformin HCl has been studied at room temperature and at different pH. It has been found that caffeine forms stable 1:1 molecular complexes with gliclazide and metformin HCl. The studies have been carried out by various UV spectrophotometric and conductometric methods. Observation of the UV spectra of the two molecules in presence of caffeine has indication that it reacts with the anti-diabetic agents. The conductometric method was used to further ascertain about the nature of interaction and stoichiometries. The Ardon's Spectrophotometric method confirmed the formation of 1:1 molecular complexes and led to calculate the stability constants. It has been observed that the stability constants for caffeine-gliclazide system were higher than that of caffeine-metformin HCl system in all pH conditions. (*Journal of Pharmacology and Toxicology 4 (5): 194-204, 2009*; ***doi:*** *10.3923/jpt.2009.194.204*)

Study on Release Pattern and Potency Status of Ketoprofen Solid Dosage Forms Available in the Pharma-Market of Bangladesh

M.E. Ali, M.A. Salam, M.A. Asad and M. Saifuzzaman

Ketoprofen, a widely used analgesic drug is available in two solid dosage forms in the pharma-market of Bangladesh: enteric-coated tablet and capsule of sustained-release pattern. Seven brands of ketoprofen enteric-coated tablets and four brands of ketoprofen sustained release capsules were studied for their *in vitro* release behavior as well as potency status. From the seven samples of tablets, two brands (KT-03 and KT-07) were found noncompliant in respect of disintegration test in acid stage, whereas all the brands complied with BP (British Pharmacopoeia) specification in buffer stage at pH 6.8. The dissolution study of ketoprofen tablets were carried out in both acid and buffer stages and all the samples satisfied with USP specification in both stages. All of the brands of

ketoprofen capsule also complied with the USP specification. Potency was determined by UV spectroscopic method according to BP. Two brands (KT-03 and KT-07) of tablets were found non-compliant, whereas all the brands of capsules exerted compliance in respect of potency. (*Journal of Pharmacology and Toxicology 4 (5): 205-212, 2009*; ***doi:*** *10.3923/jpt.2009.205.212*)

Effects of Sedative Agent JM-1232(-) ((-)-3-[2-(4-methyl-1-piperazinyl)-2-oxoethyl]-2-phenyl-3,5,6,7-tetrahydrocyclopenta[f]isoindole-1(2H)-one) on the Carotid Arteries of Rats

H. Miki, J. Morita, R. Kato, Y. Ijiri and K. Tanaka

In the present study, we investigate whether JM-1232(-) ((-)-3-[2-(4-methyl-1-piperazinyl)-2-oxoethyl]-2-phenyl-3,5,6,7-tetrahydrocyclopenta[f]isoindole-1(2H)-one) affects vessels directly or indirectly. We examined the effects of JM-1232(-) with several antagonists on rat carotid arteries using the Magnus method. JM-1232 (-) suppressed contraction non-specifically on norepinephrine, potassium chloride and calcium chloride at a high concentration (E_{max}: 10^{-5}-10^{-4} M). There were no significant change in each pretreated group consisting of flumazenil, propranolol, atropine, cimetidine, imetit and N(omega)-nitro-L-arginine methyl ester, whereas a significant suppression was observed ($p<0.05$) in PK11195 (50% inhibition concentration (IC_{50}): 3.2±0.9 ($\times10^{-5}$) M) and diphenhydramine (IC_{50}: 5.6±1.7 ($\times10^{-5}$) M). These results suggest that only a high concentration of JM-1232(-) reacts for carotid artery relaxation directly (EC_{50}: about 10^{-5} M). Thus JM-1232 (-) (less than 10^{-6} M) might not directly induce a vessel relaxation that can cause hypotension. (*Journal of Pharmacology and Toxicology 4 (6): 213-220, 2009*; ***doi:*** *10.3923/jpt.2009.213.220*)

Hepatic Histopathological Abnormalities in Rats Treated Topically with Para-Phenylene Diamine (PPD)

Manuj Kr. Bharali and Karabi Dutta

Drug and chemical mediated hepatotoxicity for wide numbers of chemicals has been recognized. The drug mediated hepatotoxicity and its evaluation is an important aspect in the development of drugs intended for therapeutic usages as well as chemicals used as food and cosmetic additive. Para-Phenylene Diamine (PPD), a widely used chemical in almost all hair dye formulation has been tested for its hepatotoxicity after 30 days continuous topical application in three different

dosages (0, 1, 2 and 3 mg kg^{-1}) in Sprague-Dawley rats. Serum biomarker (ALT, AST and ALP) of liver injury exhibit a dose dependent increases over control animals. Histopathological findings include centrilobular coagulative necrosis, periportal inflammation, fibrinous deposition, hemorrhages and increased accumulation of neutrophils within hepatic parenchyma. The PPD mediated hepatotoxicity is seems to be enhanced by increased accumulation of neutrophils. (*Journal of Pharmacology and Toxicology 4 (6): 221-228, 2009*; ***doi:*** *10.3923/jpt.2009.221.228*)

Quantum Dots Biodistribution in Tissue Organs of Healthy Male and Female Mice

B.A. Ali, X.M. Wang, G.X. Xu, X.F. Zhao, X.T. Lin, X.Y. Zhang and H.B. Niu

Quantum Dots (QDs) are autoflorescence semiconductor nanocrystals that can be used for *in vivo* biomedical imaging. However, we know a little about their *in vivo* distribution in tissue organs and health consequences. The aim of this study was to detect QDs biodistribution in different organs from healthy female and male mice after single intravenous injection at the dose of 2.98 pmol CdSe/CDs/ZnS QDs/mouse for up to 14 day in female and 8 h in male mice. Laser scanning confocal microscope and/or florescence light microscopy was used to detect QDs in different samples. The results revealed that most of QDs were highly accumulated in spleen, liver, lung of treated mice; however, small amount of QDs was detected in kidney. There is no QDs were observed in other organs such as heart of female mice and brain of male mice of treated group. We also didn't find QDs in all samples prepared from control group and blood sample of treated mice at different time points. Effective and rapid (1 h) detection of tissue organs and blood samples using fluorescent imaging of quantum dots was demonstrated. This work was done using a very low dose (2.98 pmol/mouse) of injected Qds. (*Journal of Pharmacology and Toxicology 4 (6): 229-235, 2009*; ***doi:*** *10.3923/jpt.2009.229.235*)

Atropine Sulphate Induced Changes in Uterine, Adrenal, Liver and Thyroid Gland in Female Albino Rats

Madhu M. Patil, Sharangouda J. Patil and Saraswati B. Patil

In the present study, effect of atropine sulphate on uterine cytotoxicity, gravimetric changes, histopathology and biochemical analysis has been evaluated. Three groups of healthy adult female albino rats having six rats in each group were taken.

The rats of groups II and III were administered atropine sulphate at the dose level 0.1 mg and 0.2 mg/100 g b.wt., respectively intraperitoneally everyday between 10:00 and 11:00 am for 30 days. However, the rats of group I (control) were given saline alone. After the experimental periods, the rats were sacrificed and the histopathological study of uteri was performed. The uterine tissue of the rats of group II and III showed marked vascular congestion, epithelial necrosis and fibrous tissue proliferation. The fibrosis was extensive resulting into compression of endometrial glands. Desquamation of glandular epithelium was also observed. Histometric changes observed in uterine parameters like diameter, thickness of myometrium and endometrium and surface epithelial cell height were reduced significantly. Biochemical changes are parallel to the gravimetric changes, the protein and glycogen contents are reduced significantly with respective administration of graded dose of atropine sulphate. Although, the gravimetric analysis of adrenal, liver and thyroid gland were increased significantly due to administration of atropine sulphate. (*Journal of Pharmacology and Toxicology 4 (7): 236-245, 2009*; ***doi:*** *10.3923/jpt.2009.236.245*)

Immunomodulatory Effects of Swainsonine from *Ipomoea carnea* in Healthy Mice

A.O. Latorre, I.M. Hueza, D.P. Mariano-Souza, M. Haraguchi and S.L. Górniak

The objective of this study was to more clearly characterize the immunomodulatory effects of swainsonine and an *Ipomoea carnea* aqueous fraction using two different mouse strains: Swiss outbred mice and C57BL/6 inbred mice. The swainsonine is the main toxic principle found in the *Ipomoea carnea* a poisonous plant native from Brazil and other tropical countries. Many studies have shown that swainsonine promotes biological response modifications in different cell lines, such as increased murine splenic NK lymphocyte activity, improvement of peritoneal macrophage activity and macrophage cytotoxicity against tumor cells. In addition, it is suggested that swainsonine stimulates bone marrow cell proliferation in inbred mice. Therefore, we evaluated in this study the immunomodulatory effects of swainsonine and *I. carnea* aqueous fraction using for this analyses of macrophages activities and histology evaluation of lymphoid organ. Thereby, analyses of peritoneal macrophage activities showed decreased phagocytosis of aqueous fraction-treated Swiss mice and enhancement of both the spreading activity and PMA-induced H_2O_2 production of swainsonine-treated Swiss mice; however, no alterations in these parameters were observed in C57BL/6 mice. In addition, swainsonine and aqueous fraction treatment showed no differences for both Swiss and C57BL/6 mice in the thymus, spleen and bone

marrow evaluations and histological analyses of liver and kidney. In conclusion, a clear difference in swainsonine immunostimulant effect was observed when considering mouse strain, while the use of swainsonine alone did not induce bone marrow cellularity in healthy mice. (*Journal of Pharmacology and Toxicology 4 (7): 246-253, 2009*; ***doi:*** *10.3923/jpt.2009.246.253*)

Sub-Acute Toxicity Study of Fixed Dose Combination of Sulbactomax (Ceftriaxone-Sulbactam) in Swiss Albino Mice and Wistar Rat

A. Tamta and M. Chaudhary

The present study investigated safety/toxicity profile of Sulbactomax (Ceftriaxone-Sulbactam for injection), a fixed dose combination, in *Mus musculus* mice and SD rats at three dose levels, 10, 50 and 150 mg kg^{-1} ranging from asymptomatic to high dose. Sulbactomax was introduced in order to enhance the antimicrobial efficacy and to combat resistance towards beta-lactamase producing bacteria. The combination has been reported to be highly effective as well as synergistic for many resistant strains and carry the potential for its usage in empirical therapy for various bacterial infections. To establish the safety profile of combination, 28 days repeated dose sub-acute toxicity study was conducted on mice and rat (male and female). Various hematological parameters were studied in addition to physiological and biochemical parameters in order to study toxicity profile of Sulbactomax. There were no signs of toxicity observed at any of the dose levels used in this study. Animals from control and different treated groups exhibited normal body weight gain throughout the dosing period of 28 days. No mortality was observed in any of the treatment groups during the course of whole study. Hematological as well as biochemical parameters were unaltered at all three dose levels in Sulbactomax treated rat and mice. From the present study, it can be concluded that Sulbactomax (the fixed dose combination of Ceftriaxone-Sulbactam) is safe even at the dose level which is several folds of the intended human dose. (*Journal of Pharmacology and Toxicology 4 (8): 291-299, 2009*; ***doi:*** *10.3923/jpt.2009.291.299*)

Adaptogenic Activity of *Lagenaria siceraria*: An Experimental Study using Acute Stress Models on Rats

B.V.S. Lakshmi and M. Sudhakar

This study was conducted to evaluate the anti-stress potential of ethanolic extract of fruits of *Lagenaria siceraria* in rats. The present study was to investigate the

influence of forced swimming endurance stress on swimming endurance time, organ weights and changes in biochemical parameters in rats. The purpose of the study was also to investigate the acute heat stress induced changes in biochemical parameters, adrenal gland weight and stress induced perturbations in blood cell counts in albino Wistar rats. These activities were tested at oral doses of 100-400 mg kg^{-1} of the extract using *Withania somnifera* as a standard reference drug. Pretreatment with the extract at different doses significantly ($p<0.05$) ameliorated the stress-induced variations in this biochemical parameters-serum glucose, triglyceride, cholesterol, BUN and cortisol levels, blood cell counts and organ weights in these stress models. The extract treated animals also showed increase in swimming endurance time. This ability of *Lagenaria siceraria* to prolong the swimming time and ameliorate the stress induced changes in both stress models, therefore, suggests an antistress and adaptogenic property. (*Journal of Pharmacology and Toxicology 4 (8): 300-306, 2009*; ***doi:*** *10.3923/jpt.2009.300.306*)

In vitro and *in vivo* Effects of Glipizide and Gliclazide on the Protein Binding, Plasma Concentration and Serum Glucose, Cholesterol and Creatinine Levels of Ibuprofen

Mohammad Abdus Salam, Mohammad Abdullahil Baki, A.T.M. Zafrul Azam, Md. Shah Amran, Farhad Mohammad Amjad, Begum Rokeya and Md. Amjad Hossain

The *in vivo* and *in vitro* study of effects of glipizide and gliclazide on protein binding and plasma concentration of ibuprofen has been conducted by equilibrium dialysis method at physiological temperature (37±0.5)°C and pH (7.4) and the measurements have been done by UV-spectrophotometry. It has been found that the percentage of protein binding of ibuprofen alone was 91% and in 1:1 mixtures with glipizide and gliclazide were 80 and 82%, respectively, at the saturation levels. The binding sites for ibuprofen-gliclazide system were found to be 3.1 and 2.11 and the binding constants were 0.37 and 0.45, respectively. Both glipizide and gliclazide lowered the affinity and percentage of binding of ibuprofen to serum albumin. It has been found that the interaction of glipizide and gliclazide with ibuprofen increased the free drug concentration of ibuprofen in plasma. It has been found that plasma concentration of ibuprofen after oral administration with glipizide and gliclazide is lowered than in the case of ibuprofen alone. On the other hand, it has been found that co-administration of ibuprofen and glipizide reduces blood sugar slightly but gliclazide reduces significantly but the values of cholesterol and creatinine are not lowered in the cases of gliclazide and glipizide in presence of

ibuprofen, rather they are seen to be higher. But the management of cholesterol and creatinine by gliclazide and glipizide are difficult tasks and leads to complications in many cases. It is thus clear that ibuprofen can be safely used in a combination therapy with gliclazide and better affectivity can be achieved. (*Journal of Pharmacology and Toxicology 4 (8): 307-313, 2009*; ***doi**: 10.3923/jpt.2009.307.313*)