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

G. Saravanan and L. Pari

The aim of the present study was to investigate the hypoglycaemic and antihyperglycaemic effect of *Syzygium cumini* (*S. cumini*) bark in diabetic rats. Diabetes was induced in male albino Wistar rats by a single intraperitoneal injection of streptozotocin (45 mg kg^{-1} body weight). An aqueous extract of *S. cumini* bark (SBEt) was administered orally (75, 150 and 300 mg kg^{-1} body weight) for 45 days and changes in blood glucose, urine sugar, food and fluid intakes and body weight were examined in diabetic rats. Glibenclamide was used as a standard reference drug. The levels of blood glucose and urine sugar were increased significantly in diabetic rats. Oral administration of SBEt to diabetic rats led to significantly decreased levels of blood glucose and urine sugar. The effect exerted by the extract at a dose of 300 mg kg^{-1} body weightwas greater than that of doses 75 and 150 mg kg^{-1} body weight. The daily food and fluid intakes were significantly increased while the body weights were significantly reduced in diabetic rats when compared to normal rats. Treatment with SBEt significantly restored the above physiological parameters to near normal in streptozotocin diabetic rats. During oral glucose tolerance test (OGGT), long-term administration of SBEt was able to significantly decrease the blood glucose concentrations at 30, 60, 90 and 120 min when compared to the OGTT pattern of diabetic rats. The effect of SBEt at 300 mg kg^{-1} body weight was better than glibenclamide (600 μg kg^{-1} body weight). These results suggest that SBEt possesses a significant antidiabetic effect by attenuating the above biochemical and physiological alterations in streptozotocin diabetes. Further, our findings revealed the possible therapeutic value of *S. cumini* bark for the better control, management and prevention of diabetes mellitus progression. *(Journal of Pharmacology and Toxicology 3 (1): 1-10, 2008;* ***doi:*** *10.3923/jpt.2008.1.10)*

Molecular Modelling Analysis of the Metabolism of Methimazole

Fazlul Huq

Molecular modelling analyses based on molecular mechanics, semi-empirical (PM3) and DFT (at B3LYP/6-31G* level) calculations show that MET and its major metabolites have LUMO-HOMO energy differences ranging from 4.1 to

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

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

M. Mohamed Essa and P. Subramanian

Effect of *Pongamia pinnata* (an indigenous plant used in Ayurvedic Medicine in India) leaf extract (PPEt) on the levels of circulatory ammonia, urea, lipid peroxidation products such as TBARS (thio barbituric acid reactive substances), HP (hydroperoxides) and liver markers such as bilirubin, AST (aspartate transaminase), ALT (alanine transaminase), ALP (alkaline phosphatase), LDH (Lactate dehydrogenase), Gamma glutamyl-S-transferase (GGT) were studied for its hepatoprotective effect during ammonium chloride induced hyperammonemia. Ammonium chloride treated rats showed a significant increase in the levels of circulatory ammonia, urea, bilirubin, AST, ALT, ALP, LDH, GGT, TBARS and HP. These changes were significantly decreased in PPEt and ammonium chloride treated rats. Our *in vitro* studies have shown that PPEt effectively scavenge reactive oxygen species including superoxide anion, hydroxyl and 1,1-diphenyl-2-picrylhydrazyl (DPPH) radicals. Our results indicate that PPEt offers hepatoprotection by influencing the levels of lipid peroxidation products and liver markers in experimental hyperammonemia and this could be due to its ability to detoxify excess ammonia, urea and creatinine and free radical scavenging property (both *in vitro* and *in vivo*) by means of reducing lipid peroxidation and the presence of natural antioxidants. *(Journal of Pharmacology and Toxicology 3 (1): 20-26, 2008; **doi:** 10.3923/jpt.2008.20.26)*

Molecular Modelling Analysis of the Metabolism of Venlafaxine

Fazlul Huq

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

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

R. Malathi and Patric Gomaz

The methanolic leaves extract of *Tylophora asthmatica* was screened for its toxicological and biochemical effects on rats, because of the traditional healers of India uses this plant as an anti-inflammatory and anti-anaphylactic. The extract was safe in the smaller doses needed to produce a therapeutic effect, (LD_{50} = 223.6 mg kg^{-1} body weight) and had significant toxic effect on the liver at extremely high doses leading to death of the animal. In acute toxicity study (72 h), single dose of the methanolic extract of *Tylophora asthmatica* (META) leaves (50, 100, 200, 500 and 1000 mg kg^{-1} body weight) were given to male rats. Smaller doses of META (50, 100 and 200 mg kg^{-1} body weight) produced no signs of poisonous or death in animals while 500 mg kg^{-1} body weight caused death of two animal and 1000 mg kg^{-1} body weight caused death of four animals within 72 h. The degree of protection was also measured by evaluating biochemical indices like serum AST, ALT, ALP, total protein, albumin, globulin and bilirubin. In addition, sub-chronic administration for 15 days showed a significant ($p<0.05$) increase in the serum ALT, ALP and reduction in total protein, albumin and globulin showing that the plant leaves extract i.e. META has

hepatoprotective effects after prolonged use. These studies demonstrated that the META is (50-200 mg kg^{-1} body weight) safe and did not cause any detrimental effects *in vivo* under the conditions investigated in this study. *(Journal of Pharmacology and Toxicology 3 (1): 34-40, 2008;* ***doi:*** *10.3923/jpt.2008.34.40)*

Molecular Modelling Analysis of the Metabolism of Entecavir

Fazlul Huq

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

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

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

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

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

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

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

Molecular Modelling Analysis of the Metabolism of Terbinafine

Fazlul Huq

Terbinafine (TBN) is an orally active allylamine derivative that has fungicidal activity against dermatocytes and many pathogenic fungi. The drug is extensively metabolized in humans with systemic clearance being dependent primarily on its biotransformation. The five most prominent metabolites found in plasma are N-desmethylterbinafine (DTBN), hydroxyterbinafine (HTBN), N-desmethylhydroxy- terbinafine (DHTBN), carboxyterbinafine (CTBN) and N-desmethylcarboxyterbinafine (DCTBN) that together account for 25% of the total urinary excretion. Four other metabolites are 1-naphthaldehyde (NAL), 1-naphthalenemethanol (NM), 1-naphthanoic acid (NA) and N-desmethylterbinafine aldehyde (DATBN). Molecular modelling analyses based on molecular mechanics, semi-empirical (PM3) and DFT (at B3LYP/6-31G* level) calculations show that TBN and its metabolites have LUMO-HOMO energy differences ranging from 4.22 to 4.73 eV based on from DFT calculations. The values suggest neither TBN nor any of its metabolites would be highly reactive or extremely inert. The molecular surface of TBN and the metabolites DATBN, NAL and DTBN are found to have significant electron-deficient regions so that they may be subject to

nucleophilic attack by glutathione and nucleobases in DNA. DATBN that has been implicated as a possible cause for toxicity of TBN is found to abound most in electron-deficient regions although it has a slightly higher LUMO-HOMO energy difference than NAL. Reaction with glutathione would cause glutathione depletion resulting into oxidative stress and therefore cellular toxicity whereas the oxidation of nucleobases in DNA would cause DNA damage. *(Journal of Pharmacology and Toxicology 3 (2): 64-74, 2008;* ***doi:*** *10.3923/jpt.2008.64.74)*

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

M. Muthulingam

The aim of the present study was to investigate the antihepatotoxic effect of aqueous leaf extract of *Boerhaavia diffusa* (BDEx) on rifampicin induced liver injury. The activities of serum hepatic marker enzymes viz., aspartate aminotransferase (AST, 95.30±2.96), alanine aminotransferase (ALT, 51.27±2.52) and alkaline phosphatase (ALP, 167.04±2.59), levels of bilirubin (0.96±0.01), cholesterol (95.88±3.29) and protein (8.43±0.10) were estimated in control rats. Significant elevation of serum hepatic marker enzymes (AST, 254.59±3.10; ALT, 181.95±2.45; ALP, 316.57±2.35), bilirubin (3.46±0.28) and cholesterol (151.09±1.15) whereas protein (5.28±0.07) level decreased in rats treated with rifampicin (1 g kg^{-1} b. wt. orally one day only). Oral administration of BDEx (250 and 500 mg kg^{-1} b. wt. once daily for 28 days) and silymarin to rifampicin induced liver injury rats caused significantly ($p<0.05$) attenuated the aforementioned parameters. The maximum antihepatotoxic effect against rifampicin induced liver injury was achieved with BDEx 500 mg kg^{-1} b. wt. but doses higher than 500 mg kg^{-1} b. wt. were less effective. These results are compared to the reference hepatoprotective agent silymarin. These results suggest that BDEx possess the antihepatotoxic activity against rifampicin induced liver injury. *(Journal of Pharmacology and Toxicology 3 (2): 75-83, 2008;* ***doi:*** *10.3923/jpt.2008.75.83)*

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

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

In present study, the release profiles of hydrochlorothiazide from polyacrylic acid polymer (carbopol 71G) matrices in hydro-ethanolic media were done. Percent drug released increased with increasing levels of ethanol in the dissolution media,

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

Molecular Modelling Analysis of the Metabolism of Zolpidem

Fazlul Huq

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

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

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

A series of twenty four newly synthesized 1-aroyl-3-aryl-5-hydroxy-5-(2,4-dichloro-5-fluorophenyl) pyrazolines (3) and 1H-3-aryl-5-hydroxy-5-(2,4-dichloro-5-fluorophenyl)-pyrazoles (6) were tested for cytostatic and cytotoxic effects on in a primary three cell line-one dose anticancer assay against NCI-H 460 (Lung), MCF 7(Breast) and SF 268 (CNS). Proliferation of these cancer cell

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

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

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

The effects of graded doses of *Tamarindus indica* pulp extract on the haematological, toxicological and histopathological indices in rats were evaluated. Hematological parameter was determined using micro-hematocrit method and Neubauer hemocytometer counting chamber. The haematological parameters (PCV, WBC, Lymphocytes and Monocytes) of the treated groups showed no significant difference ($p<0.05$) when compared with the control. Although there was a significant increase ($p<0.05$) ($p<0.01$) in the nuetrophils in group 3 and 4 and decrease ($p<0.05$) ($p<0.01$) in eosinophils at group 4 and 5, respectively. There was no fatality recorded in the acute toxicity tests when the animals received 900-4500 mg kg^{-1} body weight of the extract, however the higher doses of the extract (2700-4500 mg kg^{-1} body weight) exhibited some behavioral changes in the rats such as aggressive scratching of the body and mouth part, anorexia, mild restlessness and sensitive to slight sound. There was no significant difference ($p<0.05$) in the toxicological parameters investigated when compared with the control. The gastro intestinal tract revealed no apparent congestion or hemorrhage while the histopathological examination of liver and kidney showed no visible

lesions indicating its non toxic effect to these organs. These results have provided scientific evidence to justify the safety of this plant in tradition medicine. *(Journal of Pharmacology and Toxicology 3 (2): 111-118, 2008;* ***doi:*** *10.3923/jpt.2008.111.118)*

Molecular Modelling Analysis of the Metabolism of Ramelteon

Fazlul Huq

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

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

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

The anticonvulsant effects of the ethanolic flower extract of *Newbouldia leavis* (Bignoniaceae) were studied in mice. Preliminary phytochemical analysis of ethanolic flower extract revealed the presence of cardiac and saponins glycosides, flavonoids, steroids and tannins. The ethanolic flower extract had an intraperitoneal (i.p.) LD_{50} of 1264.9 mg kg^{-1} body weight in mice. Anticonvulsant studies were carried out on pentylenetetrazole (PTZ)-induced and 4-amino pyridine (4-AP)-induced seizures in mice. The results showed that the extract under study possesses slight dose-dependent anticonvulsant activities between 40-60%

(50-200 mg kg^{-1} body weight) protection against PTZ-induced convulsion; and also a dose-dependent delay on the onset of convulsion was observed in 4-AP-induced convulsion in mice ranging from 8.0±0.45 to 11.2±1.31 min (50-200 mg kg^{-1} body weight). The data obtained correlate to the traditional claim of this plant in the treatment of convulsion due to petit mal seizure. *(Journal of Pharmacology and Toxicology 3 (2): 127-133, 2008;* ***doi:*** *10.3923/jpt.2008.127.133)*

Evaluation of Toxicity of *Rhanterium epapposum* in Wistar Rats

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

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

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

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

The effect of different doses of Black caraway (*Carum carvi* L.) oil on the body weights of alloxan-induced diabetic rats was studied. Forty white male albino rats of the Winster strain weighing between 145-240 g were used for this study. Diabetes was induced in the experimental rats with alloxan (70 mg kg^{-1} body weight). Group 1 rats served as the normal control, group 2 served as the caraway control, whereas group 3 rats served as the diabetic control. Groups 4, 5, 6, 7 and 8 were the test groups. All the test groups were administered various doses of the black caraway oil ranging from 5, 10, 20, 40 and 80 mg kg^{-1} body weights,

respectively. Group 2 (the caraway control) rats were administered 10 mg kg^{-1} body weight of black caraway oil. The duration of the experiment was 10 weeks. The weights of the animals in each group were recorded daily throughout the duration of the experiment. The blood glucose levels in the different groups were assayed. The results show that the normal control, the caraway control and the diabetic rats treated with 10 mg kg^{-1} body weight of black caraway oil showed progressive and steady increase in the % mean weekly body weights, while the diabetic untreated rats and the other test groups showed decreasing and alternating increments, respectively in the % mean weekly body weights. The blood glucose level in the 10 mg caraway treatment group was significantly reduced ($p<0.01$) compared to the diabetic control and the other treatment groups. This shows that the black caraway oil increases the % mean weekly body weights of the diabetic/non-diabetic rats at a dose not more than 10 mg kg^{-1} body weight. It can also be inferred that the 10 mg kg^{-1} body weight of caraway oil is the safe dose that can be used in managing Diabetes mellitus. The information obtained from this study would be used in the management of diabetic patients. *(Journal of Pharmacology and Toxicology 3 (2): 141-146, 2008;* ***doi:*** *10.3923/jpt.2008.141.146)*

Molecular Modelling Analysis of the Metabolism of Ambroxol

Fazlul Huq

Ambroxol (AMB) is used to treat acute and chronic bronchitis, bronchiectasia and lung tuberculosis and possesses antioxidant properties. Molecular modelling analyses based on molecular mechanics, semi-empirical (PM3) and DFT (at B3LYP/6-31G* level) calculations show that AMB and its metabolites DHTQ and DBABA have LUMO-HOMO energy differences of 5.11, 5.01 and 4.28 eV, respectively from DFT calculations. The values indicate that AMB and DHTQ would be significantly more inert kinetically than DBABA. The molecular surfaces of AMB, DHTQ and DBABA are found to abound in neutral green regions so that the compounds can undergo lyophilic attack. The molecular surfaces of the three compounds are also found to possess significant amounts of electron-rich (red and yellow) regions so that they may be subject to electrophilic attacks as well. However, the compounds may not undergo significant nucleophilic attacks as their molecular surfaces do not abound in electron-deficient regions. The presence of neutral and electron-rich regions may impart antioxidant properties to AMB and its metabolites. *(Journal of Pharmacology and Toxicology 3 (2): 147-152, 2008;* ***doi:*** *10.3923/jpt.2008.147.152)*

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

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

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

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

The hepatoprotective activity of ethanol (95%) extract of (250 mg kg^{-1}) *Cansjera rheedii* J. Gmelin whole plant was evaluated against paracetamol induced hepatotoxicity by evaluating biochemical parameters such as Serum Glutamate Pyruvate Transaminase (SGPT), Serum Glutamate Oxaloacetate Transaminase (SGOT), Alkaline Phosphatase (ALP), Total bilirubin, Total Protein and Gamma Glutamate Transpeptidase (GGTP). A 10% of liver homogenate was used for estimation of enzyme such as Superoxide Dismutase (SOD), Glutathione S-Transferase (GST), Lipid Peroxidase (LPO) and Glutathione Peroxidase (GPx) for antioxidant study. Treatment of rats with ethanol extract significantly ($p<0.001$)

altered serum marker enzymes and antioxidants level near to normal against paracetamol intoxicated rats. Silymarin (50 mg kg^{-1}, p.o.) used as control. *(Journal of Pharmacology and Toxicology 3 (2): 158-162, 2008; **doi:** 10.3923/jpt.2008.158.162)*

Study of Aspartate Aminotransferase Activity in Intoxified Rat by Cadmium

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

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

Molecular Modelling Analysis of the Metabolism of Rasagiline

Fazlul Huq

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

be low. This may explain why RSG and ADN have little side effects. *(Journal of Pharmacology and Toxicology 3 (2): 168-172, 2008;* ***doi:*** *10.3923/jpt.2008.168.172)*

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

Geetha Surendran and Hassan A.N. El-Fawal

Chemicals, including heavy metals, are of health and ecological concern due to environment release from industrial and agricultural activity. Neurotoxicity is of particular concern because of effects on the developing Nervous System (NS) and contribution to neurodegeneration in later life. A pressing need exists to develop and validate biomarkers of neurotoxicity to monitor those at risk and implement successful intervention strategies. Fischer 344 rats were given one of three documented neurotoxic organometals: trimethyltin (TMT), methylmercury (MeHg) or trimethyl lead (TML) at 16 ppm in the drinking water and compared to water-only controls (n = 8/group). Detection of serum antibodies, IgM and IgG isotypes, against neurofilaments (NF), astrocytic Glial Fibrillary Acidic Protein (GFAP) and Myelin Basic Proteins (MBP) were used as biomarkers of neurotoxicity confirmed by measurement of brain GFAP, a marker of astrogliosis, in rats on day 12 of exposure. While sera from control rats did not have detectable levels of antibodies against neural proteins, sera from rats exposed to all three metals had antibodies, both IgM and IgG, against all neural antigens, with the exception of IgM against MBP which was not detected in sera of MeHg-exposed rats. Serum IgM titers against NF-L and MBP were significantly ($p \leq 0.001$) higher with TML exposure. Serum IgG titers against NF and GFAP were more prevalent and significantly ($p \leq 0.001$) higher in TMT-exposed rats, compared to the other two organometals. This suggests that neurotoxicity was more advanced with TMT, an observation substantiated by greater generalized toxicity indicated by reduced body weight and hyperexcitability after the first week of exposure. Furthermore, anti-GFAP, IgM and IgG, were consistently higher in this group, the only metal of the three, reported to be gliotoxic. Brain GFAP was significantly ($p \leq 0.001$) elevated in hippocampus of rats exposed to TMT or TML and in the cerebellum for those exposed to MeHg. This regional vulnerability of the brain is consistent with the neurotoxicity of these agents. Despite treatment of rats with equivalent levels of oragnaometals in the drinking water and similarities as electrophiles that complex with nucleophilic molecules, other mechanisms underlie their differential neurotoxicity. Proposed mechanism of neurotoxicity and immune activation are

reviewed and discussed. This study further supports the utility of neuroantibody detection as a biomarker of neurotoxicity. *(Journal of Pharmacology and Toxicology 3 (3): 173-189, 2008; **doi:** 10.3923/jpt.2008.173.189)*

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

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The objective of the present study is to evaluate the antioxidant potential of ethanolic extract of *Murraya koenigii* leaf on enzymatic, non enzymatic antioxidants and ultrastructural changes in liver of streptozotocin (STZ) induced diabetic rats. Effect of oral administration of *M. koenigii* leaves extract (200 mg kg^{-1} body weight) on the levels of blood glucose, plasma insulin, glycosylated hemoglobin, Thiobarbituric Acid Reactive Substances (TBARS), hydroperoxides, enzymatic and non-enzymatic antioxidants were estimated in STZ induced diabetic rats. Ultrastructural changes in the liver were also examined. Glibenclamide was used as a standard drug. The elevated levels of blood glucose, glycosylated hemoglobin, TBARS, hydroperoxides and decreased level of insulin observed in diabetic rats were significantly altered after treatment with the *M. koenigii*. The altered enzymatic and non-enzymatic antioxidants in the liver of streptozotocin induced diabetic rats, were restored to near normal levels by treatment with the *M. koenigii* leaves extract. Ultrastructure analysis of the liver of diabetic rat revealed a reduction in the Rough Endoplasmic Reticulum (RER) and swelling of mitochondria in the hepatocytes and these abnormalities were restored to near normal morphology by the treatment of rats with *M. koenigii* leaf extract. Our results suggested that the ethanolic extract of *M. koenigii* possess potent antioxidant properties which may be due to the presence of biologically active ingredients such as carbazole alkaloids, glycosides, triterpenoids and phenolic compounds. Thus the hepatoprotective and antidiabetic properties of *M. koenigii* leaves were probably of its antioxidant property. *(Journal of Pharmacology and Toxicology 3 (3): 190-202, 2008; **doi:** 10.3923/jpt.2008.190.202)*

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

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

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

M. Ayyanar and S. Ignacimuthu

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

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

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

Monitoring Ames Assay on Urine of Clinical Pathology Laboratories Technicians

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Forty urine samples of clinical pathology laboratory technicians were examined for the presence of mutagenic substance in urine. Mutagenic substance in this study was formaldehyde, formaline, hematoxyline-eosin, Xylole and Xyline which are used for smear fixation and staining in clinical pathology laboratories. We used Ames test to determine the mutagenic potential of above mentioned substances. Mutagenicity was evaluated by TA100 strain of *S. typhimurium*. Urine extracts were prepared using XAD-2 resin in column. The resin was then rinsed with Milli-Q water. This procedure eliminates traces of water soluble growth factors (especially histidine) from the resin. Residual water was removed by vacuum aspiration and adsorbed substance were eluted with a mixture of methanol/acetonitrile v/v. After evaporation to dryness with N_2 gas, the residue was dissolved in DMSO to reach 100 to 250 fold concentration and then urine extraction were kept frozen in liquid nitrogen gas until use. Mutagenicity was evaluated in TA100 *Salmonella thyphimurium* tester stain (overnight cultures)

with and without addition of S-9 mix. The results of this study has been shown that 20% of urine samples from technicians of clinical pathology laboratories in Tehran (Iran) were contained mutagen materials. The staff with working history in clinical pathology laboratories may excrete mutagenic compounds in urine. *(Journal of Pharmacology and Toxicology 3 (3): 230-235, 2008;* ***doi:*** *10.3923/jpt.2008.230.235)*

Effect of Chloroquine Sensitive *Plasmodium berghei* in Pregnant Mice

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

Pregnant mice were examined to determine whether or not they transmitted *Plasmodium berghei* to their fetuses. On the 14th day of pregnancy, mice were inoculated with approximately 3×10^6 *P. berghei* infected red blood cells by intraperitoneal injection. The parasitemia in 20 adult females and 145 neonates was assessed using thin blood films fixed with methanol and stained with 10% giemsa solution. The average parasitemia of females at delivery was 7.5%. Malaria parasites were microscopically confirmed in 8 of the 145 neonates. Maternal parasitemia at the time of delivery was not correlated with the incidence of vertical infection (8.71%). Present study showed that this model may be used to examine vertical transmission of malaria. *(Journal of Pharmacology and Toxicology 3 (3): 236-240, 2008;* ***doi:*** *10.3923/jpt.2008.236.240)*

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

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

The aim of this study is evaluate the curative and protective effects of penicillin G in mice poisoned with the lyophilized extract of *Chlorophyllum molybdites*. Fifty Swiss albino mice were divided into 5 groups of 10 mice each. Mice in group 1 were pretreated with penicillin G at 38, 280 IU kg^{-1}, i.p. and then dosed with LD_{99} of *C. molybdites* (741 mg kg^{-1}) i.p., mice in group 2 were dosed with the extract and then treated with penicillin G, while mice in group 3 were dosed with the extract only. Mice in groups 4 and 5 were dosed with penicillin G and physiological saline solution, respectively. The mice were monitored for clinical signs of toxicity, pathological lesions and death over a period of 72 h. The mean time of death in mice from penicillin-treated groups 1 and 2 were compared with

those in the extract-treated group using one-way analysis of variance (ANOVA) and values of $p<0.05$ were considered significant. The result showed a significant reduction in the severity of clinical signs and mortality in penicillin-treated groups 1 and 2 compared to the group dosed with only the extract. There was a significant difference in the mean time of death in mice from groups 1, 2 and 3. However, there was no reduction in the severity of lesions in mice from groups 1 and 2 treated with penicillin G compared with extract-treated group. Therefore, this study has shown that penicillin G has significant curative and protective effects in mice poisoned with the lyophilized extract of *C. molybdites*. This result may prove useful in the treatment of humans and animals suffering from *C. molybdites* poisoning. *(Journal of Pharmacology and Toxicology 3 (3): 241-245, 2008; **doi:** 10.3923/jpt.2008.241.245)*

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

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

to protect the chronic arsenic toxicity during exposure of As in laying hen. *(Journal of Pharmacology and Toxicology 3 (4): 246-253, 2008; **doi:** 10.3923/jpt.2008.246.253)*

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

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

Fifteen plants were screened for *in vivo* antimalarial activity in albino mice. The plants are *Mormodica balsamina*, *Artemisia maciverae*, *Xylopia aethiopica*, *Cyperus articulatus*, *Guiera senegalensis*. *Syzygium aromaticum*, *Zingiber officinale*, *Thonningea sanguinea*, *Sorghum* sp., *Securinega virosa* B, *Chrozophora senegalensis*, *Feretia apodanthera*, *Diospyrous mespiliformis*, *Centaurea perrottetti* and *Acacia nilotica* Del. The petroleum ether, chloroform and methanol extracts from the various parts of the plants were screened for *in vivo* antimalarial activity in mice experimentally infected with *Plasmodium berghei*. Three days after inducing the malaria, the plant extracts were administered intraperitoneally to the mice daily for four days, while chloroquine was used as a standard drug control. Parasitaemia was monitored microscopically in all the groups for four days using thick and thin blood films obtained from tail vein of each mouse. At the end of this study, it was observed that the chloroform extracts of *Artemisia maciverae* (whole plant), *Xylopia aethiopica* (fruits) and *Acacia nilotica* Del (Leaves) have antimalarial activity. The methanol extracts of *Syzygium aromaticum* (cloves) and *Zingiber officinale* (tuber stem) showed slight antimalarial activity, while the rest of the plant extracts earlier listed showed no noticeable activity. These results suggest that many plants used as recipes in ethnomedical preparation for malaria, have no direct antimalarial activity. *(Journal of Pharmacology and Toxicology 3 (4): 254-260, 2008; **doi:** 10.3923/jpt.2008.254.260)*

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

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

This study evaluated the central action of *Waltheria indica* extract. Aqueous ethanolic extract of the plant showed bioactivity in acetic-acid induced stretches

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

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

K. Sri Rama Murthy and Nagamani Kandimalla

Indigenous uses of *Walsura trifoliata* (A. Juss.) Harms. (Meliaceae) bark in different parts of Eastern Ghats of Southern Peninsular India, curing skin allergies, astringency and diarrhoeia is wide spread. The objective of the present study was to evaluate the antimicrobial and phytochemical activity of bark extract against pathogenic microorganisms. Successive petroleum ether, methanol, benzene and aqueous extracts of *Walsura trifoliata* bark were tested for their phytochemical constituents, antibacterial and antifungal activity. The methanol and aqueous extracts were found to be most effective against most of the tested organisms. The present findings significantly conform the uses of *Walsura trifoliata* in the indigenous systems of medicine to treat various diseases like skin allergies, astringency and diarrhoea. *(Journal of Pharmacology and Toxicology 3 (4): 267-271, 2008; **doi:** 10.3923/jpt.2008.267.271)*

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

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The present study aimed to investigate for a possible hepatoprotective activity of *Raphanus sativus* against carbon tetrachloride induced hepatotoxicity beside its toxicity and phytochemistry of the plant. Thirty albino rats were divided into 6

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

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

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

The Mechanism of Cryptolepine-Induced Cell Death

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

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

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

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Bacopa monnieri belonging to family Scrophulariaceae has been used since time immemorial by Ayurvedic medical practitioners in India as brain tonic. In the present clinical trial, efficacy of BacoMind®, an enriched phytochemical composition from *Bacopa monnieri* on cognitive function in children requiring individual education programme was evaluated. Twenty-eight volunteers with Intelligent Quotient between 70-90 were enrolled in the clinical trial. The study was conducted as outpatient procedure in hospital settings with close monitoring. BacoMind® at 225 mg as single oral dose for a duration of four months showed significant change in the baseline value of working memory and short term verbal memory from 5.21±0.32 to 6.38±0.25 ($p \leq 0.05$) and 5.33±0.44 to 6.54±0.35 ($p \leq 0.05$), respectively in 70.83% of study population. Significant improvement

($p \leq 0.05$) was also seen in logical memory, memory related to personal life and also in visual as well as auditory memory. BacoMind® was also found to be well tolerable with no major side effects. The findings of the current study revealed the cognitive enhancing effect of the BacoMind® in children requiring individual education programme. *(Journal of Pharmacology and Toxicology 3 (4): 302-310, 2008; **doi:** 10.3923/jpt.2008.302.310)*

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

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The aim of the present study was to elicit the therapeutic effect of *Andrographis* extract on oxidative stress in aorta as well as liver and kidney of streptozotocin diabetic rats. Aqueous leaf extract of *Andrographis paniculata* (*Andrographis*) [400 mg (kg body weight)$^{-1}$ day^{-1}] was administered to the animals 30 days before diabetes induction and continued for next 6 months after the diabetes induction. There was a significant decrease in the activity of superoxide dismutase (SOD), catalase and glutathione (GSH) in liver and kidney of the diabetic rats. *Andrographis* administration to diabetic rats resulted in increase in the activity of SOD, catalase and GSH both in liver as well as kidneys. The diabetic rats exhibited endothelial dysfunction as it was evident from the loss of vasodilatory response to the acetyl choline (Ach). This vasodilatory response was restored in the diabetic animals treated with *Andrographis*. Based on these observations, we conclude that *Andrographis* reverses the endothelial dysfunction associated with diabetes. This effect appears to be due to its antioxidant properties. *(Journal of Pharmacology and Toxicology 3 (4): 311-317, 2008; **doi:** 10.3923/jpt.2008.311.317)*

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

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

The aqueous leaf extract of *Pterocarpus erinaceus* (Leguminoceae) was investigated for possible antimycotic effect in Sprague dawley rats. The extract was tested against moulds (*Aspergillus niger* and *Aspergillus flavus*) and dermatophytes (*Trichophyton rubrum* and *Microsporum gypseum*). The extract at 20-40 mg kg^{-1} body weight significantly ($p<0.05$) and dose dependently inhibited the growth rate of the moulds and dermatophytes by over 60 and 97%, respectively. In the *in vivo* study, there was also a significant reduction in the

number of dermatophyte spores recovered from the infected sites treated with the extract as compared with the non treated sites. The extract produced no sign of acute toxicity or death when a limit dose of 2 g kg^{-1} body weight was administered orally in rats. Collectively, these results suggest that the extract possess antimycotic effect and appears to be safe when given orally at a limit dose of 2 g kg^{-1} body weight of the rats. This therefore supports the use of *Pterocarpus erinaceus* leaf extract traditionally for the treatment of fungal skin diseases. *(Journal of Pharmacology and Toxicology 3 (4): 318-323, 2008;* ***doi:*** *10.3923/jpt.2008.318.323)*

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

Syamsudin, Soesanto Tjokrosonto, Subagus Wahyuono and Mustofa

The study of *in vivo* antiplasmodial activity and acute toxicity of the active fraction of *Garcinia parvifolia* Miq. has been conducted. The fraction was obtained by maceration of n-hexane extract with methanol. A standard 4-day test on *P. berghei* infected Swiss mice was used to evaluate the *in vivo* antiplasmodial activity after an oral administration of the fraction in series dose of 25 to 200 mg kg^{-1} b.wt. once daily for 4 consecutive days. The *in vivo* antiplasmodial activity was expressed by the dose inhibiting 50% of parasite growth (ED_{50}). Acute toxicity was evaluated in Swiss mice after oral administration of the active fraction in series dose of 2000 to 8000 mg kg^{-1} b.wt. The acute toxicity was expressed by the dose leading 50% deaths (LD_{50}). The results showed that the active fraction of *G. parvifolia* Miq. was active against *P. berghei* in mice with an ED_{50} of 74.45 mg kg^{-1} b.wt. day^{-1}. In addition, the active fraction was also relatively safe as expressed by the LD_{50} of 8000 mg kg^{-1} b.wt. *(Journal of Pharmacology and Toxicology 3 (4): 324-329, 2008;* ***doi:*** *10.3923/jpt.2008.324.329)*

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

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

The effect of crude aqueous suspension of the root of *Hyphaene thebaica* (L.) mart on some indices of liver and kidney function in rats were studied. Sixteen white albino rats of wistar strain were divided into 4 groups of 4 rats each. Groups

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

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

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

depressants and therefore caution needs to be taken in the concomitant administration of *Cryptolepis* and other CNS depressants. *(Journal of Pharmacology and Toxicology 3 (5): 335-343, 2008;* ***doi:*** *10.3923/jpt.2008.335.343)*

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

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The ethanol extract of *Indigofera trita* (EIT) was studied for its antioxidant and hepatoprotective properties. The ethanol extract exhibited potent *in vitro* antioxidant activity as evidenced by the low IC_{50} values in the scavenging of ABTS, DPPH and hydroxyl radical methods. The IC_{50} values obtained were 9.50±0.50 and 19.91±1.73 μg mL^{-1}, respectively for ABTS and DPPH methods. The IC_{50} values obtained for hydroxyl radical scavenging by p-NDA and deoxyribose methods were found to be 104.50±4.50 and 99.00±0.28 μg mL^{-1}, respectively. The treatment with the EIT at 200 and 400 mg kg^{-1} body weight showed a significant and dose dependent decrease in the levels of SGOT, SGPT, ALP and TBARS and significant increase in the levels of albumin, total protein, SOD and catalase, when compared to CCl_4 treated rats. The treatment with EIT exhibited better results than the standard vitamin-E treatment in some of these parameters. Thus, the EIT showed significant antioxidant and hepatoprotective activity. These results were also confirmed by the histological observation. *(Journal of Pharmacology and Toxicology 3 (5): 344-350, 2008;* ***doi:*** *10.3923/jpt.2008.344.350)*

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

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The anticonvulsant effects of the crude flavonoid fraction of the stem bark of *Ficus sycomorus* were studied using the subcutaneous Pentylenetetrazole (PTZ) and Maximal Electroshock Test (MEST) models in mice and chicks respectively. The crude flavonoid fraction exhibited a significant ($p<0.05$) latency in mean onset and mean time of death of convulsed animal with a 20% protection at a dose of 10 mg kg^{-1} body weight i.p. (comparable to Valproic acid at 200 mg kg^{-1}) while it showed a significant ($p<0.05$) and dose dependent maximal protection (83.3%)

in the Maximal Electroshock Test (MEST) at an optimal dose of 20 mg kg^{-1} body weight i.p. (comparable to Phenytoin at 20 mg kg^{-1}). The results obtained supported the claim in the traditional use of the stem bark of the plant in the management of epilepsy. *(Journal of Pharmacology and Toxicology 3 (5): 351-356, 2008; **doi:** 10.3923/jpt.2008.351.356)*

Larvicidal and Anti-Microbial Potentials of *Nymphaea odorata*

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

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

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The current study was designed to scrutinize the putative hepatoprotective potential of the methanolic leaf extract of *Ficus hispida* Linn. (FH) (400 mg kg^{-1} body weight) on cyclophosphamide (CP) elicited oxidative injury in rat liver. CP administration (150 mg kg^{-1} body weight, i.p., twice, in 2 consecutive days) caused liver injury, featuring substantial increase in serum aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), lactate dehydrogenase (LDH), gamma-glutamyl transpeptidase (GGT) and bilirubin levels. In contrast, treatment with FH significantly precluded all these alterations. CP intoxicated rats depicted a remarkable oxidative stress, as evidenced by a significant elevation in lipid peroxidation (LPO) with a concomitant decrease in the GSH activity. These changes were coupled with a marked decline in the activities of enzymic antioxidants [superoxide dismutase (SOD), catalase (CAT), glutathione

peroxidase (GPx), glutathione-S-transferase (GST) and glutathione reductase (GR)] in the liver tissue of CP-administered rats. FH treated rats displayed a significant inhibition of lipid peroxidation (LPO) and augmentation of endogenous antioxidants. Taken together, these findings emphasize the hepatoprotective effect of *F. hispida* leaf extract against CP-induced oxidative liver injury. Hence, *F. hispida* might serve as a promising medicinal herb in complementary chemotherapeutic modalities. *(Journal of Pharmacology and Toxicology 3 (5): 363-372, 2008;* ***doi:*** *10.3923/jpt.2008.363.372)*

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

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Prototype agents such as Acetylcholine (1.0×10^{-9} to 5.0×10^{-9} M), Nor-adrenalin (2.5×10^{-8} to 4.2×10^{-7} M) and Potassium (50 mM) which stimulate different receptor populations in smooth muscle contraction have been examined on the contractility in Rat Vas Deferens (RVD) and Rat Stomach Strip (RSS) in various Physiological Salt Solution (PSS), varying the extra- cellular calcium in the medium shows a reversed sigmoidal curve in both tissues. In Ca^{2+}-free medium, the rat vas deferens contractility diminished rapidly <10 min, but the rat stomach strip, maintained successively diminished and remained stable after 1 h of this treatment. The contractile heights diminished as extracellular Ca^{2+} decreases in the bathing PSS from 1.8 mM Ca^{2+} to 0.9 mM Ca^{2+} and 0.45 mM Ca^{2+} and Ca^{2+}-free medium, (64, 81 and 98.2% in RVD and 31, 68 and 87% in RSS. In Depolarising medium, both tissues looses contractility rapidly less than five minutes in RVS and RSS maintained diminished contractions for over 1 h. The results in this study suggest that the rat stomach strip under the experimental conditions has more intra cellular calcium storage when compared to contractility in rat vas deferens. *(Journal of Pharmacology and Toxicology 3 (5): 373-377, 2008;* ***doi:*** *10.3923/jpt.2008.373.377)*

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

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The antipyretic activity of ethanol (95%) extracts of *Cansjera rheedii* J. Gmelin aerial parts of the plant was evaluated against brewer's yeast-induced pyrexia in rats to assess their antipyretic activity. Rectal temperatures were recorded before

and after inducing pyrexia at interval of one hour to five hours. At the same time parallel experiments were run with a standard antipyretic paracetamol (100 mg kg^{-1}) and control (Normal Saline 5 mL kg^{-1}). Ethanol extract of *Cansjera rheedii* J. Gmelin at dose of 250 mg and 500 mg kg^{-1} body weight showed the antipyretic activity significantly ($p<0.001$) compared to that of control. *(Journal of Pharmacology and Toxicology 3 (5): 378-381, 2008; **doi:** 10.3923/jpt.2008.378.381)*

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

Goudarz Sadeghi-Hashjin and Hovig Manokzadeh

This study was designed to challenge this important issue in healthy animals. The effects of atropine, cyclopentolate and tropicamide was studied on IOP in the rabbit. For this, 12 healthy and adult white New Zealand rabbits were used. Drugs were applied topically once daily for 14 days. IOP was measured using Schiötz tonometer 5 min after surface anesthesia before the instillation of the next dose of the antimuscarinics. Three drops of a 1% concentration was applied on one eye and the other eye served as control and received saline solution only. IOP was increased during the treatment period with a peak value up to 39, 29 and 39% with atropine, cyclopentolate and tropicamide, respectively ($p<0.001$). The IOP was still high one day after cessation of the treatment and returned to the baseline levels 7 days after termination of the treatment. In conclusion, chronic administration of antimuscarinics may lead to a critically increased IOP of normotensive eyes. These agents should be considered serious risks not only for patients with glaucoma, but also for subjects with no ophthalmologic problems. *(Journal of Pharmacology and Toxicology 3 (5): 382-385, 2008; **doi:** 10.3923/jpt.2008.382.385)*

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

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Biocompatibility and preliminary toxicity of a novel gentamicin-loaded monoolein gel (implant) intended for the local treatment of chronic osteomyelitis were

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

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

Moustapha Ouedraogo, Eric Camille Nacoulma, Rasmané Semdé, Issa Touridomon Somé, Innocent Pierre Guissou, Viviane Henschel, Brigitte Evrard, Karim Amighi and Jacques Dubois

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

Protective Effects of Propolis Against the Amitraz Hepatotoxicity in Mice

Attalla Farag El-Kott and Ayman Ahmed Owayss

The present study was aimed to study the protective effects of honeybee propolis against the amitraz hepatotoxicity in mice. Forty-eight male Swiss albino mice of 8 weeks of age, 22 to 25 g body weight was divided into four groups. The 1st was control, the 2nd treated orally with 150 mg kg^{-1} propolis extract, the 3rd treated with 160 mg kg^{-1} amitraz and the 4th one had 160 mg kg^{-1} amitraz +150 mg kg^{-1} propolis extract. These daily treatments lasted for 8 weeks and laboratory assays were measured weekly. Results, after mice sacrificed, histopathology and immunohistology tests were carried out. The obtained results revealed that amitraz had affected liver biochemicals concentrations, whereas propolis led to a significant decrease in these levels in treated group. But, hepatocytes of mice treated with amitraz + propolis demonstrated positive stained nuclei, by using Ki67 immunostaining, less than those of amitraz treated only. The study suggests that propolis ameliorated the recovery of hepatotoxicity of amitraz in the tested mice. *(Journal of Pharmacology and Toxicology 3 (5): 402-408, 2008;* ***doi:*** *10.3923/jpt.2008.402.408)*

Pharmacodynamic Drug Interaction of Metformin with Statins in Rats

N. Anitha, J.V. Rao, S. Kavimani and V. Himabindu,

The present study is aimed to explore the pharmacodynamic interaction of metformin with statins like atorvastatin and rosuvastatin in rats. Wistar albino rats of either sex (150-200 g) were induced diabetes by administering alloxan and they were divided into six groups, each consisting of six rats. Normal control group (1) is treated with 1%w/v carboxy methyl cellulose (CMC) suspension. Group 2 served as diabetic control. To the diabetic 3rd, 4th and 5th group metformin, atorvastatin and rosuvastatin were administered orally respectively for 7 days. The combination of metformin + atorvastatin and metformin + rosuvastatin were administered to the 6th and 7th group of diabetic rats for 7 days. On the last day blood samples were collected, serum was isolated and subjected to glucose, triglycerides (TG), total cholesterol (TC), low density lipoprotein (LDL) and high density lipoprotein (HDL) estimation. Body weight

was also calculated. Metformin significantly reduced the serum glucose level in diabetic rats. Atorvastatin and rosuvastatin produced mild hypoglycemia. On the other hand the combination of metformin + atorvastatin and metformin + rosuvastatin significantly reduced the serum glucose level when compared to metformin alone. Atorvastatin and rosuvastatin significantly reduced the serum TG, TC and LDL and increased HDL level. Metformin also altered the lipid profile of diabetic rats. Whereas the combination of metformin + atorvastatin and metformin + rosuvastatin significantly reduced the lipid profile when compared to atorvastatin and rosuvastatin alone. The combination of drugs also increased the body weight of diabetic animals. The antidiabetic drug metformin enhanced the hypolipidemic activity of atorvastatin and rosuvastatin. Similarly atorvastatin and rosuvastatin enhanced the hypoglycemic activity of metformin due to pharmacodynamic interactions. *(Journal of Pharmacology and Toxicology 3 (5): 409-413, 2008;* ***doi:*** *10.3923/jpt.2008.409.413)*

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

S.M.B. Asdaq, M.N. Inamdar, M. Asad and P.K. Nanjundan

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

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

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A randomized double blind placebo controlled study was designed to evaluate the efficacy and tolerability of BacoMind®, an enriched phytochemical composition from *Bacopa monnieri* on memory improvement upon chronic administration in elderly subjects as memory loss in elderly people is one of the leading health problems worldwide and its uncertain recovery with conventional therapies has paved way to elucidate the use of complementary and alternative system of medicine. Elderly individuals with mini mental state examination score of twenty four and above were enrolled. BacoMind® or placebo was given as a single oral dose of 450 mg daily for the duration of 12 weeks. The combination of well established battery of neuropsychological tests revealed that BacoMind® improved performance in tests associated with attention and verbal memory in elderly participants. Significant interaction effects between group and time were observed in digit span backward test ($p = 0.008$), list learning delayed recall test ($p = 0.014$), paired associates dissimilar delayed recall test ($p = 0.047$) and in visual retention-I test ($p = 0.035$). In conclusion, the study findings suggested that BacoMind® improved the cognitive functions such as attention and verbal memory in elderly individuals and was also found to be well tolerated. *(Journal of Pharmacology and Toxicology 3 (6): 425-434, 2008;* ***doi:*** *10.3923/jpt.2008.425.434)*

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

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Earlier, we have demonstrated that a hydro-alcoholic extract of the stone of *Euterpe oleracea* Mart., commonly known as Açaí, exerts a significant endothelium-dependent vasodilator action *in vitro*. The present study has

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

Anticancerous Effect of *Typhonium flagelliforme* on Human T4-Lymphoblastoid Cell Line CEM-ss

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Typhonium flagelliforme (Lodd.) Blume, commonly known as rodent tuber in Malaysia, is one of the widely used alternative medicines in cancer therapy by South East Asian population. Intake of this plant is common among patients with malignancies especially Leukaemia, breast and cervical cancer; however no data available regarding the possible direct effect of *T. flagelliforme* in these cancers. The purpose of the present study was to investigate the potential *in vitro* cytotoxic effect of leaves and tubers of *T. flagelliforme* extracts against human T4-lymphoblastoid cell line CEM-ss. Among the 8 extracts Dichloromethane and Ethyl acetate extracts of *T. flagelliforme* demonstrated significant anti proliferative effect with a marked level for both leaves (10.8 and 5.8 μg mL^{-1}) and tuber (6.5 and 8.2 μg mL^{-1}), against CEM-ss cells. Considering all the results collectively *T. flagelliforme* appears to be a promising plant demonstrating anti cancer activity, that requires further investigation. *(Journal of Pharmacology and Toxicology 3 (6): 449-456, 2008; **doi:** 10.3923/jpt.2008.449.456)*

The Hepatoprotective Effect of β-Carotene Against Cadmium Toxicity in Rats

S.A. Bashandy and I.M. Alhazza

The present study was carried out to investigate the potential protective effect of β-carotene against cadmium (Cd) induced hepatotoxicity. Male albino rats were used in the present experiments and divided into three groups. First group served as control, second group injected with $CdCl_2$ (sc) at dose level of 2.5 mg kg^{-1} b.wt. and third group injected intramuscularly with β-carotene (10 mg kg^{-1} b.wt.) and $CdCl_2$ (sc). The injections were 3 times weekly for 6 weeks. Results obtained showed that $CdCl_2$ significantly ($p<0.01$) elevated blood hydroperoxide, AST (Aspartate amino transferase), ALT (Alanine amino transferase), ALP(Alkaline Phosphatase), cholesterol and hepatic cadmium levels. The results demonstrated the beneficial influences of β-carotene in reducing the harmful effects of $CdCl_2$. *(Journal of Pharmacology and Toxicology 3 (6): 457-463, 2008;* ***doi:*** *10.3923/jpt.2008.457.463)*

Histological Evaluation of the Rats Testis Following Administration of a Herbal Tea Mixture

M.B. Maina, S.H. Garba and T.W. Jacks

This research was carried out as a preliminary study to determine the histological effect of a herbal tea mixture on the rat testis. A total of 25 adult male albino rats of the Wister strain were used, they were randomly divided into five groups of five rats each. Group I served as control, while rats in groups II-IV were administered 2, 4 and 8 g kg^{-1} body weight of the herbal tea, respectively for 28 days. Rats in group V were administered 8 g kg^{-1} of the herbal tea for 28 days and allowed to stay for 14 days post treatment to observe for reversibility, persistence or delayed occurrence of toxic effects. At the end of the experimental periods, the animals were sacrificed and the weights of the testes recorded, fixed and processed for routine histological technique. Administration of the herbal tea to rats showed a significant increase in body weights, but testicular weights were unaffected. Histological examination of the rat's testis revealed interstitial edema and congestion of blood vessels in the testes of the treated rats. Withdrawal of the herbal tea for 14 days showed a slight degree of recovery in the rats. These findings suggests that the histological organization of the testis can significantly be altered with continuous and increase use of the herbal tea mixture. Further studies to determine the effect of the tea on the morphometry, biometry and hormonal profile of the rat's testes following long term exposure will be useful. *(Journal of*

*Pharmacology and Toxicology 3 (6): 464-470, 2008; **doi:** 10.3923/jpt.2008.464.470)*

Effects of Folic Acid and Vitamin C on Arsenic Induced Mice

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In this study, 5 weeks old mice weighing 22±2 g were grouped in four, each group consisting of six animals. Group-I, II, III and IV of the animals were fed by a standard diet quantity sufficient, normal diet with dissolved arsenic, arsenic with folic acid mixed and arsenic with vitamin C mixed, respectively. Blood was collected from the sacrificed animals and the blood glucose levels were determined by spectrophotometrically and glucometer. The average blood glucose level of arsenic induced animals was 9.37 mmol L^{-1} compared to 6.53 mmol L^{-1} in control animals whereas the blood glucose level of Group-III and Group-IV were 6.73 and 7.03 mmol L^{-1}, respectively. Weight gain of the arsenic induced animals was lower compared to that of the animals fed with normal diet, folic acid mixed diet or vitamin C mixed diet. After sacrifice, the weight of kidney, heart and lung of arsenic induced animals were less than that of the Group-III and Group-IV. The reduction of arsenic induced higher blood glucose level by folic acid and vitamin C demonstrates that folic acid and vitamin C has significant effect in preventing arsenic induced disease. *(Journal of Pharmacology and Toxicology 3 (6): 471-477, 2008; **doi:** 10.3923/jpt.2008.471.477)*

Comparative Effect of Gasoline Vapours on Renal Functions in Male and Female Albino Wistar Rats

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The effect of gasoline vapours (17.8±2.6 $cm^3/h/m^3/day$) on renal functions was assessed from the total kidney weights and the levels of serum creatinine, urea and Blood Urea Nitrogen (BUN) in male and female rats, following 64 days of exposure. The results showed an insignificant ($p>0.05$) increase in percentage kidney weight per total body weight (PKW/BW), decrease in total serum protein and a significant increase ($p<0.05$) in serum creatinine, urea and BUN levels in both male and female test rats, compared respectively with the control. However, the percentage changes in the PKW/BW, serum creatinine and urea levels obtained for female rats were observed to be significantly higher ($p<0.05$), compared to the respective percentage changes obtained for male rats. This observation indicates that frequent exposure to gasoline vapours may cause renal dysfunction in rats, with females at greater risk. *(Journal of Pharmacology and Toxicology 3 (6): 478-484, 2008; **doi:** 10.3923/jpt.2008.478.484)*