

# Toxicol. Int. Vol. 16, No. 2, 2009

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#### **Comparative liver metabolism and toxicity of carbon disulfide influenced by various inducers of P450 isoenzymes in rats**

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#### **Abstract**

The objective of this study was to examine differential metabolism of CS<sub>2</sub> by various hepatic cytochrome P450 (CYP) isoenzymes including CYP1A1, CYP2B1, CYP2E1 and CYP3A2 induced by their selective inducers and to determine if there is a correlation between its metabolic activation and hepatotoxicity. Because 3-methylcholanthrene (3-MC), phenobarbital (PB), isoniazid (INH), and pregnenolone-16 $\alpha$ -carbonitrile (PCN) are typical selective inducers of CYP1A1, CYP2B1, CYP2E1, and CYP3A2, respectively, they were chosen in this study to pretreat male Sprague-Dawley rats for induction of the CYP isoforms. Twenty-four h following the final dose of 3 daily doses of the inducers, rats were treated ip with a single dose of 380 mg/kg of CS<sub>2</sub>. Half of the rats in each group were sacrificed at 3 h after CS<sub>2</sub> treatment to identify inhibited isoenzymes since CS<sub>2</sub> is metabolized by them in a suicide substrate manner. The remaining animals in the group were sacrificed at 24 h following CS<sub>2</sub> treatment to determine hepatic damage using serum ALT activity and liver histopathology as the indices of toxicity. At 3 h after treatment, activities of all CYPs (1A1, 2B1, 2E1 and 3A2) were inhibited by CS<sub>2</sub> significantly and differentially. However, the inhibition of CYP1A1 and CYP3A2 was reversed at 24 h post-treatment with no serious liver damage. On the other hand, the inhibition of CYP2B1 and CYP2E1 was irreversible and accompanied by severe liver damage especially in phenobarbital-pretreated rats. The results of this study suggest that induced CYP2B1 and to a lesser extent CYP2E1 are responsible for the bioactivation of CS<sub>2</sub> and the observed liver damage.

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## **Protein metabolic profiles and histopathological studies in heart tissue of rats during cypermethrin toxicosis**

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### **Abstract**

Cypermethrin is the most widely used Type II pyrethroid pesticide because of its high effectiveness against target species and its low mammalian toxicity reported so far. It is a fast-acting neurotoxin and is known to cause free radical-mediated tissue damage. On exposure to oral sublethal doses (41 mg/kg bw) of cypermethrin as single dose, double dose and multiple dose with 48 h interval the various profiles of protein metabolism were studied in different groups of rat heart tissue. Total proteins showed decrement; whereas free amino acids, the activities of protease, aspartate aminotransferase, alanine aminotransferase and glutamate dehydrogenase and ammonia significantly increased in cypermethrin exposed rats. Urea content increase at all doses of exposure was not statistically significant. Thus variation in the protein metabolic profiles of the rat exposed to cypermethrin indicates its toxic effect on the cellular metabolism thereby leading to impaired protein synthetic machinery is clearly evidenced by histopathological studies.

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## **Single dose neurotoxicity screening studies of insecticide combination (Cypermethrin and Profenofos) in Wistar rats**

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### **Abstract**

The present investigation has been taken up to determine the toxic effects of combination insecticide (Profenofos 40% + Cypermethrin 4% EC) on nervous system of rats. A single oral dose of test substance was administered to five rats per sex at a concentration of 25, 75 and 225mg/kg body weight to experimental animals. The animals were observed under carefully standardized conditions with sufficient frequency to ensure the detection and quantification of behavioral and/or neurologic abnormalities. In addition, serum cholinesterase was estimated after 24 hours of dosing. Motor activity of individual animal was measured using an automated device. Perfused (*in-situ*) nervous tissues were examined microscopically. The test article at the dose level of 75 and 225 mg/kg induced treatment related and dose dependent neurobehavioural alterations in rats of either sex. However, observed alterations were reversible, further no structural/ histopathological alterations were apparent. Single dose of test article at 25 mg/kg did not reveal any toxic signs or neurobehavioral alterations hence, it is considered to be the No Observed Adverse Effect Level (NOAEL).

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## **Treatment of sewage waste water using water hyacinth -**

## ***Eichhornia* sp and its reuse for fish culture**

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### **Abstract**

The absorption of heavy metals like chromium, copper and zinc present in the sewage waste water using aquatic plant, water hyacinth - *Eichhornia* sp were studied. The experimental setup (100% untreated and treated sewage samples) was prepared and the water hyacinth plants were introduced into the tubs. After 96 hrs, sewage samples were analysed and the results showed an active reduction in physicochemical parameters and heavy metals. The biotreated sample was reused for Aquaculture of fish - *Tilapia mossambica* for a period of 60 days. The growth study was carried out and the maximum growth was recorded in biotreated samples. After the growth study, the histology procedures were carried out on the target organs such as brain, gills, liver and muscles. The histology and histopathology results revealed the degeneration of nerve cells, fusion of secondary lamella of gills, vacuolization of hepatocytes, swelling and longitudinal splitting of muscle fibres were seen in 100% untreated and treated sample but the 100% biountreated and biotreated sample resembled as like control animals.

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## **Toxicity studies on a Unani herbal formulation “Capsule Hudar” in albino rats**

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### **Abstract**

Capsule Hudar, a very effective compound formulation of Unani System of Medicine, contains Azraqi (*Strychnos nux vomica*) a deadly poison as one of its constituents. However, it (*Strychnos nux vomica*) is detoxified, using a classical crude method, before its use to prepare the drug. Results on the evaluation of the drug at dose rate of 5 mg/kg body weight, orally as aqueous extract for 60 days in either sex for its toxicity in Wistar albino rats (150 ± 10g body weight) did not show any significant change in the blood glucose, blood urea and blood urea nitrogen and serum albumin and proteins levels. The activities of GOT/GPT and ACP/ALP levels in serum, brain, kidney, liver and spleen were also not significantly different when compared to controls.

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## **Phenotypic alterations and cytokine expression by cadmium in murine lymphocytes: An *in vitro* and *in vivo* study**

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### Abstract

Cadmium (Cd) a potent immunotoxicant causes oxidative stress and apoptosis in murine lymphocytes. In the present study, an *in vitro* and *in vivo* experiment was planned, to understand the effect of Cd on splenic (CD3 and CD19) and thymic (CD4<sup>+</sup> and CD8<sup>+</sup>) cell population and cytokine (IFN-g and IL-2) released, a function of CH4<sup>+</sup> cells. Around 1.5 fold loss in T and B cell population *in vivo*, corresponded to *in vitro* data of 25 µM Cd. The cytokine data of 25 µM Cd corroborated with altered T-phenotypes (lowered CD4<sup>+</sup> cells) and is comparable to the 72 h data of Cd *in vivo*. The above results further elucidate the immunotoxic potential of Cd and dose effect relationship can be established. Since the *in vitro* data with 25 µM Cd are similar to the 72 h effect of Cd *in vivo*, detailed *in vitro* studies may be an alternate to animal models for delineation of Cd induced immunotoxicity.

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## Impact of di-n-butyl phthalate on haematology and biochemistry of albino rat

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### Abstract

Di-n-butyl phthalate is a low volatile chemical added to plastic, paint, glue, hair spray, toys and household products. Human being and animal are exposed to di-n-butyl phthalate through air, water and food contamination in the environment. For present study, a group of six infection free rats were acclimatized under laboratory condition and divided into two groups three in each. Group I (control) albino rat fed commercial feed with corn oil. Group II albino rats were given 50mg/kg/day di-n-butyl phthalate with corn oil for 2 weeks. The study revealed that haemoglobin gm%, RBC and lymphocytes were decreased, 14.6% to 7.8%, 6.17-4.19millions/cmm and 78 to 44% respectively. However, number of neutrophils were increased. A significant decrease in cholesterol level (121- 51 mg/dl), protein (10 to 4.6 gm/dl) and glucose was observed in di-n-butyl phthalate exposed rats.

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## Embryotoxic and teratogenic evaluation of cyfluthrin in Swiss albino mice

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### Abstract

Pesticides are known for their toxicity on the mammalian systems including the embryonal development. Cyfluthrin (trade name: Baygon, Solfac) is used commonly in almost every household in India. It is reported to be neurotoxic, hepatotoxic and haematotoxic in rats and to cause miscarriages and resorptions in pregnant

rabbits. It was therefore planned to assess its teratogenic potential in Swiss albino mice. Pregnant dams were orally administered two doses of the insecticide (16 mg/kg and 32 mg/kg body weight) during the organogenetic phase i.e. days 5-14 of gestation. There occurred a dose related decrease in the weight gained by the females during the gestation period. The higher dose affected the litter size, number of live fetuses, resorptions and the average fetal weight significantly. The fetal anomalies observed were reduced ossification of the skull bones and phalanges and widened cranial sutures.

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## **Biodegradation of selected insecticides by *Bacillus* and *Pseudomonas* sps in ground nut fields**

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### **Abstract**

Bacterial cultures isolated by selective enrichment technique were identified as species of *Bacillus* and *Pseudomonas*. These isolates were tested for their ability to degrade the respective insecticides in mineral salts medium. Within 7 days of incubation, nearly 75% of chlorpyrifos and phorate and 50% of dichlorvos, methyl parathion and methomyl were degraded by cultures of soil bacteria. Qualitative analysis of chlorpyrifos and methyl parathion residues by gas chromatography revealed the formation of one unidentified metabolite in inoculated samples. Whereas no metabolite formation was detected in case of other insecticides inoculated samples. Moreover, dichlorvos and phorate were completely degraded by soil isolates at the end of 14 days. Order of microbial degradation of selected insecticides in the present experiment is as follows: phorate > dichlorvos > methyl parathion > chlorpyrifos > methomyl.

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## **Studies on organochlorine pesticide residues in butter in Punjab**

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### **Abstract**

The present study was conducted to investigate the magnitude of contamination of butter with pesticide residues in Punjab. Organochlorine pesticide residues were analyzed in twenty eight samples of commercially available butter brands and of home made butter collected from various parts of Punjab. The estimation was carried out by using multi residue analytical technique employing GC-ECD. All the samples of butter showed detectable residues of one or more organochlorine pesticides such as DDT, HCH, endosulphan and aldrin. The range of levels of SHCH residues was 0.092- 0.645 mg kg<sup>-1</sup>. Mean a, b- and g- and d- HCH residue concentration in butter was 0.098, 0.048, 0.196 and 0.01 mg kg<sup>-1</sup>, respectively. The range of levels of S DDT residues in butter was BDL - 0.469 mg kg<sup>-1</sup>. Mean concentration of p,p' SDDD, p,p'-DDE and p,p'-DDT was 0.142, 0.114 and 0.022 mg kg<sup>-1</sup> respectively. All samples of butter had SDDT residues below MRL of 1.25 ppm but 53 per cent butter samples had gamma-HCH residues more than MRL of 0.2 ppm as prescribed by PFA in India.

## **A study on free radical-induced renal toxicity due to cyclophosphamide and its amelioration with N-acetyl cysteine**

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### **Abstract**

A study was conducted to evaluate the protective effect of N-acetyl cysteine (NAC) against experimentally-induced renal toxicity due to cyclophosphamide (CYP) in rats. Three groups (2, 3 and 4) of female *Wistar Kyoto* rats with 6 animals in each group were administered with CYP @ 40 mg/kg bwt on 1<sup>st</sup>, 3<sup>rd</sup>, 5<sup>th</sup> and 7<sup>th</sup> day by intraperitoneal route. Group 2 remained as toxic control. Group 3 received NAC from 1st to 14th day @ 0.2% of feed and group 4 was treated with NAC from 8<sup>th</sup> to 14<sup>th</sup> day. Group 1 was maintained on basal diet for 14 days. The study revealed a significant ( $P < 0.05$ ) increase in the concentration of serum creatinine, blood urea nitrogen, thiobarbituric acid reacting substances (TBARS) and protein carbonyls, and a decrease in the reduced glutathione (GSH) concentration of kidney. These results are suggestive of CYP-induced oxidative stress resulting in renal damage. Feeding of NAC could not offer protection against CYP-induced renal damage in this study.

## **Toxic effects of sub-chronic oral exposure of indoxacarb on biochemical parameters in buffalo calves**

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### **Abstract**

Repeated oral administration of Indoxacarb, an oxadiazine insecticide, at the dose rate of 1 mg/kg/day for 90 consecutive days produced mild signs of toxicity in buffalo calves. Indoxacarb significantly elevated the plasma levels of aspartate aminotransferase (38.3%), alanine aminotransferase (52.9%), alkaline phosphatase (29.5%) and acid phosphatase (36.6%). Cholinesterase levels in plasma, whole blood and erythrocyte also showed elevation. Indoxacarb did not produce any significant alterations in levels of blood urea nitrogen and creatinine. However there was an increase in blood glucose (16.9%), plasma cholesterol (19.6%) and total plasma proteins (10.8%). It can be concluded from the present study that indoxacarb is a low risk insecticide in buffalo calves.