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Anti-Teratogens: A mini review

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Abstract

That the developing embryos and fetuses are vulnerable to adverse influences in the environment is now a well-established fact. Hence, to discover the means of protection of the unborn child from environment insult is a challenge to the teratologists. Although protecting the child from all the birth defects is a difficult proposition at this stage, yet things are becoming more attainable with the advancement of science and technology. Few compounds, which include natural as well as synthetic products, have been reported to have protective effects against some teratogens. Recently, methods have been developed for screening these compounds for the antiteratogenic property by using in vivo or in vitro testing system. Work reported so far on this subject is very scanty, but it is appreciable for providing a new lead in this direction. This review attempts to focus on various reports, published on this topic and also discusses them for the possibilities of further studies in this direction.

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Inhibition of Zea mays phosphoenolpyruvate carboxylase by sulfur dioxide

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Abstract

Ten - days old plants of Zea mays were exposed to different concentrations of sulfur dioxide (0.8 to 23 ppm) for 4 hours in a continuous flow exposure chamber under illumination (500W tungsten bulb). The visible injury symptoms in leaves produced due to the exposure were correlated with sulfur dioxide concentration. The effect of sulfur dioxide exposure on the activity of phosphoenol pyruvate carboxylase was studied in the leaf extracts of Zea mays plants. A concentration dependent decrease in the activity of the enzyme was observed in relation to sulfur dioxide exposure. The kinetic studies of the enzyme were used to determine the rate constants, V_{max} and K_m for different substrates. The effect of sulfur dioxide on the kinetic parameters was evaluated in terms of the inhibitor constant, K_i . K_m values of PEP-carboxylase were 58, 76.9 and 83 μM for HCO_3^- , PEP and Mg^{2+} respectively, suggesting a higher affinity for HCO_3^- related to PEP and Mg^{2+} . The inhibitory profiles suggested that the nature of inhibition was competitive with respect to HCO_3^- , whereas PEP and Mg^{2+} went through non - competitive inhibition. The K_i values obtained were 38, 87.5 and 68.5 ppm sulfur dioxide with respect to HCO_3^- , PEP and Mg^{2+} respectively. The higher K_i values indicate the low inhibitory effect of sulfur dioxide. Since the K_i value for competitive inhibition is lower than that for the non - competitive one, this indicates that competitive inhibition against HCO_3^- predominate at low sulfur dioxide concentrations.

Reproductive failure associated with chronic interactive mixture toxicity of diethyl phthalate and Clophen A60 after gestational and lactational exposure over two generations in Wistar rats

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Abstract

The study undertaken evaluates the interactive reproductive toxic effect of DEP and PCB (Clophen A60) over two generations in Wistar rats. Healthy male and female albino rats of Wistar strain weighing 75 -100 g (6-7 weeks old) were randomly assigned to four groups of six each. Group I male rats were fed on normal diet and water ad libitum. Group II and III male rats were given Clophen A60 and DEP respectively dissolved in corn oil mixed with the diet at 50 mg/ kg of the diet /day to each group. Group IV male rats received a mixture of DEP and Clophen A60, dissolved in corn oil mixed with the diet at 50 mg/kg of the diet /day. 100 days after the treatment, females were mated with males for 10 days. Exposure to DEP and Clophen A60 was continued throughout mating, and till termination at weaning (21 days post partum) through the gestation period, which was 150 days of total treatment period of the parental generation. After F1 generation pups (six males and females of each group) attained weights of approximately 75 – 100 g, treatment was carried similar to parental generation for a period of 150 days at doses of Clophen and DEP were reduced to 25mg / kg of the diet/ day and after 100 days the animals were put to mate. The experiment was terminated at 150 days due to reproductive failure in F1 generation Clophen A60 and Clophen A60 + DEP treated groups. A significant decline in relative body and testis weight was observed in F1 generation Clophen A60 and Clophen A60 + DEP treated male rats as compared to other treated groups. On the other hand, a significant increase in relative ovary weights was observed in F1 generation Clophen A60, DEP and Clophen A60 + DEP treated female rats, while relative body weights of female rats were significantly decreased in all three treated groups. A significant increase in testis and ovary ACP, LDH activity, cholesterol and glycogen levels were observed in F1 generation Clophen A60 + DEP treated male and female rats as compared to other treated male and female rats and control rats. Significant increase in ACP, LDH activity, cholesterol and glycogen levels were observed in testis while significant increase in cholesterol level was observed in the ovary of F1 generation Clophen A60 treated male and female rats as compared to DEP treated rats, but not against the mixture treated male and female rats. It can be concluded from this study, that continuous exposure over two generations to PCB and DEP in spite of dose reduction leads to loss of reproductive ability and potentiated interaction in the F1 generation animals.

Biological monitoring of exposure to inorganic lead with special reference to women - A case study of Indian bangle makers

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Abstract

Gender differences in the toxicity of lead have been observed in a selected human population engaged in glass industries of Firozabad (India). Duration of exposure, age, food habits and alcohol intake were found to be confounding factors affecting lead toxicity in women. Lead concentration in urine was found to be higher in male subjects than female workers. Contrarily, δ -amino levulinic acid concentration in urine was higher in females than

male workers. It is concluded that women of all ages (premenopausal and postmenopausal) release lead more slowly than males. Therefore, we suggest that both the parameters in both the sexes should be applied for health risk assessment. Further, studies on δ -amino levulinic acid dehydratase (ALAD) genetic polymorphism are needed so as to confirm susceptible and protective genotypes.

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Evaluation of experimental aflatoxicosis and its amelioration by chromium and methionine on performance of broilers

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Abstract

A total of fifty, day old, male broiler chicks were randomly divided into five groups consisting of 10 birds in each group. Group 1 was maintained on basal control feed and groups 3, 4 and 5 were maintained on AFB1 (1 ppm) + methionine (5 g/kg), AFB1 (1 ppm) + chromium (200 ppm) and AFB1 (1 ppm) + methionine (5 g/kg) + chromium (200 ppm), respectively, while group 2 was kept as aflatoxin toxic control (AFB1 1 ppm) throughout the experiment without any treatment. The study was carried out for a period of 6 weeks. Body weights, feed consumption and FCR were recorded at weekly intervals. At the end of the study the average body weights did not reveal any significant difference among treatment groups 3, 4 and 5, though they were significantly ($P < 0.01$) higher as compared to group 2. The weekly body weight gains of the treatment groups 3, 4 and 5 did not differ significantly though they are significantly ($P < 0.01$) higher as compared to group 2. A significant ($P < 0.01$) decrease in cumulative body weight gain was observed in group 2 at the end of 6th week as compared to all the other groups. The average FCR values of group 3, 4 and 5 were relatively higher as compared to group 1 and relatively lower as compared to group 2 at their respective time intervals. At the end of 6th week, a higher average FCR was observed in group 2 as compared to groups 1, 3, 4 and 5. In all the treatment groups supplemented with either methionine or chromium or a combination, there was a dramatic improvement in the body weight gain and FCR.

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A study on maduramicin toxicity and its amelioration by ginseng in broiler chicks

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Abstract

Maduramicin toxicity was studied in broilers and ginseng (2.5 g/Kg feed) was evaluated for prophylactic and therapeutic management of maduramicin toxicity. Day old male broiler chicks were randomly divided into 4 groups consisting of 6 chicks in each. Group 1 was maintained as basal diet control for 6 wks, group 2 on maduramicin (8 mg/Kg feed) for 6 wks, group 3 on a combination of maduramicin and ginseng for 6 wks and group 4 on maduramicin for the first 4 wks and during the subsequent 2 wks on ginseng containing feed (2.5 g/Kg feed) with out maduramicin. Weekly body weights, feed conversion efficiency, glutathione concentration and high density lipoproteins (HDL) were significantly ($P < 0.05$) reduced, while the activities of antioxidant enzymes, biomarkers of liver and the lipid profile, and the renal profile biomarkers were increased significantly ($P < 0.05$) in group 2 and 4 at the end of 4th wk as compared to group 1. Following treatment with ginseng during the last 2 wks in group 4, all

the parameters in study revealed improvement. From this study, it is concluded that maduramicin induces toxicity by oxidative stress and supplementing ginseng in feed is useful in preventing and treating the toxicity.

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Ovarian cytotoxicity by oestrogen in rat

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Abstract

Ethinyl oestradiol was administered to the rats of groups 2, 3 and 4 @ 250, 500 and 750 µg/kg body weight, respectively orally once a week for 8 weeks and to the rats of groups 5, 6 and 7, respectively for 12 weeks. At the 9th week, mild to severe congestion along with infiltration of lymphocytes in the interstitial tissue of the ovaries was observed in groups 2-4. At the 13th week (groups 5-7), these changes were more prominent. In higher dose group (EO @ 750 µg/kg), swelling of endothelial cells, thickening of blood vessel walls, degeneration and fibrous tissue proliferation were also observed. The extent and severity of ovarian damage were found to be dose and time dependent, suggesting that the higher dose and prolonged duration of oestrogen administration successively, may cause more cytotoxic changes in the ovary. The standard cytotoxic doses of oestrogen were assessed to be 500 to 750 µg/kg, orally weekly for a period of 12 weeks.

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Inhibition of aflatoxin induced liver damage in broilers by curcumin and silymarin

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Abstract

The present study was undertaken to evaluate the hepatoprotective effect of curcumin and silymarin alone and in combination, against aflatoxicosis in male broiler chicken. Liver damage was assessed by quantifying the serum levels of Total Protein, Alanine aminotransferase (ALT) and Aspartate aminotransferase (AST) supported by histopathological examination. Aflatoxin administration at 1 ppm level resulted in increase in serum ALT and AST, decrease in total serum protein with varying degrees of liver damage ranging from diffuse vacuolar degeneration of hepatocytes, necrosis and tendency for fibrosis. Curcumin (10mg, 20mg) and silymarin (500ppm, 1000ppm) produced dose dependant improvement in all the parameters studied and they were more or less similar in their hepatoprotective effect. The combined effect of both the drugs, Curcumin 10mg + Silymarin 500ppm and Curcumin 20mg + Silymarin 1000ppm, produced better results in a dose dependant manner indicating the synergistic effect of the two flavonoids.

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In vitro and in vivo lymphocyte proliferation studies of toxins of Bracken and Polystichum ferns

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Abstract

High Performance Liquid Chromatography of aqueous extract of young fronds of Bracken, Polystichum and Dryopteris indicated the presence of 6.04, 20.34 and 18.13mg ptaquiloside/kg dry wt basis respectively. Terpenoids, flavanoids and glycosides was found to be present in ethanolic extract. In vitro studies of methanolic and aqueous extract of bracken and Polystichum fern with PMN cells of healthy cattle revealed increased lymphoproliferative response than the known mitogen Con A and PHA. The degree of lymphocyte proliferation was in the following order: standard ptaquiloside < Con A < PHA < Fraction K < Fraction H < Fraction aqueous < Fraction G. In vivo lymphocyte proliferation response carried out with the PMN cells of Bracken and Dryopteris fed groups showed higher mitogenic activity to the known mitogen Con A and PHA as compared to PMN cells of control animals.

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Effect of lithium on developmentally relevant neuronal enzymes in embryonic chick brain

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Abstract

Lithium, a drug used for several decades for the treatment of manic depression, is a well known modulator of embryonic development. In the last decade lithium has been extensively reported to be neuroprotective in vitro and in vivo systems and is likely to be more widely used against neurodegenerative diseases. Despite its use for several years, the exact mechanism of action of lithium in modulating the physiological parameters of the brain has remained elusive. Though the details of its effects on second messenger systems and regulation of gene expression have been investigated actively, not much has been reported on its effects on the down stream molecules, such as the neuronal enzymes, that play a major role in cellular responses during physiological functions. We have, therefore, investigated the effect of lithium on three key neuronal enzymes relevant to cell differentiation and connectivity, Na⁺K⁺ATPase, acetyl cholinesterase (AChE) and nitric oxide synthase (NOS) using chick developing brain as a model. Lithium causes significant increase in specific activity of AChE and NOS while decreasing the specific activity of Na⁺K⁺ATPase indicating that lithium action results in change in pathophysiology of the brain by altering the biochemical milieu of the embryonic chick neuronal tissue.

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Evaluation of prophylactic potential of Withania somnifera for chlorpyrifos-induced neurotoxicity in rats

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Abstract

The present studies were conducted to evaluate the protective potential of Withania somnifera root for chlorpyrifos-induced changes in neurobehavioral profile and acetylcholinesterase inhibition in adult male wistar rats. The Withania somnifera root extract given @ 25 mg/kg and 50 mg/kg i.p. daily for 21 days before chlorpyrifos administration @ 85 mg/kg i.p. did not prevent neurobehavioral toxicity, rather aggravation of symptoms alongwith more inhibition of acetylcholinesterase enzyme in dose dependent manner was observed.

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Inhibitory effect of melanoidins, phenols and sulphate present in post methanated distillery effluent (PMDE) for detoxification by Defluviobacter lusatie ITRC PK1 (DQ 659618)

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Abstract

The effect of melanoidin, phenol and sulphate for detoxification of post methanated distillery effluent (PMDE) by Defluviobacter lusatie ITRC PK1 (DQ 659618) was assessed. The physico-chemical analysis of PMDE revealed high biological oxygen demand (BOD, 29120±10.00 ppm), chemical oxygen demand (COD, 58018.33±23.63 ppm) and dark colour (55026.33 ±30.00 Co-Pt) with slight alkaline pH (8.53). Phenol (775.66±16.93 ppm) and sulphate (20732.33±28.57 ppm) content were also detected very high in PMDE. Besides, PMDE contained Copper (Cu, 0.228±0.09 ppm), Manganese (Mn, 1.651±0.02 ppm), Iron (Fe, 4.593±0.09 ppm), Nicle (Ni, 0.652±0.00 ppm) and Zinc (Zn, 0.028±0.00 ppm). All physico-chemical properties decreased after extraction of melanoidin, phenol and sulphate. While chloride ions were increased after phenol extraction. However, colour decrease was observed only after extraction of melanoidin rather than phenol and sulphate, which indicated that melanoidin, was directly linked with colour of effluent. The uniform sigmoid bacterial growth in effluent was observed after extraction of melanoidin, sulphate and phenol in comparison of control. The toxicity studies on various growth parameters of Lemna minor L. revealed that the growth of Lemna minor L. was inversely proportional to the concentration of pollutants present in PMDE. Thus study revealed that high content of melanoidin, phenol and sulphate in PMDE are inhibitory for bacterial growth and effluent detoxification.