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Chemical N-nitrosation of metaprim [(5-(4-chlorophenyl)-6-ethyl-2,4-pyrimidinediamine] prophylactic dose regime and the toxicological consequences in rats fed diets containing varying levels of protein of the derivable nitrosamine content

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A 50 gm portion of metaprim [(5-(4-chlorophenyl)-6-ethyl-2,4-pyrimidinediamine] was nitrosated and the nitrosamine formed were identified qualitatively and quantitatively, before calculating the amount measuring to an adult metaprim prescribed regimen of 25 mg per week, and using the pure compound for toxicity studies in rats fed diets containing varying levels of protein. Twenty four 130 gm rats in six animals per group were fed with semi-purified diets of 18% normal-protein-diet; 8% low-protein-diet; 64% high-protein-diet; or 0% protein-free-diet, with drinking water *ad libitum* for 14 days, before dosing orally with 0.1 mg authentic nitrosamine, sacrificing *in extremis* and conducting liver function tests, urine nitrite analysis, liver histopathology, *in vitro* metabolisms, and identifying formed nitrosamine by double-dimensional thin-layer-chromatography, using reference pure nitrosamine, recommended color spray reagents and UV irradiation (240 nm). N-Nitrosodimethylamine (NDMA) was detected. There was a significant increase in mean nitrite content of urine of the high-protein-diet rats (0.083 mg/ml) and a lower level in either the low-protein or protein-free-diet animals (0.010 and 0.001 mg/ml, respectively), compared to normal-protein-diet rats (0.003mg/ml). A higher increase in nitrite was found on exposure to UV irradiation, thereby indicating presence of a nitrosamine in voided urine. There were significant increases ($P < 0.05$) in ALT and AST levels of serum (81.47 ± 7.91 and 204.15 ± 22.33 IU/L, respectively) in the high-protein-fed rats. The direct serum bilirubin of both the low-protein and protein-free-diet rats were much increased. A mild liver lobular inflammation and accumulation of mononuclear cells in the perivascular area was seen in the high-protein-diet rats. *In vitro* degradation of NDMA increased in the high-protein-diet rats and decreased in lower-protein-diet species, as compared to normal-protein-diet rats. Metaprim is an exogenous source of NDMA, and its endogenous nitrosation is likely to cause mild toxicity to liver, preventable by a low-protein-diet and accentuated by high-protein-diet intake.

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Effect of sub lethal cadmium concentrations on serum biochemical parameters in sea bream (*Sparus aurata*) fingerlings

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Cadmium (Cd), is a heavy metal with limited biological function, is widely distributed in the aquatic environment as a result of natural and anthropogenic activities. The effect of exposure of gilthead sea bream (*Sparus aurata*) fingerlings to sub-lethal concentrations of Cd was evaluated as levels of Cd content. The main objective of this study was to determine the effects of cadmium at sub-lethal concentrations (1 and 3 $\mu\text{g/l}$) on serum biochemical parameters including enzymes, i.e. alkaline phosphatase (ALP), aspartate aminotransferase (AST) and alanine aminotransferase (ALT), glucose, triglyceride, cholesterol and total protein in sea bream (*S. aurata*) fingerlings, sea bream were exposed to cadmium at intervals of 1, 15, and 30 days, selected parameters were evaluated. Triglyceride and cholesterol decreased transiently at day 15 and then increased at day 30. Total protein, AST, ALT and ALP increased linearly with time and Cd concentration. This investigation suggests that growth and serum biochemical parameters could be used as important and sensitive biomarkers in eco toxicological studies concerning the effects of metal contamination and fish health.

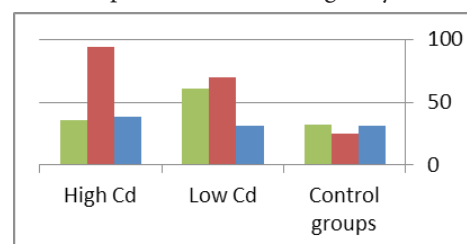


Figure 1: Serum glucose level.

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