Adverse Effects of Exposure to Analgesic/Antipyretic Drug "Paracetamol" and an Organo Phosphorus Insecticides "Diazinon" on the Liver of Male Rats

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Abstract:

The interaction of chemicals (e.g. drugs and pesticides) with the biological system may be a complex phenomenon and is ultimately an expression of the interplay between the environment, the host and chemical substance. It is evident from the literature, which is extremely limited, that drug/insecticide interactions may result in altered response/toxicity, which is of clinical relevance. Thepresent study was conducted to evaluate the adverse effect of exposure to diazinon (DIA) and paracetamol (PARA) and their combination on liver of male rats. Rats were orally administered PARA at a dose of 66.66 mg a.i. kg-1 weight (maximum administration dose) and DIA at a dose 12.50 mg a.i. kg-1 b.wt. (1/100 LD50) for 28 consecutive days. Significantly, decreasedbody weights were observed in all treated groups, while significant increase in relative liver weight were recorded in DIA andDIA+PAQ-@treated groups compared to control rats. Liver dysfunction enzymes (e.g., aspartate aminotransferase, AST; alanineaminotransferase, ALT; alkaline phosphatase, ALP and lactate dehydrogenase, LDH) and lipidperoxidation level (LPO) were increased in DIA, PARA and DIA+PAQ-@treated groups. Treatment of DIA and DIA+PARA caused significant decrease in theactivity of serum cholinesterase (ChE). PARA, DIA and PARA+DIA treatments caused histopathological changes and decreasein DNA content in liver cells of rats. The severities of such observations were more pronounced in their combined exposure. We can conclude that both paracetamol at maximum administration dose and diazinon caused biochemical and histopathological alteration within the liver of male rats. The severities of such observations were more pronounced in their combined exposure. The data throw light on the matter of simultaneous exposure to OPIs and commonly used drugs especially among agriculture sector workers in developing countries, where the handling of medicine (e.g., PARA) is mainly without medical prescription. Further studies, applied to pregnant women, newborns and childhood may be of great significance.

Introduction:

Every day, people are exposed simultaneously to a mixture of environmental and occupational stressors as a routine part of their existence. Up until recently, about 95% of all chemical toxicity studies were performed on individual chemicals. The biological activity of a chemical may be modified through prior or simultaneous exposure of a test organism to another chemical agent and such interactions might result in a potentiation, summation, or reduction of the ultimate effect of the chemical. Pesticides are occasionally used indiscriminately in large amounts causing environmental pollution and therefore, are a cause of concern. Organophosphorus insecticides (OPIs) are a major component of many pesticides with widespread use in both agricultural and domestic situations. However, approximately 85%-90% of applied agricultural pesticides never reach target organisms, but disperse through the air, soil, and water Diazinon (DIA) (0,0-diethyl-0-[2- isopropyl-6-methyl-4-pyrimidinyl] phosphorothioate) is a contact OPIs with a broad range of insecticidal activity and widely used throughout the world with applications in agriculture and horticulture. Various reports have been published with respect to DIA and its effects on biochemical and hematological parameters of rats, rabbits, and mice In fact, the interaction of chemicals with the biological system is a complex phenomenon and is ultimately anexpression of the interplay between the environment

Materials and Methods

Chemicals: Diazinon (Nasr-Cidol® 60% EC) was obtained from ElNasr Mediate Chemical Co., Egypt. Paracetamol® tablets(The Arab Drug Co., Egypt), each tablet contain 500 mg paracetamol, was purchased from local pharmacies. All other chemicals were of reagent grades and obtained from the local scientific distributors in Egypt.

Animals: Male Wistar rats (weighting 150-160 g) were purchased from Animal Breeding House of the National Research Centre (NRC), Dokki, Cairo, Egypt. Animals received humane care according to the criteria outlined in the "Guide for the Care and Use of Laboratory Animals." The experimental protocols and procedures were approved by the Local Ethics Committee at the National Research Centre (NRC), Dokki, Cairo, Egypt. Animals were housed in clean plastic cages with free access to food (standard pellet diet) and tap water ad-libitum, under standardized housing conditions (12h light/dark cycle, the temperature was and a minimum relative humidity of 40%) .

Experimental protocols: After 1 week of acclimatization to laboratory conditions, the animals were randomly assigned to four groups, each consisting of eight rats as follows: First group (control), the second group (DIA), the third group (PARA) and the fourth group (DIA + PARA). Dosages of DIA and PAR were freshly prepared in distilled water, given via oral route for28 consecutive days and adjusted weekly for body weight changes.

Body weights and relative liver weights: After blood collection, the rats were sacrificed by cervical dislocation. Liver of rats was quickly removed and weighte dindividually. Then, the organ/ body weight ratios were calculated.

Results

During the course of present investigations, it was observed that the body weights of the control animals increased progressively throughout the study and recorded a net weekly body weight gain of 13.35%.

Discussion:

In the present study, body weight gains were decreased significantly in rats exposed to diazinon, paracetamol and their mixture. Also, significant ($P \leq 0.05$) increase in the relative liver weights were recorded in treating groups. We thought that this decrease in body weight gain may be due to reduced food consumption of exposed-rats (un-tabulated data) and may be due to the overall increased degradation of lipids and proteins as a result of the direct effects of organophosphate compound. Stromborg found that dietary levels of diazinon above 50 mg/kg were associated with reduced food consumption, weight loss, and reduction in egg production in northern bobwhites. In addition, others OPIs cause reduction of body weight in rats and mice.

Conclusion:

We can conclude that both paracetamol at maximum administration dose (66.66 mg a.i. kg-1 b.wt) and diazinon at 12.50 mg a.i. kg-1 b.wt. caused biochemical and histopathological alteration in the liver of male rats. The severities of such observations were more pronounced in their combined exposure. The data of this study throw light on the problem resulting from simultaneous exposure to OPIs and some commonly used drugs especially among agriculture sector workers in developing countries, where the handling of such drugs (e.g. PARA) is mainly without medical prescription.

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