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Effect of pioglitazone on plasma concentration of phenytoin on subchronic concurrent use

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Background and Aims: An antiepileptic drug, phenytoin has a narrow therapeutic index and a change in bioavailability may lead to toxic effects or therapeutic failure. Pioglitazone is a synthetic ligand for peroxisome proliferator-activated receptors (PPAR) and through its action at PPAR-γ receptors improves insulin sensitivity and glycaemic control in Type.2 diabetes. In this study the effect of pioglitazone on plasma concentration of phenytoin on sub-chronic (30 days) concurrent administration was investigated.
Methods: Male adult Wistar rats (250-300 g, n= 10 in each group; breed locally) were used in this study. The rats were divided into control and test groups. In the control group the animals received saline (1 ml/kg po) at 10 AM and phenytoin (30 mg/kg po) at 11 AM for 30 days. In test group animals received pioglitazone (10 mg/kg po) at 10 AM and phenytoin (30 mg/kg po) at 11 AM for 30 days. In 31th day, two hours after the last intragastric gavage, animals were anesthetized and 2 ml of blood drawn via cardiac puncture and concentration of phenytoin in plasma was determined using a high performance liquid chromatographic (HPLC) method.
Results: The phenytoin levels in control and test groups were 2.08±0.25 µg/ml and 1.2±0.15 µg/ml, respectively. Statistical analysis (independent-samples T test) showed that there is a significant reduction in plasma concentration of phenytoin in test group in comparison with the control group ($p<0.01$).
Conclusions: Results of this experimental study indicated that pioglitazone has significant effect on plasma concentration of phenytoin.

Keywords: Peroxisome proliferator; Activated receptors (PPAR); Pioglitazone; Phenytoin