Abstract:

Introduction

Nicotine is a depolarizing ganglionic blocker alkaloid found in the Solanaceae family. It is metabolized by the liver enzymes and to some extent in the kidneys and lungs. Isoniazid is a bacteriostatic drug against Mycobacterium tuberculosis, that inhibits CYP450 enzyme and interferes with the metabolism of nicotine to cotinine.

Aim

This study was indicated to evaluate the effect of isoniazid on pharmacokinetic profile of nicotine from nicotine patches and its major metabolite (cotinine) in rats.

Methodology

The animals were divided into two groups (control and treated) and housed as per the animal ethics guideline. The animals of treated group were treated with isoniazid (100 mg/kg b.wt. intraperitoneally) for 30 days, while the animals of control groups received equivalent amount of normal saline. The liver function tests (aspartate aminotransferase, alanine aminotransferase and alkaline phosphatase) of all the animals were conducted after 30 days to monitor liver toxicity. On 31st day, the animals of both groups were treated with nicotine patches (15 mg/patch) for 2 hours and the blood samples were collected at different time intervals (0, 0.5, 1, 2, 2.5, 3, 4, 5 and 6 h) from tail vein, the animals were sacrificed post experiment and different organs were collected for histopathological examinations. The plasma samples were collected and analyzed for the nicotine and cotinine concentrations using Gas Chromatograph equipped with flame ionization detectors (GC-FID) using reported method.

Results and Discussion

The biochemical evaluations of samples indicate that there were significant increases in the liver transaminase enzymes level, due to the chronic effect of isoniazid which causes hepatotoxicity and hepatic injury was manifested by the histological evaluation of liver tissues.

The results indicated that the Cmax of nicotine was significantly higher in the animals of treated group than control group (115.3%, p <0.05), the confidence limits were 108.8-122.1% and the mean ratio of area under the curve of nicotine in the treated group was slightly increased (AUCtau = 105.3%), the percent confidence interval ranged from 97.98-113.64%. These increases in the Cmax and AUC of nicotine in treated group compared to control group might be due to suppression of the liver enzymes that are responsible for metabolism of the drug by isoniazid. At this juncture, we can state that the rats treated with isoniazid and nicotine requires dose adjustment as the high dose of nicotine may produce more side effect and toxicity due to slow metabolism of the nicotine.

Study the effect of isoniazid on the pharmacokinetic profile of nicotine from nicotine patches in rats by using GC-FID

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