Comparative Assessment of the Effect of Solanine Administered Orally and Intraperitoneally on Hepatic Dysfunction in Male Rats

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ABSTRACT. An oral dose of 250 mg/kg of solanine did not alter the activities of serum glutamic oxalacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT) and serum cholinesterase (ChE) in male rats 24 hr following the treatment. However, i.p. administered solanine (20 mg/kg) significantly increased the levels of SGOT and SGPT, and decreased the activities of ChE and microsomal enzymes, including cytochrome P-450, suggesting ingested solanine is several times less hepatotoxic than i.p. administered solanine, probably due to its poor absorption from the stomach.—KEY WORDS: liver toxicity, solanine.

Solanine is considered to be one of the highly toxic alkaloids. It is found in many plants belonging to the genus Solanum [1]. However, the most common source of solanine poisoning in humans and farm animals has been the tuber of potato. It is present in toxic levels in sprouted, cull and green potatoes. Potatoes containing over 0.02% solanine are considered toxic to humans [9]. Toxicity of solanine generally involves gastrointestinal disturbances and neurological disorders [1, 9, 13]. Little is known about the toxic action of solanine on liver. Satoh [10] reported that blood sugar levels were increased and liver glycogen levels decreased in rats following an i.p. administration of solanine. Other studies indicate that the alkaloid increased pentobarbital sleeping time in experimental rats, suggesting inhibition of hepatic microsomal enzymes [2, 5, 6]. The present study was undertaken to compare the toxic effect of orally and intraperitoneally administered solanine on the liver of male rats using changes in the activities of some serum and hepatic microsomal enzymes as indicators of liver dysfunction.

Purified solanine was obtained as a gift from Dr. T. J. Fitzpatrick, ARS-USDA, Philadelphia, Pa. Glucose-6-phosphate, glucose-6-phosphate dehydrogenase and nicotinamide-adenine dinucleotide phosphate (NADP) were purchased from Boehringer and Mannheim Corp. (Indianapolis, Ind.) and used to prepare NADPH-generating system required for studying the activity of microsomal drug-metabolizing enzymes. All other chemicals used in these studies were of analytical or reagent grade.

Male Sprague-Dawley rats (Southern Animal Farms, Prattville, Ala.) weighing 180-220 g were used throughout these studies. They were housed in standard stainless steel cages placed in a temperature-controlled room (25°C) on a 12-hr light-dark cycle and allowed free access to water and Purina rat chow. Solanine was suspended in corn oil (Mazola brand) and was either given per os (p.o.) by gavage to a group of 5 rats fasted overnight or administered intraperitoneally (i.p.) to another group of 5 rats at dosage levels of 250 mg/kg and 20 mg/kg, respectively. The respective control groups receiv-
ed corn oil alone. The animals were sacrificed by decapitation at 24 hr following the treatment and blood samples were collected to prepare serum for the determination of the activity of serum glutamic oxalacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT) and serum cholinesterase (ChE). Activities of SGOT and SGPT were determined spectrophotometrically using kits purchased from Sigma Chemical Co. (St. Louis, Mo). The transaminase reactions utilize for the activity a co-factor NADPH which is oxidized to NADP and the resulting decrease in absorbance at 340 nm is followed in a spectrophotometer. The change in absorbance is taken as a measure of the activity of the transaminases, which is expressed as Karnen units. The ChE activity was measured colorimetrically using a kit obtained from Pitman-Moore, Inc. (Washington Crossing, N.J.). The cholinesterase assay is based on the enzymatic breakdown of acetythiocholine to acetic acid and thiocholine, and the reaction between thiocholine and dithiobisnitrobenzoate to form a yellow color complex which is measured on a spectrophotometer to assay the enzyme activity.

After decapitation, livers of the animals were collected for the isolation of microsomes. The liver microsomes from the treated and untreated animals were isolated and incubated as described previously [3]. Benzphetamine N-demethylase activity in the microsomes was assayed according to the procedure reported earlier [3], whereas microsomal cytochrome P-450 content was determined by the method of Omura and Sato [7]. Microsomal protein concentration in each sample was measured by Biuret method modified to include 0.1 mL of 1% deoxycholate [4]. Data were analyzed using standard t-test. Significance of treatment mean differences was based on a P-value of 0.05.

The data presented in Table 1 show that the increase in SGOT and SGPT activities caused by 250 mg/kg oral dose of solanine was not statistically significant; however, a significant increase in the activities of these enzymes was noticed in rats given 20 mg/kg i.p. dose of solanine, suggesting that intraperitoneally administered solanine is more toxic to liver than ingested solanine. This may be attributed to its slower absorption and faster degradation in the gastrointestinal tract. In fact, solanine is poorly absorbed from and rapidly hydrolyzed in the gastrointestinal tract to a less toxic product known as solanidine, thus showing low oral toxicity [6]. Determination of ChE activity revealed that the enzyme activity was not significantly inhibited when 250 mg/kg dose of solanine was given orally. In contrast, there occurred a significant inhibition of the enzyme activity following an i.p. administration of solanine,
indicating that this route of administration exerts much more toxic effect on liver than does the oral route. This toxic manifestation caused by solanine further confirms that it is a hepatotoxic compound since liver damage is usually accompanied by a decrease in serum cholinesterase levels [11, 12]. A similar observation on in vitro plasma cholinesterase activity by solanine has also been reported by others [8]. However, in body whether solanine inhibits the ChE directly or its synthesis remains unknown.

The effect of solanine on hepatic microsomal enzyme system in vivo can be seen in data presented in Table 2 where the inhibition of benzphetamine N-demethylase activity and the loss of cytochrome P-450 are taken as additional indices of liver damage. Here again, a significant loss of hepatic microsomal cytochrome P-450 and nearly 50% inhibition of the benzphetamine N-demethylase activity were caused by i.p. administered solanine whereas the changes in these parameters effected by ingested solanine were non-significant. Thus, our observation that solanine is an inhibitor of hepatic microsomal drug-metabolizing enzymes is consistent with previous reports demonstrating an increase in pentobarbital sleeping time induced by solanine [2, 5, 6]. It is concluded that i.p. administered solanine is several-fold more toxic to liver than ingested solanine and thus being a hepatotoxic compound, it may potentiate the toxicity of other hepatotoxic agents that are detoxified in liver.

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