

Absence of Teratogenic Effect of Liv.52 in Albino Rats

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ABSTRACT

The teratogenic potential of Liv.52, a commonly used liver protective and rejuvenating agent of herbal "Ayurvedic" origin, was studied. The crude powder suspended in normal saline was administered orally to female pregnant rats in a dose of 100 mg/100 g of body weight during the entire period of gestation. This dose of Liv.52 had no adverse effect on body weight, growth and size of the offspring as compared to controls (non-drug treated). It did not induced any limb deformity in any of the offspring of the treated animals. There was no significant difference in fertility index (FI), lactation index (LI), gestation index (GI), live birth index (LBI) and Teratogenicity index (TI) in the Liv.52-treated animals as compared to the normal control group of animals. Thus, Liv.52 was found to be devoid of any teratogenicity in rats.

INTRODUCTION

Liv.52, a compound herbal remedy, is one of the most extensively used preparations for a variety of liver disorders in this country. A number of experimental and clinical studies have provided ample proof of its liver protective effect in these disorders. As the remedy is used for prolonged periods, particularly in cases of infective hepatitis both in males and females, the possibility of any teratogenicity in spite of its innocuous nature cannot be excluded. Therefore, the present study was carried out to evaluate the presence of such activity, if any.

EXPERIMENTAL PROCEDURES

Liv.52 powder supplied by The Himalaya Drug Company was suspended in normal saline and given orally to pregnant female rats in this study. The study was carried out by the method of Persaud and Ellington (1968), Shott *et al.*, (1971) and Singh *et al.*, (1981) in healthy female, non-pregnant albino rats weighing between 180-200 g. They were maintained on a special semifluid diet consisting of whole-wheat flour (10.0 g), milk powder (1.0 g), glucose (0.1 g) and water (100 ml). This diet was allowed *ad libitum*. The animals were divided in two groups consisting of 12 animals each and co-habited with healthy adult male rats of proven fertility. Vaginal smears were examined daily under the microscope and the day they showed thick clumps of spermatozoa was designated as day '0' of pregnancy. Animals of the first group served as controls and were treated with normal saline. Animals of the second group were treated with Liv.52 powder suspended in normal saline which was administered orally with the help of a feeding cannula at a dose of 100 mg/100 g body weight daily during the entire period of gestation, beginning from day '0' of pregnancy. The pregnant animals were watched daily for abortions. The animals were allowed to continue to term till delivery for any evidence of teratogenicity and malformations. Further, the offspring were sacrificed and their internal organs such as the heart, lungs, spleen, gastrointestinal viscera and gonads were examined grossly and microscopically for any evidence of teratogenicity.

The reproductive indices, viz. fertility index (FI), gestation index (GI), live birth index (LBI), lactation index (LI) and teratogenicity index (TI) were calculated according to Shott *et al.*, (1971).

RESULTS

The results are summarized in Table 1.

Treatment	Dose, route & administration	Number of rats				Gestation period (days)	Total No. of pups born			No. of weanings	Indices %				
		Mated	Pregnant	Aborted	Delivered		Alive	Dead	Deformed		Fertility index	Gestation index	Live birth index	Lactation index	Teratogenic index
Control (Saline)	0.5 ml/100 gm p.o. x 21 days	12	8	1	7	21.5	60	0	0	55	67	100	100	91	0
Liv.52	100 mg/100 gm p.o. x 21 days	12	9	1	8	21	72	0	0	60	75	100	100	83	0

The fertility index in the control, untreated group was found to be 67%; 8 out of 12 rats became pregnant and delivered healthy litters between 21 and 22 days of gestation. The mean litter size in the control group was five (range 4 to 6). On the other hand, the fertility index in the Liv.52-treated group was 75% (9 out of 12 rats became pregnant). One animal each aborted in the control and Liv.52-treated groups on the 12th and 14th day respectively. All the offspring in the control as well as treated groups were born alive (live birth index = 100). The survival rate of offspring at weaning (lactation index) in the control group was 85% (55 out of 65 offspring survived), whereas in the Liv.52-treated group the lactation index of the offspring was 83% (60 out of 72 offspring survived). The offspring in both groups (control and Liv.52-treated) had mean weights of 6.5 ± 0.52 g and 6.3 ± 0.35 g at birth respectively and there was no difference in body size or skull size and no sign of teratogenicity such as limb deformities. Further, no abnormality could be detected in the internal organs on gross and microscopic examination at autopsy (teratogenicity index was '0' for both groups).

DISCUSSION

Liv.52 is one of the most popular health remedies prescribed by physicians of different disciplines including doctors of modern medicine for a variety of liver disorders (Arora, 1969, Sama *et al.*, 1976) and for the protection of the liver against chronic alcoholism (Kulkarni, 1980). Singh *et al.*, (1978) while studying the hepatoprotective effect of several indigenous drugs, found that Liv.52 not only had a protective effect against CCl₄-induced liver toxicity in mice but it also increased the survival rate of the animals against CCl₄-induced mortality. As it is imperative for all modern drugs to be evaluated for this activity before their use in human subjects, this study is a must for herbal drugs also, particularly for those which are to be used for prolonged periods in patients. Furthermore, this test and its authenticity have gained maximum importance after the thalidomide (a sedative drug of West Germany) tragedy, which led to malformations like limb deformities resulting in thousands of seal babies (phocomelia), and ruined hundreds of families due to its teratogenic effect. However, this fact is ignored for Ayurvedic medicines in this country as their innocuous nature is taken for granted which may not be true. Therefore, to be on the safe side, this parameter should be studied for each and every drug irrespective of its origin. In view of this fact, the present study was conducted to evaluate any teratogenic effect in Liv.52. Table 1 shows that

Liv.52 has no teratogenic activity in rats. The fertility, gestation, live birth and lactation indices did not differ significantly from the normal control group and no foetal anomaly was observed (teratogenicity index=0). Thus, Liv.52 has been found to be devoid of any teratogenicity in rats. Absence of such toxicity provides a base for its safety value for prolonged clinical use even in pregnant females suffering from liver disorders. Although this study provides some proof for the absence of such toxicity in Liv.52, yet this work in a single species of animal cannot provide foolproof conclusions on the subject and needs further work, both in other species of animals and close observations in human pregnant females using Liv.52, to prove our contention.

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