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SUBACUTE TOXICITY STUDY OF THE COMBINATION OF GINSENG (PANAX GINSENG) AND ASHWAGANDHA (WITHANIA SOMNIFERA) IN RATS : A SAFETY ASSESSMENT

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Abstract : Ginseng (Panax ginseng) and Ashwagandha (Withania somnifera) are widely used as geriatric tonics. Both individually have not shown any toxicity on long term administration. Study was planned to assess the safety of the combination by doing subacute toxicity study in rats with 90 days oral administration using three doses.

Food consumption, body weight, haematological, biochemical and histopathological parameters were studied.

There was significant increase in body weight, food consumption and liver weight, and improved haematopoesis was observed.

Brain, heart, lung, liver, spleen, kidneys, stomach, testis and ovaries were normal on gross examination and histopathologically.

Subacute toxicity studies in rats did not reveal any toxicity.

Key words: ginseng ashwagandha subacute toxicity

INTRODUCTION

Recently, many Chinese as well as Indian medicinal plants have been subjected to detailed chemical, pharmacological and therapeutic investigations. Ginseng, a Chinese medicine, alone and in combination is being promoted as a general tonic.

Similarly, Ashwagandha, an indigenous medicinal plant, claimed to have many properties similar to Ginseng is also in wide use.

In the past, a number of studies have been carried out on these plants for testing their pharmacological activities (1-4). Though some isolated chronic toxicity studies are reported of individual agents, no systemic long term subacute and chronic toxicity studies have done using a combination of the two drugs.

Therefore, in order to substantiate the claim of safety of this combination, this particular study was planned, as subacute

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toxicity studies are particularly valuable in determining the cummulative toxicity of the drug following exposure to intermediate duration.

METHODS

Albino rats of Haffkine strain, Bombay were used for the study. The animals were divided into four groups. Each group comprised of 20 rats (10 male and 10 female), weighing between 150–250 gms.

Roots of Ginseng and Ashwagandha were pulverized. Five litres of plain water was added to 1 kg powdered roots and then reduced the volume to ¼ by boiling. The aqueous extract contained Ginseng and Ashwagandha in a ratio of 10:1 respectively.

Group I acted as control and received plain boiled water in the dose of 1 ml/100 gm body weight each. Group II, III and IV received the extract of Ginseng and Ashwagandha in the doses of 8.50 mg/kg, 12.75 mg/kg and 17.00 mg/kg respectively. The doses administered were the fractions of LD_{50} of the combination, approximating 4, 6 and 8 times the therapeutic dose. LD_{50} was determined in our laboratory prior to this study. The drug was administered orally for 90 days with the help of 18 guage long, blunt and bent needle fitted to a tuberculin syringe. It was ensured that the needle was in oesophagus.

Measured amount of fresh food was replenished daily at 10.00 a.m. and their food intake of previous day was measured. General well being and behaviour of the animals was observed daily, throughout the study. Body weight recorded and urine analysis was carried out weekly. After 45 days, half of the animals and after 90 days, rest of the animals were sacrificed and subjected to haematological, biochemical and histopathological studies. Biochemical parameters estimated were Blood glucose, Serum bilirubin, Serum GOT, Serum GPT, Alkaline phosphatase, Blood urea, Serum creatinine and Serum cholesterol. The data was analysed by student's paired 't' test.

RESULTS AND DISCUSSION

In this study, food consumption and weight gain in treated animals was significantly more than control group.

Food consumption was increased by 70–80% in treated animals as against 41% in control animals after 90 days (Table I).

Weight gain after 45 days was 25.13% – 38.16% in treated group against 8.99% in control group. After 90 days, total weight gain was 31.24%–53.02% in treated group, which was significantly more ($P<0.01$) as compared to control group i.e. 12.98% (Table II).

There was an increase of 1.7–1.9 gm% in haemoglobin which correlated with an increase of 2.0–2.1 million/cumm in RBC count. Total and differential leucocyte count did not vary much. Nothing abnormal was detected in urine microscopically or in physical characters.

All biochemical parameters were found to be within normal limits in treated as well as in control group (Table III).

Animals from group III and IV showed increase in liver weight after 45 days. After

TABLE I : Mean (±SE) food consumption (grams) per 100 gm body weight of rats.

Group	*Food consumption*			*Percentage increase*	
	0 Days	*45 Days*	*90 Days*	*45 Days*	*90 Days*
I (Control)	10.20±0.06	12.54±0.11	14.38±0.32	23	41
II (8.50 mg/kg)	10.00±0.18	14.01±0.08	17.04±0.09	40	70
III (12.75 mg/kg)	11.10±0.08	15.30±0.76	18.21±0.07	42	71
IV (17.00 mg/kg)	10.08±0.26	14.12±0.62	18.04±0.11	41	80

No significant dose dependent change.

90 days, animals from all the three treated groups showed increase in liver weight. There was no appreciable change in weight of spleen and kidneys.

TABLE II : Effect of the combination of Ginseng and Ashwagandha extract on body weight in rats.

Group	*Dose mg/kg*	*%Weight gain After*	
		45 days	*90 days*
I (Control)	—	08.99	12.98
II	08.50	25.13*	53.02**
III	12.75	38.16*	31.24**
IV	17.00	30.16*	38.18**

*P<0.05

**P<0.01

Histopathology of brain, heart, lung, liver, spleen, kidneys, stomach, testis and ovaries was normal on gross examination as well as microscopically.

All the animals appeared alert and in good health. There was no mortality in any of the drug treated or control animals during the 90 days period of study.

Sharma et al (5) showed that Ashwagandha alone was devoid of any toxic effects even after 8 months of continuous daily administration in rats.

Similarly, Trabucci (6) observed no toxicity in rats with Ginseng along after long term administration in rats.

TABLE III : Effect of the combination of Ginseng and Ashwagandha on different biochemical parameters.

Parameter	*Group I (Control)*	*Group II*	*Group III*	*Group IV*
Blood glucose (mg%)	74.4 ±0.43	80.0 ±0.86	73.0 ± 1.30	88.0 ±2.40
Total bilirubin (mg%)	0.5 ±0.18	0.6 ±0.08	0.5 ± 0.14	0.6 ±0.21
SGOT (IU/L)	20.0 ±0.20	22.0 ±0.48	22.0 ± 1.00	24.0 ±0.84
SGPT (IU/L)	20.0 ±1.84	16.0 ±2.00	21.0 ± 1.74	22.0 ±2.00
Alkaline phosphatase (KAU%)	16.0 ±2.00	18.0 ±3.12	15.0 ± 1.67	15.0 ±1.80
Blood urea (mg%)	28.0 ±1.80	25.0 ±1.62	19.0 ± 2.00	20.0 ±2.11
Serum creatinine (mg%)	0.8 ±0.07	0.8 ±0.05	0.6 ± 0.10	0.7 ±0.01
Serum cholesterol (mg%)	115.0 ±5.0	90.0 ±8.0	112.0 ± 2.0	118.0 ±5.0

Results are means ± SEM

In our study, no specific organ pathology was found except two incidental findings, wherein, one animal revealed emphysema on gross examination as well as microscopically. Similarly, one animal was found to have focal calcification in seminiferous tubules as an isolated finding.

Normal bilirubin as well as serum enzyme levels indicate normal functioning of the liver.

Increase in liver weight may be due to increased liver protein biosynthesis. Increased food consumption, weight gain and improved haematopoesis with this combination validate the use of these drugs as haematinic and growth promoters.

In conclusion, it can be said, that subacute toxicity studies in rats did not show any significant toxic effect with this combination in the doses studied and thus substantiate the claim of safety of the combination.

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