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Research Article

PROTECTIVE ACTION OF LIVOL AGAINST PARACETAMOL INDUCED HEPATOTOXICITY

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ABSTRACT
Protective action of Livol (a herbal formulation) against paracetamol induced experimental hepatotoxicity was observed in dog. Increased values of serum glutamate oxaloacetate transaminase, serum glutamate pyruvate transaminase, serum total cholesterol and its fractions, globulin, icterus index, prothrombin time and bromosulphalein retention by paracetamol (250 mg/kg, once orally) were decreased after Livol treatment (250 mg/kg, orally upto 72 hr of the experiment) in dog. However, the decreased values of total plasma protein, albumin, fibrinogen and albumin:globulin ratio were increased after administration of Livol. The improvement in these biochemical parameters indicates that Livol exerts beneficial effect on liver dysfunction.

KEYWORDS: Biochemical parameters, Dogs, Liver improvement, Livol, Hepatotoxicity, Paracetamol.

INTRODUCTION
Several chemicals and drugs have been stated[1-2] to cause liver damage in humans and animals both, resulting into a significant increase in different liver function tests (LFTs) or biochemical functions. In the present study, paracetamol was taken as a hepatotoxic agent since it has been reported to produce standard experimental hepatotoxicity in animals[2-4]. Until recently it has been accepted like a dogma that no effective treatment of liver diseases exists. However, with the discovery of a plethora of drugs of plant origin, the situation has now markedly changed and a substantial volume of evidence indicates that these drugs exert a specific influence on the hepatic parenchyma[1-2]. A herbal formulation, Livol manufactured by the Indian Herbs Research & Supply Co. Ltd., Saharanpur, UP, India has been reported to be a good remedy for various liver disorders, and ensures proper performance and growth in animals[1-2,5-7]. Livol is composed of four medicinal plants, viz., *Boerhaavia diffusa* (Punarnava), *Citrullus colocynthis* (Indrayan, colocynth), *Solanum nigrum* (Makoi) and *Terminalia arjuna* (Arjuna).
In view of the above facts, the present study was undertaken to assess the protective action of Livol against paracetamol induced experimental hepatotoxicity in dog by estimating some of the LFTs or biochemical functions.

MATERIALS AND METHODS
The study was performed in six mongrel dogs (5-10 kg) of either sex. All the dogs were dewormed by a single oral dose of tetramisole (Nilverm) @ 5 ml/15 kg body weight. The blood for biochemical estimation was collected from the femoral vein of each 18 hr fasted dog under pentobarbitone (35 mg/kg, iv) anaesthesia. Hence, the normal biochemical functions of all the six dogs were determined at the 1st hr of the experiment, and the biochemical values so obtained were served as normal values. Before 12 hr of inducing hepatotoxicity, a protective dose of Livol powder with drinking water was administered (through stomach tube) @ 250 mg/kg, orally to three dogs. Later on, Livol was administered daily at the same dose rate upto 72 hr of the experiment. Thereafter, to induce the standard hepatotoxicity, all the six

dogs showing normal biochemical functions were given paracetamol @250 mg/kg, once orally with milk after 12 hr of the first dose of Livol (given in three dogs). The blood samples were collected from three dogs of paracetamol alone treated group and from three dogs of Livol plus paracetamol treated group after 24, 48 and 96 hr of the experiment to estimate the extent of damage caused by paracetamol and improvement brought up by Livol.

The biochemical parameters estimated and the methods used for their estimation are as follows:

1. Serum glutamate oxaloacetate transaminase (SGOT) (Method of Yatzids)[8];
2. Serum glutamate pyruvate transaminase (SGPT) (Method of Yatzids)[8];
3. Serum total cholesterol and its fractions, viz., free and esterified cholesterols (Method of Kind outlined by Wooten)[9];
4. Plasma total protein and its fractions, viz., albumin, globulin, fibrinogen and albumin:globulin ratio (A:G) (Biuret method modified by Weichselboum)[10];
5. Icterus index (Method of Oser)[11];
6. Prothrombin time (PT) (Method of Quick)[12]; and
7. Bromosulphalein (BSP) retention or clearance test (Method of Oser)[11]- BSP was injected @ 5 mg/kg, iv just after the collection of blood and subsequently blood sample was collected after 45 minutes for the estimation of BSP retention.

The serum for GOT, GPT, cholesterol and icterus index was obtained for each blood sample by centrifugation. The plasma for protein, PT and BSP retention was obtained by centrifuging each blood sample containing 1 ml of sodium oxalate (1.34 M) as anticoagulant for 9 ml of blood.

RESULTS

The estimated mean values of different biochemical parameters are shown in Table 1. The blood of dogs taken at 24 hr after paracetamol alone treatment, showed the increased levels of SGOT, SGPT, all serum cholesterols, globulin, icterus index, PT and BSP retention. However, total protein, albumin and fibrinogen values were decreased, resulting into decreased A:G. The blood taken at 48 hr after dosing of paracetamol alone, showed further increase in the levels of SGOT, SGPT, globulin, icterus index, PT and BSP retention; whereas, there was decrease in the levels of serum cholesterols, total protein, albumin, fibrinogen and A:G. The blood samples collected after 96 hr, the paracetamol alone treated dogs revealed slight improvement towards normal levels of SGOT, SGPT, serum cholesterols and plasma proteins (except globulin); while the values of globulin, icterus index, PT and BSP clearance test did not reached at their normal levels. On contrary to these results, the paracetamol increased values of SGOT, SGPT, all serum cholesterols, globulin, icterus index, PT and BSP retention were found to be subsequently decreased towards normal levels after 24 and 48 hr and the values reached nearby normal after 96 hr when dogs were treated with Livol and paracetamol; however, the decreased values of plasma proteins (except globulin) were subsequently increased towards normal after 24 and 48 hr and came at normal levels after 96 hr of the experiment.

DISCUSSION

The normal and hepatotoxic values of different biochemical parameters estimated in the present study correspond with the values reported earlier[1-2,5-6,13]. As resulted in the present study, the paracetamol induced hepatotoxicity both in humans and animals has also been reported earlier[2-6].

The prior treatment with Livol in paracetamol induced hepatotoxic dogs seemed to provide protection with regard to values obtained for transaminases (SGOT and SGPT) after 24 hr of the experiment. Similarly, transaminases seemed to resume mormalcy from the observation recorded after 48 and 96 hr. The decrease in the activities of transaminases as a result of Livol treatment may be correlated with the earlier finding[14] that a significant reduction in these enzymes was noticed after administration of another indigenous hepatoprotective agent, silymarin (isolated from the seeds of *Silybum marianum*) in carbon tetrachloride induced hepatotoxicity. The levels of serum cholesterols obtained after 24 hr of the experiment also indicate slight protective effect of Livol, and the values obtained after 48 and 96 hr indicate the trend of improvement in total, free and esterified cholesterols. Although, total protein contents in blood did not show appreciable change with different treatments, the albumin was found to be

normal after 48 hr in Livol plus paracetamol treated group contrary to its diminished value in paracetamol alone treated group after the same period. The globulin did not appreciably increase after 48 hr in Livol plus paracetamol treated group as compared to paracetamol alone treated group after the same period, resulting into the maintenance of A:G within normal limits. Livol also seemed to regularize the icterus index, PT and BSP retention at the end of 96 hr in Livol plus paracetamol treated group, while the remarkable improvement in these parameters could not be observed in paracetamol alone treated group during the same period. The alterations caused by paracetamol in all the biochemical parameters determined in the present study have also been caused by another standard hepatotoxic agent, carbon tetrachloride[1].

The hepatogenic effect of Livol as observed in the dogs of the present study has also been noticed in dogs with carbon tetrachloride induced hepatotoxicity[1], and in mice and rabbits with paracetamol induced hepatotoxicity[2]. Therapeutic efficacy of Livol in experimentally induced hepatotoxicity in sheep was also found[7]. Similarly, the ingredients of Livol, viz., *B. diffusa,* colocynth, *S. nigrum* and *T. arjuna* also possess the hepatogenic activity and may be used against various liver disorders[2,6-7,15-16]. All these findings further support the results of the present study. It appears that these herbal drugs reduce the toxic hazards of paracetamol metabolically by acting on the hepatic microsomal drug metabolizing enzyme systems[2,5-6]. A herbal drug, Tefroli similar to Livol as it contains some ingredients of Livol, has been found[17] to have a possible antiinflammatory action since it caused fast decline in SGPT level increased in human infective hepatitis and cirrhosis of liver. Hence, the similar possible mechanism of action of Livol may be postulated on the basis of these reports.

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REFERENCES

1. Pandey Govind P. Pharmacological studies of Livol® with special reference to liver function. MVSc & AH thesis. Jabalpur, MP, India: JNKVV; 1980.
2. Pandey GP 1990. Hepatogenic effect of some indigenous drugs on experimental liver damage. PhD thesis. Jabalpur: JNKVV; 1990.
3. Pandey Govind, Srivastava DN, Madhuri S. A standard hepatotoxic model produced by paracetamol in rat. Toxicol Int 2008; 15(1):69-70.
4. Pandey Govind, Srivastava DN, Madhuri S. An experimental model of hepatocellular necrosis produced by paracetamol in mouse. Indian J Vet Pathol 2008; 32(1):62-3.
5. Pandey, Govind. Hepatogenic effect of some herbal drugs on paracetamol altered serum transaminases activity in rabbit. biomed 2007; 2(2):202-5.
6. Pandey, Govind. Hepatogenic efficacy of Livol, *Eclipta alba* and *Silybum marianum* against paracetamol altered serum protein levels. biomed, 2008; 3(1):62-5.
7. Wagh KR, Bidwai CS. Therapeutic efficacy of Livol® in experimentally induced hepatotoxicity in sheep. Indian J Pharmacol 1989; 21(1):48-9.
8. Yatzids H. Measurement of transaminases in serum. Nature 1960; 186:79-80.
9. Wooten IDP. Microanalysis of Medical Biochemistry. 4th ed. London: J & A Churchill Ltd.; 1964. p. 138-40.
10. Weichselboum TE. Am J clin Pathol 1946; 16:40 (In: Kaneko JJ, Cornelius CE, editors. Clinical Biochemistry of Domestic Animals. Vol. I, 2nd ed. New York: Academic Press; 1963. p. 177
11. Oser BL. Hawk's Physiological Chemistry. 4th ed. New York; 1965. p. 1073-80.
12. Quick AJ. Haemorrhagic Diseases and Thrombosis. 2nd ed. Philadelphia: Lee & Febriger; 1966. p. 391-5 & 437-9.
13. Sharma IJ. Effect of experimental hepatic damage on certain liver function tests in stray

dogs. MVSc & AH thesis. Jabalpur: JNKVV; 1975.
14. Vogel G. New Natural Products and Plant Drugs with Pharmacological, Biological or Therapeutical activity. New York: Springer-Verlag; 1977. p. 249-62.
15. Chopra RN, Nayar SL, Chopra IC. Glossary of Indian Medicinal Plants. New Delhi, India: CSIR; 1986.
16. Kirtikar KR, Basu BD. Indian Medicinal Plants. Vol. II & III. Dehradun, India: BSMP Singh; 1975.
17. Reddy KD. Tefroli- A clinical trial in hepatic malignancy and cirrhosis of liver. Indian Medical Gazette 1986; CXX(6):215-7.

Table 1: Mean values of different biochemical parameters during paracetamol and Livol treatments in dogs

Biochemical parameter (with unit)	Normal value (Normal group)*	Value after paracetamol administration (Parcaetamol alone treated group)**			Value after paracetamol and Livol administration (Parcaetamol + Livol treated group)**		
		24 hr	48 hr	96 hr	24 hr	48 hr	96 hr
1. SGOT (μ/ml)	70.30	99.30	103.00	80.23	83.10	78.16	72.00
2. SGPT (μ/ml)	76.20	106.00	109.30	84.16	89.52	80.12	77.68
3. Serum cholesterols:							
a. Total (mg%)	240.12	270.16	262.0	256.00	258.00	250.23	242.50
b. Free (mg%)	151.33	165.26	162.00	160.10	160.31	159.78	152.00
c. Esterified (mg%)	88.79	104.90	100.00	95.90	97.69	91.45	90.50
4. Plasma proteins:							
a. Total (g%)	6.70	6.62	6.31	6.68	6.48	6.59	6.78
b. Albumin (g%)	3.95	3.70	2.90	3.58	3.56	3.98	4.12
c. Globulin (g%)	2.52	2.71	3.22	2.88	2.67	2.32	2.36
d. Fibrinogen (g%)	0.23	0.21	0.19	0.22	0.47	0.29	0.30
e. A:G (Ratio)	1.56:1	1.36:1	0.90:1	1.24:1	1.33:1	1.71:1	1.74:1
5. Icterus index	4.8	8.0	12.0	10.0	7.0	6.2	4.9
6. PT (Second)	12.0	20.0	25.0	18.0	14.0	13.8	12.6
7. BSP retention (mg%)	6.9	11.3	16.8	17.3	10.3	8.2	6.0

* Mean value obtained from 6 dogs. ** Mean value obtained from 3 dogs.

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