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HEPATOPROTECTIVE EFFECT OF CHITRAKAPIPPALI GHRITA IN PARACETAMOL INDUCED HEPATOTOXICITY- AN IN VIVO STUDY.

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ABSTRACT

Background & Objectives - Methods: 42 male Wistar rats were divided into 7 equal groups as follows. All drugs were administered orally. **Group I**: Untreated group. **Group II**: Control group, paracetamol (3gm/kg body weight of animal) for 1 day after over night fasting. **Group III:** Low dose CP (chitrakapippali ghrita) for 5 days, 6th day- CP(low dose) followed by paracetamol and on 7th day- CP(low dose) alone. **Group IV:** Therapeutic/intermediate dose CP for 5 days, 6th day- CP(intermediate dose) followed by paracetamol and on 7th day- CP(intermediate dose) alone. **Group V:** High dose CP for 5 days, 6th day- CP(high dose) followed by paracetamol and on 7th day- CP(high dose)only. **Group VI:** Silymarin (100mg/kg body weight of animal) for 5 days, 6th day- silymarin followed by paracetamol and on 7th day-silymarin alone. **Group VII:** High dose CP alone for 7 days. Biochemical parameters such as serum bilirubin, ALT, AST, ALP, albumin globulin ratio were analysed for the estimation of hepatotoxicity. **RESULT:** The animals treated with paracetamol showed significant elevation in serum parameters especially bilirubin, AST, ALT and a slight elevation in ALP when compared to other groups. Animals treated with CP at therapeutic and low doses show hepatoprotectivity in a dose dependant manner. The therapeutic/intermediate dose of CP was proved to have the most hepatoprotective effect through the estimation of serum parameters, and histopathological observations even than silymarin when serum ALT, AST are considered; bilirubin remains the same.

Keywords : Chitrakapippali ghrita; hepatoprotective; paracetamol;

1. INTRODUCTION

Abuse of drugs is a common source of hepatotoxicity nowadays. So in this guise, Ayurvedic medicines can offer a protective action against development of serious health hazards.

Chitrakapippali ghrita mentioned in Bhaishajya ratnavali pleeha yakrit rogaadhikara, is selected to find the efficacy in hepatoprotective aspect[1]. (C. Kathiravan et al., 2019) Since chitraka and pippali are the rasayanas told by our acharyas, this study also aims to check the efficacy of this drug against hepatotoxicity.

2. IN VIVO EXPERIMENTAL STUDY

2.1 EXPERIMENTAL PHARMACOLOGY

The Animals:

All animal experiments were conducted after getting prior permission from Institutional Animal Ethics Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), Ministry of Environment and Forest, (D. C. Kathiravan, 2019) Government of India. Male Wistar rats (Average weight 200g) of 7-8 weeks old were purchased.

Dose fixation: The dose for the study was fixed by converting human dose to animal dose on the basis of body surface area ratio by referring to the table of Paget and Barnes (1969).

- Standard(intermediate/therapeutic) dose of chitraka pippali ghrita = **1 ml**
- High dose administered = **2 ml**
- Low dose administered = **0.5 ml**
- **Paracetamol** was administered at a dose of **3gm/kg body weight orally.**
- **Silymarin** was administered at a dose of **100mg/Kg body weight orally.**

Paracetamol is given by dissolving the concerned dose in distilled water and that suspension is being administered to the experimental animals as per their body weight. Silymarin, available for research purposes is in powder form. It is dissolved in ethanol (minimum quantity) and in 1% gum acacia (1gm gum acacia in 100 ml distilled water)**.** This is heated for 15 min at 75˚C.

Animal groupings: The animals were divided into the following 7 groups containing 6 animals.

Group I : Normal

Group II : Paracetamol (3gm/kg body weight) for 1 day, after overnight fasting. Sacrifice after 48 hrs.

Group III : Low dose of chitrakapippali ghrita (CP) for 5 days.
5th day overnight- fasting
6th day- CP (low dose) then after 1 hr paracetamol (3gm/kg body weight).
7th day- CP (low dose) only.
8th day- sacrifice.

Group IV : Therapeutic/intermediate dose of chitrakapippali ghrita (CP) for 5 days.
5th day overnight- fasting.
6th day- CP (intermediate dose) then after 1 hr paracetamol (3gm/kg body weight).
7th day- CP (intermediate dose) only.
8th day- sacrifice.

Group V : High dose of chitrakapippali ghrita (CP) for 5 days.
5th day overnight- fasting.
6th day- CP (high dose) then after 1 hr paracetamol (3gm/kg body weight).
7th day- CP (high dose) only.
8th day- sacrifice.

Group VI : Silymarin (100mg/kg body weight) for 5 days.
5th day overnight- fasting.
6th day- silymarin then after 1 hr paracetamol (3gm/kg body weight).
7th day- silymarin only.
8th day- sacrifice.

Group VII : High dose of chitrakapippali ghrita (CP) for 7 days.
8th day- sacrifice.

Experimental protocol:

- On the 8th day animals were weighed again and sacrificed in carbondioxide chamber. Blood samples were collected by cardiac puncture for the estimation of serum biochemical parameters

2.2 PARAMETRES RECORDED FOR THE STUDY

- **Biochemical parameters :** Serum
- **Biochemical parameters in serum**

1. **Liver function test**

- Serum Bilirubin
- Serum Aspartate amino transaminases (AST/SGOT)
- Serum Alanine aminotransferase (ALT/SGPT)
- Serum alkaline phosphatase (ALP)
- Serum albumin globulin ratio.

3. ESTIMATION OF SERUM PARAMETRES

3.1 ESTIMATION OF LIVER FUNCTIONS

The serum was preserved at -80 degree Celsius and the liver function tests were carried out with the help of commercial kits purchased.

4. OBSERVATION AND ANALYSIS

The mean and standard deviation of various groups were compared with the untreated, control and the standard drug using one way analysis of variance (ANOVA) in which Dunnet multiple comparison test was employed to analyze the level of significance of variation of group means. The analysis was performed using statistical software GraphPad InStat (DATASET1.ISD).

Table 1 : OBSERVATIONS FROM LIVER FUNCTION TEST

Group	BILIRUBIN	AST/SGOT	ALT/SGPT	ALP	ALB:GL0
Untreated	0.27 ± 0.06^{B}	166.27 ± 23.54^{B}	27.12 ± 11.25^{B}	35.34 ± 8.83^{B}	3.1 : 3.5
Paracetamol alone (control)	$4.41 \pm 1.6^{**,b}$	$417.78 \pm 146.7^{**,b}$	$244.04 \pm 141.5^{**,b}$	$76.52 \pm 13.8^{**,a}$	4.6 : 4.4
Drug(0.5ml)+ paracetamol	0.43 ± 0.26^{B}	179.02 ± 63.26^{B}	73.08 ± 20.11^{B}	$64.24 \pm 14^{**}$	2.7 : 5.6

Drug(1ml)+ paracetamol	0.39±0.17^{B}	169.65±32.70^{B}	89.02±22.74^{B}	62.79±3.94**	2.5 : 6.1
Drug(2ml)+ paracetamol	0.68±0.49^{B}	214.75±73.67^{B}	59.83±13.97^{B}	69.32±12.80^{**,a}	3.8 : 6.0
Silymarin+ paracetamol	0.38±0.30^{B}	255.13±34.94^{B}	112.94±12.24^{B}	52.05±17.51^{A}	3.7 : 5.9
Drug(2ml) only	0.30±0.25^{B}	197.29±25.43^{B}	63.79±9.82^{B}	58.37±13.86*	4.5 : 5.9

Each value represents the mean ± SD of 6 wistar rats. *, P<0.05; **, P<0.01; ***,P<0.001; when compared with normal. A, P<0.05; B, P<0.01; C, P<0.001; when compared with control. a- P<0.05, b- P<0.01, c- P<0.001 when compared with standard drug.

5. DISCUSSION

In this work, the hepatotoxicity was induced by the oral administration of paracetamol to the experimental animals. Here the hepatotoxicity that we induced was later confirmed by the serum parameters analysis. The serum parameters for the estimation of liver function include bilirubin, AST, ALT, ALP, albumin and globulin. On analyzing the serum parameters it is proved that the order of efficacy of chitrakapippali ghrita is therapeutic/intermediate dose > low dose > high dose. The therapeutic dose is even more effective than the standard hepatoprotective drug used in this study ie, silymarin, as far as ALT and AST are concerned; serum bilirubin remains almost the same. Chitraka and pippali are mentioned by acharyas as rasayanas, proven to potentiate vyadhikshamatva. Hence in addition to provide hepatoprotection, this test drug can act as immune boosting agent. Chitrakapippali ghrita mainly contains chitraka, pippali, ghrita and goksheera. Among these, goksheera as per acharya Vagbhata, is a rasayana. This is also an added benefit as we consider paracetamol as an aganthuja nidana for vyadhi .

Among the chatusnehas, ghrita is the most potent of the unique characteristic feature shown by it ie, samskaarasyaanuvartanat ie, without losing its own properties it can imbibe the features of drugs added to it. Ghrita is the best drug of choice when there is vata pitta kopa and also when we require a rasayana property too. Besides, the visha induced here can also be subsided by the vishahara property of ghrita. Chitrakapippali ghrita is mentioned in the pleehayakrit rogadhikara (41/219) of Bhaishajya ratnavali.

Here it has been proved that chitrakapippali ghrita if consumed in high dose (2ml/animal) resulted in slight elevation of some liver function enzymes in blood. It is evident from this that chitrakapippali ghrita is not suitable for snehapana in sodhana aspect; yet it gives better results if administerd in therapeutic dose and also in low dose. Anyway, the therapeutic dose was found to be most effective hepatoprotective agent against paracetamol induced hepatotoxicity. Actually, the therapeutic dose was determined as per human uttama sneha maatra ie, 48ml. The therapeutic dose of chitrakapippali ghrita is even more effective than silymarin thereby emphasizing its hepatoprotectivity.

6. CONCLUSION

Although the study was conducted using three different doses of chitrakapippali ghrita, the maximum hepatoprotection was shown by the therapeutic/intermediate dose. Though this ghrita had been proven as a better hepatoprotective agent than silymarin, administration in high doses is not at all encouraged; as it tends to elevate certain liver enzymes in blood. In people who are prone to hepatic dysfunction due to the drug abuse and xenobiotics, this ghrita can be administered in therapeutic dose if with proper agnibala; if not, in low dose can be taken.

7. REFERENCES

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