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Effect of Aerial Part Extract of *Cassia Sophera* (Linn) on Ranitidine induced Hepatotoxicity in Rats

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Abstract:
The present study was carried out to assess the hepatoprotective activitiy of aqueous extract of aerial part extract of *Cassia Sophera* (Linn) (AQEACS) in rats. Preliminary phytochemical studies revealed the presence of phytoconstituents like carbohydrates, amino acids, fixed oils, fats, Ascorbic acid, glycosides and sterols. Toxicity profile of the crude extract was conducted in albino mice by following OECD Guideline No-425. It was found that even at 2g/kg the extract is safer to be used which was confirmed in mice which have not shown any mortality.
The hepatoprotective activity was studied in ranitidine induced hepatotoxic animal models in rats. The biochemical parameters studied were ALT, AST, ALP, BILD, BILT, ALB, PRO, CHO and TRG levels in serum. Prevention of elevation in biochemical parameter levels like ALT, AST, ALP, BILD, BILT, CHO and TRG and increase in ALB, PRO in serum after treatment with the extracts confirmed that hepatoprotective effect of these extracts against ranitidine induced liver injury. Drug induced hepatotoxicity was significantly prevented by pretreatment with the extract.

Key words - Hepatoprotective, OECD, ranitidine, *Cassia Sophera*

I. Introduction:

Hepatotoxicity may be defined as the effect of any agent on liver which results in a deviation from normal function, morphology and implies chemical/drug/microbial-driven liver-damage[1]. Toxicants lead to necrosis, steatosis, cirrhosis, carcinoma, other cause is jaundice or with little or no overt injury to the hepatic parenchyma and some agents produce degenerative or vascular lesions. Hepatotoxicity can also be related to chemical change of numerous drugs during biotransformation to reactive metabolites. These metabolites can accumulate due to lack of their disposal mechanism leading to liver damage. Hepatic damage is inturn related to the metabolites chemical nature and its affinity towards the hepatocytes.
Domestic exposure to hepatotoxins includes accidental exposure to ccl_4, phosphorous, toxic/over doses of hepatotoxic medicinal agents such as acetaminophen or ferrous sulphate, ingestion of hepatotoxic mushrooms.
Liver plays an important role in regulation of physiological processes, involved in several vital functions such as storage, secretion and metabolism. It also detoxifies a variety of drugs and xenobiotics and secrete bile that has an important role in digestion.
The liver plays a central role in transforming, clearing the chemicals and is susceptible to the toxicity from these agents. Certain medicinal agents when taken in overdoses and sometimes even when administered within therapeutic ranges may injure this organ. Other chemical agents such as those used in laboratories, industries, natural chemicals (e.g. microcystins) and herbal remedies can also induce hepatotoxicity, and chemicals that cause liver injury are called hepatotoxins.
Cassia sophera, Linn. (Caesalpiniaceae) known as 'Kasondi' is an important drug of Unani System of Medicine. According to the physicians of Unani medicine, three plants viz., Cassia occidentalis Linn. Cassia sophera Linn. and Cassia sophera, Linn. var. purpurea, Roxb. are varieties of 'Kasondi' and are invariably used in similar pathological conditions. ''Kasondi'is described in Unani literature to be repulsive of morbid humours (specially phlegm), resolvent, blood purifier, carminative, purgative, digestive, diaphoretic, and reported to be useful in epilepsy, ascites, dyscrasia of liver, skin disorders, piles, jaundice, fever, articular pain and palpitation[2]. Therefore the present study was planned to screen the beneficial effect of aerial part extract of *Cassia sophera* (linn) against ranitidine induced hepatotoicity in rats.

II. Material and Methods:

1. Collection and identification of Plant Material

Aerial part of *C. sophera* were collected in the month of August from local fields of Raichur and were identified by a botanist Prof. Hemanth kumar and were dried in shade at room temperature then subjected to size reduction to a fine powder with the help of grinder.

2. Preparation of aqueous extract[3]

About 100 g of powder was taken in a round bottom flask (2000 ml) and macerated with 500 ml of distilled water with 10 ml of chloroform (preservative) for 24 h with shaking for every hour in a closed vessel. Then the marc was removed by filtering the extract

and then it was concentrated on a water bath maintained at 50ºC. The preliminary phytochemical investigations were carried out with aqueous (AQEACS) extracts for qualitative identification of phytochemical constituents present by following standard methods.

3. Experimental animals:

Albino rats (Wistar strain) of either sex weighing between 150-200 g and Albino mice 20-30g were procured from National Centre for Laboratory Animal sciences, C/O Sri. Venkateswara Enterprises, Bangalore for experimental purpose. Then the animals were acclimatized for 7 days under standard husbandry conditions. The animals were fed with a synthetic standard diet from Amrut laboratories & Pranav Agro Industries Ltd. Sangli. Water was allowed *ad libitum* under strict hygienic conditions. All animal studies were performed in accordance to guidelines of CPCSEA and Institutional Animal Ethical Committee (IAEC) of V.L. College of Pharmacy, Raichur (Karnataka).

Determination of acute toxicity (LD_{50}):

The acute toxicity of AQAECS were determined by using female albino mice (20-30 g) those maintained under standard husbandry conditions. The animals were fasted 3 h prior to the experiment and "up and down" (OECD guideline No. 425) method was adopted for toxicity studies. Animals were administered with single doses of extracts and observed for their mortality during 48 h study period (short term toxicity). Based on the short-term toxicity profile of drug the dose for the next experimentation was determined.[4]

4. Experimental Procedure:

Ranitidine induced hepatotoxicity[5,6]:

Albino rats weighing between 150-200 g each group containing 6 animals will be divided in 9 groups.

Group A -Normal Control (vehicle treated, p.o)
Group B -Toxicant (Ranitidine 50 mg/kg, i.m)
Group C -Standard (Silymarin 100 mg/kg, p.o)
Group D -AQEACS (low dose100 mg/kg, p.o)
Group E -AQEACS (medium dose 200 mg/kg, p.o)
Group F -AQEACS (high dose 400 mg/kg, p.o)

Experimental procedure[7]:

Group A were administered vehicle for 10 days and served as normal control, group B with ranitidine (50 mg/kg, i.m), and group C with silymarin (100 mg/kg, p.o) which was serve as standard. Animals in group D, E, F were treated with three different doses (low, medium and high) of AQEACS for 10 days, animals of group B, C, D, E and F were intoxicated with ranitidine (50 mg/kg, i.m). On the 10th day after drug treatment, blood was collected from retro orbital puncture under anaesthesia and liver biochemical parameters were studied.

III. Results:

In toxicant group, when compared to normal control animals biochemical parameters like ALT (U/L) (147.76 ± 3.84), AST (U/L) (208.41 ± 15.68), ALP (U/L) (243.58 ± 12.14), BILD (U/L) (2.361 ±0.10), BILT (U/L) (2.145 ± 0.05), CHO (U/L) (255.5 ± 7.82) and TRG (U/L) (148.25 ± 7.19) except ALB and PRO (mg/dl) (1.606 ±0.11, 6.423± 0.06) were significantly enhanced.

Table no. 01 Hepatoprotective effect of different extracts of *C. sophera* on Ranitidine induced hepatotoxicity in rats

Groups	Treatment	ALT U/L	AST U/L	ALP U/L	BILD U/L	BILT U/L	ALB mg/dl	PRO mg/dl	CHO U/L	TRG U/L
Normal	Vehicle 10 ml/kg p.o	42.07 ± 0.705	107.4 ± 3.30	109.1 ± 2.61	0.19 ± 0.008	0.23 ± 0.015	4.38 ± 0.14	13.94 ± 0.43	132.5 ± 0.97	31.72 ± 0.51
Toxicant	Ranitidine 50 mg/kg i.m	147.7 ± 3.84	208.4 ± 15.6	243.5 ± 12.14	8.36 ±0.10	2.14 ± 0.05	1.60 ±0.11	6.42 ±0.06	255.5 ± 7.82	148.2 ± 7.19
Standard	Silymarin 100 mg/kg p.o	43.47 ± 2.35**	109.7 ±2.48**	128.2 ± 6.91**	0.46 ± 0.11**	0.34 ± 0.04**	4.26 ±0.15**	13.21 ± 0.03**	153.7 ± 16.3**	39.74 ± 3.67**
AQEACS	Low dose 100 mg/kg p.o	8.76 ± 0.11^{ns}	9.34 ± 0.12 **ns**	139.3 ± 5.14 ^{ns}	7.4 ± 3.47 ^{ns}	2.8 ± 3.84*	2.15 ± 0.03**	1.96 ± 0.03*	1.85 ± 0.11 ^{ns}	6.59 ± 0.11 ^{ns}
AQEACS	Med dose 200 mg/kg p.o	6.83 ±0.19**	7.01 ±0.11**	73.73 ± 1.14**	6.9 ± 4.15**	2.6 ± 4.99**	1.53 ± 0.05**	0.78 ± 0.07**	3.69 ±0.08**	9.52 ± 0.10**
AQEACS	High dose 400 mg/kg p.o	5.84 ± 0.29**	6.02 ±0.12**	64.66 ± 1.42**	6.0 ± 2.26**	2.5 ± 4.10**	1.7 ± 0.01**	0.52 ± 0.06**	4.23 ±0.05**	12.05 ± 0.25**

n = 6, Significant at P < 0.05*, 0.01** and 0.001***, ns = not significant

AEACS-Alcoholic extract of aerial part of *C. sophera*, AQEACS- Aqueous extract of aerial part of *C.sophera*

In Standard treated group, when compared to toxicant control animals biochemical parameters like ALT (U/L) (43.47± 2.35), AST (U/L) (109.7±2.48), ALP (U/L) (128.2±6.91), BILD (U/L) (0.46±0.11), BILT (U/L) (0.34±0.04), CHO (U/L) (153.7±16.33) and TRG (U/L) (39.74±3.67) were significantly reduced except ALB, PRO (mg/dl) (4.26±0.15, 13.21±0.03) which were significantly increased.

When compared to toxicant control animals AQEACS has shown dose dependent activity (low, med, high) on all biochemical parameters like ALT, AST, ALP, BILD, BILT, CHO and TRG (U/L) by decreasing the elevated levels significantly in med and high dose and similarly increased ALB and PRO (mg/dl) levels significantly.

IV. Discussion:

Reactive oxygen species (ROS), such as superoxide anion, hydroxyl radical and hydrogen peroxide, have a causal relationship with oxidative stress. Over production of ROS can aggravate the oxidative stress and the result is a unifying mechanism of injury that occurs in many developments of clinical disease processes such as heart disease, diabetes, liver injury, cancer and aging, etc.

Liver injury induced by ranitidine is due to its metabolite which may leads to hepatic oxidative damage and one of its metabolite is generating immunoallergic reaction[8, 9]. Chronic administration of ranitidine to rats increased the levels of marker enzymes like ALT, AST and ALP as these are stored in the liver cells and increase in the levels of these marker enzymes in serum indicate damage to the liver cells. Pretreatment with aqueous extracts of aerial parts of *C. sophera* decreased the levels of ALT, AST, ALP, BILD, BITD, CHO, TRG levels and increased PRO and ALB levels an indication for the hepatoprotective activity of these extracts against drug induced hepatotoxicity. The protective effect shown by the extracts in various biochemical parameters (ALT, AST & ALP) clearly depicts that aerial part extracts of *C. sophera* possess hepatoprotective activity.

V. Conclusion:

The preliminary pharmacological studies on different parts of the plant revealed significant anticonvulsant[2], hepatoprotective, hypnotic–sedative[2], analgesic[2] and antidiabetic[10] activity.

The preliminary phytochemical analysis of the aerial part extracts of *C. sophera* revealed the presence of carbohydrates, sterols, amino acids, glycosides, fixed oils and fats. In addition to these phytoconstituents it exhibited the presence of emodin, chrysophanic acid and vitamin C.

It can be concluded that AQEACS showed significant hepatoprotective effect against ranitidine induced hepatic damage as depicted by biochemical analysis. The medium and higher doses of AQEACS (200 and 400mg/kg) treated groups showed better hepatoprotective activity when compared to standard drug silymarin (100mg/kg p.o) treated group.

VI. References:

1. Haley Thomas J, Berndt William O. Toxicology 1987; 4: 74-75

2.Ahmad Bilal, Naeem A. Khan, A. Ghufran. Inamuddin. Pharmacological investigation of cassia sophera, linn. Var. Purpurea, roxb. Med J islamic world aca sci 15:3, 105-109, 2005

3. Kokate CK. "Practical Pharmacognosy". New Delhi: Vallabh Prakashan;1994, 4:110-111

4. OECD 2001-gudeline on acute oral toxicity (AOT) Environmental health and safety monograph series on testing and adjustment no.425

5. Valois Maria, Copper Mary Anne, Shear Neil H, An organized approach to drug induced hepatitis. Can J Clin Pharmacol 2003; 10(2):59-62.

6. Hemieda Faried AE, Abdel Hady El-Sayed. Biochemical and histological studies on H2- receptor antagonist ranitidine-induced hepatotoxicity in rats. Indian J Exp Biol 2005; 43:782-785.

7. Gujarati Vipul, Patel Nilesh, Venkat Rao N, Nandakumar K, Gouda TS, Md. Shah Alam. Hepatoprotective activity of alcoholic and aqueous extracts of leaves of Tylophora indica in rats. Indian J Pharmacol 2007; 39(1): 43-47

8. Lee WL. Drug induced hepatotoxicity.N Engl J Med 2003; 349:474-485.

9. Valois Maria, Copper Mary Anne, Shear Neil H, An organized approach to drug induced hepatitis. Can J Clin Pharmacol 2003; 10(2):59-62

10. Khan DI, Pharmacological screening of Cassia sophera for hypoglycemic activity in normal and diabetic rabbits, Proceeding sheikh Zayed Postgraduate Med Inst, 2002;16(1):1-4