Original Research Article

Annals of Plant Sciences
ISSN: 2287-688X
www.annalsofplantsciences.com
OPEN ACCESS

Toxicity studies of *Ervatamia coronaria* Stapf., leaves on experimental animals

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Received for publication: April 05, 2014; Accepted: April 21, 2014

Abstract: The present study was carried out to evaluate the toxicity methanol extract *Ervatamia coronaria* leaves (MEEC) on experimental animals. This was determined by the administration of MEEC intraperitoneally to male mice weekly at a single dose of 200 mg/kg for 6 weeks. The results of this study showed no abnormalities in the test groups as compared to the controls. Biochemical and renal parameters values in treated groups were normal in comparison with the control group. Therefore, the methanol extract of MEEC given intraperitoneally to male mice did not produce toxicities.

Key Words: *Ervatamia coronaria*, Toxicity, Biochemical parameters, Renal parameters

Introduction

Toxicology, the study of the harmful effects of substances on living systems, has been of interest since the earliest days of science. Toxicity testing in animals is carried out on new drugs to identify potential hazards before administering them to man. It involves the use of a wide range of tests in different species, with long-term administration of the drug, regular monitoring for physiological or biochemical abnormalities and a detailed post-mortem examination at the end of the trial to detect any gross or histological abnormalities [1]. Such studies are performed with doses well above the expected therapeutic range and determine which tissues or organs are likely 'targets' of toxic effects of the drug. The basic premise is that toxic effects caused by a drug are similar in man and other animals. This is inherently reasonable in view of the similarities between higher organisms at the cellular and molecular levels. There is a spectrum of toxicity test using whole animals, which evaluate chemical hazards ranging from carcinogenicity to teratology and reproduction studies as well as mutagenicity, neurotoxicity and others. The studies can be loosely categorized as acute, subacute, subchronic or chronic toxicity tests[2].

Toxicological evaluation was performed in serum samples following the administration of dose regimens of the agents that were previously shown to be effective in suppressing malignant tumor growth or to prolong survival in tumor bearing animals. Hepatic and renal toxicity was evaluated by measuring enzyme activity or concentrations of alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, total cholesterol, glucose, blood urea nitrogen and uric acid.

The present study was undertaken to determine the effect of multiple intraperitoneal administration of the different doses of the extract of *Ervatamia coronaria* on hepatorenal functions and metabolism in mice.

Materials and Methods

Test Compound

The methanol extract of *Ervatamia coronaria* (MEEC) 200mg/kg body weight, dissolved in normal saline and administered intraperitoneally.

Experimental animals

Male Swiss albino mice (20-25 g) were used for the present study. They were maintained under standard environmental conditions and were fed with standard pellet diet (Hindustan Lever, Bombay) and water *ad libitum*.

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Chemical reagents

Sodium chloride, Hydrochloric acid (Ranbaxy Chemicals, India), Sulphanilic acid, Sodium nitrite, Chloroform, Methanol (BDH, India), Potassium hydroxide, Sodium hydroxide, Ferric chloride, Anhydrous Sodium sulphate, Dipotassium hydrogen phosphate, Potassium dihydrogen phosphate, Barium hydroxide (Sarabhai M. Chemicals, India); L-Aspartic acid, Acetic acid; 2,4-dinitrophenyl hydrazine, DL-alanine (E. Merck, Germany); Tris buffer (Sigma Chemicals Co, USA), cholesterol, bilirubin, oxaloacetic acid (Sigma Chemicals Co, USA) Glacial acetic acid, Propylene glycol (BDH, India), Sulphuric acid, Phosphoric acid (Ranbaxy, India Ltd), Sodium potassium tartarate, Sodium hydroxide, Copper sulphate, Mercuric iodide, (Sarabhai M. Chemicals, India, Ltd), Urea (Basic and Synth Chemicals, Calcutta, India) Ammonium sulphate, Potassium iodide, Sodium tungstate (Loba Chemicals, Bombay, India).

Treatment schedule

Mature male Swiss albino mice were weighed (20-25g) and divided into 2 Groups (n=10) and given food and water *ad libitum*. On group receives normal saline (5 ml (0.9 % w/v)/ kg body weight) and the other group receives MEEC at the dose of (200 mg/kg body weight) intraperitoneally once in a week and continued for 6 weeks.

All mice were sacrificed after the blood collection at the end of the treatment schedules**.** The changes in the biochemical parameters due to the treatment of MEEC were evaluated. Serum biochemical enzymes such as serum glutamic oxaloacetic (SGOT) and glutamic pyruvic transaminase (SGPT) activities[3] and alkaline phosphatase (SALP) [4] were determined. The total protein concentration and bilirubin were measured by the method of Lowry *et al.,* 1951[5] and Oser, 1965[6].

The changes in the renal parameters due to the treatment of MEEC were evaluated by measuring serum urea [7], creatinine [8] and uric acid level [9].

Statistical analysis

Results are expressed as mean ± SEM. The unpaired student's 't' test was done to evaluate the statistical significance of the data.

Results and Discussion

The methanol extract of *Evatamia coronaria* was evaluated for its chronic toxicity in mice. Results are summarized in Table 1 and 2.

Table 1: Effect of MEEC on biochemical parameters of liver function in mice

Treatment	SGOT (U/l)	SGPT (U/l)	SALP (U/l)	Cholesterol (mg/dl)	Glucose (mg/dl)	Bilirubin (mg/dl)
Saline (5ml/kg)	50.2 ± 0.6	33.1 ± 0.7	98.4 ± 1.3	61.4 ± 1.8	89.1 ± 3.5	1.1 ± 0.001
MEEC (200mg/kg)	52.3 ± 0.7	35.3 ± 0.6	104.4 ± 1.4	63.6 ± 1.7	92.4 ± 3.7	1.3 ± 0.001

P<0.001, Experimental groups compared with control group.

Table 2: Effect of MEEC on biochemical parameters of kidney function in mice

Treatment	Urea (mg/dl)	Uric acid (mg/dl)	Creatinine (mg/dl)	Protein (gm/dl)	Nonprotein Nitrogen
Saline (5ml/kg)	31.7 ± 0.55	3.2 ± 0.23	1.0 ± 0.001	5.8 ± 0.12	16.8 ± 0.44
MEEC (200mg/kg)	29.1 ± 0.57	3.9 ± 0.13	1.1 ± 0.002	5.9 ± 0.14	21.1 ± 0.57

P<0.001, Experimental groups compared with control group

Liver function parameters

Liver function can be assessed by serum transaminase activity[10]. In normal subjects the levels of serum transaminases is usually low but after any tissue injury these enzymes are liberated into serum. It has been found that, patients with acute hepatic diseases have increased SGOT, SGPT levels and thus increased transaminase level may serve as an indicator of liver damage [11]. Moreover, according to the reports of Friend *et al.,* SGOT and SGPT activity is also found in mice liver cell injury caused by the viral hepatitis [12]. The results indicate that the MEEC at a dose of 200mg/kg body weight on

weekly administration does not have any significant alteration in SGOT, SGPT and SALP levels.

Hypercholesterolaemia is found most characteristically in the primary hyperlipoprotinaemia type IV and in the nephratic syndrome, myxoedema, obstructive jaundice and diabetes mellitus[13]. The treatment with MEEC does not alter the plasma cholesterol level at a dose of 200mg/kg body weight.

Bilirubin is formed from degeneration of hemoglobin in the whole of the reticulo endothelial system. The level of bilirubin was not altered by the 6 weeks treatment of MEEC at a dose of 200mg/kg body weight.

Kidney function parameters

Kidney primarily serves to eliminate the waste products of metabolism from the body. It has been found that in case of renal failure, insufficiency of the kidneys to excret urea often leads to an increase in blood urea level [14,15]. Similarly, when accumulation of other waste products like nitrogenous substances takes place, the NPN titre of blood increases. The urea concentration over a period is proportional to the amount of protein in the diet[16] and urea nitrogen forms the greater part of plasma nonprotein nitrogen. Variations in nonprotein nitrogen mainly reflect alterations in blood urea level and as urea rises its nitrogen forms increase the percentage of nonprotein nitrogen. Blood urea and consequently nonprotein nitrogen level is found raised in the terminal stages of chronic nephritis, in some cases of acute nephritis and in congenital cystic kidneys[17].

Creatinine is the least variable nitrogenous constituents of blood. The value is increased in early nephritis and in chronic hemorrhage nephritis with uremia. Similarly increased blood content of creatinine has been reported in renal injury subsequent to trauma or anuria, in traumatic injuries to the muscles and in muscular dystrophy. Treatment with MEEC at a dose of 200mg/kg body weight does not have any significant alteration in blood creatinine level.

The important functions of plasma protein is are to maintain the viscosity of the blood, blood pressure, colloidal osmotic pressure of blood and to aid in regulating the distribution of fluid between blood and tissues[18]. An increase in total plasma protein may be caused by the dehydration and decrease catabolism of protein[16]. Total plasma protein increment is also an indication of liver diseases. The MEEC did not alter the protein content significantly at a dose of 200mg/kg body weight.

Conclusion

Since many drugs are detoxified by the liver and some are stored there, liver damage is often a prominent feature of the body's reaction to toxic drugs. Conversely, liver damage from any cause may prevent the metabolic transformation of drugs and of other regulatory substances. Thus profound systemic disturbances may arise from damage to a single organ. Hepatotoxic reactions sometimes arise acutely, they sometimes occur only during prolonged treatment with a drug or they may have a delayed onset appearing sometime after treatment has ceased.

Kidney is regarded principally as an organ responsible for the removal of metabolic wastes from the body. Any toxic substance present in the blood stream is eventually excreted out of the body by the kidney vulnerable to damages by a variety of chemicals. Chemically induced nephrotoxicity can result from physical damage and/or through biochemical alteration.

Thus from the above investigation, it can be concluded that MEEC at a dose of 200mg/kg body weight don't alter the liver and kidney functions significantly, thus it is found to be safe at this dose.

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Source of support: Nil
Conflict of interest: None Declared