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TOXICOLOGICAL STUDIES OF "ASTAVARGA KVATHA CURNA (AST)" ON KIDNEY FUNCTION PARAMETERS OF RATS' PLASMA AFTER CHRONIC ADMINISTRATION

Kaiser Hamid[1]*, Kaniz Fatima Urmi[2], M Obayed Ullah[3], Md. Sohel Kabir[2], MSK Choudhuri[2]
[1]Lecturer, Department of Pharmacy, East West University, Mohakhali, Dhaka-1212
[2]Department of Pharmacy, Jahangirnagar University
[3]School of Chemistry and Molecular Biosciences, University of Queensland, QLD, Australia

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***Corresponding author**
Email: kaiserpharm_1134@yahoo.com, kaiserpharm@gmail.com

ABSTRACT
The present study was designed for observing the effect of AST (an Ayurvedic formulation) on the kidney function parameters of rats' plasma after its chronic administration. The animal used was albino rats (*Rattus novergicus*: Sprague-Dawley strains) and the drug was administered per oral route at a dose of 40 ml/kg body weight, once daily, up to 41 days for all the experiments. Forty rats, equally of both sexes, were randomly grouped into four where one male and one female group were used as control and other groups were used as test. Almost similar trend of result was observed in both male and female rats except the level of Creatinine. Incase of male rats there was an increase in all the studied parameters in comparison with the control group. The increase in Creatinine level was not statistically significant. But it was statistically highly significant (p=0.001) incase of urea and uric acid. On the other hand in the female rats, there was statistically highly significant (p=0.001) decrease in the Creatinine level. But there was statistically highly significant (p=0.001) increase in the urea and uric acid level.
Key words: Ayurvedic formulation, AST, kidney function parameters

INTRODUCTION

The demand of complementary and alternative medicines among the public is more due to the increased side effects of the presently used drugs, lack of curative treatment for several chronic diseases, high cost of new drugs, microbial resistance and emerging diseases. It has been postulated that by the year 2010 at least two-thirds of the United States population will be using one or more of the alternative therapeutic approaches[1].

Though the traditional and complementary method of treatment have health benefits and are normally practiced safely, over recent years there have been several concerns raised over the safety of some forms of complementary medicine, traditional/herbal medicines in particular.[2-3]

Ayurveda is one type of complementary and alternative medicine and is based on experience from the time immemorial, some of which has been proven experimentally. Formulations and dosage forms have great importance in Ayurveda. Generally Ayurvedic formulations are multi-component mixtures, containing plant and animal-derived products, minerals and metals.[4-7]

Astavarga Kvatha Curna (AST) is an Ayurvedic formulation that is included in the Bangladesh National Formulary (BNF) of Ayurvedic Medicine 1992. It is widely used in the treatment of vata roga (neurological diseases) in the country. Actually, it is a preparation of eight important medicinal plants that were used in equal amount (Table 1)

Considering the safety concerns in the long term use of Ayurvedic medicines, we are investigating the effect of some widely used Ayurvedic formulations of Bangladesh on lipid profile, liver and kidney function parameters of rats' plasma after their chronic administration. The present study is the continuation of our effort in which the effect of AST on the kidney function parameters of rats' plasma was reported.

MATERIALS AND METHODS

Chemicals and Reagents

All the reagents and chemicals that were used in this work were of analytical grade and were prepared in all glass-distilled water. To evaluate the effect of Astavarga Kvatha Curna (AST) on kidney function parameters of rat plasma, it was collected from Sree Kundeshawri Aushadhalaya Ltd, Chittagong.

Dose and route of administration

The liquid "Astavarga Kvatha Curna (AST)" was administered to the animals at a volume such that it would permit optimal dosage accuracy without contributing much to the total increase in the body fluid. For investigating the kidney function parameters, the drug was administered per oral route at a dose of 40 ml/kg body weight. For all the studies, the drug was administered orally. [per oral (p.o.) route]. Ketamine was administered intra-peritoneally (500 mg/kg i.p.).

Experimental animals and their Management

Forty eight-week old albino rats (*Rattus novergicus* : Sprague-Dawley strain,) of both sexes, bred and maintained at the animal house of the Department of Pharmacy, Jahangirnagar University were used in this experiment. These animals were apparently healthy and weighed 50-70 g.

The animals were housed in a well ventilated hygienic experimental animal house under constant environmental and adequate nutritional conditions throughout the whole investigational period. All of the rats were kept in plastic cages having dimensions of 30 x 20 x 13 cm and soft wood shavings were employed as bedding in the cages. Feeding of animals was done ad libitum, along with drinking water and maintained at natural day night cycle.

They were fed with "mouse chow" (prepared according to the formula developed at BCSIR, Dhaka). All experiments on rats were carried out in absolute compliance with the ethical guide for care and use of laboratory animals. Before starting the experiment the animals were carefully marked on different parts of their body, which was later used as identification mark for a particular animal, so that the response of a particular rat prior to and after the administration could be noted separately.

A group of equal number of rat as the drug treated group was simultaneously employed in the experiment. They were administered with distilled water as placebo as per the same volume as the drug treated group for the same number of days and this group served as the control. Prior to the experiment, they were randomly divided into 4 groups of 10 animals / sex. Thus ten rats were taken for each group for both control and the experimental group.

Preparation of Plasma for the Test

At the due of the 41-day treatment period, the animals were fasted for 18 hours and also twenty-four hours after the last administration, the animals were anaesthetized using i.p. Ketamine (500 mg/kg i.p.). Blood samples were collected from post vena cava and transferred into heparinised tubes immediately. Blood was then centrifuged at 4,000 g for 10 min using bench top centrifuge (MSE Minor, England) to remove red blood cells and recover plasma. Plasma samples were separated and were collected using dry Pasteur pipette and stored in the refrigerator for analyses. All analyses were completed within 24 h of sample collection.

Determination of kidney function Parameters

To assess the state kidney function, biochemical analyses was carried out on plasma. These studies involved analysis of parameters such as creatinine, blood urea nitrogen (BUN) and uric acid. The procedure of Tietz et al was used to determine serum creatinine concentration while the serum urea concentration was determined by the method of Kaplan.[8-9]

Statistical Analysis

The group data are expressed as Mean ± SEM (Standard Error of the Mean). Unpaired "t" tests were done for statistical significance tests. SPSS (Statistical Package for Social Science) for WINDOWS (Ver. 11) was applied for the analysis of data. Differences between groups were considered significant at $p < 0.05$, 0.01 and 0.001.

RESULTS AND DISCUSSION

Incase of male rats, there was an increase in the Creatinine, urea and uric acid level in comparison with the control group. The increase in Creatinine was not statistically significant but it was statistically highly significant (p=0.001) incase of uric acid and urea. On the other hand in the female rats, there was a statistically highly significant (p=0.001) increase in the both urea and uric acid. The reverse trend of result was observed incase of Creatinine. There was statistically highly significant (p=0.001) decrease in the Creatinine. (Table 2, Graph 1 and 2)

Blood urea nitrogen is derived in the liver from proteins/amino acids, diet or tissue sources and is normally excreted in the urine. In renal disease, the serum urea accumulates (resulting in uremia) because the rate of serum urea production exceeds the rate of clearance. Other causes of uremia include high protein diet, increased catabolism due to starvation, tissue damage, sepsis or steroid treatment and absorption of amino acids and peptides from digested blood after hemorrhage into the gastrointestinal lumen or soft tissue.[10]

Creatinine is a waste product derived from creatinine and it is excreted by the kidneys. Creatinine values are used as indicators of renal function; usually increased Creatinine do not appears unless significant renal impairment exists. Thus the increased serum Creatinine seems to corroborate the noticeable damage to the cortex and glomerulus.[11]

CONCLUSION

AST is a widely used drug for the treatment of vata roga (neurological disorders) by the rural people of Bangladesh. In the present study, it was shown that it affect the kidney function parameters of rats' plasma after chronic administration. However, the observed result was not congruent incase of all the studied parameters incase of male and female rats. So, it necessitate further closer study to find out this discrepancies

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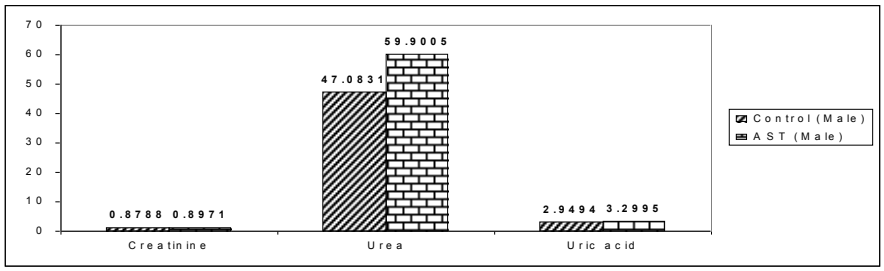
Table 1: Formulary of Astavarga Kvatha Curna (AST)

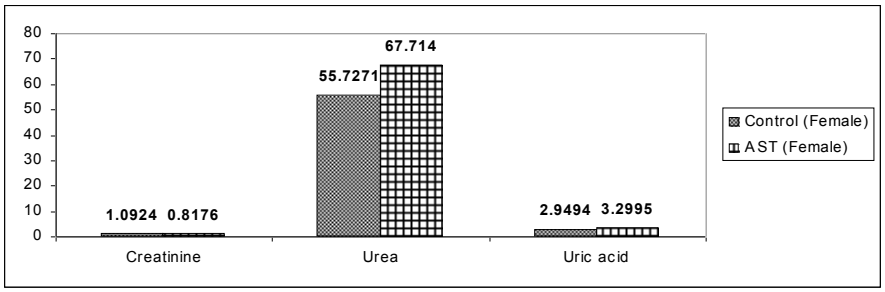
Ayurvedic Name	Parts Used	Botanical Name	Amount Used
**Bala	Root	*Sida cordifolia*	1 part
****Sahacara	Pulp	*Barleria prionitis* Linn	1 part
****Eranda	Root	*Ricinus communis* Linn	1 part
*Sunthi	Rhizome	*Zingiber officinale* Roxb.	1 part
***Rasna	Root / leaf	*Pluchea lanceolata*	1 part
**Suradruma (kastha sara)	Heart wood	*Cedrus deodara*	1 part
******Sinduvara mula. (nirgundi)	Root	*Vitex negundo*	1 part
****Lasuna	Bulb	*Allium sativum* Linn	1 part

Table 2: Effect of AST on kidney function parameters of rats' plasma after chronic administration

Parameters	Male rats			Female rats		
	Control (n=10)	AST (n=10)	P value	Control (n=10)	AST (n=10)	P value
Creatinine	0.8788 ± 0.02173	0.8971 ± 0.02668	(2.08 %, increase, p=0.139) NS	1.0924 ± 0.0399	0.8176 ± 0.4312	(-25.15 %, decrease, p=0.001)***
Urea	47.0831 ± 0.8715	59.9005 ± 0.9727	(-21.39 %, increase, p=0.001)***	55.7271 ± 1.0302	67.7140 ± 1.2386	(-17.70 %, increase, p=0.001)***
Uric acid	2.9494 ± 0.07584	3.2995 ± 0.0531	(11.87 %, increase, p=0.001)***	2.9494 ± 0.07584	3.2995 ± 0.0531	(11.87 %, increase, p=0.001)***



Graph 1: Effect of AST on kidney function parameters of male rats.



Graph 2: Effect of AST on kidney function parameters of female rats.

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