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Toxicity Study of *Garcinia Mangostana Linn.* Pericarp Extract in Rats

Vishnu Priya V[1*], Mallika Jainu[2], Surapaneni Krishna Mohan[3], Karthik B[2], Saraswathi P[4], Chandra Sada Gopan V S[5].

[1]Department of Biochemistry, Saveetha Dental College & Hospital, Saveetha University, Velappanchavadi, Chennai – 600 077, T.N, INDIA.

[2] Department of Bio – Medical Engineering, SSN Engineering College, Chennai, T.N, INDIA.

[3] Department of Biochemistry, Saveetha Medical College & Hospital, Saveetha University, Saveetha Nagar, Thandalam, Chennai – 602 105, T.N, INDIA.

[4] Department of Anatomy, Saveetha Medical College & Hospital, Saveetha University, Saveetha Nagar, Thandalam, Chennai – 602 105, T.N, INDIA.

[5]PhD Supervisor, Saveetha University, Chennai, T.N, INDIA.

ABSTRACT

Garcinia mangostana Linn is used as a phytomedicine in South East Asia for the treatment of trauma, diahorrea and skin infections. In the present study oral toxicity studies of G. mangostana methanolic extract powder was carried out in rat model. G. mangostana extract (1, 2 and 3 g/kg) was given orally for 7 and 14 days to Wistar rats. They were observed each hour for 24h and each day for 14 days for any changes in behavioural activity and mortality. The blood was collected for hematological parameters and serum was used to perform the biochemical and enzymatic analysis. Clinical and neurobehavioral observations, growth, feed and water consumption, hematology, clinical chemistry, organ weights and histopathological examination were carried out and it was experimentally observed that there were no significant effect on body weight and mild increase in the hematological parameters were observed in the control group. The study showed that there was neither death nor alterations in the body weight, relative organ weight, cytoarchitecture of organs, clinical biochemistry, serum marker enzymes and hematological parameters in the G.mangostana treated groups when compared to the control.

KEYWORDS: *Garcinia mangostana Linn. Toxicity, hematology, organ weight*

INTRODUCTION

Toxicity is the extent to which a compound causes harm to animals or human beings. Toxicity can be acute, sub chronic, or chronic. Acute toxicity involves harmful effects in an organism through a single or short-term exposure. Sub chronic toxicity is the ability of a toxic substance to cause effects for more than one year but less than the lifetime of the exposed organism. Chronic toxicity is the ability of a substance or mixture of substances to cause harmful effects over an extended period, usually upon repeated or continuous exposure. Determining the toxicological profile of a substance or preparation is required by regulations for the use and marketing of a product and is also an essential prerequisite for guaranteeing public health. Every drug before being declared as a potential medicine for any disease has to be tested for its chemical, bio-physiological and pathological characters. This process ensures that the compound that becomes a medicine is safe for consumption and can be commercially marketed.

Garcinia mangostana Linn. commonly known as " mangosteen", is a tropical evergreen tree and is an emerging category of novel functional foods sometimes called "superfruits" presumed to have a combination of appealing subjective characteristics, such as taste, fragrance and visual qualities, nutrient richness, antioxidant strength [1] and potential impact for lowering risk of human diseases [2]. The pericarps of *G. mangostana* have been widely used as a traditional medicine for the treatment of diarrhea, skin infection and chronic wounds in South East Asia for many years [3].

These are the nature's most abundant sources of xanthones, which are the natural chemical substances possessing numerous bio-active properties that help to maintain intestinal health, neutralize free radicals, help and support joints and cartilage functions and promotes immune systems [4]. These are extracted from the rind of mangosteen containing 95% xanthones also isoflavones, tannin and flavonoids [5]. In the present communication, we have shown the safety use of *G. mangostana* pericarp extract by conducting the oral toxicity study in rats.

MATERIALS AND METHODS

Test drug and chemicals

G. mangostana pericarp extract powder was obtained from Avasthagen Company, California, USA as a compliment and used for the present investigation. All other chemicals used were of analytical grade.

Animals

Specific-pathogen-free bred Wistar rats were obtained and acclimatized to the laboratory conditions. A set of 6 rats of 6 weeks old were chosen for the present study. They were housed under conventional conditions in polypropylene cages in a controlled environment. They were provided with water and food to acclimatize them before starting the experiment. Experimental protocols were approved by the institutional ethical committee.

Test compound and dose administration levels

Acute toxicity test is performed according to the World Health Organization (WHO) guideline (WHO, 2000) and the Organization of Economic Co-operation and Development (OECD) guideline for testing of chemicals (OECD, 2001). An initial test was carried out to determine the approximate lethal and non-lethal doses of the extract. Four groups of six rats each was used in the experiment. The extract in doses of 1.0, 2.0 and 3.0 g/kg body weight respectively dissolved in 1ml distilled water was administered in a single oral dose by gavages using a feeding needle. The control group received an equal volume of distilled water. Observations on toxic symptoms were made and recorded systematically at 1, 2, 4 and 6 hours after administration. The number of survivors was noted after 24hours and these animals were maintained for further 7 days with daily observations and for 14 days with observations on alternate days.

Observation and examination methods

After the treatment period of 14 days all survivors were anesthetized for blood collection from a common carotid artery. Blood samples were collected for analyzing hematological parameters.

Organ weights

After blood collection, the animals were sacrificed for tissue examination. The various organs under study were excised from the animal and weighed to the maximum accuracy possible. The weights of the Heart, Liver, Kidneys, Brain and Lungs was evaluated and studied for any abnormal gain or loss of weight from normal. This gives a preliminary confirmation regarding the adverse effects (if any) of the drug under test.

Hematological parameters

The heparinized blood was used for hematological study which included RBC, hemoglobin (Hb), packed cell volume, WBC, neutrophil, lymphocyte, eosinophils, monocytes, basophils, platelet count, mean corpuscular volume and mean corpuscular hemoglobin concentration.

Statistical Analysis

Results will be expressed as mean ± S.E.M. Statistical significance is determined by one-way analysis of variance (ANOVA) and post hoc least-significant difference (LSD) test. The data obtained from acute toxicity studies will be analyzed using Student's paired t-test. P values less than 0.05 will be considered significant.

RESULTS

Body weights

Continued oral administration of the drug at 1.0, 2.0 and 3.0 g/kg body weight did not induce any mortality to the animals however there were slight increase in the body weight of the animals which is non-significant compared to that of control group as shown in Table 1.

Organ Weights

Though a slight decrease in the brain weights was noted and a non-significant change was noted in the organs like liver and kidney. A mild increase in the weights of heart and lung were observed which is not significantly observed as shown in table 2.

Hematological parameters

The estimation of the blood parameters showed not much deviation from the normal group, but indicated the increase in the number and volume of blood components. A significant rise in the number of WBC cells especially lymphocytes, neutrophils and the platelet count increased mildly as shown in Table 3.

Table 1: Body weights of rats in the toxicity study of the extract

Body weight (g)	Control	Extract
Day 0	175 ± 12.5	175 ± 13.8
Day 7	175 ± 11.9	175 ± 14.1
Day 14	175 ± 13.1	180 ± 15.5
Mortality	Nil	Nil
Results are expressed as mean ± S.E.M, n = 6.		

Table 2: Organ weights of rats in the toxicity study of the extract

Parameters (g)	Normal Control	G. mangostana (1.0g/kg)	G. mangostana (2.0 (2.0g/kg)	G. mangostana (3.0g/kg)
Heart	0.35±0.02	0.37±0.02	0.34±0.01	0.36±0.02
Liver	4.1±0.26	3.94±0.18	3.96±0.21	4.01±0.31
Kidney	0.69±004	0.65±0.03	0.64±0.04	0.67±0.05
Lung	0.51±0.02	0.53±0.03	0.52±0.04	0.58±0.03
Brain	0.79±0.06	0.65±0.04*	0.69±0.03*	0.74±0.05
Results are expressed as mean ± S.E.M, n = 6. * P < 0.05 as compared to the control.				

Table 3: Hematological values of rats in the toxicity study of the extract

Parameters	Normal Control	G. mangostana (1g/kg)	G. mangostana (2g/kg)	G. mangostana (3g/kg)
RBC (millions/cu.mm)	5.13 ± 0.41	5.15 ± 0.41	5.26±0.32	5.32±0.41
Hb (g/dl)	13.01 ± 0.28	13.83± 0.98 \	14.0±1.1	14.12±1.0
PCV (%)	42.11 ± 1.05	44.5±4.1	44.0±2.5	45±1.1*
WBC (cells / cu.mm)	7375 ± 440.17	8050±330.9 a	8325±417.3*	8633±513.3*
Neutrophil (%)	54.66 ± 4.80	42±2.9 a	47±3.2*	47±3.9*
Lymphocyte (%)	39.08 ± 1. 42	50 ±3.3 a	48±3.9	46±4.1*
Eosinophils (%)	7.0 ± 0.48	5.0±0.85*	5±0.4*	5±0.3*
Monocytes (%)	4.0 ± 0.02	3.0±0.24	4.0±0.3	2±0.1*
Basophils (%)	0 ± 0	0± 0	0±0	0± 0
Platelet count (10^5 cells/cu.mm)	1.52 ± 0.05	1.86±0.09*	1.89±0.12*	2.1±0.14*
Mean Corpuscular volume (Fl/red cell)	78.5±2.6	80.8±1.6	83.5±2.4*	84.6±5.6*
Mean corpuscular Hemoglobin concentration (pg/red cell)	27.3±1.6	24.91±1.1	29.6±1.3	30.15±2.3*
Results are expressed as mean ± S.E.M, n = 6. *P < 0.05 as compared to the control; a P < 0.01 as compared to the control.				

DISCUSSION

With reference to various discoveries that lead to the identification of medicinal properties of *G. mangostana*, numerous studies are being carried out to identify the potential use of this compound. These studies have been carried out using natural extracts as well as synthetic derivatives. They have proved to exhibit strong antimicrobial and pharmacological activities [6]. The fruit of G. mangostana is rich in prenylated xanthones [6, 7]. They are found to exhibit antibacterial [8], antifungal [9] and anti-inflammatory [10]. Further, studies on commercial implementation of this *G. mangostana* as a potential drug are being carried out.

The toxicity of this compound, when administered orally to a set of Wistar strain rats under controlled conditions and the observations made during the study form the base of this study. No lethality was observed for any dose during the course of administration of the extract. There was no evidence of deviations for physiological responses and neuro behavioral changes between the control and any of the treated groups. There were no significant rise or fall of body weight of the animals under Extract and their food and water consumption were least deviating from the controlled group of normal animals. No macroscopical abnormalities were detected in the examined organs. The organ weights though indicated some changes from that of the normal in particular the weights of liver and kidney slightly decreased but it is non-significant.

Hematological parameters provide vital information regarding the status of bone marrow activity and intra vascular effect such as hemolysis. In the estimation of hematological parameters it was distinctly found that there was considerable increase in the blood components especially the WBCs. There was a notable rise in the level of lymphocytes and this was found to be due to the initiation of reactions against the drug by the animals own defense system.

CONCLUSION

Toxicity at doses 1.0, 2.0 and 3.0 g / kg body weight of *G. mangostana* pericarp extract did not produce any significant dose – related change of hematological parameters and in organ weights of any internal organs. Therefore it is concluded that *G. mangostana* pericarp extract at the given dose did not produce any significant

toxic effect in rats during the period of treatment for 14 days. Further studies on chronic toxicity evaluation are needed to determine the long term safety of the extract.

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CORRESPONDENCE TO AUTHOR: Vishnu Priya V, Assistant Professor, Department of Biochemistry, Saveetha Dental College & Hospital, Saveetha University, Velappanchavadi, Chennai – 600 077, Tamilnadu, India. Email: vishnupriya_v9@yahoo.co.in