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# ACUTE AND CHRONIC TOXICITY EVALUATION OF SIDDHA DRUG KANTHAATHI CHOORANAM

**Gowri V.[1*], Mahendran M.[2], Thangadurai K.[3] and Raman R.[4]**

[1]Reader, Maria Siddha Medical College, Thiruvattar, Kanyakumari District, Tamilnadu, India.

[2]Reader, Velumailu Siddha Medical College, Sriperumbudur, Tamilnadu, India.

[3]Associate Professor, National Institute of Siddha, Tambaram, Chennai, India.

[4]Professor, Maria Siddha Medical College, Thiruvattar, Kanyakumari District, Tamilnadu, India.

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***Corresponding Author**
**Dr. Gowri V.**
Reader, Maria Siddha Medical College, Thiruvattar, Kanyakumari District, Tamilnadu, India.

## ABSTRACT

Siddha system of Medicine has its origin in southern part of India and it has a vast traditional literature. The unique feature of Siddha medicines is the preparation of high order pharmaceutical forms of medicines which is a combination of herbals, minerals and metals. The Drug Kanthathi Choornam (KC) is one such herbomineral formulation that has been indicated in "Anuboga Vaithiya Navaneetham Part- I", for En-vagai Gunmam (Acid peptic diseases), Peruvayiru (Ascitis), Manneeral Veekam (Spleenomegaly) and Neer Kovai (Sinusitis). In this study Acute and Chronic Toxicity study was carried out in Wistar albino rats to evaluate the safety of Kanthaathi Chooranam. Acute toxicity evaluation was carried in 30 rats were divided into 6 groups with, each group consisting of 5 rats for a period of 24 Hour in various doses. Group I served as Control. Group II, Group III, Group IV, Group V and Group VI (40 mg, 160mg, 320mg and 640mg of KC/body weight of animal respectively) according to WHO guidelines. The results showed no signs of toxicity such as change in general behavior, mortality, or change in gross appearance of internal organs. Chronic toxicity (90-days oral toxicity) was carried by giving KC for a period of 90 days. Group -I Served as control. Group II and Group III received 40mg and 80mg of KC/body weight of animal respectively. The results showed no abnormalities in sensory reactivity to stimuli, and no changes were observed in body weight, The observed Hematological values were within limits. No histopathological abnormalities

were observed Liver and Kidney tissues. Hence the drug *Kanthaathi Chooranam* was found to be safe.

**KEYWORDS**: *Kanthaathi Chooranam*, Siddha, herbomineral formulation, Acid peptic diseases, Spleenomegaly, Toxicity studies.

## INTRODUCTION

Herbal and herbo mineral preparations are being traditionally used in Indian system of Medicine such as Siddha due to their longer Shelf life.[1] *Kanthaathi Chooranam* is one such formulation indicated in Siddha classical text "Anuboga Vaithiya Navaneetham Part- I", for the management of En-vagai Gunmam (Acid peptic disease and Gastrointestinal disorders), Peruvayiru (Ascitis), Manneeral Veekam (Spleenomegaly) and Neer Kovai (Sinusitis). Gastrointestinal disorders cause considerable economic and social impact on our society.[2] Currently the incidence for duodenal ulceration is 1-3.5/1000 per year for men which constitutes 25-40% of this figure in women and the incidence of gastric ulcer is 0.5/1000 per year in men which constitutes 60-80% in women.

The male preponderance for both duodenal and gastric ulceration is still strong in most parts of the world, especially for duodenal ulceration, but is probably decreasing.[3] Though there are many causes for peptic ulceration and the data suggesting a dietary cause for peptic ulceration is unconvincing, positive correlations have been found with cigarette smoking and peptic ulcer but not with coffee or alcohol consumption.[4] Accumulation of fluid within the peritoneal cavity results in ascites almost always due to portal hypertension resulting from cirrhosis.[5] The incidence of ascites is approximately 60,000 per 100,000 individuals with cirrhosis worldwide. The incidence of ascites is approximately 75,000 per 100,000 cirrhotic individuals with a mortality rate of 50%, within 3 years. The male to female ratio is approximately 2.5 to 1.[6]

Spleenomegaly is a feature of a broad range of diseases, and presents to clinicians in many fields. The ‘‘gold-standard" definition of spleenomegaly is spleenic weight: the normal adult spleen weighs about 50–250 g, and this decreases with age. The clinical finding of a palpable spleen was previously considered to be evidence of spleenic enlargement. A patient presenting with spleenomegaly may therefore have a collection of symptoms, signs and test results that are common to various diseases: some benign and self-limiting, some infective and others malignant.[7] Approximately 0.5% of all upper respiratory tract infections are

complicated by sinusitis. The incidence of acute sinusitis ranges from 15 to 40 episodes per 1000 patients per year, depending on the setting. It is much more common in adults than it is in children.[8,9]

Kanthaathi Chooranam is a herbomineral combination which has been indicated for the managent of all the above said disorders. Since toxicity evaluation is the need of the hour, this Siddha formulation has been investigated for its safety through the acute and chronic toxicity studies and also for Histopathological evaluation.

**PREPARATION OF KANTHAATHI CHOORANAM**

The Drug Kanthathi Choornam was prepared as per the Siddha classical text Anuboga Vaithiya Navaneetham Part- I. The raw drugs Kantham (Magnet), Dried *Zingiber officinale* (Chukku), Feruka safoetida (Perungayam), Kodiveli ver pattai, Karunjeerakam, (*Piper longum*) Milagu and Cinnabar (*Lingam*) were purchased from local markets of Palayamkottai. All the herbomineral raw drugs were purified as per standard methods prescribed in standard texts. 8 ¾ gms of Purified Kantham was taken in a clean mortar and grinded after which purified lingam (3 ½ gm) was added and grinded. Finally the ingredients such Chukku (21gm) and all other herbal ingredients Feruka safoetida (Perungayam), Kodiveli ver pattai, Karunjeerakam, (*Piper longum*) Milagu were added (each 3 ½ gm) were added with the above mixture and minced well. The final mixture was filtered using a clean mesh cloth and stored in an air tight container.

**Selection of Animal species**

Wistar albino rats of both sexes weighing between 80 – 120 gm and bred in the animal house attached to the Post Graduate, Pharmacology Department, Govt. Siddha Medical College, Palayamkottai were used for the study. The animals were maintained with standard animal feed and water ad-libitum. The temperature in the animal house was maintained at 19˚C - 25˚C with 30% humidity. The animals were allowed to be in the cage for 5 days before drug administration in-order to make them accustomed to the new environment. The 12 hrs dark and 12hrs light cycle was maintained in the cage.

**Grouping of Animals**

For acute toxicity study, 30 rats were divided into 6 groups with, each group consisting of 5 rats. Group I served as Control. Group II received KC 40mg/body weight of animal. Group III, Group IV, Group V and Group VI received 160mg, 320mg and 640mg of KC/body

weight of animal respectively. The behavioral signs and mortality were observed once in 30 minutes up to 24 hours. Changes in the skin, eye, mucous membrane, blood circulation, respiratory movements and the neurological problems were observed and recorded.

For chronic toxicity study, 15 rats were divided into 3 groups each group consisting of 5 rats. Two doses of test drug KC which did not produce any acute toxicity and presumed to be safe for long term administration in animals were selected for Chronic toxicity. Group -I Served as control. Group II and Group III received 40mg and 80mg of KC/body weight of animal respectively for a period of 90 days. The Body weight of the animal and Hematological parameters such as WBC Total count, WBC Differential count, Haemoglobin %, SGOT, SGPT were recorded before the beginning of drug administration and also at at 30 days, 60 days and at the end of the experiments and the results were tabulated. At the end of the study, one animal from each group, were sacrificed dissected for Histopathological studies.

**Histopathological study**

The viscera like Liver and Kidney were removed from each animal and were preserved in 40% formalin and sent for Histo-pathological studies. The sections were stained with haemotoxilin and eosin and the histopathological report was given. The study was performed at the Department of pathology, Government Medical College, Tirunelveli.

**Preparation of the test drug for administration**

The drug was weighed and taken. Then water and honey was added as a suspending agent. The mixture was ground well before the administration. The preparation was done in such a way such that 1ml of suspension containing doses ranging from 40-640mg of KC for Acute toxicity study and 40mg and 80mg for chronic toxicity study. Before drug administration, the animal were fasted for a period of 12hrs. The weight of the animal has to be noted before drug administration. After administration of the drug, the animal should be fed after a lapse of 3-4 hrs.

## RESULTS

**Table 1: Acute toxicity study of kanthathi choornam from 1 to 24 hrs.**

| Observation | G 1 (Control) | G-2 (40mg) | G-3 (80mg) | G-4 (160mg) | G-5 (320mg) | G-6 (640mg) |
|---|---|---|---|---|---|---|
| **I Stimulation:** | | | | | | |
| Hyper activity | - | - | - | - | - | - |
| Pyloerection | - | - | - | - | - | - |
| Twitching | - | - | - | - | - | - |
| Rigidity | - | - | - | - | - | - |
| Irritability | - | - | - | - | - | - |
| Jumping | - | - | - | - | - | - |
| Clonic convulsion | - | - | - | - | - | - |
| Tonic convulsion | - | - | - | - | - | - |
| **II Depression:** | | | | | | |
| Ptosis | - | - | - | - | - | - |
| Sedation | - | - | - | - | - | - |
| Sleep | - | - | - | - | mildly+ after 24 hrs | mildly+ after 24 hrs |
| Loss of Pinna Reflex | - | - | - | - | - | - |
| Ataxia | - | - | - | - | - | - |
| Loss of muscle tone | - | - | - | - | - | - |
| Analgesia | - | - | - | - | - | - |
| **III Autonomic effects:** | | | | | | |
| Straub tail | - | - | - | - | - | - |
| Laboured respiration | - | - | - | - | - | - |
| Cyanosis | - | - | - | - | - | - |
| Blanching | - | - | - | - | - | - |
| Reddening | - | - | - | - | - | - |
| **IV Number of animals dead:** | - | - | - | - | - | - |

+ Positive sign - Negative sign

**Table 2: Effect of *Kanthaathi Chooranam* on hematological parameters.**

| Parameters | Group I (Control) | | Group-II (40 mg/bwt) | | Group-III (80mg /bwt) | |
|---|---|---|---|---|---|---|
| | 0 Day | 90$^{th}$ Day | 0 Day | 90$^{th}$ Day | 0 Day | 90$^{th}$ Day |
| WBC | 6100/cumm | 6000/cumm | 7790/cumm | 7786/cumm | 7600/cumm | 7600/cumm |
| Neutrophil | 65% | 63% | 58% | 63% | 59% | 68% |
| Basophil | - | - | - | - | - | - |
| Eosinophil | - | - | 3% | 1% | 3% | 2% |
| Lymphocyte | 33% | 37% | 39% | 36% | 38% | 30% |
| Monocyte | - | - | - | - | - | - |
| Haemoglobin % | 11 gm | 11.6 gm | 13.5 gm | 16gm | 14 gm | 16.2gm |
| SGOT | 551U/L | 581U/L | 54IU/L | 56IU/L | 61IU/L | 58IU/L |
| SGPT | 251U/L | 271U/L | 23IU/L | 24IU/L | 25IU/L | 24IU/L |

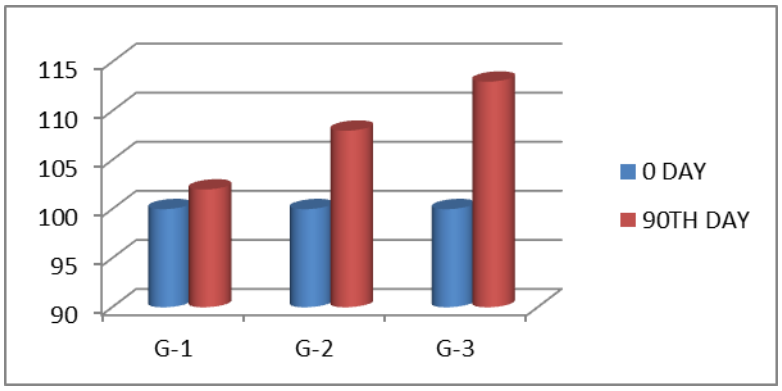
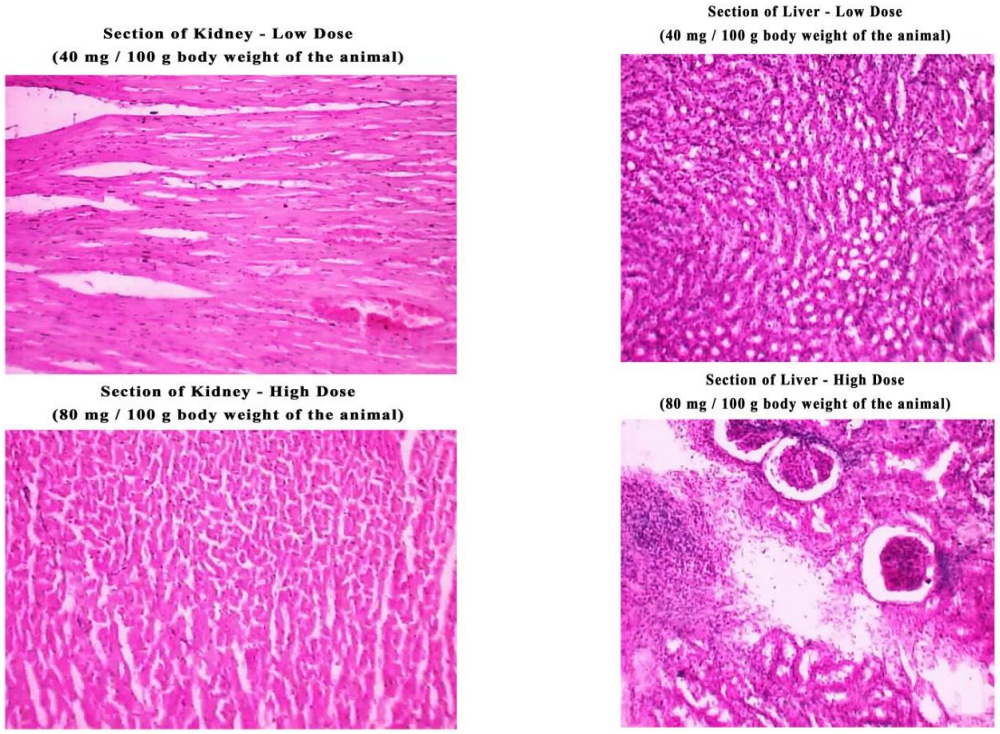



**Figure 1: Effect of Kanthathi Chooranam on Body weight in rats.**

**Histopathological study report of kidneys and liver**




## DISCUSSION

Acute and chronic toxicity studies in Wistar albino rats were performed as per WHO guidelines to assess the safety profile of KC, as there were no earlier reports on the safety assessment of this Siddha herbomineral drug. Significant changes were not found in behaviour pattern and locomotor activity, convulsion, tremor, excessive salivation, diarrhea, sedation and edema were not observed. Body weight changes are perceptive and analytical marker for the first sign of toxicity when exposed to toxic substances.

In this study all animals were found to show an increase in body weight in chronic toxicity study. Hence the results support normal food and water consumption throughout the study period. The most sensitive target for toxic substances and the important index of physiological and pathological status is Hematopoietic system. No abnormality was observed in hematopoietic function indices for KC treated groups compared with control groups indicating the drug is safe. SGOT, SGPT levels of the experimental animals were monitored as they are the specific markers for liver damage or injury. No significant changes in SGOT, SGPT were observed in all the treated group animals. Thus animals treated with KC were found to be non-hepatotoxicas shown in Table-1 and Table-2. The drug *Kanthathi Choornam* did not produce any mortality even up to 640 mg/body weight of the animal except a symptom of mild sleep which was observed on animals administered with 320mg and 640 mg/body weight of the animal (Group V & VI), that was noted after 24hrs.[10]

## CONCLUSION

Based on our results, we conclude that Kanthaathi Chooranam was found to be safe in both acute and chronic toxicity studies with no mortality even up to 640 mg/body weight of the animal except a symptom of mild sleep which was observed on animals administered with 320mg and 640 mg/body weight of the animal (Group V & VI), that was noted after 24hrs. Hematological, biochemical and histopathological investigations clearly demonstrates that Kanthaathi chooranam may be valuable medicinal formulation for further clinical studies.

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