

## ***STUDY OF HISTO-PATHOLOGICAL EFFECTS OF RASAGARBHA POTTALI ON ALBINO RATS***

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### **ABSTRACT**

*Ayurvedic Rasaoushadhis* containing heavy metals are used therapeutically since ages. *Rasagarbha Pottali* is one of the formulations being possessed with mercury, sulphur and Gold as ingredients. The safety of these formulations is questioned on time to time by modern counterparts as metals in their elemental form are very toxic. The present study was carried out with an aim to screen out **Histopathological changes** on different organs of wistar strain Albino rats on administration of *Rasagarbha Pottali* in TED, TEDx5 & TEDx10 level dose. With this experimental study it was concluded that *Rasagarbha pottali* even at 5 times of its therapeutic dose and 10 times of its therapeutic dose was well tolerated and on overall assessment, slight changes observed in organs at higher dose level with no specific & serious toxic effects found at the therapeutic dose level treated. But however, caution may be exercised while it is administered in persons prone to hyperuremic condition.

**Keywords:** *Rasagarbha Pottali* (RGP), Toxicity study, Histopathological Effects.

### **INTRODUCTION**

Rasaushadhis are integral part of Ayurveda, and describes the use of metals and minerals for chronic disorders in various combinations, dosage forms and at various levels of purities. The recent concern raised about safety by researchers from contemporary science about these classical metallic-based preparations has led to an attempt to re-

validate the safety of these medicines in a more rigorous way, to improve the global acceptance.

Out of *chaturvidha rasa kalpas* explained in classics, *Pottali rasayana* is very potent because of its unique method of preparation and the easy way of administration, easy to carry with no chances of destruction due to its hard and solid form.

*Rasagarbha Pottali*<sup>1</sup> is one of the *Pottali kalpana* consisting of *Hingulotha parada* of 1 karsha, *Gandhaka* of 1 tanka, *Swarnatantu khanda* of 6 rattika & *kajjali* of 4 pala separately. This was prepared by *Gandhaka drava paka* method to get a solid compact form and this formulation is therapeutically very effective in *Sannipataja Jwara*, *Rasayana* (Rejuvenative), as per reference it is *sarvaroga hara*.

Since *Rasagarbha Pottali* containing one of most important ingredient Mercury which is listed in Drug & Cosmetic Act Schedule E-1 of poisonous substances in ASU Drugs, so it has become very important for all to have knowledge of toxicity profile of the formulations containing Metals & minerals. *Ayurvedic* experts have estimated that approximately 20% of the *Ayurvedic* formulations contain mercury sulphide as a component<sup>2</sup> Mercury sulphide in low dose shows good therapeutic effect without producing toxic effects in the human beings<sup>3</sup>.

The present study was designed with an aim to screen out Histopathological changes occurred in albino rats after Repeated dosing where Sub acute Toxicity studied according to AYUSH 170 guidelines on wistar albino rats.

## MATERIALS AND METHODS

The present experimental study was conducted in Animal house attached to SDM Research centre, SDM Ayurveda College, Udipi after getting approval of the Institutional Animal Ethical committee (IAEC) NO: SDMCRA/IAEC/BL/RS/03.

**Test drug:** *Rasagarbha Pottali* (RGP) was prepared in pharmacy of TGAMC Ballari. Where the

RGP took 6hr of paka kala for complete attaining *Pottali siddhi lakshana*, the details can be cited at *sapna et.al*<sup>4</sup> about pharmaceutical study of *Rasagarbha Pottali*.

**Test animal and housing:** Total 40 Wistar Albino rats of both sex weighing 150-250g were selected for the study. Animals were randomly divided into 4 groups and were marked with saturated picric acid solution in water for proper identification. They were kept in colony cages in Animal house of SDM Research center Udipi at an ambient temperature of (24±5°C) and at a relative humidity of 55-65% in 12 hrs light and 12 hrs dark sequences. They were fed with Sai Durga feeds, Bengaluru rat pellets and tap water *ad libitum*. Animals were allowed to acclimatized one week prior to commencement of experiment.

## Experimental design

This study was conducted strictly following Ayush 170 guidelines. The rats were divided into 4 groups of 40 rats consisting of 10 rats (5male & 5 Female) of in each group The repeated oral dose toxicity was conducted for 28 days. The rats were given daily Tap water to control group. For Test Drug Groups RGP , RGP in 5times (5x) and RGP 10 times to the therapeutic dose (table 1) dissolved in 20 % gum acacia by oral gavage , once daily for 28 consecutive days. Animals were observed for mortality and general clinical and behavioural changes viz. routine activity, irritability, food intake and external appearances etc.

**Table 1:** Showing the drug schedule for Sub acute Toxicity Study

Group	No of animal	Drug	Dose	Duration	Purpose
Control Group	10	Water	Sufficient quantity	28 days	To serve as Control group
TED Group	10	RGP	11.25mg/Kg body weight	28 days	To serve as trial group
TEDx5 Group	10	RGP	11.25mg×5 /kg body weight	28 days	To serve as trial group
TEDx10 Group	10	RGP	11.25mg×10 / kg body weight	28 days	To serve as Trail Group

### HISTOPATHOLOGICAL STUDIES:-

On 29<sup>th</sup> day for Histopathological study, the animals were sacrificed with over dose of ether anesthesia. The abdomen was opened through midline incision to record the autopsy changes followed by dissecting out the important organs like Brain, heart, liver, spleen, lungs, kidney, stomach, jejunum, testis, uterus and extraneous tissues was removed and weighed. The organs were transferred to bottles containing 10% formalin and sent to a commercial laboratory for preparation of slides. The slides with sections obtained were scanned in Trinocular Carl Zeiss's microscope (Germany) under different magnifications. Changes, if any in the cytoarchitecture were noted down.

### OBSERVATIONS AND RESULTS

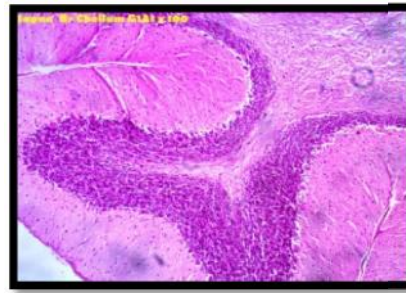
No mortality was observed in control and all the treated groups, neither any treatment related clinical signs were observed. All the animals were well oriented and active during and after the trial period. Weekly changes in body weight of animals were noted.

#### Histopathological examination:

**Brain:** Microscopic examination of sections of different parts of the brain belonging to both control and test drug administered groups was carried out under microscope at different magnifications. Comparison of the cytoarchitecture profile of the test drug administered groups with that of control group were done to assess the drug induced changes. All the four parts- fore brain, mid brain, hippocampus and cerebellum in all the test drug administered groups were examined. The results have been enumerated below.

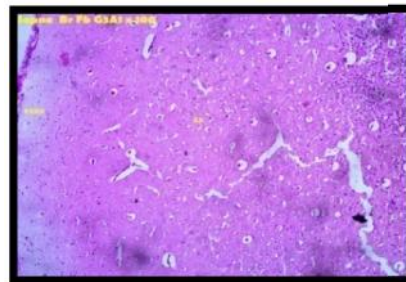
**Cerebellum:** The sections of the cerebellum from all the three test drug administered groups- TED, TED x5 and TED x 10 exhibited normal cytoarchitecture.

**Fig 1:** Photomicrograph of cerebrum of TED group



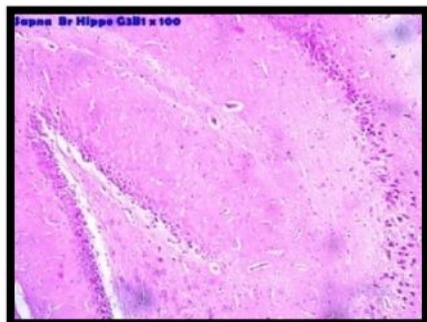
**Fore brain:** The sections from TED and TED x 5 treated group exhibited normal cytoarchitecture where in TED x 10 treated group mild increase in the neurofil proportion was observed- otherwise the sections appeared normal.

**Fig 2:** Photomicrograph of Fore Brain of TED x 10 group



**Hippocampus and midbrain region:** Hippocampal sections from TED and TED x 5 exhibited normal cytoarchitecture. In TED x 10 dose administered group decreased cellularity was observed in section of one rat. Cell infiltration of moderate intensity was observed in midbrain section of one rat in this group. The midbrain sections from other two groups were found to be normal.

**Fig 3:** Photomicrograph of Hippocampus of TED x 10 group



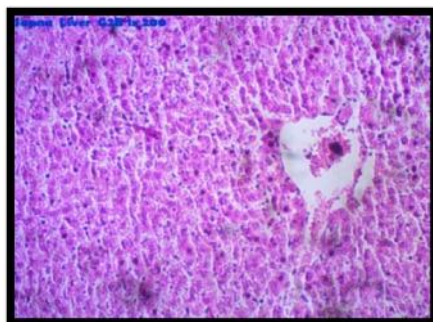
**Heart, Testis, Uterus:**

Microscopic examination of these in all groups showed normal cytoarchitecture.

**Liver:**

Sections from most of the rats in TED and TED x 5 dose groups exhibited normal cytoarchitecture. However, in section from one rat in both these groups exhibited mild cell infiltration and sinusoidal dilatation. The sections from TED x 10 dose given group were found to be normal.

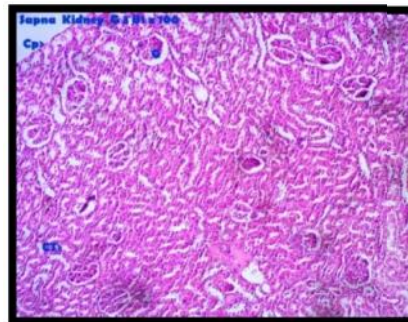
**Fig 4:** Photomicrograph of Liver of TED x 5 group



**Kidneys:**

The kidney sections from TED and TED x 5 dose groups exhibited normal cytoarchitecture. In section from one kidney in TED x 10 dose given group mild cell infiltration and proteus changes were observed.

**Fig 5:** Photomicrograph of Kidney of TED x 10 group

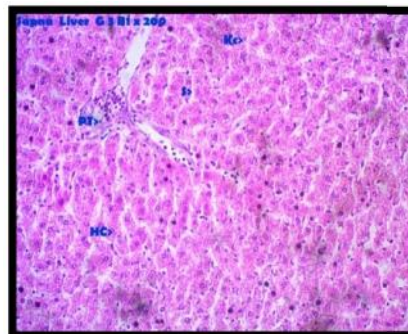


**Spleen:** The proportion of white pulp was found to be significantly increased in sections from the entire three test drug administered group in comparison to the sections from control group.

**Jejunum:** Mild erosion of the epithelium was observed in few sections from all the three groups.

**Lungs:** In TED dose group sections from two rats were found to exhibit cell infiltration. In TED x 5 dose group the lung sections were found to be almost normal. In TED x 10 dose administered group cell infiltration was observed in section from one rat.

**Fig 6:** Photomicrograph of Liver of TED x 10 group



**DISCUSSION**

Rasagarbha Pottali is a Sagandha, Sagni, Bahirdhooma, Gandhaka jarita, Pottali Kalpana. This formulation consists of Shuddha parada Shuddha



*gandhaka*, *Swarna tantu Khanda* & *samaguna kajjali*, these ingredients were triturated with *Kumari* (Aloevera pulp) for Seven days to bind into a single molecular form then subjected to *gandhaka drava paka* to form a complete compound form.

The present study was aims for evaluation of toxicological & Histopathological aspect of RGP on the different organs functioning to revalidate it changes. In compare to normal treated group, the body weights of TED x 5 treated group was decreased significantly in 3<sup>rd</sup> and 4<sup>th</sup> week that may be due to less food Intake and not related to test drug. In Histological examination, there are no major changes in Therapeutic dose level group where as in higher dose treated group minimal changes were observed.

## CONCLUSION

After careful analysis of the data generated related to Histopathological parameters it can be suggested that the test drug *Rasagarbha Pottali* (RGP) is not likely to produce any serious toxic effects especially at the dose level studied. But however, caution may be exercised while it is administered in persons prone to hyperuremic condition.

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