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ACUTE AND SUB-ACUTE TOXICOLOGICAL STUDY OF VANGA BHASMA

Nayana

Associate professor, Department of Rasashastra Evam Bhaishajya Kalpana, Dhanvantari Ayurveda College, Koydam, Gujrat , India,

Corresponding Author: drnayanahegde@gmail.com

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ABSTRACT

Introduction: Vanga is a dhatu, that has been used externally since the Samhita period. During the rasa shastra era, vanga was utilized internally for *Prameha, (urinary disorder) Medoroga(diseases of medadhatu – fat tissue), Kapha Vikaras(diseases of kapha-bodily constitution)*, and other purposes after *Bhasmikarana*.(preaparation of Bhasma - medicine) **Objective:** Evaluate Acute and Sub-acute toxicity of Vanga Bhasma. **Materials &Methods:** The acute and sub-acute toxicity studies of Vanga Bhasma were carried out on Wistar Albino rats using 425 and 407 OECD guidelines, respectively. Acute oral toxicity study of the test drug was carried out at the limit dose of 2000 mg/kg orally in rats. In a sub-acute toxicity study, Vanga bhasma was administered to rats for 28 consecutive days at doses of 22.5(TED-therapeutic equivalent dose), 112.5(TEDX5), and 225 mg/kg(TEDX10). The effects of the drug were assessed on haematological, biochemical, histological, and ponderal parameters. **Results**: **Acute toxicity: the** study showed the LD 50 value of Vanga Bhasma is greater than 2000mg/kg. **Sub-acute toxicity:** this study did not produce any signs or symptoms of toxicity at TED, TEDX5, and TEDX10. **Conclusion: The** single dose of 2000mg/kg body weight evaluated by acute toxicity study is proved to be non-toxic. Overall analysis reveals that test drug vanga bhasma is very well tolerated at rat human therapeutic equivalent dose and multiples of it. Therefore, Vanga bhasma, prepared and administered in accordance with customary protocols, is safe to consume at therapeutic dose levels.

Keywords: Vanga Bhasma , Actue Oral Toxicity , Subacute Toxicity , OECD

INTRODUCTION

Ayurveda is an ancient health science. One important aspect of clinical Ayurveda is Rasaushadhis. Among the Rasaushadhis, Bhasma Kalpana is so effective that it has gained a significant place. One such versatile bhasma is vanga bhasma, which has applications for treating a variety of diseases such as *Medoroga, Krimiroga, Prameha, And Kaphavikaras* [1]. Currently, there are claims that Ayurvedic medications made from minerals and metals are hazardous to living things. The metals and minerals are used to make *Bhasmas*, which Ayurveda claims are not only highly helpful to human health but also non-toxic. Despite considerable testing, aversion persists due to the scarcity of scientific data. The timeless principles of Ayurveda, which were developed by the great sages of ancient times, are still relevant today because of their scientific base and enduring features. Such fundamentals require scientific investigation to support their validity and deepen our understanding of this issue. Therefore, screening for the toxicity of "*Vanga Bhasma*," which is frequently utilized in therapeutic practice, is necessary. The adverse effects of a substance are referred to as "toxicity." In Rasashastriya preparations, dosage is crucial, but it's also critical to express efficacy and toxicity and implement suitable production techniques to ensure a high-quality final product. According to OECD guidelines 425 and 407, respectively, the acute and sub-acute toxicity of Vanga Bhasma are evaluated in the current study using the in vivo method.

AIMS AND OBJECTIVES:

1. To evaluate the acute and sub-acute toxicity of Vanga Bhasma on Wistar albino rats at various doses.

MATERIAL AND METHODS:

Experimental animals:

For this study, Wistar albino rats of both sexes weighing 150–200g were used. They underwent the normal day-night cycle while being in ideal laboratory conditions with respect to humidity and ambient temperature. They were fed with tap water and standard rat pellets. The animals were obtained from an animal house attached to the Pharmacology Laboratory at the S.D.M. Centre for Research in Ayurveda and Allied Sciences. Institute's Animal Ethics Committee approval no. SDM-CAU-13-14-21

Dose selection: As per classical reference, the therapeutic dosage of Vanga Bhasma is 250mg [(2).] The appropriate dosage for rats was estimated using Paget and Barnes' [(3)] table and was calculated to be 22.5 mg/kg rat (called the therapeutic equivalent dose, TED). The test drug was administered orally through a cannula as a suspension in the distilled water solution.

Acute toxicity study [(4):]

A total of 5 healthy either Sex, young, healthy, wistar-strain albino rats were selected according AOT Software Guidelines and acclimatized for seven days before the experiment. The animals were marked with saturated picric acid solution in water for proper identification.

Table 1: The marking within the cage are as follows:

Animal Number	Marking
1.	Head
2.	Neck
3.	Middle of the back
4.	Base of the tail
5.	No mark

A suitable concentration of vehicle gum acacia was used to create a fine suspension of the test formulation, vanga bhasma. Constant dosage volumes (1 ml/100 g of body weight) were administered to each

animal, equal to 175 mg/kg, 550 mg/kg, and 2000 mg/kg. In this study, 75 mg and 550mg doses of 40 mg/ml stock solution were taken, and a 2000mg dose of 200 mg/ml stock solution was taken. A single dose per animal was administered through the oral route at different **dose** levels to the respective animal through an oral feeding needle on a disposable syringe.

Observation:

1. **Examination of physical and behavioural changes:**

The animal was under constant observation for 4 hours following the dosage. It was carefully observed from its cage without being disturbed, and after each hour, it was taken out into the open arena to look for any changes in behavior, like increased or decreased motor activity, convulsions, Straub's reaction, muscle spasm, catatonia, spasticity, salivation, diarrhea, writhing, mode of respiration, changes in skin colour, exitus, cns depression—hypo activity, passivity, relaxation, ataxia, narcosis, etc.

2. **Mortality**

All animals were checked for mortality at 12, 24, and 48 hours after the dose and thereafter once daily for the duration of this study, i.e., 14 days.

Sub-acute study (repeated dose toxicity) [5]

For this experimental study, albino rats of the Wistar strain weighing between 150 g and 250 g,both sexes, were chosen. In addition to being under ideal laboratory circumstances with regards to humidity and ambient temperature, they were exposed to the natural day-night cycles. Ten rats—five males and five females—per group were divided into four groups. Group (I) was retained as the control group, which was given an oral 2% gum-acacia solution. The test drug vanga bhasma TED (22.5 mg/kg orally), TED X5 (112.5 mg/kg orally), and TED X10 (225 mg/kg orally) were given to groups II to IV in that order. For 28 days, including the experiment day, they received control and suspensions of the test medicines in the morning session orally between 9 and 10 a.m. The rats were observed daily, carefully for any apparent signs and symptoms of toxicity. Assessments of food and water intake and body weight gain were done weekly. Both the wet and dry faecal matter weight and faecal water content were assessed weekly. The food conversion ratio was calculated for each week. On the 28th day, all animals were kept for overnight fasting. The next day, the body weight of each rat was noted, and blood was collected by supra-orbital puncture with the help of microcapillary tubes under mild ether anaesthesia for estimation **of serum biochemical and haematological parameters**, followed by sacrifice with an overdose of ether anaesthesia. The abdomen was opened through the midline incision to record the autopsy changes, followed by dissecting out the important organs as mentioned below, and extraneous tissues were removed and weighed. The tissues were transferred to bottles containing 10% formalin for the purpose of **histopathological study.**

Ponderal changes: The weight of important organs like brain, heart, liver, spleen, lungs, kidney, thymus, jejunum, testis, uterus were recorded and expressed in terms of relative values.

Sperm aberration test:

Sperm motility: the sperm motility was observed by viewing the sperm under microscope and counting the number of live cells in percentage under high power microscope.

Sperm count: The count was done with a Haemocytometer (Neubauer-improved counting chamber). The count was calculated in million/caudal epididymal tissue suspension.

Statistical analysis:

All the values were expressed as mean± SEM (standard error of mean). The data were analyzed by one-way ANOVA followed by Dunnett's multiple 't' test. A level of $P<0.05$ was considered statistically significant. The level of significance was noted and interpreted accordingly.

Results & discussion

Acute oral toxicity: -

Table no 2: shows the acute oral toxicity dose and its short- and long-term results.

Test sequence	Animal id	Dose(mg/kg	Short term result	Long term result
1	1	175	O	O
2	2	550	O	O
3	3	2000	O	O
4	4	2000	O	O
5	5	2000	O	O

(X = Died, O = Survived)

An acute toxicity study of the test drug was carried out to record immediate adverse signs and symptoms of the drug at dose levels that are several folds higher than the therapeutic equivalent dose. There were no physical or behavioural changes except a mild increase in motor activity seen in one rat at 2000mg. Thus, the data obtained from the study on single-dose oral administration of vanga bhasma and observation for 14 days indicate that it does not result in any physical or behavioural changes. All the animals survived the 14-day observation period after dosing, which suggests that the LD50 value may be higher than 2000 mg/kg by oral route.

Sub-Acute Toxicity

A. Effect on haematological parameters.

Table N0.3: Consolidated statement of hematological parameters on administration of Vanga bhasma at different concentrations

SL NO	Parameters	TED	TEDX5	TEDX10
1.	HB%	NSI	NSI	NSI
2.	Total Count	NSD	NSI	NSI
3.	RBC	NSD	NSD	NSI
4.	PCV	NSI	NSI	NSI
5.	MCV	NSI	NSI	NSI
6.	MCH	NSI	NSI	NSI
7.	MCHC	NSD	NSD	NSD
8.	RDW CV	NSD	NSI	NSI
9.	RDW SD	NSI	NSI	NSI
10.	Platelet	NSI	NSI	NSI

Here SI – Significant Increase, NSI – Non-Significant Increase

SD – Significant Decrease NSD – Non-Significant Decrease

By analyzing the **hematological parameters**, it is found that none of the hematological parameters examined at the three dose levels—TED, TEDX5, and TEDX10 groups—shows a statistically significant change when compared to the control group. The values of all 10 parameters exhibit a slight increase or decrease, which is statistically not significant and suggests that no adverse effects were seen in any of these parameters for any of the vanga bhasma groups. This indisputably demonstrates that test medication does not have the potential to negatively affect any blood component. At the levels used in clinical settings, prolonged treatment is unlikely to result in any alterations to the hematological composition.

Effect on biochemical parameters:

Table No. 4: Consolidated statement of biochemical parameters on administration of *Vanga bhasma* at different concentrations

Sl. No	Parameters	TED	TED X 5	TED X10
1	Glucose	NSD	NSD	NSD
2	SGOT	NSI	NSI	NSI
3	SGPT	NSD	NSD	NSI
4	Alkaline Phosphate (ALP)	NSI	NSD	NSI
5	Bilurubin (Total)	NSI	NSI	NSI
6	Bilurubin (Direct)	**SD**	NSD	**SD**
7	Albumin	**SI**	NSD	NSD
8	Globulin	**SD**	**SD**	NSD
9	Total Proteins	NSD	**SD**	NSD
10	Sr.urea	**SD**	NSD	NSD
11	Sr.Creatinine	**SI**	**SD**	NSD
12	Cholesterol	NSD	NSD	NSI
13	Triglycerides	NSI	NSI	NSI

Out of the 13 **biochemical** parameters studied, none were found to be affected at all at the three dose levels. A decrease in direct bilirubin level was observed at two dose levels; five parameters were found to be affected at the TED dose level, three parameters at the TED x5 dose level, and only one parameter was found to be affected at the TED x10 dose level.

Effect on Liver Function Test Parameters:

Three enzymes, SGOT, SGPT, and ALP, are measured with the bilirubin level to assess the status of liver function. Other parameters like total protein, albumin level in serum, and blood glucose also provide information about the functional status of the liver. None of the three studied enzymes were found to be significantly affected by the test drug at the three dose levels. Similar is the case with total bilirubin. Surprisingly, a decrease in direct bilirubin level was observed at two dose levels. Elevated bilirubin is indicative of liver function impairment; hence, based on the above, it can be suggested that the test drug, even at high dose levels and on medium-term administration, is not likely to affect liver function. A decrease in direct bilirubin requires analysis.

The enzyme glucuronyltransferase in the liver conjugates bilirubin with glucuronic acid to make it soluble in water. This conjugated, water-soluble portion is called direct bilirubin. The majority of this bilirubin is secreted into the bile and, through it, into the small intestine. Additionally, it should be noted that, in addition to the conjugated form, direct bilirubin also contains delta bilirubin, which is bound to albumin. As a result, the decreased direct bilirubin may be the result of increased excretion into the bile or increased binding with albumin. It's interesting to note that the level of serum albumin is elevated at the TED dose level. As a result, this fact and the fact that this effect is non-dose-dependent can be regarded as having no pathological significance.

Effect on parameters related to kidney function:

Serum creatinine and blood urea level are considered as important biomarkers for the assessment of kidney function status. In the present study, a complex activity profile was observed. At TED dose level elevated creatinine and decreased urea level were noted, whereas at TED x 5 dose significant decrease and no effect at TED x 10 dose level was observed. This profile does not reflect impairment in the kidney function. The elevated level at TED dose level may be due to increased formation in the muscles; decreased urea level suggests decreased turnover of nitrogenous substances. Other parameters -The blood sugar and lipid related parameters were not affected to a significant extent indicating that the test drug has no toxicological implications when considered in the context of biochemical parameter related data.

B. **Effect on sperm analysis:**

Table No.5: Consolidated statement of SPERM ANALYSIS on administration of *Vanga Bhasma* at different concentrations

Sl. No	Parameters	TED	TED X 5	TED X 10
1	Sluggish motile	NSI	SD	NSD
2	Non motile	NSI	SI	NSI
3	Sperm count	SI	NSD	NSI
4	Morphology- Normal	NSI	NSI	NSI
5	Morphology- Small head	NSD	NSD	NSD
6	Morphology-Large Head	NSD	NSI	NSI

In all parameters related to **sperm analysis,** we can observe that there was a significant decrease in sluggish motility and a significant increase in non-motility in the TEDx5 group compared to the control group. It is to be noted here that the motility of sperm from epididymal suspension—sperms from this source—is less motile, and even whatever motility is there, it gets reduced over a short period of time in comparison to the sperm collected after ejaculation. Hence, this requires further analysis. This was estimated to give an indication. A significant increase in the sperm count of the TED group compared to the control group may be due to the *Shukravardhaka (increases sperm) ,Vrushya (Aphrodisiac)* [6] property of *Vanga bhasma*. Other parameters, like morphology -Normal, morphology -small head and morphology- large Head, show a mild increase or decrease. It is difficult to assess because sperms quality and quantity vary from individual to individual, and in rats, we are testing the epididymal sperms rather than the ejaculated sperms. However, an increased percentage of sperms with abonormal morphology may be indicative of the effect of the test drug on germinal tissue; hence, this is an important parameter. The test drug did not produce any significant change in the percentage of sperms with abnormal morphology; Therefore, it doesn't seem to be a tendency for it to cause genotoxicity.

D.**Ponderal Changes:**

Table No. 6: Consolidated statement of **WEIGHT OF ORGANS** on administration of *Vanga Bhasma* at different concentrations

Sl. No	**Name of the Organ**	**TED**	**TED X 5**	**TED X 10**
1	**Wt of Brain**	NSI	NSI	NSI
2	**Wt of thymus**	NSD	NSD	NSD
3	**Wt of Lungs**	NSI	NSI	NSI
4	**Wt of Heart**	NSI	NSI	NSI
5	**Wt of Liver**	NSI	NSI	NSI
6	**Wt of Kidney**	NSI	NSD	NSI
7	**Wt of Jejunum**	**SD**	**SD**	**SD**
8	**Wt of Testes**	NSI	NSI	**SI**
9	**Wt. of Uterus**	NSI	**SD**	**SD**
10	**Wt of Spleen**	NSD	NSI	NSI

The analysis of the ponderal changes associated with organs reveals that of the 10 recorded organ weights, there is a significant decrease in wt of jejunum in TED, TEDx5, and TEDx10, a significant increase in wt of testes in TEDx10, and a significant decrease in wt of the uterus in TEDx5 and TEDx10 in comparison to the control group. Other organ weights such as wt of brain, wt of thymus, wt of lungs, wt of heart, wt of liver, wt of kidney, and wt of spleen in all groups

only exhibit a slight increase or decrease in organ weights in relation to the control group.

The organ weight changes are indicators of morphological changes in the organ in focus. A decrease in weight is indicative of degenerative changes and organ loss, and an increase in weight is indicative of hypertrophy, hyperplasia, or oedematous changes in the components of the organs. In the present study, one of the significant changes observed is with respect to jejuna weight. Decreased weight was observed in all three dose levels studied. The correlation with the histological study revealed epithelial erosion of mild to moderate intensity. This alone may not be the contributing factor, but it is one of them. It may perhaps be due to the absorption of water content from jejunum into the GI tract, as reflected in the increased water content in the faecal matter.

The weight of the testis was found to be increased at the TED x 10 dose level; histological examination ruled out oedema or hyperplasia, but it may be indicative of increased size. The weight of the uterus was found to be reduced in the TED x 5 and TED x 10 groups. Histological examination did not indicate degenerative or necrotic changes; hence, the exact reason is not known. Considering all the above factors, it can be suggested that the organ weight changes do not indicate the possibility of any serious pathological changes at the dose level used in the study.

Table No. 7: Changes in Food intake.

Group	Changes in Body weight			
	7th Day	14th Day	21st Day	28th Day
TED	NSI	NSD	NSI	NSI
TED x 5	NSI	NSI	NSD	NSI
TED x 10	NSD	NSD	NSD	NSD

Data related to the changes in food intake can be seen in a consolidated form in the table above.

Overall, there is a trend toward more food consumption, particularly at the TED dosage and TED x 10 dose levels. A higher appetite or poorer food absorption could be the cause of an increased food intake. From a pathological perspective, consuming less food is crucial. Since this increase was not associated with increased body weight gain it can be suggested that it is indicative of the deepana [7] effect.

Table No. 8: Body weight changes

Group	Changes in Food Intake			
	7th Day	14th Day	21st Day	28th Day
TED	**SI**	**SI**	NSI	NSI
TED x 5	NSD	**SI**	NSD	NSI
TED x 10	NSI	NSD	**SI**	**SI**

The body weight gain changes were not significant in any of the group. Body weight change is an important parameter for assessing the effect of test drug on nutritional status of an animal. If there is decrease it is indicative of improper nourishment or gross pathology involving tissue loss in some major organs. All these can be ruled out in the present case.

Table No. 9:
Changes in Faecal wet weight & dry weight

Group	Changes in faecal wet weight	Changes in faecal dry weight

	7th Day	14th Day	21st Day	28th Day	7th Day	14th Day	21st Day	28th Day
TED	NSI	NSI	NSD	NSD	**SI**	NSI	NSD	NSD
TED x 5	**SI**	NSI	**SI**	NSD	NSI	NSI	NSD	NSD
TED x 10	NSI	NSI	NSI	NSD	NSI	NSI	NSI	NSI

Variations in the wet and dry weight of the feces can reveal details about the quantity and quality of the stool. In the current study, TED was associated with an increase in dry weight during the first week; thereafter, no noticeable variations were seen. The primary determinant of both wet and dry stools is the amount of food consumed and absorbed by the body. When we compare the weights of the wet and dry feces with the amount of food consumed, we can see that there was an initial increase in the wet and dry feces due to an increase in food intake. However, in the later stages, even though there was an increase in food, wet and dry feces decreased in all groups. Hence this change is self-limiting, perhaps indicative of decreased pachana effect in the initial stages which gets remedied as the duration increases.

Table No. 10: Changes in Faecal water

Group	Changes in Faecal water			
	7th Day	14th Day	21st Day	28th Day
TED	NSD	NSI	NSD	NSD
TED x 5	NSI	NSI	**SI**	**SD**
TED x 10	**SD**	NSI	NSI	NSI

The estimation of fecal water provides an understanding of the consistency of the stool, giving information on stool formation and also indicating a drug's propensity to cause diarrhea. There was no apparent effect at the TED dosage level. At the TED x 5 dosage level, an increase was seen by day 21 and a decline by day 28. Therefore, other factors may be more relevant to this outcome than medication. On the seventh day, there was a notable drop at the TED x10 dosage level that persisted for the following three weeks. As a result, all of the alterations that were seen inconsistent, suggesting that the test medication has no discernible impact on fecal water and is hence unlikely to cause diarrhea or impair the formation of stool.

Table No. 11: Changes in Food conversion ratio:

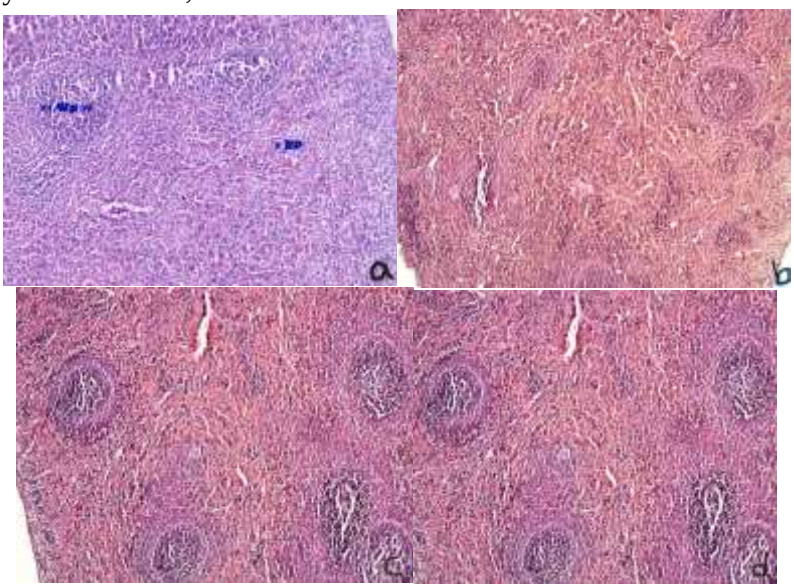
Group	Changes in Food conversion ratio			
	7th Day	14th Day	21st Day	28th Day
TED	NSI	**SI**	NSI	**SI**
TED x 5	**SD**	**SI**	NSD	**SI**
TED x 10	NSD	NSD	**SI**	**SI**

The food conversion ratio indicates the ratio expressing the weight of food required to produce a unit gain in the body weight of an animal. It is also an index of how much food consumed is assimilated. It is considered a parameter for the assessment of *Pachana* (digestion of undigested food) property. In TED, the trend is towards increased food conversion; at the TED x 5 dose level, there was a biphasic decrease in the first week and then an increase, a decrease again, and an increase in the final, and at the TED x 10 dose level, a significant increase was observed at the 3rd and 4th weeks. Thus, the overall trend is towards increased food assimilation. Thus, in most of the above parameters, the activity profile observed is that of one that promotes tissue development. This may be due to the rasayana property of vanga bhasma.

Because of this property, there is an increase in the *Jataragni(digestive fire)* as well as the Dhatwaagni (agni-fire at tissue/cellualar level), and an increase in the food conversion ratio was observed. The increase can be considered to indicate enhanced pachana properties in the test drug [8].

Histopathology:

All four parts—the forebrain, midbrain, hippocampus, and cerebellum—in all three groups were found to exhibit a normal cytoarchitectural profile. The hearts of rats belonging to both the control and TEDx5 and TEDx10 groups showed normal cytoarchitecture. In the TED group, focal cell infiltration was observed in sections from one rat, while sections from the remaining rats were found to be normal. One rat in group 1 (TED dose) exhibited erosion in the epithelial layer of the jejunum. The remaining sections from this group and the TEDx5 and TEDx10 groups exhibited normal cytoarchitecture. In the TEDx5 dose group, in one rat, moderate focal cell infiltration of the kidney was observed, while normal cytoarchitecture was observed in sections from the remaining rats. TED and TEDx5 groups revealed the presence of mild fatty changes in liver and cell infiltration in sections from one rat: the remaining exhibited a normal profile. In the TEDx10 dose group, sections from two rats exhibited cell infiltration with fatty changes, while the remaining exhibited a normal profile. The proportion of white pulp in the spleen was found to be moderately increased in all the sections from the TED, TEDx5, and TEDx10 groups. An increase in white pulp in the spleen may be non-specific. In the TED group, one rat showed moderate spermatogenesis with an increase in interstial cells; the rest of the sections from this group were found to be normal. All the sections from the TEDX5 and TEDx10 groups exhibited normal cytoarchitecture with evidence of good spermatogenesis. In the TED, TEDx5, and TEDx10 groups, the serosal, muscular, and sub-mucosal layers of the uterus were found to be normal.



Photomicrographs of a section of spleen taken at 1 ×100 magnification. (a) normal cytoarchitecture, (b), (c), & (d) increase in white pulp proportion.

CONCLUSION

Acute toxicity study showed the LD50 value of Vanga Bhasma is greater than 2000 mg/kg. Hence, it is concluded that vanga bhasma is not toxic on acute administration at a maximum oral dose level of 2000 mg/kg.

Sub-acute toxicity (repeated dose): Overall analysis reveals that Vanga bhasma, the test drug, is very well tolerated at therapeutic equivalent dosages for rats and multiples thereof,

The absence of significant negative effects on ponderal, histological, biochemical, and hematological measures

is evidence of this. Additionally, sperm morphology displayed a normal profile, indicating that there were no apparent effects on germinal tissue or risk for genotoxicity. Therefore, Vanga bhasma, prepared and administered in accordance with customary protocols, is safe to consume at therapeutic dose levels.

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REFERENCES

1. Shree Vagbhatacharya, Rasa Ratna Samuchchaya Edited by Kaviraja Shree Ambikadatta Shastri, 8th Edn, Varanasi, Chaukhambha Amarabharati Publication, 1988, 5th Chapter,162nd verse ,113pp.
2. Sadhananda Sharma, Rasa Tarangini, Edited by Kasinatha Shastri, 11th Edn, Varanasi, Motilal Banarasi Das, 1979, 8th Taranga, 46 verse, 445pp.
3. Paget GE, Barnes JM. Toxicity tests. In: Laurance DR, Bacharach AL, editors. Evaluation of drug activities: pharmacometrics. New York: Academic Press; 1964. p. 205-10
4. https://www.oecd.org/env/test-no-425-acute-oral-toxicity-up-and-down-procedure
5. https://www.oecd.org/env/test-no-407-repeated-dose-28-day-oral-toxicity-study-in-rodents
6. Acharya Madhava, Ayurveda Prakasha, Gulraj Sharma Mishra Ed, Varanasi, Chaukhamba Bharati Academy, 1999, 3rd Chapter, 148th verse, 373pp.
7. Sadhananda Sharma, Rasa Tarangini, Edited by Kasinatha Shastri, 11th Edn, Varanasi, Motilal Banarasi Das, 1979, 8th Taranga, 40verse, 443pp.
8. Acharya Madhava, Ayurveda Prakasha, Gulraj Sharma Mishra Ed, Varanasi, Chaukhamba Bharati Academy, 1999, 3rd Chapter, 148th verse, 373pp.

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