www.ThePharmaJournal.com

The Pharma Innovation

ISSN (E): 2277- 7695
ISSN (P): 2349-8242
NAAS Rating: 5.03
TPI 2020; SP-9(9): 118-122

www.thepharmajournal.com
Received: 12-07-2020
Accepted: 20-08-2020

VI Borekar
Department of Veterinary Pharmacology & Toxicology, Nagpur Veterinary College, Seminary Hills, Nagpur, Maharashtra, India

AP Somkuwar
Professor & Head, Department of Veterinary Pharmacology & Toxicology, Nagpur Veterinary College, Seminary Hills, Nagpur, Maharashtra, India

NV Kurkure
Professor & Head, Department of Veterinary Pathology, Nagpur Veterinary College, Seminary Hills, Nagpur- 06 (MS)

SW Bonde
Professor & Head, Department of Veterinary Biochemistry, Nagpur Veterinary College, Seminary Hills, Nagpur, Maharashtra, India

M Hedau
Assistant Professor, Department of Veterinary Pathology, Nagpur Veterinary College, Seminary Hills, Nagpur, Maharashtra, India

Corresponding Author:
VI Borekar
Department of Veterinary Pharmacology & Toxicology, Nagpur Veterinary College, Seminary Hills, Nagpur, Maharashtra, India

Safety evaluation of *Zingiber officinale* rhizomes extract in Wistar rats

VI Borekar, AP Somkuwar, NV Kurkure, SW Bonde and M Hedau

Abstract
The present study was conducted to evaluate the safety of 50% ethanolic extract of *Zingiber officinale* rhizomes on 30 Wistar rats divided into 5 groups, each comprised of 6 rats. Group T_1 served as control and Group T_2, T_3, T_4 and T_5 administered with extract @ 100, 200, 400, 800mg/kg body weight, respectively for 28 days. During the experiment, there were not any mortalities and abnormalities in general body condition of rats while, reduced body weight from Group T_5 was observed. No significant changes were observed in haematological values. There was slight elevation of AST, ALT & ALP level at high dose of extract (800mg/kg BW) whereas, no significant alterations observed in the levels of serum creatinin, total protein and albumin. Decreased total cholesterol level was noticed in all extract treated groups indicating the lipid lowering effect of plant. The histopathological studies revealed that high dose of extract (@ 800mg/kg BW) caused mild degenerative changes in liver & kidney. Finally, it was concluded that, 50% ethanolic rhizome extract of *Z. officinale* @ 100, 200, 400mg/kg BW considered to be safe without any adverse effect, whereas extract @ 800mg/kg BW has adverse effect on body weight and weight gain with mild degenerative changes in liver & kidney of rats.

Keywords: Medicinal plants, *Zingiber officinale*, safety evaluation, rats

1. Introduction
The herbal remedies are being used as replacement for modern medicine and also increasing their regards in the population in developing countries also has an important role in traditional system of medicine in India used for treatment in the field of Veterinary as well as in human being. Medicinal plants are the part and parcel of society to combat diseases from the dawn of civilization in world [1] and also continued in providing valuable therapeutic agents, both in modern and in traditional medicine [2]. Ginger, the rhizomes of the plant *Zingiber officinale* (Family *Zingiberaceae*), is arguably one of the most widely used culinary agent and spice in the world [3]. It is popularly known as 'Aale' in Marathi and 'Adrak' in Hindi. It is a creeping herb with thick, branching rhizomes and sturdy upright stem with pointed lance like leaves. The ginger plant has long history of cultivation originating from Asia and widely grown in India, Southeast Asia, West Africa and Caribbean. Ginger is widely employed in Chinese, Ayurvedic, Unani medicines and home remedies since antiquity for many ailments including pain, inflammation, and gastrointestinal disorders and the nutracuetical attributes of ginger are its positive influence on gastrointestinal tract including digestive stimulant action, anti-inflammatory influence and anticancer effect [4].
Despite its widespread use, few scientific validations need to be undertaken to ascertain the safety of traditional remedies which can provide the information on the toxicological properties of such remedies. Various bioactive phytochemicals present in herbal plant possesses ability to significantly change the mechanism concerned to pathology of diseases or toxicities. Therefore, the present investigation was carried out to evaluate the safety of 50% ethanolic extract of *Zingiber officinale* rhizomes at different oral dose level in Wistar rats.

2. Materials and Methods
2.1 Preparation of 50% Ethanol cold extract
The plant material i.e. roots of plant *Zingiber officinale* was collected from the local market of Nagpur and were dried at room temperature. 500 gram of powder of dried rhizome of *Zingiber officnale* was mixed with 2000ml of 50% Ethanol in stoppered flask and allowed to stand at room temperature for 72 hrs with frequent agitation until the soluble matter get dissolved. After 72 hrs, the mixture was filtered through muslin cloth, so as to remove the insoluble material.

The filtrates were again filtered through filter paper and then poured in clean and already weighed petri plate and allowed for complete evaporation at room temperature and finally stored in desiccators in cool and dry place.

2.2 Experimental animals
The Institutional Animal Ethics Committee (IAEC) (CPCSEA Reg. No. 244/GO/ReBi/S/2000/CPCSEA Dated 01.08.2000) approved the experimental protocol. The experimental protocol met the national guidelines as per the guidelines of the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), Ministry of Social Justice and Empowerment, Government of India. The present research work was carried out on 30 Wistar rats, which were procured from National Centre For Laboratory Animal Sciences, National Institute of Nutrition, Hyderabad (TS) (CPCSEA Reg. No. 154/GO/RBiBt-S/RL/99/CPCSEA Dated 25.11.1999). Rats were kept under standard management conditions as per the norms of CPCSEA. They were provided with 12 hrs light and 12 hrs dark periods and were maintained in polypropylene cages (47×34×18cms) lined with sterilized rice husk was used as a bedding material. The maximum numbers of rats in each cage were six and space was sufficient as per the norms

2.3 Experimental protocol
The safety evaluation of the extract of rhizomes *Zingiber Officinale* was carried out on rats by analyzing body weight, hematobiochemical parameters and histopathology of liver and kidney [5]. A total of thirty Wistar rats, used in this study were divided into five groups, as T_1, T_2, T_3, T_4 and T_5 comprised of six rats in each group. The rats were acclimatized for seven days to the environment, before the start of the experiment. Group T_1 served as control and Group T_2, T_3, T_4 and T_5 administered with the plant extract @ 100, 200, 400 and 800mg/kg body weight, respectively. After 28th day of experiment, prior to sacrifice, the rats were weighed and fasted for 12hr. Blood was collected by retro orbital bulbar method in glass vials containing 1% Ethylene Diamine Tetra Acetic Acid (EDTA) for haematological estimation and non-heparinized tubes for the serum biochemical analysis.
After collection of blood, the rats from all experimental groups were sacrificed (Ether Anaesthesia) with proper euthanization. Thereafter, liver and kidney were removed and washed with normal saline and immersed in 10% buffered formalin solution immediately. On dehydration liver and kidney tissue, were embedded in paraffin and cut into 5µm sections. These sections were stained with hematoxylin and eosin for histopathological examination according to standard procedure [6]. Haematological studies such as haemoglobin concentration (Hb), using Sahli's Method (acid hematin), total RBC count, total WBC count and Packed Cell Volume (PCV) by micro tube method [7]. Biochemical estimations were carried out by using commercial reagent kits (Robonik Ltd).

3. Results
3.1 Live body weight and gain in body weight (gm) of rats
The results of weekly live body weights and gain in body weight are detailed shown in table no.1. The initial mean body weights were non-significantly different from each other. At the end of first and second week, the body weights of rats in respective treatments does not show any significant difference, but at the end of fourth week, the body weights of group T_5 were found to be reduced significantly (P<0.05) as compared to normal control (T_1) & other treatment groups. As depicted in table 1, group T_2 (Ext. @ 100mg/kg BW) showed significant increase in overall gain in body weight followed by group T_3 (Ext. @ 200mg/kg BW) as compared to other treatment groups. Similarly, rats fed with extract @ 800mg/kg BW (T_5) showed significant reduction in overall gain in body weight when compared with normal (T_1) and other extract treatment groups. However, the values recorded for live body weight at 4th week of experiment, revealed that extract @ 100, 200 and 400mg/kg BW does not show significant difference (P<0.05).

3.2 Haematological parameters in rats
The mean values recorded for total RBC, WBC, Haemoglobin and PCV% does not show significant differences between all the treatment groups. (Table 2)

3.3 Serum biochemical parameters in rats
There was significant increased levels of AST, ALT and ALP were found in Group T_5 (Ext. @800mg/kg BW) (P<0.05) as compared to normal and other extract treated groups. The mean values for serum creatinin, total protein and albumin were does not differs whereas, a significant decrease in cholesterol level was observed (P<0.05) from all extract treated groups when compared with normal control group. (Table 3)

3.4 Histopathology of liver and kidney of rats
a) Liver: No marked histopathological alterations caused by extract @ 100, 200 and 400mg/kg body weight (T_2, T_3 & T_4) as shown in plate no. 1 & 2. Group T_5 exposed with extract @ 800mg/kg BW showed mild hemorrhages with vacuolar degenerative changes (plate no.3 & 4).

b) Kidney: Extract @ 100, 200 and 400mg/kg body weight (T_2, T_3 & T_4) did not causes any histopathological alterations (plate no. 5, 6 & 7), where as mild granular degenerative changes were noticed in group T_5 exposed with extract @ 800mg/kg body weight (plate no. 8).

Table 1: Effect of *Zingiber officinale* rhizomes extract on live body weight & gain in body weight of Wistar rats

Parameters	Group	T_1	T_2	T_3	T_4	T_5
	Week	Control Group	*Zingiber officinale* Extract @ 100 mg/kg B.W.	*Zingiber officinale* Extract @ 200 mg/kg B.W.	*Zingiber officinale* Extract @ 400 mg/kg B.W.	*Zingiber officinale* Extract @ 800 mg/kg B.W.
	Initial	120.00±3.82	122.50±4.04	123.33±7.92	120.50±5.79	119.16±7.25
Live Body Weight (g)	I	126.33±3.79	129.00±4.13	131.33±7.51	124.33±5.82	121.66±7.24
	II	136.33±4.46	140.66±3.65	146.00±1.50	133.33±5.14	125.33±7.58
	III	140.33±4.91^{ab}	154.83±0.79^{a}	155.00±1.50^{a}	137.50±1.13^{ab}	130.83±1.73^{b}
	IV	147.83±5.78^{abc}	164.00±4.73^{a}	160.50±7.25^{ab}	141.83±4.79^{bc}	135.16±7.60^{c}
Gain in Body Weight (g)	I	6.33±0.84^{ab}	6.50±0.88^{a}	8.00±0.68^{a}	4.33±0.76^{bc}	2.50±0.34^{c}
	II	10.00±0.93^{bc}	11.66±0.98^{b}	14.66±0.49^{a}	8.50±0.92^{c}	3.66±0.42^{d}

	III	4.00±0.51^{c}	14.16±0.94^{a}	9.00±0.73^{b}	4.16±0.70^{c}	5.50±0.67^{c}
	IV	7.50±0.95^{ab}	9.16±0.79^{a}	5.50±0.76^{bc}	4.33±0.76^{c}	4.33±0.84^{c}
	Total	27.83±2.16^{c}	41.50±0.56^{a}	37.17±0.60^{b}	21.33±1.20^{d}	16.00±1.91^{e}

Values are mean S.E. for 6 rats in each group. Values not sharing a common superscript in a column differ significantly (P<0.05)

Table 2: Effect of *Zingiber officinale* rhizomes extract on haematological parameters in Wistar rats

Group	Treatment	RBC (x 10^6 Cells/dl	WBC (x 10^3 Cells/dl	Hb (g/dl)	PCV (%)
T_1	Control Group	8.39±0.92	7.13±0.57	14.85±1.27	42.55±3.81
T_2	*Zingiber officinale* Extract @ 100 mg/kg B.W.	6.30±0.72	6.38±1.10	14.40±0.91	41.20±2.74
T_3	*Zingiber officinale* Extract @ 200 mg/kg B.W.	6.48±0.98	6.86±1.88	14.46±1.86	41.40±5.58
T_4	*Zingiber officinale* Extract @ 400mg/kg B.W.	7.76±0.25	6.27±1.39	13.99±1.08	39.99±3.25
T_5	*Zingiber officinale* Extract @ 800 mg/kg B.W.	7.25±0.88	6.41±0.11	14.14±1.22	40.44±3.66

Values are mean S.E. for 6 rats in each group. Values in a column does not differ significantly (P<0.05)

Table 3: Effect of *Zingiber officinale* rhizomes extract on serum biochemical parameters of Wistar rats

Serum Biochemical Parameters	T_1 Control Group	T_2 *Zingiber officinale* Extract @ 100 mg/kg B.W.	T_3 *Zingiber officinale* Extract @ 200 mg/kg B.W.	T_4 *Zingiber officinale* Extract @ 400 mg/kg B.W.	T_5 *Zingiber officinale* Extract @ 800 mg/kg B.W.
SGPT (IU/L)	43.16±1.13^{b}	42.83±0.87^{b}	43.16±1.24^{b}	44.5±0.71^{b}	56.50±1.47^{a}
SGOT (IU/L)	62.50±1.17^{b}	62.66±1.20^{b}	63.16±0.74^{b}	61.83±1.49^{b}	70.66±1.45^{a}
ALP (IU/L)	55.29±1.93^{b}	57.28±3.54^{b}	56.09±3.44^{b}	51.20±1.83^{b}	67.56±0.76^{a}
Total Protein (g/dl)	6.78±0.52	7.72±0.35	7.27±0.45	7.89±0.28	6.65±0.11
Albumin (g/dl)	3.31±0.23	3.85±0.04	3.84±0.20	3.52±0.17	3.64±0.08
Cholesterol (mg/dl)	74.84±1.48^{a}	60.72±1.63^{b}	55.00±1.95^{b}	48.14±1.52^{b}	50.95±1.31^{b}
Creatinin (mg/dl)	2.02±0.04	1.82±0.27	1.76±0.32	1.96±0.32	1.87±0.10

Values are mean S.E. for 6 rats in each group. Values not sharing a common superscript in a column differ significantly (P<0.05)

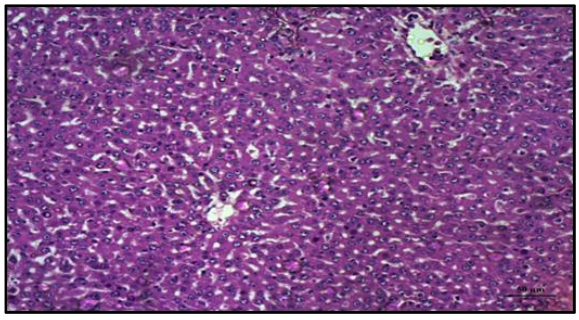

Plate 1: Showing Normal Architecture of Liver of rat with hepatocytic cords (H & E Stain 200X)

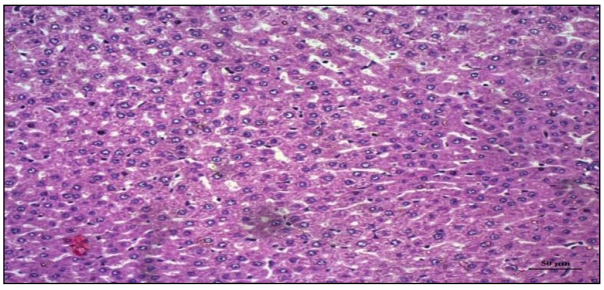

Plate 2: Showing Normal Architecture of Liver Section in Rat (H & E Stain 200X)

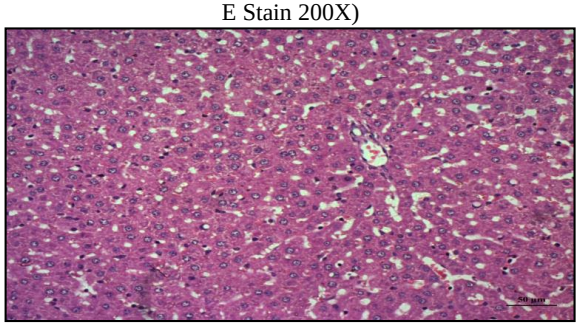

Plate 3: Showing relatively normal architecture of liver of rat with mild haemorrhages (H & E Stain 200X)

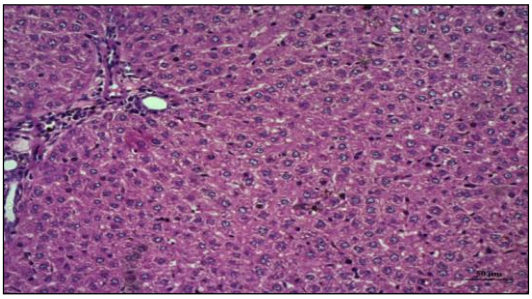

Plate 4: Showing relatively normal architecture of liver of rat with mild vacuolar degenerative changes (H & E Stain 200X)

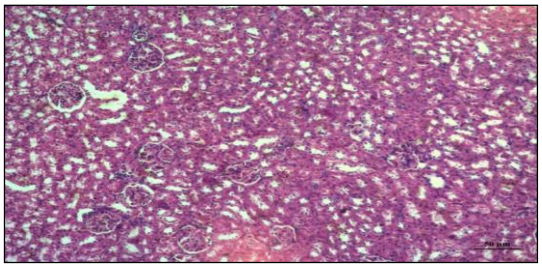

Plate 5: Showing normal architecture of kidney of rat (H & E Stain 100X)

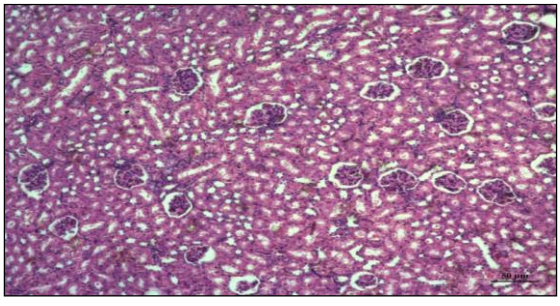

Plate 6: Showing normal architecture of kidney of rat (H & E Stain 100X)

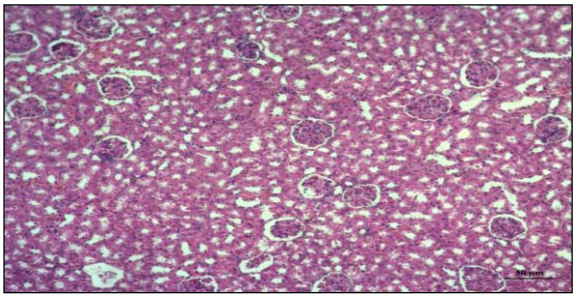

Plate 7: Showing relatively normal architecture of Kidney of rat (H & E Stain 100X)

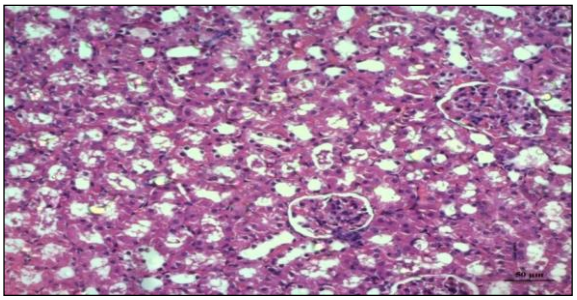

Plate 8: Mild Granular Degenerative Changes in Kidney of rat (H & E Stain 200X)

4. Discussions

The findings showed that extract @ 100, 200 and 400mg/kg BW does not cause any mortalities and abnormalities in general body conditions in Wistar rats throughout the experiment of four weeks. However, high dose of the plant extract (800mg/kg BW) affected the body weights of rats, may be due to its adverse effect. In the earlier studies, studied methanolic extract @ 75, 150 and 300mg/kg BW of *Z. officinale* and reported that it does not affect body weight of rats where as @ 600 mgkg bw, the body weight of rats were lower down for which he has mentioned that extract may increased the functional activity of liver causing increase in removal of bilirubin that could negatively affected the health of rats [8]. Ginger oil at doses of 100, 250, and 500 mg/kg per day to 6 groups of rats (5/sex per dose) shows no mortality and no decrease in body weight or food consumption [9].

Hematological parameters are most sensitive to assess the toxicity and the blood profile of the animal usually gives most important information regarding response of the body to the injury or adverse effect of the drug [10]. In our investigation *Z. officinale* extract did not cause any significant changes in values of RBC, WBC, Hb and PCV % in all extract treatment groups when compared with normal control. In earlier study, oral administration up to 2000 mg/kg powder of ginger to rats does not associate with any mortalities and abnormalities in general conditions, behaviour, growth, food and water consumption in rats and parameters of haematology and blood biochemistry [11].

The levels of AST, ALT and ALP which are the valuable indicators of increased function of organ tissue (Liver and Kidney) as well as plasma due to adverse effect of any drug [12]. In our investigation, the extract @100, 200 and 400 mg/kg BW does not show significant difference in serum AST, ALT and ALP values. However, significant elevated AST, ALT & ALP level were observed at high dose of *Z. officinale* extract (800mg/kg bw). It may be due to the hepatic & renal tissue damage which was histopathologically proved with mild vacuolar degenerative changes in liver & mild granular degenerative changes in kidney. Different organ like intestine, bone, liver and kidney, ALP has located inside of their tissues; therefore, alteration in ALP level could be a specific biomarker of tissue injury [13].

Evaluation of miss functioning of kidney can be assessed by detecting increased level of serum creatinine [14]. In present investigation, serum creatinine level in all *Z. officinale* extract treatment groups did not show significant difference compare to normal control which indicated normal functioning of kidney with minor degenerative changes at high dose of the extract (800mg/kgBW). Alcoholic extract of ginger @ 10, 20 and 40 mg/kg every 48 hours for 20 days in mice does not affect the serum creatinine compared to control animals [15]. It was also reported that ginger oil at doses of 100, 250, and 500 mg/kg per day to Wistar rats did not produce any treatment related changes in haematological parameters, hepatic, renal functions, serum electrolytes and histopathology of selected organs and also confirmed that ginger oil was not toxic to rats following sub chronic oral administrations of up to 500 mg/kg per day [9].

In the present investigation, the total protein & albumin levels did not show any significant changes in all *Z. officinale* extract treated rats compared to the normal control. In earlier studies, there was no change in total protein, albumin, globulin and albumin/globulin ratio by giving aqueous extract of ginger 500mg/kg bw for four weeks, similarly aqueous extract at 500mg/kg by IP and PO [16, 17]. 28 days administration of methanol extract of *Zingiber officinale* at 75 mg/kg to 600 mg/kg bw does not revealed any alterations in serum concentrations of ALT, AST, ALP, albumin and total proteins when compared with the control [8].

The total cholesterol level significantly decreased was in all extract treated groups when compared to normal group in present study which indicated the lipid lowering effect of the *Z. officinale* extract. It has been reported earlier that, ginger may be acted on the liver to reduce cholesterol biosynthesis and may stimulate cholesterol's conversion to bile acids and may increase its faecal excretion [18]. Further, presence of chemical constituent which inhibited absorption of dietary fat by inhibiting its hydrolysis which also stimulate hepatic pathway of elimination of cholesterol from the body. The hypocholesterolmic effect of *Zingiber officinale* could be attributed to down regulated of HMG-CoA reductase activity [19]. The findings of our studies are in agreement with [20] who reported decrease in total cholesterol level by aqueous and ethanolic extract of *Z. officinale* @200 and 400mg/kg BW daily for 30 days in rats. Significant decrease in total cholesterol level in rats treated with high fat diet by *Zingiber officinale* extract and serum cholesterol level in hypercholesterlomic rats treated with *Zingiber officinale* extract [21]. Reduced cellular cholesterol biosynthesis is often related with amplified activity of LDL receptor, which leads to the removal of cholesterol from plasma resulting in reduced plasma cholesterol concentration [22]. Further, it was also reported that *Zingiber officinale* has increased fecal excretion of cholesterol, signifying that ginger may block absorption of cholesterol in the gut [23]. Lipid lowering effects of *Zingiber officinale* may be due to single or various effects of its active components present in the extract.

The histopatholigcal studies of present investigation revealed mild degenerative change in the tissue of liver and kidney which are in agreement with study reported earlier as absolute ethanolic extract of *Z. officinale* @400mg/kg BW daily for 30 days causes vacuolar degeneration in liver tissue and

granularity of the cytoplasm of epithelium lining of the renal tubules [20]. As, in our investigation, 50% ethanol is used as a solvent to prepare the extract from *Z. officinale* which may diverge the chemical composition in more or less, that may be the reason, extract given at 400mg/kg BW above caused some pathological alterations in liver & kidney tissue.

5. Conclusion

Form this investigation it can be concluded that, 50% ethanolic rhizome extract of *Z. officinale* @ 100, 200, 400mg/kg BW considered to be safe without any adverse effect, where as extract @ 800mg/kg BW has adverse effect on body weight and weight gain with mild degenerative changes in liver & kidney of rats..

6. Acknowledgements

The author is very much thankful to Associate Dean, Nagpur Veterinary College, Nagpur and Head, Department of Veterinary Pharmacology & Toxicology, Nagpur Veterinary College, Nagpur for providing necessary facility & infrastructure to carry out the above research investigation.

7. References

1. Nayak AZ, NG Nayak Ganganath, B Soumya. Evaluation of antibacterial and anticandidial efficacy of aqueous and alcoholic extracts of neem (*Azadirachta indica*). International Journal of Research in Ayurveda and Pharmacy. 2011; 2(1):230-235.
2. Krentz AJ, CJ Bailey. Oral antidiabetic agents: current role in type 2 diabetes mellitus, Drugs. 2005; 65:385-411.
3. Srinivasan Krishnapura. Ginger rhizomes (Zingiber officinale): A spice with multiple health beneficial potentials. Pharma Nutrition. 2017; 5:18-28.
4. Baliga MS, R Haniadka, MM Pereira, KR Thilakchand, S Rao. Radioprotective effects of *Zingiber officinale* Roscoe (ginger), Past, present and future. Food Funct. 2012; 3:714-723.
5. Adedapo AA, OM Mogbojuri, BO Emikpe. Safety evaluations of the aqueous extract of the leaves of *Moringa oleifera* in rats Journal of Medicinal Plants Research. 2009; 3(8):586-591.
6. Ross MH, EJ Reith, LJ Romrell. Histology a text Atlas (Ki sp k) Willams and Wikins, Baltimore, Maryland, 1989, 1-2.
7. Benjamin MM. Outline of Veterinary Clinical Pathology. 3rd edn, 1985, 65.
8. Yusuf Abubakar A, Bashir Lawal, Asmau N Abubakar, Eustace B Berinyuy, Yemisi O Omonije, Sheriff I Umar *et al*. *In-vitro* antioxidants, antimicrobial and toxicological evaluation of Nigerian Zingiber officinale. Clinical Phytoscience. 2018; 4(12):1-8.
9. Jeena Kottarapat, Vijayastelter B Liju, Ramadasan Kuttan. A Preliminary 13-Week Oral Toxicity Study of Ginger Oil in Male and Female Wistar Rats. International Journal of Toxicology. 2011; 30(6):662-670.
10. Liju V B, Jeena K, Kuttn R. Acute and sub chronic toxicity as well as mutagenic evaluation of essential oil from turmeric (Curcuma longa L.) Food Chem. Toxicol. 2013; 53:52-61
11. Rong Xianglu, Gang Peng, Takuya Suzuki, Qinglin Yang, Johji Yamahara, Yuhao Li *et al*. A 35-day gavage safety assessment of ginger in rats. Regul Toxicol Pharmacol. 2009; 54(2):118-123.
12. Sandeghi LA, Farzeen T, Vahid YB. Antioxidant effect of alfalfa can improve iron oxide nanoparticle damage: *In vivo* and *in vitro* studies. Regulatory Toxicology & Pharmacology. 2016; 81:39-46.
13. Goldstein DJ, Rogers C, Harris H. Evolution of alkaline phosphatises in primates. PNAS USA. 1982; 79:879-883.
14. Kaneko JJ, Harvey JW, Michael LB. Clinical Biochemistry of Domestic Animals. 5th ed., Academic press, New York, 1997, 182-189.
15. Mehrdad M, Messripour M, Ghobadipour M. The effect of ginger extract on blood urea nitrogen and creatinine in mice. Pakistan J Biol Sci, 2007; 10:2968-2971
16. Ismail HA, HY Al- Nahari. The protective effect of ginger (*Zingiber officinale*) on some biochemical parameters in rats. Egypt. J Exp. Biol (Zool.). 2009; 5:411-417
17. Alnaqeeb MA, Thomson M, Al-Qattan KK, Kamel F, Mustafa T, Ali M *et al*. Biochemical and histopathological toxicity of an aqueous extract of ginger. Kuwait J Sci Eng. 2003; 30:35-48.
18. Verma SK, Singh M, Jain P, Bordia A. (2004) Protective effect of ginger, *Zingiber officinale* Rosc on experimental atherosclerosis in rabbits. Indian J. Exp. Biol. 2003; 42:736-738.
19. Srinivas N, Moon SK, Navnath SG, George Q Li, Basil DR. Regulation of low density lipoprotein receptor and 3-hydroxy-3 methylglutaryl coenzyme A reductase expression by *Zingiber officinale* in the liver of high-fat diet-fed rats. Journal Compilation Nordic Pharmacological Society.Basic & Clinical Pharmacology & Toxicology. 2010; 106:389-395.
20. Al-Kishu AG, ME El-Boshy, NA Elsawy, OA Omar, EA Header. Pathological comparative studies on aqueous and ethanolic extract of *Z. officinale* on antioxidants and hypolipidemic effects in rats. Life Science Journal. 2013; 10(2):2393-2403
21. Ajayi OB. Effect of Ginger Powder (*Zingiber officinale*) on plasma lipid profile and liver *e*nzyme activities of hypercholesterolemic rats. Journal of Life Sciences. 2011; 5:712-716.
22. Srinivas N, Satyanarayana S, Basil DR. Protective effects of ethanolic extract of *Zingiber officinale* Rhizome on the development of metabolic syndrome in High-Fat Diet-Fed Rats. Journal compilation Nordic Pharmacological Society. Basic & Clinical Pharmacology & Toxicology. 2009; 104:366-373.
23. Han L, Gong X, Kawano S, Saito M, Kimura Y, Okuda H. Antiobesity actions of *Zingiber officinale* Roscoe. Yakugaku Zasshi. 2005; 125:3-7.