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EVALUATION OF CHRONIC TOXICITY OF GOWRI CHINTHAMANI CHENDURAM IN WISTAR ALBINO RATS

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ABSTRACT

Aim and Objectives: The aim of the present study was to carry out 90 days repeated oral toxicity of *Gowri chinthamani chenduram* (GCC) in Wistar albino rats and to assess in a 30 days recovery period for delayed onset of any toxicity of *Gowri chinthamani chenduram*. **Methods:** Cronic toxicity of *Gowri chinthamani chenduram* was evaluated in wistar albino rats with reference to haematological, bio-chemical and histopathological studies. **Results:** No GCC-related changes in body weights, food and water intake, cage side observations, clinical observations, clinical pathology, mortality, macroscopic examinations and organ histopathology were noted during treatment period and post recovery period. **Conclusion:** Based on the results of this study, the no-observed-adverse-effect-level (NOAEL) of *Gowri chinthamani chenduram* in rats is >400 mg/kg/day when administered orally for 90 days

Key words: Cronic toxicity, *Gowri chinthamani chenduram*, metallomineral, Siddha.

No: of Tables: 13 **No: of Figures : 02** **No: of References: 09**

Introduction

India has different recognized systems of medicine. They are Ayurveda, Siddha, Unani, Yoga, Naturopathy Homoeopathy and Sowa Rigpa [1]. Among them Siddha is the unique system of medicine "Siddha" means "established truth" [2]. Siddha system of medicine is claimed to alleviate the root cause of the diseases by maintaining the ratio of Vatham, Pitham and Kapham. In this system of medicine the commonly used formulations in combination with minerals are Parpam (mineral/metallic oxides), Chendhooram (mineral/metallic sulphides), Chunnam (caustic or major oxides) and Pathangam (sublimation). Among them Parpam and Chenduram type of medicines are widely used, having potential therapeutic values [3].

Gowri chinthamani chenduram (GCC) is a Siddha metallomineral formulation and it contains Mercury, Sulphur and Borax [4]. *Gowri chinthamani chenduram* at a dose of 100 – 200 mg thrice a day with honey is one of the best and potent compound drugs for osteoarthritis mentioned in *Agasthiar Vaidhya Kaviyam – 1500* [5]. It has a long history in Siddha system of medicine for various ailments especially for the treatment of inflammation [6]. GCC is also known to cure 18 types of colic, 16 types of gastritis, chronic fevers, rat bite, pneumonia, bronchitis, dyspnoea, Tuberculosis (TB), bronchial asthma, piles, jaundice, inflammation of male and female genital organs accompanied by severe pain, pain in the tongue and ulcerative bites[7] . The duration of the treatment is depends on the severity from 30 – 60 days [6]. As mentioned earlier, GCC is a metallomineral formulation and is being used for prolong period to treat several diseases. Chronic usage of these metal formulation may grounds toxic effects, hence, the need for its safety has to be ascertained. So the present work was carried out in wistar albino rats by following OECD guideline 408[7].

Materials and Methods:

Procurement of *Gowri chinthamani chenduram*: *Gowri chinthamani chenduram* was collected from The Indian Medical Practitioner's Co-operative Pharmacy & Stores LTD (GMP certified) Thiruvaanmiyur, Chennai.

Preparation of Vehicle: The vehicle in the study was prepared as follows;

5 ml of dabur honey diluted with 95 ml R.O water and made the volume up to 100 ml (5%v/v). 0.5% CMC was prepared by triturating the 500 mg of CMC in 100 ml of 5% v/v honey till formation of a clear solution.

Preparation of *Gowri chinthamani chenduram*: The test doses were prepared by triturating a weighed quantity of test drug in required volume of 0.5 % carboxy methyl cellulose (CMC) prepared in 5% v/v honey to obtain a concentration of 40 mg/kg, 200 mg/kg and 400 mg/kg.

Animals and Husbandry: A total of 80 wistar albino rats (40/sex) of 5 to 6 weeks age were received from TANUVAS, Chennai, Tamil Nadu. The body weight variation of the animals selected for the study on the day of randomization did not exceed □□20 % of the mean body weight of each sex. This study was performed as per the recommendations of the Committee for the Purpose of Control

and Supervision of Experiments on Animals (CPCSEA) guidelines for Laboratory Animal Facility after approval of Institutional Animal Ethics Committee (IAEC) of Siddha Central Research Institute, Central Council for Research in Siddha (Ministry of AYUSH), Arumbakkam, Chennai-106. The study was approved by the Institutional Ethical Committee (164/PHARMA/SCRI/2017).

Feed and water were provided *ad libitum*, except on study day (SD) 30-31, 60-61, 90-91 (before terminal sacrifice) and SD 119-120 (before recovery sacrifice) when food-fasting was implemented and rats were fasted for 12 hours before termination at those 4 occasions. The animals were maintained in polypropylene cages at room temperature 18-25^{0}C, humidity 30 to 65% and light cycle 12-hour light/12-hour dark.

Chemicals: The chemicals used in this study such as Carboxy methyl cellulose, Sodium chloride, Formaldehyde, Anesthetic ether and Sodium ethylenediaminetetraacetic acid (sodium-EDTA) of analytical grade were purchased from Theres scientific works, Chennai.

Dose calculation of *Gowri chinthamani chenduram*: The clinical dose of *Gowri chinthamani chenduram* is 200 mg. The animal (rat) doses are calculated as per the FDA guidelines[8] and the calculated therapeutic dose (TD) was found to be 40mg/kg of body weight. In the present study to evaluate the dose correlated effects, 5 times TD and 10 times TD i.e. 200 mg/kg & 400 mg/kg of bodyweight were chosen correspondingly.

Experiment Design: The present study was carried out according to OECD 408 guidelines. Animals were initially divided into four groups, each group contains 20 animals (10/sex) based upon descending body weights and physical examinations. Male and females were randomized into groups separately based on bodyweight. After the randomization process, each study animal was assigned a unique number and identified by a picric acid mark. Group-I served as normal control, Group-II, Group-III and Group-IV administered with test drug at a doses of 40 mg/kg, 200 mg/kg and 400*p.o.* mg/kg respectively for 90 days. At 90th day 50% of the experimental animals (40 animals) in each group were subjected to euthanasia. The necropsy was carried out on all euthanized animals and the organs were isolated and observed macroscopically for abnormalities. After 30days of post treatment the remaining half animals (40animals) were euthanized and organs were collected and observed macroscopically for abnormalities. The organs of treatment and post treatment were preserved in 10% neutral formalin and were subjected for histopathology.

Observations: Cage side observations included observation for mortality, morbidity, general health, and signs of toxicity. Clinical observations included evaluation of skin and fur characteristics, eye and mucous membrane, sensory responses and

reflexes, respiratory and autonomic effects, motor activity and behavior patterns.

Hematology: The hematology parameters viz., hemoglobin concentration (HB), packed cell volume (PCV), total red blood cell count (RBC), total white blood cell count (WBC) and platelet count (PLT) were analyzed.

Serum Biochemistry: Following serum biochemical parameters were estimated using RA-50 auto analyzer(Bayer).Glucose, Alkaline phosphatase Total proteins, Albuminn, Creatine phosphotase, Uric acid and Calcium.

Histopathology: All tissue samples from each group viz., brain, pancreas, adrenal glands, heart, thymus, liver, kidneys, spleen, stomach, testes / ovaries, epididymides/ uterus, sciatic nerve, skin and femur bone from each group test animals(1/sex) were processed and evaluated. Those tissue samples were embedded in paraffin, sectioned, stained with hematoxylin and eosin and examined microscopically by a board-certified veterinary pathologist.

Statistical Analysis:

Body weights, food intake, water intake, relative organ weights, and clinical pathology data were analyzed statistically. All the data was expressed as mean ± SEM. Statistical significance between more than two groups was tested using one-way ANOVA followed by Tukey's post hoc using Graph pad prism version-5. The significance level was set at $P<0.05$ for all tests. Group II, III, and IV will be statistically compared with Group I to find the treatment related effects[9].

Results and Discussions:

The dose volume was 1ml/100g body weight per day for all animals. The total volume of administration was calculated based on the weekly body weights of the animals. In the present study changes in body weight, feed and water consumption, biochemical parameters and histopathological studies were carried out and the results are expressed in the form of tables and figures.

Blood urea, Creatinine, Total Cholesterol,T

No compound-related mortality or signs of toxicity were noted. Other observations noted included alopecia, excessive grooming, Straube's phenomenon, abscess formation and hyperactivity; these observations were considered unrelated to treatment because they occurred in both the compound-treated and control groups or only appeared sporadically in low incidence throughout the study with no correlation to treatment or sex.

No compound-related body weight changes were noted. No significant differences were noted in total body weight change over the course of the study for either sex. Group summary of body weight data for males and females are presented in table 1 and 2 respectively.

A significant change in the feed intake was not observed in animals during treatment period and post recovery period between the groups. The data are presented in table 3.

No significant change in the water intake was observed in animals during treatment

period and post recovery period between the groups. The data are presented in table 4.

The clinical pathology evaluation and data reports are presented in table 5-12. No compound-related changes in hemoglobin concentration, packed cell volume, total red blood cell count, total white blood cell count and platelet count were noted (table 5-8). No compound-related changes in serum glucose, serum Urea, serum Creatinine, serum Total Cholesterol, serum Triglycerides, serum HDL, serum LDL, serum Total bilirubin, serum SGOT, serum SGPT, serum ALP, serum Total proteins, serum Albumin, serum CRP, serum Uric acid, serum Calcium (table 9-12) were noted.

Macroscopic observations were listed in table 13. All findings listed in table 13 were considered incidental because they occurred in frequently, in both treated and control animals, exhibited no dose relationship.

The histopathology of brain and stomach (glandular & non glandular) shown normal characteristic features with regular cell arrangements at the end of the treatment (90^{th} day) and post recovery period (120^{th} day) in both control and GCC treated animals. Liver histopathology showed congestion, multifocal moderate vesicular (micro to macro) fatty degeneration of hepatocytes. The histopathology of heart in all groups shown normal characteristic features at the end of the treatment (90^{th} day) and post recovery period (120^{th} day). Congestion and mild tubular epithelial cell degeneration was noticed in the histopathology of kidneys of control and test drug GCC treated animals. Pulmonary congestion, haemorrhages, peribronchiolar and interstitial mononuclear cell infiltration was observed in the lungs histopathology of both control and test drug treated animals at end of the treatment (90^{th} day) and post recovery period (120^{th} day). Congestion was noticed in the spleen of group-II (animal No .GCC20; dose 40mg/kg) at post recovery period (120^{th} day). The histopathology of thymus has shown mild lymphoid cell depletion in group-III (animal No.66; dose 200mg/kg) and group-IV (animal No.37; dose 400mg/kg) animals at end of the treatment. No abnormalities and damaged cells were noticed in the histopathology of sciatic nerve, adrenal gland, spleen, skin, femur bone, eye, ovary and uterus. Images of the organs were shown in figure 1 and 2 at end of the treatment and post recovery period respectively.

Table1. Effect of GCC on body weight (g) of male rats

S.NO.	Group	Treatment Period				Post recovery Period
		0th Day	30th Day	60th Day	90th Day	120th Day
1	I	216.0±11.77	246.1±28.35	272.5±30.98	304.5±34.20	325.5±12.95
2	II	224.3±9.804	269.2±12.02	312.4±15.01	333.2±14.81	351.6±23.57
3	III	224.7±4.847	271.1±4.927	314.8±6.751	336.4±6.822	353.5±11.59
4	IV	221.3±6.683	276.9±4.334	321.5±4.865	338.3±5.880	362.0±6.988

All values were expressed as Mean ± S.E.M; n=10

Table 2. Effect of GCC on body weight (g) of female rats

S.NO.	Groups	Treatment Period				Post Recovery Period
		0th Day	30th Day	60th Day	90th Day	120th Day
1	I	171.1±6.923	201.0±5.903	207.8±5.085	215.9±5.982	229.3±14.40
2	II	168.9±6.163	201.4±5.027	211.2±4.991	222.2±5.921	232.0±5.779
3	III	166.8±3.991	185.9±21.23	171.3±30.27	160.0±35.55	229.3±16.25
4	IV	183.6±8.887	195.4±4.768	183.3±20.89	190.0±21.67	225.0±5.447

All values were expressed as Mean ± S.E.M; n=10

Table 3. Effect of GCC on Feed intake (g) of experimental animals

Weeks	Treatment Groups			
	Group I	Group II	Group III	Group IV
Treatment Period				
Week 1	235±34.74	255±45.43	242±38.49	302±9.09
Week 2	323.5±6.15	344±4.28	344±6.95	331.5±3.47
Week 3	343.5±6.15	361.5±2.41	366.5±1.34	351±4.81
Week 4	342.5±0.27	362.5±1.87	335.5±5.08	356±1.60
Week 5	322.5±1.87	341.5±2.41	334±2.14	301.5±9.34
Week 6	338±3.21	368.5±2.41	326.5±0.27	343±0.53
Week 7	338.5±6.68	364.5±0.80	336±3.21	340.5±9.35
Week 8	338.5±5.61	368.5±1.34	332.5±0.27	343.5±7.75
Week 9	351.5±1.34	365±2.67	315±4.28	350±1.60
Week 10	326±2.67	377.5±4.54	327±3.74	347.5±7.75
Week 11	335±9.62	367.5±1.34	305±3..21	346.5±3.47
Week 12	344±8.02	366.5±2.94	311.5±9.35	338.5±5..08
Week 13	247.5±43.56	276±46.5	217±48.11	253.5±48.37
Post Recovery Period				
Week 14	166.5±2.94	192.5±1.34	128±0.53	156.5±4.01
Week 15	171±3.21	181±3.74	132±0	159.5±1.87
Week 16	156.5±6.15	180.5±2.41	151.5±0.27	142.5±1.87
Week 17	160.9±1.60	190.5±0.80	136.5±0.27	170.5±0.80

All values were expressed as Mean ± S.E.M; n=10

Table 4. Effect of GCC on water intake (ml) of experimental animals

Weeks	Treatment Groups			
	Group I	Group II	Group III	Group IV
Treatment Period				
Week 1	592.5±6.68	600±0	630.5±18.98	625±2.67
Week 2	615±29.40	630±42.76	567.5±14.70	636±8.55
Week 3	616.5±48.91	674±23.52	612.5±22.72	664±34.21
Week 4	747.5±14.70	782.5±9.35	690±21.38	742.5±14.7
Week 5	697.5±25.39	670±42.76	655±61.47	705±45.43
Week 6	775±8.02	735±13.36	725±13.36	760±0
Week 7	785±8.02	780±10.69	757.5±6.68	775±13.36
Week 8	795±2.67	760±10.69	730±16.04	770±5.35
Week 9	770±5.35	730±10.69	695±8.02	730±0
Week 10	795±2.67	790±5.35	765±2.67	780±0
Week 11	750±0	760±0	770±5.35	760±10.69
Week 12	925±24.05	955±13.36	835±29.40	935±2.67
Week 13	675±168.37	675±136.30	660±165.7	645±157.68
Post Treatment Period				
Week 14	395±13.36	435±8.02	290±5.35	335±2.67
Week 15	305±8.02	305±8.02	270±0	310±5.35
Week 16	385±8.02	425±2.67	300±10.69	315±2.67
Week 17	355±18.71	385±24.05	260±5.35	320±0

All values were expressed as Mean ± S.E.M; n=10

Hematology results:

Table 5. Effect of GCC on Hematological parameters at 30th day

Parameter	Group I	Group II	Group III	Group IV
Hb (g/dl)	12.66±0.559	12.71±0.398	11.79±0.374	12.43±0.191
PCV (%)	33.63±1.448	33.77±1.085	31.32±0.954	32.94±0.507
RBC (m/µl)	6.906±0.282	6.936±0.206	6.520±0.209	6.827±0.106
WBC (/cmm)	10285±900.6	8881±687.7	9800±660.1	8553±575.8
Platelets (L / µL)	7.564±0.451	7.038±0.491	8.000±0.307	7.888±0.244
Neutrophils (/cmm)	20.74±0.801	18.50±1.072	16.72±0.726	18.84±0.693
Lymphocytes (/cmm)	74.11±0.884	76.65±1.208	79.63±0.780	76.21±0.890
Monocytes (/cmm)	2.737±0.365	2.550±0.328	1.842±0.115	2.526±0.377
Eosinophils (/cmm)	2.556±0.166	2.350±0.181	2.105±0.169	2.474±0.177

All values were expressed as Mean ± S.E.M; n=10

Table 6. Effect of GCC on Hematological parameters at 60th day

Parameter	Group I	Group II	Group III	Group IV
Hb (g/dl)	12.43±0.425	11.47±0.235	39.07±6.366	38.05±8.067
PCV (%)	33.55±1.224	30.81±0.675	29.73±1.037	29.89±0.562
RBC (m/µl)	6.702±0.258	6.198±0.140	6.029±0.209	5.951±0.121
WBC (/cmm)	9050±1087	8055±494.5	7595±421.9	7625±647.0
Platelets (L / µL)	7.903±0.398	8.219±0.277	8.337±0.376	8.389±0.254
Neutrophils (/cmm)	23.60±1.072	21.75±1.135	22.7±1.363	24.38±1.064
Lymphocytes (/cmm)	69.80±2.677	73.00±1.277	72.75±1.442	71.81±1.141

Monocytes (/cmm)	2.80±0.277	2.90±0.190	2.85±0.283	2.25±0.111
Eosinophils (/cmm)	1.750±0.123	1.850±0.150	1.700±0.105	1.800±0.144

All values were expressed as Mean ± S.E.M; n=10

Table 7. Effect of GCC on Hematological parameters at 90th day

Parameter	Group I	Group II	Group III	Group IV
Hb (g/dl)	11.21±0.381	11.96±0.327	11.92±0.207	11.73±0.329
PCV (%)	31.48±1.055	33.92±0.945	33.72±0.504	33.12±0.863
RBC (m/µl)	5.955±0.210	6.286±0.218	6.405±0.114	6.248±0.178
WBC (/cmm)	9620±881.2	8605±685.8	8118±591.2	15606±4731
Platelets (L / µL)	7.791±0.281	8.481±0.287	8.700±0.198	8.549±0.340
Neutrophils (/cmm)	26.20±1.167	42.25±18.75	21.76±0.779	26.50±1.049
Lymphocytes (/cmm)	69.4±1.148	70.35±1.487	73.94±0.829	69.83±1.055
Monocytes (/cmm)	2.550±0.245	3.400±0.515	2.353±0.331	4.167±1.681
Eosinophils (/cmm)	1.850±0.150	2.100±0.160	1.941±0.159+	1.313±0.150

All values were expressed as Mean ± S.E.M; n=10

Table 8. Effect of GCC on Hematological parameters at 120th day

Parameter	Group I	Group II	Group III	Group IV
Hb (g/dl)	10.42±0.494	11.03±0.209	10.84±0.527	10.06±0.395
PCV (%)	28.80±1.357	31.27±0.322	30.31±1.412	28.65±1.057
RBC (m/µl)	5.591±0.296	5.851±0.156	5.825±0.318	5.450±0.240
WBC (/cmm)	7313±841.6	8800±801.9	7500±847.7	8163±731.4
Platelets (L / µL)	7.274±0.447	8.179±0.203	7.575±0.436	7.149±0.367
Neutrophils (/cmm)	23.75±1.556	24.40±1.157	22.50±0.823	23.63±1.569
Lymphocytes (/cmm)	69.00±1.822	68.80±1.519	72.50±1.052	69.88±1.608
Monocytes (/cmm)	5.500±0.566	5.100±0.622	3.375±0.532	4.500±0.731

Eosinophils (/cmm)	1.750±0.250	1.700±0.213	1.625±0.183	2.00±0.267

All values were expressed as Mean ± S.E.M; n=10

Biochemical parameters:

Table 9. Effect of GCC on serum biochemistry (30th day):

Group	Glucose (mg/dl)	Urea (mg/dl)	Creatinine (mg/dl)	T. Cholesterol (mg/dl)	Triglyceride (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	T. bilirubin (mg/dl)	SGOT (U/L)	SGPT (U/L)	ALP (U/L)	T. proteins (g/dl)	Calcium (mg/dl)
G-I	83.28 ±5.428	30.50 ±1.279	0.43± 0.018	79.17± 3.853	103.1 ±6.027	25±1.281	32.22 ±3.916	0.127 ±0.010	227.6 ±14.14	54.61 ±1.942	167.2± 12.06	6.889 ±0.094	8.367 ±0.090
G-II	87.83 ±5.227	28.72 ±1.218	0.43± 0.016	71.76± 2.838	85.29 ±5.629	23.88 ±0.973	32.29 ±2.721	0.138 ±0.011	214.6 ±11.29	51.35 ±3.587	194.8± 14.46	6.876 ±0.115	8.341 ±0.078
G-III	98.63 ±4.204	27.95 ±1.225	0.38± 0.024	72.37± 3.424	95.37 ±4.179	23.63 ±0.799	30.84 ±3.22	0.121 ±0.009	183.9 ±5.414*	53.05 ±1.486	205.4± 15.54	6.868 ±0.118	8.374 ±0.095
G-IV	87.28 ±5.195	26.11 ±1. 242	0.42± 0.018	66.89± 2.175*	87.53 ±4.559	23.68 ±0.787	28.32 ±3.027	0.131 ±0.010	175.5 ±7.605*	50.05 ±2.085	197.7± 12..41	6.879 ±0.102	8.379 ±0.095

All values were expressed as Mean ± S.E.M; n=10

* indicates $p<0.05$ when compared to vehicle control

Table 10. Effect of GCC on serum biochemistry (60th day):

Group	Glucose (mg/dl)	Urea (mg/dl)	Creatinine (mg/dl)	T. Cholesterol (mg/dl)	Triglyceride (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	T. bilirubin (mg/dl)	SGOT (U/L)	SGPT (U/L)	ALP (U/L)	T. proteins (g/dl)	Calcium (mg/dl)
G-I	109.4±3.363	32.68±1.475	0.494±0.022	75.32±3.355	103.6±5.771	25.26±1.037	29.16±3.137	0.105±0.005	191.7±6.776	63.26±2.343	225.6±10.81	7.437±0.088	9.579±0.098
G-II	96.43±3.310	32.05±1.22	0.476±0.01	68.33±2.69	100.1±4.29	22.76±1.29	25.52±2.02	0.110±0.01	221.7±13.0	66±3.101	242.8±13.5	7.310±0.26	9.550±0.
		4	5	2	0	6	0	0	6		7	3	089
G-III	101.3±3.314	34.44±1.659	0.455±0.023	67±3.166	91±4.771	22.33±1.079	26.44±2.923	0.105±0.005	193.8±7.912	57.11±1.615	246.7±10.80	7.050±0.171	9.456±0.130
G-IV	93.68±3.295	32.16±1.195	0.421±0.021	61.16±1.653	85.37±4.694	21.11±0.888	24.74±1.731	0.100±0.00	177.5±6.845	57.74±2.761	234.2±21.12	7.121±0.075	9.500±0.080

All values were expressed as Mean ± S.E.M; n=10

Table 11. Effect of GCC on serum biochemistry (90th day):

Group	Glucose (mg/dl)	Urea (mg/dl)	Creatinine (mg/dl)	T. Cholesterol (mg/dl)	Triglyceride (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	T. bilirubin (mg/dl)	SGOT (U/L)	SGPT (U/L)	ALP (U/L)	T. proteins (g/dl)	Calcium (mg/dl)
G-I	99±3.432	29.58±1.143	0.463±0.015	73±3.196	93.89±6.431	28.84±1.700	26.42±3.650	0.115±0.008	172±8.520	324.3±268.1	156.4±10.10	7.521±0.063	9.395±0.144
G-II	95.25±3.298	27±0.746	0.450±0.011	66.75±3.109	73.3±3.608	26.30±1.517	25.40±3.326	0.120±0.009	182.9±6.311	51.85±1.555	154.2±9.356	7.315±0.111	8.870±0.398
G-III	91.06±6.025	28.71±1.107	0.438±0.014	65.65±2.767	84.82±9.785	27.18±1.809	23.53±3.429	0.118±0.010	173.3±8.021	52.19±2.019	171±11.73	7.281±0.103	8.982±0.644
G-IV	100.6±11.09	32.16±2.410	0.447±0.011	61.79±2.102	76.72±4.796	26.47±1.974	20.32±2.143	0.126±0.010	182±6.749	54.11±2.338	182.5±14.80	7.368±0.076	9.500±0.088

All values were expressed as Mean ± S.E.M; n=10

Table 12. Effect of GCC on serum biochemistry (120th day):

Group	Glucose (mg/dl)	Urea (mg/dl)	Creatinine (mg/dl)	T. Cholesterol (mg/dl)	Triglyceride (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	T. bilirubin (mg/dl)	SGOT (U/L)	SGPT (U/L)	ALP (U/L)	T.	Calcium (mg/dl)
G-I	97.67±5.180	29.89±1.620	0.422±0.014	74.56±3.571	93.22±10.44	25.78±1.164	30±4.327	0.144±0.017	186.6±7.680	5311±3.195	189.8±19.46	6.456±0.766	8.856±0.146
G-II	113.1±9.390	29.3±1.5	0.480±0.02	76±2.996	105.7±9.43	27±1.011	27.5±3.468	0.100±0.00	206.7±13.3	56.7±1.535	227.3±40.6	7.390±0.13	9.040±0.

		64	4		2				2		5	2	164
G-III	103.1±17.26	26±1.464	0.428±0.018	75.29±5.846	89.14±17.62	26.43±1.494	31.29±7.470	0.100±0.00	193.9±15.98	52.57±2.359	215.7±40.65	7±0.189	8.686±0.112
G-IV	105.9±8.138	29±0.963	0.487±0.012	68±3.273	95.38±7.732	22.5±0.944	23.25±3.416	0.112±0.012	188.8±8.502	57.113±2.216	259.4±50.98	7.363±0.106	8.912±0.208

All values were expressed as Mean ± S.E.M; n=10

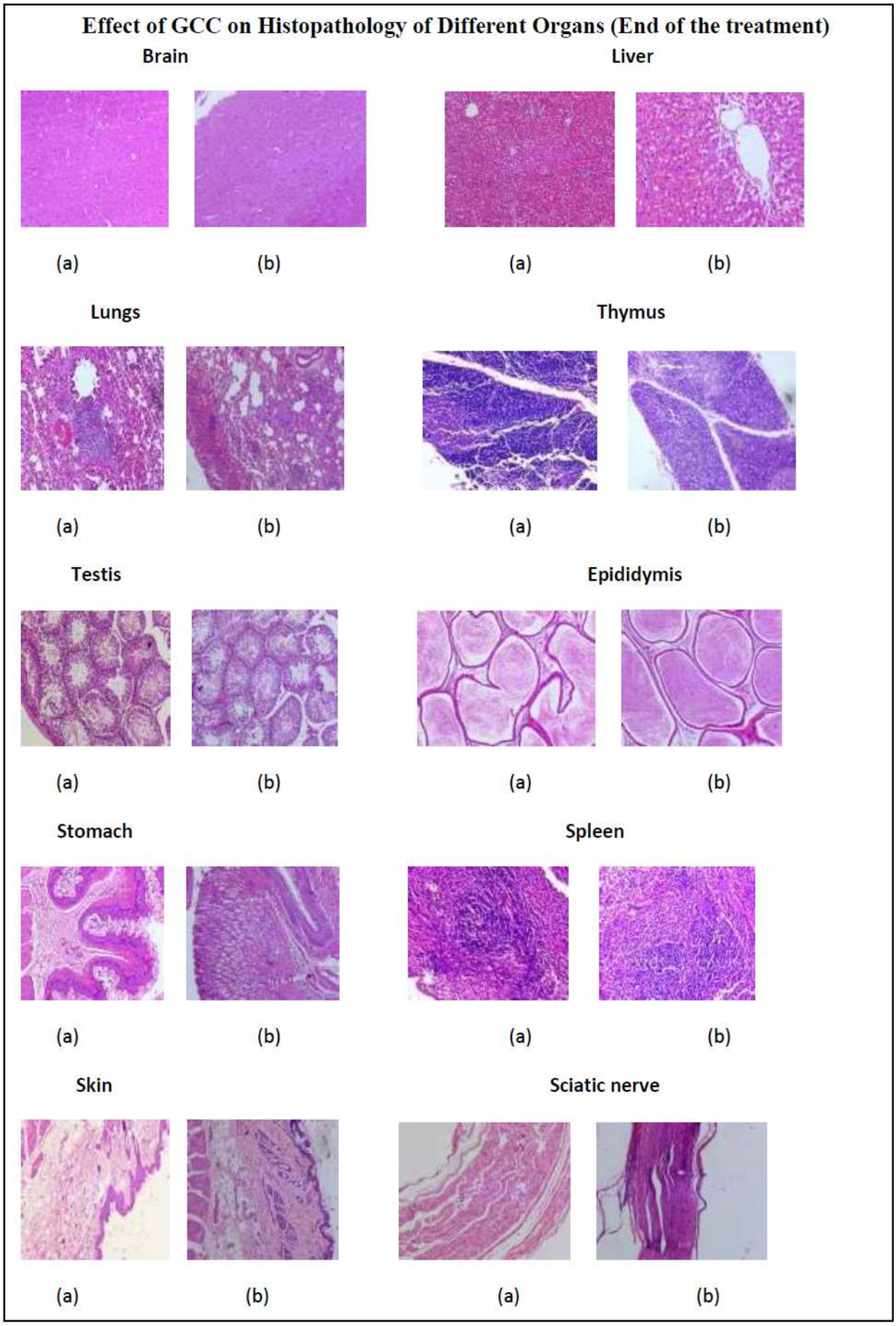
Macroscopic Observations:

Table13. Effect of GCC on Macroscopic Observations

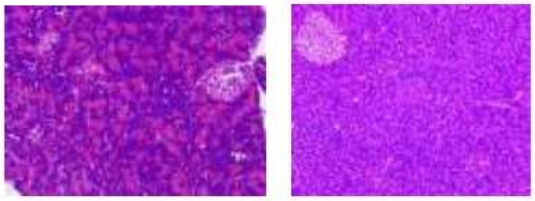
S. No	**Group**	**Total No. of Animals**	**Macroscopic Findings**	
			Terminal sacrifice	**Post recovery sacrifice**
1	**G-I**	**20**	**NAO**	A cyst in left kidney (animal No.GCC50; male). Presence of black pores, pale colored liver and kidneys (animal No.GCC58; female).
2	**G-II**	**20**	Cystic ovary (animal No.GCC18;female)	Presence of black pores, pale colored liver and kidneys (animal No. GCC55; male).
3	**G-III**	**20**	Nodules at the base of the pancreas (animal No.GCC22; male)	Cyst in left kidney (animal No.GCC54; male).
4	**G-IV**	**20**	**NAO**	**NAO**

NAO= No Abnormality Observed

Figure 1. Effect of GCC on histopathology of rat organs (at end of the treatment)

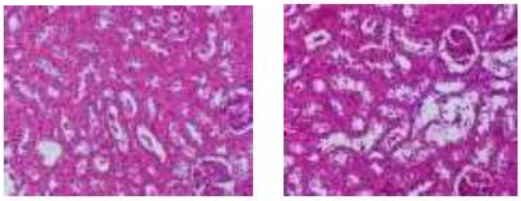


Pancreas



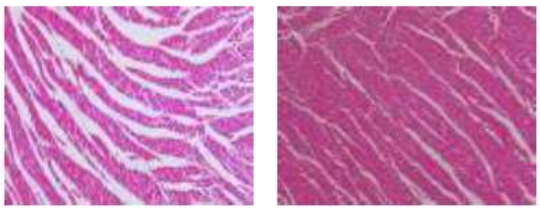
(a) (b)

Kidney



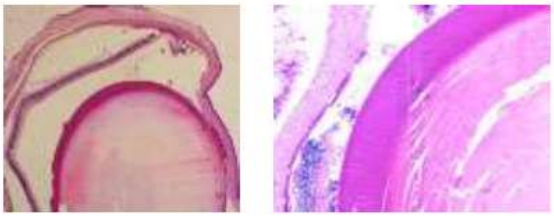
(a) (b)

Heart



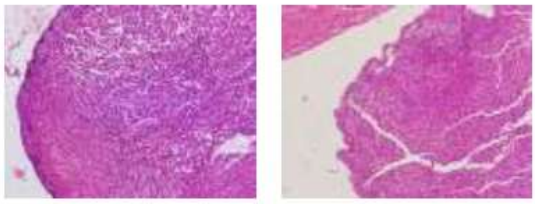
(a) (b)

Eye



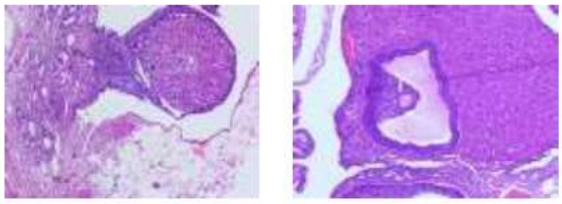
(a) (b)

Adrenal gland



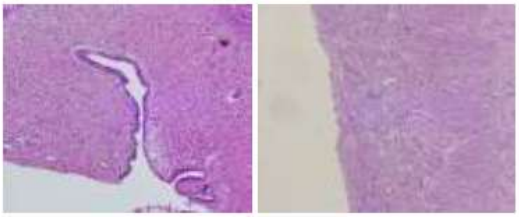
(a) (b)

Ovary



(a) (b)

Uterus



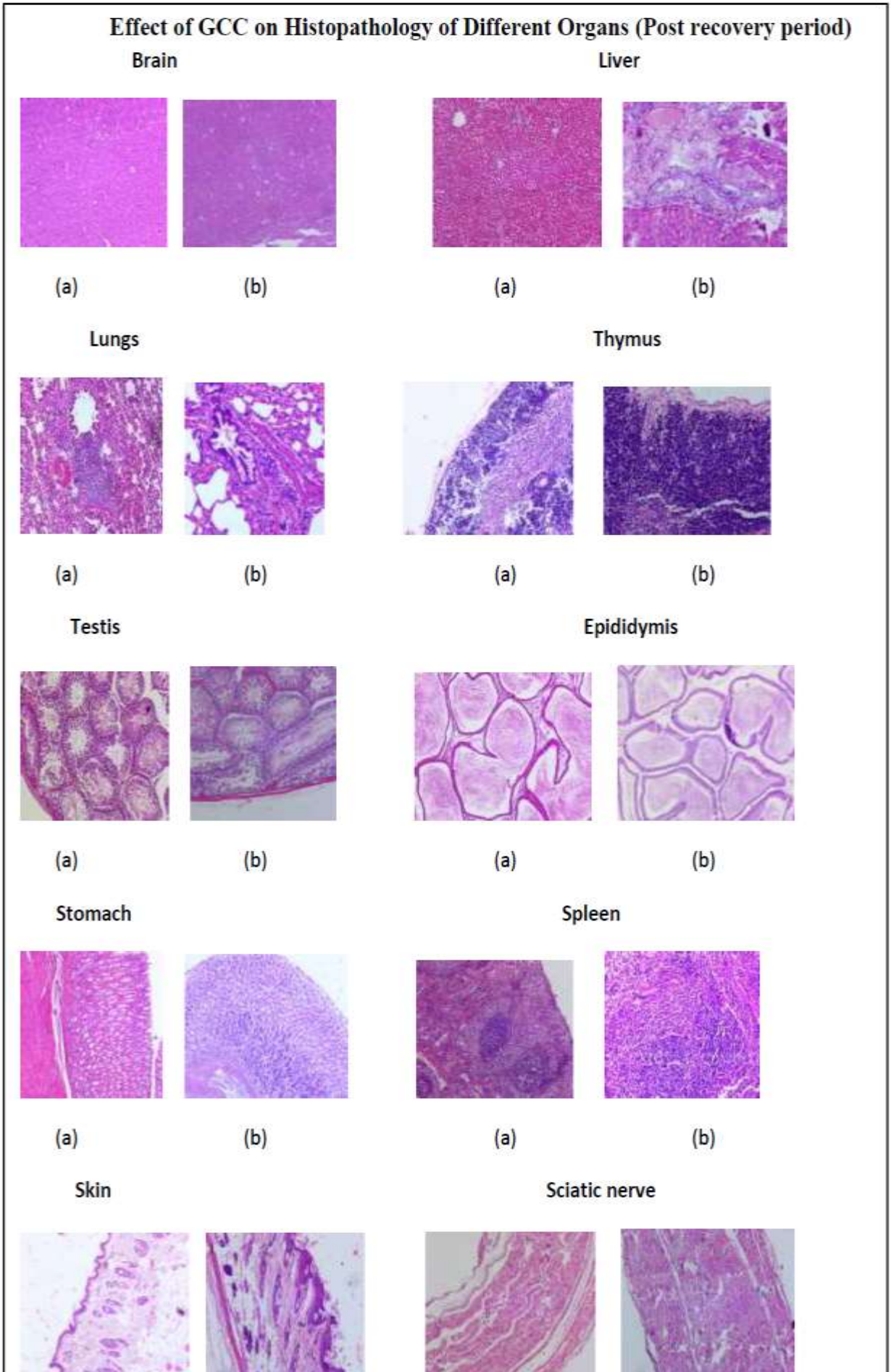
(a) (b)

Microscope magnification: 10X

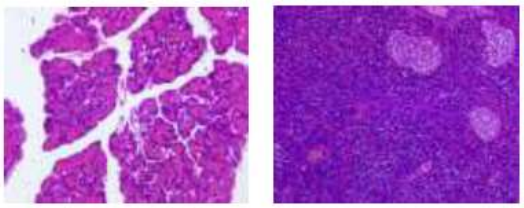
(a)- denotes organs of the normal control animals

(b)- denotes organs of the animals treated with high dose of *Gowri chinthamani chenduram*

Figure 2. Effect of GCC on histopathology of rat organs (Post recovery period)

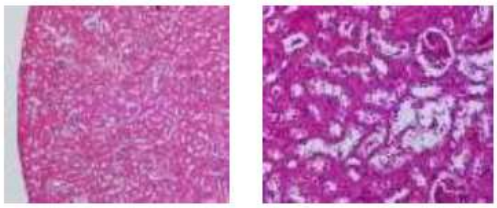


Pancreas



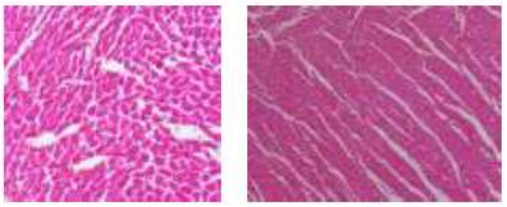
(a) (b)

Kidney



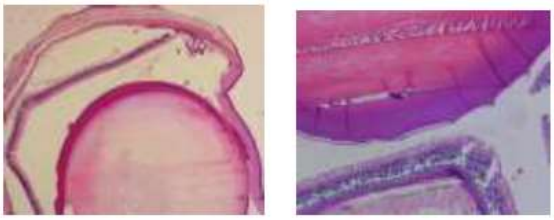
(a) (b)

Heart



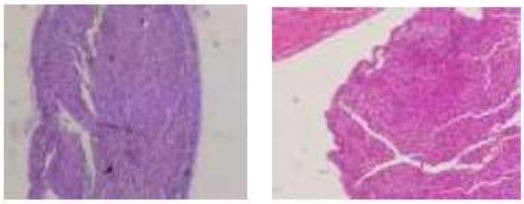
(a) (b)

Eye



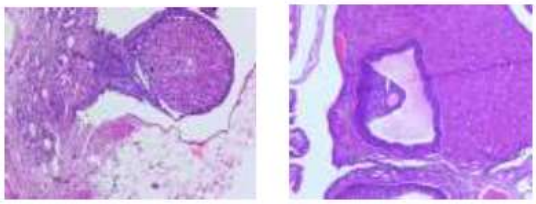
(a) (b)

Adrenal gland



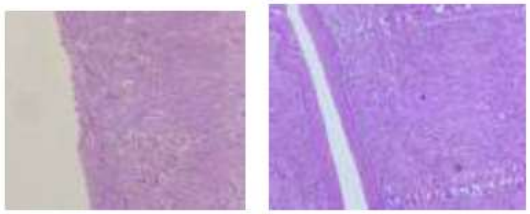
(a) (b)

Ovary



(a) (b)

Uterus



(a) (b)

Microscope magnification: 10X

(a)- denotes organs of the normal control animals

(b)- denotes organs of the animals treated with high dose of ***Gowri chinthamani chenduram***

ACKNOWLEDGEMENT

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CONCLUSION:

Under the conditions of the present study, daily oral administration of *Gowri chinthamani chenduram* at doses of up to 400 mg/kg/day was well tolerated in rats. The no-observed-adverse-effect-level (NOAEL) of *Gowri chinthamani chenduram* in rats is >400 mg/kg/day when administered orally for 13 consecutive weeks (90 days).

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