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ACUTE AND SUB ACUTE TOXICITY STUDY ON SIDDHA DRUG *CUṆṬIYĀTI CŪRAṆAM*

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Abstract
*The bronchial Asthma is the most common disease in India, because our country have more industrial area . It is the most common in allergic disease of human beings leading to more complication. The present study was investigated the acute sub-acute toxicity study of **cuṇṭiyāti cūraṇam** for the management of **CUVĀCA KĀCAM** (Bronchial Asthma), following OECD guidelines 423 and 407 method 28 days repeated oral toxicity studies were done on both sex of Wister albino rats.In acute and sub-acute toxicity studies no toxic effects were observed upto the dose level of 2000 mg/kg body weight and carried in five different groups in CC was administrated and dose ranging from 5, 50, 300, 1000, 2000 mg/kg for rat respectively. No mortality effect was observed up to 2000 mg/kg of body weight in acute and sub-acute toxicity study.*
Keywords: *cuṇṭiyāti cūraṇam, acute toxicity, sub-acute toxicity.*

Introduction

Bronchial Asthma is a very common disease in the society due to increasing exposure to air pollution and western life style often starts in childhood. It is a disease characterized by recurrent attacks of breathlessness and wheezing, which vary in severity and frequency from person to person. In an individual it may occur from hour and day to day. Bronchial asthma common in both sex but more prevalent among males, while during adolescence and adulthood, it affect girls and women more. Bronchial Asthma has been seen as one of the leading cause of morbidity and mortality in rural India (Smith 2000). Worldwide, deaths from this condition have reached over 180,000 were affected annually and it is estimated to add 100 million more asthmatic patients by the year 2025.

Aim

To evaluate the safety profile for Acute and sub-acute toxicity study of **cuṇṭiyāti cūraṇam** in **CUVĀCA KĀCAM** (Bronchial Asthma).

Materials and Methods

Preparation of the cuṇṭiyāti cūraṇam:

6 Parts of Chukku, 4 Parts of Milagu, 5 Parts of Thippili, 3 Parts of Adhimadhuram, 2 Parts of Lavangapattai, 1 Parts of Elakkai, (Equal Part of Sarkkarai were cleaned dried powdered and mixed well.

Result and Discussion

Toxicity Studies of CC:

Effect of Acute Toxicity Study (14 Days) of CC

Table no –1 Physical and behavioural examinations

Group no.	Dose(mg/kg)	Observation sign	No. of animal affected.
Group-I	5mg/kg	Normal	0 of 3
Group- II	50mg/kg	Normal	0 of 3
Group-III	300mg/kg	Normal	0 of 3
Group-IV	1000mg/kg	Normal	0 of 3
Group-V	2000mg/kg	Normal	0 of 3

Statistical significance (p) calculated by one way ANOVA followed by Dennett's (n=6); $^{ns}p>0.05$, *p<0.05, **p<0.01, ***p<0.001, calculated by comparing treated groups with control group

Data obtained in this study indicated $^{ns}p>0.05$ no significance physical and behavioural signs of any toxicity due to administration of *CC* at the doses of 5mg/kg, 50mg/kg , 300mg/kg, 1000mg/kg and 2000mg/kg to rats.

Table no-2 Home cage activity

Functional and Behavioural observation	Observation	5mg/kg Group (G-I)	50mg/kg (G-II)	300mg/kg (G-III)	1000mg/kg (G-IV)	2000mg/kg (G-V)
		Female n=3	Female n=3	Female n=3	Female n=3	Female n=3
Body position	Normal	3	3	3	3	3
Respiration	Normal	3	3	3	3	3
Clonic involuntary Movement	Normal	3	3	3	3	3
Tonic involuntary Movement	Normal	3	3	3	3	3
Palpebral closure	Normal	3	3	3	3	3
Approach response	Normal	3	3	3	3	3
Touch response	Normal	3	3	3	3	3
Pinna reflex	Normal	3	3	3	3	3
Tail pinch response	Normal	3	3	3	3	3

Statistical significance (p) calculated by one way ANOVA followed by Dennett's (n=6); $^{ns}p>0.05$, *p<0.05, **p<0.01, ***p<0.001, calculated by comparing treated groups with control group

Data obtained in this study indicated $^{ns}p>0.05$ 05 no significance changes in Home cage activity, signs of any toxicity due to administration of *CC* at the doses of 5mg/kg, 50mg/kg , 300mg/kg, 1000mg/kg and 2000mg/kg to rats.

Table no-3 Hand held observation

Functional and Behavioral observation	Observation	Control	5 mg/ kg (G-I)	50 mg/kg (G-II)	300mg/kg (G-III)	1000mg/kg (G-IV)	2000mg/kg (G-V)
		Female n=3	Female n=3	Female n=3	Female n=3	Female n=3	Female n=3
Reactivity	Normal	3	3	3	3	3	3
Handling	Normal	3	3	3	3	3	3
Palpebral closure	Normal	3	3	3	3	3	3
Lacrimation	Normal	3	3	3	3	3	3
Salivation	Normal	3	3	3	3	3	3
Piloerection	Normal	3	3	3	3	3	3
Pupillary reflex	Normal	3	3	3	3	3	3
Abdominal tone	Normal	3	3	3	3	3	3
Limb tone	Normal	3	3	3	3	3	3

Statistical significance (p) calculated by one way ANOVA followed by Dennett's (n=6); $^{ns}p>0.05$, *p<0.05, **p<0.01, ***p<0.001, calculated by comparing treated groups with control group

Data obtained in this study indicated $^{ns}p>0.05$ no significance changes in hand held observation and signs of any toxicity due to administration of *CC* at the doses of 5mg/kg, 50mg/kg , 300mg/kg, 1000mg/kg and 2000mg/kg to rats.

Table no-4 Mortality

Group no	Dose no(mg/kg)	Mortality
Group-I	5(mg/kg)	0 of 3
Group-II	50(mg/kg)	0 of 3
Group-III	300(mg/kg)	0 of 3
Group-IV	1000(mg/kg)	0 of 3
Group-V	2000(mg/kg)	0 of 3

Statistical significance (p) calculated by one way ANOVA followed by Dennett's (n=6); nsp>0.05, *p<0.05, **p<0.01, ***p<0.001, calculated by comparing treated groups with control group. From acute toxicity study it was observed $^{ns}p>0.05$ that the administration of *CC* at a dose of 2000 mg/kg to the rats do not produce drug-related toxicity and mortality. So No-Observed-Adverse-Effect- Level (NOAEL) at *CC* is 2000 mg/kg.

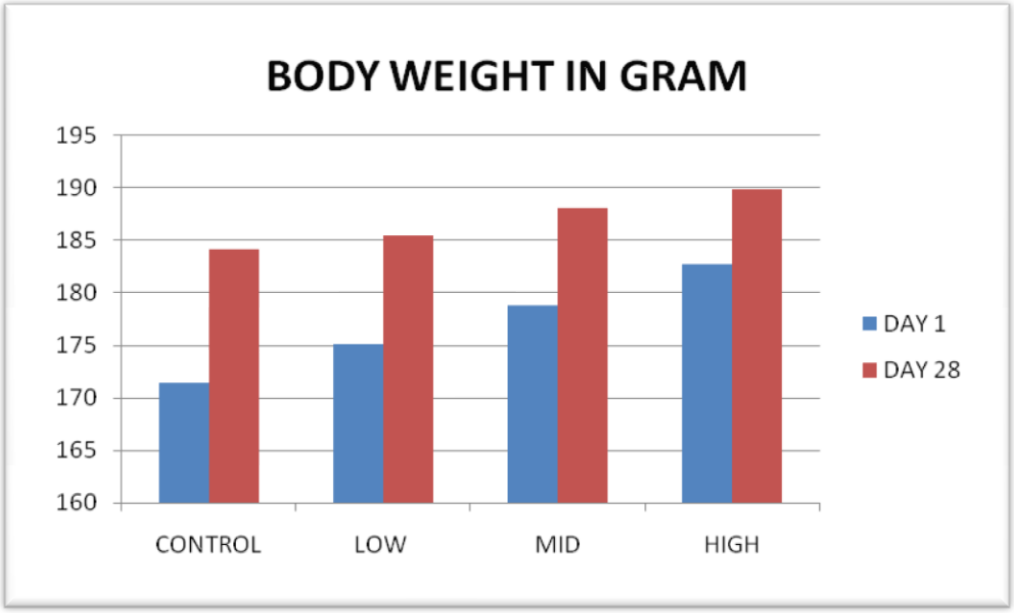
Sub-Acute Toxicity Study in Wistar Rats to Evaluate Toxicity Profile of *CC*

Table no-5 Body Weight in Gram

GROUP	CONTROL	LOW	MID	HIGH
1st day	**171.37±0.80**	**175.15±0.80**	**178.80±0.80**	**182.75±0.84**
7th day	**174.13±0.72**	**178.21±0.73**	**181.29±0.82**	**184.75±0.84**
14th day	**177.11±0.69**	**179.17±0.80**	**184.98±0.84**	**186.81±0.76**
21st day	**180.03±0.76**	**183.09±0.707**	**187.42±0.83**	**188.95±0.71**
28th day	**184.15±0.77***	**185.46±0.70***	**188.05±0.74***	**189.86±0.75***

Values are expressed as mean ± SEM Statistical significance (p) calculated by one way ANOVA followed by Dennett's (n=6); nsp>0.05, *p<0.05, **p<0.01, ***p<0.001, calculated by comparing treated groups with control group.

Figure No: 1 Body Weight in Gram



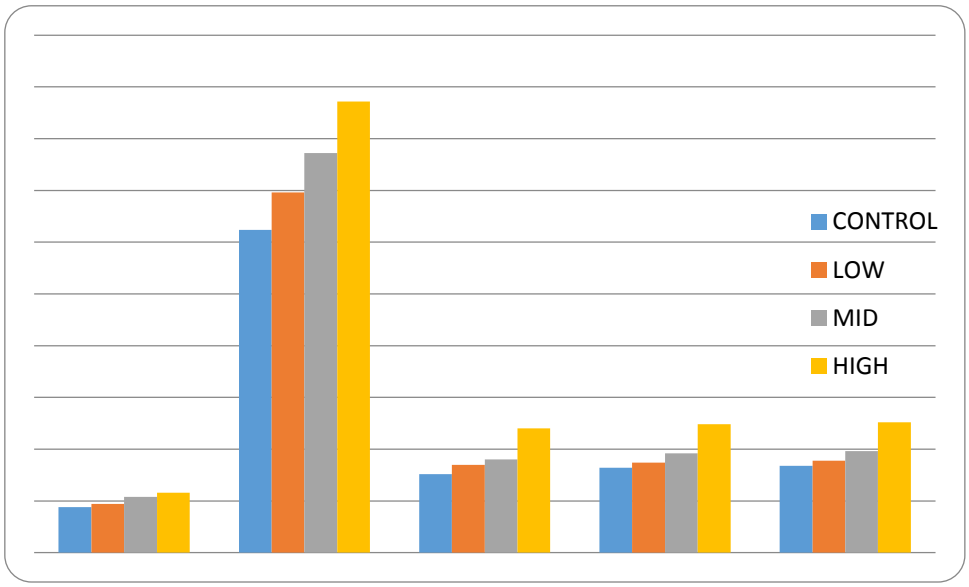
The effect of CC was observed, on the body weight changes, significant increase (*p<0.05) in body weight in all the treated animals were observed. The values are expressed as mean ± S.E.M. n=6. The results of group I were compared with other groups such as II, III, IV.

Table no-6 Effect of Sub acute Dose (28 Days) *CC on* Organ Weight (Physical Parameter) in Gram

GROUP		CONTROL	LOW	MID	HIGH
HEART		0.44±0.02	0.47±**0.03**	0.54±**0.06**	0.58±**0.08**
LIVER		3.12±**0.03**	3.48±**0.06**	3.86±**0.08**	4.36±**0.07**
LUNGS		0.76±**0.06**	0.85±**0.02**	0.90±**0.06**	1.20±**0.08**
KIDNEY	L	0.82±**0.07**	0.87±**0.07**	0.96±**0.07**	1.24±**0.07**
	R	0.84±**0.04**	0.89±**0.04**	0.98±**0.044**	1.26±**0.044**

Values are expressed as mean ± SEM Statistical significance (p) calculated by one way ANOVA followed by Dennett's (n=6); ^{ns}p>0.05, *p<0.05, **p<0.01, ***p<0.001, calculated by comparing treated groups with control group.

Figure No: 2 Organ Weight (Physical Parameter) in Gram



The effects of CC on kidney, heart, liver and lung so the rats were recorded. Not significant p>0.05 changes in the weights of various organs of the animals occurred with higher doses of the extract but macroscopic examinations visualized no changes in colour of the organs of the treated animals compared with the control group.

Effect of Sub- Acute Dose (28 Days) of *CC on* Haematological Parameters

Table no-7

Drug treatment	RBC 10^{12}/litre	WBC 10^{9}/litre	Haemoglobin /litre	Differential count %			
				Neutrophils	Eosinophil's	Monocyte	Lymphocyte
Control	5.02±0.08	5.99±3.54	12.55±0.03	58.54±0.08	1.62±0.04	3.16±0.06	38.16±0.03
LOW	5.16±0.03	6.57±3.64	12.78±0.08	59.86±0.46	1.65±0.05	5.37±0.08	35.67±0.08
MID	5.26±0.05	6.54±3.87	12.94±0.05	60.43±0.25	1.68±0.08	5.48±0.07	34.34±0.07
HIGH	5.31±0.08	7.20±3.04	13.58±0.08	57.75±0.87	1.70±0.07	6.54±0.08	36.16±0.04

Values are expressed as mean ± SEM Statistical significance (p) calculated by one way ANOVA followed by Dennett's (n=6); ^{ns}p>0.05, *p<0.05, **p<0.01, ***p<0.001, calculated by comparing treated groups with control group.

Figure No: 3 Haematological Parameters

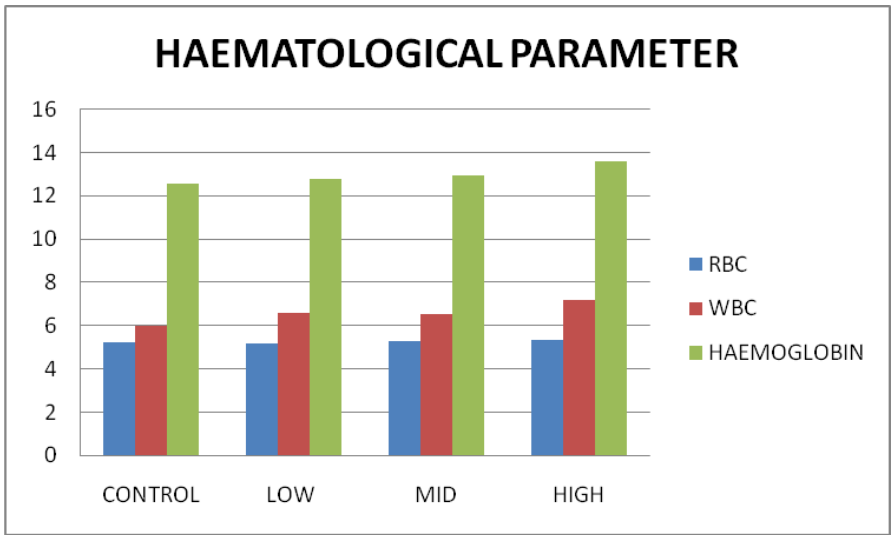


Figure No: 4 Haematological Parameters

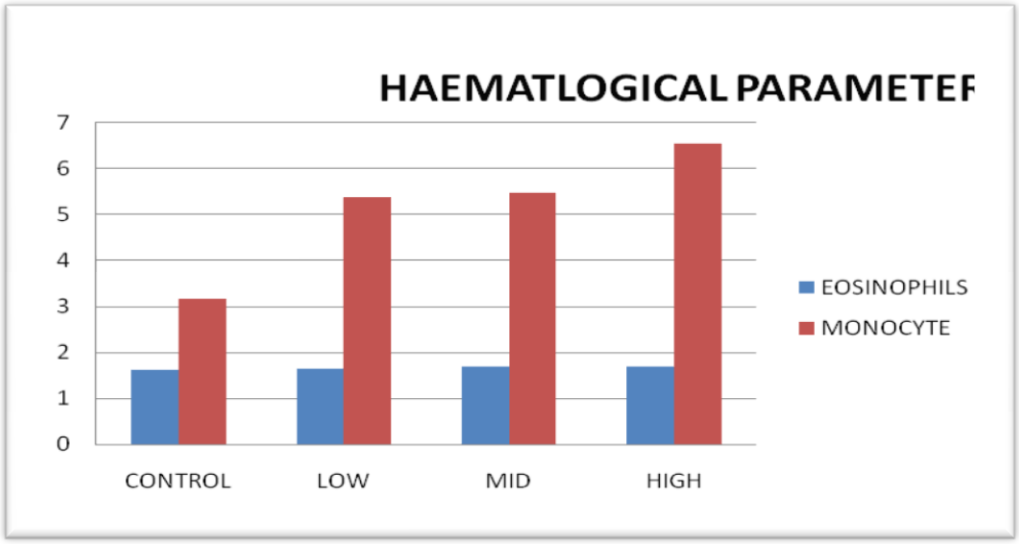
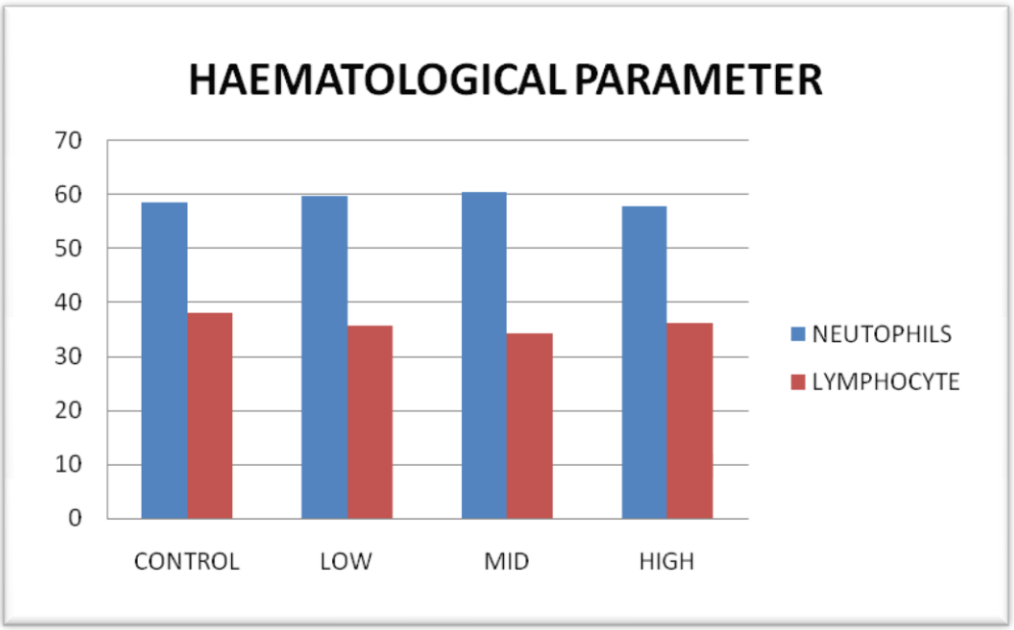


Figure No: 5 Haematological Parameters



The effects of **CC** were observed for its effect on haematological parameters in experimental rat. Final study, not significant ($p<0.05$) in the values of treated groups. The values are expressed as mean ± S.E.M. n=6. The results of group I were compared with other groups such as II, III, IV.

Table no-8 Effect of Sub- Acute Dose (28 Days) of *CC* on Biochemical Parameters

Drug treatment	SGPT (U/L)	SGOT (U/L)	ALP(U/L)	Urea (mg/dl)	Creatinine (mg/dl)
Control	**26.44±0.06**	**48.68±0.06**	**122.56±0.08**	**30.66±0.07**	**0.93±0.07**
Low	**28.69±0.27**	**52.78±0.08**	**130.76±0.06**	**34.45±0.04**	**0.96±0.08**
Mid	**30.28±0.58**	**56.34±0.86**	**137.98±0.54**	**37.55±0.76**	**0.98±0.07**
High	**32.16±0.76***	**62.56±0.77***	**143.23±0.76***	**40.23±0.23***	**1.04±0.08***

Values are expressed as mean ± SEM Statistical significance (p) calculated by one way ANOVA followed by Dennett's (n=6); $^{ns}p>0.05$, *$p<0.05$, **$p<0.01$, ***$p<0.001$, calculated by comparing treated groups with control group.

GROUP	CONTROL	LOW	MID	HIGH
TOTAL BILIRUBIN (mg/dl)	**0.35±0.06**	0.38±**0.07**	0.42±**0.07**	0.45±**0.08**

Values are expressed as mean ± SEM Statistical significance (p) calculated by one way ANOVA followed by Dennett's (n=6); $^{ns}p>0.05$, *$p<0.05$, **$p<0.01$, ***$p<0.001$, calculated by comparing treated groups with control group.

Figure No: 6 Biochemical Parameters

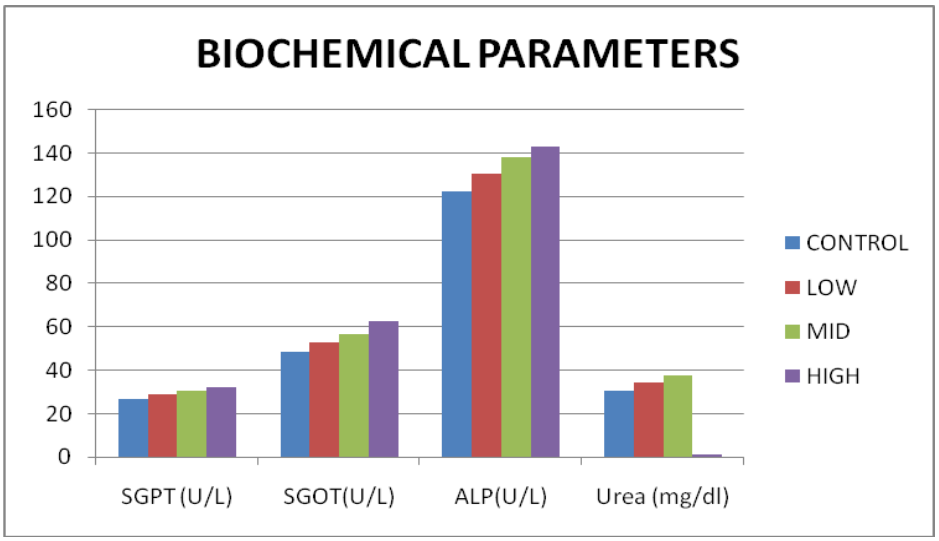
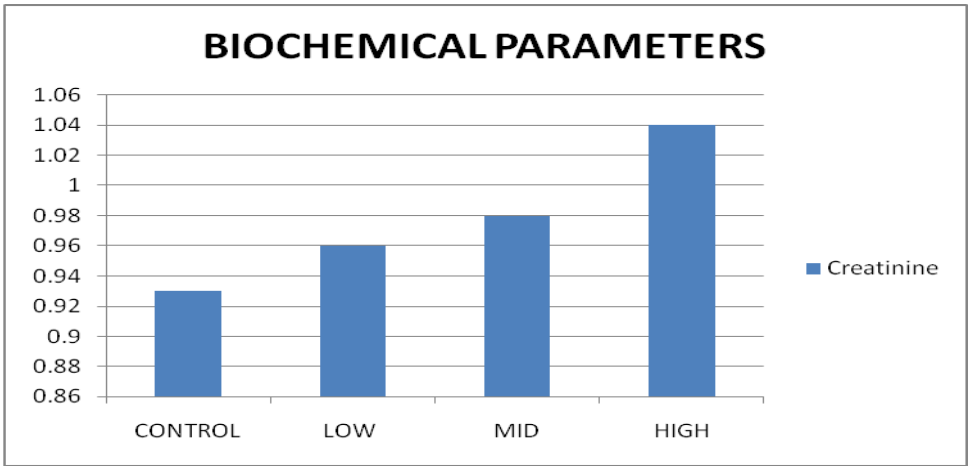
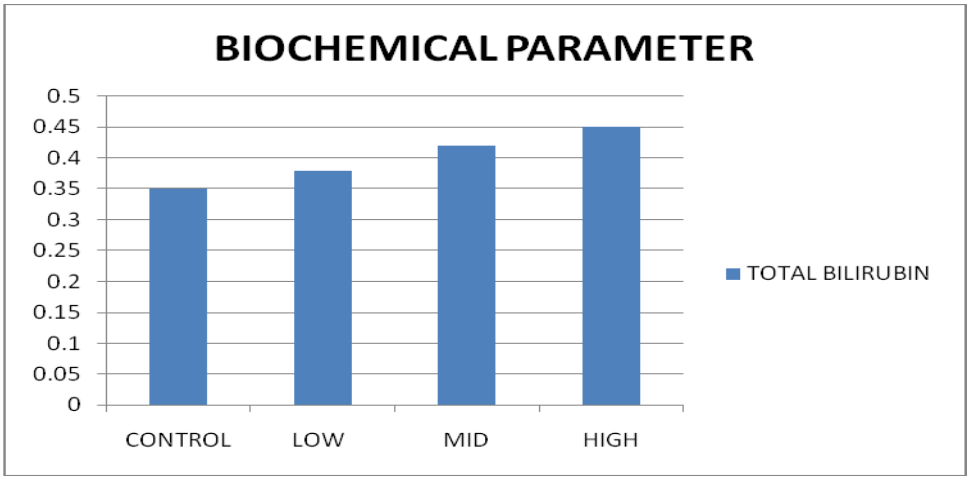


Figure No: 7 Biochemical Parameters



The SGPT, SGOT, ALP, UREA and Creatinine values was compared in Group I and other groups II, III, and IV. The biochemical Parameters in experimental rat is Not significant ($p<0.05$) in The SGPT, SGOT, ALP, urea and Creatinine values. The values are expressed as mean ± S.E.M. n=6.

Figure No: 8 Biochemical Parameters



The Bilirubin values in experimental rat. Final study, not significant ($p<0.05$) in the bilirubin values are. The values are expressed as mean ± S.E.M. n=6 were compared in Group I and other groups II, III, IV, and V.

Table no-9 Effect of Sub- Acute Dose (28 Days) on Food Intake in Gram

GROUP	CONTROL	LOW	MID	HIGH
1st DAY	10.32±**0.07**	11.45±**0.07**	11.56±**0.08**	10.34±**0.07**
7th DAY	11.34±**0.07**	12.45±**0.07**	12.65±**0.07**	11.78±**0.08**
14th DAY	12.54±**0.06**	12.78±**0.08***	13.67±**0.08***	12.89±**0.08***
21st DAY	13.23±0.07	13.57±0.07**	13.98±0.071**	13.97±0.06**
28th DAY	13.55±0.08***	14.23±0.06***	14.36±0.05***	14.45±0.06***

Values are expressed as mean ± SEM Statistical significance (p) calculated by one way ANOVA followed by Dennett's (n=6); $^{ns}p>0.05$, *p<0.05, **p<0.01, ***p<0.001, calculated by comparing treated groups with control group.

The Food intake values were compared in Group I to other groups II, III, IV, and V. in experimental rat. Final study, significantly increase in the Food intake values. The values are expressed as mean ± S.E.M. n=6.

Table no-10 Water Intake in ml

GROUP	CONTROL	LOW	MID	HIGH
1st DAY	12.40±0.04	12.20±0.07	13.66±0.06	13.87±0.08
7th DAY	13.59±0.06	13.67±0.07	14.87±0.04	14.21±0.08
14th DAY	14.40±0.07*	14.77±0.06*	15.34±0.08*	15.91±0.07*
21st DAY	15.69±0.05**	15.78±0.08**	16.23±0.07**	16.67±0.09**
28t9h DAY	16.15±0.08***	16.32±0.07***	16.58±0.06***	16.94±0.08***

Values are expressed as mean ± SEM Statistical significance (p) calculated by one way ANOVA followed by Dennett's (n=6); $^{ns}p>0.05$, *p<0.05, **p<0.01, ***p<0.001, calculated by comparing treated groups with control group.

Table no-11 On Electrolytes

GROUP	CONTROL	LOW	MID	HIGH
Sodium (mmol/L)	140.15±**0.04**	139.39±**0.06**	139.07±**0.07**	137.05±**0.07**
Chloride(mmol/L)	102.45±**0.07**	101.56±**0.04**	100.20±**0.08**	102.31±**0.06**
Potassium(mmol/L)	3.97±**0.02**	4.16±**0.08**	4.24±**0.06**	4.28±**0.08**

There were no significant changes in the Electrolyte level in all the treated animals compared to the control. The values are expressed as mean ± S.E.M. n=6. The results of group I were compared with other groups such as II, III, IV and V.

Discussion

All animals from control and all the treated dose groups survived throughout the dosing period of 28 days. The results for body weight determination of animals from control and different dose groups show comparable body weight gain throughout the dosing period of 28 days. During dosing period, the quantity of food and water consumed by animals also significantly increase. The results of haematological investigations conducted on day 29th day revealed no significant changes in the haematological values when compared with those of respective controls. This gave clear justification that bone marrow and spleen were not influenced by *CC*. The clinical biochemistry analysis was done to evaluate the possible alterations in hepatic and renal functions not influenced by the test drug. Results of Biochemical investigations conducted on days 29 and recorded in revealed the no significant changes in the values of different parameters studied when compared with those of respective controls; Urea, SGOT,SGPT, Bilirubin were within the limits. Group Mean Relative Organ Weights are recorded Comparison of organ weights of treated animals with respective control

animals on day 29 was found to be normal comparable with respective control group.

Conclusion

Acute and sub-acute toxicity were carried out in Wister albino rats according to OECD guidelines (423) this drug has no acute toxicity as there was no mortality seen. Sub-acute toxicity is carried by repeated dose of test drug for 28 days. Mortality, the functional observation, haematological and biochemical investigations were done. There were no significant changes in the biochemical and haematological profile. So the toxicological study of these test drug, CC wasthe safe to use for long time administration.

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