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Evaluation of Anti-Obesity Potential of Capparis Spinosa

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ABSTRACT
Ischemic heart disease, cancer, and stroke are the leading causes of death worldwide, in recent years. These diseases are related to the "epidemic of obesity," one of the major global health concerns. Due to high-calorie diet and sedentary lifestyle, obesity is highly prevalent. Obesity is a chronic disease in the same sense as hypertension and atherosclerosis. The etiology or cause of obesity is an imbalance between the energy ingested in food and the energy expended. The excess energy is stored in fat cells that enlarge and/or increase in number. Capparis spinosais an economical species in Caparidaceae family with high medicinalvalues and play a pivotal role in traditional health care system. Studies have revealed the presence of phenolics, alkaloids, flavonoids (kaempferol, rutin, quercetin), glucosinolates (glucobrassicin, glucoiberin, glucocapparin, sinigrin), antioxidants, carotenoids, terpenoids and essential oils in different parts of the Capparisspinosa. The aqueous extracts of aerial parts of Capparisspinosa for it shep at oprotective effect against the paracetamol and carbonte trachloride induced hepatotoxicity in rats. Study revealed that acute toxicity and free radicle scavenging activity. Two groups , each containing 3 animals were randomly selected for the treatment with hydroalcoholic and ethanol extractof *Capparisspinosa* leaves. Results showed that hydroalcoholic & ethanolic extract of *Capparisspinosa* leaves on high fat induced obesity was reduced

Keywords: anti-obesity, *Capparisspinosa* leaves, acute toxicity, Ischemic heart disease, rats.

Introduction

Ischemic heart disease, cancer, and stroke are the leading causes of death worldwide, in recent years. These diseases are related to the "epidemic of obesity," one of the major global health concerns. Due to high-calorie diet and sedentary lifestyle, obesity is highly prevalent [1]. Obesity generally is defined as excess body fat. The definition of excess, however, is not clear-cut. Adiposity is a continuous trait not marked by a clear division into normal and abnormal. Moreover, it is difficult to measure body fat directly. Consequently, obesity often is defined as excess body weight rather than as excess fat. In epidemiologic studies, body mass index (BMI) calculated as weight in kilograms divided by height in meters squared is used to express weight adjusted for height [2]. Obesity is a chronic disease in the same sense as hypertension and atherosclerosis. The etiology or cause of obesity is an imbalance between the energy ingested in food and the energy expended. The excess energy is stored in fat cells that enlarge and/or increase in number. It is this hyperplasia and hypertrophy of fat cells that is the pathological lesion of obesity. Enlarged fat cells produce the clinical problems associated with obesity either because of either the weight or mass of the extra fat or because of the increased secretion of free fatty acids and numerous peptides from enlarged fat cells.

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The consequence of these two mechanisms is other diseases, such as diabetes mellitus, gallbladder disease, osteoarthritis, heart disease, and some forms of cancer[3].Obesity is an increasingly prevalent health burden upon modern society. Most obese women are not infertile; however, obesity and its negative impact upon fecundity and fertility are well documented. Obese women are three times more likely to suffer infertility than women with a normal body mass index[4]. The adipose tissue plays an essential role in regulating energy homeostasis and can be classified into two types: brown adipose tissue (BAT) and white adipose tissue (WAT). WAT is further subcategorized into subcutaneous and visceral WAT. In general, excess accumulation of visceral WAT is associated with high incidence of metabolic disease, while subcutaneous WAT has been found to be beneficial for the maintenance of metabolic homeostasis. In contrast, the anatomical location of BAT is more specific around the neck and clavicle, containing multilocular small lipid droplets (LDs) and a large number of mitochondria. BAT possesses specialized thermoregulatory functions and its unique expression of uncoupling protein 1 (UCP1) is responsible for non-shivering thermogenesis. Thus, molecular mechanisms controlling brown adipocyte thermogenesis have been investigated as a potential therapeutic target to counteract obesity and metabolic diseases [5]. In 2019, an estimated 38.2 million children under the age of 5 years were overweight or obese. Once considered a high-income country problem, overweight and obesity are now on the rise in low- and middle-income countries, particularly in urban settings. In Africa, the number of overweight children under 5 has increased by nearly 24% percent since 2000. Almost half of the children under 5 who were overweight or obese in 2019 lived in Asia. The World Health Assembly welcomed the report of the Commission on Ending Childhood Obesity (2016) and its 6 recommendations to address the obesogenic environment and critical periods in the life course to tackle childhood obesity. The implementation plan to guide countries in taking action to implement the recommendations of the Commission was welcomed by the World Health Assembly in 2017 [6]. Overweight and obesity are estimated to cause approximately 320,000 deaths in 20 countries in Western Europe each year. Obesity mainly results from an imbalance between energy intake and expenditure [7]. Activation of constitutive androstane receptor (CAR), a xenobiotic-sensing nuclear receptor, has been shown to inhibit obesity [8]. Recently, awareness of the importance of the composition of gut microbiota has increased with the revelation that various diseases are associated with dysbiosis, that is, a microbial imbalance inside the body. Although the alteration of the gut microbiota by obesity is not clearly explained, dysbiosis and obesity might be correlated. When dysbiosis occurs with obesity, major species of gastrointestinal microbiota and their beneficial metabolites, such as short chain fatty acids (SCFAs), vitamin B12, and indole, are lost, and intestinal permeability and endotoxemia are increased, which induces inflammation and gluconeogenesis in the liver, decreases satiety in the brain, and increases triglyceride incorporation and inflammation in adipose tissues. In addition, increased gut permeability maintains low-grade inflammation, and such chronic inflammation induces obesity. Individual or multiple strains of probiotics have been actively studied to improve obesity [9].A new generation of DGAT1 inhibitors that have progressed into clinical development, with the leading compound LCQ-908 (Novartis AG) now in phase II clinical trials. This exciting progress has led researchers to anticipate that an understanding of the human pharmacology of DGAT1 inhibitors, as well as their potential as therapeutic agents for the treatment of diabetes and obesity [10].Capparisspinosais an economical species in Caparidaceae family with high medicinalvalues and play a pivotal role in traditional health care system [11,12]. Capparisspinosaisconsidered as a hybrid between Capparisorientalis and Capparissicula[13]. Capparisspinosa distributed geographically from Morocco to the black sea,Atlantic Coastof Canary

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Island, East of Caspian Sea, Crimea, Armenia, Iran, Europe, North Africa, WestAsia, Australia and Afganistan[14]. Several studies have revealed thepresence of phenolics, alkaloids, flavonoids (kaempferol, rutin, quercetin), glucosinolates(glucobrassicin, glucoiberin, glucocapparin, sinigrin), antioxidants, carotenoids, terpenoidsandessentialoilsindifferentpartsoftheCapparisspinosa. The leaves and stemofCapparisspinosaisrich in presence ofkaempferol 3-Rha-7-G, quercetin 3-Rut,quercetin7-Rut,quercetin3-G-7-Rhaw1 [15]. The different extracts of the arial parts of Capparisspinosa have found to contain reducingsugar, flavonoids, tanins,and alkaloids. Terpene, Quercetin3-O-rutinoside,quercetin3-O-glucoside, quercetin 3-O-glucoside-7-O-rhamnoside, Quercetin 3-O-(6‴ -a-L-rhamnosyl-6″-b-D-glucosyl)-b-D-glucoside. [15,16]. The flower buds of Capparisspinosa contains 5-Caffeoyl quinic acid, 1-Caffeoyl quinic acid,5-p-Coumaroylquinic acid,4-Feruloylquinic acid, Rutin, Quercetin3-O-glc, Kaempferol3-O-rutinoside,Methyl-quercetin-O-rutinoside,Kaempferol3-O-glucoside, acids, flavonols[17]. The Capparisspinosafruit have also been investigated many times to identify the present phyto constituents. The studies have shown that the fruit part is abundant in term of phenolics,flavonoids and carotenoids, and moreover racemic benzofuranone, tetrahydroquinoline acid,p-hydroxy benzoic acid, 5-(hydroxymethyl)furfural, bis(5-formylfurfural)ether, daucosterol,a-D-fructofuranosides methyl, uracil, stachydrine, Capparisine A, capparisine B, capparisineC, 2-(5-hydroxymethyl-2-formylpyrrol-1-yl) propionic acid lactone, N-(30-maleimidy1)-5-hydroxymethyl-2-pyrrole formaldehyde, Protocatechuic aldehyde, E-butenedioic acid, ethyl3,4-dihydroxybenzoate, syringic acid, protocatechuic acid, vanillic acid, succinic acid, 4-hydroxybenzoic acid, Cappariside, 5-hydroxymethylfurfural, 5-hydroxymethyl furoic acid, 2-furoic acid, Flazin, guanosine, capparine A, capparine B, 1-H-Indole-3-carboxaldehyde, 4-hydroxy-1H-indole-3-carboxaldehyde, chrysoeriol, apigenin, kaempferol, thevetiaflavone, 5-hydroxymethylfuraldehyde,vanillicacid,cinnamicacid(6S)-hydroxy-3-oxo-a-ionolglucoside,Corchoionoside C, prenylglucoside, indol-3-acetonitrile glycoside, capparillosideA, capparilloside B [18,19,20,21,22]. Seeds are rich in proteins,fibres andoils with high contents of sterols, tocopherols, linoleic and oleic acids [23].Capparisspinosa (caper) is being used in food and culinary as pickles(usingflowerbuds),asappetizer, flavoring agents to manage pungencytosauces, salads, in pastas and pizzas [24,25]. The aqueous extracts of aerial parts of Capparis spinosaforits hepato protectiveeffect against the paracetamol and carbonte trachloride induced hepatotoxicity inrats [26]. In another study, the significant loss of weight was observed in high fat diet fed rats, using aqueous fruit extract of Capparis spinosa [27]. Capparisspinosa decreases the systolic blood pressure by excreting various electrolytes and inhibiting angiotensin converting enzyme [28]. Inanother study different extracts of Capparisspinosa root ware analysed for antimicrobial activity. A significant inhibitory effect was observed against the Staphylococcus,Streptococcus, Salmonella, Shigella, Klebsiella, Bacillus, Candida, Aspergillus[29].

Acutetoxicitystudies:

Selection of animal species: Healthy young adult (8 to 12 weeks old), nonpregnent female rats(180-200gm)wereselectedfortheexperimentalpurpose. Housing and feeding conditions: Animal house was maintained at temperature range of 22ºC ±3ºC and relative humidity at 50-60%. The animals were acclimatized on 12 hours light, 12 hoursdark cycle. Conventional laboratory diets were usedfor feeding with water add libitum. Theacute toxicity study was performed in overnight fasted animals for dose calculation of collected extracts for further pharmacological studies.

Grouping of animals: Two groups,each containing 3 animals were randomly selected for the treatment with hydroalcoholic and ethanolextract of *Capparisspinosa* leaves.

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Preparation of Doses and Dosing: The hydroalcoholic and ethanol extract of *Capparisspinosa* leaves were suspended in normal saline. The animals were treated with various doses viz. 5, 50, 300 and 2000 mg/kg body weight orally with the help of intubation canula (*OECDguideline423,2001*).The animals were observed for behavioral and physiological responses continuously for first 4 h, then hourly for the next 24 hand then 6hourly for 48 hrs after administering the extracts.

Table 1. Animal group for determination of dose and acute toxicity

Animal Group	HACS (mg/ kg)	ECS (mg/ kg)	No.ofanimals ineachgroup
1	Normal Saline	Normal Saline	03
2	5	5	03
3	50	50	03
4	300	300	03
5	2000	2000	03

Evaluation ofAnti-obesity Activity:
The hydroalcoholic and ethanol extract of *Capparisspinosa* leaves was evaluated for their anti obesity effect according to the method described in animals using high fat diet induced obesity model in rats.

Selection of animal species: Healthy young adult (8 to 10 weeks old), male rats (200-250 gm)were selected for the experimental purpose.The animals were kept on regular observation forone weektofindoutanybehavioralandsocialdifference amongthe whole group.

Housingand feeding conditions:The animalswere kept in polypropylene cages, 6 in eachcage. Animal house was maintained at temperature range of 22ºC ± 3ºC and relative humidity at50-60%. The animals were acclimatized on 12 hours light, 12 hours dark cycle. Conventional laboratory diet was used for feeding with water add libitum. The rats were allowed to acclimatize to the experimentalroom conditions for a period of seven days.

Preparation of High Fat Diet:
The rat chow diet,which was purchased from local market of Guntur District AndhraPradesh, was grinded finely with home mixture. The mixture of vanaspati ghee and coconut oil (ratio 3:1)along with 25% fructose was prepared separately. The powdered chaw material and preparedmixture was then added (in 50: 50 ratios). This mixture was mixed thoroughly using distilledwater, in such a manner, that the small balls (semi dried pellets) of the feed material may beprepared. The prepared feed material was considered as high fat diet(HFD). Grouping of animals: Total 42 rats were selected for the study purpose. They were divided randomly into eleven groups,each containing 06.The grouping was done as mentioned in table

no. 2.

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Table 2. Animal group for evaluationof anti-obesity activity

Groups	Treatment(mg /Kg,BW)	No. ofanimals
Groups1	Receivedonlystandardpelletdiet(NormalControlGroup)	6
Groups2	Receivedonlypreparedhighfatdiet(PositiveControlGroup)	6
Groups3	Receivedpreparedhighfatdiet+HACS(400)	6
Groups4	Received preparedhighfatdiet+ECS(400)	6
Groups5	Receivedpreparedhighfatdiet+Orlistat(25)	6

Procedure:

Before commencing the experimental procedure, the weight, and waist circum ference of the individual animals of the respective groupw as measured. It was considered as day first values. The animals of respective groups were treated as mentioned in table no. 2. The changes inbody weight, and waist circumference of the animals was subsequently recorded on day 7^{th}, day14^{th},day21^{st}, day 28^{th} , day 35^{th} andd ay 42^{nd}. To investigate and established the anti-obesity effect of collected extracts, it is important to analyze various serum lipid profile in experimental rats on different days. Keeping in view the safety of experimental animals, the blood was collected on the day I andsubsequently at the interval of two weeks, i.e. on day14^{th}, day 28^{th} and day 42^{nd},from retro-orbital puncture, under light anesthesia, using anti coagulant (EDTA) coated glass capillaries.The collected blood samples were used for analysis of biochemical parameters (Serum lipid profile). All the groups were treated orally, using intubation tube daily at morning hours (10 to 11 AM).The extracts and standard drug (orlistat) were dissolved in normal saline and accordingly dosewas adjusted. The free access for the feed item and water was kept during whole experiment.The fresh feed material and water was placed for animals daily early in the morning and evening, and residual feed part was also removed to maintain hygienic conditions.

Results:

The percentage yield of the collected extract of *Capparisspinosa* leaves was calculated accordingly and was foundas mentioned in table no.3

$$\text{Percentageyield} = \frac{\text{Weightofextracts}}{\text{Weightofcrude drug}} \times 100$$

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Table 3. Percentage yield of the extracts

S.no	Extract	Weight ofcrude drugs(ingram)	Wightofextracts(ingram)	Percentageyield
3	Hydroalcoholicextractof *Capparisspinosa(HACS)*	500	84	16.8%
4	Ethanolicextract of *Capparisspinosa*(ECS)	500	67	13.4%

Phytochemical Screening Results Of *Capparisspinosa* Leaves

Table 4. Phytochemicalscreeningresultsof*Capparisspinosa*leaves

S. No.	Phytochemicals		Hydroalcoholicextract of*Capparisspinosa(HACS)*	Ethanolicextract of*Capparisspinosa*(ECS)
1.	Alkaloids	GeneralTest	-	+
2.	Carbohydrates(Monosaccharides,Oligosaccharides &Polysaccharides)	GeneralTest	+	-
		Reducing Sugars	+	-
		Monosaccharides	-	+
		PentoseSugars	+	+
		HexoseSugars	-	+
		Non Reducing Sugars	++	+
		Non Reducing Polysaccharides	+	+
		Gums	+	-
		Mucilage	-	-
3.	Proteins&Aminoacids	Proteins	+	-
		AminoAcids	+	-

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4.	Glycosides	GeneralTest	+	+
		Cardiac Glycosides	+	++
		Cardenoloids	-	-
		Deoxysugars	+	++
		Bufadenoloids	+	+
		Anthraquinone Glycosides	+++	-
		SaponinGlycosides	-	+
		CyanogeneticGlycosides	+	-
		CoumarinGlycosides	+	-
5.	Flavonoids		+++	++
6.	Tannin&Phenolic Compounds	GeneralTest	++	++
7	Steroids		+++	-
8.	VolatileOils		-	+
9.	Fats& Oils		+	+

#Theresultsshowninthetablearepresentedonthebasisofobservationalstudies,where;

*+++:withhighintensity, *++:Moderateintensity, *+:Slightintensity, *- Absent.

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Total phenol contents:

Table 5.Absorbance recorded for Standard Gallic Acid Curve (Dataare representedasmean±S.E.M,where n=3)

Sr.No.	Concentration(µg/ml)	AbsorbanceofSTD(GallicAcid)
1	10	0.138± 0.011
2	20	0.211±0.007
3	30	0.299±0.021
4	40	0.388±0.019
5	50	0.468±0.006
6	60	0.571±0.007
7	70	0.692±0.018
8	80	0.767±0.022
9	90	0.878±0.010
10	100	0.945±0.013

Table 6. Absorbance recorded for hydroalcoholic extract of *Capparisspinosa*

(Dataarerepresentedasmean±S.E.M,wheren=3)

S.No.	Concentration(µg/ml)	AbsorbanceforHACS
5	50	0.354± 0.011
6	100	0.433± 0.009
7	200	0.527±0.013
8	300	0.642± 0.018
9	400	0.757± 0.021
10	500	0.839± 0.027

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Table 7. Absorbance recorded for ethanol extract of *Capparisspinosa*
(Data are represented as mean±S.E.M,wheren=3)

S.No.	Concentration(µg/ml)	AbsorbanceforECS
1	50	0.257±0.013
2	100	0.348± 0.021
3	200	0.439± 0.019
4	300	0.514± 0.026
5	400	0.612± 0.011
6	500	0.711± 0.021

Table 8.Total Phenolcontent

S.No	Extract	Total flavanoid content (mg/G GallicAcid equivalent)
1.	Hydroalcoholic extract of *Capparisspinosa* (HACS)	35.88
2.	Ethanolic extract of *Capparisspinosa*(ECS)	25.75

Total flavonoid contents:

Table 9.Absorbance recorded for Standard Quercetin Curve (Data are represented as mean ±S.E.M,where n=3)

S.No.	Concentration(µg/ml)	AbsorbanceofSTD(Quercetin)
1	10	0.187± 0.018
2	20	0.218± 0.032
3	30	0.298± 0.012
4	40	0.461± 0.022

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5	50	0.523± 0.009
6	60	0.639± 0.017
7	70	0.793± 0.006
8	80	0.891± 0.019
9	90	0.982± 0.028
10	100	1.0821± 0.042

Table 10.Absorbance recorded for ethanol extract of *Capparisspinosa*(Data are represented as mean ±S.E.M,wheren=3)

Sr.No.	Concentration(µg/ml)	AbsorbanceforECS
1	50	0.144±0.007
2	100	0.211±0.010
3	200	0.398±0.087
4	300	0.487±0.039
5	400	0.597±0.011
6	500	0.719±0.027

Table 11.Total flavanoid content

S.No	Extract	Totalflavanoidcontent (mg/G Quercetinequivalent)
1.	Hydroalcoholicextractof *Capparisspinosa*(HACS)	10.66
2.	Ethanolic extract of *Capparisspinosa* (ECS)	8.33

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Antioxidant assay of extracts:

Results for DPPH Free Radical Scavenging Activity

Scavenging activity of hydroalcoholic and ethanolic extract of *Commiphoramukul* and *Capparisspinosa* leaves and ascorbic acid was studied on DPPH radicals and result indicated decrease in the concentration of DPPH radical. The ascorbic acid (standard) was found to decrease in the concentration of DPPH radicalin dose dependant manner.

Table 12. % DPPH radical scavenging activity of Ascorbic acid

S. No.	Conc.µg/ml	Absorbance Blank	I		II		III	
			Sample1	%Inhib.	Sample2	%Inhib.	Sample3	%Inhib.
1.	10	0.833	0.524	37.09	0.531	36.25	0.521	37.45
2.	20	0.833	0.507	39.13	0.517	37.93	0.524	37.09
3.	30	0.833	0.487	41.53	0.491	41.05	0.477	42.73
4.	40	0.833	0.406	51.26	0.411	50.66	0.403	51.62
5.	50	0.833	0.372	55.34	0.384	53.90	0.366	56.06
6.	60	0.833	0.308	63.02	0.315	62.18	0.302	63.74
7.	70	0.833	0.273	67.22	0.279	66.51	0.269	67.71
8.	80	0.833	0.256	69.26	0.261	68.67	0.257	69.14
9.	90	0.833	0.231	72.26	0.236	71.66	0.238	71.42
10.	100	0.833	0.204	75.51	0.208	75.03	0.202	75.75

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Table 13.%DPPH radicals cavenging activity of hydroalcoholic extract of *Capparisspinosa*

S.No.	Conc.µg/ml	Absorbance Blank	I		II		III	
			Sample1	%Inhib.	Sample 2	%Inhib.	Sample3	%Inhib.
1.	20	0.833	0.686	17.64	0.689	17.28	0.683	18.01
2.	40	0.833	0.612	26.53	0.607	27.13	0.614	26.29
3.	60	0.833	0.572	31.33	0.574	31.09	0.571	31.45
4.	80	0.833	0.511	38.65	0.508	39.01	0.506	39.25
5.	100	0.833	0.429	48.49	0.432	48.13	0.428	48.62
6.	120	0.833	0.364	56.30	0.361	56.62	0.367	55.94
7.	140	0.833	0.292	64.94	0.287	65.54	0.288	65.42
8.	160	0.833	0.184	77.91	0.181	78.27	0.182	78.15
9.	180	0.833	0.101	87.87	0.097	88.35	0.102	87.75
10.	200	0.833	0.068	91.83	0.067	91.95	0.064	92.31

Table 14. IC $_{50}$ value of DPPH by hydroalcoholic extract of *Capparisspinosa*

S.No.	Sample	IC50µg/ml				
		I	II	III	Mean	SD (±)
1	Hydroalcoholicextractof *Capparisspinosa*	100.41	100.11	100.13	100.22	0.1677

The results of the antioxidant activity assay of hydroalcoholic extract of *Capparisspinosa* leaves, against DPPH was found to produce concentration dependent response. It was found thatthe120 µg/mloftheextractshowed >50% Inhibition.The IC$_{50}$ value was found100.22±0.1677.

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Table15.%DPPH radical scavenging activity of ethanolic extract of *Capparisspinosa*

S.No.	Conc.µg/ml	Absorbance Blank	I		II		III	
			Sample1	%Inhib.	Sample2	%Inhib.	Sample3	%Inhib.
1.	50	0.833	0.795	04.56	0.792	04.92	0.789	05.28
2.	100	0.833	0.703	15.61	0.698	16.21	0.701	15.85
3.	150	0.833	0.617	25.93	0.615	26.17	0.619	25.69
4.	200	0.833	0.523	37.21	0.531	36.25	0.521	37.45
5.	250	0.833	0.427	48.74	0.431	48.26	0.433	48.02
6.	300	0.833	0.301	63.86	0.304	63.51	0.299	64.11
7.	350	0.833	0.209	74.91	0.204	75.51	0.211	74.67
8.	400	0.833	0.144	82.71	0.146	82.47	0.141	83.07
9.	450	0.833	0.091	89.07	0.089	89.31	0.086	89.67
10.	500	0.833	0.018	97.84	0.021	97.47	0.017	97.96

Table 16 .IC_{50}valueofDPPHbyethanolicextractof*Capparisspinosa*

S.No.	Sample	IC50µg/ml				
		I	II	III	Mean	SD (±)
1	Ethanolicextractof*Capparisspinosa*	256.16	256.39	255.48	256.01	0.4731

The results of the antioxidant activity assay of ethanol extract of *Capparisspinos a*leaves,against DPPH was found to produce concentration dependent response. It was found that the 300 µg/ml of the extract showed > 50% Inhibition.TheIC_{50}value wasfound256.01±0.4731.

Table17. IC_{50} values of DPPH by hydroal coholic & ethanoli cextract of *Capparisspinosa* leaves

S.No.	Sample	IC50µg/ml				
		I	II	III	Mean	SD (±)
3	HACS	100.41	100.11	100.13	100.22	0.1677

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4	ECS	256.16	256.39	255.48	256.01	0.4731
5	Ascorbicacid	39.76	41.50	39.53	40.26	1.077

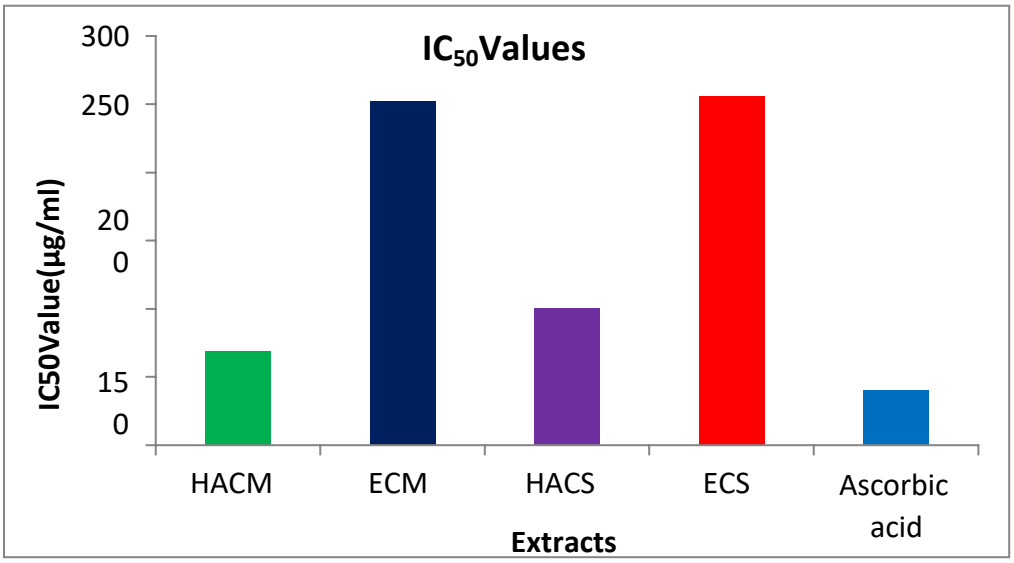

Figure 1. IC_{50}Values of hydroal coholic & ethanolic extract of *Capparisspinosa* leaves

Results of Pharmacological Studies:

Results of acutetoxicity studies:

The acute toxicity study was carried out to establish a suitable dose of plant extracts for furthers creenin gpur pose.The results of toxicity studies were found as follows;

Table 18.Resultsofacute toxicity studies

Sr. No	Parameter	Observationatdifferent timeintervalafterextractadministration				
		01	04	12	24	48
1	Bodyweight	NoChange	NoChange	NoChange	NoChange	NoChange
2	Foodand waterintake	Optimum	Optimum	Optimum	Optimum	Optimum
3	Skincolor	NoChange	NoChange	NoChange	NoChange	NoChange
4	PostureRelatedToxicity					
	Restlessness	Notobserved	Notobserved	Notobserved	Notobserved	Notobserved
	Irritability	Notobserved	Notobserved	Notobserved	Notobserved	Notobserved

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	Fearfulness	Notobserved	Notobserved	Notobserved	Notobserved	Notobserved
5	CNS–toxicity					
	Convulsion	Notobserved	Notobserved	Notobserved	Notobserved	Notobserved
	Sleepingtime	NoChange	NoChange	NoChange	NoChange	NoChange
	Sedation	Notobserved	Notobserved	Notobserved	Notobserved	Notobserved
	CNSDepression	Notobserved	Notobserved	Notobserved	Notobserved	Notobserved
	Hyperactivity	Notobserved	Notobserved	Notobserved	Notobserved	Notobserved
	TouchResponse	NoChange	NoChange	NoChange	NoChange	NoChange
	Respiratorydistress	NoChange	NoChange	NoChange	NoChange	NoChange
6	ANS–toxicity					
	Salivation	Notfound	Notfound	Notfound	Notfound	Notfound
	Lacrimation	Notfound	Notfound	Notfound	Notfound	Notfound
	Diarrhea	Notobserved	Notobserved	Notobserved	Notobserved	Notobserved
	Urination	Optimum	Optimum	Optimum	Optimum	Optimum
	Optical signs	Notobserved	Notobserved	Notobserved	Notobserved	Notobserved
	Pupilsize	Optimum	Optimum	Optimum	Optimum	Optimum
7	Cagebehavior (Socialcoordination)	NoChange	NoChange	NoChange	NoChange	NoChange
8	Bodytemperature	NoChange	NoChange	NoChange	NoChange	NoChange
9	Mortality	NotFound	NotFound	NotFound	NotFound	NotFound

The experimental animals did not show any mortality on oral administration of dose up to 2000mg / kg b.w., of hydroalcoholic& ethanolic extract of *Commiphoramukul & Capparisspinosa*leaves, separately. Therefore, 2000 mg / kg b.w., was considered as maximum safe dose withhydroalcoholic& ethanolic extract of *Commiphoramukul&Capparisspinosa*leaves. For InVivostudies, the 1/ 5^{th} of maximum tolerated safe dose i.e. 400 mg / kg b.w. of hydroalcoholic & ethanolic extract of *Commiphoramukul & Capparisspinosa* leaves separately was selected.

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Results of Anti-obesity studies:

Effecton waist circumference:

The effect of hydro alcoholic & ethanolic extract of *Capparisspinosa* leaves on abdominal circumference of the experimental rats was found.The abdominal circumference was estimated using standard plastic non extensible measuringtape. The results indicated a graded increase in abdominal circumference of the normal diettreated (groups 1) and high fat diet treated (group 2) animal groups. The orlistat is commonly used agentto manage the obesity inindividuals.The increase in abdominal circumference,treated withor listat (groups7) was found minimum, although these animals were also consuming high fat diet regularly. It established the well defined anti obesity effect of the orlistat.On anlysing the result data we can strongly denote that hydroalcoholic& ethanolic extract of *Capparisspinosa* leaves also contains the anit obesity effect, as all the extracts were opposing rise in waist circumference of experimental animalsas compared to risein waist circumference in only high fat diet treated animals. The maximum protection was found in the hydroalcoholic extract of *Capparisspinosa*, ethanol extract of *Capparisspinosa* against high fat diet induced obesity.

Table: 19 Effect of hydroalcoholic & ethanolic extract of *Capparisspinosa* leaves on waist circumference (cm)

Groups	Day1	Day7	Day14	Day21	Day28	Day35	Day42
NormalControl	14.41 ± 0.12	14.67 ± 0.09	14.98 ± 0.12	15.27 ± 0.31	15.88 ± 0.16	16.19 ± 0.13	16.79 ± 0.21
HFDOnly	13.81 ±0.18	14.49 ±0.19	15.39 ±0.22	16.12 ±0.11	17.01 ±0.14	17.96 ±0.31	18.36 ±0.18
HFD+HACS(400)	14.32 ± 0.11	14.53 ± 0.10	14.93 ± 0.16**	15.88 ± 0.21**	16.23 ± 0.08**	16.89 ± 0.06**	17.19 ± 0.18**
HFD+ECS (400)	14.27 ±0.16	14.76 ±0.08	15.17 ± 0.17***	15.94 ± 0.19***	16.47 ± 0.27***	16.91 ± 0.16***	17.41 ± 0.11***
HFD+Orlistat(25)	14.14 ±0.29	14.21 ±0.12	14.39 ± 0.08**	14.91 ± 0.21**	15.11 ± 0.17**	15.44 ± 0.22**	15.77 ± 0.17**

Values are expressed as mean ± SEM (n=6)

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Data were analyzed by one-way analysis of variance (ANOVA) followed by dunnet test.

P values<0.05 were consideredas highly significant**, and<0.01were considered as significant***.

Effectonbodyweight:The high fat diet causes graded increase in overall adipose tissue mass of experimental animals leading increase in body weight. The body weight of the rats was measured using standard and calibrated weighing machine, on day1st, day 7th , day 14th , day 21st,day 28th, day 35thand day 42nd. The % change in body weight was calculated using followingformula;

$$\% \text{ Weightgain} = \frac{\text{Bodyweightonspecificday(g)} - \text{Initialbodyweight(g)}}{\text{Initialbodyweight(g)}} \times 100$$

Table 20.Effect of hydroalcoholic & ethanolic extract of *Capparisspinosa* leaves on body weight (ingrams)

Treatment	Day1	Day7	Day14	Day21	Day28	Day35	Day42
NormalControl	217.83 ±3.24	226.83 ±3.1	230.83 ±2.99	233.83 ±2.87	238.5 ±3.2	240.66 ±3.00	243.66 ±3.13
HFDOnly	221.5 ±4.53	251.66 ±4.57	265.16 ±3.94	277.5 ±3.16	288.33 ±3.03	302.16 ±2.79	313.16 ±1.84
HFD+HACS(400)	222.83 ±4.79	239.83 ± 4.91**	248.66 ± 4.99**	258.16 ± 4.8**	266.33 ± 4.47**	269.66 ± 4.58**	275.33 ± 4.58**
HFD+ECS(400)	219.16 ±4.91	244.83 ±3.86	255.66 ±3.92	264.5 ±3.43	270.83 ±3.54	276.83 ±3.82	283.83 ±3.60
HFD+Orlistat(25)	226.66 ±5.44	232.66 ± 5.31**	237.83 ±5.022**	241.83 ± 5.06**	246.16 ± 4.98**	248.83 ± 5.08**	250.16 ± 5.08**

Values are expressed as mean± SEM(n=6)

Data were analyzed by one-way analysis of variance(ANOVA) followed by dunnet test

P values<0.05were considered as highly significant**, and<0.01were considered as significant***

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Table 21.Percent change in body weight

Treatment	Day7	Day14	Day21	Day28	Day35	Day42
NormalControl	4.13	5.96	7.34	9.48	10.48	11.85
HFDOnly	13.61	19.71	25.28	30.17	36.41	41.38
HFD+HACS(400)	7.62	11.59	15.85	19.52	21.01	23.56
HFD+ECS (400)	11.71	16.65	20.68	23.57	26.31	29.51
HFD+Orlistat(25)	2.64	4.93	6.69	8.6	9.78	10.36

The effect of hydro alcoholic& ethanolic extract of *Capparisspinosa*l eaves on the body weight of the experimental rats again ststandard pellet dietand prepared high fat diet (HFD), was estimated and was found. The body weight was estimated using standard weighing machine available indepart mental laboratory.The result data indicating here that both the hydro alcoholic & ethanolic extract of *Capparisspinosa* leaves are quite able tooppose the riseinbody weight of the experimental animals.Yet the potency to oppose increase in body weightof the rats was significantly differing. The rise in body weight with respect of time is normal physiologicalprocess of the individuals, and it can be observed from the animals of group-I, i.e. in animalstreated with standard pellet diet. It was also observed that normal weakly rise in body weightwasabout1to 2 percent.The animals treated with only high fatdiet, was foundto gain very high body weight with respect of time. After start of the treatment with high fat diet, it was observed that the body weight was increasenear by 40%.,Which is approximately 4 times higher as compared to the risein body weight of the animals of normal control group, who was consuming normal conventionalpelletdiet. These results are alsoestablishing the high calorie production,by the prepared high fat diet. Moreover; thea nimals, which were simultaneously treated with orlistat,which is a well established anti-obese agent, along with high fat diet, were showing aboutequal results, ascompared to standard pellet diet, yet the continuous rise in body weight was there. It indicating here that the or list at also oppose the rise in body weight.On the other hand, the animals treated with plant leave extract were also found to oppose rise inbody weight of the animals, yet they were consuming the prepared high fat diet. Among all fourextracts, the hydroalcoholic extract of both the plants were found to produce highly significant results. The hydroalcoholic extract of *Capparisspinosa.*The resultswere highly significant with these two extracts.The ethanol extract of *Capparisspinosa* leaves were also producing promising results. Both extracts were also opposing rise in body weight of the experimental animals.

Conclusion

Capparisspinosa leaf extract showed anti-obese like activity on high fat diet induced obesity in rats by reducing their weights after giving leaf extracts. At high doses it may reducing the total cholesterol and may help in reducing the obesity as well. In acute toxicity studies the plant extract is showing low LD 50 and may have less potency and less toxicity. So *Capparisspinosa*may be having anti-obese activity.

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