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Garden cress *(Lepidium sativum* L.*)* Seed - An Important Medicinal Source: A Review

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ABSTRACT

Lepidium sativum, commonly known as garden cress is a fast growing annual herb that is native to Egypt and West Asia, although it is now cultivated in the entire world. Its seeds are rich source of proteins, dietary fiber, omega-3 fatty acids, iron, other essential nutrients and phytochemicals. Garden cress is widely used in folk medicine for the treatment of hyperactive airways disorders, such as asthma, bronchitis and cough. Seeds are considered to be galactogogue, emmenagogue and recommenced in inflammation, bronchitis, muscular pain and rheumatism. The present review deals with nutritional, phytochemical, antimicrobial, toxicology and medicinal potential of garden cress seeds. It highlights anti-diabetic, laxative, hypocholesterolemic, fracture healing, analgesic, coagulant, diuretic, hepatoprotective, antiashthamatic, antidiarrheal, antispasmodic and anti cancer activities of garden cress seeds. It also focuses on food products developed using garden cress seed or its fractions.

Keywords: *Lepidium sativum*, phytochemicals, antimicrobial activities, medicinal properties

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INTRODUCTION

Garden cress (Gc), *Lepidium sativum* is an annual, herbaceous edible plant that is botanically related to mustard and watercress. Gc plant is native to Egypt and South west Asia. It is cultivated in India [1], North America and parts of Europe [2]. In some regions, Gc is known as garden pepper grass, pepper cress, pepperwort or poor man's pepper. The plant is cultivated as culinary vegetable all over Asia [3]. Gc seeds are well known for their various ethno pharmacological properties [4].

Gc seeds are used in South Asia as traditional medicine to treat bronchitis, asthma and cough. It is considered aborfacient, diuretic, expectorant, aphrodisiac, antibacterial, gastrointestinal stimulant, gastro protective, laxative and stomadic [5, 6].Gc seed is reported to exhibit antirheumatic [7] and bronchodilatory potential [8].The paste of GC seeds is applied in rheumatic joints to relieve the pain and swelling. It is also useful in hiccup, dysentery, diarrhea and skin disease caused by impurities of blood [9, 10]. Ethanolic extracts of Gc seed were effective in treating inflammatory bowel disease. Traditional sweets for lactating mothers are prepared from the Gc seeds [11]. The present review deals with the nutritional, nutraceutical, antimicrobial properties and phytochemical constituents of Gc seeds. It also highlights the potential of Gc seeds and its extracts for various medicinal uses.

The taxonomic classification [12]

Kingdom: Planate
Division: Magnoliophyta
Class: Magnoliopsida
Order: Brassicales
Family: Brassicaceae
Genus: *Lepidium sativum*

Vernacular names of Garden cress Plant in India:

Aadalu:	Telugu	**Candriki:**	Assamese
Chand Shura :	Sanskrit	**Chandasura:**	Oriya
Chansur:	Hindi	**Common Cress:**	English
Halim:	Urdu	**Halim:**	Bengali
Holan:	Punjabi	**Haliv:**	Marathi
Alian:	Kashmiri	**Allibija:**	Kannada
Allivirai:	Tamil	**Asali:**	Malayalam
Aseliyo:	Gujrati		

Morphology of Gc seeds: Gc seeds are small, oval-shaped, pointed and triangular at one end, smooth, about 3-4 mm long, 1-2 mm wide, reddish brown in color. A furrow present on both surfaces extending up to two thirds downward, a slight wing like extension present on both the edges of seed. On soaking in water seed coat swells and gets covered with transparent, colorless, mucilage with mucilaginous taste [13]. The seed length and width are 298 ± 3.2μm and 100 ±1.9 μm respectively [14].

Microscopic characters of Gc seeds: P Bigoniya et al. (2011) revealed that, endosperm was composed of thick walled polygonal cells and embryo appeared as innermost structure surrounded by endosperm cells. The cells of embryo were small in size and polygonal in shape [13].

Table 1 Chemical Constituents of Garden cress seed

Nutrient	Whole Meal	Endosperm	Bran
Moisture Content	4.14±0.05	2.58±0.01	4.27±0.01
Protein	22.47±0.78	27.74±0.02	12.58±0.21
Fat	27.48±0.14	33.06±0.16	6.34±0.19
Carbohydrates*	34.24±0.92	28.45±0.21	50.31±0.08
Crude Fiber	7.01±0.08	4.00±0.13	14.29±0.06
Ash	4.65±0.09	4.06±0.08	6.19±0.01
Energy (Kcal)**	474±1.06	523±0.82	363±0.87
Insoluble Dietary Fiber	28.49±0.38	13.10±0.62	74.07±1.48
Soluble Dietary Fiber	1.51±0.09	0.50±0.01	0.93±0.01
Total Dietary Fiber	30±0.47	13.6±0.62	75±1.49

** By difference, ** Calculated Source: [14]*

Table 2 Carbohydrate profile of Garden cress seed

Carbohydrate Profile	% in Gc seeds
Starch	10.3±0.69
Pentosans	11.0±0.38
Free reducing sugars	0.76±0.03
Crude fiber	16.5±1.05
Acid detergent fiber	27.3±0.43
Neutral detergent fiber	35.7±0.82
Hemi cellulose	8.4±0.39
Cellulose	9.4±0.03
Acid insoluble lignin	17.9±0.40
Lignin	29.4±0.63

Source: [15]

Table 3 Mineral Content (mg/100g) of Garden cress seed

Mineral	Whole Meal	Endosperm	Bran
Potassium	1193.95±10.51	945.15±5.81	1934.57±18.82
Phosphorous	514.59±10.67	625.81±14.59	209.92±0.70
Magnesium	315.25±3.63	334.95±3.16	303.63±1.37
Calcium	296.60±1.04	210.51±1.08	556.32±3.03
Sulphur	293.02±14.27	149.31±3.48	239.48±10.47
Sodium	24.64±0.02	15.34±1.04	57.06±2.69
Iron	7.62±0.04	8.31±0.06	6.61±012
Copper	5.53±0.09	2.21±0.03	1.63±0.04
Zinc	5.05±0.07	5.31±0.02	2.98±0.41
Aluminium	2.82±0.13	2.55±0.05	4.82±0.05
Manganese	2.57±0.04	3.03±0.05	1.87±0.03
Boron	1.41±0.03	1.17±0.03	1.98±0.06
Molybdenum	0.43±0.08	0.33±0.16	0.58±0.10

Source: [14]

Table 4 Amino Acid profile of Garden cress seed

Non-essential amino acids	g/100g protein	Essential amino acids	g/100g protein
Aspartic Acid	9.76±0.03	Histidine	2.66±0.09
Glutamic Acid	19.33±0.19	Threonin	4.51±0.03
Serine	4.96±0.09	Arginine	8.04±0.03
Glycine	-	Valine	5.67±0.02
Alanine	-	Metheonine	0.97±0.02
Tyrosine	-	Phenyl Alanine	5.65±0.03
Proline	-	Isoleucine	5.11±0.03
		Leucine	8.21±0.01
		Lysine	6.26±0.39
		Total (%)	47.08
		Essential Amino Acid score (%)	28.53

Source: [14]

BR Moser et al. (2009) reported that the Gc seed oil has 1.3 % of free fatty acids, acid value of 2.6 mg KOH/g and iodine value of 130 g I_2/100 g. The calculated molecular weight of Gc seed oil is about 891.94 g/mol. The primary phytosterols detected in Gc seed oil includes sitosterol (5.82 mg/g), campesterol (3.95 mg/g), and avenasterol (3.44mg/g), with cholesterol (0.50 mg/g), stigmasterol (0.30 mg/g), dihydrolanosterol (0.25 mg/g), and ß-amyrin (0.16 mg/g) and other steroidal constituents. The combined phytosterol content of Gc seed oil was 14.41mg/g [16]. Extraction of Gc seed oil by cold press, solvent and supercritical CO_2 extraction methods by BT Diwakar et al. (2010) showed 21.54, 18.15 and 12.60% oil in Gc seed respectively. The cold pressed oil has been reported to have low peroxide value and free fatty acid content compared to the oil extracted by other methods. The total carotenoid content of Gc seed oil was 1.0 µmol/100 g oil. The oil was stable up to 4 months at 4 °C [17]. Gc seed oil is rich source of natural antioxidant tocopherol. It contains total 139.73 ± 0.91mg/100gm tocopherol which constitutes of α-tocopherol (17.19 ± 0.52), γ-tocopherol (γ-Tocopherol) and δ-tocopherol (111.56 ± 0.37) [18].

Table 5 Fatty Acid Profile (%) of Garden cress seed oil

Fatty Acid	BT Diwakar et al. (2010)	M Zia-Ul-Haq et al. (2012)	RF Mohammed (2013)
Palmitic Acid (16:0)	10.1	10.30±0.12	9.10
Palmitoleic Acid (16:1)	-	0.70±0.30	0.16
Stearic Acid (18:0)	2.9	1.90±0.19	4.40
OleicAcid (18:1)	22	30.50±0.16	26.42
Linoleic Acid (18:2)	11.8	8.60±0.38	8.64
α-Linolenic Acid	34	32.18±0.59	41.17
Arachidic acid(20:0)	3.4	2.10±0.57	3.57
Eicosaenoic Acid (20:1)	12	13.40±0.66	-

Source: [17, 18, 19]

Phytochemical constituents of Gc seeds:
RK Sharma et al. (2012) and YC Yadav et al. (2011) reported the presence of phenolic compounds, alkaloids, cardiac glycosides, anthroquinones glycosides, tannins, steroids, flavonoids in Gc seeds [20, 21].M Zia-Ul-Haq et al. identified phenolic compounds in Gc seeds based on their mass spectral characteristics [18].

Table 6 Phenolic compounds identified in Garden cress seed

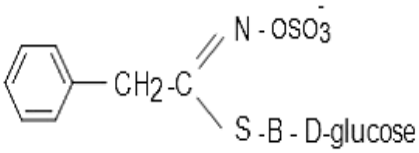
Compound	$[M-H]^-$ (m/z)	Qualifier ions (m/z)
Gallic Acid	169	125
Protocatechuic Acid	153	109
Coumaric Acid	163	119
Caffeic Acid	179	135
Coumaric acid- hexoside	325	163, 119
Caffeic Acid-hexoside	341	179, 135
Ferulic Acid-hexoside	355	193, 134
Vanillic Acid-hexiside	353	167
Caffeoylquinic acid	337	191, 179,173,135
Coumaroylquinic Acid	447	191, 173
Kaemferol-hexoside	463	301
Querecetin-hexoside	461	285
Kaemferol-glucuronide	301	151

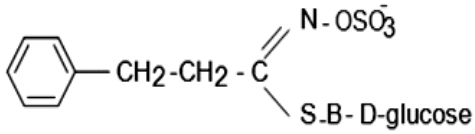
Source: [18]

UH Maier et al. (1998) identified dimeric imidazole alkaloids *viz.* lepidine B, C, D, E and F and two new monomeric imidazole alkaloids semilepidinoside A and B in Gc seeds [22].

PS Nayak et al. (2009) identified and quantified sinapic acid from Gc seed methanolic extract by high performance thin layer chromatography (HPTLC). The sinapic acid was separated on a thin layer of silica gel and determined by HPTLC-photo densitometry and reported about 0.4710 % of sinapic acids in Gc seeds [23].

HM Radwan et al. (2007) studied the glucosinolates of Gc seed. They reported the presence of glucotropaeolin and 2- Phenyl ethyl glucosinolate also called gluconasturiin in Gc seeds.





They also investigated the insecticidal activity of Gc seed extracts and glucosinolates against the white fly, *Bemisia tabaci*. The results revealed that the mortality reached to 92.5% when pest was treated with the Gc seed glucotropaeolin [24].

Antioxidant Activity
Highly reactive free radicals and oxygen species are present in biological systems from a wide variety of sources. These free radicals may oxidize nucleic acids, proteins, lipids or DNA and can initiate degenerative diseases. Antioxidant has ability to trap these free radicals. Antioxidant compounds like phenolic acids, polyphenols and flavonoids scavenge free radicals such as peroxide, hydro peroxide or lipid peroxyl and thus inhibit the oxidative mechanisms that lead to degenerative diseases.

M Zia-Ul-Haq et al. (2007) assayed the total phenolic content and antioxidant capacities (TEAC: Trolox equivalent antioxidant capacity; FRAP: Ferric reducing antioxidant power; TRAP: Total radical-*trapping* antioxidant parameter) of Gc seed methanolic extract. Total phenol content was 120.26 ± 1.52 mg CAE/g. TEAC, FRAP, and TRAP as reported were 168.10 ± 1.32µmol TE/g, 1317.04±5.74µmol Fe++/g and 506.40 ± 14.87µmol TE/g respectively [18].

P Bhasin et al. (2011) investigated the antioxidant activity of Gc seed extracts in different solvents (viz. ethanol, chloroform, methanol, benzene, hexane, propanol, glacial acetic Acid, petroleum ether, acetone, and ethyl acetate)

and antioxidant activity of extracts of Gc seeds was quantitatively determined using reducing power assay. Ethanolic extract of Gc seeds was reported to possess the strongest antioxidant activity [25].

YC Yadav et al. (2011) studied the *in vitro* antioxidant potential of ethanolic extract of Gc seeds. Total polyphenol and total flavonoid content of extract were 4.46±0.14 mg GAE/gm and 3.57±1.2 mg QE/gm respectively. Free radical scavenging activities of the ethanolic extract of Gc seeds were assessed by DPPH, FeCl3 and phosphor-molybdenum assay. The IC_{50} values for scavenging DPPH, ferric chloride, phosphor-molybdenum were 18.46±0.27 µg/ml, 9.11±0.40µg/ml and 18.41±0.08µg/ml respectively [21].

R Indumathy and A Aruna (2013) evaluated the free radical scavenging activity of total phenolic and flavonoid compounds extracted from Gc seeds. The methanolic extract was found to contain a noticeable amount of total phenols (8.651mgGAE/gm) and flavonoids (4.023 mg CAE/gm). Methanolic extract of Gc seeds showed maximum antioxidant activity by inhibiting DPPH and hydroxyl radical, super oxide anion scavenging, nitric oxide and hydrogen peroxide scavenging activities than the reference standards studied [26].

Reported results strongly support the *in vitro* antioxidant potential of Gc seeds.

Antimicrobial Activity

SIY Adam et al. (2011) studied the antimicrobial activity of the petroleum ether, methanol and water extracts of GC seeds against six pathogenic micro-organisms viz. *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumonae*, *Proteus vulgaris*, *Pseudomonas aeruginosa* and fungus *Candida albican*. The petroleum ether extract of Gc seeds in different concentrations (2.5, 5 and 10%) were found to be active antimicrobials against all the 6 pathogens with a strong antifungal activity at the concentration of 2.5 and 10% [27].

RK Sharma et al. (2012) studied the antifungal activity of ethanolic extract of Gc seeds against *Fusarium equiseta, Aspergillus flavus* and *Alternaria alternate, by* employing various concentrations of Gc seed extracts (2-8%) in Potato Dextrose Agar (PDA).They concluded that all the concentration of seed extract inhibited the fungal growth and among the different concentrations, the diameter of zone of inhibition ranged from 4 to 22 mm in various fungal species. The studies indicate that the Gc seeds have strong antimicrobial activity [20].

Toxicology of Gc Seeds

MA Al-Yahya et al. (1994) performed acute and chronic toxicity test of Gc seeds in mice. The acute toxicity tests showed that the administration of extract in single doses of 0.5 to 3.0g/kg of body weight of mice did not produce any adverse effects or mortality in mice. Chronic toxicity (100 mg/kg/day for a period of 3 months in drinking water) studies revealed that there were no symptoms of toxicity except a statistically insignificant higher mortality rate in the mice [28].

AI Abuelgasim et al. (2008) carried out the toxicity studies of Gc seed methanolic extract at the dose level of 200mg/kg and 400mg/body weight in albino Wistar rats for 21 days. Toxicity evaluation of the extract revealed no alteration in the parameters measured except few scattered fatty changes in the liver at higher dose [29].

PK Datta et al. (2011) assessed the safety of Gc seeds by conducting acute and sub chronic toxicity studies in adult Wistar rats. Gc seed powder (0.5 –5 g/kg body weight) was fed through diet to rats for the acute toxicity study and obvious symptoms of toxicity and mortality were monitored for 72 hrs. There were no symptoms of toxicity or mortality. 1.0 – 10 % of Gc seed powder was administered to rats in sub chronic toxicity study, through diet for 14 weeks. Dietary feeding of Gc seed powder did not produce any mortality. No significant changes in food intake, gain in body weight, relative weight of organs, hematological parameters, macroscopic and microscopic changes in vital organs in the rats. They concluded that the acute and sub chronic feeding of Gc seed powder did not produce any toxic effects in male and female rats and thus, Gc seed can be considered non-toxic and safe [30].

Medicinal Properties:

Antidiabetic and hypocholesterolemic Activity of Gc seeds

AP Patole et al. (1998) studied the effect of five mucilaginous seeds (Garden cress seeds, niger seeds, linseed, holybasil and basil) on *in-vitro* rate of starch hydrolysis for testing their potential to slow down the hydrolysis of starch to glucose in diabetic subjects. They observed that Gc seeds showed highest reduction in *in-vitro* rate of starch hydrolysis (41%) and therefore Gc seeds were tested *in-vivo* on 11 NIDDM subjects as well as in 14 normal

healthy subjects. Studies revealed that for both control and diabetic subjects meal with Gc seeds lowered the glycemic response as compared to the meal without Gc seeds. They also reported that diabetic subjects showed higher reduction in glycemic response compared to healthy subjects. In long term (21 days) administration of diabetics with Gc seeds (15 gm/day) 9 out of 11 subjects showed reduction in the levels of blood glucose from 10.2 mM/L to 8.3 mM/L at the end of the study period. Results of this investigation indicate that Gc seeds have a potential of activity as hypoglycemic activity [31].

M Eddouks et al. (2005) investigated the hypoglycemic activity of Gc seed aqueous extract in normal and streptozotocin (STZ) diabetic rats. There was a significant ($p < 0.001$) decrease in blood glucose levels in STZ diabetic rats after acute and chronic oral treatments with aqueous Gc seed extract (20 mg/kg body weight) and the blood glucose levels were normalized after two weeks of daily oral administration of aqueous Gc seed extract (20 mg/kg body weight). Authors concluded that the aqueous extract of Gc seeds exhibit a potent hypoglycemic activity in rats and the mechanism of hypoglycemic activity of Gc seeds was independent of insulin secretion as no changes were observed in basal plasma insulin concentrations after treatment either in normal or STZ diabetic rats [32].

The mechanism underlying the hypoglycaemic activity of the aqueous extract perfusion of Gc seed in normal and streptozotocin-induced diabetic rats was determined by M Eddouks and M Megharani (2008). Authors reported that the aqueous Gc seed extract caused a potent inhibition of renal glucose reabsorption which in turn reduced blood sugar which explained that the renal effect is at least one mechanism explaining the observed hypoglycemic activity of Gc seed extract in normal and diabetic rats [33].

WA Al-Hamedan (2010) reported the protective effect of Gc seed extract and powder on hypercholesterolemic rats. In comparison to positive control group, hypercholesterolemic rat groups with oral administration of Gc seed extract and powder showed a significant lower value of weight gain, feed efficiency ratio, serum cholesterol, triglycerides VLDL-c (very low density lipoprotein cholesterol), LDL-c (low density lipoprotein cholesterol) level, cholesterol/ HDL-c (high density lipoprotein cholesterol levels) , LDL-c/ HDL-c , serum ,serum creatinine, urea, liver cholesterol and total lipids with a significant increase in both serum globulin and liver triglycerides [34].

K Chauhan et al. (2012) reported the hypoglycemic and hypolipidemic effects of Gc seed powder in alloxan induced diabetic male Wistar rats. Diabetic and hyperlipidemic rats administered with Gc seed (3g/kg body weight) showed a significant decrease ($p \leq 0.05$) in fasting blood glucose levels, glycosylated haemoglobin, lipid profile, total cholesterol, triglycerides and lipoprotein fractions (LDL-c and VLDL-c) with a significant increase in HDL-c levels. Increased thiobarbituric acid reactive substances levels were neutralized, reduced glutathione and antioxidant enzyme activity in diabetic control and high fat high cholesterol diet fed experimental rats and was restored in Gc seed fed diabetic and hyperlipidemic rats [35].

A Shukla et al. (2012) investigated the hypoglycemic activity of total alkaloids from Gc seed on alloxan induced diabetic rats. Diabetic rats were fed with total alkaloid (50,150 and 250 mg/kg of body weight) for continuous 21 days. At the dose level of 250mg/kg, there was significant ($p< 0.001$) reduction in the blood glucose, cholesterol, triglyceride, and urea level in diabetic rats. Authors reported that total alkaloid from Gc seed at the dose level of 250mg/kg body weight showed potent hypoglycemic activity [36].

K Amawi and A Aljamal (2012) studied the effect of Gc seed aqueous extract on lipid profiles and blood glucose levels of hypercholesterolemic and alloxan induced diabetic albino rats. Gc seed extract (20mg/kg) was orally administered for four weeks to hypercholesterolemic and diabetic rats and they reported better lipid profile and reduction in blood glucose level in both the cases [37].

Antidiarrheal, antispasmodic, prokinetic and laxative activity of Gc seeds:

M Divanji et al. (2009) investigated the antidiarreal activity of methanolic extract of Gc Seeds. The antidiarrheal activity was studied using three experimentally induced diarrhea models i.e. Castor oil induced diarrhea; Prostaglandin E2 (PG-E2) induced enteropooling in rats and charcoal meal test in mice. The methanolic extracts of Gc seeds showed significant reduction in the weight of faeces in dose dependent manner in castor oil induced diarrhea. In PG-E2 induced diarrhea significant inhibition of PG-E2 induced intestinal secretions was observed. There was decrease in propulsion of charcoal meal in charcoal meal test, indicating its antimotility activity. Authors concluded that methanolic extract of Gc seeds possess significant antidiarrheal activity due to their inhibitory effect both on gastrointestinal propulsion and fluid secretion [38].

N Rehman et al. (2012) investigated antidiarrheal activity and antispasmodic activities of Gc seed crude extract in rats using *in-vivo* and *in-vitro* assays. Extract inhibited castor-oil induced diarrhea in rats. In isolated rat ileum, Gc seed extract (0.01–5 mg/mL) reversed carbachol (CCh, 1mM) and K+ (80mM)-induced contractions with higher potency against CCh, similar. Pre-incubation of rat ileum with a lower concentration of extract (0.03 mg/mL) caused a rightward parallel shift in the concentration– response curves (CRCs) of CCh without suppression of the maximum response, while at the next higher concentration (0.1 mg/mL), it produced a non-parallel rightward shift with suppression of the maximum response. Gc seed extract shifted the CRCs of Ca++ to the right with suppression of the maximum response. Authors concluded that Gc seed possess antidiarrheal and antispasmodic activities which are mediated possibly through dual inhibition of muscarinic receptors and Ca++ channels [39].

N Rehman et al. (2011) carried out charcoal meal *gastrointestinal* tract transit test and laxative activity test in BALB/c mice and also carried out *in vitro* experiments in isolated tissues of mouse, guinea-pig and rabbit to evaluate the prokinetic and laxative activities of aqueous-methanolic extract of Gc seed. Authors reported prokinetic and laxative effects of Gc seed in mice, which are partially mediated through a cholinergic pathway. The *in vitro* spasmodic effect of the Gc seed extract is also mediated through a similar mechanism with species and tissue-selectivity [40].

Fracture Healing Ability of Gc seeds

ABHA Juma (2007) investigated the fracture healing ability of Gc seeds in adult New Zealand White rabbits. The midshaft of the left femur were exposed in the surgery and subperiosteal transverse fractures were induced. The test animals had 6 g of *Gc* seeds in their food daily. After 6 and 12 weeks postoperatively left femurs of rabbits (control and test) were X-rayed. Results showed that the callus formations in the test rabbits fed with Gc seeds with the induced fractures, there was significant increase in the healing of fractures compared to the control group. This indicates that Gc seeds played a major role in promoting and accelerating callus formation in fractures. They concluded that Gc seeds have a marked effect on fracture healing in rabbits. The results support their effects on human beings for fracture healing as described in traditional medicine [41].

YC Yadav et al. (2011) investigated fracture healing ability of ethanolic extract of Gc seeds in internally fixed rats using femoral osteotomy model. Test group was administered (400mg/kg body weight) Gc seed ethanolic extract for 8 weeks. At 2nd, 4th and 8th weeks X- Ray photographs were taken for control and test groups. After fourth week, X-ray photographs of test groups showed significantly larger callus formation and more disposing of osseous material as compared to control group. After eight weeks, X-Ray photographs indicated that the fractured bone of test group animals was completely joined whereas fractured bone was not joined in control group. The study revealed that the ethanolic extract of Gc seeds has significant fracture healing ability [42].

Antihypertensive, hepatoprotective, diuretic, nephrocurative and nephroprtective Activity: The antihypertensive and diuretic effects of the aqueous extract of Gc seed were studied both in normotensive and spontaneously hypertensive rats were studied by M Maghrani et al. (2005). Authors reported that daily oral administration of aqueous Gc seed extract for 3 weeks exhibited antihypertensive and diuretic activities [43].

AI Abuelgasim et al. (2008) examined hepatoprotective effect of Gc seed methanolic extract for the prevention of carbon tetrachloride (Ccl_4) induced liver damage. Gc seed methanolic extract (200 and 400 mg/kg body weight) was administered to rats having induced liver injury. Serum activity of alkaline phosphatase (ALP), aspartate aminotransferase (AST), alanine aminotransferase (ALT) and bilirubin concentration were increased significantly in the group of rats received only Ccl_4. There was a significant reduction in these parameters in groups administered with Gc seed extract, the severe fatty changes in the livers of rats caused by Ccl_4 were also decreased. On the basis of results obtained authors concluded that the methanolic extract of Gc seeds seems to possess hepatoprotective activity in rats [29].

U Patel et al. (2009) assessed the diuretic effect of aqueous and methanolic extracts of the Gc seeds in adult male Wistar rats Extracts were administered orally to experimental rats at doses of 50 and 100mg/kg body weight. Both the extracts of Gc seeds showed a dose-dependent increase in urine excretion. The excretion of sodium was increased by both the extracts and potassium excretion was increased only by the aqueous extract at a dose of 100 mg/kg. The methanolic extract had the additional advantage of a potassium-conserving effect. Aqueous and methanolic extracts of Gc seeds showed notable diuretic effect which is comparable to that produced by the reference diuretic hydrochlorothiazide [44].

The nephrocurative and nephroprotective activity of ethanolic extract of Gc seeds were studied by YC Yadav et al. (2009). Ethanolic extract (200mg/kg body weight) of Gc seeds was used against cisplatin induced nephrotoxicity in adult male Wistar rats. The neproprotective test group received Gc seed ethanolic extract for 1st to10th day and cisplatin was administered on 11th day. Nephrocurative test group received single dose of cisplatin on day 1st, and after 6th day Gc seed ethanolic extract was administered up to 16th day. A dose of cisplatin induced loss in body weight, increased urea and creatinine level in serum in model control group , it was a significantly recovered in test groups which indicates increased glomerular filtration rate. There was significant increase in glutathione level and decrease in lipid peroxidation in nephroprotective and curative test groups. The study suggests that ethanolic extract of Gc seeds may possess nephrocurative and nephrprotective activity [45].

Anti cancer activity of Gc seeds:

SH Mahassni and RM Al-Reemi (2013) investigated the cytotoxic effect of Gc seed aqueous extract on human breast cancer cells using human breast cancer cell line MCF-7 (Michigan Cancer Foundation–7), an epithelial invasive breast ducal carcinoma cell line, which is estrogen and progesterone receptor positive by trypan blue dye exclusion and sulforhodamine B assays compared to its effect on normal human skin fibroblasts (HSF). The results revealed that Gc seed extract had a significant cytotoxic effect on MCF-7 cells. It caused significant time and dose dependant decrease in cancer cell viability. The effect of Gc extract on cancers is generally attributed to the constituent isothiocyanates, specifically benzyl isothiocyanate, presence of which in Gc seed extract was also confirmed by authors using HPLC. The study provides strong evidence that Gc seed aquoues extract has ability to inhibit the growth of breast cancer cells [46].

SH Mahassni and RM Al-Reemi (2013) also investigated the potential of aqueous extract of Gc seeds to induce apoptosis and necrosis in human breast cancer cells. The potential of Gc seed extract to induce apoptosis and necrosis in the human breast cancer cell line MCF-7, compared to HFS, was determined. Apoptosis was induced in cells, more in MCF-7, when they were treated with 25% and 50% extract, while necrosis was observed mainly after exposure to elevated extract concentrations (75%). DNA fragmentation resulted for both cells, in a time and dose-dependent manner. Authors reported that Gc seed extract was equally, and in some experiments more, effective against MCF-7 cells compared to HFS cells and the highest (75%) dose of extract was cytotoxic for both MCF-7 and HFS cells in most assays [47].

Bronchoprotective Activity:

AN Paranjape et al. (2006) evaluated the efficacy and safety of Gc seeds in patients (15-80 years old) having mild to moderate bronchial asthma. Patients were given finely powdered dried seeds at a dose of 1g thrice a day with water for 4 weeks. The bronchial asthma patients showed statistically significant improvement in various parameters of pulmonary functions after 4 weeks of Gc seed powder administration. Also, significant improvement was observed in clinical symptoms and severity of asthmatic attacks. None of the patient showed any adverse effect with Gc seeds. The results suggest the usefulness of Gc seeds in patients with bronchial asthma [48].

N Rehman et al. (2012) reported the bronchodilator activities (anticholinergic, Ca++ antagonist and phosphodiesterase inhibitory effects) of Gc seed crude extract which indicates its medicinal use in the hyperactive airways disorders, such as cough and asthma [49].

Galactagogue Potential:

Galactagogue properties of Gc seeds were studied by MA Al-Yawer et al. (2006) in adult female virgin Norway rats. Each experimental rat was administered 1.6 mg seeds powder /gm body weight /day for fourteen days. Different parameters (gross assessment, histological examination, enzymatic histochemical study, and hormonal assay of follicle-stimulating hormone, luteinizing hormone, prolactin, estrogen and progesterone) were assessed to study the effect of Gc seeds on the mammary gland of young adult virgin rats. All the parameters significantly exhibited a strong mammotrophic and lactogenic effects of Gc seeds on the non-primed mammary gland of adult virgin rats. Authors concluded that Gc seeds are most probably a real galactagogue and might be useful in induction of lactation [50].

Neurobehavioral effects:

A Shukla et al. (2011) investigated the neurobehavioral effects of the total alkaloid from Gc seeds in Swiss Albino mice and Wistar albino rats. The animals were intraperitonealy treated with total alkaloids (50, 150 and 250 mg/kg body weight) from Gc seeds. Total alkaloids considerably potentiated the thiopental induced hypnosis, decreased

locomotor activity and motor coordination, and increased preference to plus maze open arm. Gc seed alkaloids also increased the reaction time in caudal immersion and decreased the number of writhes in acetic acid induced writhing. Researchers concluded that Gc seed total alkaloids exhibit sedative, anxiolytic, myorelaxant and analgesic activity [51].

Antinflammatory, antipyretic and analgesic activities:
MA Al-Yahya et al. (1994) investigated the anti-inflammatory, antipyretic and analgesic activities of an ethanolic extract of Gc seeds in rats. The extract significantly inhibited carrageenan-induced pedal oedema in rats. However, only a weak inhibition of cotton pellet-induced granuloma was observed in rats fed with extract. Gc seed extract administration significantly prolonged the hot plate reaction time revealing its analgesic activity. The coagulation studies showed that the extract produced a significant increase in fibrinogen level and insignificant decrease in prothrombin time [28].

ND Raval and B Ravishankar (2010) studied the analgesic effect of Gc seeds in Charles Foster Albino rats and Swiss albino mice using different experimental models. Experiments were carried out in two groups – low dose of Gc seeds and high dose of Gc seeds. In the acetic acid-induced writhing syndrome, latency of onset was significantly increased in both low and high dose group. In the formaldehyde-induced paw licking response, there was a significant inhibition of neurogenic pain in the high dose group and significant inhibition of inflammatory pain in the lower dose group. In the tail flick response, a mild to moderate effect in both low and high dose group and also in the high dose group was reported by authors [52].

Effect on Sperm Parameters:
NS Naji (2013) studied the effect of phenol extract of Gc seeds on sperm parameters of adult male rabbits. Medium Effect Dose (MED_{50}) of phenols was obtained by Dose-Response Curve. MED_{50} of Gc seed phenols was 36.1 mg /kg body weight. There was a significant increase in testicular sperm concentration, epididymus sperm concentration and in the sperm count per gm of the testis, sperm motility percent, grade activity, sperm viability percent, and abnormal sperm morphology percent of epididymis caudal at MED_{50} of Gc seed phenol. Authors reported that supplementation with low doses of Gc seed phenols could enhance rabbit fertility. Author concluded that phenol extract of Gc seeds improves some parameters of sperm [53].

Health benefits of Gc seed oil:
In-vivo and *in-vitro* modulation of platelet aggregation and eicosanoids (Thromboxane B_2, Leukotriene C_4) by eugenol and a-linolenic acid rich Gc seed oil in adult Wistar rats were studied by RH Raghavendra and KA Naidu (2011). Eugenol and Gc seed oil showed synergistic effect against platelet aggregation and thromboxane B_2 levels in spleen and lung tissues of Wistar rats [54].

BT Diwakar et al. (2011) reported the modulatory effect of a-linolenic acid (ALA) rich Gc seed oil on lipid composition, spleen lymphocyte proliferation and inflammatory mediator production by peritoneal macrophages in rats. Vegetable oils containing a-linolenic acid have been shown to modulate the functions of immune competent cells. Female Wistar rats were fed with diets containing either Gc seed oil (2.5, 5 and 10 %, w/w) or sunflower oil (10% w/w) for 8 weeks. Gc seed oil modulated inflammatory mediators such as nitric oxide and leukotriene B_4, and thus may play a role in alleviating inflammatory conditions favorably [55].

SS Umesha and KA Naidu (2012) developed vegetable oil blends with ALA rich Gc seed oil and assessed their modulatory effect on lipid metabolism. Sunflower oil, rice bran oil, sesame oil were blended with Gc seed oil at different ratios to obtain n-6/n-3 polyunsaturated fatty acids (PUFA) ratio of 2.3-2.6. Native and Gc seed oil blended oils were fed to Wistar rats at 10% level in the diet for 60 days. Blending of vegetable oils with Gc seed oil increases ALA, decreases n-6 / n-3 PUFA ratio and beneficially modulates lipid profile in rats [56].

Food and Food Ingredients from Gc seeds:
SS Gokavi et al. (2004) developed dietary fiber formulation using Gc seed coat fraction. The powdered seed coat (5 kg) was blended with fresh carrot pulp (500 g), lime extract (100 g) and lecithin (100 g) and the blend was dispersed in potable water (100ml), boiled for 5 min and homogenized in a colloidal mill and the slurry was spray dried. The formulation was a free flowing smooth powder with yellowness index of 37.2. Its water holding capacity, viscosity (5% slurry) and dietary fiber content were 23.6 ml/g, 5100 mPas and 74.3% respectively [14].

N Agarwal and S Sharma (2011) analyzed proximate and phenol content of Gc seeds in two forms; whole Gc seed powder (WGCSP) and roasted Gc seed powder (RGCSP). Both the forms were rich in nutrients and phenols. They developed food product (Sev) using both the forms of Gc seeds. Sensory evaluation of Gc enriched sev on nine point hedonic scale showed that the Sev developed from RGCSP was more acceptable than that of WGCSP incorporated Sev but less acceptable than that of control one. Authors reported that the products developed from both forms of Gc seed powders were loaded with various nutrients along with antioxidants which are beneficial for curing a plethora of diseases [57].

SY Mohite et al. (2012) developed a health drink with processed Gc seeds keeping in view the health benefits of Gc seeds. The Gc seeds were boiled at 95°C for 15 minutes in potable water, dried and powdered. Health drinks were prepared with different concentration (1-5% w/v) of processed Gc seeds in skimmed milk. Sensory analysis of health drink showed that the overall acceptability of health drink containing 3% (w/v) of processed Gc seed powder was highest (8.75) compared to other drinks [58].

N Agarwal and S Sharma (2013) prepared different forms of Gc seed powder (GCSP) such as whole GCSP, husk removed GCSP, husk GCSP, roasted GCSP and microwave processed GCSP. *Mathri* (a wheat based food product) was developed by incorporating different forms of GCSP at different levels (2.5%, 5% and 7.5%).They found that only 5% incorporation gave the acceptability scores on sensory analysis. *Mathri* incorporated with 5% husk removed GCSP showed maximum overall acceptability score of 7.66 next to standard (8.46) *mathri*. Authors reported that GCSP incorporated *mathri* is more nutritious than standard *mathri* and has the potential to acts as nourishing as well as therapeutic agent due to antioxidant potential of Gc seed [59].

Gc seed protein isolate was prepared and evaluated by RF Mohammed (2013).Protein isolate of Gc seed contained 86.90% protein. Authors concluded that high water absorption capacity (229 ml H_2O/100 g) of Gc seed protein isolate makes it a potential ingredient in meat, bread, and cakes industries. Also, high oil absorption capacity (3.5 ml oil/gm) of Gc seed protein isolate makes it a good ingredient for the cold meat industry, particularly for sausages, where the protein can bridge the fat and water in these products. Therefore, the protein isolated from Gc seed could be a desirable food ingredient and can be used as nutrient substitution or supplementation and as functional agent in food systems [19].

Microencapsulation of Gc seed oil using different wall materials such as sodium caseinate whey protein concentrate, blend of maltodextrin, gum arabica and skimmed milk powder was carried out using spray-drying method by SS Umesha et al. (2013). Authors concluded that the microencapsulated Gc seed oil powder can be supplemented in food products to enhance plant based *n*-3 fatty acid [60].

CONCLUSION

Gc seeds are rich source of proteins, dietary fiber, minerals and essential amino acids. Gc seeds contain phenolic compounds which might be responsible for its strong antioxidant capacity. Toxicology studies of Gc seeds revealed that Gc seeds can be considered as non-toxic and safe. Gc seeds shows many medicinal properties such as antidiabetic, hypocholesterolemic, antihypertensive**,** antidiarrheal, antispasmodic and laxative activities. It also has fracture healing hepatoprotective, diuretic, nephrocurative, nephroprtective, galactogogue, antinflammatory, antipyretic and analgesic potential. Health drink and food products incorporated with Gc seed or its fractions were sensorily acceptable. Gc seed can be used as a promising multipurpose medicinal source whereas further clinical trial is required to prove its efficacy.

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