

Review Article

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Biological and medicinal application of *Cucumis sativus* Linn. – review of current status with future possibilities

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Abstract

Objectives: The increasing demand for herbal drugs for the human application is causing a growing demand for the cultivation of Medicinal Plants. This demand has developed because of cost-effective, plant-derived products rather than commercially available synthetic drugs. *Cucumis sativus* Linn. (Ver. Kheera) is a vegetable climber, species belongs to family Cucurbitaceae. This species has a wide range of medicinal and biological applications thanks to its richness in carbohydrate, proteins, minerals (calcium, iron, magnesium, phosphorus, potassium, zinc) and secondary metabolites like alkaloids, tannins, flavonoids, saponins, and phenolic compounds. These phytoconstituents may be responsible for allied therapeutic application. So, *C. sativus* possess wider applications for preventing certain ailments.

Content: The literature in various national and international journals and reports pertaining to the medicinal and nutritional uses were reviewed. The result revealed the current therapeutic applications of *C. sativus* whole plants other than the nutritional value. *C. sativus* pharmacological action includes antioxidant, anti-diabetic, UV protectant, hepatoprotective, gastroprotective, anti-helminthic, wound healing, antimicrobial, and anticancer. So, it could

be useful for both preventive and additive therapy along with modern medicine for the better management of certain disorders.

Summary and Outlook: This review furnishes updated information about the phytoconstituents and their medicinal applications so that it can pose a path for the young researchers to do future findings.

Keywords: bioactive; *Cucumis sativus*; Cucurbitaceae; phytoconstituents; protective.

Introduction

Cucumis sativus L. (Cucumber), belongs to the Cucurbitaceae, and commercially cultivated as a vegetable crop. It is native to India, found wild in the Himalayas from Kumaun to Sikkim [1]. The traditional systems of medicine specifically in Ayurveda, the leaves, fruits, and seeds of *C. sativus* have been widely used for various skin problems [2], include Puffy eyes, sunburn and the plant extract or paste believed to promote cooling, healing, soothing, emollient, lenitive, anti-itching effect to irritated skin, and have extended cosmetic effects [3]. The fruits are used as hemostatic, diuretic, and tonic. It is also used as add-on therapy in other physiological conditions like in pitta, hyperdipsia, fever, insomnia, cephalgia, bronchitis, jaundice, haemorrhages, strangury, and general debility [4, 5]. Further, numerous literatures revealed its anthelmintic [6], anti-diabetic [7] antiulcer, moisturizing, and antimicrobial activity [8] of the fruit extracts in different doses. Cucumber pulp and seeds are useful as folk cosmetic for certain skin complications like hyperpigmentation and also for face cleaning, further from centuries to present *C. sativus* is recommended globally in cosmetic industry to produce cosmetics. The data on *C. sativus* were reviewed and collected through literature from various national and international journals and reports related to the medicinal and nutritional uses.

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Diversity of cucumbers species

It is a large group of vegetable crops cultured widely in the subtropical and tropics countries. The family comprises of 118 genera and 825 species [9]. Plants of this family have many therapeutic and nutritional benefits [10]. Cucumbers are botanically categorized as berries and are available in many different sizes, shapes, and colors. They range from thick, stubby little fruits (10–12 cm long) to Dutch greenhouse diversities (of up to 50 cm long) as shown in Figure 1 *C. sativus* Linn. Show (A) Tree growing in flowering & fruiting stage while (B) fruits of *C. sativus*.

Cucumber may not be very distinguished for its food value, but they make up this by providing some extensive variety of healthy substances [11]. The most popular variety is the long smooth salad cucumber which has a smooth, dark-green skin. The true gherkin is a different species (*Cucumis anguria*), widely grown in the West Indies. The vernacular name and their botanical classification are detailed in Table 1.

Nutritional values of fruits of *C. sativus*

This vegetable possesses high water content but very low in calories. It has potent antilipidemic, anti-diabetic [13], and antioxidant activity [14]. It is commonly used in salads or fermented pickles. Consumption of antioxidant compounds from food is a very significant factor for the defense of human health, and it is broadly known that Mediterranean diet, which is rich in natural antioxidants, thus prevent cardiovascular diseases and cancer [15]. The main component of fruit is water (95%) and only small amounts of protein (0.6%), lipids (0.1%), and carbohydrates (2.2%). Cucurbitacins A, B, C, D, E, and I were identified in cotyledons of different varieties of *C. sativus* seedlings [16]. The bitter taste of fruits is due to Cucurbitacins [17]. On maturity, the fruits of cucurbitacins are hydrolyzed to its

non-bitter principles, in presence of enzyme elaterase [18]. The amount of bitterness in cucumber appears to vary from year to year and from location to location. This might be due to elaterase production which is stimulated or depressed under certain environmental situations such as cool temperatures can enhance bitterness of the fruit [19]. Another study discloses that the bitterness of cucumber is due to the presence of cucurbitacin C but the amount was very less i.e. 0.001 mg, as summarized in Table 2. The stem of the fruits contains a higher concentration of cucurbitacin C than the center or blossom end of the fruit, therefore it is common practice to cut the stem end first before using the fruits [17].

Traditional uses

Traditional uses of various parts of *C. sativus* were mentioned below according to their applications [20, 21].

Fruits are a good source of nutrition. Fruit juice use as demulcent, depurative, diuretic, emollient, purgative, and resolvent. The fresh fruit used internally for the treatment of blemished, skin rash etc. Whereas the half-ripen fruits were used as purgative. The whole fruit used externally as a poultice for burns, sores scold, wounds, and also in cosmetic for skin softening and whitening. The decoction

Table 1: Vernacular name and botanical classification of *Cucumis sativus* (with permission from ref. [12]).

Vernacular name	Botanical classification
English Cucumber	Kingdom Plantae
Hindi Kheera	Division Mangoliophyta
Marathi Tavsini	Class Mangoliopsida
Chinese Huang Gua	Order Cucurbitales
Malayalam Vellari	Family Cucurbitaceae
Panjabi Khira	Genus <i>Cucumis</i>
Sanskrit Sakusa	Species <i>C. sativus</i>
Arabic Kheyar	
Urdu Kheera	



Figure 1: *Cucumis sativus* Linn. (A) Tree growing in flowering & fruiting stage. (B) Fruits.

Table 2: Nutritional values of fruits of *C. sativus* (with permission from ref. [11]).

Nutritional value per 100 g of fruit	
Source	Quantity, mg
Carbohydrates	3,630
Sugars	1,670
Dietary fiber	500
Fat	110
Protein	650
Vitamins	
Thiamine (B1)	0.027
Riboflavin (B2)	0.033
Niacin (B3)	0.098
Pantothenic acid (B5)	0.259
Vitamin B6	0.04
Folate (B9)	7
Vitamin C	0.0028
Vitamin K	0.0164
Minerals	
Calcium	16
Iron	0.28
Magnesium	13
Manganese	0.079
Phosphorus	24
Potassium	147
Sodium	2
Zinc	0.2
Other constituents	
Water	95,230
Fluoride	0.0013

of the green fruit was used for cough exclusion. Further evidence suggests, fruits were useful in the treatment of bronchitis, asthma, dyspepsia, piles, hepatitis, diarrhea, as a laxative, anthelmintics, antipyretic, and in menstrual disorder, also was useful externally as astringent and reduces burning pain in scorpion-sting, in eye infections and used as hair tonic [22].

In Chinese folk medicine the leaves, stems, and roots were used as anti-diarrheal, detoxicant, and anti-gonorrheal agents. The leaf juice was used as emetic. It is used for treating dyspepsia in children when given in combination with cumin seeds and was useful in throat infections [5]. Seed oil useful in rheumatism, diuresis, and anthelmintic effect. A Gum obtained from the bark is used as demulcent and purgative.

Phytoconstituents present in different parts were different in ratio and were summarized in Table 3. it is believed that these were responsible for their exclusive medicinal applications. various products of *C. sativus* like fresh or lyophilized juice, oil, ethanolic/methanolic/ethyl acetate/aqueous extracts of different parts were evaluated via *in vitro* or methods for certain activities and the findings were tabulated in Table 4. *C. sativus* showed high therapeutic potential for ethnopharmacological, phytochemical and therapeutic applications due to the presence of important bioactive like cucurbitacin & cucumerin.

Table 3: Various phytoconstituents from different parts of *C. sativus*.

Plant parts	Chemical constituent
Fruits	Fruits contain water, protein, fat, carbohydrate, mineral, calcium, phosphorus, iron, and vitamin B. Crepsin and proteolytic enzyme, ascorbic acid, oxidase, succinic, and malic dehydrogenase reported in fruits [23]. Fruits contain a high concentration of ascorbic acid [24].
Leaves	Leaves are sources for some major phytoconstituents. Vitexin-6-(4-hydroxy-1-ethylbenzene) (cucumerin A) and isovitexin-8-(4-hydroxy-1-ethylbenzene) (cucumerin B) are the two new major C glycosyl flavonoids products, identified in leaves, with other flavonoids as apigenin 8-C-β-D-Glucopyranoside (vitexin), apigenin-6-C-β-D-glucopyranoside (isovitexin), luteolin-8-C-β-D glucopyranoside (orientin), luteolin-6-C-β-D-glucopyranoside (isoorientin), and 4-hydroxycinnamic acid (26,27) isolated two new megastigmane, cucumegastigmanes I [(6S,7E,9S)-6,9,10-trihydroxy-4,7-megastigmadien-3-one], and cucumegastigmanes II [(6S,7E,9S)-6,9,10-trihydroxy-4,7-megastigmadien-3-one, 10-O-β-D-glucopyranoside] and a known megastigmane (+) – dehydrovomifoliol from the leaves of <i>C. sativus</i> . Other five known compounds are: lutein; (+) (1R,2S,5R,6S)-2,6-di-(4'-hydroxyphenyl)-3,7-dioxabicyclo (3,3,0) octane; indole-3-aldehyde, indole-3-carboxylic acid, and adenosine were also identified from the same.
Flowers	Quercetin 3-O-glucoside, kaempferol 3-O-glucoside, isorhamnetin 3-O-glucoside, and kaempferol 3-Orhamnoside are other phyto-constituents were present in the methanolic extract of the flowers [27].
Peel	Pulp and peel extracts contain lactic acid, which showed antioxidant activity [8] essential oils isolated from it further found 21 compounds, include Z-6-nonenol, E-2-nonenol, E,Z-2,6-nonadienal, E-2- nonenal, Z-3-nonenol, 3-nonenol, pentadecanal, 9,12,15 octadecatrienal, and 9,17-octadecadienal from three distinct cultivators.
Seeds	Seeds contain crude proteins, fats, and oil. The fatty acid components are palmitic, stearic, linoleic, and oleic acid [23]. It contains a number of sterols such as codisterol, 25 (27) dehydroporifersterol, clerosterol, isofucosterol, stigmaterol, campesterol, 22-dihydrobrassicasterol, sitosterol, 25 (27)-dehydrofungisterol, 25 (27) hydrocondrillasterol, 24-β-ethyl-25 (27)-dehydrofungisterol, avenasterol, 22-dihydrispinosterol, and 24-methylenecolesterol. The gibberellin hormone was also found in seeds.

Table 4: Pharmacological activities of *C. sativus* extracts.

S.No.	Types of extract and parts used	Types of activity	Models used	Doses	Experimental test	Findings	References
1	Volatile oil of cucumber	Antioxidant and antimicrobial activity	DPPH assay	100 µg/mL	<i>In vitro</i>	- The cucumber pulp and peel extracts contain a high concentration of lactic acid (~7–8% w/w) which could explain, as a matter of fact, the traditional use of cucumber in skin treatment. - The extracts, showed interesting antibacterial and moderate antifungal activity.	[8, 28]
2	Lyophilized juice of cucumber fruit	Antioxidant, anti-hyaluronidase, and anti-elastase activity	DPPH, superoxide radical scavenging assay and HPLC	1.56–50 µg/mL	<i>In vitro</i>	- The juice showed DPPH-free radical and superoxide radical scavenging activity, IC50 at a concentration of 14.73 ± 1.42 and 35.29 ± 1.30 µg/mL, respectively. - The lyophilized juice also showed strong anti-hyaluronidase ($p < 0.001$) and anti-elastase ($p < 0.001$) activity, IC50 at a concentration of 20.98 ± 1.78 and 6.14 ± 1.74 µg/mL, respectively. - The ascorbic acid content was found to be $3.5 \pm 0.23\%$ w/w as compared with the standard. - The juice is the rich source of ascorbic acid and this study thereby rationalizes the use of <i>C. sativus</i> as the potential anti-wrinkle agent in cosmetic products.	[29]
3	Methanolic extract of seeds	Antioxidant and anti-ulcer activity	Pyloric ligation and water immersion stress induced ulcer model in rats	150 and 300 mg/kg	<i>In vitro</i> & <i>in vivo</i>	- The seeds extract showed maximum antioxidant activity measured by DPPH method. - The extract showed significant reduction of gastric acid volume, free and total acidity as 41, 29, and 48% at 300 mg/kg dose.	[30]
4	Aqueous extract of <i>C. sativus</i> fruit	Antacid and carminative properties	Carbondioxide evolution method & Rossette Rice test	2.5–7.5 g	<i>In vitro</i>	The extract of <i>C. sativus</i> significantly neutralized acid and showed resistance against change in pH and also illustrates good carminative potential compared to NaHCO_3.	[31]
5	Ethanollic extract of <i>C. sativus</i> fruit	Anti-ulcerogenic activity	NSAID Aspirin (–) induced gastric ulcer	100, 200, and 400 mg/kg	<i>In vivo</i>	The ethanollic extracts of cucumber showed a significant less ulcer index when compared to control at 400 mg/kg, dose. The ulcer protective activity of cucumber may be due to the presence of alkaloids, steroids, flavonoid, polyphenols.	[32]

Table 4: (continued)

S.No.	Types of extract and parts used	Types of activity	Models used	Doses	Experimental test	Findings	References
6	Ethanollic extract of <i>C. sativus</i> leaves	Antilulcer activity	Indomethacin (–) induced ulcer models	150 mg/kg	<i>In vivo</i>	– Antilulcer activity of leaves was found near equivalent to standard drug Ranitidine at 150 mg/g. Histopathological study of the stomach also showed almost normal architecture compared to indomethacin treated group.	[33]
7	Methanolic extracts of <i>C. sativus</i> leaves	Antidiarrheal activity	Castor oil induced diarrhea	250 and 500 mg/kg body weight	<i>In vivo</i>	– The extract showed significant ($p < 0.001$) dose-dependent inhibitory activity against castor oil induced diarrhea. – The extract might exert its antidiarrheal activity by the antisecretory mechanism	[34]
8	Aqueous extract of fruit	Ulcerative colitis	Acetic acid induced colitis in Wistar rats	100, 250 and 500 mg/kg	<i>In vivo</i>	– Pre-treatment with fruit extract for 7 days showed the significant reduction in ulcer area, ulcer index and neutrophil infiltration at 250 and 500 mg/kg compared with prednisolone.	[35]
9	Ethanollic extract of <i>C. sativus</i> seed	Anthelmintic activity	<i>Hymenolepis nana</i> and <i>Aspicularis tetraptera</i> infection in mice	5 g/kg	<i>In vivo</i>	– Cucumis seeds showed potent effect against <i>H. nana</i> (tapeworm) and <i>A. tetraptera</i> (pinworm) infection in mice compared with piperazine citrate.	[36]
10	Ethanollic extract of the fruits of <i>C. sativus</i>	Hepatoprotective activity	Paracetamol (–) induced hepatotoxicity in albino rats	250 and 500 mg/kg	<i>In Vivo</i>	– Treatment with ethanolic extract of the fruits of <i>C. sativus</i> had significant protection against hepatic damage by maintaining the different liver marker enzymes. – Liver histopathology also showed that reduced the space formation, loss of cell boundaries, and hepatic necrosis induced by paracetamol in albino rats.	[37]
11	Ethanollic extract of <i>C. sativus</i> leaves	Hepatoprotective activity	Paracetamol (–) induced hepatotoxicity	150 mg/kg	<i>In Vivo</i>	– The leaves extract was showed significant hepatoprotective effect as compared to silymarin through maintaining the different liver biomarkers enzymes.	[33]
12	Ethanollic extracts of fruit	Anti-diabetic activity and hypolipidemic effect	Streptozotocin (–) induced diabetes	200 and 400 mg/kg	<i>In vivo</i>	– The ethanolic extracts of powder fruit showed significant anti-diabetic effects in streptozotocin induced rats as compared to glibenclamide. The extracts also significantly lowered the elevated cholesterol as well as LDL level.	[7]

Table 4: (continued)

S.No.	Types of extract and parts used	Types of activity	Models used	Doses	Experimental test	Findings	References
13	Methanolic fruit pulp extract	Hypoglycemic activity	Alloxan (–) induced diabetes mellitus	500 mg/kg	<i>In vivo</i>	– The extract was significantly reduced the blood glucose level from 231 ± 1.11 to 82 ± 1.55 mg/dL body weight. The presence of saponins, terpenes, phenolics, flavonoids, alkaloids, and glycosides in extract could be responsible for management of diabetes.	[38]
14	Aqueous extract of <i>C. sativus</i> fruit	Wound healing	Excision wound model	2.5, 5, and 10% (w/w) of extract cream using soft white paraffin base	<i>In vivo</i>	– Topical treatment of extract based cream formulation significantly increased the wound healing rate. By virtue of its antioxidant property and presence of the flavonoids, content in <i>C. sativus</i> may be responsible for wound contraction and the elevated rate of epithelization in wound healing. It may act either by increasing the myofibroblasts contractile property or causes enhancement of myofibroblasts number that was incorporated into mesenchymal cells of wound area.	[35]
15	Ethyl acetate fraction of <i>C. sativus</i> flowers	Anti-cancer activity	HepG2 cell line by MTT assay	50–1,000 µg/mL	<i>In vitro</i>	– The IC_{50} value of the sample was found at 103.7 µg/mL against liver cancer HepG2 cell lines.	[39]
16	Methanolic extracts of leaves and stems	Skin-whitening agent	DOPA oxidase activity, Measurement of melanin content, Western blotting, tyrosinase activity in B16 crude lysates, and mushroom tyrosinase assay	100 µg/mL	<i>In vitro</i>	– Methanolic extracts of leaves and stems inhibited melanin production in melanoma B16 cells by down regulation of tyrosinase expression.	[40]
17	Fresh aqueous extract from fruits of <i>C. sativus</i>	Sun protection	Sun protection (SPF) determination	100 & 200 µg/mL	<i>In vitro</i>	– These results suggest that lutein in leaves of <i>C. sativus</i> can contribute to the inhibition of melanin synthesis and can also decrease the expression of tyrosinase. – The SPF value of marketed cucumber lotion was found to be 0.61 ± 0.059 at 200 µg/mL concentration while SPF value of cucumber extracts at 100 & 200 µg/mL were found to be 0.39 ± 0.039 and 0.67 ± 0.54 respectively. – The fresh cucumber extracts absorb skin erythema producing UV-B radiation suggesting more potent sun protection as compared to marketed formulation contains cucumber lotion.	[41]

Table 5: Pharmacological activities of purified molecules from *C. sativus*.

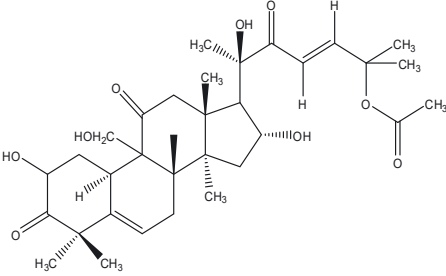
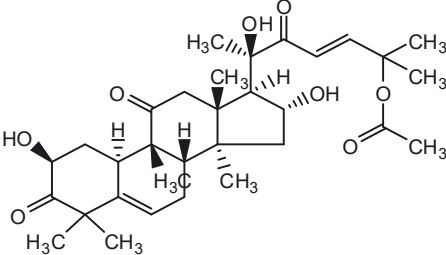
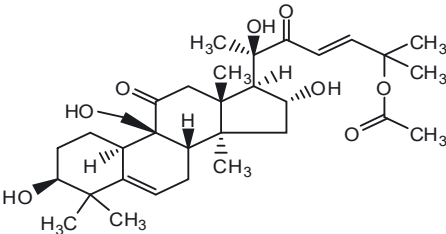
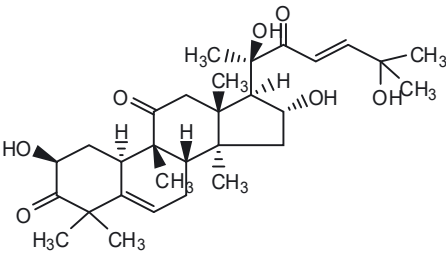
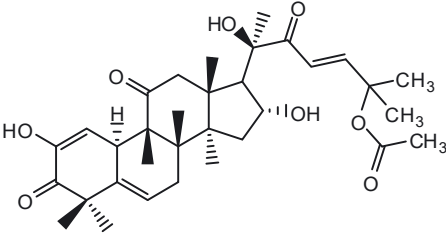
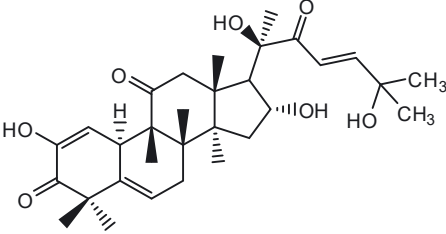
Name	Structure	Activity	References
1. Cucurbitacin A (C ₃₂ H ₄₆ O ₉)		—	[42]
2. Cucurbitacin B (C ₃₂ H ₄₆ O ₈)		Chemotherapy of lung cancer, breast tumor growth. Chemopreventive for prostate cancer.	[43, 44]
3. Cucurbitacin C (C ₃₂ H ₄₈ O ₈)		Cytotoxic and antitumor activity	[45].
4. Cucurbitacin D (C ₃₀ H ₄₄ O ₇)		Lung cancer Breast cancer Immunomodulating activity	[46–48]
5. Cucurbitacin E (C ₃₂ H ₄₄ O ₈)		Breast cancer metastasis Inhibited triple negative breast cancer (TNBC) Cell cycle regulators in cancer cells using, lung cancer (A549) Liver cancer (Hep3B) and Colon cancer (SW480)	[49–51]
6. Cucurbitacin I (C ₃₀ H ₄₂ O ₇)		Adjunct chemotherapy agent	[52]

Table 5: (continued)

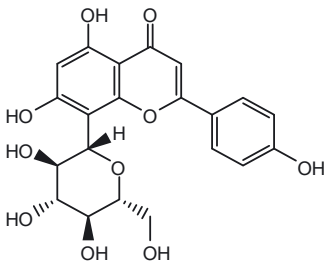
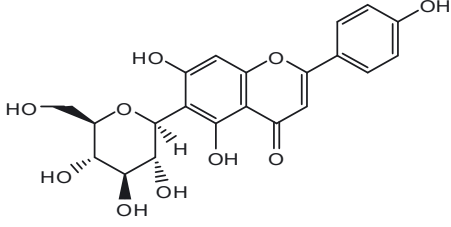
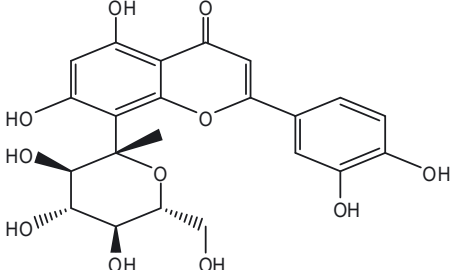
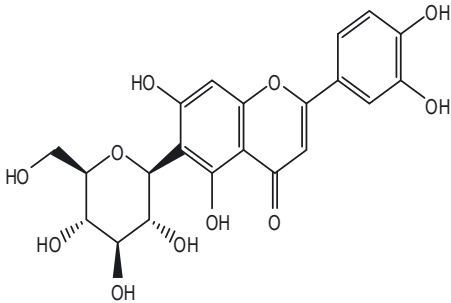
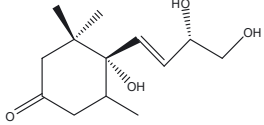
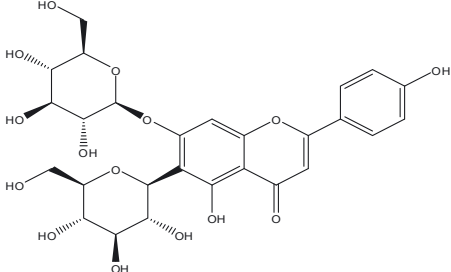
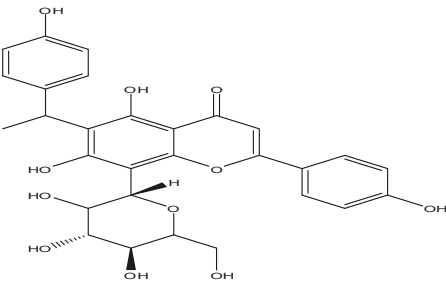
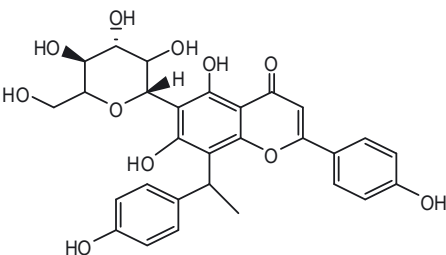
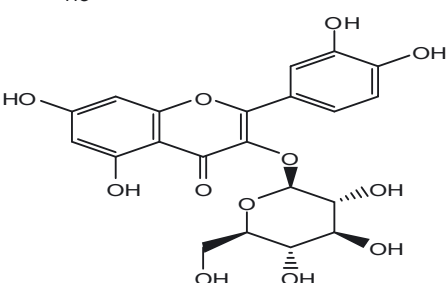
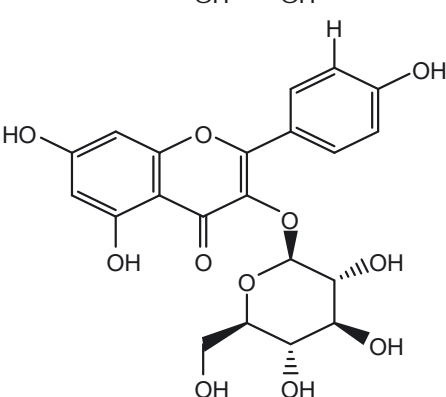
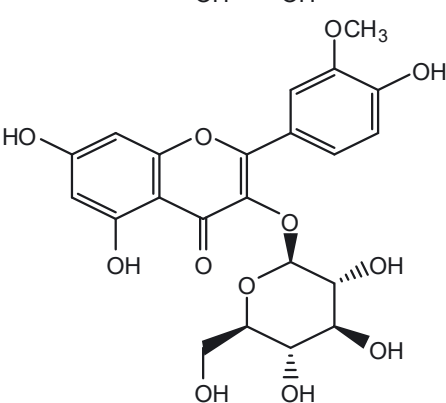
Name	Structure	Activity	References
7 Vitexin ($C_{21}H_{20}O_{10}$)		Neuroprotective activity Anti-diabetic, anti-Alzheimer's disease, and anti-inflammatory activities	[53, 54]
8 Isovitexin ($C_{21}H_{20}O_{10}$)		Anti-diabetic, anti-Alzheimer's disease, and anti-inflammatory activities	[54]
9 Orientin ($C_{21}H_{20}O_{11}$)		Antioxidant action	[55]
10 Isoorientin ($C_{21}H_{20}O_{11}$)		Anti-inflammatory activity using murine macrophages	[55, 56]
11 Cucumegastigamanes I		—	[26]
12 Saponarin ($C_{27}H_{30}O_{15}$)		Hepatoprotective & antioxidant against paracetamol induced hepatotoxicity	[57, 58]

Table 5: (continued)

Name	Structure	Activity	References
13 Cucumerin A (C ₂₉ H ₂₈ O ₁₁)		–	[25]
14 Cucumerin B (C ₂₉ H ₂₈ O ₁₁)		–	[25]
15 Quercetin 3-O-glucoside		Wound healing activity	[59]
16 Kaemferol 3-O-glucoside		Anti-inflammatory and analgesic activity	[60]
17 Isorhamnetin-3-O-glucoside		Preventive for CCL4 induced hepatotoxicity	[55, 61]

Necessitate for future research on purified molecules of *C. sativus*

Other than the nutritional and traditional application today more focus is given to the active phytoconstituents. Important bioactives were Cucurbitacin, vitexin, isovitexin, orientin and isoorientin, and Cucumegastigamanes I, Table 5 covered these phytoconstituents along with their structure.

Discussion

According to the literature, it is confirmed that beyond each biological or pharmacological response there must be a specific bioactive. The major components are listed in this review like Cucurbitacin A, B, C, D, E, and I out of which B, C, D, and E are mostly responsible for their *in vitro* anticancer activity though cytotoxicity [43, 46, 47, 50, 51, 62, 63]. whereas Cucurbitacin I only be useful as adjunct chemotherapy [52]. The Anti-diabetic, Anti-Alzheimer's activities in preclinical models are confirmed due to presence of Vitexin [53, 54]. Whereas the anti-inflammatory effects may be due to the presence of isoorientin [55, 56]. Further, the hepatoprotective action is confirmed due to the presence of saponarin [57, 58]. Furthermore, there were no studies has been carried out yet on Cucurbitacin A, Cucumegastigamanes I, Cucumerin A, and Cucumerin B, what may be the reason behind may not be clear regarding their bioavailability or some other issues with stability, yet has to explore, so research needs to be focused on these untarn constituents to get some new sights for their beneficial effects in case of specific ailment.

Conclusions

In recent years more scope has been given to herbal drugs because of their minimal adverse effects as compared to other synthetic or semisynthetic derivatives in addition to their good acceptability. Cucumber is used as a vegetable food, with their various therapeutic applications against specific ailments as explained in the traditional ayurvedic medicines. This plant is rich in various phytoconstituents, out of which few are summarized in this review for their nutritional properties and medicinal application against many disorders including cancer, Alzheimer's, and diabetes. Still, there are many more secrets need to be discovered about its phytoconstituents and their pharmacological effect through further researches, such as isolation of bioactive and their preclinical and clinical studies

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