

Pharmacognostical and Pharmacological Review of Cucumis Melo L. Including Unani Medicine Perspective

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Review Article

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Abstract

Cucumis melo which is commonly known as musk melon or Kharbuzah belongs to the family Cucurbitaceae. It is an annual climbing or creeping herb with angular, scabrous stem, simple soft hairy orbicular-reniform leaves and bears tendrils, by which it is readily trained over trellises. Musk melons are extensively cultivated throughout India particularly in the hot and dry North-Western areas. Main parts used are pulp, root, seeds and seed oil. It is having diuretic, emmenagogue, and cooling, demulcent, properties. Fruit has been used for several centuries to treat kidney disorders such as kidney and bladder stones, painful and burning micturition, ulcers in the urinary tract, suppression of urine and to treat cough, hot inflammation of the liver, liver and bile obstruction, eczema, etc. The oil from seeds is said to be very nourishing and contains linoleic acid (60-70%), lecithin, cephalin and cerebroside isolated from seed oil. The seeds of melon contain multiflorenol, isomultiflorenol, and 24-methylenecycloartenol. Its antimicrobial, antioxidant, anti-hyperlipidemic, anti-inflammatory, analgesic, diuretic, anthelmintic, nephroprotective and cytotoxic activity, Analgesic and Anti-inflammatory Activity, Anti-oxidant and free radical scavenging activity, Anti-Vitiligo Effect, Anti-ulcer activity, Anti-cancer activity, Hepato-protective activity, Diuretic effect, Protects against Hypothyroidism, Anti-diabetic activity, Haemagglutination and Haemolysis, Antibacterial and Anthelmintic activity, Antimicrobial activity, Antifungal, Nematicidal have been proved by research studies.

Keywords: Tukhm-e-Kharpaza; *Cucurbitaceae*; Diuretic

Abbreviations: TPC: Total Phenolic Compounds; BAL: British Anti-lewisite; EDTA: Ethylene Diamine Tetra Acetic Acid; SOD: Superoxide Dismutase.

Introduction

Cucumis melo Linn. is a well-known plant of Cucurbitaceae indigenous and largely cultivated in India,

particularly in hot, dry, North-Western areas, Northern Bengal, Kashmir and Afghanistan [1-3]. There are 40 species of herbs under this genus; seven species are native to India. It is a perennial trailing herb and distributed throughout India [4]. Plants are soft and hairy, leaves are round-ovate, obtuse, lobed or divided, angled and tendrils are simple. The plants of cucurbitaceous family are monoecious or with both male and female flowers. Flowers are yellow, 2.5 cm in diameter. Fruits are globose to oblong or slender and curved or coiled, pubescent and flavoured with musky scent [5].

Taxonomical Classification

Kingdom: Plantae
 Class: Magnoliopsida
 Order: Cucurbitales
 Family: Cucurbitaceae
 Genus: Cucumis
 Species: Cucumis melo Linn.

Vernaculars

Arabic- Battikh, **Bengali-** Kharmuj; **Bombay-** Kharabuja, Chibuda, Kakadi, Kharbuja, Kharbuj; **Cannada-** Kalingada; **Chinese-** Kankua, Then kwa, Hiang-kwa, Tien Kua; **English-** Sweet melon, Musk melon, Melon; **French-** Cantaloup, Melon; **German-** Melonegurke, Melone; **Gujarati-** Turbuch, Kharbuja, Teti, Chibdu, Shakarateli, Tarbucha; **Hindi-** Khurbuza, Sakkarteli, Kharbuja, Kachra, Patkira, Phut, Tuti, Kharbuza, Kakni, Kakri; **Latin-** Cucumis melo; **Madras-** Mulam; **Marathi-** Kharbuja, Khurbuj, Valuk, Chibunda, Kharbuja; **Persian-** Kharbuzeh, Kharpaza; **Punjabi-** Kharbuja, Gilas, Girasa; **Russian-** Melon; **Sanskrit-** Kalinga, Kharvuja, Kharbuja, Madhupaka, Amritavha, Dashangula, Karkati, Madhupaka, Madhuphala, Phalaraja, Shadbhuja, Shadrekha, Tikta, Tiktaphala, Vrittakarkatti, Vrittervaru; **Sindhi-** Gidhro; **Tamil-** Vealapalam, Vellari-verai, Mulampazham, Mulam; **Telugu-** Velipanda, Kharbuzadosa, Putzakova, Velipandu, Mulam; **Unani-** Khafis; **Urdu-** Kharbuzah [2,3,6-14].

Morphology

Cucumis melo Linn. is an annual herb with stems creeping, angular, scabrous, leaves about 7.5 cm in diameter, orbicular-reniform in outline, 5-angled or lobed, scabrous on both surfaces and also often with soft hairs, lobes neither deep nor acute, petiole 5 cm, petals are 1.6 cm long. Female peduncles are sometimes 5 cm [10]. Flowers yellow, monoecious, males clustered in the axila, female solitary, all shortly peduncled. Male: calyx-tube top-shaped or campanulate, 5lobes, 3 stamens; free anthers, one 1-celled, or two 2-celled, cells conduplicate or

much flexuose, connective produced in a crest. Female: Calyx and corolla as in the male flower; ovary ovoid, style short, with three obtuse stigmas, many ovules, horizontal, 3placentas [15]. Fruit is spherical, ovoid, elongated or contorted, glabrous or hairy, not spinous nor tuberculate [10].

Macroscopic

Fruits 15x10 cm White, Flat, Oblong, longitudinal stripe, Apex and Base blunt narrow at the tip [1]. The seeds are oval-oblong, cream coloured, about 10 mm long and 2 mm wide, laterally flattened having a smooth outer surface. Seeds one end broader but tapering at the other exalbuminous with prominent cotyledons. Seeds have sweet taste but no odour and ten seeds weigh about 0.29 gram in average [16].

Microscopic

Cross section of seed shows the outer test which is bounded externally by epidermis, made up of characteristic palisade cells but with pointed unbranched ribs, often only the ribs are present. Immediately within the epidermis are several layers of pitted stone cell. This region is terminated internally by single layer relatively thin walled lignified pitted cells. The rest of the testa consists of spongy cells. Perisperm consists of 3 or 4 layers of small cells, the other most layer of which is of regular cells having thickened fatty walls. Endosperm is in form of single layer of thin walled cells having oil drops and aleurone grains. Embryo is also parenchymatous and cell rich in oil drops and aleurone grains [16].

Geographical Distribution

It is found throughout the world [16], but popular as native of Africa, extensively cultivated in India, chiefly in hot, dry, North-Western areas [1], particularly in Uttar Pradesh and Punjab [17].

Description According to Unani Literature

It is creeper having rough surface, leaves are round in shape, flowes are of different shapes and colours, plant commonly found in India and Pakistan [18]. Galen mentioned *Cucumis melo* as Qissa Nazeej (Pukhta kakdi/Mature cucumber). Descorides mentioned *Cucumis melo* with the name of flush and said that it is found in different shape, colour and size depending upon the geographical locations. He further described its various name for example- Bukharai, Samarqandi and Darabi. He mentioned that Garmak and bapaza are its best and medium varieties respectively [13].

Parts Used

Seed [12]; Fruit [13].

Temperament (Mizaj)

Hot (1^o) and Wet (2^o) [7,11,13,14,18-21], Hot (2^o) and Wet (1^o) [22,14], Hot (1^o) and Wet (1^o) [14], Hot (2^o) and Wet (2^o) [13], Cold (2^o) and Wet (2^o) [8,23].

Doses

2-6 gram [19], 6.79-16.99 gms [21], 5-7 gram [7], 8.73 gm [14,22], 7-17gm [13].

Adverse Effect

Spleen [13-15,19,20], Cold temperament [13,19,21], Excessive use may cause Cholera [13,24].

Correctives

Honey [13,19,20,25], Honey and Banafsha [14,19,22], (*Viola odorata*) Zarishk (*Berberis Vulgaris*) [13,21], Shahad (Honey), Banafsha (*Viola odorata*) [21], Saunf (*Foeniculum vulgare*) Sikanjabeen and Honey [14], Filfil siyah (*Piper nigrum*) [26].

Substitute

Tukhm-e-Khayarein (*Cucumis sativa*) [19,21], Badam Shireen (*Prunus amygdalus*), Chilgoza (*Pinus geradiana*) [14,19,21,22].

Pharmacological Action (Afa'al)

Lithotriptic (*Mufattit-e-Hasat*) [18,26], Demulcent (*Mulattif*) [9,10], Diuretic (*Mudirr-e-Baul*) [1-3,8,10,11,14,17,18,20,22,24,26], Emmenagogue (*Mudirr-e-Haiz*) [14,18,22,26], Purgative (*Mushil*) [3], Cooling (*Mubarrid*) [1,2,9,10,17], Relaxant (*Murkhi*) [2], Tonic (*Muqawwi*) [3,4,10], Laxative (*Mulaiyyin*) [10,19], Nutritive value (*Mughazzi*) [1,4,6,9,10,14,17,18], Aphrodisiac (*Muqawwi-e-Bah*) [10,27-29], Lactagogue (*Muwallid-e-Laban*) [19,11,13,14], Cardio tonic (*Muqawwi Qalb*) [10], Nervine tonic (*Muqawwi Asaab*) [10], Astringent (*Qabiz*) [10], Liver deobstruent (*Mufatteh sudad-e-jigar*) [8,13,14,18,21,22,26], Anti ulcer (*Nafe Quruh*) [20], Stomachic (*Muqawwi-e-Meda*) [4], Sedative (*Musakkin*) [4], Emetic (*Muqi*) [3,8,25,14], Detergent (*Jali*) [13,18], Quenching Thirst (*Musakkin-e-Atsh*) [24].

Medicinal Uses (Mahalle Istemal)

Acute and Chronic Eczema (*Haad wa Muzmin Naar-e-Farsi*) [10,1,3], Freckles (*Namash*) [8,14], Dyspepsia (*Zoaf-e-Hazm*) [10], Epilepsy (*Sar'a*) [3], Prickly Heat (*Hasf*) [8], Burning micturition (*Hirqat-ul-Baul*)

[5,8,10,13,14,21,22,26], Urinary infection (*Tadiya Majariy-e-Baul*) [3], Kidney and Bladder stone (*Sang Gurda wa Masana*) [8,13,26], Anuria (*Ehtebas-e-Baul*) [8,10,17,26], Amenorrhoea (*Ehtebas-e-Haiz*) [8,26], Ophthalmia (*Iltihab-e-Ain*) [10], Bronchitis (*Iltihab-e-Sho'abtur Riya*) [10,29], Sore throat (*Khashunat-e-Halaq*) [8,13,21], Hepatitis (*Warm-e-Jigar*) [8,10,18,19,21,28], Fever (*Humma*) [9,10,13,18,19,23,29], Cough (*Su'al*) [8,13,19], Thirst (*Atash*) [10,23], Insanity (*Junoon*) [10], Ascites (*Istisqa*) [10,13,14], Allays fatigue (*Thakan*) [10], Headache (*Sud'a*) [3,10], Chest pain (*Waja-al-Sadr*) [8,19,21], Cirrhosis of the liver (*Talaiyyuf-e-Kabid*) [28], Gonorrhoea (*Sozak*) [9,18,21], General debility (*Zoaf-e-Umoomi*) [9], Cholasma (*Jhaiyan*) [14,19], Jaundice (*Yarqan*) [11,13,14,18,28], Constipation (*Qabz*) [3,11,19], Indigestion (*Sue Hazm*) [3], Renal stone (*Hasat-e-Kuliya*) [14], Ulcers (*Quruh*) [29], Dermatitis (*Iltehab-e-Jild*) [29], Strangury (*Taqteer-ul-Baul*) [10,18].

Important Formulation

Banadiq-e-buzoor, Sharbat-e-buzoori [18,26], Qurs-e-Sartan kafoori, Majoon-e-Kaknaj[30], Qurs-e-Kafoor, Qurs-e-Sartan, Sharbat-e-Mudir, Lubub-e-barid, Majoon-e-Hajrul Yahood [31].

Phytochemistry

Protein content of seed meal 49.93% amino acid composition also determined [32]. Fixed oil, starch, resin and sugar [9]. Sulphur compounds (mostly thioesters) are responsible for the characteristic aroma of the fruit. 3-Methylpropanenitrile originating from 2-methyl-thioethyl glucosinolate through the action of myrosinase activity of myrosinase activity in fruit because of 3-methyl propanenitrile. This activity seems to increase with the maturation of the fruit [29]. The melon contains elaterin or melotoxin and cucurbitacins B and E. The seeds contain melonin and some trypsin-inhibitors, CMeTI-A and CMeTI-B. Recently, a special protein, cucumisin, has been isolated from the juice of the melon fruit [28]. Total kernel lipids contained neutral lipids (91.5), glycolipids (6.4) and phospholipids (2.1%). Neutral lipids consisted mostly of triacylglycerols (90.7%). Monoand diacylglycerol identified as major glycolipids, and phosphatidylcholine and phosphatidylglycerolamine as major phospholipids [33]. The research on *C. Melo* suggested that the regulation of sugar metabolism differs between oriental melons and other types of melons. The KEGG pathway results and DEG analysis in the study suggest that genes involved in the glucose and fructose metabolic pathways were up-regulated early during fruit development (8 DAP), which is consistent with the previous results. The genes involved in sucrose

synthesis were activated early in fruit development and subsequently down-regulated from 16 DAP to 32 DAP [34]. The main fatty acids identified so far were linoleic, oleic, palmitic and stearic acids with respective contents 60.1%, 25.3%, 10.1% and 4.5%. Mineral analysis revealed significant levels of potassium, magnesium, calcium and sodium, namely 509.80, 101.71, 55.39 and 41.17 mg/100g respectively [35]. Terpenoid profile of *C. melo* Linn. was elucidated using high performance thin layer chromatography (HPTLC). The R_f value of the different compounds present in the extract was found to be 0.06, 0.21 and 0.93 of peak 1, 2 and 3 respectively. Among them, peak 1 was found to be terpenoid compounds. *C. melo* fruit extract showed the presence of terpenoids and it was confirmed from the chromatogram after derivatization [36]. The effect of freeze-drying on the antioxidant compounds and antioxidant activity tests showed that there were no significant ($p < 0.05$) differences found between the fresh and freeze-dried fruit of muskmelon in the amounts of total phenolic compounds (TPC) and change observed in the ascorbic acid content [37].

The methanolic extract of the seeds of *C. melo* L. var. *reticulatus* afford three new chromone derivatives; 5, 7-dihydroxy-2-[2-(4-hydroxyphenyl)ethyl] chromone, 5, 7-dihydroxy-2-[2-(3,4-dihydroxyphenyl)ethyl] chromone and 7-glucosyloxy-5hydroxy-2-[2-(4-hydroxyphenyl)ethyl] chromone, together with three known compounds; beta-amyrin, beta-sitosterol and beta-sitosterol-3-O-beta-glucopyranoside [38].

A new phenolic glycoside (E)-4-hydroxycinnamyl alcohol 4-O-(2'-O-β-D-apiofuranosyl) (1"→2')-β-D-glucopyranoside was isolated and identified from *Cucumis melo* seeds together with benzyl 0-β-D-glucopyranoside, 3, 29-O-dibenzoylmultiflor-8-en-3α, 7β, 29-triol and 3-O-p-amino-benzoyl-29-O-benzoylmultiflor-8-en-3α, 7β, 29-triol [39].

21 cucurbitane-type triterpenoids, including 9 new compounds and 12 known compounds were isolated and identified from the stems of *Cucumis melo*. 2 known compounds, cucurbitacin-B and cucurbitacin-A showed significant cytotoxic activity against the proliferation of A549/ATCC and BEL7402 cells in vitro. Out of 9 new compounds, only compound 7 were weakly cytotoxic [40].

Pharmacological Studies

Analgesic and Anti-inflammatory Activities

The methanolic extract of *C. melo* seeds possesses potent analgesic property. Carrageenin induces accumulation of leukocytes in the pleural cavity, as well as

the enhancement of LTB₄ levels in pleural exudates after inflammatory stimulus. Migration of neutrophils to the affected area constitutes an important pro-inflammatory factor, as they liberate toxic oxygen radicals in the extracellular medium. *C. melo* inhibited the leukocyte influx and diminished LTB₄ levels, thereby producing anti-inflammatory effect [41].

Anti-Oxidant And Free Radical Scavenging Activity

The methanolic extract of cantaloupe has shown DPPH and hydroxyl radicals scavenging activity. This activity of cantaloupe extracts is particularly due to the presence of phenolic compounds especially flavonoids. High antioxidant activity was observed in the leaf and stem extracts of cantaloupe [42]. The methanolic extract of the seeds has the highest DPPH radical scavenging activity than methanol extracts of leaf, stem, skin and flesh of the melon. The high antioxidant activity of the water and methanol-water extract may be due to the high amounts of caffeic acid present in these extracts [43]. Differential *CmADHs* expression suggested tight adaptation of the fruit to the developmental events [44].

Anti-Vitiligo Effect

An open observational study to evaluate the efficacy and safety of the investigated product containing phenylalanine, *C. melo* extract and acetyl cysteine, given alone or in combination with 311-nm narrow band microphototherapy, excellent repigmentation (>75%) was achieved by 38-73% of patients, depending on the treatment regimen. Mild to moderate side effects were observed only in patients treated with clobetasol 0.05% ointment. The tested gel formulation showed a good efficacy in improving vitiligo repigmentation. No side effects were observed [45].

Anti-Ulcer Activity

The methanolic extract of *C. melo* seeds exhibited anti-ulcerogenic activity. The mechanism of its gastro-protective activity may be attributed to reduction in vascular permeability, scavenging of free radicals and diminished lipid peroxidation along with strengthening of mucosal barrier. Presence of phytoconstituents, triterpenoids and sterols are responsible for these actions [41].

Anti-Cancer Activity

Cucurbitacins are extremely oxygenated tetracyclic-triterpenes, primarily establish in the cucurbitaceae

family. Cucurbitacin B is an anticancer (oncogenic) agent naturally isolated from the stems of *C. melo*. In human leukemia cells, the anti-cancer activity of cucurbitacin B has been reported. Cucurbitacin B inhibit Raf/MEK/ERK and STAT 3 activation pathway in leukemia cell line K562. Cucurbitacin A along with cucurbitacinE also own major anti-tumour activity [40]. Significant reduction in odd ratio (95%) was seen with consumption of melon [3].

Hepato-Protective Activity

The dried pedicel of *C. melo* L. has been observed to improve hepatic function and to increase gluconeogenesis. It has a protective effect against CCl₄ intoxication. It is used to treat toxic and chronic hepatitis, jaundice and cirrhosis of liver [46].

Diuretic Effect

The ether extract of seeds (0.5 ml/kg bw, i.v.) in dogs caused diuresis by increasing the glomerular filtration rate and also by interfering with the reabsorption of chloride and possibly sodium ions in the tubules. Further, the diuretic as well as chloruretic activity of the extract was antagonised by the compounds like BAL (British anti-lewisite), and EDTA (Ethylene diamine tetra acetic acid). The mechanism of the action may be similar to mercurial [3]. *C. melo* at a dose 400mg/kg showed an extremely significant ($p < 0.0001$) diuretic effect compared to the positive control Furosemide. *C. melo* possessed more diuretic activity when compared to the standard (Furosemide) [47].

Gentamicin treated group showed increased levels of blood urea nitrogen and serum creatinine, which were significantly retrieved in group pretreated with methanolic extract of *C. melo* (ME-CM) seed kernel. The level of superoxide dismutase, catalase, glutathione peroxidase and reduced glutathione were increased with decrease in malondialdehyde content in ME-CM pretreated group when compared with gentamicin alone treated group. The histopathological analysis also showed the protective nature of ME-CM in gentamicin-induced renal damage [48].

Protects Against Hypothyroidism

Administration of 3 test fruit peel extracts (*M. indica*, *C. vulgaris* and *C. melo*) significantly increased both the thyroid hormones (T₃ and T₄) with a concomitant decrease in tissue lipid peroxidation, suggesting their thyroid stimulatory and antiperoxidative role. This thyroid stimulatory nature was also exhibited in propylthiouracil induced hypothyroid animals [49].

Anti-Diabetic Activity

The ethanolic extract of plant in a dose of 250mg/kg p.o. did not lower the blood sugar level in streptozotocin-induced diabetic male albino rats [3]. Although the fruit peel extracts of *C. melo* reversed the CCT-diet (supplemented with 4% cholesterol, 1% cholic acid and 0.5% 2-thiouracil) induced increase in the levels of tissue lipid peroxidation, serum lipids, glucose, creatinine kinase-MB. Furthermore, Musk melon increased the levels of thyroid hormones and insulin indicating their potential to ameliorate the diet induced alterations in serum lipids, thyroid dysfunctions and hyperglycemia/diabetes mellitus. These beneficial effects could be due to the rich content of polyphenols and ascorbic acid in the peel extracts [49]. Oxykine is the cantaloupe melon extract rich in vegetal superoxide dismutase (SOD) covered by polymeric films of wheat matrix gliadin. The treatment of oxykine ameliorated the progression and acceleration of diabetic nephropathy in type-2 diabetic rodents. The oxykine reduced the diabetes induced oxidative stress and renal mesangial cell injury. Oxykine might be a novel approach for the prevention of diabetes nephropathy [50].

Haemagglutination and Haemolysis

The lectins from the seeds, when tested for haemagglutinating activity with erythrocytes of human, rabbit, cow, sheep, guinea pig, dog, monkey, chicken, horse, goat and pig haemolysed the red cells of rabbit, dog and monkey only [3].

Antibacterial and Anthelmintic Activity

The seeds growing on cattle dung heaps showed inhibition of the spores of *B. subtilis*, *E. coli*, *P. cichorii* and *S. Typhi* (Anonymous, 2009). The n-hexane and methanolic extracts of the seeds of *C. melo* L. have shown good antimicrobial and anthelmintic activity [38].

Antimicrobial Activity

The aqueous, heptane, petroleum ether and acetone extract of the whole plant of *C. melo* Linn, *P. daemia* Frosk. (Asclepiadaceae) was screened for the antibacterial and antifungal activity by highest Zone of Inhibition was shown by whole plant and fruit extract of *C. melo* Linn with aqueous and acetone with *C. albicans* and *E. coli* 08 and 12 mm respectively. Very poor response was observed with acetone and aqueous extract in other bacterial and fungal stains. Highest zone of inhibition was shown by whole extract of *Pergularia daemia* with heptane with *E. coli* and *C. albicans*, 16 and 21 mm respectively [51].

Antifungal Activity

The aqueous and ethanolic extract of the fruits were found to be devoid of antifungal activity against *A. niger* and *T. rubrum*. The oil cake inhibited mycelial growth of *Rhizoctoniasolani* causing stem rot of chilli [3].

Nematicidal Activity

The seed extract showed concentration dependent mortality of *Meloidogyne incognita* and *R. Reniformis* [3].

Anti-Angiogenic Activity

In this study, the purified trypsin inhibitor from *Cucumis melo* seeds using a procedure and the effectiveness of its anti-angiogenic activity on three dimensional cultures of HUVECs was determined. *C. melo* seeds are rich in urease, lipase, lipoxygenase and trypsin inhibitor which is considered for their enzyme inhibitor activities. Treatment with TICMS at six doses resulted in a significant decrease of endothelial cell proliferation with an IC₅₀ value of about 20 µg/ml [52].

Nutritive Value

The study revealed that melon (*C. melo* L. *Inodorus*) seeds are an important source of minerals, namely K, Ca and Mg. Magnesium is showing increasing interest for the adequate heart function; its presence would be taken advantage of for people with limited resources. Moreover this oil showed interesting amounts of unsaturated fatty acids as compared to other known edible oils. As nutritionists generally recommend a Mediterranean diet especially for cardiovascular concerns, melon seeds oil could be taken advantage of for its content of both linoleic and oleic acids palmitic and stearic acids with respective contents 60.1%, 25.3%, 10.1% and 4.5%. are food supplements to improve health conditions [35].

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