Semen Cucurbitae

Definition

Semen Cucurbitae consists of the dried seeds of *Cucurbita pepo* L. (Cucurbitaceae) or its cultivars (*1–3*).

Synonyms

Cucurbita aurantia Willd., *C. courgero Ser.*, *C. esculenta* Gray, *C. fastuosa* Salisb., *C. melopepo* L., *C. ovifera* L., *C subverrucosus* Willd., *C. verrucosus* L., *Pepo melopepo* Moench., *P. verrucosus* Moench., *P. vulgaris* Moench. (*4*, *5*).

Selected vernacular names

Abobora, bitter bottle gourd, bucka, calabaza, cubini, duraffere, dubba, dynia, étkezési tök, Garten-Kürbis, geonwomu, ghia kaddu, giramonte, giraumon, gourd, græskar, guicoy, harilik kõrvits, herkules-keule, jerimum, kadu, kadu I maghrebi, kadu I rumikao montini, kaula, kurlaru, kumra, lob-abyad, lob-kar-e-asal, malange, mandelgræskar, marrow, navadna buca, ntite, ntsuudya, pepokabocha, pompion, pompoen, pottaigummadi, pumpkin, qar, qar maghrebi, qar rumi, qara'a, safed kaddu, Schmuckkürbis, shada kumra, summer pumpkin, uritök, zapallo, zapayo, zerri at l-ger-a, zucca indi, zucchette, zucchini (*6–8*).

Geographical distribution

Native to North America and cultivated worldwide (*4*, *9*, *10*).

Description

Annual, running, monoecious herbs with dark green, non-glossy, 3–5 lobed leaves; prostrate or climbing; branched, prickly stems, up to 10 m long. The solitary flowers are large and yellow being arranged singly in the axils of leaves; the male flowers have a peduncle of 10–17 cm, a calyx with very small sepals, a campanulate deep yellow corolla (7–10 cm in diameter) gradually widening towards the top. Calyx lobes are narrow. Female flowers are similar to the male ones, but with a shorter peduncle, small stamin-

odes, and inferior ovary of various shapes. The gourd-fruit varies in size (15–40 cm in diameter) and shape in the many cultivated varieties, and the toughened, furrowed peduncle does not enlarge near it (*4*, *10*).

Plant material of interest: dried seeds

General appearance

The seeds are ovate, constricted at one end forming a short, blunt extension; flat or weakly biconvex; up to 25 mm long and 8–14 mm wide, 3–4 mm thick; on both faces, close to the edge, is an encircling ridge and groove, 1–2 mm wide, absent from projection; testa creamy-white to pale beige with a satiny sheen, smooth or with irregular wrinkles; texture brittle, somewhat papery; inner surface of seed coat fawnish-white, dull, rough or scurfy. The seed is non-endospermic. Embryo easily separated from testa, more or less entirely covered in a dark olive-green pellicle, with metallic lustre; light patches of inner seed coat may be adherent. Embryo pale greenish-yellow, oily; large, almost flat cotyledons, small conical radical at constricted end of seed; inner surfaces of cotyledons with three or five rudimentary veins, palmately arranged (*11*).

Organoleptic properties

Odour: indistinct; taste: bland, oily and slightly nut-like (*2*, *10*).

Microscopic characteristics

Epidermal cells of testa erect, prismatic, up to 200 µm long; walls thin, bearing slender vertical strips of thickening, usually sinuous in upper portion; in surface view polygonal, large with conspicuous beads; starch grains abundant, up to 5 µm, simple but frequently clumped; a band, about six cells deep, of small, thin-walled, isodiametric or small, elongated parenchymatous cells, finely reticulately thickened and strongly lignified; a few larger, irregular simple pits; a single layer of large, sub-rectangular sclereids, lumen narrow, ovoid, walls very thick and conspicuously layered, pits few and not well-defined, only middle lamella and primary wall strongly lignified; in surface view the sclereids are somewhat elongated and the anticlinal walls deeply sinuous. Internal to the sclereid band several layers of progressively larger lignified parenchymatous cells with very fine reticulate thickening; the cells, having short arm-like projections, form a spongy, lacunose tissue; areas of contact between branches of cells have quite large simple perforations. Innermost layers less well-defined, parenchymatous, largest cells internally; greenish chromoplasts present. Cotyledon cells variable, very thin-walled, containing oily globules and aleurone grains up to 4 µm in diameter (*2*).

Powdered plant material
To be established in accordance with national requirements.

General identity tests

Macroscopic and microscopic examinations (*2*, *4*, *10*), and thin-layer chromatography (*2*).

Purity tests

Microbiological
Tests for specific microorganisms and microbial contamination limits are as described in the WHO guidelines for assessing quality of herbal medicines with reference to contaminants and residues (*11*).

Foreign organic matter
Not more than 1% (*1*).

Total ash
Not more than 7% (*2*).

Acid-insoluble ash
To be established in accordance with national requirements.

Water-soluble extractive
To be established in accordance with national requirements.

Loss on drying
Not more than 12.0% (*1*).

Pesticide residues
The recommended maximum limit of aldrin and dieldrin is not more than 0.05 mg/kg (*12*). For other pesticides, see the *European pharmacopoeia* (*12*) and the WHO guidelines for assessing quality of herbal medicines with reference to contaminants and residues (*11*) and pesticide residues (*13*).

Heavy metals
For maximum limits and analysis of heavy metals, consult the WHO guidelines for assessing quality of herbal medicines with reference to contaminants and residues (*11*).

Radioactive residues
Where applicable, consult the WHO guidelines for assessing quality of herbal medicines with reference to contaminants and residues (*11*).

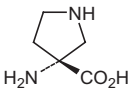
Chemical assays

To be established in accordance with national requirements.

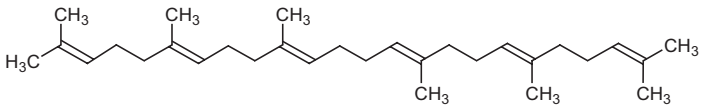
Major chemical constituents

Major constituents of the seed include a fixed oil (30–53%), phytosterols (1%) and terpenes. The main fatty acids found in the fixed oil are linoleic acid (35–68%) and oleic acid (15–48%). Squalene is a characteristic constituent and accumulates in the non-saponifiable fraction of the oil to a concentration of 39–46%. The primary phytosterols are Δ^7-sterols including spinasterol, α-spinasterol, Δ^7-avenasterol, Δ^7-ergostenol and Δ^7-stigmastenol, together with smaller amounts of Δ^5-sterols (e.g. campesterol, stigmasterol, clerosterol and isofucosterol). Rare amino acids, including γ-aminobutyric acid, ethylasparagine, citrulline and cucurbitine (3-aminocarboxypyrrolidine) are also found (*4*, *6*, *14*). Structures of the potential markers, squalene and cucurbitine are presented below.

Cucurbitine



Squalene



Medicinal uses

Uses supported by clinical data

For symptomatic treatment of difficulties with micturition associated with stage I–II prostatic adenoma and irritable bladder (*15–17*).

Uses described in pharmacopoeias and well established documents

No information was found.

Uses described in traditional medicine

Used for the treatment of asthma, burns, constipation, eczema, fever, tapeworms and toothache (*4*, *6*).

Pharmacology

Experimental pharmacology

Anti-androgenic activity

A supercritical carbon dioxide extract of the seeds (dose not stated) antagonized the development of the prostate gland when administered with

testosterone in castrated rats (*4*). A sterol mixture isolated from the seeds dose-dependently inhibited the binding of labelled dihydroxytestosterone to cultured human prostate fibroblasts. Following preincubation of one sample of the fibroblasts with 120 ng of sterol mixture and another with 240 ng of the mixture, dihydroxytestosterone binding was reduced from 68.3% to approximately 47% in the first sample and from 68.3% to 38% in the second (*4*).

Anthelminthic activity

A dried methanol extract of the seeds administered orally to mice, at a dose of 20.0 mg/kg body weight (bw), for 3–4 days had weak activity against *Hymenolepis diminuta*, inducing a 37% clearance of worms in 6 days (*18*). Cucurbitine (3-aminocarboxypyrrolidine) is reported to be one of the most actively anthelminthic constituents of the crude drug (*4*).

Anti-inflammatory activity

The anti-inflammatory effects of intragastric administration of the seed oil to rats with arthritis induced by Freund's complete adjuvant, at a dose of 100 mg/kg bw (*19*), were compared with the effects of indometacin, a classical anti-inflammatory agent. Two models of inflammation were investigated. In the acute inflammatory phase model only seed oil was used, and in the chronic inflammatory phase model both seed oil and indometacin were used. Treatment with the seed oil normalized blood glutathione and serum *N*-acetyl-β-D-glucosaminidase levels, which were elevated in the acute phase of inflammation. Plasma total proteins and albumin, which were reduced during the chronic phase of inflammation, were increased after treatment. Liver glucose-6-phosphate dehydrogenase activity, which was markedly increased during the induction of inflammation, was also reduced after treatment. Also, a remarkable inhibition of paw oedema was observed. A similar pattern was noted following treatment with indometacin (*19*).

Intragastric administration of a supercritical carbon dioxide extract of the crude drug (dose not stated) reduced carrageenan- or dextran-induced oedema in castrated rats (*4*).

Antischistosomal activity

Oral administration of 3.0 g of the seeds daily to mice for 28 days reduced the number of *Schistosoma japonicum* parasites (*20*).

Inhibition of 5α-reductase

The effect of an extract of the seeds on the activity of 5α-reductase, the enzyme responsible for the conversion of testosterone to dihydrotestosterone, was assessed in vitro in cultured human prostate fibroblasts (*4*).

The extract inhibited the activity of the enzyme with a median inhibitory concentration of 128 µg/ml. The affinity of the extract for the dihydrotestosterone receptors was very weak.

Clinical pharmacology

A 12-month randomized, placebo-controlled, multicentre study assessed the efficacy of a 92% ethanol extract of the seeds (15–25:1) in 476 men with benign prostatic hyperplasia stages I and II (mean age 63 years) (*15*). The men were treated with two capsules (500 mg extract per capsule) of the extract (n = 233) or placebo (n = 243) for 12 months. One capsule of the active treatment contained 500 mg pumpkin seed extract (15–25:1, 92% ethanol w/w). The outcome measured was a change in the International Prostate Symptom Score (IPSS). The median baseline IPSS for the placebo group was 17.7 and that for the treatment group was 17.6. A mean reduction of the IPSS of 6.8 in the treatment group and 5.6 in the placebo group (p = 0.014) was reported. A decrease in the IPSS by > 5 points was reported in more patients in the treatment group than in the placebo group, 65% versus 54% (p = 0.021). Urological flow parameters, quality of life, residual urine, prostate volume and prostate-specific antigen remained unchanged in both groups (*15*).

In a 3-month open multicentre study involving 2245 patients with benign prostatic hyperplasia stages I and II according to Alken, the effects of a seed extract (15–25:1, 92% ethanol w/w) were assessed (*22*). Patients were treated with 1–2 capsules of the extract (500 mg per capsule). The results of this study demonstrated an improvement in the IPSS by 41.4% and in quality of life by 46.1%. Micturition (average number of times patients urinated) decreased during the day from 6.7 to 4.8, and at night (nocturia) from 2.7 to 1.1.

In an open study involving 79 male patients with benign prostatic hyperplasia, treatment with the seed fixed oil (dose not specified) reduced the amount of residual urine and led to better bladder emptying and greater volume of emptying after 12 weeks of treatment (*22*).

In a 3-month multicentre open study involving 39 women and 19 men with irritable bladder, patients were treated with 6 g of the crude drug three times daily for 8 weeks. Subjective symptoms such as polyuria and nocturia improved in more than 80% of patients (*17*).

In a study in men, a mixture of Δ^7-sterols, isolated from the crude drug, was administered to patients with benign prostatic hyperplasia. Patients received 90 mg of the mixture by the oral route on days 3 to 4 prior to prostatectomy. A significant decrease in the level of dihydrotestosterone in the prostate tissue was observed (p < 0.05), as well as a significant decrease in serum acid phosphatase (*23*). Oral administration of 30.0 g of the

seed to a single human volunteer decreased urine output, but increased urea and uric acid output over a 3-day period (*24*).

Toxicology
Intraperitoneal administration of an aqueous or aqueous alcoholic extract of the seeds to mice had a median lethal dose of > 5000 mg/kg bw (*25*).

Adverse reactions
Gastrointestinal disorders (heartburn, nausea, stomach ache and diarrhoea), allergic skin reactions and tinnitus.

Contraindications
Hypersensitivity or allergy to the crude drug.
Pregnancy: in traditional medicine, the crude drug has been used as an emmenagogue (*6*), thus extracts of the crude drug should not be ingested during pregnancy.

Warnings
No information was found.

Precautions
No information was found.

Pregnancy: non-teratogenic
See contraindications.

Nursing mothers
Due to the lack of safety data, extracts of the crude drug should not be used during breastfeeding.

Paediatric use
Due to the lack of safety data, extracts of the crude drug should not be used in children aged under 12 years.

Other precautions
No information was found.

Dosage forms
Crude drug and extracts.

Posology

(Unless otherwise indicated)
Oral daily dose: 10 g of seed; equivalent preparations (*16*).

References

1. *Deutsches Arzneibuch*. Stuttgart, Deutscher Apotheker Verlag, 1999.
2. *British herbal pharmacopoeia*. Exeter, British Herbal Medicine Association, 1996.
3. *PharmaMed: Aufbereitungsmonographien (Komm. E)* [CD-ROM]. Stuttgart, Deutscher Apotheker Verlag, 2002 [in German].
4. Bombardelli E, Morazzoni P. *Cucurbita pepo* L. *Fitoterapia*, 1997, 68:291–302.
5. *Hagers Handbuch der Drogen* [CD ROM]. Heidelberg, Springer Verlag, 2003 [in German].
6. Farnsworth NR, ed. *NAPRALERT database.* Chicago, University of Illinois at Chicago, IL (an online database available directly through the University of Illinois at Chicago or through the Scientific and Technical Network [STN] of Chemical Abstracts Services), 30 June 2005.
7. Nadkarni AK. *Dr. K.M. Nadkarni's Indian materia medica*. Bombay, Popular Prakashan, 1976.
8. Bedevian AK. *Illustrated polyglottic dictionary of plant names*. Cairo, Medbouly Library, 1994.
9. Wichtl M. *Herbal drugs and phytopharmaceuticals*, English ed. [Bisset NG, translated and edited]. Boca Raton, FL, CRC Press, 1994.
10. Youngken HW. *Textbook of pharmacognosy,* 6th ed. Philadelphia, PA, Blakiston Company, 1950.
11. *WHO guidelines for assessing quality of herbal medicines with reference to contaminants and residues.* Geneva, World Health Organization, 2007.
12. *European Pharmacopoeia*, 5th ed. Strasbourg, Directorate for the Quality of Medicines of the Council of Europe (EDQM), 2005.
13. *Guidelines for predicting dietary intake of pesticide residues*, 2nd rev. ed. Geneva, World Health Organization, 1997 (WHO/FSF/FOS/97.7).
14. Bruneton J. *Pharmacognosy, phytochemistry, medicinal plants*. Paris, Lavoisier Publishing, 1995.
15. Bach D. Placebokontrollierte Langzeittherapiestudie mit Kürbissamen-extrakt bei BPH-bedingten Miktionsbeschwerden [Placebo-controlled long-term study with pumpkin seeds in BPH-induced problems with micturition]. *Urologe* [B], 2000, 5:437–443.
16. Blumenthal M et al., eds. *The complete German Commission E monographs: Therapeutic guide to herbal medicines*. Austin, TX, American Botanical Council, 1998.
17. Nitsch-Fitz R et al. Ergebnisse einer Praxisstudie über das Kürbiskern-Diätetikum "Kürbis-Granufink" bei Patienten mit Miktionsbeschwerden

verschiedener Genese. *Zeitschrift für die Ärztliche Praxis,* 1979, 3:38–40 [in German].
18. Sharma LD, Bahga HS, Srivastava PS. In vitro anthelmintic screening of indigenous medicinal plants against haemonchus contortus (Rudolphi, 1803) Cobbold, 1898 of sheep and goats. *Indian Journal of Animal Research*, 1971, 5:33–38.
19. Fahim AT et al. Effect of pumpkin-seed oil on the level of free radical scavengers induced during adjuvant-arthritis in rats. *Pharmacological Research*, 1995, 31:73–79.
20. Chou HJ, Hu HK, Ch'iu TW. Prophylactic and therapeutic effect of pumpkin seed on *Schistosoma japonicum*. *Chinese Medical Journal*, 1958, 77:565.
21. Friederich M et al. Forte capsules in the treatment of benign prostatic hyperplasia. *Forschende Komplementarmedizin Klassische Naturheilkunde*, 2000, 7:200–204.
22. Sabo E et al. Pharmacodynamic effect of pumpkin seed oil (Oleum cucurbitae pepo) in patients with adenoma prostate. *Fundamentals in Clinical Pharmacology*, 1999, 13(Suppl 1):360.
23. Koch E. Pharmakologie und Wirkmechanismen von Extrakten aus Sabalfrüchten (Sabal fructus), Brennesselwurzeln (Urticae radix) und Kürbissamen (Cucurbitae peponis semen) bei der Behandlung der benignen Prostatahyperplasie. In: Loew D, Rietbrock N, eds. *Phytopharmaka in Forschung und klinischer Anwendung*. Steinkopff Verlag, Darmstadt, 1995.
24. Masurovsky B. Study of the effects of *Cucurbita pepo* seeds on kidney excretion. *Proceedings of the National Academy of Sciences*, 1922, 8:39–43.
25. Desta B. Ethiopian traditional herbal drugs. Part I: Studies on the toxicity and therapeutic activity of local taenicidal medications. *Journal of Ethnopharmacology*, 1995, 45:27–33.