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PHYTOCHEMICALS AND PHARMACOLOGICAL POTENTIALS OF CUCURBITA PEPO SEEDS: AN INTEGRATIVE REVIEW

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ABSTRACT :

Pumpkin (Cucurbita pepo) and its seeds are rich in bioactive compounds such as flavonoids, alkaloids, fatty acids, phytosterols, tocopherols, and essential minerals, which contribute to significant medicinal and nutritional benefits. Pumpkin seeds exhibit diverse pharmacological properties, including anti-inflammatory, antioxidant, antidiabetic, antimicrobial, anticancer, hepatoprotective, and cardioprotective effects. Advanced extraction techniques such as ultrasound, microwave, and supercritical CO_2 enhance the recovery of valuable phytochemicals. Their nutraceutical potential supports applications in managing conditions like diabetes, PCOD, cancer, and liver disorders. This review highlights phytochemistry, pharmacology, and formulation approaches of pumpkin seeds, underscoring their relevance in functional food development and modern herbal medicine.

KEYWORDS Pumpkin seeds, Cucurbita pepo, phytochemicals, pharmacological activities, extraction techniques, nutraceuticals.

INTRODUCTION

Pumpkin is one of the well-known edible plants and has substantial medicinal properties due to the presence of unique natural edible substances. It contains several Phyto-constituents belonging to the categories of alkaloids, flavonoids, palmitic, oleic and linoleic acids. Various important medicinal properties including anti-diabetic, antioxidant, anti-carcinogenic, anti-inflammatory and others have been well documented.

PUMPKIN SEED

Pumpkin seeds are also a good source of vitamin E. This vitamin in the seeds includes four tocopherol and tocotrienol isomers .The pumpkin seeds possess a significant amount of valuable minerals .The seeds are rich in potassium (K) and relatively lower in sodium (Na), high in calcium (Ca), manganese (Mn), phosphorus (P), and magnesium (Mg). Pumpkin seeds are also good source of trace elements such as zinc (Zn), iron (Fe), not to mention copper (Cu). Minerals such as Zn, Cu, Mn, and Fe possess antioxidant potential hence serve as cofactors of vital antioxidation-dependent bio catalyst .
Pumpkin seeds may be tiny, but they are densely packed with useful nutrients and nutraceuticals such as amino acids, phytosterols, unsaturated fatty acids, phenolic compounds, tocopherols, cucurbitacin and valuable minerals.
Bioactive compounds in pumpkin seeds exhibit promising activities such as anthelmintic, antidiabetic, antidepressant, antioxidant, antitumor and cytoprotective.
Pumpkin seeds also include the beneficial ω-3 fatty acids that can help control the elevated insulin and cholesterol levels associated with PCOD. They also include beta-sitosterol, which can reduce too much androgen and treat PCOD symptoms like hirsutism, acne, and weight gain.[1]

FIGURE NO.01
PUMPKIN SEEDS

FIGURE NO.02
PUMPKIN

MORPHOLOGICAL CHARACTERS

SYNONYM

Curcubitae Peponis Semen

BIOLOGICAL SOURCE

Pumpkin seeds are obtained from the dried, ripe seeds *Cucurbita pepo Linn.*

FAMILY

Cucurbitaceae

GEOGRAPICAL SOURCE

Pumpkin seeds are obtained from the pumpkin plant (*Cucurbita pepo*), which is native to North America.[2]

MACROSCOPIC FEATURES

COLOUR : Light yellow
ODOUR : Odourless
TASTE : Mildy nutty, slightly sweet
SHAPE : Flat and oval
SIZE : Length : 1.0 to 2.5 cm
Width : 0.5 to 1.5 cm

FIGURE NO:03

MACROSCOPIC FEATURES OF PUMPKIN SEEDS

MICROSCOPICAL CHARACTERS

EPIDERMAL CELLS

Elongated polygonal, thick-walled with straight anticlinal walls.

TRICHOMES

Absent or rarely unicellular hairs.

OILGLOBULES

Numerous, due to the high fixed oil content.

PARENCHYMAL CELLS

Contain aleurone grains and oil globules **.**

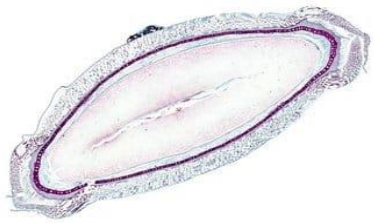

FIGURE NO:04

STONE CELLS **MICROSCOPIC CHARACTER OF PUMPKIN SEEDS**

Irregular, thick-walled, and lignified.[3]

MEDICINAL USES OF PUMPKIN SEED

- ❖ Anti-parasitic Activity
- ❖ Cardio-protective Effects
- ❖ Neuro-protective & Antidepressant Activity
- ❖ Anti-inflammatory & Antioxidant Effects
- ❖ Prostate Health
- ❖ Anti-diabetic Properties
- ❖ Weight Management & Metabolism
- ❖ Skin & Hair Health[4]

CHEMICAL CONSTITUENTS

Proteins, Amino Acid, Fatty Acid, Phytosterols, Tocopherols (Vitamin E), Minerals, Carotenoids, Phenolic Compounds, Alkaloids & Saponins, Cucurbitacin[5].

EXTRACTION METHOD

VARIOUS TECHNIQUES FOR THE EXTRACTION OF BIOACTIVES FROM PUMPKIN BY PRODUCTS

Extraction is the most important step, which is normally carried out with various solvents, acids, alkalis, and hydro distillation methods depending on the type of extracted component**.**

- Conventional Techniques
- Modern Extraction Techniques
  - → Ultra Sound Assisted Extraction
  - → Microwave Assisted Extraction
  - → Supercritical Fluid Extraction

CONVENTIONAL TECHNIQUES

One of the most often used methods is conventional extraction (CE). The effectiveness of extraction is influenced by the chemicals' volatility and solubility in the selected solvent. Carotenoids are fat-soluble in polar aprotic solvents (acetone, ethanol, acid acetic) or nonpolar solvents (ethyl acetate and benzene), whereas phenolic compounds are readily soluble in polar protic media (methanol, ethanol, and acetone). Traditionally, maceration, hydro-distillation, or Soxhlet extraction methods using organic or inorganic solvents are used to extract natural pigments. Conventionally, colours that are water soluble are extracted using water or diluted alcohol, whereas pigments that are lipophilic (such as methanol, acetone, or hexane) are extracted using non-polar solvents. Although most of them are toxic by nature, their volatile nature allows them to efficiently degrade target pigments, which facilitates removal. These solvents are hazardous for human consumption and can contaminate the environment, despite their technical advantages[7]. Traditional extraction techniques are not economically viable, require a long time to extract, consume a lot of energy, and have low extraction efficiency. Because of these problems, new environmentally friendly techniques are needed to facilitate effective extraction using green solvents made from renewable resources, like edible oils obtained from plants. A study looked at the effects of several techniques for extracting carotenoids from pumpkin pulp. For carotenoid extraction, the solid-to-solvent ratio (1:50, 1:100, and 1:150), extraction time (8, 12, and 16 hours), and temperature (15, 30, and 45 °C) were all optimized. Lycopene and β-carotene are examples of nonpolar solvents that are required to purify nonpolar carotenoids from pumpkin pulp.[8] Furthermore, it was shown that carotenoid synthesis was enhanced by raising the solid-to-solvent ratio to a maximum of 1:150.

MODERN EXTRACTION TECHNIQUES

The shortcomings of traditional methods have led to the introduction of new methods. The challenges of achieving high purity, the use of expensive solvents, lengthier extraction times, the possibility of heat-labile chemical degradation, and low extraction selectivity are the characteristics of traditional extraction processes. The extraction procedure is currently being carried out using a number of innovative and evolvingtechniques. These techniques are more common than conventional extraction methods because of their many benefits, which include the need for fewer solvents, speed, convenience, and the capacity to increase extraction output while preserving pigments from deterioration and enhancing the quality of natural colourants.

- **ULTRASOUND ASSISTED EXTRACTION**

Mechanical vibrations with an ultrasonic frequency higher than 20 kHz are used by UAE. This results in a cavitation effect, which accelerates the particles' mass and heat transmission, rupturing cells and permitting the release of chemicals. The qualities of the bioactives are better preserved when ultrasound is used during the extraction process. This method lowers the required temperature, speeds up the extraction process, and greatly increases extraction efficiency.[9] In contrast to traditional solvent extraction, the effectiveness of ultrasound-assisted extraction (UAE) technology. It is well recognized that the UAE approach can be used to assist in the extraction of carotenoids from natural sources because of its high efficiency, short extraction time, and simple and easy operation.

Trans-lutein and trans-carotenoids were produced in greater amounts by ultrasound-assisted extraction (UAE) than by the traditional solvent extraction technique.[10] This is because the UAE can stop the chemicals from degrading and isomerizing. The pumpkin peel investigation by employing conventional techniques to identify the best solvent for carotenoids extraction. They found that the best solvent was a mixture of petroleum ether and ethanol. To do this, researchers evaluated the effects of the main factors that influence the yield of carotenoids, such as extraction time, ultrasonic power, and liquid–solid.[10]

When compared to traditional extraction techniques, UAE produced a 92% higher yield with a carotenoid content of 363 μg/g at ideal conditions (203 W, 30 min, and a solvent-to-material ratio of 31mL/g). Sharma and Bhat separated carotenoids from the pulp and peel of two pumpkin cultivars using three different extraction methods (ultrasound-assisted extraction, microwave-assisted extraction, and conventional extraction) and maize oil as an environmentally friendly solvent[11]. It was also found that the amount of carotenoids differed according to the part of the plant, with the peel powder having more than the pulp powder. Total carotenoids were nearly twice as high using ultrasonic (38.03 ± 4.21; 33.78 ± 1.76 μg/g) as compared to traditional extraction (19.21 ± 4.39; 16.21 ± 2.52 μg/g)

The antioxidant capacity of pumpkin peel and identify the ideal extraction parameters for an ultrasonic-assisted extraction method to extract complete carotenoids.[12] For the extraction of carotenoids from pumpkin peel, the best conditions were 80 °C, 10 mL of solvent, and 100 minutes of extraction time. This led to an antioxidant activity of 7.25 μM TE/g D.W. and a carotenoid concentration of 0.97 mg/g D.W.

- **MICROWAVE ASSISTED EXTRACTION**

MAE is a technique that uses nonionizing electromagnetic radiation at microwave wavelengths between 0.3 and 300 GHz in conjunction with traditional solvent extraction. Due to the effects of ionic conduction and dipole rotation, the chemicals are then extracted by heating the entire sample at once. The method uses the material's ability to absorb radiation particle by particle. By using a solvent that is not polar and does not absorb microwave radiation, the sample is heated and the heat is transferred to the extractant. Because the extraction process is shortened and less solvent is used, the method is economical.[13] [14] During microwave heating, dipole particles move and use friction to produce heat energy.

Compared UAE, MAE, and the conventional method for recovering phenolic components from pumpkin seeds (Curcubita sp.) using ethanol and hexane as the extraction solvents. Under subcritical solvents (ethanol and water, 8.12 and 8.71 mg GAE/g, respectively), MAE produced the highest phenolic content and antioxidant activity with good extraction yields.[15] The extract made using subcritical ethanol, however, contained more phenols (83.95 mg GAE/g of extract) than the extract made with subcritical water (55.52 mg). These outcomes outperformed those from conventional extraction, with 3.93 mg GAE/g matrix and 42.42 mg GAE/g extract.

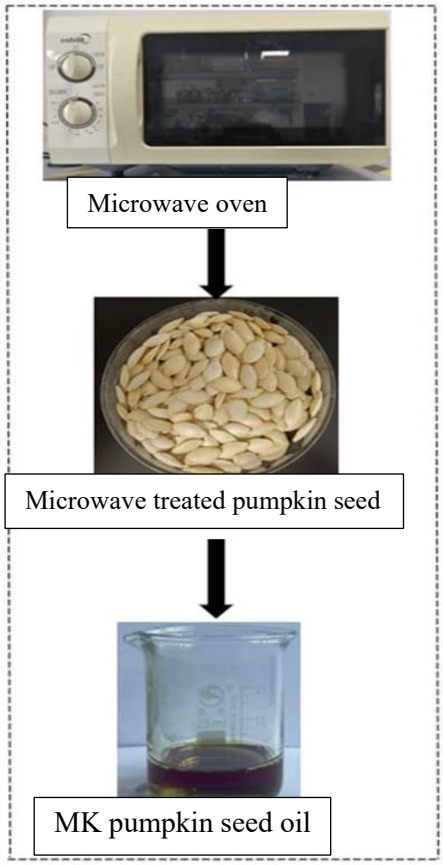

FIGURE NO:05

MICROWAVE ASSISTED EXTRACTION

- **SUPERCRITICAL FLUID EXTRACTION:**

Compared to the critical points of fluids like CO_2, water, methanol, ethanol, n-butane, and ethylene, SFE functions at higher pressures and temperatures. CO_2 is the most widely used supercritical fluid because it is inexpensive, easily accessible, highly pure, combustible, chemically inert, and recyclable. The main advantages of using supercritical CO_2 are low temperature and low pressure, which are essential for extracting natural chemicals, particularly those containing thermally unstable components. The extraction of thermolabile compounds can be done at room temperature and low pressure because the critical point for CO_2 is at 31.1 °C (304.2 K) and 7.3 MPa (72.8 bar).[16]

By extracting pumpkin seed oil and the fruit's peel, a high-quality extract that is acceptable for use in food, medicine, and cosmetics has been produced By including the pumpkin peel during the oil extraction process, bioactive components from the peel, including carotenoids, phytosterols, tocopherols, and antioxidant activity, were added to the extract. The solvent solution for the simultaneous extraction was sub- and supercritical CO_2. The utilization of optimal pressured extraction conditions, including temperature and pressure, using CO_2 resulted in the production of a higher quality extract compared to those obtained through conventional and ultrasonic methods, as evidenced by the concentration of β-carotene, phytosterols, tocopherols, phenolics, antioxidant activity, and thermal stability.

Mitra *et al.*[17] examined the Soxhlet method of extracting oil from pumpkin seeds using hexane and CO_2 supercritical extraction, achieving comparable yields with both methods. SFE also made it possible to shorten extraction times and use less organic solvent in both studies. Consequently, the oil yield obtained at the ideal conditions (68.1°C, 94.6 min, 32,140 kPa) was 31%. Supercritical CO_2 extraction was also used by Wang *et a*l.[18] extract β-carotene (18.50 mg/100 g sample) from pumpkin seeds.

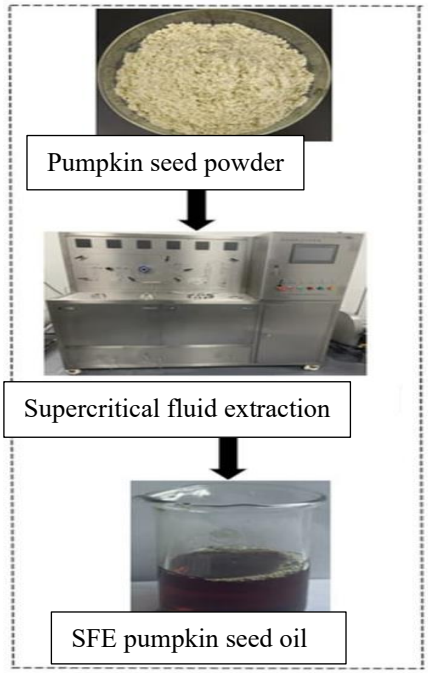

FIGURE NO:06

SUPERCRITICAL FLUID EXTRACTION

PHARMACOLOGICAL ACTIONS OF PUMPKIN

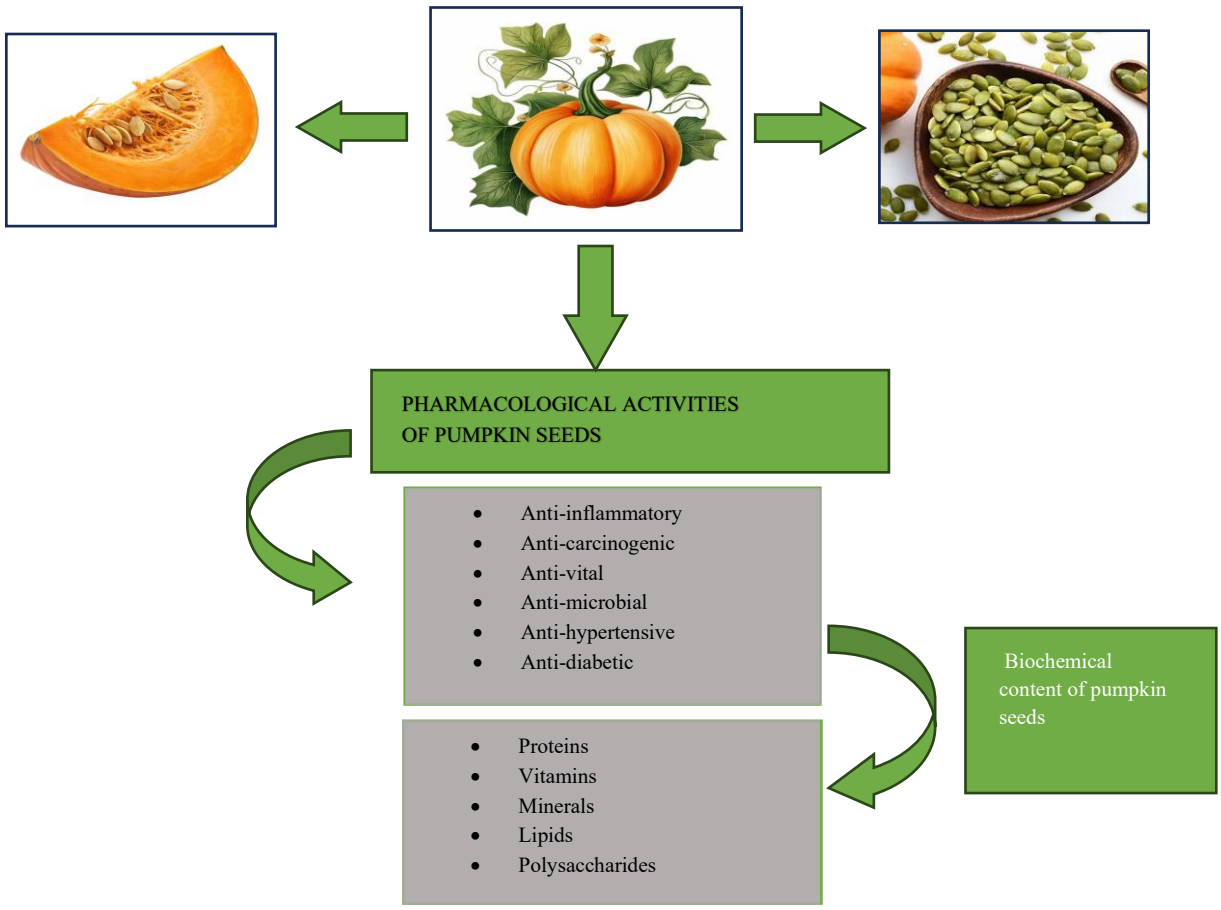

FIGURE NO:07

PHARMACOLOGICAL ACTIONS OF PUMPKIN SEED[19]

ANTI-DIABETIC PROPERTIES

The most common ailment among the elderly is diabetes mellitus. Diabetes mellitus is a metabolic disease that arises when the body either generates too little insulin or responds improperly to the insulin that is produced. Teugwa *et al.* employed rats in an oral glucose tolerance test and discovered that the most widely used storage protein is globulin (295.11 mg/g) dry matter, which reduces blood sugar (88-137.80%).[20] Among the several plants in the Cucurbitaceae family that shown hypoglycemic activity was Cucurbita moschata. Pumpkin and flax seeds together have hypoglycemic and antioxidant effects in diabetic rats; lower levels of malondialdehyde, growth-stimulating hormone, superoxide dismutase, chloramphenicol acetyltransferase, and antioxidant enzymes are among the histological abnormalities. elevations in total lipid, glucose plasma levels, cholesterol resistance, and triglycerides.[21]

ANTI-CARCINOGENIC PROPERTIES

Carotenoids, which have been linked to a lower risk of cancer, are found in pumpkin seeds. Furthermore, Aghaie *et al.*[22] state that cyclophosphamide is a cancer treatment drug that is detrimental to reproductive systems. A study by Rathinavelu *et al*.[23] found that the in vitro fatal effects of pumpkin seed ethanolic and aqueous extracts on prostate cancer were caused by oxidative stress, mitochondrial depolarization, and apoptotic pathways.[24] Additionally, the Cucurbita pepo extract might be created as a potential chemotherapeutic treatment to stop or slow the growth of tumors and cancer.[25]

ANTI-OXIDANT ACTIVITY

Numerous chronic diseases and their aftereffects, such as diabetes, obesity, cardiovascular disease, and cancer, have been linked to oxidative stress. A potentially hazardous imbalance between pro-oxidants and antioxidants favouring the former is found. Szasz *et al*.[26] claim that some pumpkin extracts may have strong antioxidant properties that could help people with diabetes, pre-diabetes, and vascular damage. Pumpkin seeds contain trace amounts of zinc and selenium, both of which are believed to be powerful antioxidants. Zinc can prevent the effects of the release of free radicals.
antioxidant vitamin E, which is abundant in pumpkin seed extract, or establish a direct bond with the copper or iron-binding sites of proteins, lipids, and DNA molecules. Pumpkin supplementation dramatically reduced the amount of malonaldehyde seen in mice and increased the serous and hepatic activity of glutathione peroxidase and superoxide dismutase.[27]

ANTI-INFLAMMATORY PROPERTIES

The pathologic reaction of living tissue to damage is inflammation, which causes a local buildup of blood cells and plasmatic fluid. Despite being a defence mechanism, many diseases can be caused, maintained, or made worse by the many events and mediators involved in the inflammatory reaction.[28] As an anti-inflammatory, antiviral, analgesic, antiulcer, anti-diabetic, and antioxidant, *Cucurbita pepo* L. (Cucurbitaceae) is one of those that has been used traditionally in many nations to treat a variety of illnesses.[29]

FORMULATION

FOR EVERY 100 GRAMS (OR ML IN A LIQUID BATCH)

INGREDIENTS	QUANTITY	PURPOSE
SUCROSE SYURP	75 ML	BASE
PUMPKIN SEED EXTRACT	10 ML	API
ORANGE SYRUP	15 ML	FLAVOURING AGENT
SODIUM BENZOATE	0.2 ML	PRESERVATIVE

PREPARATION OF SUCROSE SYRUP
Put 66.7 grams of sucrose in a clean, well-maintained beaker and fill it with enough distilled water. Bring the mixture to a boil until the sucrose dissolves completely**.**

FIGURE NO:08

PUMPKIN SEEDS

PREPARATION OF PUMPKIN SEEDS POWDER
Buy pumpkin seeds at your neighborhood market. In a dry pan over low heat, roast the seeds. The seeds were roasted, ground into a powder, and then sieved. Keep it in a shelf shield cover that is airtight.

FIGURE NO:09

PUMPKIN SEEDS POWDER

PREPARATION OF ORANGE SYRUP

Grab the oranges that are fresh. After removing the skin, put the oranges in a clean, tidy bowl. Add enough sugar, cover, and refrigerate for three days. Mix thoroughly and then separate the liquid extract after three days. To get a syrup-like consistency, the extract was boiled for a while before being filtered and kept in a tight container**.**

FIGURE NO:10

ORANGE SYRUP

PROCEDURE FOR 0.2 ML SODIUM BENZOATE PREPARATION

1. Weigh 0.2 grams of sodium benzoate powder accurately using a fine scale.
2. Dissolve the powder in about 10 ml of distilled or sterilized water at room temperature. Stir until fully dissolved.
3. Filter the solution if needed to remove undissolved particles.
4. Use this prepared solution directly by adding the required volume (0.2 ml) to your syrup batch while stirring well for even distribution.
5. Store any leftover sodium benzoate solution in a clean, airtight container for future use.

FORMULATION FOR PUMPKIN SEED TABLET

No.	INGREDIENT	QUANTITY (MG)
1.	*C. pepo* seeds powder	250
2.	Microcrystalline cellulose	50
3.	Lactose	30
4.	Corn starch	40
5.	Crosscarmellose	10
6.	Kaolin	10
7.	Sodium lauryl sulphate	4
8.	Colloidal silicon dioxide	2
9.	Talc	2
10.	Magnesium stearate	2
	Total	400

Preparation of seed powder from raw pumpkin seeds:

The dried pumpkin seeds were ground to a fine powder using the Maulinex standard grinder (180W). The obtained powder was sieved through 710um sieve and packed in an air tight plastic container.

Maulinex grinder and seed powder

FIGURE NO:11

SEED POWDER

PROCEDURE:

Pumpkin seed powder tablets were prepared using the wet granulation technique with 250 mg of raw powder per tablet to retain phytochemical efficacy. Powder was sieved (710 µm) and mixed with microcrystalline cellulose and lactose as fillers, kaolin as absorbent, and sodium lauryl sulphate to enhance wettability. The mixture was dry blended for five minutes and moistened with binder solution; binders and disintegrants were incorporated intragranularly. Wet massing was done for ten minutes, screened (1700 µm), and oven-dried at 50 °C for two hours. The dried granules were resized (710 µm) and mixed with colloidal silicon dioxide and talc as extragranular excipients. Finally, magnesium stearate was added, and the granules were compressed into tablet

CONCLUSION:

Pumpkin seeds (Curcubita pepo) are rich in essential nutrients such as zinc, magnesium, omega-3 fatty acids and phytoestrogens, which contribute significantly to hormone regulation, insulin sensitivity and reduction of inflammation core concerns in the management of Polycystic Ovarian Disease (PCOD). Current scientific literature supports their potential role in improving reproductive health, though specific formulation –based studies are limited. The review underscores the importance of further research into pumpkin seed-based interventions for PCOD.As part of our future work, we can aim to develop a syrup formulation containing standardized pumpkin seed extract, designed to be both effective and patient friendly. This approach may offer a natural, safe and effective accessible option for managing PCOD symptoms and improving quality of life in affected women

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