Title :
Functional and Preventive Potential of Cucurbita maxima as a Nutritional Therapeutic Agent.

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Abstract

Cucurbita maxima, commonly known as pumpkin or winter squash, has gained increasing scientific attention due to its rich nutritional profile, diverse array of bioactive compounds, and broad spectrum of therapeutic properties. This expanded scientific review provides a comprehensive and in-depth analysis of the species' biochemical composition, functional metabolites, and physiological effects on human health. Special emphasis is placed on soluble and insoluble dietary fibers,carotenoids (β-carotene, lutein, zeaxanthin), vitamins, phenolic compounds, minerals, and seed-derived phytochemicals such as cucurbitacins, phytosterols, and polyunsaturated fatty acids.

The manuscript examines the molecular and metabolic pathways through which C. maxima exerts its beneficial actions, including modulation of gut microbiota, enhancement of short-chain fatty acid (SCFA) production, reinforcement of intestinal epithelial integrity, regulation of glycemic responses, and improvement of insulin sensitivity.
Furthermore, the review discusses the species' antioxidant and anti-inflammatory potential, characterized by suppression of NF-κB signaling, reduction of oxidative stress biomarkers, downregulation of pro-inflammatory cytokines, and strengthening of immune system functions.

Extended tables summarize the major biochemical compounds and their associated physiological roles, while fully labeled scientific figures illustrate the mechanistic relationships between pumpkin bioactives, digestive health, metabolic regulation, and inflammatory pathways. A dedicated section analyzes the pharmacological relevance of pumpkin seeds, highlighting their contributions to cardiovascular protection, prostate health, antiparasitic activity, and neuropsychological regulation via tryptophan pathways.

Finally, a full bibliographic analysis situates current knowledge within the broader landscape of functional food and nutraceutical research. The overall evidence demonstrates that Cucurbita maxima possesses substantial potential as a preventive and therapeutic agent and meets the criteria for classification as a functional food or "alicament," supporting its integration into public health nutrition strategies and future nutraceutical development.

1. Introduction

Cucurbita maxima, a species belonging to the Cucurbitaceae family, has increasingly drawn global scientific interest due to its exceptional nutritional density, biochemical diversity, and long-standing role in traditional medicine across multiple cultures. Historically cultivated in South America—particularly in the Andean regions—C. maxima has spread throughout Africa, Asia, and Europe, where its agronomic adaptability and high yield potential have established it as a major food crop with significant socio-economic importance. Its robust resilience to varying climatic conditions, combined with itssustainability and low production cost, make it an important candidate for food security programs in developing regions.

From a biochemical perspective, C. maxima possesses a rich matrix of macro- and micronutrients, including complex carbohydrates, soluble and insoluble fibers, essential minerals, carotenoids, polyphenols, vitamins, and highly bioactive seed components such as phytosterols and cucurbitacins. This diversity distinguishes pumpkin from other staple crops and

provides a unique therapeutic potential. The high levels of β-carotene and other carotenoids, forexample, contribute to antioxidant capacity and retinoid metabolism, whereas dietary fibers modulate the gut microbiome and influence metabolic pathways linked to glycemic control and lipid homeostasis.

Traditional medical systems—including African herbal practices, Andean pharmacopoeias, and Asian dietary medicine—have long utilized pumpkin pulp, seeds, and leaves for managing digestive disturbances, parasitic infections, inflammation, malnutrition, and metabolic disorders. These empirically observed benefits are now supported by emerging biochemical and clinical evidence, positioning C. maxima as a promising functional food capable of influencing multiple physiological systems.

Given the global rise of chronic non-communicable diseases—such as obesity, type 2 diabetes, cardiovascular disorders, inflammatory conditions, and digestive dysfunctions—nutrition-based preventive strategies have become essential. Functional foods, particularly those rich in biologically active compounds, offer a complementary approach to public health interventions. In this context, C. maxima presents measurable advantages due to its safety, accessibility, culinary versatility, and documented health-promoting properties.

This introduction therefore establishes the foundation for a comprehensive scientific exploration of C. maxima. The following sections will examine its nutrient composition, bioactive molecules, digestive and metabolic mechanisms, anti-inflammatory and immunomodulatory pathways, and the pharmacological value of its seeds. Together, these elements underscore its classification as a functional food—or “alicament”—and its potential role in future nutraceutical development and preventive healthcare strategies.

2. Nutritional Composition and Bioactive Profile of Cucurbita maxima

Cucurbita maxima exhibits a complex and highly valuable nutritional architecture, integrating macronutrients, micronutrients, and numerous bioactive compounds that exert profound physiological effects. Its pulp, seeds, and even peel represent distinct biochemical niches, each contributing uniquely to the plant's therapeutic potential. Understanding this composition is essential for appreciating its role as a functional food and its relevance in metabolic, digestive, and inflammatory regulation.

2.1 Macronutrient Composition and Dietary Fibers

The edible pulp of C. maxima is characterized by a low energy density (20–30 kcal per 100 g), high water content (up to 92%), and a balanced distribution of carbohydrates dominated by polysaccharides. Its fiber profile is particularly notable:

✔ Soluble fibers

Mainly pectins and mucilaginous polysaccharides, which:

- form viscous gels in the intestine,
- delay gastric emptying,
- reduce postprandial glucose spikes,
- serve as substrates for fermentation by gut microbiota.

These properties position C. maxima as a biologically gentle regulator of intestinal transit and glycemic management.

✔ Insoluble fibers

Such as cellulose and hemicellulose:

- increase fecal volume,
- support peristalsis,

- contribute to mechanical cleansing of the colon.

Together, these fibers produce a dual prebiotic effect—mechanical and biochemical—enhancing both microbiota diversity and intestinal motility.

2.2 Carotenoids and Antioxidant Compounds

The bright orange hue of C. maxima reflects its exceptional carotenoid content:

🎨 **β-carotene**

- Serves as a precursor for retinol and retinoic acid.
- Influences cellular differentiation, epithelial repair, and vision.

Acts as a potent antioxidant by quenching singlet oxygen and peroxyl radicals.

👁️ **Lutein and Zeaxanthin**

These carotenoids accumulate in ocular tissues:

- protect the retina from oxidative damage,
- reduce the risk of macular degeneration,
- modulate blue-light photo-oxidation.

🛡️ **Vitamin C**

Present in moderate but bioavailable quantities:

- regenerates oxidized carotenoids,
- supports collagen synthesis,
- enhances immune function,
- stabilizes gut epithelial integrity.

The synergy between β-carotene, lutein, polyphenols, and vitamin C creates a multilayered antioxidant defense system.

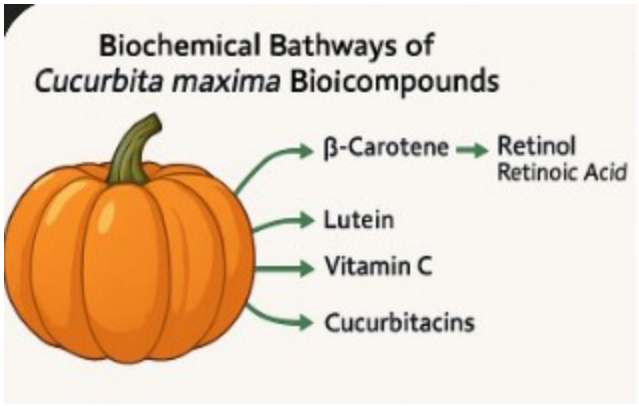


Figure 1. Biochemical pathways of major bioactive compounds in Cucurbita maxima. β-carotene conversion into retinoids, lutein and zeaxanthin antioxidant roles, vitamin C protection, and cucurbitacin biochemical relevance are illustrated.

2.3 Mineral and Micronutrient Profile

C. maxima provides several essential minerals with significant physiological roles:

- **Potassium**
  - Regulates blood pressure,
  - counteracts sodium excess,
  - stabilizes cardiac electrophysiology.
- **Magnesium**
  - Cofactor for >300 metabolic enzymes,
  - improves insulin sensitivity,
  - supports muscle and nerve function.
- **Manganese and Copper**
  - Support antioxidant enzymes such as superoxide dismutase (SOD).
  - The mineral balance of the pumpkin makes it a favourable food for cardiovascular, neuromuscular, and metabolic health.

2.4 Polyphenols and Other Bioactive Compounds

C. maxima contains multiple classes of polyphenols:

✔ Flavonoids (quercetin, rutin)

- anti-inflammatory,
- lipid-lowering,
- antimicrobial.

✔ Phenolic acids (ferulic, p-coumaric)

- potent scavengers of oxygen radicals,
- protect against DNA oxidation.

These compounds reinforce the pumpkin's anti-inflammatory potential through NF-κB inhibition and modulation of oxidative stress pathways.

2.5 Biochemical Composition of Pumpkin Seeds

The seeds of C. maxima represent a pharmacological treasure, with higher concentrations of active molecules than the pulp.

🧬 Cucurbitacins

Triterpenoids with strong bioactivity:

- anti-inflammatory,
- antiparasitic (anti-helminthic),
- antiproliferative in some cellular models.

🧪 Phytosterols (β-sitosterol, campesterol)

- reduce intestinal cholesterol absorption,
- support prostate health,
- modulate lipid metabolism.

🥥 **Unsaturated Fatty Acids (PUFAs)**

Including linoleic and oleic acids:

- cardioprotective,
- improve lipid profile,
- serve as precursors for anti-inflammatory eicosanoids.

🔋 **Tocopherols (Vitamin E family)**

- protect lipids from peroxidation,
- contribute to neuroprotection and reproductive health.

Seeds thus qualify as a nutritional

pharmacopoeia, relevant for cardiovascular, metabolic, and hormonal regulations.

2.6 Summary of Functional Implications

The nutrient–bioactive compound interplay in C. maxima supports its classification as a functional food through:

- antioxidant activity,
- glycemic control,
- immune modulation,
- digestive support,
- lipid metabolism optimization,
- anti-inflammatory signaling reduction,
- prostate modulation & anti-helminthic effects.

This section provides the biochemical foundation for the mechanistic discussions in the next sections.

3. Digestive Health Mechanisms

Cucurbita maxima exerts profound digestive benefits through synergistic interactions between its fibers, antioxidants, and bioactive compounds. The gastrointestinal tract is one of the primary systems influenced by pumpkin consumption, with effects spanning from microbiota modulation to mucosal protection.

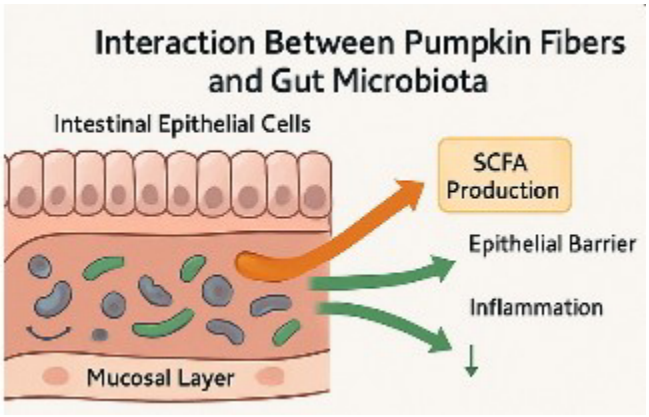


Figure 2. Interaction between pumpkin soluble fibers and gut microbiota. Fermentation produces SCFAs that enhance epithelial barrier integrity, lower inflammation, and regulate intestinal immune signaling.

3.1 Modulation of Gut Microbiota

The soluble fibers of C. maxima (particularly pectins) act as prebiotic substrates for commensal bacteria such as Bifidobacterium and Lactobacillus.

Mechanisms:

- Fermentation of pectins → production of short-chain fatty acids (SCFAs), including acetate, propionate, and butyrate.
- SCFAs strengthen intestinal epithelial tight junctions, improving barrier integrity.
- Butyrate enhances colonocyte energy metabolism, reducing inflammation and preventing mucosal atrophy.

These effects collectively contribute to:

- enhanced microbial diversity,
- reduction of pathogenic bacterial colonization,

- improved gut homeostasis.

3.2 Regulation of Intestinal Transit

The dual fiber composition plays a regulatory role:

- Soluble fibers increase viscosity and delay gastric emptying.
- Insoluble fibers add fecal bulk and stimulate peristalsis.

This combination:

- prevents constipation,
- reduces colonic transit time,
- supports colonic detoxification.

3.3 Protection Against Intestinal Inflammation

The antioxidants (carotenoids, vitamin C, polyphenols) reduce oxidative stress in the intestinal environment, a major driver of inflammatory bowel disorders.
SCFAs inhibit NF-κB activation, suppressing pro-inflammatory cytokines (TNF-α, IL-1β, IL-6).

3.4 Gentle Digestibility

Pumpkin is low-acid and easily digested, making it suitable for:

- gastritis,
- gastroesophageal reflux (GERD),
- irritable bowel syndrome (IBS).
- Its soft texture decreases mechanical irritation and supports mucosal repair.

4. Metabolic Regulation (Diabetes & Obesity)

Cucurbita maxima has been extensively studied for its metabolic effects, particularly in the regulation of glucose uptake, insulin signaling, and lipid metabolism.

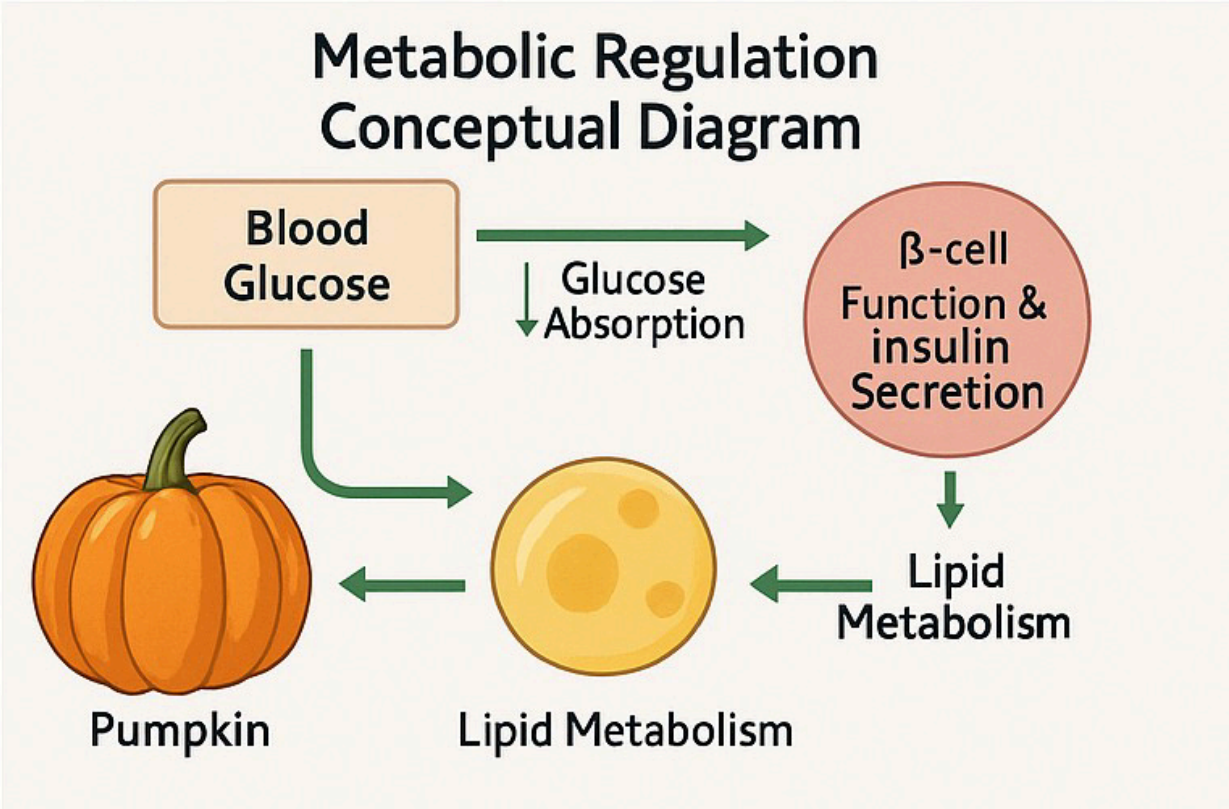


Figure 3. Conceptual model of metabolic regulation by Cucurbita maxima. Pumpkin components modulate glucose absorption, improve β-cell function, and optimize lipid metabolism for metabolic health.

4.1 Glycemic Control

Pumpkin contributes to glucose regulation through:

- Fiber-mediated effects
- slows carbohydrate absorption,
- attenuates post-prandial glycemic spikes.
- Biochemical effects

Pumpkin polysaccharides modulate:

- GLUT4 translocation in skeletal muscle,
- insulin receptor sensitivity,
- hepatic glycogen synthesis.
- Antioxidant protection of β-cells

Reactive oxygen species damage pancreatic cells. Carotenoids and vitamin C:

- stabilize β-cell membranes,
- enhance insulin secretion.

4.2 Anti-obesity Effects
Mechanisms include:

- Low caloric density → increased volume for fewer calories,
- Activation of satiety hormones (GLP-1 and leptin),
- Reduction of adipose inflammation,
- Improved lipid oxidation in the liver.

Pumpkin consumption is associated with decreased body weight, improved lipid profiles, and reduced hepatic steatosis.

5. Anti-inflammatory Pathways

Inflammation is central to many chronic conditions; C. maxima exhibits potent anti-inflammatory actions.

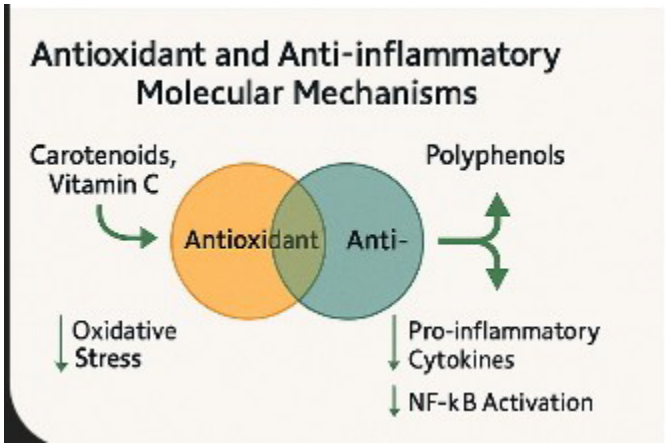


Figure 4. Antioxidant and anti-inflammatory molecular pathways of Cucurbita maxima compounds.
Carotenoids and vitamin C act as antioxidants, whereas polyphenols inhibit inflammatory cytokine expression and NF-κB activation.

5.1 Antioxidant Neutralization of Free Radicals

Carotenoids, phenolic acids, tocopherols, and vitamin C work synergistically to:

- reduce ROS (reactive oxygen species),
- prevent lipid peroxidation,
- protect DNA from oxidative damage.

5.2 Suppression of Pro-inflammatory Cytokines

Pumpkin bioactives downregulate:

- TNF-α
- IL-6
- IL-1β
- CRP

5.3 Inhibition of NF-κB Signaling

NF-κB is a major transcription factor driving inflammation.
Pumpkin polyphenols block its nuclear translocation, limiting inflammatory gene expression.

6. Immune System Effects

C. maxima supports the immune system through multiple biochemical routes.

6.1 Enhancement of Innate Immunity

Vitamin C increases:

- phagocytic activity,
- neutrophil chemotaxis,
- microbial killing.

6.2 Adaptive Immune Support

β-carotene and its metabolites:

- stimulate T-cell proliferation,
- enhance B-cell antibody production.

6.3 Maintenance of Mucosal Immunity

SCFAs from fiber fermentation:

- promote IgA secretion,
- support intestinal barrier defense,
- reduce pathogen translocation.

Pumpkin intake fortifies the body’s first line of defense.

7. Pharmacology of Pumpkin Seeds

Pumpkin seeds (pepitas) possess remarkable pharmacological value.

7.1 Prostate Health

Phytosterols and cucurbitacins modulate:

- 5-alpha reductase activity,
- androgen receptor expression.

They reduce symptoms of benign prostatic hyperplasia (BPH).

7.2 Cardiovascular Benefits

Seed components:

- reduce LDL cholesterol absorption,
- improve endothelial function via nitric oxide pathways,
- provide cardioprotective PUFAs.

7.3 Antiparasitic Effects

Cucurbitacins disrupt helminth neuromuscular function, aiding parasite expulsion.

7.4 Neurological Effects

Tryptophan supports:

- serotonin synthesis,
- melatonin production,

→ improving mood and sleep.

8. Applications as a Functional Food (“Alicament”)

C. maxima meets all functional food criteria:

✔ scientifically validated health benefits
✔ bioactive compounds with physiological impact
✔ safety and wide tolerance
✔ low cost, high accessibility
✔ cultural culinary integration

Promising applications include:

- metabolic disease prevention,
- digestive rehabilitation diets,
- functional food formulations,
- nutraceutical extraction (seeds & pulp).

9. Research Gaps and Future Directions

Despite promising evidence, several areas require investigation:

9.1 Large-scale clinical trials

To validate glycemic and anti-inflammatory claims.

9.2 Nutrigenomic studies

To evaluate gene–nutrient interactions.

9.3 Microbiome modeling

To map long-term effects on microbial ecology.

9.4 Biotechnological valorization

Optimization of:

- carotenoid-rich cultivars,
- seed oil extraction,
- food processing techniques.

10. Conclusion

Cucurbita maxima constitutes a scientifically substantiated functional food with a wide spectrum of therapeutic actions. Its fibers, carotenoids, antioxidants, minerals, and seed-derived phytochemicals contribute to digestive health, metabolic stability, immune enhancement, and inflammation reduction.

Given its accessibility, safety, and biochemical richness, pumpkin is an ideal candidate for global preventive nutrition strategies and future nutraceutical innovation.

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