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Full Length Research Paper

Bioactive compounds in pumpkin (*Cucurbita* species) seeds as natural alternatives in the management of erectile dysfunction: A focus on cucurbitacin

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Sexual dysfunction, particularly erectile dysfunction (ED), is a prevalent health concern in men with substantial physical, psychological, and interpersonal implications. ED currently affects over 150 million men globally, with projections exceeding 322 million by 2025, and is increasingly recognised as an early marker of systemic conditions, including cardiovascular disease, type 2 diabetes, and endocrine disorders. Standard therapy relies on phosphodiesterase type 5 inhibitors, which are effective but limited by adverse side effects, prompting interest in complementary therapies, including the use of pumpkin seeds. This review employed a systematic literature search across PubMed, Scopus, and Google Scholar, using keywords including "pumpkin seeds," "Cucurbita pepo," "cucurbitacins," "benign prostatic hyperplasia (BPH)," and "erectile dysfunction (ED)," focusing on peer-reviewed articles published between 2015 and 2025. Studies reporting mechanistic insights, preclinical findings, or clinical outcomes related to pumpkin seed bioactive compounds were included. Pumpkin (*Cucurbita* species) is highlighted for its phytochemical richness, particularly cucurbitacins, and its potential role in improving erectile function. The review highlights the need for further research to confirm the efficacy of cucurbitacins in directly enhancing erectile function and to elucidate their mechanisms of action.

Key words: Erectile dysfunction, alternative therapies, *Cucurbita* species seeds, bioactive compounds, Cucurbitacin.

INTRODUCTION

Sexual dysfunction and low libido are significant concerns in men's health, impacting physical, emotional, and relational well-being. Sexual dysfunction encompasses various conditions such as erectile dysfunction (ED), premature ejaculation, and inhibited sexual desire, while a reduction in sexual interest or activity marks low libido. Together, they affect millions of men worldwide and warrant serious attention due to their multifaceted implications for health and relationships (Pastuszak et al., 2015; Imprialos et al., 2021). Sexual dysfunction often serves as a precursor to serious health conditions such as cardiovascular diseases (CVDs), diabetes, and hormonal imbalances. For example, ED has been recognised as an early warning sign for atherosclerosis and heightened cardiac risk, often due to shared risk factors like endothelial dysfunction and reduced nitric oxide availability

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(Pastuszak et al., 2015; Goodale et al., 2017; Imprialos et al., 2021; Kaur and Werstuck, 2021). This connection emphasizes the importance of recognizing sexual health issues as markers for broader systemic health problems in men.

ED, sometimes referred to as impotence, is the most common form of sexual dysfunction in men (Sin et al., 2021). ED is defined as the ongoing or repeated difficulty in getting and/or keeping an erection firm enough for satisfying sexual activity (Leisegang and Finelli, 2021; Sin et al., 2021). Although not life-threatening, ED can have a serious negative effect on a man's overall quality of life, affecting both emotional well-being and relationships. It leads to loss of self-confidence, anxiety, depression and avoidance of intimacy, which in turn aggravate sexual dysfunction. As a result, this puts a strain on the relationship and well-being of the couple (Masuku et al., 2020; Leisegang and Ferelli, 2021). ED is associated with various endocrine disorders, including hypogonadism, type 2 diabetes mellitus, hyperthyroidism, and hypo-thyroidism. It poses an increased mortality risk as it is also seen as a standalone risk factor for developing metabolic syndrome and CVDs, sharing common underlying mechanisms (Chen et al., 2019; Leisegang and Ferelli, 2021).

The clinical assessment of patients with ED includes a thorough review of their family, medical, sexual and social history. Family history covers conditions such as CVDs and diabetes mellitus (Patel et al., 2017), while medical history involves reviewing any medications the patient has taken for ailments such as heart diseases and mental illnesses (Chen et al., 2018). Sexual history includes use of unrestricted questions that encourage the patient to share more details about their sexual performance in past and current relationships, as well as their overall sexual health (Patel et al., 2017). Social history, on the other hand, encompasses the history of alcohol and drug use, smoking, diet and exercise (Patel et al., 2017). For research and diagnosis, doctors often use a tool called the International Index of Erectile Function (IIEF) to diagnose ED and determine how severe it is. The IIEF is also used as an international standard to evaluate how well an ED treatment works (Bilal and Abbasi, 2020).

Current interventions for treating ED involve using medications, hormonal replacement, vacuum constriction devices, intracavernosal injection therapy of vaso-active substances, and penile prosthesis surgery. Phosphodiesterase-5 inhibitors (PDE5) are the most commonly used drugs for ED treatment. They block the flow of blood out of the penis to help create and maintain an erection. Most commonly used PDE5 inhibitors include sildenafil citrate, tadalafil, vardenafil and avanafil (Kim et al., 2021; Sin et al., 2021). Although generally well tolerated with a high efficacy rate, PDE5 inhibitors present adverse effects including headaches, visual disturbances, flushing, dyspepsia, nasal congestion, flushing, and heart attack (Anand et al., 2021). Therefore, this has increased the use of natural and alternative therapies for treating ED, including herbal remedies and dietary supplements, used alone or in combination with other treatments (Leisegang and Ferelli, 2021; Napolitano et al., 2022).

Various studies have reported the potential of different plant species for the treatment of ED (Anand et al., 2021; Sin et al., 2021; Xu et al., 2023). Plants have a diverse array of bioactive compounds, including polyphenols, vitamins, minerals, and amino acids. Several plant species, including members of the Cucurbitaceae family, are used in traditional medicine to increase libido, sexual arousal, potency and/or sexual pleasure (Sin et al., 2021; Napolitano et al., 2022). Pumpkin (*Cucurbita* species) is one of the most cultivated vegetable crops across the globe. It has been widely used as a functional food or herbal remedy for several ailments due to its promising health benefits. The fruit of the pumpkin, including the seed, peel, and flesh, is a rich source of nutrients and phytochemicals which offer many health benefits, such as reducing inflammation and protecting against ulcers, anti-microbial, and improving symptoms of sexual dysfunction in males, which in turn supports both prostate and vascular health pertinent to ED management (Pellicorio et al., 2025). While studies by Vahlensieck et al. (2015); Leibbrand et al. (2019) and Theil et al. (2022) have reported the potential of pumpkin seed oil to treat BPH, the specific contribution of its constituents, particularly cucurbitacins, to improving erectile function remains largely unexplored. Notably, BPH and ED often coexist and share underlying mechanisms such as vascular issues, inflammation, and hormonal imbalances, and pumpkin seeds may beneficially target these pathways. Pumpkin seeds are rich in bioactive compounds such as unsaturated fats, vitamins, minerals, antioxidants, and phytocompounds, including cucurbitacin, that can improve male sexual health (Dotto and Chacha, 2020). However, there is limited documentation on the potential of these bioactive compounds to alleviate ED symptoms directly. Therefore, this review will explore the potential of pumpkin seed-derived compounds, particularly cucurbitacins, as a natural therapeutic option for improving erectile function and overall sexual health.

METHODOLOGY

This review was developed through a structured and systematic approach to ensure that the evidence considered was both relevant and reliable. We searched three major databases, PubMed, Scopus, and Google Scholar, to identify studies published between 2015 and 2025. The search was built around a combination of keywords, including “pumpkin seeds,” “*Cucurbita pepo*,” “cucurbitacins,” “benign prostatic hyperplasia (BPH),” and “ED.” Boolean operators (AND, OR) were used to refine results and capture as many relevant studies as possible. We included peer-reviewed articles that reported either mechanistic insights, preclinical findings, or clinical outcomes related to pumpkin seeds or their bioactive compounds in the context of BPH or ED. Elig ible studies covered a range of designs, from cell culture and animal experiments to clinical trials and systematic reviews. Only English-language publications within the defined

Table 1. Taxonomic classification of *C. pepo.*

Rank	Classification
Kingdom	Plantae
Clade	Tracheophytes
Clade	Angiosperms
Clade	Eudicots
Order	Cucurbitales
Family	Cucurbitaceae
Genus	Cucurbita
Species	*C. pepo L.*

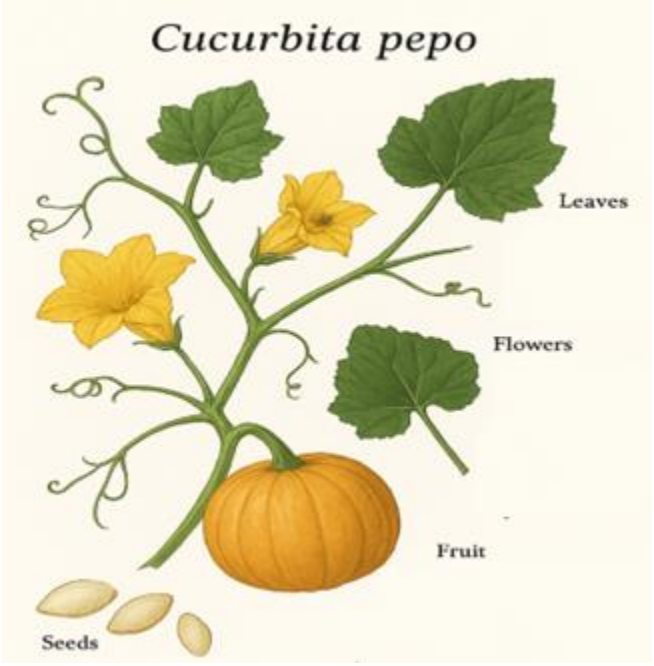

Figure 1. Botanical description of *C. pepo*.

timeframe were considered. Studies were excluded if they were editorials, commentaries, non-peer-reviewed reports, or if they did not specifically address pumpkin seeds, cucurbitacins, or their relevance to prostate or sexual health. Articles published before 2015 were also excluded.

RESULTS AND DISCUSSION

Taxonomy and botany of pumpkins (*C. pepo*)

Taxonomy

Pumpkins belong to the genus *Cucurbita* in the family Cucurbitaceae, which comprises more than 800 species of mostly climbing or trailing vines. The cultivated pumpkins commonly used for food and medicinal purposes are primarily derived from *C. pepo*, although related species such as *Cucurbita maxima* and *Cucurbita moschata* are also widely grown (Himani et al., 2023). The formal taxonomic classification of *C. pepo* is as follows (Table 1). The species name pepo is derived from the Greek word pepon, meaning “large melon.” While *C. pepo* is the primary source of medicinal pumpkin seeds, other species within the genus contribute regionally important cultivars with overlapping phytochemical and nutritional profiles (Swamy, 2022; Himani et al., 2023).

Botanical description

C. pepo is an annual herbaceous plant that grows as a creeping or climbing vine with long, branched, angular stems covered in coarse hairs. The plant produces tendrils that facilitate spreading and climbing. The species is monoecious, bearing separate male (staminate) and female (pistillate) flowers on the same plant. Flowers are large, bright yellow to orange, funnel-shaped, and unisexual. Male flowers are borne on long peduncles, while female flowers have shorter stalks and are distinguished by the presence of an inferior ovary. Pollination is predominantly entomophilous, with bees playing a central role. The leaves are large, simple, alternate, and broadly ovate to cordate, with rough pubescence and serrated or lobed margins. Long petioles support them, and their size and shape can vary across cultivars**.** The fruit of *C. pepo* is botanically classified as a pepo, a type of berry with a hard outer rind. Fruits show remarkable variability in size, shape, colour, and surface texture depending on the cultivar, ranging from round to oblong and from smooth to ribbed. The rind may be green, yellow, or orange, often with mottled or striped patterns. The seeds are flattened, ovate, and cream to whitish in colour, enclosed within the fibrous pulp of the fruit. They contain a hard testa surrounding a white kernel rich in oils, proteins, and bioactive phytochemicals such as cucurbitacins, tocopherols, phytosterols, and poly-unsaturated fatty acids. The plant develops a shallow but extensive root system adapted to spreading horizontally in the soil, which allows efficient nutrient and water uptake (Muimba-Kankolongo, 2018; Gbemenou et al., 2022; Swamy, 2022) (Figure 1).

Cultivation of pumpkins

Pumpkins thrive in warm climates with well-drained soils. Key climatic requirements include temperatures between 18°C and 30°C, with seasonal rainfall, and irrigation is often required in arid regions (Imtiaz et al., 2024; Prajapati et al., 2024). Proper and advanced agricultural technologies, including mechanised farming and pest-resistant hybrids, enhance productivity in developed regions. In contrast, developing countries rely more on traditional practices, leading to variable yields (Dhatt et al., 2020). However, pumpkin production faces challenges

from pests and diseases, such as Powdery mildew and downy mildew, which are the most common fungal infections reducing yields (Chinnadurai et al., 2018; Subhalakshmi, 2019). Pests such as the squash vine borer and cucumber beetle are significant threats. Integrated pest management strategies are required to mitigate losses. Other challenges hindering cultivation are limited access to markets, poor and low seed quality, as well as shifting weather patterns, including unpredictable rainfall and rising temperatures, which impact pumpkin growth, particularly in rain-fed regions. Prolonged droughts threaten yields in Africa and parts of Asia (Imtiaz et al., 2024; Prajapati et al., 2024).

Key bioactive compounds in pumpkin seeds and their potential health benefits

Pumpkin seeds, derived from the fruit of *Cucurbita* spp., are highly valued for their nutritional and therapeutic properties. Rich in essential nutrients, bioactive compounds, and functional components, they have been widely recognised for their potential health benefits (Batool et al., 2022; Bedi and Tewari, 2024).

Proteins and amino acids

Pumpkin seeds are a significant source of high-quality protein that provides all the essential amino acids. They are particularly rich in tryptophan, which is essential for serotonin production, aiding in mood regulation and sleep (Kokturk and Kambayi, 2015; Yousef et al., 2024). Additionally, arginine, an amino acid found in abundance, supports cardiovascular health by promoting nitric oxide synthesis, which is important for penile vascular relaxation and blood flow, directly affecting erectile function (McRae, 2016).

Fats and fatty acids

The seeds contain a high concentration of healthy fats, predominantly unsaturated fats like linoleic acid (omega-6) and oleic acid (omega-9). These fats contribute to cardiovascular health by reducing LDL cholesterol and increasing HDL cholesterol levels (Dotto and Chacha, 2020; Batool et al., 2022). Additionally, pumpkin seed oil is a source of phytosterols, which help lower serum cholesterol (Patel et al., 2023).

Minerals

Pumpkin seeds are an excellent source of magnesium, zinc, iron, and potassium. Magnesium supports strong bones, healthy muscles, and sustained energy levels, while zinc is vital for immune function and male fertility (Allouche-Fitoussi and Breitbart, 2020; Lima et al., 2023). Iron helps combat anaemia, and potassium contributes to maintaining electrolyte balance (Kumari et al., 2025).

Vitamins

Pumpkin seeds provide significant amounts of vitamins, particularly vitamin E (tocopherols and tocotrienols), which exhibit strong antioxidant properties. They also contain B vitamins, including niacin, riboflavin, and folate, supporting metabolic and neurological health (Patel et al., 2023; Fatima et al., 2025).

Dietary fibre

The seeds contain dietary fibre, beneficial for gut health and digestion. Fibre aids in regulating blood sugar levels and cholesterol, reducing the risk of heart diseases and diabetes mellitus (Yang et al., 2022).

Other phytochemicals

Pumpkin seeds are packed with beneficial compounds, including phenolic acids (such as, caffeic and ferulic acids) and flavonoids, which have antioxidant and anti-inflammatory effects (Hussain et al., 2022). The presence of cucurbitacins, a class of triterpenes, provides antifungal and anticancer potential (Chung et al., 2015). Cucurbitacins also reduce prostate inflammation and hyperplasia, making them beneficial in improving associated sexual health issues (Basha et al., 2021).

Role of cucurbitacins in addressing sexual dysfunction

Cucurbitacins are a class of tetracyclic triterpenoids predominantly found in plants of the Cucurbitaceae family, including pumpkins, cucumbers, and gourds. They are derived from the cucurbitane skeleton, which is based on a 19-(10→9β)-abeo-10α-lanost-5-ene framework (Mir et al., 2019). Their core structure consists of four fused carbon rings (A–D) with diverse oxidation states, unsaturations, and functional groups that give rise to significant structural diversity. Typically, cucurbitacins feature multiple hydroxyls, keto, and acetoxy substituents, as well as an α, β-unsaturated ketone moiety at C-23, which is believed to be critical for their toxicity, pharmacological activity and their characteristic bitter taste (Kaushik et al., 2015).

Known for their potent pharmacological activities, cucurbitacins exhibit anti-inflammatory, antioxidant, and hormonal modulation properties, which have gained attention for their potential applications in managing sexual dysfunction (Kaushik et al., 2015; Silvestre et al., 2022). Cucurbitacins have been used to address sexual

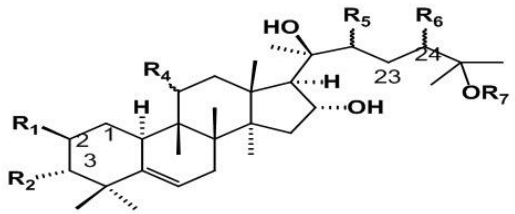

Figure 2. General structure of Cucurbitacin.
Source: Mir et al. (2019).

dysfunction issues, which include ED, libido enhancement, prostate health and psychogenic sexual dysfunction (Russo et al., 2021). The general structure of Cucurbitacin is as shown in Figure 2.

Erectile dysfunction (ED)

Cucurbitacins enhance endothelial function by reducing oxidative stress and inflammation, restoring nitric oxide-mediated vasodilation critical for penile erection (Chung et al., 2015). Experimental studies on animal models have demonstrated improved penile blood flow and erectile response following cucurbitacin administration (Jimoh et al., 2017; Ademiluyi et al., 2019).

Libido enhancement

Hormonal imbalances are one of the key physiological causes of sexual dysfunction, affecting both libido and sexual performance. Testosterone, the primary male sex hormone, plays a central role in regulating sexual desire and erectile function. Low testosterone levels, or hypogonadism, can lead to reduced libido, difficulty achieving or maintaining erections, and diminished sexual satisfaction. Testosterone deficiency disrupts nitric oxide synthesis, which is essential for penile vascular relaxation and blood flow, directly impacting erectile function. This imbalance may result from ageing, chronic illnesses, or endocrine disorders such as pituitary dysfunction (Nassar and Leslie, 2023; Patil et al., 2023).

In addition to testosterone, other hormones like prolactin, cortisol, and thyroid hormones also influence sexual health. Hyperprolactinemia, characterised by elevated prolactin levels, suppresses gonadotropin-releasing hormone (GnRH) secretion, leading to reduced testosterone levels and sexual dysfunction (Haidenberg-David et al., 2024). Similarly, excessive cortisol production, often caused by chronic stress or Cushing's syndrome, can impair sexual desire and erectile function by disrupting the hypothalamic-pituitary-gonadal (HPG) axis and contributing to metabolic issues such as obesity and reduced sensitivity to insulin (Pressman et al., 2018; Odetayo et al., 2024). Thyroid hormone imbalances, including both hyperthyroidism and hypothyroidism, also affect sexual performance and libido due to their impact on metabolism and psychological well-being (Yavuz et al., 2019).

The interplay between hormonal imbalances and psychological factors further exacerbates sexual dysfunction. Hormonal deficiencies often lead to symptoms like fatigue, mood disturbances, and depression, which can amplify sexual health challenges. For instance, low testosterone levels are closely linked to depressive symptoms, creating a vicious cycle of reduced libido and emotional distress (Määttänen et al., 2021). Addressing these imbalances through hormone replacement therapy (HRT), stress management, and lifestyle interventions can significantly improve intimacy and overall well-being, highlighting the importance of a holistic approach to treating hormonally driven sexual dysfunction. Hormonal modulation, particularly the upregulation of testosterone, is a significant mechanism through which cucurbitacins may enhance libido (Ohiri et al., 2024). These effects, combined with reduced oxidative stress, create a favourable environment for improved sexual desire and function (Basha et al., 2021).

Prostate health and sexual function

Cucurbitacins' anti-inflammatory and antiproliferative properties have been effective in managing BPH, a condition often linked to reduced sexual function. By alleviating prostate-related symptoms, cucurbitacins indirectly enhance sexual health outcomes (Chen et al., 2020; Liu et al., 2021).

Psychogenic sexual dysfunction

Cucurbitacins' neuroprotective effects, coupled with their anti-anxiety properties, address psychogenic causes of sexual dysfunction. By reducing stress and enhancing neurological resilience, these compounds support overall sexual well-being (Dai et al., 2023).

Pharmacology of cucurbitacins

Anti-inflammatory properties

Chronic inflammation is a significant contributor to sexual dysfunction, particularly ED and conditions like prostatitis (Kaya-Sezginer and Gur, 2020). Cucurbitacins reduce inflammation through the suppression of inflammatory cytokines such as TNF-α, IL-6, and IL-1β (Dai et al., 2023). They also inhibit the NF-κB pathway, a central mediator of inflammatory responses, thus potentially alleviating inflammation-induced ED (Chung et al., 2015).

Antioxidant activity

Oxidative stress damages the lining of blood vessels and

lowers the availability of nitric oxide, both critical for penile vascular health (Poredos et al., 2021; Kaltsas et al., 2024). Cucurbitacins act as strong antioxidants, neutralising free radicals and boosting antioxidant enzymes such as superoxide dismutase and catalase (Yang et al., 2020). These properties help restore endothelial integrity and improve blood flow, key factors in addressing ED (Salehi et al., 2021).

Hormonal modulation

Regarding its hormonal modulation properties, evidence suggests cucurbitacins may modulate hormonal balance, particularly by influencing androgen activity, such as inhibiting 5α-reductase activity (Salehi et al., 2019). Studies in experimental animal models indicate that cucurbitacin-rich seed extracts increase levels of follicle-stimulating hormone, testosterone and luteinizing hormone, potentially enhancing libido and addressing hormone-related sexual dysfunction (Ademiluyi et al., 2019; Elakhdar et al., 2020; Purnamasari et al., 2021; Obembe et al., 2023).

Neuroprotective effects

Stress and anxiety, major contributors to sexual dysfunction, can be mitigated by the neuroprotective properties of cucurbitacins. These compounds exhibit anxiolytic and neurorestorative effects, supporting the role of cucurbitacins in alleviating psychogenic sexual dysfunction (Chen et al., 2020; Liu et al., 2021). A study conducted by Wahid et al. (2023) showed a reduction in anxiety and depression behaviours, improved memory and elevated norepinephrine levels in mice administered with *C. maxima* seed extracts, an indicator of the anxiolytic effects of the cucurbitacins in the pumpkin seeds. Another study has also reported the anti-depressive-like activity of cucurbitacins, indicating their potential as a neuroprotective compound (Ge et al., 2023).

Pharmacokinetics of cucurbitacins

Cucurbitacins' pharmacokinetics is versatile, dynamic and complex. In terms of its absorption and bioavailability, Cucurbitacins exhibit moderate oral bioavailability due to their hydrophobic nature, which limits solubility in water (Dai et al., 2023). Studies suggest that formulation improvements, such as liposomal delivery systems or nanoparticle encapsulation, enhance the absorption and systemic availability of triterpenoids such as cucurbitacins (Milan et al., 2022; Chowdhury et al., 2024). Metabolically, cucurbitacins undergo hepatic metabolism primarily through cytochrome P450 enzymes, producing both active and inactive metabolites (Shu et al., 2023; Liu et al., 2024). The metabolic pathway can influence the pharmacological effects, particularly their anti-inflammatory and antioxidant activities (Wang et al., 2017; Siyuan et al., 2020).

Regarding its distribution, the lipophilic nature of cucurbitacins allows them to cross biological membranes efficiently, suggesting good tissue distribution. This property facilitates their action on vascular endothelial tissues, reproductive organs, and the central nervous system, relevant sites for addressing sexual dysfunction (Yang et al., 2020; Dai et al., 2023). In terms of elimination and excretion, cucurbitacins are primarily excreted via the biliary route, with minimal renal clearance. Their elimination half-life varies depending on the specific compound and delivery method, but is generally sufficient for maintaining therapeutic plasma levels (Shu et al., 2023).

Although numerous studies support the anti-inflammatory and antioxidant roles of cucurbitacins, mechanisms directly relevant to ED and sexual dysfunction and available evidence of hormonal modulation and prostate health benefits, broadening their therapeutic potential, several limitations were noted in this review. First, human clinical trials evaluating cucurbitacins for sexual dysfunction are limited, with most evidence derived from *in vitro* or *in vivo* studies (Chung et al., 2015). Additionally, most research is preclinical, with insufficient human trials to validate its safety and effectiveness in clinical applications.

Secondly, the poor bioavailability of cucurbitacins in traditional formulations, where low solubility and rapid metabolism restrict their efficacy in systemic applications (Delgado-Tiburcio et al., 2022; Shu et al., 2023). Finally, most studies often lack comprehensive pharmacokinetic evaluations, leaving questions about optimal dosing and long-term safety. Other significant and crucial limitations regarding the use of pumpkin seeds as a remedy for ED are associated with toxicity at high doses. Cucurbitacins are associated with gastrointestinal irritation and hepatotoxicity at high doses, which limits their therapeutic window (Shaban and Sahu, 2017; Siyuan et al., 2020).

Conclusion

Pumpkin seeds and their bioactive compounds, particularly cucurbitacins, represent a promising natural intervention for addressing sexual dysfunction and low libido in men. Their rich composition of essential nutrients such as zinc, arginine, and antioxidants positions them as a functional food with profound benefits for male reproductive health. By enhancing testosterone production, supporting nitric oxide synthesis for improved blood flow, and reducing oxidative stress and inflammation, pumpkin seeds offer a holistic approach to improving sexual health. Furthermore, the neuroprotective and mood-enhancing properties of compounds like tryptophan add a critical psychological dimension to their efficacy.

The therapeutic potential of cucurbitacins in managing ED through reducing inflammation and improving prostate

health broadens the therapeutic scope of pumpkin-based remedies. However, while preclinical studies have shown encouraging results, further clinical research is needed to validate their safety, efficacy, and optimal dosages in treating sexual dysfunction in men. Ultimately, integrating pumpkin seeds into a balanced diet not only supports sexual health but also contributes to overall well-being, addressing broader health concerns such as cardiovascular and metabolic health. As scientific exploration continues to unveil the therapeutic potential of this remarkable functional food, pumpkin seeds stand as a beacon of hope for natural and sustainable solutions to complex health issues, including male sexual dysfunction and low libido. Future research should focus on overcoming bioavailability challenges and assessing the potential for cucurbitacins in integrated therapeutic approaches.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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