Bitter Melon (*Momordica charantia*) Endocrine Disruption: A Review

**ABSTRACT**

*Momordica charantia*, commonly known as bitter melon, is a tropical vine that has a long history of use in traditional medicine. Recent studies have focused on its potential therapeutic applications, particularly in the management of diabetes, metabolic syndrome, and polycystic ovary syndrome (PCOS). The plant contains various bioactive compounds, including charantin, momordicin, and polypeptide-p, which contribute to its hypoglycemic, anti-inflammatory, and antioxidant properties. Bitter melon has been shown to modulates glucose metabolism, insulin signaling, and adipokine production, making it a promising natural intervention for metabolic disorders. However, the endocrine-disrupting potential of bitter melon raises safety concerns, especially in individuals with hormonal imbalances or in those taking hormone-sensitive medications. Bitter melons may interact with reproductive hormones, thyroid function, and adrenal hormones, necessitating caution in its use. Future research should address knowledge gaps such as the precise mechanisms of action, optimal dosage, and long-term safety profiles. Developing targeted therapies based on bitter melon's bioactive compounds holds promise but requires further investigation and clinical trials. Long-term safety studies are crucial to establish guidelines for the use of bitter melons and identify potential contraindications. Although bitter melon shows significant therapeutic potential, its use should be approached with caution and under medical supervision. As research progresses, a better understanding of the effects of bitter melon on the endocrine system will help maximize its therapeutic benefits while minimizing potential risks.

**Keywords**: Bitter Melon; *Momordica charantia*; Endocrine Disruption; Bioactive Compounds; Charantin; Momordicin; Polypeptide-p; Hypoglycemic; Anti-inflammatory; Antioxidant; Metabolic Disorders; Reproductive Hormones; Thyroid Function; Adrenal Hormones; Traditional Medicine

**Introduction**

*Momordica charantia*, commonly known as bitter melon or bitter gourd, is a tropical and subtropical vine belonging to the Cucurbitaceae family (Bortolotti et al., 2019). Native to Asia, Africa, and the Caribbean, it is now cultivated worldwide for its edible fruits and medicinal properties. This plant has gained significant attention in the scientific community because of its diverse array of bioactive compounds and potential health benefits (Zannou et al., 2022). Bitter melon has been used for centuries in traditional medicine across various cultures to treat a wide range of ailments, including diabetes, digestive issues, and skin conditions (Basch et al., 2003). Its most significant traditional use is in the management of diabetes as it is believed to help regulate blood sugar levels. Modern scientific research has begun to investigate these traditional claims, with some studies supporting the potential of plants in managing diabetes and other health conditions (Nam et al., 2023). Understanding endocrine disruption (the interference of natural or synthetic compounds with the normal functioning of hormones in the body) can lead to various health issues. properties of *Momordica charantia* are crucial for several reasons (Krawinkel & Keding, 2006). Recent studies have shown that certain compounds in bitter melon may act as endocrine disruptors, potentially interfering with hormone signaling pathways in the body. This interaction could have both positive and negative effects on human health depending on the specific context and dosage (Basch et al., 2003). Studying these mechanisms is essential for developing safe and effective therapeutic applications of bitter melon as well as for assessing the potential risks associated with its consumption. The major bioactive compounds found in bitter melon include charantin (a steroidal saponin known for its hypoglycemic properties), momordicin, vicine, and polypeptide-p (Tan et al., 2015). These phytochemicals work synergistically to impart bitter melon with potential therapeutic effects, including antidiabetic, anticancer, anti-inflammatory, and immunomodulatory properties. However, some of these compounds may also act as potential endocrine disruptors, affecting glucose metabolism, insulin signaling, and the production of various hormones (Yang et al., 2018). This introduction sets the stage for a comprehensive exploration of the endocrine disruption properties of Momordica charantia, its potential therapeutic applications, and the importance of understanding its effects on human health.

**Overview of *Momordica charantia* (bitter melon)**

*Momordica charantia* is a tropical and subtropical vine that belongs to the Cucurbitaceae family. Native to Asia, Africa, and the Caribbean, it is now cultivated worldwide for its edible fruits and medicinal properties (Bortolotti et al., 2019). The plant has lobed leaves, yellow flowers, and oblong fruits, with a warty exterior. The fruit is green when unripe, turning yellow or orange as it matures, with a white interior and red seeds (Shahrajabian & Sun, 2025). The distinctly bitter taste intensifies as the fruit ripens. Nutritionally, bitter melon is low in calories and rich in vitamins C and A, folate, potassium, and dietary fiber (Lopes et al., 2020). It is used in various cuisines, particularly in Asian and Indian dishes, and has been employed in traditional medicine for treating diabetes, digestive issues, and skin conditions (Efird et al., 2014). Scientific research has explored its potential antidiabetic properties, possible anticancer effects, and antioxidant activities (Choi et al., 2012). Bitter melons grow best in warm climates, requiring well-drained soil and full sun exposure, and can be grown annually in temperate regions. However, it may interact with certain medications, particularly those for diabetes, and pregnant women should avoid consuming large amounts owing to potential risks (Efird et al., 2014).

**Traditional uses and medicinal properties**

*Momordica charantia* has been used for centuries in traditional medicine across various cultures. This climbing vine, which is native to tropical and subtropical regions, is renowned for its distinctive bitter taste and numerous health benefits (Efird et al., 2014). In traditional medicine, bitter melon is used to treat a wide range of ailments, including diabetes, digestive disorders, and skin conditions. The fruits, leaves, and seeds of the plant are utilized for their medicinal properties (Mahwish et al., 2021). One of the most significant traditional uses of bitter melon is the management of diabetes, as it is believed to help regulate blood sugar levels. The plant is also used to alleviate digestive problems such as constipation, indigestion, and ulcers (Yung et al., 2016). In some cultures, bitter melon is topically applied to treat skin infections, wounds, and burns. Additionally, it is believed to possess anti-inflammatory, antiviral, and antimicrobial properties, making it useful for treating various infections and reducing inflammation throughout the body (Dwijayanti et al., 2019). Some traditional practitioners use bitter melon to support liver function, boost the immune system, and even act as a potential anti-cancer agent. Modern scientific research has begun to investigate these traditional claims, with some studies supporting the potential of plants in managing diabetes and other health conditions (Efird et al., 2014). However, further research is needed to fully understand the medicinal properties of bitter melon and its potential applications in modern healthcare. Given its historical application in managing diabetes—a condition intricately linked to hormonal activity—investigating the endocrine-disrupting properties of bitter melon has emerged as a critical area of study.

**Importance of understanding endocrine disruption**

Understanding endocrine disruption in relation to *Momordica charantia*, commonly known as bitter melon, is crucial for several reasons. Bitter melon has traditionally been used in various cultures for its potential health benefits, including its ability to regulate blood sugar levels (Gao et al., 2021). However, recent studies have shown that certain compounds in bitter melon may act as endocrine disruptors, potentially interfering with hormone signaling pathways in the body (Yang et al., 2022). This interaction could have both positive and negative effects on human health depending on the specific context and dosage. For instance, while some endocrine-disrupting properties might contribute to the plant's anti-diabetic effects, they could also potentially lead to unintended consequences in other hormonal systems (Chan et al., 2020). Understanding these mechanisms is essential for developing safe and effective therapeutic applications of bitter melon as well as for assessing the potential risks associated with its consumption. Moreover, studying the endocrine-disrupting properties of bitter melon can provide valuable insights into the broader fields of phytochemistry and endocrinology, potentially leading to the discovery of novel compounds with therapeutic potential (Tan et al., 2015). As the use of natural remedies and functional foods continues to gain popularity, a thorough understanding of their endocrine-disrupting potential has become increasingly important for ensuring consumer safety and maximizing potential health benefits (Xu et al., 2022). Having established the background and importance of studying the endocrine effects of *Momordica charantia*, we will now examine its phytochemical composition in more detail.



**Figure 1**: Unveiling the multifaceted nature of bitter lemon

**Phytochemical Composition of Bitter Melon**

**Major bioactive compounds**

*Momordica charantia* is a tropical and subtropical vine belonging to the Cucurbitaceae family. This plant has gained significant attention from the scientific community because of its diverse array of bioactive compounds and potential health benefits (Mozaniel et al., 2018). The major bioactive compounds found in bitter melon are charantin, momordicin, vicine, and polypeptide-p. Charantin, a steroidal saponin, is known for its hypoglycemic properties and has been studied for its potential in diabetes (Saeed et al., 2018). Momordicin, a triterpene glycoside, contributes to the bitter taste of fruits and has anti-inflammatory and antioxidant effects. Vicine, an alkaloid, has been associated with antimicrobial and anthelmintic activities. Polypeptide-p, also referred to as p-insulin, has insulin-like effects and may play a role in glucose regulation (Krawinkel & Keding, 2006). Additionally, bitter melon contains various other compounds such as triterpenoids, flavonoids, and phenolic acids, which contribute to its overall bioactivity. These phytochemicals work synergistically to impart bitter melon with potential therapeutic effects, including antidiabetic, anticancer, anti-inflammatory, and immunomodulatory properties (Arif et al., 2021). The concentration and composition of these bioactive compounds can vary depending on factors such as plant variety, growth conditions, and extraction methods, highlighting the importance of standardization in research and the potential medicinal applications of *Momordica charantia*.

**Potential endocrine-disrupting components**

*Momordica charantia* is a tropical and subtropical vine that is widely used in traditional medicine and cuisines. Although celebrated for its potential health benefits, including antidiabetic properties, recent research has raised concerns about its possible endocrine-disrupting effects (Mozaniel et al., 2018). The plant contains various bioactive compounds such as charantin, vicine, and momordicin, which may interfere with hormonal pathways. Charantin, a steroidal saponin, affects insulin secretion and glucose metabolism, potentially affecting the endocrine system (Sidorkiewicz et al., 2017). Vicine, a pyrimidine glycoside, may influence the thyroid function and reproductive hormone levels. Momordicin, a triterpene, affects steroidogenesis and alters the production of sex hormones (Nguyen et al., 2020). Additionally, bitter melon contains phytoestrogens that can mimic or antagonize estrogen activity in the body. These compounds may bind to estrogen receptors, potentially disrupting normal hormonal signaling (Sur & Ray, 2020). Cucurbitacins present in bitter melon have also been associated with endocrine-modulating effects, particularly in the hypothalamic-pituitary-adrenal axis (Dwijayanti et al., 2019). Although the potential health benefits of *Momordica charantia* are widely recognized, the presence of these bioactive compounds underscores the need for further research to fully understand their impact on the endocrine system and to establish safe consumption guidelines, especially for individuals with hormonal imbalances or those undergoing hormone-sensitive treatments (Mozaniel et al., 2018). By understanding the key bioactive compounds in bitter melon, we can now explore how these components interact with the endocrine system.

**Endocrine System Interactions**

**Effects on glucose metabolism**

*Momordica charantia* has attracted considerable attention for its potential impact on glucose metabolism. This tropical vine fruit contains various bioactive compounds including charantin, vicine, and polypeptide-p, which are believed to contribute to its hypoglycemic properties (Lo et al., 2017). Studies have shown that bitter melon can enhance glucose uptake in peripheral tissues, stimulate insulin secretion from pancreatic beta cells, and improve insulin sensitivity (Arif et al., 2021). The ability of the fruit to activate AMP-activated protein kinase (AMPK)pathway plays a crucial role in regulating glucose metabolism by promoting glucose uptake and fatty acid oxidation (Lee et al., 2011). Additionally, bitter melon inhibits glucose absorption in the intestines and suppresses key enzymes involved in glucose metabolism, such as alpha-glucosidase and alpha-amylase (Gao et al., 2021). These mechanisms collectively contribute to lowering blood glucose levels and improving overall glycemic control. Although numerous preclinical and small-scale clinical studies have demonstrated promising results, larger randomized controlled trials are needed to establish the efficacy and safety of bitter melon as a potential therapeutic agent for managing diabetes and related metabolic disorders. Despite these encouraging findings, it is essential to note that bitter melon should not be considered as a substitute for conventional medical treatments, and individuals with diabetes should consult healthcare professionals before incorporating it into their diet or treatment regimen.

**Impact on insulin signaling**

*Momordica charantia* has garnered significant attention for its potential effects on insulin signaling and glucose metabolism (Han et al., 2018). This tropical vine fruit contains bioactive compounds including charantin, vicine, and polypeptide-p, which are associated with hypoglycemic properties (Wen et al., 2019). Research suggests that bitter melon may enhance insulin sensitivity by increasing glucose uptake in the peripheral tissues and suppressing hepatic glucose production (Gao et al., 2021). Studies have demonstrated that bitter melon extract can activate the AMP-activated protein kinase (AMPK)pathway, a key regulator of cellular energy homeostasis and insulin signaling. Additionally, bitter melon has been shown to improve the phosphorylation of insulin receptor substrates and enhance the translocation of glucose transporter 4 (GLUT4) to the cell membrane, facilitating glucose uptake in muscle and adipose tissues (Ansari et al., 2024). These fruit components may also protect pancreatic β-cells from oxidative stress and promote insulin secretion. Furthermore, bitter melon modulates the expression of genes involved in glucose and lipid metabolism, potentially contributing to its insulin-sensitizing effects (Gao et al., 2021). Although these findings are promising, it is important to note that the exact mechanisms of action and optimal dosage for therapeutic use remain subjects of ongoing research. As with any potential natural remedy, further clinical studies are necessary to fully elucidate the efficacy and safety of bitter melon in managing insulin resistance and diabetes.

**Influence on adipokine production**

*Momordica charantia* has attracted considerable attention for its potential impact on adipokine production and metabolic health. This tropical fruit contains bioactive compounds that may modulate the secretion of adipokines, which are signaling proteins produced by the adipose tissue (Gao et al., 2021). Research suggests that bitter melon extract can influence the expression of key adipokines such as adiponectin, leptin, and resistin (Smitka & Marešová, 2015). Studies have shown that *Momordica charantia* may increase adiponectin levels, which are associated with improved insulin sensitivity and reduced inflammation (Rubino et al., 2016). Conversely, it may decrease leptin and resistin levels, potentially contributing to improved metabolic function and reduced obesity-related complications. The mechanisms underlying these effects involve activation of AMP-activated protein kinase (AMPK)and peroxisome proliferator-activated receptor gamma (PPARγ)pathways (Bednarska-Makaruk et al., 2017). Although promising, further research is needed to fully elucidate the precise molecular mechanisms and long-term effects of bitter melon on adipokine production and its potential therapeutic applications in metabolic disorders. Beyond its effects on glucose metabolism and insulin signaling, bitter melon also influences other hormonal pathways in the body (Hussain et al., 2022)

**Hormonal Modulation**

**Effects on reproductive hormones**

Research suggests that bitter melon may influence the production and regulation of various reproductive hormones. Some studies have indicated that bitter melon extract can affect testosterone levels in males, potentially leading to changes in sperm production and quality. In females, bitter melon has been observed to affect estrogen and progesterone levels, which play crucial roles in menstrual cycle and fertility (Hussain et al., 2022). Additionally, the plant has been associated with alterations in follicle-stimulating hormone (FSH)and luteinizing hormone (LH)secretion, both of which are essential for reproductive functions (Santi et al., 2020). Although these findings are promising, it is important to note that the exact mechanisms and long-term effects of bitter melon on reproductive hormones are not fully understood (Sur & Ray, 2020). Further research is needed to elucidate the precise impact of *Momordica charantia* on the endocrine system and its potential application in reproductive health management.

**Interactions with thyroid function**

*Momordica charantia* has garnered attention for its potential effects on thyroid function. This tropical vine, which is native to Asia, Africa, and the Caribbean, contains bioactive compounds that may influence thyroid hormone production and metabolism (Xiao et al., 2024). Some studies suggested that bitter melon extract can modulate thyroid-stimulating hormone (TSH)levels and affect the conversion of thyroxine (T4) to triiodothyronine (T3) (Kuzmenko et al., 2021). The hypoglycemic properties of the plant, attributed to its ability to enhance insulin sensitivity, may indirectly affect thyroid function by altering glucose metabolism. Additionally, the antioxidant properties of bitter melon could potentially protect the thyroid tissue from oxidative stress (Ansari et al., 2024). However, research on the direct interactions between *Momordica charantia* and thyroid function remains limited and inconclusive (Fan et al., 2019). Although some animal studies have shown promising results, human clinical trials are needed to establish the precise mechanisms and potential therapeutic applications of bitter melon in thyroid disorders. As with any herbal supplement, individuals with thyroid conditions should consult healthcare professionals before incorporating bitter melon into their diet or treatment regimen to avoid potential adverse effects or interactions with existing medications (Basch et al., 2003).

**Impact on adrenal hormones**

*Momordica charantia* has attracted interest because of its potential impact on adrenal hormones. This tropical vine, native to Asia, Africa, and the Caribbean, contains bioactive compounds that may influence adrenal hormone production and regulation of adrenal hormones (Gao et al., 2021). Studies have suggested that bitter melon extract can modulate cortisol levels, the primary stress hormone produced by adrenal glands (Alisofi et al., 2019). Some studies indicate that bitter melon may help reduce elevated cortisol levels, potentially mitigating stress-related symptoms and improving overall adrenal function (Sur et al., 2019). Additionally, bitter melon has been associated with changes in aldosterone secretion, which is another important adrenal hormone involved in blood pressure regulation and electrolyte balance. Although the exact mechanisms are not fully understood, it is believed that the plant's unique phytochemicals, including charantin and momordicin, play a role in the hormonal effects (Zannou et al., 2022). However, more comprehensive research is needed to fully elucidate the impact of *Momordica charantia* on adrenal hormones and its potential therapeutic applications in adrenal-related disorders (Krawinkel and Keding, 2006b). As with any natural remedy, individuals should consult healthcare professionals before using bitter melon for adrenal hormone management (Gao et al., 2021). To better understand the hormonal effects of bitter melon, the molecular mechanisms underlying its endocrine-disrupting properties must be examined.



**Figure 2**: Bitter Mellon’s impact on endocrine system

**Molecular Mechanisms of Endocrine Disruption**

**Receptor-mediated pathways**

*Momordica charantia* exerts its therapeutic effects via various receptor-mediated pathways. The plant's bioactive compounds interact with insulin receptors, enhancing glucose uptake and metabolism in the peripheral tissues (Lo et al., 2017). Bitter melon activates the AMP-activated protein kinase (AMPK)pathway, promoting glucose utilization and fatty acid oxidation. It also stimulates the peroxisome proliferator-activated receptor (PPAR)pathway, thereby improving insulin sensitivity and lipid metabolism (Smith & Steinberg, 2017). Plant components interact with glucagon-like peptide-1 (GLP-1) receptors to enhance insulin secretion and reduce glucagon release. Bitter melons modulate the expression of glucose transporters, particularly GLUT4, facilitating glucose uptake in muscle and adipose tissues (D’Souza et al., 2020). Additionally, it influences the PI3K/Akt signaling pathway, which is crucial for insulin-mediated glucose metabolism. The antioxidant properties of plants are mediated through the activation of nuclear factor erythroid 2-related factor 2 (Nrf2), which enhances cellular defense against oxidative stress. These receptor-mediated pathways collectively contribute to the antidiabetic, anti-inflammatory, and antioxidant effects of bitter melon, making it a potential therapeutic agent for metabolic disorders (Younis & Ghanim, 2022).

**Enzyme inhibition or activation**

*Momordica charantia* (bitter melon) exhibits significant enzyme inhibition and activation. The potential therapeutic effects of this plant have been extensively studied, particularly in relation to diabetes management (Bortolotti et al., 2019). Bitter melon contains various bioactive compounds, including charantin, vicine, and polypeptide-p, which have been shown to inhibit α-glucosidase and α-amylase enzymes. These enzymes are responsible for carbohydrate digestion and their inhibition can help regulate blood glucose levels (Hsieh et al., 2021). Additionally, bitter melon activates AMP-activated protein kinase (AMPK), which is a key enzyme involved in cellular energy homeostasis and glucose uptake. This activation enhances glucose utilization and fatty acid oxidation in the peripheral tissues (Gao et al., 2021). Bitter melon also inhibits 11β-hydroxysteroid dehydrogenase type 1 (11β-HSD1), an enzyme associated with obesity and metabolic syndrome (Alam et al., 2015). Furthermore, the plant has been found to inhibit pancreatic lipase, potentially aiding in weight management. The enzyme-modulating effects of bitter melon extend to its antioxidant properties, as it activates antioxidant enzymes such as superoxide dismutase, catalase, and glutathione peroxidase, contributing to its overall health-promoting effects (Gao et al., 2021).

**Gene expression alterations**

*Momordica charantia* exhibits significant gene expression alterations in response to various environmental factors and developmental stages (Sheikhalipour et al., 2022). Studies have shown that genes involved in primary metabolism, secondary metabolism, and stress responses are differentially expressed in different tissues under different conditions (Nerurkar et al., 2010). For instance, genes related to terpenoid biosynthesis, which contribute to bitter taste and medicinal properties of plants, show increased expression during fruit development (Li et al., 2021). Transcriptomic analyses have revealed that genes associated with antioxidant activity, such as superoxide dismutase and catalase, are upregulated under abiotic stress conditions such as drought and salinity. Additionally, genes involved in the biosynthesis of triterpenoids and phenolic compounds, which are responsible for the antidiabetic and anticancer properties of the plant, show tissue-specific expression patterns (Sun et al., 2019). The expression of genes related to fruit ripening, including those involved in ethylene biosynthesis and cell wall modification, is tightly regulated during fruit maturation (Dwijayanti et al., 2019). Understanding these gene expression alterations provides valuable insights into the molecular mechanisms underlying the unique nutritional and medicinal properties of bitter melon, potentially leading to improved cultivation practices and the development of enhanced varieties. The molecular interactions between bitter melon and the endocrine system give rise to several potential therapeutic applications (Basch et al., 2003)

**Potential Therapeutic Applications**

**Diabetes management**

*Momordica charantia* has attracted interest for its potential role in diabetes management. This fruit from a tropical vine is rich in bioactive compounds, such as charantin, vicine, and polypeptide-p, all of which have been shown to lower blood sugar levels (Lo et al., 2017). Studies have suggested that bitter melon may enhance insulin sensitivity, promote glucose uptake in peripheral tissues, and inhibit glucose absorption in the intestines. Its mechanisms of action include stimulating pancreatic beta cells to produce insulin, increasing glucose utilization in the liver and muscles, and reducing hepatic glucose production (Basch et al., 2003). Clinical trials have shown varying degrees of efficacy in lowering blood glucose levels in patients with type 1 and type 2 diabetes mellitus (Rahman et al., 2015). However, the optimal dosage, preparation method, and long-term effects of bitter melon remain the subject of ongoing research (Mahwish et al., 2021). While promising, it is essential to note that bitter melon should not replace conventional diabetes treatments without medical supervision (Basch et al., 2003). Potential side effects and interactions with other medications necessitate caution and consultation with healthcare providers before incorporating bitter melon into diabetes management strategies (Yung et al., 2016).

**Metabolic syndrome**

*Momordica charantia* has garnered significant attention for its potential role in the management of metabolic syndrome. The bitter taste of this tropical vine fruit contains bioactive compounds that may affect various aspects of metabolic health (Han et al., 2018). Research suggests that bitter melon can help regulate blood glucose levels by enhancing insulin sensitivity and promoting cellular glucose uptake. Additionally, it may contribute to weight management by affecting lipid metabolism and reducing fat accumulation (Martínez-Abundis et al., 2016). Studies have indicated that bitter melon extracts can lower cholesterol levels and improve lipid profiles, potentially reducing the risk of cardiovascular complications associated with metabolic syndromes (Raygan et al., 2015). The antioxidant properties of the fruit may also play a role in mitigating oxidative stress and inflammation, both of which are implicated in the development and progression of metabolic disorders (Lee et al., 2015). Although promising, it is important to note that more comprehensive clinical trials are needed to fully elucidate the efficacy and safety of bitter melon as a therapeutic agent for metabolic syndrome. Nonetheless, its potential as a natural intervention continues to be a subject of interest in both traditional medicine and modern scientific research (Hussain et al., 2022).

**Polycystic ovary syndrome (PCOS)**

*Momordica charantia*, commonly known as bitter melon, has shown potential therapeutic effects in (PCOS). PCOS is a complex endocrine disorder characterized by hormonal imbalance, ovulatory dysfunction, and metabolic disturbances (Hernández-Jiménez et al., 2021). The effect of bitter melon on PCOS is primarily attributed to its ability to improve insulin sensitivity and regulate glucose metabolism (Nerurkar et al., 2008). The fruit contains bioactive compounds, including charantin, vicine, and polypeptide-p, which have been found to exert insulin-like effects (Saeed et al., 2018). By enhancing insulin sensitivity, bitter melon may help address the insulin resistance commonly observed in patients with PCOS. This improvement in insulin function can lead to better glucose uptake by cells, potentially reducing hyperinsulinemia and its associated symptoms (Basch et al., 2003). Additionally, bitter melon has demonstrated anti-inflammatory and antioxidant properties, which may help alleviate the chronic low-grade inflammation often present in PCOS (Chao et al., 2014). Some studies have suggested that bitter melon consumption may contribute to weight loss and improve lipid profiles, both of which are beneficial for PCOS management (Hussain et al., 2022). Furthermore, bitter melon has been reported to have potential effects on hormonal balance, possibly by influencing the regulation of androgens and other reproductive hormones implicated in PCOS (Cermik et al., 2003). While promising, it is important to note that more extensive clinical research is needed to fully elucidate the efficacy and safety of bitter melon as a therapeutic intervention for PCOS (Basch et al., 2003). As with any natural remedy, individuals with PCOS should consult healthcare professionals before incorporating bitter melon into their treatment regimens (Shahrajabian & Sun, 2025). Although bitter melon shows promise for treating various conditions, it is crucial to consider the safety implications of its use.

**Safety Considerations and Side Effects**

**Potential risks of endocrine disruption**

*Momordica charantia* is widely used in traditional medicine and as a dietary supplement. However, their potential effects on the endocrine system have raised concerns (Krawinkel & Keding, 2006). Bitter melons contain compounds that may interfere with hormone production, signaling, and metabolism (Basch et al., 2003). One primary concern is its effect on blood glucose regulation. Although often touted for its hypoglycemic properties, excessive consumption of bitter melon may lead to hypoglycemia, particularly in individuals with diabetes or those taking glucose-lowering medications (Uebanso et al., 2007). Additionally, bitter melon has been reported to affect thyroid function, potentially altering the thyroid hormone levels and metabolism. Some studies suggest that bitter melon may influence reproductive hormones, potentially affecting fertility in both males and females (Alam et al., 2015). Its phytoestrogenic properties can interfere with estrogen-dependent processes, raising concerns for individuals with hormone-sensitive conditions. Furthermore, bitter melon may interact with the hypothalamic-pituitary-adrenal axis, potentially affecting cortisol levels and stress responses (Alisofi et al., 2019). The effects of plants on insulin sensitivity and secretion could also affect other hormones regulated by insulin, such as growth and sex hormones (Uebanso et al., 2007). While more research is needed to fully understand the endocrine-disrupting potential of bitter melon, caution is advised, especially for individuals with pre-existing endocrine disorders, pregnant women, and those taking hormone-related medications (Nagasawa et al., 2002). Healthcare professionals should be aware of these potential risks when advising patients about bitter melon consumption or supplementation.

**Interactions with medications**

*Momordica charantia* has been reported to interact with various medications, potentially affecting their efficacy or causing adverse effects. One of the most significant interactions is with antidiabetic drugs, as bitter melon has hypoglycemic properties that may enhance the blood glucose-lowering effects of these medications, potentially leading to hypoglycemia (Han et al., 2018). Patients taking insulin or oral hypoglycemic agents should closely monitor their blood glucose levels when consuming bitter melon (Arif et al., 2021). Additionally, bitter melon may interact with anticoagulant medications, such as warfarin, potentially increasing the risk of bleeding. Plants contain compounds that may affect the metabolism of certain drugs processed by the liver cytochrome P450 enzyme system, potentially altering their effectiveness or increasing the risk of side effects (Zhu et al., 2012). Some studies have suggested that bitter melon may interact with chemotherapy drugs, potentially interfering with their efficacy or exacerbating side effects. Bitter melon has also been reported to have a mild diuretic effect, which could potentially interact with diuretic medications or affect the electrolyte balance (Feng et al., 2023). Furthermore, plants may interact with immunosuppressant drugs, potentially altering their effectiveness in transplant patients or those with autoimmune conditions (Alisofi et al., 2019). Because of its potential to lower blood sugar levels, bitter melon consumption should be carefully monitored in patients scheduled for surgery as it may interfere with blood glucose control during and after the procedure (Laczkó-Zöld et al., 2024). Given these potential interactions, it is crucial for patients to consult healthcare professionals before incorporating bitter melon into their diet or supplement regimen, especially if they are taking medications for chronic conditions or undergoing medical treatment (Bortolotti et al., 2019).

**Contraindications and precautions**

*Momordica charantia* should be used with caution because of several contraindications and precautions. Pregnant women should avoid consuming bitter melon, as it may induce uterine contractions and potentially lead to miscarriages (Efird et al., 2014). Individuals with diabetes must exercise caution because bitter melon can lower blood sugar levels and may interact with diabetes medications, necessitating close monitoring of glucose levels (Basch et al., 2003). Those with G6PD deficiency should refrain from using bitter melon, as it may exacerbate hemolytic anemia. Bitter melons may interact with certain medications, including blood thinners and chemotherapy drugs, potentially altering their effectiveness (Gao et al., 2021). People with liver or kidney disorders should consult a healthcare professional before using bitter melon because it may affect organ function (Basch et al., 2003). Children and elderly individuals should use bitter melon under medical supervision because of its potential side effects. Allergic reactions, although rare, have been reported; therefore, individuals with known allergies to plants of the Cucurbitaceae family should exercise caution. It is advisable to discontinue bitter melon use for at least two weeks before any scheduled surgery to prevent potential complications. Despite the wealth of research on bitter melon, several knowledge gaps remain to be addressed in future studies (Alam et al., 2015)

**Figure 3**: Weighing risk and benefits of bitter lemon

**Future Research Directions**

**Gaps in current knowledge**

Despite extensive research on *Momordica charantia* (bitter melon), several knowledge gaps remain. The precise mechanisms of action of its antidiabetic effects remain incompletely understood, particularly regarding the interplay between various bioactive compounds (Laczkó-Zöld et al., 2024). The optimal dosage and preparation methods for maximizing therapeutic benefits have yet to be standardized, hindering their clinical application. Long-term safety profiles and potential drug interactions require further investigation, particularly in vulnerable populations such as pregnant women and children (Bortolotti et al., 2019). The genetic diversity of bitter melon cultivars and their impact on phytochemical composition and efficacy requires comprehensive exploration (Kole et al., 2012). The potential synergistic effects of bitter melon with other herbal remedies or conventional medications remain largely unexplored (Basch et al., 2003). The role of gut microbiota in mediating the health benefits of bitter melon requires further elucidation. Advanced clinical trials are needed to establish its efficacy in managing various health conditions beyond diabetes, such as cancer and cardiovascular disease. The molecular targets and signaling pathways involved in the anti-inflammatory and immunomodulatory properties of bitter melon warrant further investigation (Nerurkar & Ray, 2010). The bioavailability and metabolism of the key compounds in bitter melon, as well as their distribution in different tissues, require further clarification. Additionally, the potential environmental and cultivation factors affecting the medicinal properties of plants remain understudied, limiting efforts to optimize cultivation practices for therapeutic use (Sur & Ray, 2020).

**Potential for developing targeted therapies**

*Momordica charantia* has attracted considerable interest in the realm of targeted therapies because of its wide range of bioactive compounds and its potential for therapeutic use. This plant's rich phytochemical profile, including triterpenoids, saponins, and polyphenols, exhibits various pharmacological activities, including anti-diabetic, anti-inflammatory, and anti-cancer properties (Bortolotti et al., 2019). Recent studies have focused on isolating and characterizing specific compounds from bitter melon to develop targeted therapies for chronic diseases. For instance, studies have shown promising results using bitter melon extracts to modulate glucose metabolism, potentially offering new avenues for diabetes management (Yang et al., 2018). Additionally, certain compounds isolated from bitter melon have demonstrated selective cytotoxicity against cancer cells, suggesting their potential in the development of targeted anti-cancer treatments. The ability of plants to interact with multiple cellular pathways makes them attractive candidates for developing multi-targeted therapies (Kwatra et al., 2013). As research progresses, the potential of *Momordica charantia* in targeted therapy development continues to expand, offering hope for novel natural-based interventions in the treatment of various diseases.

**Need for long-term safety studies**

*Momordica charantia* has garnered significant attention for its potential health benefits, particularly in the management of diabetes and other metabolic disorders (Mahmoud et al., 2017). Despite its widespread use in traditional medicine and growing popularity as a dietary supplement, there is a pressing need for comprehensive long-term safety studies (Rahman et al., 2015). Although short-term studies have shown promising results, the long-term effects of regular bitter melon consumption remain largely unknown. (Basch et al., 2003) Potential concerns include interactions with medications, effects on liver function, and reproductive health. Additionally, the optimal dosage and duration of use for various health conditions have not yet been firmly established (Feng et al., 2023). Given the increasing incorporation of bitter melon into functional foods and nutraceuticals, it is crucial to conduct rigorous long-term clinical trials to assess its safety profile, potential side effects, and interactions with other medications (Basch et al., 2003). Such studies would provide valuable insights for healthcare professionals, regulatory bodies, and consumers to ensure the safe and effective use of *Momordica charantia* in both traditional and modern healthcare practices.

**Conclusion**

*Momordica charantia*, commonly known as bitter melon, has emerged as a promising plant with potential therapeutic applications for various health conditions, particularly in the management of diabetes, metabolic syndrome, and polycystic ovary syndrome. Its diverse array of bioactive compounds, including charantin, momordicin, and polypeptide-p, contribute to its hypoglycemic, anti-inflammatory, and antioxidant properties. The ability of this plant to modulate glucose metabolism, insulin signaling, and adipokine production highlights its potential as a natural intervention for metabolic disorders. However, the endocrine-disrupting potential of bitter melon raises important concerns regarding its safety and long-term effects. While some of these disruptions may contribute to therapeutic benefits, they also present potential risks, particularly for individuals with pre-existing hormonal imbalances or those taking hormone-sensitive medications. The interactions of plants with reproductive hormones, thyroid function, and adrenal hormones underscore the need for caution in its use. Future research should focus on addressing the gaps in current knowledge, including the precise mechanisms of action, optimal dosage and preparation methods, and long-term safety profiles. The development of targeted therapies based on bitter melon's bioactive compounds holds promise but requires further investigation and clinical trials. Additionally, comprehensive long-term safety studies are essential to establish guidelines for its use and identify potential contraindications. Although *Momordica charantia* shows significant potential in managing various health conditions, its use should be approached with caution. Healthcare professionals and consumers should be aware of its potential benefits and risks, and its incorporation into treatment regimens should be performed under medical supervision. As research progresses, a more comprehensive understanding of the effects of bitter melon on the endocrine system will help harness its therapeutic potential while minimizing potential risks.

**References**

Alam, M. A., Uddin, R., Reza, H. M., Jain, P., Subhan, N., & Rahman, M. M. (2015). Beneficial role of bitter melon supplementation in obesity and related complications of metabolic syndrome. *Journal of Lipids*, *2015* (9): 1–18. https://doi.org/10.1155/2015/496169

Alisofi, S., Einali, A., Sangtarash, M. H. (2019). Jasmonic acid-induced metabolic responses in bitter melon (*Momordica charantia*) seedlings under salt stress. *The Journal of Horticultural Science and Biotechnology*, *95* (2): 247–259. https://doi.org/10.1080/14620316.2019.1663135

Ansari, P., Abdel-Wahab, Y. H. A., Paul, S. R., Chowdhury, S., Khan, J. T., Flatt, P. R., Soultana, M., Hunter, L., Priyanka, S. K. (2024). Insulin secretion by *Momordica charantia* regulates glucose homeostasis in alloxan-induced type 2 diabetic rats. *RPS Pharmacy and Pharmacology Reports*, *3* (1). https://doi.org/10.1093/rpsppr/rqae005

Arif, R., Mahrosh, H. S., Ahmad, S., Tahir Ul Qamar, M., Mustafa, G., Dar, H. R., & Ali, M. (2021). Molecular docking and simulation studies of Antidiabetic Agents devised from hypoglycemic polypeptide-P of *Momordica charantia*. *BioMed Research International*, *2021* (7), 1–15. https://doi.org/10.1155/2021/5561129

Basch, E., Gabardi, S., & Ulbricht, C. (2003). Bitter melon (*Momordica charantia*): a review of efficacy and safety. *American Journal of Health-System Pharmacy*, *60* (4), 356–359. https://doi.org/10.1093/ajhp/60.4.356

Bednarska-Makaruk, M., Sławińska, K., Bochyńska, A., Ługowska, A., Graban, A., Łojkowska, W., Wehr, H., Gugała-Iwaniuk, M., Ryglewicz, D., & Wiśniewska, A. (2017). Association of adiponectin, leptin, and resistin with inflammatory markers and obesity in dementia patients *Biogerontology*, *18* (4), 561–580. https://doi.org/10.1007/s10522-017-9701-0

Bortolotti, M., Mercatelli, D., Polito, L. (2019). *Momordica charantia* is a nutraceutical for inflammation-related diseases. *Frontiers in Pharmacology*, *10* (496169). https://doi.org/10.3389/fphar.2019.00486

Cermik, D., Taylor, H. S., & Selam, B. (2003). Regulation of HOXA-10 expression by testosterone in vitro and in the endometrium of patients with polycystic ovary syndrome. *The Journal of Clinical Endocrinology & Metabolism*, *88* (1): 238–243. https://doi.org/10.1210/jc.2002-021072

Chan, D. W., Yung, M. M., Chan, Y.-S., Xuan, Y., Yang, H., Xu, D., Zhan, J.-B., Chan, K. K., Ng, T.-B., & Ngan, H. Y. (2020). The MAP30 protein from *Momordica charantia* is therapeutic and has synergistic activity with cisplatin against ovarian cancer in vivo by altering metabolism and inducing ferroptosis. *Pharmacological Research*, *161*, 105157. https://doi.org/10.1016/j.phrs.2020.105157

Chao, C.-Y., Sung, P.-J., Wang, W.-H., & Kuo, Y.-H. (2014). Anti-inflammatory effect of *Momordica charantia* in sepsis mice. *Molecules*, *19* (8), 12777–12788. https://doi.org/10.3390/molecules190812777

Choi, J. S., Seo, W. T., Cho, K. M., Kim, H. Y., & Lee, J. H. (2012). Roasting enhances the antioxidant effect of bitter melon (*Momordica charantia* L.), increasing flavan-3-ol and phenolic acid content. *Food Science and Biotechnology*, *21* (1): 19–26. https://doi.org/10.1007/s10068-012-0003-7

D’Souza, K., Mercer, A., Udenigwe, C. C., Pulinilkunnil, T., Mawhinney, H., Kienesberger, P. C. (2020). Whey Peptides Stimulate Differentiation and Lipid Metabolism in Adipocytes and Ameliorate Lipotoxicity-Induced Insulin Resistance in Muscle Cells. *Nutrients*, *12* (2): 425. https://doi.org/10.3390/nu12020425

Dwijayanti, D. R., Shimada, T., Mukai, E., Ishii, T., Nishizawa, M., Okuyama, T., Ikeya, Y. (2019). The bitter melon fruit extract has a hypoglycemic effect and reduces hepatic lipid accumulation in ob/ob mice. *Phytotherapy Research*, *34* (6): 1338–1346. https://doi.org/10.1002/ptr.6600

Efird, J., Mehra, S., Anderson, E., Davies, S., Katunga, L., Choi, Y. (2014). Potential for Improved Glycemic Control with Dietary *Momordica charantia* in Patients with Insulin Resistance and Prediabetes. *International Journal of Environmental Research and Public Health*, *11* (2), 2328–2345. https://doi.org/10.3390/ijerph110202328

Fan, M., Moon, S.-H., Tang, Y., Kim, E.-K., & Choi, Y.-J. (2019). Role of *Momordica charantia* in Resisting Obesity. *International Journal of Environmental Research and Public Health*, *16* (18): 3251. https://doi.org/10.3390/ijerph16183251

Feng, T., Wan, Y., Dai, B., & Liu, Y. (2023). Anticancer activity of bitter melon-derived vesicle extracts against breast Cancer. *Cells*, *12* (6), 824. https://doi.org/10.3390/cells12060824

Gao, Y., Li, X., Huang, Y., Chen, J., & Qiu, M. (2021). Bitter melons and diabetes mellitus. *Food Reviews International*, *39* (1), 618–638. https://doi.org/10.1080/87559129.2021.1923733

Han, J., Tuan, N. Q., Oh, J., Heo, K., Myung, C., Na, M., Quan, K. T., & Park, M. (2018). Cucurbitane triterpenoids from the fruits of *Momordica charantia* improved insulin sensitivity and glucose homeostasis in streptozotocin-induced diabetic mice. *Molecular Nutrition & Food Research*, *62* (7): 1700769. https://doi.org/10.1002/mnfr.201700769

Hernández-Jiménez, J. L., Barrera, D., Espinoza-Simón, E., González, J., Ortíz-Hernández, R., Escobar, L., Echeverría, O., & Torres-Ramírez, N. (2021). Polycystic ovarian syndrome: Signs and feedback effects of hyperandrogenism and insulin resistance. *Gynecological Endocrinology*, *ahead-of-print* (head-of-print), 2–9. https://doi.org/10.1080/09513590.2021.2003326

Hsieh, H., Chen, K., Lin, J., Hsieh, C., & Cheng, K. (2021). Thermal treatment enhances the α-glucosidase inhibitory activity of bitter melon (*Momordica charantia*)by increasing the free form of phenolic compounds and content of Maillard reaction products. *Journal of Food Science*, *86* (7): 3109–3121. https://doi.org/10.1111/1750-3841.15798

Hussain, L., Aamir, N., Hussain, M., Asif, M., Chauhdary, Z., Manzoor, F., Siddique, R., Riaz, M. (2022). Therapeutic Investigation of Standardized Aqueous Methanolic Extract of Bitter Melon (*Momordica charantia* L.)for its potential against polycystic ovary syndrome in an experimental animal model: in vitro and in vivo studies. *Evidence-Based Complementary and Alternative Medicine : ECAM*, *2022* (2), pp.1–14. https://doi.org/10.1155/2022/5143653

Kole, C., Singh, J., Bajpai, A., Abbott, A. G., Kole, P., Rao, V. K., Olukolu, B.A., Elanchezhian, R., Backiyarani, S. (2012). The First Genetic Map and Positions of Major Fruit Trait Loci of Bitter Melon (*Momordica charantia*). *Journal of Plant Science and Molecular Breeding*, *1* (1), 1. https://doi.org/10.7243/2050-2389-1-1

Krawinkel, M. B. & Keding, G. B. (2006). Bitter Gourd (*Momordica charantia):*A Dietary Approach to Hyperglycemia. *Nutrition Reviews*, *64* (7), 331–337. https://doi.org/10.1111/j.1753-4887.2006.tb00217.x

Kuzmenko, N. V., Tsyrlin, V. A., Pliss, M. G., & Galagudza, M. M. (2021). Seasonal variations in the levels of human thyroid-stimulating hormone and thyroid hormones: A meta-analysis. *Chronobiology International*, *38* (3), 301–317. https://doi.org/10.1080/07420528.2020.1865394

Kwatra D., Subramaniam D., Ramamoorthy P., Standing D., Moran E., Velayutham R., Mitra A, Umar S., Anant S. (2013). Methanolic Extracts of Bitter Melon Inhibit Colon Cancer Stem Cells by Affecting Energy Homeostasis and Autophagy. *Evidence-Based Complementary and Alternative Medicine : ECAM*, *2013* (1), 1–14. https://doi.org/10.1155/2013/702869

Laczkó-Zöld, E., Csupor-Löffler, B., Kolcsár, E.-B., Ferenci, T., Nan, M., Tóth, B., & Csupor, D. (2024). The metabolic effect of *Momordica charantia* cannot be determined based on the available clinical evidence: a systematic review and meta-analysis of randomized clinical trials. *Frontiers in Nutrition*, *10*. https://doi.org/10.3389/fnut.2023.1200801

Lee, W.-H., Liang, Y.-C., Chen, Y.-C., Lin, R.-J., Lin, S.-Y., & Lin, H.-M. (2011). Osthole enhances glucose uptake by activating AMP-activated protein kinase in skeletal muscle cells. *Journal of Agricultural and Food Chemistry*, *59* (24), 12874–12881. https://doi.org/10.1021/jf2036559

Lee, Y.-M., Song, B. C., Yeum, K.-J., & Han, S.-I. (2015). Bioactives in Commonly Consumed Cereal Grains: Implications for Oxidative Stress and Inflammation. *Journal of Medicinal Food*, *18* (11), 1179–1186. https://doi.org/10.1089/jmf.2014.3394

Li, N., Qian, L., Dong, Y., Cai, Y., Lv, M., Liu, L., Fan, H., & Sun, X. (2021). Combined analysis of volatile terpenoid metabolism and transcriptome revealed transcription factors related to terpene synthase in the two cultivars of Dendrobium officinale flowers. *Frontiers in Genetics*, *12* (e38146). https://doi.org/10.3389/fgene.2021.661296

Lo, H.-Y., Chen, F.-Y., Chen, J.-C., Ho, T.-Y., Li, C.-C., & Hsiang, C.-Y. (2017). Gastro-Resistant Insulin Receptor-Binding Peptide from *Momordica charantia* Improved the Glucose Tolerance in Streptozotocin-Induced Diabetic Mice via the Insulin Receptor Signaling Pathway. *Journal of Agricultural and Food Chemistry*, *65* (42), 9266–9274. https://doi.org/10.1021/acs.jafc.7b03583

Lopes, A. P., Petenuci, M. E., Oliveira, J. H., Canesin, E. A., Galuch, M. B., Schneider, V. V. A., Visentainer, J. V. (2020). Quantification of phenolic compounds in ripe and unripe bitter melons (*Momordica charantia*)and evaluation of the distribution of phenolic compounds in different parts of the fruit by UPLC–MS/MS. *Chemical Papers*, *74* (8), 2613–2625. https://doi.org/10.1007/s11696-020-01094-5

Mahmoud, M. F., El Ashry, F. E. Z. Z., El Maraghy, N. N. & Fahmy, A. (2017). antidiabetic activities of *Momordica charantia* fruit juice in streptozotocin-induced diabetic rats. *Pharmaceutical Biology*, *55* (1), 758–765. https://doi.org/10.1080/13880209.2016.1275026

Mahwish, M., Bigiu, N., Manea, R., Sultan, M. T., Riaz, A., Ahmed, S., Amarowicz, R., & Saeed, F. (2021). Bitter Melon (*Momordica charantia* L.) fruit bioactive charantin and vicine have potential for diabetes prophylaxis and treatment. *Plants*, *10* (4), 730. https://doi.org/10.3390/plants10040730

Martínez-Abundis, E., Mendez-Del Villar, M., González-Ortiz, M., Pérez-Rubio, K. G., Cortez-Navarrete, M., Ramírez-Rodriguez, A., & Zuñiga, L. Y. (2016). Novel nutraceutical therapies for treating metabolic syndrome. *World Journal of Diabetes*, *7* (7): 142. https://doi.org/10.4239/wjd.v7.i7.142

Mozaniel, S. D. O., Wanessa, A. D. C., Fernanda, W. F. B., Gracialda, C. F., Marilena, E. A., & Raul, N. D. C. J. (2018). English. *African Journal of Biotechnology*, *17* (27), 829–846. https://doi.org/10.5897/ajb2017.16374

Nagasawa, H., Watanabe, K., & Inatomi, H. (2002). Effects of bitter melon (*Momordica charantia* L.) and ginger rhizome (Zingiber officinale rosc)on spontaneous mammary tumorigenesis in SHN mice. *The American Journal of Chinese Medicine*, *30* (2–3), 195–205. https://doi.org/10.1142/s0192415x02000302

Nam, T., Kim, A., & Oh, Y. (2023). Effectiveness of Chickpeas on Blood Sugar: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Nutrients*, *15* (21), 4556. https://doi.org/10.3390/nu15214556

Nerurkar, P. V., Lee, Y. K., Nerurkar, V. R., Adeli, K., & Motosue, M. (2008). *Momordica charantia* (bitter melon) reduces plasma apolipoprotein B-100 levels and increases hepatic insulin receptor substrate and phosphoinositide-3 kinase interactions. *British Journal of Nutrition*, *100* (4), 751–759. https://doi.org/10.1017/s0007114508937430

Nerurkar, P. V., Lee, Y.-K., & Nerurkar, V. R. (2010). *Momordica charantia* (bitter melon) inhibits primary human adipocyte differentiation by modulating adipogenic gene expression *BMC Complementary and Alternative Medicine*, *10* (1). https://doi.org/10.1186/1472-6882-10-34

Nerurkar, P., & Ray, R. B. (2010). Bitter Melon: Antagonist to Cancer. *Pharmaceutical Research*, *27* (6), 1049–1053. https://doi.org/10.1007/s11095-010-0057-2

Nguyen, T.-V.L., Nguyen, P.B.D., Tran, B.L., Nguyen, Q.D., & Huynh, P. T. (2020). Effects of drying conditions in low-temperature microwave-assisted drying on bioactive compounds and antioxidant activity of dehydrated bitter melon (*Momordica charantia* L.). *Food Science & Nutrition*, *8* (7), 3826–3834. https://doi.org/10.1002/fsn3.1676

Rahman, I. U., Rahman, K. U., Khan, R. U., & Bashir, M. (2015). Lower hypoglycemic but higher antiatherogenic effects of bitter melon than glibenclamide in patients with type 2 diabetes *Nutrition Journal*, *14* (1). https://doi.org/10.1186/1475-2891-14-13

Raygan, F., Tehrani, D., Farrokhian, A., Asemi, Z., Rezavandi, Z. (2015). Effects of coenzyme Q10 administration on glucose homeostasis parameters, lipid profiles, inflammation biomarkers, and oxidative stress in patients with metabolic syndrome. *European Journal of Nutrition*, *55* (8), 2357–2364. https://doi.org/10.1007/s00394-015-1042-7

Rubino, E., Gentile, S., Govone, F., Zucca, M., Pinessi, L., De Martino, P., Rainero, I., Gai, A., Vacca, A., & Boschi, S. (2016). Investigation of the role of adipokines in chronic migraine. *Cephalalgia*, *37* (11), 1067–1073. https://doi.org/10.1177/0333102416665871

Saeed, F., Afzaal, M., Niaz, B., Arshad, M. U., Tufail, T., Hussain, M. B. & Javed, A. (2018). The bitter melon (*Momordica charantia*) is a naturally healthy vegetable. *International Journal of Food Properties*, *21* (1), 1270–1290. https://doi.org/10.1080/10942912.2018.1446023

Santi, D., Reiter, E., Rochira, V., Crépieux, P., Simoni, M., Brigante, G., Spaggiari, G., & Casarini, L. (2020). Follicle-stimulating Hormone (FSH)Action on Spermatogenesis: A Focus on Physiological and Therapeutic Roles. *Journal of Clinical Medicine*, *9* (4): 1014. https://doi.org/10.3390/jcm9041014

Shahrajabian, M. H. & Sun, W. (2025). Multidimensional Uses of Bitter Melon (*Momordica charantia* L.)Considering the Important Functions of its Chemical Components. *Current Organic Synthesis*, *22* (4), 516–530. https://doi.org/10.2174/0115701794285586240523101245

Sheikhalipour, M., Mohammadi, S. A., Esmaielpour, B., Zareei, E., Kulak, M., Ali, S., Nouraein, M., Bahrami, M. K., Gohari, G., & Fotopoulos, V. (2022). Exogenous melatonin increases salt tolerance in bitter melon by regulating ionic balance, antioxidant system, and secondary metabolism-related genes. *BMC Plant Biology*, *22* (1). https://doi.org/10.1186/s12870-022-03728-0

Sidorkiewicz, I., Zaręba, K., Czerniecki, J., & Wołczyński, S. (2017). Endocrine-disrupting chemicals: mechanisms of action on the male reproductive system. *Toxicology and Industrial Health*, *33* (7): 601–609. https://doi.org/10.1177/0748233717695160

Smith, B. K. & Steinberg, G. R. (2017). AMP-activated protein kinase, fatty acid metabolism, and insulin sensitivity. *Current Opinion in Clinical Nutrition & Metabolic Care*, *20* (4), 248–253. https://doi.org/10.1097/mco.0000000000000380

Smitka, K., & Marešová, D. (2015). Adipose tissue as an endocrine organ: an update on pro-inflammatory and anti-inflammatory microenvironments. *Prague Medical Report*, *116* (2), 87–111. https://doi.org/10.14712/23362936.2015.49

Sun, Y., Zahedipour-Sheshgelani, P., & Asghari, M. (2019). Foliar Spray with 24-Epibrassinolide Enhanced Strawberry Fruit Quality, Phytochemical Content, and Postharvest Life. *Journal of Plant Growth Regulation*, *39* (2), 920–929. https://doi.org/10.1007/s00344-019-10033-y

Sur, S., & Ray, R. B. (2020). Bitter Melon (*Momordica charantia*) is a Nutraceutical Approach for Cancer Prevention and Therapy. *Cancers*, *12* (8), 2064. https://doi.org/10.3390/cancers12082064

Sur, S., Nakanishi, H., Flaveny, C., Ippolito, J. E., Mchowat, J., Ford, D. A., and Ray, R. B. (2019). Inhibition of key metabolic pathways, glycolysis, and lipogenesis in oral cancer by bitter melon extract. *Cell Communication and Signaling : CCS*, *17* (1). https://doi.org/10.1186/s12964-019-0447-y

Tan, S. P., Kha, T. C., Parks, S. E., & Roach, P. D. (2015). Bioactive composition and health benefits of bitter melon (*Momordica charantia* L.): A review. *Food Reviews International*, *32* (2), 181–202. https://doi.org/10.1080/87559129.2015.1057843

Uebanso, T., Uryu, K., Mizuno, A., Arai, H., Yamamoto, H., Takeda, E., Hada, T., Taketani, Y., & Fukaya, M. (2007). Extracts of *Momordica charantia* Suppress Postprandial Hyperglycemia in Rats. *Journal of Nutritional Science and Vitaminology*, *53* (6), 482–488. https://doi.org/10.3177/jnsv.53.482

Wen, J.-J., Gao, H., Hu, J.-L., Nie, Q.-X., Nie, S.-P., Chen, H.-H., Xie, M.-Y., & Xiong, T. (2019). Polysaccharides from fermented *Momordica charantia* ameliorate obesity in HFD-induced obese rats. *Food & Function*, *10* (1), 448–457. https://doi.org/10.1039/c8fo01609g

Xiao, X., Huang, S., Yang, Z., Zhu, Y., Zhu, L., Zhao, Y., Bai, J., & Kim, K.-H. (2024). *Momordica charantia* Bioactive Components: Hypoglycemic and Hypolipidemic Benefits Through Gut Health Modulation. *Journal of Medicinal Food*, *27* (7), 589–600. https://doi.org/10.1089/jmf.2024.k.0037

Xu, B., Zeng, T., Li, S., Zhan, J., Li, Z., Wang, S., & Ho, C.-T. (2022). Bioactivities of *Momordica charantia* as Potential Anti-Diabetic/Hypoglycemic Agents. *Molecules*, *27* (7): 2175. https://doi.org/10.3390/molecules27072175

Yang, W. S., Yeo, S.-G., Sung, G.-H., Cho, J. Y., Yang, E., Kim, M.-J., Jeong, D., Lee, S., Yoo, B. C., & Yoon, D. H. (2018). *Momordica charantia* Inhibits Inflammatory Responses in Murine Macrophages via Suppression of TAK1. *The American Journal of Chinese Medicine*, *46* (2), 435–452. https://doi.org/10.1142/s0192415x18500222

Yang, Y.-S., Wu, N.-Y., Kornelius, E., Huang, C.-N., & Yang, N.-C. (2022). A randomized, double-blind, placebo-controlled trial was conducted to evaluate the hypoglycemic efficacy of mcIRBP-19-containing *Momordica charantia* L. fruit extracts in subjects with type 2 diabetes. *Food & Nutrition Research*, *66* (Suppl. 1). https://doi.org/10.29219/fnr.v66.3685

Younis, N. S., Ghanim, A. M. H. (2022). The protective role of celastrol in renal ischemia-reperfusion injury involves activating Nrf2/HO-1 and PI3K/AKT Signaling Pathways, Modulating NF-\u03bab Signaling Pathways, and Inhibiting ERK Phosphorylation. *Cell Biochemistry and Biophysics*, *80* (1), 191–202. https://doi.org/10.1007/s12013-022-01064-6

Yung, M. M. H., Hardie, D. G., Chan, D. W., Zhan, J., Ngan, H. Y. S., Ross, F. A., Leung, T. H. Y. (2016). Bitter Melon (*Momordica charantia*) extract inhibits tumorigenicity and overcomes cisplatin resistance in ovarian cancer cells by targeting the AMPK Signaling cascade. *Integrative Cancer Therapies*, *15* (3), 376–389. https://doi.org/10.1177/1534735415611747

Zannou, O., Ali Redha, A., Pashazadeh, H., Koca, I., & Ghellam, M. (2022). Enhanced ultrasonically assisted extraction of bitter melon (*Momordica charantia*)leaf phenolic compounds using choline chloride-acetic acid–based natural deep eutectic solvent: an optimization approach and in vitro digestion. *Biomass Conversion and Biorefinery*, *14* (10), 11491–11503. https://doi.org/10.1007/s13399-022-03146-0

Zhu, Y., Guo, Q., Zhou, X., Wang, Y., Zhang, Y., Cui, F., Qian, X., Xiong, Z., & Dong, Y. (2012). Effect of superfine grinding on antidiabetic activity of bitter melon powder. *International Journal of Molecular Sciences*, *13* (11), 14203–14218. https://doi.org/10.3390/ijms131114203