

## Medicinal plants as dual therapeutic agents: A comprehensive review on antidiabetic and anticancer activity

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### Abstract

Diabetes mellitus and cancer are among the most prevalent chronic diseases worldwide, sharing pathological mechanisms such as oxidative stress, chronic inflammation, and dysregulated cellular signaling pathways. The therapeutic potential of medicinal plants in addressing these dual health challenges has garnered significant interest. This review explores medicinal plants with antidiabetic and anticancer properties, focusing on their bioactive compounds, mechanisms of action, and therapeutic applications. Plants such as *Gymnema sylvestre*, *Momordica charantia*, *Curcuma longa*, and *Tinospora cordifolia* exhibit dual efficacy by regulating blood glucose levels and inducing cytotoxic effects on cancer cells. Key bioactive compounds, including gymnemic acid, curcumin, and saponins, demonstrate antioxidant, anti-inflammatory, and apoptotic activities with lower toxicity compared to synthetic drugs. The integration of traditional knowledge with modern pharmacological approaches holds promise for developing effective and holistic therapeutic strategies. Future research should emphasize standardization, pharmacokinetics, and clinical validation to optimize the use of these plants for dual-target therapy.

**Keywords:** Diabetes mellitus, cancer, medicinal plants, bioactive compounds, anti-cancer, anti-diabetic

### Introduction

Diabetes mellitus and cancer are two of the most prevalent and life-threatening chronic diseases worldwide, posing significant challenges to global healthcare systems. While diabetes is characterized by persistent hyperglycemia resulting from impaired insulin secretion or action, cancer is marked by uncontrolled cell proliferation and metastasis. Both conditions share common underlying mechanisms, such as oxidative stress, chronic inflammation, and dysregulated cellular signaling pathways. These shared pathological features highlight the need for therapeutic strategies that can address both diseases simultaneously.

Medicinal plants have long been a cornerstone of traditional medicine systems due to their rich reservoir of bioactive compounds, including alkaloids, flavonoids, terpenoids, and polyphenols. These natural compounds exhibit multifaceted

pharmacological activities, including antioxidant, anti-inflammatory, hypoglycemic, and anticancer effects. Their ability to modulate cellular pathways, improve insulin sensitivity, inhibit tumor growth, and induce apoptosis in cancer cells has drawn increasing attention from researchers.

Several plants, such as *Gymnema sylvestre*, *Momordica charantia*, and *Curcuma longa* have demonstrated dual efficacy as antidiabetic and anticancer agents. These plants not only regulate blood glucose levels but also exhibit cytotoxicity against cancer cells, making them potential candidates for integrated therapeutic approaches. Moreover, the bioactive compounds derived from these plants, such as gymnemic acids, curcumin, and saponins, offer the advantage of lower toxicity compared to synthetic drugs (Table 1).

**Table 1:** Some important Medicinal Plants with Dual Antidiabetic and Anticancer Properties

Plant Name	Family	Plant Part Used	Bioactive Compound	Biological Activity		Reference
				Antidiabetic	Anticancer	
<i>Gymnema sylvestre</i>	Apocynaceae	Leaves	Gymnemic acid, Saponins	Insulin secretion	Cytotoxicity	Khan <i>et al.</i> , 2019 Ghosh <i>et al.</i> , 2023
<i>Momordica charantia</i>	Cucurbitaceae	Fruit, Leaves, Seeds	Charantin, Lectins	Insulin mimetic	Apoptosis	Oyelere <i>et al.</i> , 2022 [30] Sur & Ray, 2020 [46]
<i>Withania somnifera</i>	Solanaceae	Roots, Leaves	Withanolides, Alkaloids	Insulin sensitivity	Apoptosis	Sarangi <i>et al.</i> , 2013 Singh <i>et al.</i> , 2021
<i>Curcuma longa</i>	Zingiberaceae	Rhizome	Curcumin, Turmerones	Glucose regulation	Metastasis inhibition	Sharma <i>et al.</i> , 2022 Gull <i>et al.</i> , 2023
<i>Tinospora cordifolia</i>	Menispermaceae	Stem, Leaves	Polysaccharides, Alkaloids	Glucose uptake	immunomodulation	Chaudhary <i>et al.</i> , 2024 [9] Malabadi <i>et al.</i> , 2024
<i>Azadirachta indica</i>	Meliaceae	Leaves, Bark, Seeds	Limonoids, Azadirachtin	Glucose utilization	Apoptosis	Jadhan <i>et al.</i> , 2024
<i>Ocimum santum</i>	Lamiaceae	Leaves, Seeds	Eugenol, Ursolic acid	Glucose regulation	Antioxidant	Arya <i>et al.</i> , 2024
<i>Allium sativum</i>	Amaryllidaceae	Bulbs	Allicin, Sulphur compounds	Insulin sensitivity	Tumour inhibition	Okoro <i>et al.</i> , 2023
<i>Zingiber officinale</i>	Zingiberaceae	Rhizome	Gingerols, Shogaols	Glucose uptake	Anti-inflammatory	Al-Radadi <i>et al.</i> , 2022 Rahman <i>et al.</i> , 2011
<i>Phyllanthus</i>	Phyllanthaceae	Fruits, Leaves	Gallic acid, Ellagic	Beta cell	Antioxidant	Huang <i>et al.</i> , 2023 [16]

<i>emblica</i>			acid	protection		Zhao <i>et al.</i> , 2015 <sup>[55]</sup>
<i>Aloe vera</i>	Asphodelaceae	Leaves, gel	Aloin, Polysaccharides	Glucose regulation	Apoptosis induction	Nagime <i>et al.</i> , 2024
<i>Triginella foenum-graecum</i>	Fabaceae	Seeds, leaves	4-hydroxyisolutrine, Diosgenin	Insulin secretion	Anti-inflammatory	Visuvanathan <i>et al.</i> , 2022 Almalki <i>et al.</i> , 2022
<i>Camellia sinensis</i>	Theaceae	Leaves	Epigallocatechin gallate (EGCG)	Insulin sensitivity	Inhibit metastasis	Chaudhary <i>et al.</i> , 2023
<i>Capperis decidua</i>	Capparaceae	Bark, fruit	Flavonoids, Alkaloids	Glucose metabolism	Cytotoxicity and antioxidant	Nazar <i>et al.</i> , 2020
<i>Berberis aristata</i>	Berberidaceae	Bark, roots	Berberine	Glucose regulation	DNA damage inhibition	Sharma <i>et al.</i> , 2024
<i>Nigella sativa</i>	Ranunculaceae	seeds	Thymoquinone	Glucose uptake	Apoptosis induction	Shaukat <i>et al.</i> , 2023 Majdalawieh <i>et al.</i> , 2016
<i>Pterocarpus marsupium</i>	Fabaceae	Bark, heartwood	Pterostilbene, Flavonoids	Beta-cell regeneration	Anti-inflammatory	Umamaheswari <i>et al.</i> , 2023 <sup>[51]</sup> Basanayake <i>et al.</i> , 2024
<i>Cinnamomum cassia</i>	Lauraceae	Bark	Cinnamaldehyde, Eugenol	Glucose metabolism	Cytotoxicity	Wang <i>et al.</i> , 2020 Banerjee & Banerjee, 2023
<i>Ficus religiosa</i>	Moraceae	Bark, leaves	Flavonoids, Tannins	Hypoglycemic effect	Antioxidant	Murugesu <i>et al.</i> , 2021
<i>Annona squamosa</i>	Annonaceae	Seeds, leaves	Acetogenins, Alkaloids	Insulin sensitivity	Cytotoxicity	Safira <i>et al.</i> , 2022 <sup>[38]</sup>

This review explores the pharmacological potential of medicinal plants with both anticancer and antidiabetic properties. It emphasizes their bioactive compounds, mechanisms of action, and therapeutic applications. By delving into recent advancements and existing knowledge, this review aims to provide a comprehensive understanding of these dual-purpose plants and their relevance in combating diabetes and cancer in a holistic manner.

### Common Mechanisms Linking Diabetes and Cancer

Diabetes mellitus and cancer, though distinct diseases, share several overlapping molecular and cellular mechanisms. These commonalities highlight how the progression of one condition may influence the other and why therapeutic approaches targeting both simultaneously are promising (Fig 1).

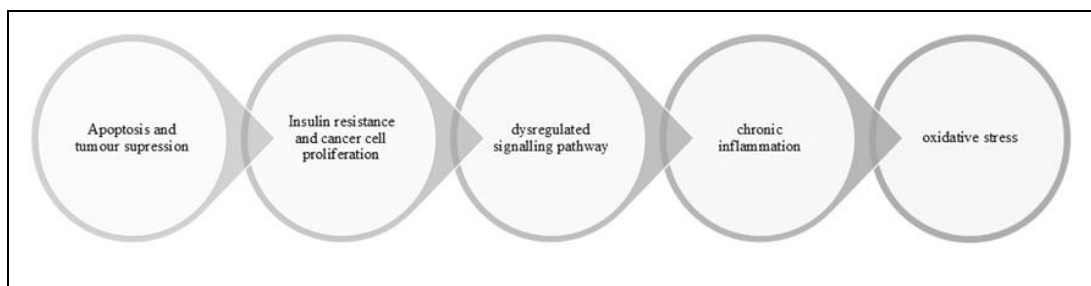


Fig 1: Showing common mechanism linking diabetes and cancer

#### 1. Oxidative Stress

Oxidative stress, caused by an imbalance between reactive oxygen species (ROS) and antioxidant defenses, is a central contributor to both diabetes and cancer.

In diabetes, excessive ROS impairs insulin signaling and damages pancreatic  $\beta$  cells, leading to insulin resistance and hyperglycemia. In cancer, oxidative stress promotes genomic instability, DNA damage and uncontrolled cell proliferation.

#### 2. Chronic Inflammation

Persistent inflammation is a hallmark of both diseases.

In Diabetes Chronic hyperglycemia induces low-grade systemic inflammation through pro-inflammatory cytokines (e.g- IL-6, TNF- $\alpha$ ). In Cancer Inflammatory mediators stimulate tumor growth, angiogenesis, and metastasis.

#### 3. Dysregulated Cellular Signaling Pathways

Common pathways involved in both conditions include:

**PI3K/Akt/mTOR Pathway:** In diabetes, this pathway is crucial for glucose metabolism and insulin signaling. Its

dysregulation leads to insulin resistance. In cancer, hyperactivation of this pathway promotes tumor survival and growth.

**AMPK Pathway:** AMPK regulates energy homeostasis. In diabetes, its inhibition contributes to metabolic imbalance. In cancer, AMPK suppression favors tumor growth.

#### 4. Insulin Resistance and Hyperinsulinemia

In diabetes, insulin resistance often leads to compensatory hyperinsulinemia. High insulin levels:

Act as a growth factor for cancer cells via the IGF-1/IGF-1R signaling axis.

Promote cell proliferation and inhibit apoptosis, creating a favorable environment for cancer development.

#### 5. Lipid Metabolism Dysregulation

Altered lipid metabolism in diabetes and cancer is characterized by increased free fatty acids and lipotoxicity.

In Diabetes Lipotoxicity impairs beta-cell function. In cancer, Cancer cells rely on lipid synthesis for rapid proliferation.

## Detailed overview of selected medicinal plants

### *Gymnema sylvestre*

*Gymnema sylvestre*, belongs to Apocynaceae family, is native to various regions across Africa, Asia, and Australia. For its diverse therapeutic applications this plant has been extensively utilized in traditional medicine. Currently, it also serves as a dietary supplement due to its wide-ranging health benefits. Notably, *Gymnema sylvestre* is recognized for reduce blood glucose levels, making it a prominent choice in Ayurvedic and traditional medicinal practices. Its hypoglycemic effect is attributed to the presence of bioactive phytochemicals, including gymnemic acid, gurmardin and gymnemasaponins. Additionally, this plant exhibits a broad spectrum of pharmacological activity, such as anti-inflammatory, antibiotic, antioxidant, hepatoprotective, antiviral, anticancer, and lipid-lowering activities, gastroprotective.

The antidiabetic properties of *Gymnema sylvestre* are largely attributed to gymnemic acids, which decrease glucose levels by inhibiting the absorption of sugar in the intestines (Tiwari *et al.*, 2014)<sup>[49]</sup>. Gymnemic acid, a compound consisting of saponins, structurally resembles glucose and blocks its intestinal receptor site. Screening using Affinity Ultrafiltration-HPLC-MS has identified  $\alpha$ -glucosidase inhibitors within this plant (Chen and Guo, 2017)<sup>[10]</sup>. Furthermore, *Gymnema sylvestre* influences insulin-dependent enzymes by enhancing hexokinase and glucose-6-phosphate dehydrogenase activity, while suppressing insulin-independent enzymes like glycogen phosphorylase (Aralelimath and Bhise, 2012)<sup>[4]</sup>. Additionally, research indicates that *Gymnema sylvestre* may stimulate insulin secretion and support the regeneration of insulin and pancreatic  $\beta$ -cells (Ahmed *et al.*, 2010).

Several studies have highlighted the anticancer potential of *Gymnema sylvestre*. Gymnemenol demonstrated significant anticancer activity against HeLa cells while ethyl, ethanolic and chloroform extracts exhibited efficacy against A549 and MCF7 cell lines (Srikanth *et al.*, 2010)<sup>[44]</sup>. Ethanolic extract also displayed cytotoxic effects on A375 cells and antitumor properties in a skin papilloma model (Chakraborty *et al.*, 2013)<sup>[8]</sup>. Moreover, it inhibited BCRP, which could enhance the effectiveness of drugs like methotrexate (Tamaki *et al.*, 2010)<sup>[47]</sup>. Polysaccharides such as GSP11, GSP22, and GSP33 demonstrated immunomodulatory and anticancer effects, with GSP33 reducing U937 cell viability by 83.8% (Wu *et al.*, 2012). Additionally, methanolic extracts decreased tumor incidence in DMBA-induced mice (Agrawal *et al.*, 2016)<sup>[1]</sup>.

### *Momordica charantia*

*Momordica charantia* (commonly known as bitter melon, karela and bitter gourd) a member of Cucurbitaceae family is a medicinal plant. It is widely cultivated across Africa, Asia, and South America (Cefalu *et al.*, 2008)<sup>[6]</sup>. *Momordica* is a rich source of bioactive compounds, including triterpene glycosides, flavonoids, triterpenoids, lectins, phenolic acids, sterols, and proteins has been traditionally used in folk medicine (Cousens, 2007)<sup>[12]</sup>.

The antidiabetic potential of *Momordica charantia* has been the focus of numerous studies. Administration of its ethanolic extract (250 mg/kg) significantly decreased blood glucose levels in alloxan-induced diabetic mice within a period of 14 days. Both aqueous and Ethanol extracts (200 mg/kg) demonstrated notable effect in glucose level in

alloxan induced diabetic rats over 21 days, with the aqueous extract yielding better results (Rathi *et al.*, 2002)<sup>[35]</sup>. Methanolic extracts exhibited antiglycemic effect in both normal and alloxan induced diabetic mice (Liu *et al.*, 2021)<sup>[24]</sup>. Furthermore, *M. charantia* delayed cataract onset in diabetic rats by up to 180 days, whereas untreated rats developed cataracts within 100 days (Srivastava *et al.*, 1993)<sup>[45]</sup>. Daily administration of aqueous extracts (400 mg/day) effectively minimized hyperglycemia and hyperinsulinemia in fructose-fed rats (Vikrant *et al.*, 2001)<sup>[52]</sup>. Additionally, consuming seared fruits improved glucose tolerance without altering insulin levels (Saeed *et al.*, 2021)<sup>[37]</sup>. Clinical evaluations showed that a homogenized suspension decreased 86 % of postprandial glucose levels in diabetes mellitus patients, while consumption of fruit juice enhanced glucose metabolism in 73% of individuals with adult-onset diabetes (Oyelere *et al.*, 2022)<sup>[30]</sup>.

Crude extracts and isolated compounds from bitter melon have been shown to elevate ROS (reactive oxygen species) levels, suppress inflammatory cytokines such as IL-23a, IL-1 $\beta$ , s100a9, IL-6, and TNF $\alpha$ , and stimulate detoxification enzymes, including superoxide dismutase, glutathione-S-transferase, and catalase, across various cancer types. The increase in ROS and detoxification enzyme activity disrupts tumor initiation, halts progression, and induces stress-related cell death, a mechanism commonly observed in natural chemopreventive agents (Qian *et al.*, 2019)<sup>[34]</sup>. Chronic inflammation, fueled by pro-inflammatory cytokines, promotes carcinogenesis by driving ROS generation, genetic mutations, epithelial-mesenchymal transition (EMT), angiogenesis, and metastasis. However, targeting and inhibiting these cytokines has demonstrated potential in clinical studies (Landskron *et al.*, 2014)<sup>[21]</sup>. Detoxification enzymes play a critical role in defending against oxidative damage and metabolizing carcinogens, thereby reducing cancer risk (Pathania *et al.*, 2018; Younus, 2018)<sup>[32, 54]</sup>. Consequently, Bitter melon stands out as a potential candidate for cancer prevention and therapy (Sur *et al.*, 2020)<sup>[46]</sup>.

### *Tinospora cordifolia*

*Tinospora cordifolia* commonly known as Guduchi or Amrita, belongs to the Menispermaceae family and is indigenous to regions like China, Myanmar, and Sri Lanka (Saha & Ghosh, 2012)<sup>[39]</sup>. This herb is widely used in traditional Ayurvedic medicine for its diverse therapeutic applications. It is known to address various ailments, including jaundice, rheumatism, skin diseases, diabetes, inflammation, urinary disorders, allergic reactions, anemia, and periodic fevers. Additionally, it exhibits radioprotective and other beneficial properties (Sharma *et al.*, 2012)<sup>[41]</sup>. The plant's key phytochemical constituents include anti-diabetic tannins, flavonoids, alkaloids, saponins, steroids and cardiac glycosides (Chougale *et al.*, 2009)<sup>[11]</sup>.

Aqueous extracts of *Tinospora cordifolia* have shown a significant ability to lower blood sugar levels. In a study, a dosage of 400 mg/kg per day led to the highest percentage reduction in glucose levels among subjects with moderate diabetes. Experimental trials, spanning 21 to 120 days, utilized Alloxan-induced diabetic rats and demonstrated remarkable glycemic control. The extract also affected key metabolic enzymes responsible for glucose regulation in individuals with mild to severe hyperglycemia. Additionally, there was an observed increase in total

hemoglobin levels, body mass and hepatic hexokinase activity (Chaudhary *et al.*, 2024) [9]. In another study, a significant reduction in both urine and blood glucose levels with *T. cordifolia* aqueous extracts in Streptozotocin-induced diabetic mice for six weeks exhibited substantial anti-hyperglycemic effects (Ruan *et al.*, 2012) [36].

Berberine demonstrates anticancer effects in mice by inhibiting topoisomerase II at 10 mg/kg in ascites carcinoma (Jagetia & Rao, 2006; Jagetia & Baliga, 2004) [17, 18]. Columbin and octacosanol show chemopreventive and antiangiogenic properties, respectively, with octacosanol also suppressing tumor growth and promoting apoptosis (Kohno *et al.*, 2002; Thippeswamy & Salimath, 2007 [19, 48]; Mishra & Kaur, 2015). Palmatine reduces tumor size by enhancing antioxidant enzyme levels and minimizing DNA damage (Ali & Dixit, 2013) [3]. G1-4A activates cytotoxic T lymphocytes via dendritic cells, while *Tinospora cordifolia* ethanolic extracts combat drug-resistant cancer and enhance chemotherapy efficacy (Maliyakkal *et al.*, 2015) [25]. Its extracts regulate key genes (p53, Cdkn2A, mdm2) and reduce chemotherapy toxicity by inhibiting CYP3A4 activity. An herbal remedy with *T. cordifolia* has shown success in treating third-stage pulmonary carcinoma by reducing symptoms and improving appetite (Bhatia & Rani, 2012; Hamsaa & Kuttan, 2012) [15].

### ***Phyllanthus emblica***

*Phyllanthus emblica* L. is commonly found in tropical and subtropical regions. Fruits of *Phyllanthus* rich in ascorbic acid, phenolic compounds like gallic acid, quercetin, ellagic acid, proanthocyanidins, and ellagitannins (Paltanov *et al.*, 2009). Research suggests that the primary bioactivity of *P. emblica* is attributed to its potent antioxidant properties (Liu *et al.*, 2008) [23]. Additionally, the *phyllanthus* fruits demonstrate a variety of pharmacological effects, such as gastroprotective and antitussive activities.

In STZ-diabetic mice treated with EPE, increase numerous beta pancreatic cells expressing insulin, along with a reduction in pancreatic  $\alpha$  cells expressing glucagon (Nahdi *et al.*, 2017) [27]. This suggests that EPE may act similarly to an insulin secretagogue, derived from the remaining  $\beta$  cells (approximately 30% in this STZ-induced diabetic model, where 70% of islets per pancreas were destroyed by STZ and later regenerated) (Lin *et al.*, 2019) [22]. These effects provide a therapeutic benefit for T1DM by enhancing insulin levels after  $\beta$ -cell damage and/or reducing glucagon-producing  $\alpha$  cells. In conclusion, the beneficial effect of EPE treatment lies in its ability to restore near-normal blood glucose and HbA1C levels while increasing insulin concentrations (Huang *et al.*, 2023) [16].

*Phyllanthus emblica* extracts demonstrate potent anti-tumor effects targeting multiple type of cancer, both *in vitro* and *in vivo*. Aqueous extracts from its fruits promote apoptosis in cancer cell lines at concentrations between 50 and 100  $\mu\text{g/mL}$ , with minimal toxicity to normal fibroblasts Nagamkitidechakul *et al.*, 2010). Likewise, when tested on triple-negative breast cancer cell lines (MDA-MB-231, MDA-MB-435, and MDA-MB-468), they showed significant cytotoxicity at 25–100  $\mu\text{g/mL}$ , while leaving normal breast epithelial cells (MCF10A) unaffected. In contrast to blueberry and strawberry extracts, which require higher concentrations (above 500  $\mu\text{g/mL}$ ) to show activity, *Phyllanthus emblica* is effective at much lower doses (Somasagara *et al.*, 2012). These results suggest that its

extract encourages apoptosis instead of merely halting cell proliferation, making it a promising option for breast cancer treatment with low toxicity to healthy cells (Zhao *et al.*, 2015) [55].

### ***Capparis decidua***

*Capparis decidua* Edgew (Forssk.) from the Capparidaceae family, is a perennial woody species thrives predominantly in equatorial and subtropical areas (Dhakad *et al.*, 2016) [13]. This plant is highly regarded for its wide range of therapeutic properties, including antibacterial, antifungal, antihemolytic, antioxidant, antidiabetic, anthelmintic, anesthetic, antirheumatic, and anti-gout effects.

*C. decidua* has been recognized as a promising candidate for antidiabetic treatment. Extracts from its fruits demonstrated a notable suppressive action on both enzymes, with the flower and leaf extracts following closely behind in efficacy. When diabetic rats induced by alloxan (80 mg/kg IP) were fed a diet containing 30% *Capparis* fruit powder for three weeks, significant hypoglycemic activity was observed. Additionally, research revealed that the alkaloid fraction of *Capparis* was effective in managing diabetes (Sharma *et al.*, 2010) [40]. Further investigation showed that both purified and methanol extracts from the stem effectively decrease glucose levels in both diabetic and normal mice, as demonstrated by glucose tolerance tests.

Stachydrine, a naturally occurring alkaloid found in various *Capparis* species, has been shown to exert strong cytotoxic effects on prostate cancer cells by significantly reducing the chemokine receptors signalling. Its ability to inhibit cancer cell invasion and metastasis highlights its potential as a promising candidate for anticancer drug development. Furthermore, lectin, a bioactive compound present in the seeds of *Capparis* species, has demonstrated remarkable inhibitory activity against HIV-1 reverse transcriptase while also suppressing the growth of HepG2 liver cancer and MCF-7 breast cancer cells.

### ***Pterocarpus marsupium***

*Pterocarpus marsupium* Roxb, known as "Vengai," is a traditionally used medicinal plant in tropical and subtropical areas to treat various ailments. Research has identified compounds such as alkaloids, proteins, carbohydrates, and flavonoids in its extracts. Research indicates that this plant exhibits diverse pharmacological properties, such as anti-cancer, antioxidant, anti-inflammatory, analgesic, antimicrobial, hepatoprotective, and anti-diabetic properties (Umamaheswari *et al.*, 2023) [51].

The ethanolic extract derived from the heartwood of *Pterocarpus marsupium* Roxb has been investigated for its potential anti-diabetic properties in streptozotocin-induced diabetic mice. Studies have shown that the pure powder, ethanolic extract, as well as hexane and n-butanol fractions, significantly enhanced oral glucose tolerance and increased serum insulin levels (Mishra *et al.*, 2013). In a separate study, Pant and colleagues compared the effects of ethanolic extracts from *P. marsupium* Roxb stem at doses of 200 mg/kg and 400 mg/kg in mice, using glibenclamide (0.43 mg/kg) as a reference standard. The acute toxicity study revealed no toxic effects within the dose range of 250–1000 mg/kg. The blood glucose-lowering effects were observed to be 57.56%, 51.30%, and 55.13% at 180 minutes for the standard drug, 200 mg/kg, and 400 mg/kg doses, respectively. These findings suggest that the anti-diabetic

activity of the extract is dependent on both dosage and duration (Pant *et al.*, 2017) [31].

Another significant compound isolated from the heartwood of *P. marsupium* Roxb is pterostilbene, a stilbenoid polyphenol. Chakraborty and his team explored its anticancer potential against breast (MCF-7) and prostate (PC3) cancer cell lines. Pterostilbene exhibited anticancer properties by inducing DNA fragmentation, generating apoptotic bodies, and disrupting cell membrane integrity. Its apoptotic mechanism involves the suppression of cell proliferation markers such as Akt and Bcl-2, while upregulating pro-apoptotic factors like Bax and caspases within the mitochondrial pathway. Furthermore, it inhibits key metastasis-promoting factors, including Matrix metalloproteinase 9 (MMP9) and  $\alpha$ -methyl acyl-CoA racemase (AMACR) (Chakraborty *et al.*, 2010) [7]. Gosetti and colleagues analyzed the aqueous extract of *P. marsupium* heartwood, identifying various volatile and non-volatile compounds, as well as metals. They evaluated its anticancer efficacy in A431, HeLa, REN, and PC-3 cell lines, reporting IC50 values of 8.7, 9.8, 12.5, and 13.4  $\mu$ g/mL, respectively, confirming its anticancer potential (Gosetti *et al.*, 2016) [14]. Pterostilbene, predominantly found in *P. marsupium* wood, has demonstrated potent anticancer activity, particularly against breast, colon, and prostate cancers. Its mechanisms include inducing apoptosis, arresting the cell cycle, enhancing autophagy-related proteins, and inhibiting metastatic processes (Tsai *et al.*, 2017) [50].

### *Annona squamosa*

*Annona squamosa*, belongs to the Annonaceae family, commonly known as custard apple. Its leaves contain various phytochemical compounds, including flavonoids, tannins, saponins, carbohydrates, coumarins, and cardiac glycosides. The biological activities of *A. squamosa* leaf extract includes antioxidant, anti-obesity, antidiabetic, hepatoprotective, lipid-lowering, and anticancer properties. (Safira *et al.*, 2022) [38].

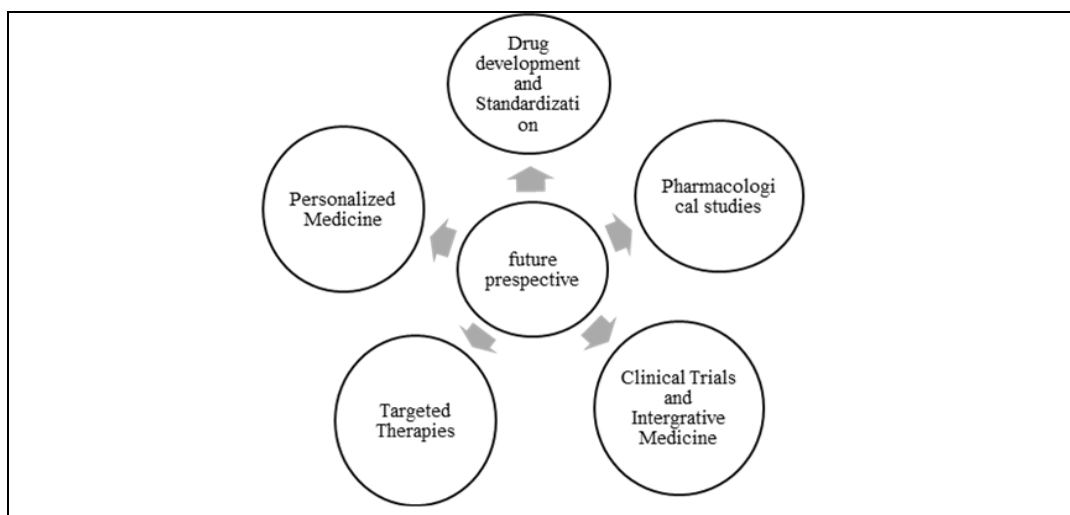
The antidiabetic activity of *Annona* leaf extract is likely attributed to its phytochemical composition. Streptozotocin (STZ) induces specific damage to islet cells, leading to elevated blood glucose levels (Nguyen *et al.*, 2020) [29]. Gliclazide, a standard drug known to induce hypoglycemia, is commonly used in STZ-induced diabetes models to assess glucose-lowering potential of various bioactive compounds (Basha & Subramanian, 2011). Administration of *Annona* leaf extract hypoglycemic effect in STZ-induced diabetic mice (Kumar *et al.*, 2021) [20].

Ethnic communities traditionally use all parts of *Annona* to treat various diseases, including cancer, skin issues, and insect bites. However, plant seeds contain toxic compounds, that serve to eliminate lice and head lice. The leaves, on the other hand, are used for their hepatoprotective and immunomodulatory properties. Previous studies have focused on *A. squamosa* non-alkaloidal compounds, particularly acetogenins, for their anticancer activity. Research on the alkaloid fraction of *A. squamosa* identified two benzyloisoquinoline alkaloids, with Alkaloid I showing strong activity against human breast cancer cells (MCF-7) and colon cancer cells (HTC116), highlighting the potential of benzyloisoquinoline alkaloids in cancer treatment (Soni *et al.*, 2013) [43].

### Future perspective

The potential for drug development from these dual-purpose plants is immense, particularly in the context of combination therapies targeting both diabetes and cancer. However, extensive pharmacological investigation are needed to better understand the pharmacokinetics, mechanisms of action and long-term safety of plant-derived compounds. Clinical trials will be essential to establish the safety and efficacy of these plants in human populations.

The future of using medicinal plants for the dual treatment of diabetes and cancer is promising, with several key areas for exploration (Fig 2):



**Fig 2:** Showing future perspective of using medicinal plants for dual treatment of diabetes and cancer

### Conclusion

The growing prevalence of both diabetes and cancer worldwide has led to an increasing need for innovative and effective therapeutic strategies. Medicinal plants, with their rich array of bioactive compounds, offer a promising avenue

for the dual management of these chronic conditions. Through the intricate mechanisms of action, many medicinal plants possess properties that can modulate insulin sensitivity, regulate glucose metabolism, inhibit

cancer cell proliferation, and induce apoptosis in malignant cells.

This review has highlighted several plants and their bioactive compounds that show potential in combating both diabetes and cancer. Compounds such as gymnemic acid, curcumin, withanolides, and alkaloids have demonstrated significant biological activities that support their inclusion in therapeutic regimes for these diseases. However, there are challenges, including the variability in plant composition, the need for standardization of dosages, and the potential toxicity of certain compounds. Addressing these challenges through rigorous pharmacological studies and clinical trials is essential to move forward with plant-based therapies.

The future of plant-based treatments lies in the integration of traditional knowledge with modern science, focusing on developing safe, standardized, and effective therapies. As research progresses, medicinal plants could play a pivotal role in offering holistic healthcare solutions for diabetes and cancer, providing a natural and complementary approach to current pharmacological treatments.

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