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Review Article

A comprehensive review on assessing paan (*Piper betle'*s) efficacy in diabetes management under environmental stress

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Abstract

The changing climate has significant impacts on human health, particularly in the management of diabetes. Worsening diabetes outcomes result from increased weather events and environmental degradation, impacting heat stress, physical activity, food security, and healthcare access. Furthermore, climate change poses indirect risks to diabetes management by threatening food security, as climate change aggravates existing vulnerabilities in diabetes management, particularly by limiting access to fresh food and healthcare resources. This review examines the impacts and investigates ways to reduce climate-related effects on diabetes. One effective adaptation method involves the integration of paan (*Piper betle*), a traditional medicinal plant native to South and Southeast Asia. The phytochemical properties of paan have displayed promise in treating diabetes. They provide an environmentally sustainable approach to help regulate blood sugar levels and enhance insulin efficiency. In regions impacted by climate change and with potential interruptions to standard healthcare services, paan provides a viable, readily accessible substitute. This multifaceted relationship between climate, healthcare, and diabetes underscores the necessity for comprehensive strategies that incorporate both medical and environmental considerations to improve health outcomes for individuals at risk. This review thoroughly explores the potential of paan as a complementary therapy for diabetes treatment by combining the effects of climate change with traditional medicinal practices. It emphasizes the potential of paan to aid in adaptive health measures in climate-impacted regions and indicates a necessity for more research to enhance its medicinal benefits.

Keywords: Climate change, Diabetes, Insulin sensitivity, Paan, Sustainable healthcare

Highlights

- Climate change influences outspread of diabetes in India
- Paan aligns with sustainable, locally accessible healthcare strategies in climate-affected regions
- Paan presents a promising complementary method for managing diabetes due to its phytochemicals
- Clinical and animal studies suggest paan lowers blood sugar and boosts insulin sensitivity
- Standardized formulations and safety tests are crucial for using betel leaf in diabetes care

INTRODUCTION

Temperature fluctuations, particularly during global warming, weather events, and long-term environmental changes, pose serious public health challenges, affects both communicable and non-communicable diseases (NCDs). While much attention has been focused on the effects of a changing climate on communicable diseases, its impact on chronic diseases such as diabetes is also becoming increasingly clear. Diabetes, a major global health problem characterized by persistent hyperglycemia, affects an estimated 537 million adults worldwide, and that number is projected to increase by 783 million by 2045 (International Diabetes Federation, 2021; Sun *et al*., 2021). This variation in number highlights the need for effective management strategies as the climate continues to change.

In this context, traditional medicinal plants such as paan offer a promising complementary approach to diabetes treatment. Native to South and Southeast Asia, traditional medicine systems, for example, in Ayurveda, paan have long been used for their potential therapeutic benefits. In Ayurveda, paan is classified as "Kashaya" (an astringent) and is used to balance the doshas of the body and regulate blood glucose levels (Singh and Desar, 2024). The phytochemical composition of paan contains a variety of bioactive compounds, namely polyphenols, alkaloids, and essential oils that contribute to its medicinal properties. Animal models and clinical trials have provided

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evidences to support the effectiveness of paan in treating diabetes (Kottaisamy *et al*., 2021). Research has highlighted that the various extracts of *Piper betle* exhibit significant antioxidant and anti-inflammatory activities (Das *et al*., 2015). Achieving uniform efficacy in paan-based treatments necessitates standardization and more rigorous research.

Paan cultivation aligns with sustainable agricultural practices, presenting an environmentally friendly option for local food production. It is important to build a health system that includes preventive health services, which are important for the treatment of diabetes during heat stress. This includes disaster preparedness and the availability of essential medicines and supplies (Satoh *et al*., 2019). Supporting local agriculture and producing climate-resilient food can ensure that people with diabetes have access to nutritious food even when living in a stressful environment. Climate-smart agriculture and disaster preparedness strategies are critical to reducing the impact of food insecurity (Levi *et al*., 2023). This review focuses on a comprehensive analysis of the role of paan in diabetes treatment by the phytochemical profile, which also helps in improving resilience against climatic challenges. By addressing existing research gaps, this review contributes to a greater understanding of how traditional treatments such as paan can complement modern health approaches, especially in climate change, which may be an effective future direction.

Effects of temperature on blood glucose

Temperature changes, especially heat waves, directly impact people with diabetes. Environmental heat stress alters physiological processes, increasing susceptibility to hyperglycemia by influencing insulin sensitivity. Ambient pressure can worsen hyperglycemia, putting people at greater risk for diabetes complications such as heart disease and kidney damage (Ratter-Rieck *et al*., 2023). Research suggests that there is a relationship between temperature and blood sugar control in people with type 1 and type 2 diabetes (Kenny *et al*., 2016; Dendup *et al*., 2018). Diabetes are more susceptible to health-related problems during extreme weather conditions, including heat stroke and heart attack. This increased risk is primarily due to poor thermoregulation in people with diabetes, especially those with obesity and heart disease. One study that investigated the hottest heat wave in July 2007 in Belgrade, Serbia, found a substantial increase in mortality among elderly individuals, particularly noting that diabetes mellitus had a marked 286% increase in related deaths during the heat wave (Bogdanovic *et al*., 2013; Ratter-Rieck *et al*., 2023).

The impact of climate change on agriculture threatens food security, which directly affects diabetes management. Extreme weather patterns such as droughts and floods disrupt food production, leading to shortages in nutritious foods, especially in low-income regions. Reduced access to fresh fruits, vegetables, and whole grains increases the risk of poorly managed diabetes as patients may rely on processed, high-sugar foods due to scarcity (Yen *et al*., 2022). The interplay between poor diet and diabetes has long been established, and climate-induced food crises exacerbate this issue. Poverty can lead to food insecurity (Al-Worafi *et al*., 2024; Tapkigen *et al*., 2024). Research has shown that countries facing severe climatic disruptions report higher rates of diabetes-related complications due to nutritional deficits (Al Shihabi *et al*., 2022). Climate change-related environmental disasters, including hurricanes, floods, and wildfires, greatly affect the delivery and accessibility of medical treatment. People with diabetes continue to rely on insulin, blood sugar monitors, and healthcare providers to manage their disease. Natural disasters limit access to these important resources, leading to serious diabetes problems. A report on diabetes management during disasters highlighted how Hurricane Katrina contributed to the diabetes crisis by destroying the clean infrastructure of healthcare (Fonseca *et al*., 2009). Similarly, another study highlights the importance of disaster planning in diabetes management (Satoh *et al*., 2019). Physical activity is fundamental to diabetes management, and climate change will change the ability to exercise outdoors. Heat, air pollution, and extreme weather conditions can affect physical activity in people with diabetes, increase obesity, and contribute to poor glycemic control (Venkatasamy *et al*., 2013; You *et al*., 2022; Al-Worafi *et al*., 2024). Climate change due to migration often leads to urbanization, leading to poorer lifestyles, increased food insecurity, and lower physical activity. These lifestyle changes contribute to the development and prevalence of diabetes (Berggreen-Clausen *et al*., 2021). Migrants in particular face difficulties in accessing healthcare, which in turn leads to higher rates of poor healthcare. The literature has documented the association between rapid urbanization and increasing diabetes in these regions (Misra and Ganda, 2007).

Effects of paan (*Piper betle*) on climate and agriculture

Paan can positively affect soil health by promoting organic matter retention and enhancing soil fertility. The integration of paan cultivation with agroforestry practices often leads to improved nutrient cycling and soil structure (Fahad *et al.*, 2022). This not only benefits the paan plants but also supports the overall agricultural productivity of the area. It also contributes to aiding carbon sequestration. The trees associated with paan cultivation,-absorb CO_2 from the atmosphere, contributing to climate change mitigation. This dual benefit of producing a marketable crop while sequestering carbon makes paan farming environmentally valuable (Ullah *et al.*, 2020). Paan cultivation is often conducted sustainably, utilizing practices that minimize deforestation and land degradation. Farmers who rely on naturally occurring trees for support may manage their harvesting practices in a way that does not threaten the integrity of the forest ecosystems. This sustainable approach not only provides livelihoods but also promotes ecological health (Saha and Azam, 2004). Cultivation of paan can enhance the resilience of agricultural communities to climate change impacts. By promoting diverse cropping systems and restoring forest cover, paan farms can help mitigate the effects of extreme weather events, such as floods or droughts. This resilience is particularly essential in coastal regions where climate variability poses significant risks to traditional agricultural systems (Das and Bhattacharji, 2023). It also contributes to biodiversity conservation, especially in forested regions. The cultivation practices often coexist with a variety of support trees, which help maintain the ecological balance within the forest ecosystems. For instance, the Khasia tribes in Bangladesh practice paan farming alongside other tree species, which fosters biodiversity and protects the natural habitat (Saha and Azam, 2004).

Role of various bioactive compounds of paan (*Piper Betle*) in diabetes management

Phytochemical constituents of paan: Paan (*Piper betle*) is an important source of bioactive compounds and holds promise for diabetes management, though its efficacy under environmental stress warrants focused attention. While it is known for its rich phytochemical composition, which includes many bioactive compounds with therapeutic potential, discussions often generalize the role of these phytoconstituents in diabetes management. This review aims to address this gap by focusing on the efficacy of Paan in managing diabetes, specifically under environmental stress, acknowledging, that these components contribute to its medicinal properties and play an important role in affecting diabetes management in varying environmental conditions.

Polyphenols: Antioxidant arsenal- Polyphenols are a diverse group of compounds characterized by their antioxidant properties. In paan, polyphenols such as flavonoids, tannins, and phenolic acids are present in significant amounts. These compounds have been shown to exert beneficial effects on blood sugar metabolism and insulin sensitivity and are crucial in combating oxidative stress, a key player in the pathogenesis of diabetes (Pandey and Rizvi, 2009; Al-Ishaq *et al.*, 2019 ; Aryal *et al.*, 2024). Among the polyphenols, flavonoids such as quercetin, kaempferol, and myricetin stand out. These compounds have been widely studied for their ability to alter glucose metabolism and improve insulin resistance (Varshney *et al.*, 2019). Quercetin, in particular, has been shown to improve glucose uptake in skeletal muscle by increasing the glucose transporter GLUT4. This effect not only lowers blood sugar but also plays a role in enhancing metabolic functions, including insulin signaling (Varshney *et al.*, 2019; Zhou *et al.*, 2023). Kaempferol has been found to activate the AMP-activated protein kinase (AMPK) pathway, which plays an effective role in maintaining energy homeostasis. Activation of the AMPK pathway also promotes the breakdown of fatty acids and reduces the accumulation of lipids in the liver and skeletal muscles, further improving insulin sensitivity (Yang *et al.*, 2022). These compounds exhibit antihyperglycemic effects by inhibiting the activity of carbohydrate-digesting enzymes such as alpha-amylase and alpha-glucosidase. Tannins reduce sugar absorption from the small intestine by blocking enzymes, which reduces the absorption of glucose, preventing postprandial blood glucose spikes, thus preventing post-diabetic conditions, a common problem in diabetes management (Omar *et al.*, 2022). Tannins also have antioxidant properties that help to neutralize free radicals and reduce oxidative stress and related problems (Bigham *et al.*, 2022). Phenolic acids, such as caffeic acid and chlorogenic acid, are known for their dual effects as antioxidants and anti-inflammatory agents. For example, chlorogenic acid has been shown to lower blood sugar levels in the intestines and improve insulin sensitivity by regulating glucose-6-phosphatase, an enzyme involved in glucose production in the liver (Meng *et al*., 2013). This dual effect makes phenolic acids important therapeutic agent in controlling blood sugar. This thereby reduces the oxidative stress (Meng *et al*., 2013). Studies comparing different *Piper betle* varieties found variations in antioxidative properties, suggesting that specific cultivars may offer strong therapeutic effects (Dutta and Banerjee, 2023).

Alkaloids: Bioactive compounds with multifaceted benefits-Alkaloids are nitrogen-containing compounds with many chemical properties. The main alkaloid in the leaves, piperine, has been widely studied for its effects on improving insulin sensitivity and glucose metabolism. It shows that piperine treatment resulted in moderate weight loss, significantly improved glycolipid metabolism, and reversed insulin resistance and glucose intolerance in MSG-induced obese mice. The antidiabetic effect of piperine is likely due to its strong inhibition of systemic and adipose inflammation. Overall, piperine, a promising natural alkaloid, holds potential for the development of antidiabetic therapies (Liu *et al*., 2020).

This action not only lowers blood sugar levels but also helps control insulin levels, a major problem in type 2 diabetes. Piperine also lowers blood sugar levels by inhibiting glucose-6-phosphatase and modulating the activity of insulin receptor substrates (IRS), proteins that play a key role in insulin resistance (Boura-Halfon and Zick, 2009; Stojanovic-Radic *et al*., 2019). Chavicine, another alkaloid found in the leaves, has been shown to have anti-inflammatory properties that are effective in treating diabetes. While research on chavicine is limited, preliminary research suggests that it may help reduce inflammation and oxidative stress, thereby protecting pancreatic beta cells from damage (Iqbal *et al*., 2016; Dinic *et al*., 2022). Another alkaloid, Piperlongumine, has also shown promise in reducing oxidative stress and improving insulin sensitivity, making it useful in combating diabetes (Xu *et al*., 2021a).

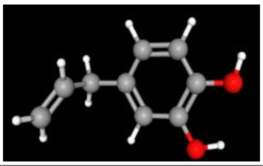
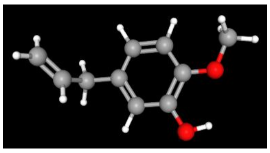
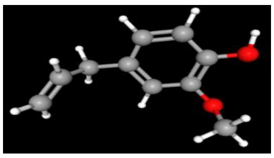
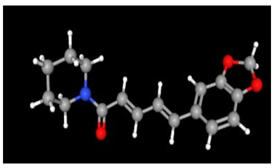
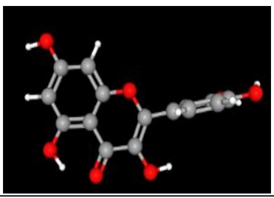
Essential oils: A therapeutic complement-The essential oil obtained from the leaves has many medicinal properties. This essential oil plays a role in the anti-inflammatory and antioxidant properties of the leaves. Research reveals Eugenol's potent antidiabetic effects, added to its ability to inhibit α-glucosidase and prevent the formation of advanced glycation end products, thereby delaying glucose absorption and minimizing blood sugar spikes. It also boosts key enzymes involved in carbohydrate metabolism, such as glucose-6-phosphate dehydrogenase and hexokinase, while lowering levels of creatine kinase and blood urea nitrogen. Tahir *et al*. (2016) demonstrated that *S. aromaticum*, which contains a high concentration of Eugenol, exhibits stronger antidiabetic activity compared to *C. cyminum*. Eugenol's inhibition of α-amylase reduces carbohydrate digestion, leading to lower blood glucose levels in a dose-dependent manner. Further studies in diabetic rats showed that Eugenol significantly increased hepatic glycogen and plasma insulin while reducing glycosylated hemoglobin and blood glucose levels (Al-Trad *et al*., 2019; Nisar *et al*., 2021). Caryophyllene is a sesquiterpene with anti-inflammatory and antioxidant properties. It has been shown to modulate inflammatory pathways and reduce oxidative damage, which can be beneficial for individuals with diabetes. It inhibits the production of pro-inflammatory cytokines, such as TNF-α and IL-6, thereby reducing inflammation and protecting pancreatic beta cells from damage. By reducing inflammation, betel leaf helps to improve insulin sensitivity and preserve beta-cell function, both of which are crucial for diabetes management. β-Caryophyllene is another essential oil component with potential therapeutic effects. It has been reported to have anti-inflammatory and antioxidant effects, which may help mitigate diabetes-related inflammation and oxidative stress (Gushiken *et al*., 2022).

Terpenoids and other compounds: Terpenoids are another class of phytochemicals found in the leaves that account for their medicinal properties. These compounds have been shown to have antioxidant and anti-inflammatory properties, making them useful for diabetes. Linalool is a monoterpene found in betel leaf that has been shown to activate the nuclear factor erythroid 2-related factor 2 (Nrf2) pathway, leading to increased production of antioxidant enzymes such as superoxide dismutase (SOD) and catalase. By activating the Nrf2 pathway, it enhances the body's antioxidant defenses, reducing oxidative stress and protecting against diabetes-related complications (Tamilmani *et al*., 2023; Bar *et al*., 2024).

Clinical and pre-clinical studies: evidence supporting paan's (*Piper betle*) antidiabetic effects

Several studies have investigated the effects of paan on diabetes through both animal models and human trials. Animal studies using diabetic rat models have demonstrated that paan extract can significantly lower blood glucose levels and improve metabolic parameters. For example, administering varying doses of red betel combination extract for 14 days led to lowered blood glucose and triglyceride levels, an increase in pancreatic Langerhans β-cell islets and HDL levels, as well as a reduction in body weight loss in diabetic rats (Safithri *et al*., 2023). Another study conducted by Sembiring *et al*. (2023) showed that red betel leaf extract effectively lowers blood glucose levels and repairs pancreatic tissue and β cells in diabetic mice. The extract reduced blood glucose most significantly at 100 mg (from 406 mg/dL to 168.6 mg/dL), followed by 300 mg and 500 mg doses. It also improved pancreatic tissue health, reducing inflammation, with no necrosis observed. The findings suggest that red betel leaf extract promotes pancreatic healing, enabling insulin production and stabilizing blood sugar may help protect against diabetes-related complications (Sembiring *et al*., 2023). While preclinical studies have provided promising results, clinical studies are needed to confirm the antidiabetic effects of betel leaf in humans. A pilot study conducted by Pane *et al*. (2023) investigated the effects of betel leaf extract on glycemic control in patients with type 2 diabetes. The results have shown that chewing paan inhibits the increase in BGL of type 2 diabetes patients-a marker of glycemic control. Additionally, the study found that paan extract was well-tolerated, with no significant adverse effects reported. This suggests that betel leaf can be a viable complementary therapy for diabetes management (Singh *et al*., 2023). The improvement in insulin sensitivity observed in animal models suggests that paan extract may serve as an adjunct therapy for diabetes. Despite the promising results from pre-clinical studies and pilot clinical trials, more extensive clinical trials are needed to confirm the efficacy and safety of paan in diabetes management.

Table 1. A list of phytochemicals found in *Piper betle*, along with their chemical structure and relation to insulin sensitivity.

Sl. No.	Phytochemicals derived from betel leaf	Chemical Structure	Biological activity	References
1	Hydroxychavicol		Hypoglycemic and hypolipidemic effects, potential diabetes treatment, and inhibition of osteoclastogenesis. Also exhibits in hibitory activity against gastrointestinal pathogens.	Jesonbabu *et al*., 2011; Srividya *et al*., 2015
2	Chavibetol		Major phytotoxic constituent of betel oil, promising volatile phytotoxin, anti - cancer, and antioxidant agent	Kemprai *et al*., 2023
3	Eugenol		Anti-inflammatory, antioxidant, traditionally used for digestive disorders, decreases glucose transport	Nangle *et al*., 2006; Baviskar *et al*., 2017; Chilukoti *et al*., 2023
4	Piperine		Anti-inflammatory and antioxidant effect, reduces body weight, fat mass, triglyceride and glucose level, improves sensitivity of exogenous insulin	Liu *et al*., 2020
5	Quercetin		Strong alpha-glucosidase inhibitory activity decreases serum glucose and blood glycated hemoglobin levels while ameliorating endothelial dysfunction.	Azahar *et al*., 2020

Cont. Table 1.

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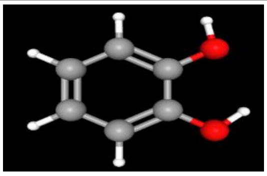
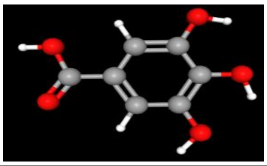
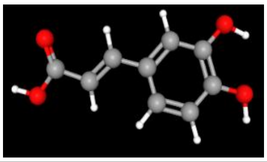
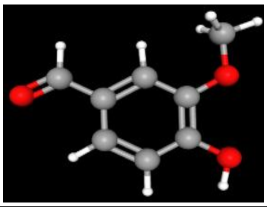
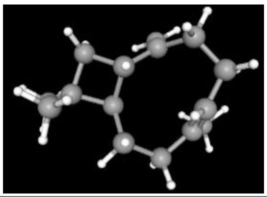
Sl. No.	Phytochemicals derived from betel leaf	Chemical Structure	Biological activity	References
6	Catechol		Redox-active, can donate electrons to quench oxidative free radicals, and can accept electrons to quench reductive free radicals	Kim *et al*., 2019
7	Gallic acid		Alleviates oxidative stress and hematological abnormalities, diminishes the oxidative stress, and inhibits hyperglycemia-induced cytokine production	Xu *et al*., 2021b
8	Caffeic acid		Exhibits different pharmacological activities like anti-diabetic, anti-inflammatory, antioxidant, and antimicrobial activities	Matboli *et al*., 2017
9	Vanillin		Potent antidiabetic effect, suppresses blood glucose, serum cholesterol, and triglyceride, improves pancreatic β-cell function, glucose tolerance, and pancreatic morphology	Salau *et al*., 2021
10	Caryophyllene		Possesses stimulant and medicinal properties, antiplatelet, anti-inflammatory effects, as well as immunomodulatory, gastroprotective, and antidiabetic activity	Hashiesh *et al*., 2020

CONCLUSION

The increasing connection between climate change and diabetes presents considerable difficulties for worldwide healthcare systems, particularly when considering the efficacy of *Piper betle* (Paan) in diabetes management under environmental stress. Especially in susceptible areas, increases in temperatures, severe weather occurrences, and food security and healthcare availability exacerbate blood sugar outcomes. Changes in agricultural productivity due to climate change impact access to nutritious and reasonably priced foods, making it more challenging to manage diabetes amid rising temperatures and reduced medical services during disasters. Prompt implementation of adaptation tactics such as improving healthcare facilities, guaranteeing food stability, and executing community-focused measures is essential in lessening the effects of climate change on diabetes management.

Paan cultivation offers several advantages concerning climate and environmental sustainability and may have direct implications for its efficacy in diabetes management under stressed environmental conditions. It plays a crucial role in biodiversity conservation, enhances soil health, and promotes effective land use practices, all of which can be affected by climate change. Paan cultivation can also provide resilience against climate-related challenges, making it an advantageous crop in various ecological settings. Furthermore, it also shows potential as an additional method for managing diabetes. It is rich in bioactive compounds like polyphenols, alkaloids, and essential oils, showing promise in managing glucose metabolism, improving insulin sensitivity, and decreasing inflammation. Research with both humans and animals backs up the idea that it can help reduce blood sugar and enhance overall metabolic health, suggesting it could be a practical substitute for traditional therapies, especially when access to conventional medications is limited due to environmental stressors. Although the evidence shows potential, there are still gaps in knowledge, especially regarding the lasting effectiveness and safety of paan in treating diabetes complications such as heart disease and nerve damage under conditions of environmental stress.

The fact that paan comes from nature, is easily found locally, and is affordable, makes it attractive in areas dealing with diabetes and climate change, where healthcare access may be limited. Utilizing it fits into sustainable health plans by offering a culturally recognized and locally obtained choice for controlling diabetes in resource-limited environments. By merging age-old treatments with contemporary medical care, societies can enhance their resistance to the twin threats of climate change and chronic illness.

Although current regulatory guidelines for herbal medicines, including betel leaves, emphasize stringent quality control and safety measures to ensure consumer protection and therapeutic efficacy. These guidelines aim to standardize the manufacturing processes, prevent contamination, and accurately determine the concentration of active compounds. Compliance with these regulations is crucial for maintaining the quality, safety, and efficacy of betel leaf products, thereby promoting their rational use and minimizing potential health risks (Balkrishna *et al*. 2024).

In a nutshell, managing the interconnected challenges of climate change and diabetes necessitates a comprehensive strategy that combines traditional medical remedies with natural solutions such as paan, while also accounting for the impacts of environmental stress on both disease management and agricultural practices. This underscores the significance of integrating paan cultivation into broader agricultural and environmental strategies for the potential treatment of diabetes. Policymakers, healthcare providers, and researchers need to work together to enhance, the resilience of health systems and maximize the healing benefits of natural remedies, particularly in the face of increasing environmental challenges.

Future studies should focus on conducting extensive, extended clinical trials to confirm these initial discoveries. More Researches is required to investigate how paan affects glucose control and insulin pathways at a molecular level, which could provide important information about its wider healing capabilities. Additionally, it is crucial to have standardized formulations and dosages to guarantee consistent results among various patient groups. The different ways through which paan are prepared and dosed in various studies make it challenging to come to definite conclusions about its clinical effectiveness. Also, a limelight should be created on understanding how paan works, setting standards, and evaluating its long-term safety to maximize its effectiveness in managing diabetes and providing a sustainable solution for health challenges related to climate change.

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Author's contribution: TD: Conducted the overall literature review, organized the manuscript's structure, and drafted and edited the main text; PP: Edited and offered valuable insights and feedback; SB: Edited and suggested the topic of the effects of climatic changes on diabetes; ERB: Conceptualized the review plan and supervised and gave her input in the final editing of the manuscript. All authors have read and approved the final review paper.

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REFERENCES

Al-Ishaq RK, Abotaleb M, Kubatka P, Kajo K and Büsselberg D, 2019. Flavonoids and their anti-diabetic effects: cellular mechanisms and effects to improve blood sugar levels. Biomolecules, 9(9): 430, doi: 10.3390/biom9090430

Al-Trad B, Alkhateeb H, Alsmadi W and Al-Zoubi M, 2019. Eugenol ameliorates insulin resistance, oxidative stress and inflammation in high fat-diet/streptozotocin-induced diabetic rat. Life Sci, 216: 183-188, doi: 10.1016/j.lfs.2018.11.034

Al-Worafi YM, 2024. Diabetes Mellitus: Causes and Risk Factors in Developing Countries. Handbook of Medical and Health Sciences in Developing Countries, Springer, Cham, pp1-26, doi: 10.1007/978-3-030-74786-2_322-1

Aryal D, Joshi S, Thapa NK, Chaudhary P, Basaula S *et al*., 2024. Dietary phenolic compounds as promising therapeutic agents for diabetes and its complications: A comprehensive review. Food Sci Nutr, 12(5): 3025-3045, doi: 10.1002/fsn3.3983

Azahar NI, Mokhtar NM and Arifin MA. 2020. *Piper betle*:

A review on its bioactive compounds, pharmacological properties, and extraction process. IOP Conf Ser: Mater Sci Eng, 991(1): 012044, doi: 10.1088/1757-899X/991/1/012044

Balkrishna A, Sharma N, Srivastava D, Kukreti A, Srivastava S *et al*., 2024. Exploring the safety, efficacy, and bioactivity of herbal medicines: bridging traditional wisdom and modern science in healthcare. Futur Integr Med, 3(1): 35-49, doi: 10.14218/FIM.2023.00086

Bar S and Kara M, 2024. Linalool exerts antioxidant activity in a rat model of diabetes by increasing catalase activity without an antihyperglycemic effect. Exp Ther Med, 28(3): 359, doi: 10.3892/etm.2024.12648

Baviskar HP, Dhake GT, Kasai MA, Chaudhari NB and Deshmukh TA, 2017. Review of *Piper Betle*. Res J Pharmacogn Phytochem, 9(2): 128, doi: 10.5958/0975-4385.2017.00024.3

Berggreen-Clausen A, Hseing Pha S, Mölsted Alvesson H, Andersson A and Daivadanam M, 2022. Food environment interactions after migration: A scoping review on low- and middle-income country immigrants in high-income countries. Public Health Nutr, 25(1): 136-158, doi: 10.1017/s1368980021003943

Bigham A, Rahimkhoei V, Abasian P, Delfi M, Naderi J *et al*., 2022. Advances in tannic acid-incorporated biomaterials: Infection treatment, regenerative medicine, cancer therapy, and biosensing. Chem Eng J, 432: 134146, doi: 10.1016/j.cej.2021.134146

Bogdanovic DC, Milosevic ZG, Lazarevic KK, Dolicanin ZC, Randelovic DM *et al*., 2013. The impact of the July 2007 heat wave on daily mortality in Belgrade, Serbia. Cent Eur J Public Health, 21(3): 140-145, doi: 10.21101/cejph.a3840

Boura-Halfon S and Zick Y, 2009. Phosphorylation of IRS proteins, insulin action, and insulin resistance. Am J Physiol Endocrinol Metab, 296(4): E581-591, doi: 10.1152/ajpendo.90437.2008

Chilukoti SR, Sahu C and Jena G, 2023. Protective role of eugenol against diabetes induced oxidative stress, DNA damage, and apoptosis in rat testes. J Biochem Mol Toxicol, 38(1): e23593, doi: 10.1002/jbt.23593

Das R, Mitra S, Mukherjee K, Paul P, Singh UP *et al*., 2015. Anti-Oxidant and anti-inflammatory activities of different varieties of piper leaf extracts (*Piper Betle* L.). J Nutr Food Sci, 5: 415, doi: 10.4172/2155-9600.1000415

Das S and Bhattacharji M, 2023. Climate change and agriculture in a coastal region: A case study of betel leaf cultivation in Sagar Island, Kakdwip, South 24 Parganas. Curr World Environ, 18(1): 381-403, doi: 10.12944/CWE.18.1.32

Dendup T, Feng X, Clingan S and Astell-Burt T, 2018. Environmental risk factors for developing Type 2 diabetes mellitus: A systematic review. Int J Environ Res Public Health, 15(1): 78, doi: 10.3390/ijerph15010078

Dinic S, Jovanovic JA, Uskokovic A, Mihailovic M, Grdovic N *et al*., 2022. Oxidative stress-mediated beta cell death and dysfunction as a target for diabetes management. Front Endocrinol, 13: 1006376, doi: 10.3389/fendo.2022.1006376

Dutta R and Banerjee ER, 2023. A comparative study on anti-oxidative properties of different cultivars of *Piper betle* collected from Howrah district (West Bengal). Inter J Sci Res, 12(03): 4, doi: 10.36106/ijsr

Fahad S, Chavan SB, Chichaghare AR, Uthappa AR, Kumar M *et al*., 2022. Agroforestry systems for soil health improvement and maintenance. Sustainability, 14(22): 14877, doi: 10.3390/su142214877

Fonseca VA, Smith H, Kuhadiya N, Leger SM, Yau CL *et al*., 2009. Impact of a natural disaster on diabetes: exacerbation of disparities and long-term consequences. Diabetes Care, 32(9): 1632-1638, doi: 10.2337/dc09-0670

Gushiken LFS, Beserra FP, Hussni MF, Gonzaga MT, Ribeiro VP *et al*., 2022. Beta-caryophyllene as an antioxidant, anti-inflammatory and re-epithelialization activities in a rat skin wound excision model. Oxid Med Cell Longev, 2022: 9004014, doi: 10.1155/2022/9004014

Hashiesh HM, Meeran MFN, Sharma C, Sadek B, Kaabi JA *et al*., 2020. Therapeutic potential of â-caryophyllene: A dietary cannabinoid in diabetes and associated complications. Nutrients, 12(10): 2963, doi: 10.3390/nu12102963

International Diabetes Federation, 2022. IDF Diabetes Atlas, 10th edn, Brussels, Belgium: International Diabetes Federation. Available at: https://diabetesatlas.org/

Iqbal G, Iqbal A, Mahboob A, Farhat SM and Ahmed T, 2016. Memory enhancing effect of black pepper in the AlCl3 induced neurotoxicity mouse model is mediated through its active component chavicine. Curr Pharm Biotechnol, 17(11): 962-73, doi: 10.2174/1389201017666160709202124

Jesonbabu J, Spandana N and Lakshmi KA, 2011. The Potential activity of hydroxychavicol against pathogenic bacteria. J Bacteriol Parasitol, 02(06), doi: 10.4172/2155-9597.1000121

Kemprai P, Bora PK, Saikia SP and Haldar S, 2023. Chavibetol: major and potent phytotoxin in betel (*Piper betle* L.) leaf essential oil. Pest Manag Sci, 79(11): 4451-4462, doi: 10.1002/ps.7645

Kenny GP, Sigal RJ and McGinn R, 2016. Body temperature regulation in diabetes. Temperature (Austin), 3(1): 119-145, doi: 10.1080/23328940.2015.1131506

Kim E, Kang M, Liu H, Cao C, Liu C *et al*., 2019. Pro- and anti-oxidant properties of redox-active catechol-chitosan films. Front Chem, 7: 541, doi: 10.3389/fchem.2019.00541

Kottaisamy CPD, Raj DS, Prasanth Kumar V and Sankaran U, 2021. Experimental animal models for diabetes and its related complications review. Lab Anim Res, 37(1): 23, doi: 10.1186%2Fs42826-021-00101-4

Levi R, Bleich SN and Seligman HK, 2023. Food insecurity and diabetes: overview of intersections and potential dual solutions. Diabetes Care, 46(9): 1599-1608, doi: 10.2337/dci23-0002

Liu C, Yuan Y, Zhou J, Hu R, Ji L *et al*., 2020. Piperine ameliorates insulin resistance via inhibiting metabolic inflammation in monosodium glutamate-treated obese mice. BMC Endocr Disord, 20(1): 152, doi: 10.1186/s12902-020-00617-1

Matboli M, Eissa S, Ibrahim D, Hegazy MGA, Imam SS *et al*. Caffeic acid attenuates diabetic kidney disease via modulation of autophagy in a high-fat diet/streptozotocin-induced diabetic rat. Sci Rep, 7: 2263, doi: 10.1038/s41598-017-02320-z

Meng S, Cao J, Feng Q, Peng J and Hu Y, 2013. Roles of chlorogenic acid on regulating glucose and lipids metabolism: A review. Evid Based Complement Alternat Med, 2013: 801457, doi: 10.1155/2013/801457

Misra A and Ganda OP, 2007. Migration and its impact on adiposity and type 2 diabetes. Nutrition, 23(9): 696-708, doi: 10.1016/j.nut.2007.06.008

Nangle M, Gibson T, Cotter M and Cameron N, 2006. Effects of eugenol on nerve and vascular dysfunction in streptozotocin-diabetic rats. Planta Med, 72(6): 494-500, doi: 10.1055/s-2005-916262

Nisar MF, Khadim M, Rafiq M, Chen J, Yang Y *et al*., 2021. Pharmacological properties and health benefits of eugenol: A comprehensive review. Oxid Med Cell Longev, 2021: 2497354, doi: 10.1155/2021/2497354

Omar N, Ismail CAN and Long I, 2022. Tannins in the treatment of diabetic neuropathic pain: research progress and future challenges. Front Pharmacol, 12: 805854, doi: 10.3389/fphar.2021.805854

Pandey KB and Rizvi SI, 2009. Plant polyphenols as dietary antioxidants in human health and disease. Oxid Med Cell Longev, 2(5): 270-278, doi: 10.4161/oxim.2.5.9498

Pane YS, Machrina Y, Arrasyid NK and Sari MI, 2023. The effect of chewing-betel habits on blood glucose levels in the *Karo* ethnic community, Karo district. F1000 research, 11: 100, doi: 10.12688/f1000research.75763.4

Ratter-Rieck JM, Roden MM and Herder C, 2023. Diabetes and climate change: current evidence and implications for people with diabetes, clinicians and policy stakeholders. Diabetologia, 66(6): 1003-1015, doi: 10.1007/s00125-023-05901-y

Safithri M, Bintang M and Syaefudin, 2023. Blood glucose level, langerhans pancreas and lipid profile of diabetic rats after administration of red betel, ginger and cinnamon combination extract. Trop Life Sci Res, 34(1): 41-50, doi: 10.21315/tlsr2023.34.1.3

Saha N and Azam MA, 2005. Betel leaf based forest farming by Khasia: tribes: a sustainable system of forest management in Moulvibazar District, Bangladesh. For Trees Livelihoods, 15(3): 275-290, doi: 10.1080/14728028.2005.9752528

Salau VF, Erukainure OL, Olofinsan KO, Msomi NZ, Ijomone OM *et al*., 2021. Vanillin improves glucose homeostasis and modulates metabolic activities linked to type 2 diabetes in fructose–streptozotocin induced diabetic rats. Arch Physiol Biochem, 130(2): 169-182, doi: 10.1080/13813455.2021.1988981

Satoh J, Yokono K, Ando R, Asakura T, Hanzawa K *et al*., 2019. Diabetes care providers' manual for disaster diabetes care. J Diabetes Investig, 10(4): 1118-1142, doi: 10.1111/jdi.13053

Sembiring ME, Nasution AN and Chiuman L, 2023. Effectiveness test of ethanol extract of red betel leaves (*Piper crocatum* Ruiz & Pav) against histopathological features of the pancreas and blood sugar levels of Alloxan-induced male mice (*Mus Musculus* L). J Eduhealth, 14(4): 65-74

Singh N and Dasar D, 2024. Harnessing the power of ayurveda for diabetes management: A narrative review. J Clin Diagn Res, 18(6): LE01-LE05, doi: 10.7860/JCDR/2024/70617.19479

Singh T, Singh P, Pandey VK, Singh R and Dar AH, 2023. A literature review on bioactive properties of betel leaf (*Piper betel* L.) and its applications in food industry. Food Chem Adv, 3: 100536, doi: 10.1016/j.focha.2023.100536

Srividya S, Devi V and Subramanian S, 2015. Hypoglycemic and hypolipidemic properties of hydroxychavicol, a major phenolic compound from the leaves of *Piper betlelinn* studied in high fat diet fed-low dose STZ induced experimental type 2 diabetes in rats. Pharm Lett, 7(11): 130-140

Stojanovic-Radic Z, Pejcic M, Dimitrijevic M, Aleksic A and Kumar NVA, 2019. Piperine-A major principle of black pepper: A review of its bioactivity and studies. Applied Sci, 9(20): 4270, doi: 10.3390/app9204270

Sun H, Saeedi P, Karuranfa S, Pinkepank M and Ogurtsova K, 2021. IDF Diabetes Atlas: Global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. Diabetes Res Clin Pract, 183: 109119, doi: 10.1016/j.diabres.2021.109119

Tahir HU, Sarfraz RA, Ashraf A and Adil S, 2016. Chemical composition and antidiabetic activity of essential oils obtained from two spices (*Syzygium aromaticum* and *Cuminum cyminum*). Int J Food Prop, 19(10): 2156-2164, doi: 10.1080/10942912.2015.1110166

Tamilmani P, Uddandrao VVS, Chandrasekaran P, Saravanan G and Naidu PB, 2023. Linalool attenuates lipid accumulation and oxidative stress in metabolic dysfunction-associated steatotic liver disease via Sirt1/Akt/PPRA-α/AMPK and Nrf-2/HO-1 signaling pathways. Clin Res Hepatol Gastroenterol, 47(10): 102231, doi: 10.1016/j.clinre.2023.102231

Tapkigen J, Harding S, Pulkki J, Atkins S and Koivusalo M, 2024. Climate change-induced shifts in the food systems and diet-related non-communicable diseases in sub-Saharan Africa: A scoping review and a conceptual framework. BMJ Open, 14(6): e080241, doi: 10.1136/bmjopen-2023-080241

Ullah ASM, Tani M, Tsuchiya J, M Rahman A and M Rahman Z, 2020. Impact of betel leaf cultivation on the protected forest area of Teknaf peninsula, Bangladesh. Small-scale For, 19: 335-355, doi: 10.1007/s11842-020-09441-w

Varshney R, Mishra R, Das N, Debarata S and Roy P, 2019. A comparative analysis of various flavonoids in the regulation of obesity and diabetes: An *in vitro* and *in vivo* study. J Funct Foods, 59: 194-205, doi: 10.1016/j.jff.2019.05.004

Venkatasamy VV, Pericherla S, Manthuruthil S, Mishra S and Hanno R, 2013. Effect of physical activity on insulin resistance, inflammation and oxidative stress in diabetes mellitus. J Clin Diagn Res, 7(8): 1764-1766, doi: 10.7860/jcdr/2013/6518.3306

Xu P, Xiao J and Chi S, 2021a. Piperlongumine attenuates oxidative stress, inflammatory, and apoptosis through modulating the GLUT-2/4 and AKT signaling pathway in streptozotocin-induced diabetic rats, 2021. J Biochem Mol Toxicol, 35(6): 1-12, doi: 10.1002/jbt.22763

Xu Y, Tang G, Zhang C, Wang N, Feng Y, 2021b. Gallic Acid and diabetes mellitus: its association with oxidative stress. Molecules, 26(23): 7115, doi: 10.3390/molecules26237115

Yang Y, Chen Z, Zhao X, Xie H, Du L *et al*., 2022. Mechanisms of kaempferol in the treatment of diabetes: A comprehensive and latest review. Front Endocrinol, 13: 990299, doi: 10.3389 /fendo.2022.990299

Yen TS, Htet MK, Lukito W, Bardosono S, Setiabudy R *et al*., 2022. Increased vegetable intake improves glycaemic control in adults with type 2 diabetes mellitus: A clustered randomized clinical trial among Indonesian white-collar workers. J Nutr Sci, 11: e49, doi: 10.1017/jns.2022.41

You Y, Wang D, Liu J, Chen Y, Ma X *et al*., 2022. Physical exercise in the context of air pollution: An emerging research topic. Front Physiol, 13: 784705, doi: 10.3389%2Ffphys.2022.784705

Zhou M, Konigsberg WH, Hao C, Pan Y, Sun J *et al*., 2023. Bioactivity and mechanisms of flavonoids in decreasing insulin resistance. J Enzyme Inhib Med Chem, 38(1): 2199168, doi: 10.1080/14756366.2023.2199168

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