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Arshu P Patel
Department of Pharmacognosy, Pravara Rural College of Pharmacy, Pravaranagar, Maharashtra, India

Sayee P Dhavan
Department of Pharmacognosy, Pravara Rural College of Pharmacy, Pravaranagar, Maharashtra, India

Pradnya A Sukhadhane
Department of Pharmacognosy, Pravara Rural College of Pharmacy, Pravaranagar, Maharashtra, India

Nikita R Kature
Department of Pharmacognosy, Pravara Rural College of Pharmacy, Pravaranagar, Maharashtra, India

Corresponding Author:
Sayee P Dhavan
Department of Pharmacognosy, Pravara Rural College of Pharmacy, Pravaranagar, Maharashtra, India

Exploring natural interventions for mitigating diabetes complications: An updated review of therapeutic potential in natural substances

Arshu P Patel, Sayee P Dhavan, Pradnya A Sukhadhane and Nikita R Kature

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Abstract
The growing prevalence of type 2 diabetes presents substantial threat to human health on a global scale. Diabetes mellitus (DM) is a chronic metabolic disorder that arises from a lack or ineffective response in insulin secretion, leading to increased blood glucose levels, known as hyperglycaemia which has the potential to give rise to various illnesses and serious complications. Compared to traditional medicine, the using natural remedies for medical purposes in the management and avoidance of various illnesses, includes diabetes, which has a historical heritage. There are multiple strategies for managing and preventing diabetes and its complications, with herbal medicine being one option. Still, the choice of herbs relies on a number of parameters such as the stage of diabetes progression, any accompanying health conditions, accessibility, cost, and safety profile. This review delves into herbal and natural remedies that can aid in treating or preventing diabetes. It examines how they a reduction in blood sugar and talks about herbal products that are currently on the market for controlling diabetes. There are many natural herbs used for the treatment of the Diabetes such as *Aloe vera*, Banaba, Coffee, Garlic, Bitter melon, Guava, etc. The emphasis of this review is on natural products that can serve as alternative therapies.

Keywords: Diabetes mellitus (DM), Hyperglycaemia, Pathogenesis, Herbal, Insulin

Introduction
In recent times, Diabetes Mellitus (DM) has emerged as a significant concern, identified by deficiencies either in the production of insulin or in its effectiveness on peripheral tissues, leading to metabolic irregularities and elevated blood sugar levels. However, the expectation is that this number will elevate to 642 million in the subsequent 25 years [1]. Diabetes affects an estimated 346 million people globally, and that figure is predicted to double by 2030, presenting a major challenge to the healthcare system, according to estimates from the World Health Organization (WHO) [2]. On April 7, 2016, World Health Day, a day devoted to raising awareness of diabetes, saw the release of the first WHO Global Report on Diabetes. Elevated blood glucose levels and abnormal lipid and protein metabolism are hallmarks of diabetes, a chronic illness. The surge in blood glucose ensues from its impaired cellular metabolism, attributed to either insufficient pancreatic insulin secretion or diminished cellular responsiveness to endogenous insulin. The disease encompasses three principal classifications: (a) Type 1, characterized by pancreatic insulin insufficiency; (b) Type 2, marked by cellular insulin resistance and a progressive decline in insulin production; and (c) gestational diabetes, manifesting during pregnancy with potential complications and heightened risks of subsequent type 2 diabetes and offspring obesity [3].
Around 90 percent of diabetes cases belong to type 2, originating from insulin resistance and deficiency [4]. Herbs and natural products persist to be very important for treating and preventing a wide range of illnesses. They work as a vast reservoir for uncovering novel compounds characterized by specific structural arrangements, demonstrating noteworthy therapeutic potential for addressing a spectrum of health conditions. Compounds derived from these sources are generally perceived as safer, cost-effective, readily available, and at times, more efficacious than entirely synthetic entities. In recent times, scientific investigations have been focused on identifying safe and highly effective medications derived from natural sources, particularly medicinal plants [5].

Pathogenesis of diabetes

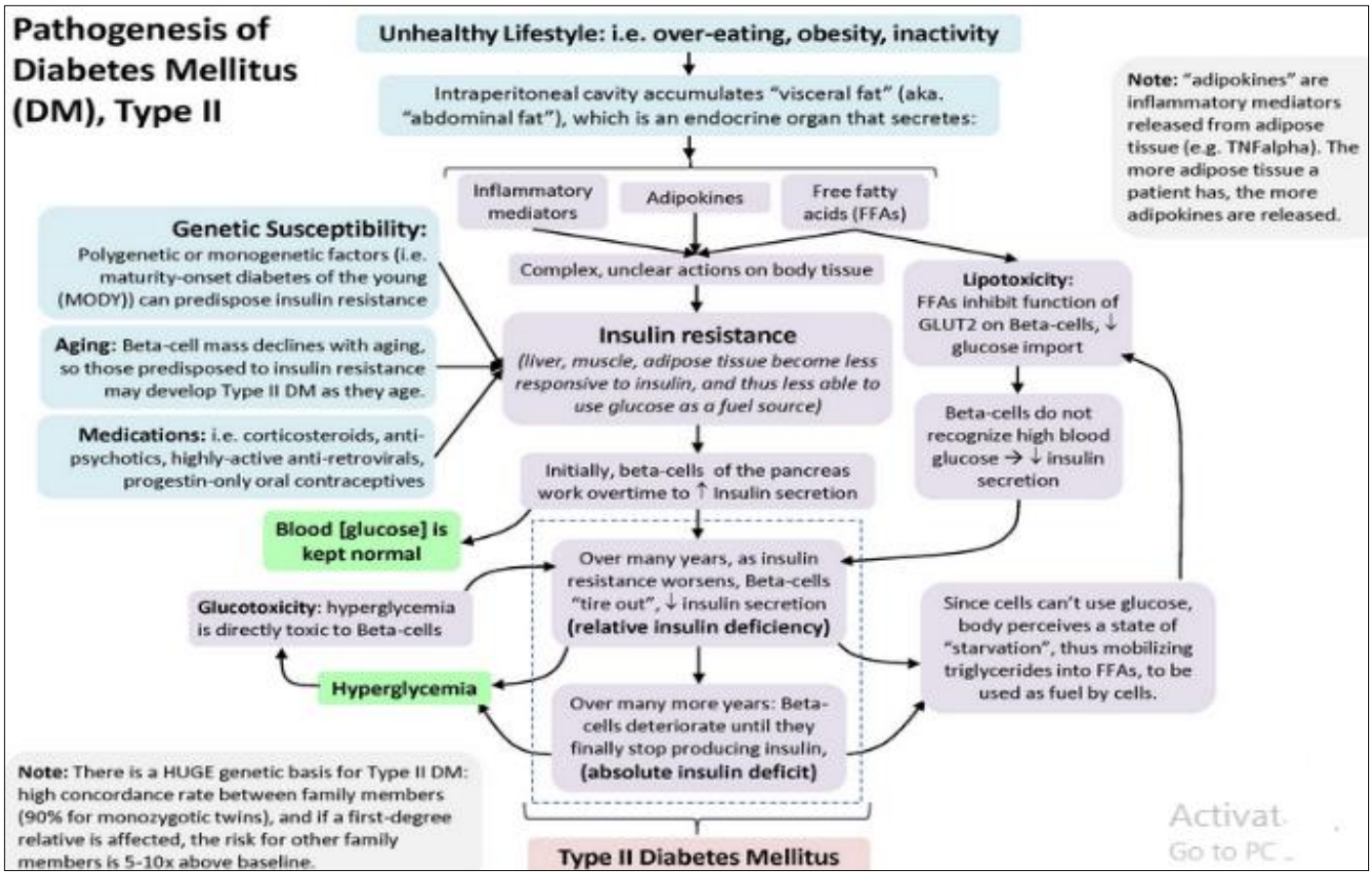

Fig 1: Pathogenesis of Diabetes

Pharmacological Potential of Natural Compounds and Herbal Substances: In developing nations, medicinal plants persist as the predominant reservoir of pharmaceutical agents. 7,295 plant species are used as medicine, mostly in China. In underdeveloped countries, some 3.4 billion people primarily use plants as their major source of medicine, according to estimates from the World Health Organization (WHO). This constitutes approximately 88% of the global population, emphasizing the substantial dependence on traditional medicine for primary healthcare in these regions [6]. Preserving the current and potential reservoir of medicinal and biological agents is a preeminent concern for public health and human well-being. Immediate measures are imperative to avert further depletion. Undocumented natural remedies, employed by humans for millennia, necessitate systematic cataloging to safeguard crucial ethnomedical knowledge from irretrievable loss. According to research by Farnsworth *et al*., at least 119 chemicals that come from 90 different plant species are considered important medications that are now being used worldwide, with 77% of these compounds coming from plants that have been used traditionally in medicine. The fact that, in 1991, natural goods or their derivatives accounted for over half of the top-selling medications highlights the importance of natural products [7].

Challenges in advancement of new pharmaceuticals predominantly constitute experienced obstacles. The following characteristics are deemed optimal for naturally sourced compounds.

- Augmented stereo complexity.
- Reduced proportion of aromatic ring atoms.
- Abundance of oxygen atoms.
- An elevated number of chiral centers.
- Dispersion of molecular properties encompassing diversity in ring systems, mass number, and partition coefficient.

These distinctive attributes encapsulate range of complexities that medicinal scientists encounter in expansion of pharmaceutical compounds. Addressing these challenges are imperative for optimizing compound enlargement, absorption enhancement, and toxicity mitigation to enhance overall efficacy [8].

Clinical Assessment of Diabetes

In the year 2000, the estimated global prevalence of diabetes among the adult population was approximately 171 million individuals, While the count rose to 422 million (approximately 1 in every 11 individuals) in 2014, the global prevalence of diabetes is anticipated to double to around 366 million by the year 2030. This escalation is attributed to demographic shifts in individuals aged over 65 years and, significantly, the adoption of sedentary lifestyles among urban populations worldwide [9]. If left untreated, this condition can lead to severe and potentially fatal complications, including diabetic ketoacidosis and coma due to a significant increase in blood glucose levels. Diabetes also contributes to adverse vascular outcomes, resulting in both macrovascular and microvascular disorders due to damage to blood vessels caused by elevated glucose levels. Microvascular complications encompass conditions such as retinopathy and neuropathy, while macrovascular complications lead to cardiovascular issues. Chronic diabetic conditions further give rise to complications such as dementia, sexual dysfunction, depression, and the need for lower-limb amputations [10].

Various classes of antidiabetic medications are available in the market for therapeutic intervention. These include insulin analogs, sulphonylureas, biguanides, dipeptidyl peptidase-4 inhibitors, thiazolidiones, alpha-glucosidase inhibitors, and more. The mechanisms employed by each category to counteract elevated glucose levels vary. (Fig.2) [11].

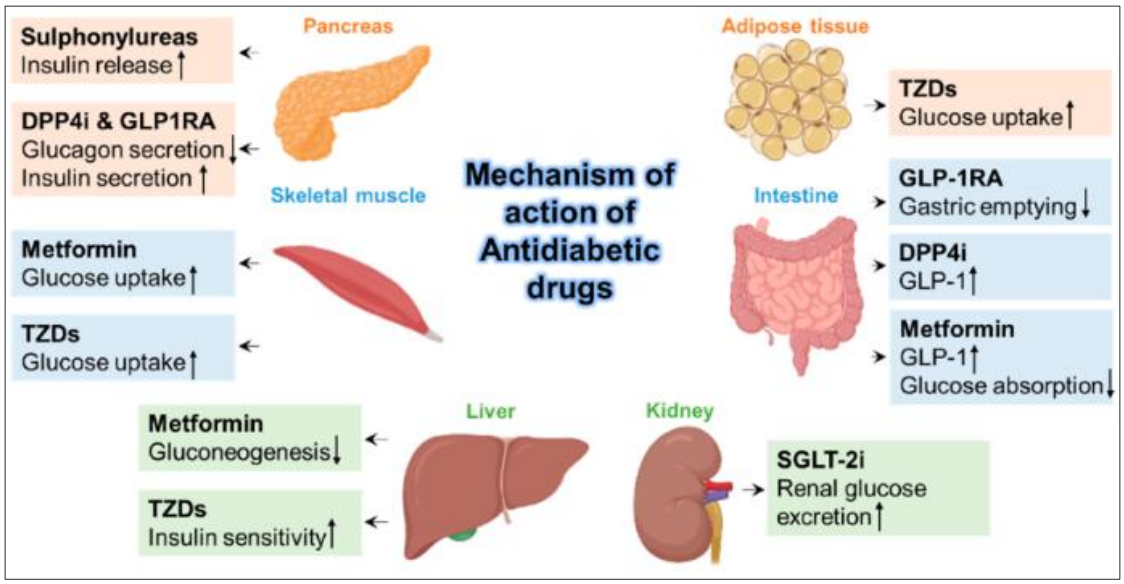

Fig 2: Mechanisms of Action of Antidiabetic Drugs

Natural treatment for diabetes

Complementary or alternative treatments utilizing herbal medicines capture the interest of many individuals with diabetes. Several commonly used herbs are purported to lower blood glucose levels, creating the enticing possibility of achieving better glycaemic control or reducing reliance on insulin injections through herbal interventions. However, the choice of herbs may be influenced by various factors, including the stage of diabetes progression, the presence of comorbidities, herb availability, affordability, and safety considerations.

Preclinical investigations have transitioned from laboratory settings to clinical application, with recent human studies reporting the antidiabetic potential of medicinal plants such as Scoparia dulcis, Cinnamomum cassia, Ficus racemose bark, and Portulaca oleracea L. seeds. Subsequent research on herbal products has moved from laboratories to diabetic patients, marketed under the brand names Diabecon®, Glyoherb®, and Diabeta Plus®. Thus, herbal supplements may serve as adjunctive or favorable alternative therapies for diabetic conditions [12].

The selection of natural treatments/ natural herbs for diabetes

Numerous medicinal plants have demonstrated effectiveness at various stages of diabetes. For instance, curcumin is suggested as a potential intervention in pre-diabetes treatment to hinder the advancement of Type 2 Diabetes Mellitus (T2DM) owing to its established advantages and safety record [13]. However, cinnamon could be a more suitable alternative for diabetic patients with concomitant hypertension [14].

Historically, treatments for various disorders, particularly diabetes, primarily relied on dietary and plant-based remedies. Ethno pharmacological studies have identified numerous plant-derived herbs as potential treatments for diabetes. A thorough examination of data concerning thousands of these herbs revealed that over 80% exhibited some level of antidiabetic activity in research studies. Notably, only one approved antidiabetic medication, metformin, originated from an herb with a longstanding history of use for diabetes—the French lilac, scientifically known as Galega officinalis [15].

The alcoholic extract derived from the gel of *Aloe vera* leaves a member of the Liliaceae family, demonstrated the ability to enhance insulin levels in regenerated pancreatic beta-cells. Additionally, administration of *Aloe vera* extract resulted in decreased plasma lipid levels, liver cholesterol, and kidney triglycerides in diabetic rats undergoing testing [16].

Banaba extracts, derived from Lagerstroemia speciosa L., have a longstanding history in traditional medicine for managing diabetes. This plant's hypoglycemic effects are credited to both Corosolic acid and ellagitannins. Research conducted across animal models, human trials, and laboratory settings has examined the effects of water-soluble Banaba leaf extracts, Corosolic acid, and ellagitannins. Corosolic acid has been shown to rapidly lower blood sugar levels in humans within an hour of ingestion, and it also possesses properties that combat hyperlipidaemia and oxidative stress. The positive impacts of Banaba and Corosolic acid on glucose and lipid metabolism involve various mechanisms, such as improved glucose uptake by cells, inhibition of sucrose and starch breakdown, reduced gluconeogenesis, and modulation of lipid metabolism [17].

Coffee consumption has been investigated for its impact on various mechanistic factors involved in the development of type 2 diabetes mellitus (T2DM), including glucose tolerance, insulin sensitivity, insulin resistance, glucose-6-phosphatase activity, intestinal glucose absorption, antioxidant properties, Inflammatory markers, inhibition of nuclear factor-κB, glucose uptake, glucose homeostasis, glucose metabolism, and insulin secretion. These factors are critical in maintaining normal blood glucose levels. Collectively, both experimental and epidemiological evidence suggests that coffee consumption exerts protective effects against T2DM through multiple preventive mechanisms. Therefore, it is suggested that coffee be recommended as a supplementary therapy to prevent further progression of T2DM in patients with diabetes or those at risk of developing the condition [18].

Garlic and its active components have undergone extensive examination for their potential to mitigate diabetes in animal models induced with either experimental or genetic factors. Additionally, human trials have reported hypoglycemic effects associated with garlic consumption. The beneficial impacts of garlic are primarily linked to the presence of volatile sulphur compounds such as alliin, allicin, diallyl disulphide, diallyl trisulfide, diallyl sulphide, S-allyl cysteine, ajoene, and allyl mercaptan. Studies indicate that garlic and its extracts exhibit effectiveness in reducing insulin resistance [19].

Bitter melon, scientifically known as *Momordica charantia*, is widely utilized in traditional medicine across Asia, South America, India, and East Africa for managing diabetes and its associated conditions. Numerous pre-clinical studies have extensively explored its potential benefits, revealing its anti-diabetic and hypoglycemic properties through various proposed mechanisms [20]+. Bitter melon, whether consumed as fresh fruit, fruit juice, or in dried powder form, has been historically employed in traditional medicine to reduce blood sugar levels. Studies indicate that a daily intake of 2000 mg of dried bitter melon fruit pulp exhibits a slight hypoglycemic effect, as evidenced by a decrease in Fructosamine levels. However, this effect appears to be less pronounced compared to the hypoglycemic action of 1000 mg of metformin. While *in vitro* and animal research supports the potential hypoglycemic properties of bitter melon, there is limited evidence from human studies to fully endorse its use for this purpose [21].

The fruit of *Capparis spinosa* L. is a traditional remedy used by diabetic patients in Iran to counteract hyperglycaemia. Despite its widespread use, there is currently no controlled human study available to definitively assess its efficacy in treating hyperglycaemia specifically in individuals with type 2 diabetes [22].

Guava, a traditional remedy for diabetes, was examined to identify its active components and how they work. Our study found that guava polysaccharides, particularly GP70, notably reduced fasting blood glucose levels and increased glycosylated serum protein (GSP) levels by 21% in type II diabetic individuals. Additionally, extracts from guava leaves demonstrated significant antidiabetic effects by inhibiting tyrosine phosphatase activity and reducing liver lipid droplets in type 2 diabetes. Similarly, extracts from Psidium guajava leaves exhibited significant antidiabetic effects through tyrosine phosphatase inhibition and reduction of liver lipid droplets. Furthermore, guava polysaccharides displayed potent antioxidant properties [23].

Herbal medications that are commercially available for the treatment of diabetes

Commercially available herbal drugs with antidiabetic effects are in high demand due to their accessibility, affordability, and lower risk of side effects compared to synthetic anti-diabetic medications. These herbal formulations are widely considered more effective for diabetes management. India, with its numerous herbal drug manufacturers, sees nearly all of them developing anti-diabetic herbal formulations alongside other products [24].

Diabecon, manufactured by Himalaya, reportedly enhances glucose utilization in peripheral tissues, increases hepatic and muscle glucagon levels, supports the repair and regeneration of pancreatic B cells, and boosts c-peptide levels. It possesses antioxidant properties that protect pancreatic B cells from oxidative stress. Additionally, Diabecon exerts insulin-like effects by reducing glycated haemoglobin levels, normalizing microalbuminuria, and modulating lipid profiles. It also helps minimize the risk of long-term complications associated with diabetes.

Diabetes Daily Care, developed by Nature's Health Supply, is a special natural formula crafted to enhance sugar metabolism in a safe and efficient manner. Specifically designed for type 2 diabetes, this product contains solely natural ingredients [25].

Epinsulin, promoted by Swastik Formulations, utilizes epicatechin, a benzopyran, as its active component. Epicatechin boosts cAMP levels in the islet, leading to increased insulin secretion. It aids in converting proinsulin to insulin by enhancing cathepsin activity. Moreover, epicatechin exhibits insulin-like properties by affecting the osmotic fragility of human erythrocytes and inhibiting Na/K ATPase activity in patients' erythrocytes [26].

References

1. Patle D, Vyas M, Khatik GL. A Review on Natural Products and Herbs Used in the Management of Diabetes. Curr Diabetes Rev. 2021;17:186-197. DOI: 10.2174/1573399816666200408090058
2. Kodra JT, Jargensen AS, Andersen B, *et al*. Novel glucagon receptor antagonists with improved selectivity over the glucose-dependent insulinotropic polypeptide receptor. J Med Chem. 2008;51(17):5387-96. DOI: 10.1021/jm7015599
3. Roglic G. WHO Global report on diabetes. Int. J Noncommunicable Dis. 2016;1(1):3-8. DOI: 10.4103/2468-8827.184853
4. Yki-Jarvinen H. Pathogenesis of non-insulin-dependent diabetes mellitus. Lancet. 1994;343(8889):91-95. DOI: 10.1016/S0140-6736(94)90821-4
5. Osadebe PO, Odoh EU, Uzor PF. Natural Products as Potential Sources of Antidiabetic Drugs. Br J Pharm Res. 2014;4(17):2075-2095. DOI: 10.9734/BJPR/2014/8382
6. Beutler JA. Natural products as a foundation for drug discovery. Curr Protoc. Pharmacol. 2019;86:e67. DOI: 10.1002/cpph.67
7. Cragg GM, Newman DJ. Natural products: A continuing source of novel drug leads. Biochim. Biophys. Acta. 2013;1830:3670-3695. DOI: 10.1016/j.bbagen.2013.02.008
8. Ehrman TM, Barlow DJ, Hylands PJ. Phytochemical databases of Chinese herbal constituents and bioactive plant compounds with known target specificities. J Chem Inf. Model. 2007;47(2):254-63. DOI: 10.1021/ci600288m
9. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projection for 2030. Diabetes Care. 2004;27(5):1047-1053. DOI: 10.2337/diacare.27.5.1047
10. Forbes JM, Cooper ME. Mechanisms of diabetic complications. Physiol Rev, 2013, 93(1). http://physrev.physiology.org/content/93/1/137.short (Accessed 24 May 2017).
11. Li W, Yuan G, Pan Y, Wang C, Chen H. Network pharmacology studies on the bioactive compounds and action mechanisms of natural products for the treatment of diabetes mellitus: a review. Front Pharmacol. 2017;8:74. DOI: 10.3389/fphar.2017.00074
12. Choudhury H, Pandey M, Hua CK, *et al*. An update on natural compounds in the remedy of diabetes mellitus: A systematic review. J Tradit Complement Med. 2018;8:361-376. DOI: 10.1016/j.jtcme.2018.03.009

13. Chuengsamarn S, Rattanamongkolgul S, Luechapudiporn R, Phisalaphong C, Jirawatnotai S. Curcumin extract for prevention of type 2 diabetes. Diabetes Care. 2012;35:2121-2127. DOI: 10.2337/dc12-0116
14. Howard ME, White ND. Potential Benefits of Cinnamon in Type 2 Diabetes. Am J Lifestyle Med. 2013;7:23. DOI: 10.1177/1559827612462960
15. Vuksan V, Sievenpiper JL. Herbal remedies in the management of diabetes: Lessons learned from the study of ginseng. Nutr Metab Cardiovasc Dis. 2005;15:149-160. DOI: 10.1016/j.numecd.2005.05.001
16. Pothuraju R, Sharma RK, Onteru SK, Singh S, Hussain SA. Hypoglycemic and Hypolipidemic Effects of *Aloe vera* Extract Preparations: A Review. Phytother Res. 2016;30:200-207. DOI: 10.1002/ptr.5532
17. Miura T, Takagi S, Ishida T. Management of Diabetes and Its Complications with Banaba (*Lagerstroemia speciosa* L.) and Corosolic Acid. Evid Based Complement Alternat Med. 2012;2012:871495. DOI: 10.1155/2012/871495
18. Akash MSH, Rehman K, Chen S. Effects of Coffee on Type 2 Diabetes Mellitus. Nutrition; c2014. DOI: 10.1016/j.nut.2013.11.020
19. Padiya R, Banerjee SK. Garlic as an Anti-diabetic Agent: Recent Progress and Patent Reviews. Recent Pat Food Nutr Agric. 2013;5:1.
20. Leung L, Birtwhistle R, Kotecha J, Hannah S, Cuthbertson S. Anti-diabetic and hypoglycaemic effects of *Momordica charantia* (bitter melon): a mini review. Br J Nutr. 2009;102:1703-1708. DOI: 10.1017/S0007114509992054
21. Fuangchan A, Sonthisombat P, Seubnukarn T, *et al*. Hypoglycemic effect of bitter melon compared with metformin in newly diagnosed type 2 diabetes patients. J Ethnopharmacol. 2011;134:422-428. DOI: 10.1016/j.jep.2010.12.045
22. Huseini FH, *et al*. *Capparis spinosa* L. (Caper) fruit extract in the treatment of type 2 diabetic patients: A randomized double-blind placebo-controlled clinical trial. Complement Ther Med. 2013. DOI: 10.1016/j.ctim.2013.07.003
23. Dange SS, Rao PS, Jadhav RS. Traditional uses of guava: a review. World J Pharm Res. 2019;9(5):452-464.
24. Kaur M, Valecha V. Diabetes and anti-diabetic herbal formulations: An alternative to allopathy. Int. J Pharmacogn. 2014;1(10):615-627.
25. Manisha M, Priyanjali D, Jayant L, Saroj G. Indian herbs and herbal drugs used for the treatment of diabetes. J Clin Biochem Nutr. 2007;40(3):163-173.
26. Mirkar PP, Pandav SS, Sanap GS. A review on: Diabetes mellitus treatment using herbal drug. World Journal of Pharmaceutical Research. 2024;9(5):452-464.