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THE CURRENT TREND IN PHARMACOGNOSY OF ANTI DIABETIC PLANTS

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Abstract: The growing prevalence of diabetes has sparked greater interest in using medicinal plants as potential treatments. Pharmacognosy, which focuses on bioactive compounds derived from plants, has highlighted several promising antidiabetic species, including *Momordica charantia*, *Cinnamomum verum*, and *Trigonella foenum-graecum*. These plants contain compounds such as flavonoids and alkaloids, which help manage blood glucose levels by enhancing insulin sensitivity, inhibiting digestive enzymes, and protecting pancreatic cells. Advanced methods like HPLC, mass spectrometry, and bioinformatics are facilitating the discovery and understanding of these bioactive compounds. While preclinical studies show promise, challenges remain in areas like standardization, safety, and clinical validation. Nonetheless, pharmacognosy holds great promise in developing natural therapies for diabetes management.

Index Terms - Diabetes mellitus,anti diabetic plant, phytoconstituents,DM therapy, diabetic cardiomyopathy (DCM),flavonoids,alkaloids

I. INTRODUCTION

Diabetes is a complex condition influenced by several factors and arises due to various risk elements. It is classified into various types, including diabetes, insulin-dependent diabetes, and non-insulin-dependent diabetes, commonly referred to as moody diabetes [1]. Type 1 diabetes and moody diabetes are associated with increased susceptibility due to genetic and/or epigenetic causes. Type 2 diabetes develops as a result of various triggering factors, particularly those related to daily dietary habits [2]. According to epidemiological studies, the frequency of type 2 diabetes has expanded rapidly worldwide during the last 70 years, particularly after World War II, mostly as a result of profound shifts in dietary habits and lifestyle. In Morocco, as in many other countries [3]. The pathophysiology of type 2 diabetes is complex, and various theories have been proposed for explain its development and the underlying mechanisms contributing to its onset. Obesity, insulin resistance, and the accumulation of body fat are recognized as the leading causes of type 2 diabetes. furthermore, additional elements, particularly the detrimental mismatch between movement and calorie intake, contribute significantly to raising the disease's incidence [4,5].

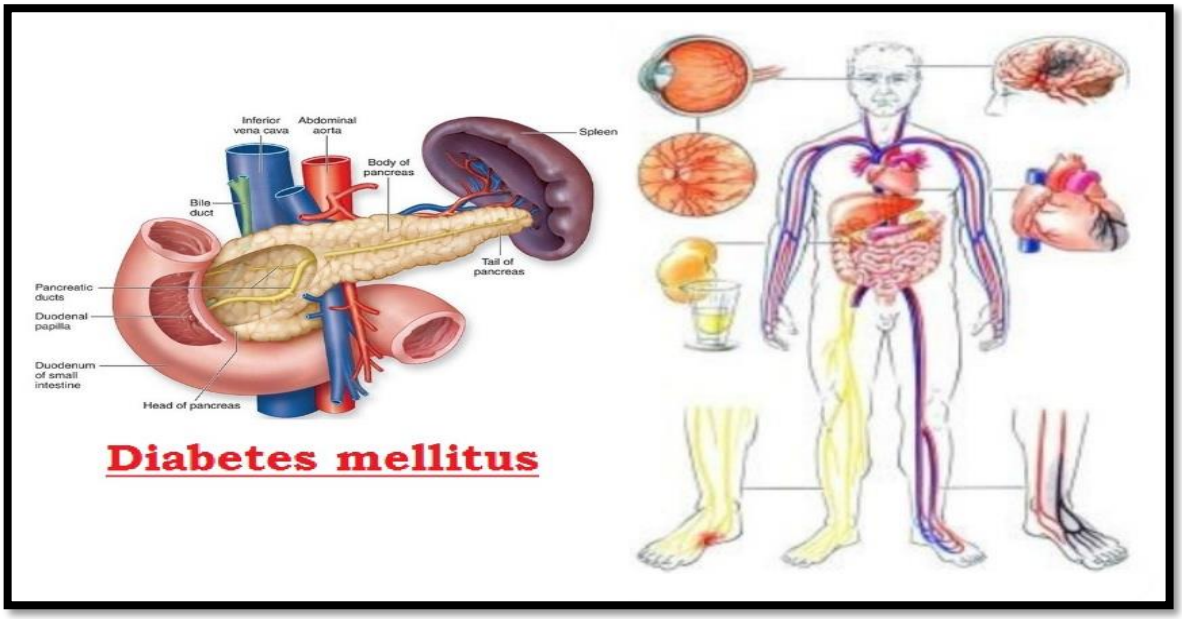

Fig 1: Diabetes Mellitus

Anti-diabetic treatments mainly focus on lowering blood glucose levels to prevent the severe complications linked to diabetes. Even after being identified for more than 3,000 years, this illness was nevertheless difficult to treat until the early 1900s [6]. Today, diabetes is widespread around the world, with a particularly high prevalence in Middle Eastern countries, including Morocco Diabetes imposes a significant social and economic burden, with severe implications for both morbidity and mortality. More than two million people in Morocco who are 18 years of age or older have diabetes, and half of them are not aware that they have the disease [7]. Over 350,000 patients in Morocco are currently receiving insulin treatment, and it is estimated that about 15,000 youngsters have diabetes. Over 12,000 fatalities are attributed to diabetes each year, while an additional 32,000 deaths are indirectly caused by the disease [8,9].

According to the latest national data from the WHO (2016), more than 12.4% of the Moroccan population is affected by diabetes. A countrywide study in 2000 found that this frequency was substantially higher in urban areas (9%) compared to rural areas (4.4%) [10]. Field studies conducted across various regions of Morocco revealed varying diabetes prevalence rates. In 2001-2002, the southern area had an 11.9% prevalence of type 2 diabetes, whereas the northern and Meknes regions had a 19% prevalence and eastern Morocco had a 10.2% prevalence. According to a survey on immigrants from Morocco, the incidence rate was 8%. In Morocco, type 2 diabetes atone for over 80% amidst all occurrences and is strongly linked to lifestyle factors and obesity. 21.7% of people are obese, while 55.1% of people are overweight. Diabetes is the primary precursor of lower limb amputations, chronic kidney failure, and blindness [11]. Common complications among diabetic patients in Morocco include retinopathy, diabetic neuropathy, nephropathy, and cardiovascular disease. Several factors contribute to the rising diabetes rate in Morocco, including the shift from a rural, traditional lifestyle to a more modern way of life. This transition has been accompanied by alterations in eating patterns and lifestyle, further fuelling the increase in diabetes cases [12,13].

Numerous medicinal plants found in Moroccan flora have long been applied in conventional medicine to treat a range of conditions, including diabetes. Numerous bioactive substances from several chemical families, including Alkaloids, terpenoids, flavonoids, and phenolic acids, are found in these plants. Approach and scope: The available research regarding the antidiabetic effects of Moroccan therapeutic herbs is the main topic of this study. It offers a thorough explanation of how those plants and the secondary metabolites they produce work [14]. The potency of these organic resources to be transformed into formidable antidiabetic medications has been highlighted by the summary of studies on the antidiabetic active molecules. It was discovered that Morocco uses a number of medicinal herbs to cure diabetes. Significant suppression of the enzymes engaged in the metabolism of carbohydrates in the gut in the intestinal process of carbohydrate metabolism was shown by the in vitro investigations. According to in vivo investigations, these plants' extracts and essential oils shown a number of antidiabetic properties, such as lowering blood glucose levels and increasing insulin production. 148 secondary metabolites were found in the active plants after phytochemical investigation. These compounds are classified into various chemical groups. 95 of the compounds that were found had their antidiabetic potential evaluated [15-17]. According to the results, these substances control diabetes via a number of methods, such as by inhibiting enzymes,

modifying signalling pathways analogous to glucose and lipidic metabolism, and controlling the manifestation of genes accountable for glucose homeostasis. In clinical studies, eighteen active medicines showed encouraging outcomes in managing diabetes and its related problems [18].

Diabetes and currently used anti-diabetic drugs

Inflammation, elevated blood sugar, insulin resistance, insufficient insulin synthesis, and pancreatic β-cell dysfunction, and excessive glucagon secretion are the hallmarks of diabetes mellitus. Globally, type 1 and type 2 diabetes are becoming more common. The rising prevalence of adult-onset type 2 diabetes is mostly caused by behavioural risk factors such as aging, obesity, smoking, excessive consuming alcohol and a diet heavy in fat, and leading a deskbound lifestyle [19]. In order to preclude type 2 diabetes, it is advised to adopt a healthful lifestyle that includes frequent consumption of functional meals high in fruits and vegetables. 5–10% of all instances of diabetes are type 1 diabetes and is typically diagnosed at a younger age. Diabetes is frequently associated with environmental variables, including viral infections, and genetic susceptibility. Pancreatic β-cells are severely damaged and destroyed in type 1 diabetes, in contrast to type 2, which causes a sharp drop in insulin output and the beginning of hyperglycaemic symptoms [20]. Numerous anti-diabetic drugs have been released in the last ten years. Based on data from the Drug Bank, more than 95% of FDA-approved anti-diabetic medications are primarily designed for management of type 2 diabetes by lowering glycemia, mainly through the enhancement of insulin secretion [21]. Usually, these medicines are used either by themselves or in conjunction with other anti-diabetic therapies. However, given the possibility of adverse consequences, long-term usage of synthetic medications might not be the best option. The main ways of synthetic anti-diabetic medications function are by increasing peripheral glucose uptake, lowering gastrointestinal absorption of carbohydrates, decreasing the release of glucose from liver and increasing insulin production in the pancreas. For instance, intestinal α-glucosidase is frequently inhibited by acarbose, valises, and miglitol [22]. These drugs do not have direct effects on insulin production but instead work by slowing the breakdown of carbohydrates in the intestines, thereby reducing post-meal blood glucose spikes. Glimepiride and glyburide, on the other hand, are sulfonylurea-based medications that directly increase insulin secretion while having little to no effect on α-amylase activity [23]. A significant nuisance of some current anti-diabetic medications is their gastrointestinal side symptoms, including stomach discomfort, which is commonly associated with α-glucosidase inhibitors. Additionally, thiazolidinediones, such as pioglitazone and rosiglitazone, have been associated with significant adverse effects, including weight gain, heart failure, and anemia. Although novel methods for screening and assessing natural and synthetic compounds have been made possible by current anti-diabetic drug development procedures, no significant advancements have been made. Because protein active sites are selective for their preferred substrates, a major problem with the proposed medicines is their limited capacity to interact with the several receptors [24,25]. Only a small number of anti-diabetic medications have been created using alkaloid backbones, according to Drug Bank. Therefore, gaining a deeper understanding of the molecular mechanisms through which alkaloids act in the context of diabetes mellitus (DM) could help researchers identify other potential alkaloid-based compounds to alleviate diabetic complications [26].

Possible targets for DM therapy

A key tactic for treating type 2 diabetes problems is to inhibit enzymes that break down carbohydrates, such as α-glucosidase and α-amylase. It plays a crucial role in breaking down polysaccharides and oligosaccharides into monomers, which can lead to elevated blood glucose levels, contributing to hyperglycaemia. Inhibiting α-amylase, which aids in the digestion of starch and glycogen, is thought to be a useful treatment for conditions involving the absorption of carbohydrates, such as diabetes and obesity. Furthermore, tooth cavities and periodontal disorders can be avoided by blocking α-amylase. By dissolving dietary carbohydrates, including starch, into smaller molecules, hydrolysing enzymes like α-amylase help the blood's free glucose levels rise. One major problem with diabetes mellitus is the ensuing high blood glucose levels, or hyperglycaemia [27,28].

Reducing or controlling the breakdown of complex carbohydrates into glucose and/or limiting its absorption from the small intestine are two strategies for treating hyperglycaemia. Hyperglycaemia negatively impacts insulin sensitivity, impairing glucose utilization by peripheral tissues. It also promotes lipolysis and proteolysis, increases the secretion of catabolic hormones and stimulates hepatic gluconeogenesis [29]. Additionally, hyperglycaemia exacerbates oxidative stress and superoxide production, resulting in cerebral intracellular acidosis, damages neurons, and causes endothelial and mitochondrial dysfunction. Therefore,

slowing down the digestion of carbohydrates by using natural or synthetic inhibitors to block or regulate these enzymes can improve glucose homeostasis. According to research, type 2 diabetes is best managed with inhibitors that have low to moderate α-amylase inhibition and substantial α-glucosidase activity [30].

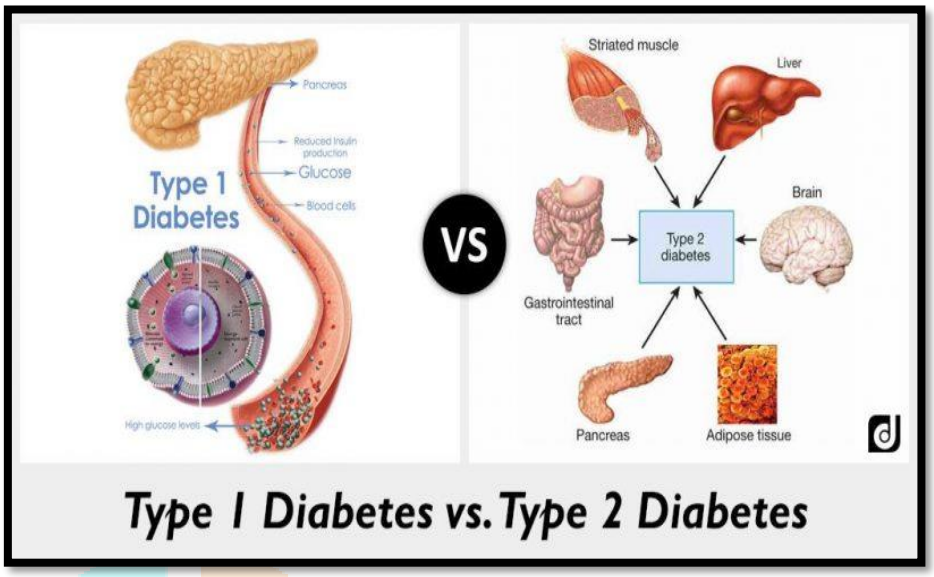

Fig 2: Types of Diabetes

In α-glucosidase's active site, the side chains of residues are likely to interact directly with the substrate inside the active site cavity. may cooperate with the primary residues to alter the conformation of the enzyme's active site, influencing its catalytic efficiency and substrate binding [31]. From this perspective, the proper structural conformation of the α-glucosidase's active site enzyme is crucial for its activity. The selectivity of the enzyme and its ability to engage with the substrate might be changed by any disturbance in this area. Consequently, α-glucosidase is a structurally sound primary target for type 2 diabetes therapy [32,33].

Potential antidiabetic phytochemicals in plant roots

Alkaloids

Alkaloids are a diverse group of natural compounds primarily found in plants, characterized by the presence of a structural nitrogen atom that is not an amide. Tryptophan, tyrosine, histidine, lysine, and ornithine are among the amino acids that are essential building blocks for most plant alkaloids. These compounds play a key protective role in plants, particularly in their roots, serving to defend against herbivores due to their pharmacological properties [34]. The main criteria used to categorize alkaloids are either the plant species from which they originate or their heterocyclic ring structure. These alkaloids are employed in the remedy of many circumstances including cardiovascular, inflammatory and mental health disorders. Alkaloids are primarily known for their effects on the CNS and their anti-inflammatory properties; however, they have also shown antidiabetic activities [35]. The rhizomes of plants in the family ‘Berberidaceae’ include benzylisoquinoline alkaloids, which have demonstrated encouraging promise in the management of diabetes [36].

Phenols and flavonoids

Phenols are the largest group of natural goods, characterized by a chemical structure that includes an aromatic ring attached to a hydroxyl group (C6H5OH). Within this group, flavonoids form the largest subgroup, and they can be further divided into anthocyanidins, flavanones, isoflavones, flavonols, flavones, and flavan-3-ols. Fruits, leaves, seeds, and flowers are usually abundant in flavonoids and phenols, though additionally, research has identified these compounds as essential chemical components of plant roots. Phenols and flavonoids are synthesized via the phenylpropanoid pathway, where L-phenylalanine is converted into p-coumaroyl-CoA, or L-tyrosine is converted by tyrosine ammonia lyase. These compounds then enter the biosynthesis pathways for phenols and flavonoids [35,37].

Phytosteroids

One significant class of secondary metabolites that plants generate are called Phyto steroids. These compounds, which are present in the roots of plants primarily in the form of lipids, play crucial roles in regulating plant growth and reproduction [34]. Mostly lipid-like compounds, steroids have demonstrated encouraging antidiabetic potential. Baker et al. conducted clinical research. demonstrated that sterols found in fruits, seeds, and vegetables have the potential to reduce cholesterol levels in diabetic patients, highlighting their potential benefits in managing diabetes-related complications [35]. Plant-based diets high in cholesterol have drawn a lot of attention because of their many health advantages. According to Nissinen et al., these meals prevent the small intestine from absorbing cholesterol, which lowers low-density lipoprotein (LDL) cholesterol levels. Furthermore, Sem ova and associates showed that sterol-rich plant-based meals helped lower blood glucose levels and improved the effectiveness of antidiabetic medications [33,36].

Terpenoids

Terpenoids are a broad class of chemicals found in many plants that are produced from one or more isoprene units. The quantity of isoprene units they contain determines their classification. Hemiterpenoids are the most basic class of terpenoids. They can be further classified into various classes, according to their carbon units [34]. Terpenoids are recognized for their diverse bioactivities, including antibacterial, antifungal, and anti-inflammatory properties [33]. In addition, they have demonstrated potential in managing diabetes, both in laboratory and animal studies. Research shows that terpenoids can improve metabolism of glucose, reduce the risk of insulin resistance, and help restore normal insulin and blood sugar levels, highlighting their significant pharmacological potential for treating diabetes and related conditions [31,37]

Anthraquinones

Anthraquinones are compounds characterized by two aromatic rings connected by two carbonyl groups, forming a flat, aromatic structure. These metabolites can be found in various parts of the plant, including the aerial tissues and roots, existing as both C- and O-glycosides, along with in their aglycone forms. Multiple in vivo research have demonstrated that anthraquinones exhibit potential for managing diabetes, positioning this class of compounds as promising antidiabetic candidates. Among the most commonly isolated aglycone anthraquinones found in plant roots. These compounds have shown notable inhibitory effects on α-glucosidase and α-amylase, two key enzymes engaged in glucose metabolism [31,34,36].

Protective effects of medicinal plant against diabetes induced cardiac disorder:

Ethnopharmacological Relevance:

Using medicinal plants as preventive and curative agents to treat diabetes and its long-term consequences, such cardiovascular disorders, has become more and more popular worldwide in recent years. This increasing interest is driven by the widespread availability of these plants and their rich traditional use in various cultures, which provide a valuable foundation for their potential therapeutic benefits. The goal of this review is to present commonly used medicinal plants that have shown cardioprotective effects in diabetes [37]. It will also explore the underlying mechanisms through which these plants exert their beneficial impact on cardiovascular health in individuals with diabetes. The medicinal plants reviewed primarily exerted cardioprotective effects by enhancing antioxidant activity, which helped reduce reactive oxygen species (ROS) production. Additionally, these plants inhibited inflammatory signalling pathways and the associated cytokines [38]. Furthermore, they contributed to the improvement of key cardiac functions. They further enhanced the manifestation of Bcl-2 protein and downregulated the manifestation of TGFβ1 and TNFα, which are key factors involved in cardiac damage and inflammation. The medicinal plants reviewed exhibited cardioprotective effects in diabetes by intervening in the mechanisms underlying diabetic heart damage, ultimately helping to restore cardiovascular function and mitigate complications associated with diabetes [33, 39]

Ethnopharmacological survey

Unlike modern medicine, medicinal plants used within traditional medicine are not only more affordable but also tend to have fewer side effects, making them an appealing alternative for many individuals seeking natural cures. Despite the widespread use of modern medicine, traditional medicine continues to hold a significant place in medical practices, especially due to the beliefs of indigenous communities, local climatic conditions, and the diverse plant species. Additionally, in countries with lower socioeconomic status, people often turn to traditional medicine as a more affordable alternative to modern treatments. As a result, the use

of medicinal plants has increased, with many individuals seeking guidance from pharmacists to ensure safe and effective use of these natural remedies [40].

Diabetic cardiomyopathy (DCM)

Diabetic cardiomyopathy (DCM) is characterized by ventricular dysfunction in individuals with diabetes, occurring independently of atherosclerosis and hypertension. It is estimated that 55% of diabetic patients may develop DCM. Several factors contribute to the progression of DCM. These processes collectively lead to the impairment of cardiac function in diabetic individuals [41].

Oxidative stress

Oxidative stress is exacerbated by high blood sugar levels in diabetics, which also weaken the body's natural antioxidant defences, such as glutathione peroxidase, catalase, and superoxide dismutase, and increase the generation of reactive oxygen species. This oxidative stress causes fat accumulation, fibrosis, and mitochondrial fatty acid oxidation in the heart, which ultimately leads to diastolic dysfunction and heart failure. Lipid peroxidation can also increase tissue permeability and harm enzymes, membrane-bound receptors, and cell membranes. Moreover, reactive oxygen species (ROS) promote protein oxidation and boost protein carbonylation, which in turn leads to impaired protein function. Apoptosis is triggered by reactive oxygen species. Increased manifestation of the poly (ADP-ribose) polymerase-1 (PARP-1) is the outcome of this process, and it alters the structure and functionality of heart tissue [42]

Cell death

Diabetic cardiomyopathy (DCM) is influenced by three distinct types of cell death: necrosis, autophagy, and apoptosis. A kind of programmed cell death known as cardiomyocyte apoptosis is brought on by the stimulation of the mitochondrial cystatin C-stimulated caspase-3 pathway, which is set off by hyperglycaemia [40]. A particular nuclease known as caspase-3 activated DNase (CAD), which is triggered by caspase-3, fragments DNA when it enters the nucleus. Furthermore, ROS promote the development of the p53 protein, which in turn can reduce anti-apoptotic proteins like Bcl-2 and activate pro-apoptotic factors like Bax, thereby accelerating the apoptotic process. Studies on rats and mice have revealed a drop in Bcl-2 levels in cardiac tissue and increased manifestation of Bax, caspase-3/9, and the ratio of Bax to Bcl-2. Cardiomyocyte apoptosis can trigger pathological remodeling of the heart, including the promotion of hypertrophy and fibrosis, which ultimately contribute to the development of heart failure [41,43].

ROLE OF AYURVEDA IN TYPE 2 DIABETES MELLITUS

Ayurveda offers a holistic approach to managing Type 2 Diabetes Mellitus (T2DM) by focusing on lifestyle, diet, and natural remedies. It identifies T2DM, known as Madhumeha, as an imbalance in the Kapha and Vata doshas, along with digestive and metabolic disturbances. Management strategies include consuming high-fiber, low-glycemic foods while avoiding sugary and processed items. Herbs like bitter gourd, turmeric and fenugreek are used to regulate blood sugar and improve insulin function. Detoxification therapies like Panchakarma help cleanse the body and restore balance. Ayurveda complements modern treatments by addressing root causes and improving overall health [44].

Herbal medications and natural products for patients with covid-19 and diabetes mellitus

Higher rates of hospitalization, morbidity, and death are associated with diabetes mellitus in COVID-19 patients. Research has indicated that hyperglycemia increases the severeness of COVID-19, especially in people with concomitant diabetes [46,47]. Clinical proof of the antidiabetic benefits and any information on the potential anti-COVID-19 properties of ten chosen natural products were presented in the selected publications. This review then included an analysis and discussion of these works [48].

COVID-19 and diabetes: the underlying mechanisms of the comorbidity

Significant testimony indicates that COVID-19 patients with diabetes mellitus (DM) experience higher disease severity and mortality rates compared to those without diabetes. Increased viral receptor binding, decreased clearance of viruses, compromised adaptive and innate immunity, elevated inflammatory reactions, and pre-existing multimorbidity linked to the secondary issues of diabetes mellitus (DM) are some of the mechanisms that have been suggested to explain this observation [49].

Virus clearance and immunological abnormalities in diabetic COVID-19 patients

The initial line of protection against viruses, such as SARS-CoV-2, is innate immunity. By IFN-1 and IFN-III (interferon types I and III) interruption of signalling or delay, SARS-CoV-2 can circumvent response of the host's innate immunity. Similarly, Hyperglycemia suppresses the synthesis and signaling of IFN-1, according to a study of human peripheral blood mononuclear cells [41]. Therefore, by interferon signaling disruption, hyperglycemia may impede viral clearance and reduce the innate immunological response of the host to the pathogen. Lympopenia is a signature of an infection with SARS-CoV-2 that has been connected to heightened illness severity. Consequently, COVID-19 patients with type 2 diabetes (T2D) have been shown to have lower lymphocyte counts than those without the disease. This suggests that diabetes mellitus could be a contributing cause to lymphopenia and, in turn, a more severe infection in these patients [45]. Furthermore, in respiratory viral infections, alveolar macrophages, dendritic cells, and inflammatory monocyte-macrophages are important interferon (IFN) makers. Therefore, the decreased count of lymphocytes in a patient with COVID-19 with diabetes mellitus comorbid condition may be related to retarded and restricted Signaling via interferons reported in SARS-CoV-2 infection [50]. Additionally, another study discovered that extended viral shedding was observed in severely sick COVID-19 patients who also had diabetes mellitus. The researchers hypothesized that this may be caused by ACE2 downregulation, a cytokine storm, or weakened innate immunity. The activation or priming of adaptive immunity is a crucial function of innate immunity, in addition to its involvement in the early response to infection [42].

In vitro Antioxidant, Antimicrobial and Antidiabetic activities of Insulin plant rhizome extracts

"Insulin plant" through traditional practice, has been the subject of further assessment of pharmacological and phytochemical. Studies on the leaves of this plant have demonstrated its broad therapeutic potential, including antioxidant, antimicrobial, and antidiabetic activities. The focus of our current investigation is to investigate the rhizome of Costus igneus through multiple extraction methods. By carrying out pertinent phytochemical and pharmacological in vitro analyses, we want to check and pinpoint the distinct the various extracts' potential for medicinal use. Techniques: The antioxidant, antibacterial, and antidiabetic properties of several rhizome extracts were evaluated using the DPPH, Disc Diffusion, and DNS techniques. All rhizome preparations exhibit a notably high and nearly consistent level of in vitro antioxidant activity. Comparing the ethyl acetate, ethanol, and methanol extracts to the standard medication Ceftriaxone sodium, the disc diffusion method shows that they have moderate bactericidal activity against gram -ve and gram +ve bacteria. However, there is no antibacterial activity in the aqueous extract. The ethyl acetate and ethanolic rhizome extracts have substantial antidiabetic action, but the methanolic and aqueous rhizome extracts have only weak activity, according to the DNS method's assessment of the α-amylase inhibitory activity [51].

Despite the availability of more recent synthetic antimicrobial medicines, life-threatening microbial infections are increasing worldwide in the contemporary context. Furthermore, the use of these agents is increasingly limited due to the rapid development of multidrug resistance after only brief exposure to these drugs. The issue of multidrug resistance could potentially be addressed by developing plant-derived drugs. In order to assess certain activities including antioxidant, antibacterial, and antidiabetic qualities, the current work focuses on the pharmacological and phytochemical examination of several extracts from Costus igneus rhizomes. The objective is to evaluate and draw conclusions on the medicinal potential of Costus igneus rhizomes [52].

Large-scale computational screening of Indian medicinal plants reveals Cassia angustifolia to be a potentially anti-diabetic

Researchers worldwide are exploring the medicinal properties of herbal plants, often leading to the identification of new plants and their bioactive compounds for human preventative requirements. Because of their therapeutic properties and non-toxic nature, natural phytochemicals are still in high demand as alternative remedies for a variety of illnesses. Large-scale phytochemical screening has been made easier in recent years by computational phytochemistry, which has enabled researchers to investigate a variety of therapeutic alternatives to conventional ethnopharmacology [53]. This approach enables the identification and evaluation of bioactive compounds more efficiently, expanding the scope of potential treatments. Through computational screening of Indian herbal plants, we hope to find an anti-diabetic plant. The therapeutic potential of the chosen plants will next be confirmed through experimental characterisation and biological validation. Creating an internal database of Indian herbal plants is part of the technique.

Molecular docking is employed to check these plants for potential anti-diabetic activity by targeting alpha-amylase. *Cassia angustifolia* was selected for further investigation due to its phytochemicals' ability to bind to alpha-amylase, suggesting its potential in anti-diabetic prophylaxis [46]. The plants underwent biological activity evaluation, botanical analysis, and experimental extraction. Additionally, molecular dynamics simulations were employed to identify the specific phytochemicals responsible for binding to alpha-amylase, helping to pinpoint the compounds that contribute to their anti-diabetic activity [53].

Computational screening

Docking energy from binding locations as well as docking scores from molecular docking are commonly used by drug discovery researchers as essential elements of the drug discovery procedure based on structure. As part of the drug development process, these metrics assist in predicting which small compounds have the highest likelihood of binding to a target protein and either activating or inhibiting its activity [54]. The initial stage was to virtually screen against the target of interest using the in-house phytochemical database. A popular molecular modeling method for finding possible candidate chemicals that might be further investigated as possible therapeutic candidates is high-throughput virtual screening. extensive database of chemicals may be methodically explored to identify substances that might attach to specific targets, such as proteins linked to a particular illness, by using computational techniques. This allows for the design of drugs with enhanced efficacy and specificity for the intended target. As a consequence, the research team may save time and money by drastically lowering the number of chemicals that require experimental testing. This streamlined process enhances the efficiency of drug discovery by focusing on the most promising candidates [48]. These poses were then sorted according to each molecule's Gibbs binding free energy estimates. A computer method for predicting the best orientation for a chemical to attach to a protein is called a molecular docking algorithm. The goal is to determine the configuration that allows for the most stable complex formation when the molecule and protein interact, ensuring effective binding and potential biological activity [49,54].

Current Trends of Plants Having Antidiabetic Activity

Studies on medicinal plants from various species and families have been conducted, focusing on different plant parts for antidiabetic research. The most commonly used solvents for extracting bioactive compounds in these studies were methanol, ethanol, and aqueous solutions. The efficacy of these plants was evaluated using streptozotocin or alloxan-induced diabetic models to assess their potential antidiabetic effects. Most of the research findings demonstrated hypoglycemic effects of the plant extracts, showing results comparable to those of typical medications. Various modes of action have been proposed for these plant extracts, suggesting multiple pathways through which they may exert their antidiabetic effects [55].

Acorus calamus (Acoraceae), when extracted using methanol from its rhizome, demonstrated potent antidiabetic action in a diabetic model generated by streptozotocin. The crude extract raised serum insulin levels, demonstrated the greatest enhancement of glucose tolerance, and dramatically lowered levels of blood glucose during a fast [49]. The active compounds, including flavonoids, tannins, and saponins, are believed to enhance the insulin effect in the plasma. These compounds may either stimulate the release of insulin from the current β-cells in the pancreas or promote the secretion of insulin from its enclosed form, contributing to improved glucose regulation [55].

Formulating antidiabetic medications using nanocarriers based on medicinal plants

Conventional anti-diabetic medications, while effective, are often linked to numerous issues and adverse consequences, which can limit their long-term use. Extracts from plants and additional bioactive substances with antidiabetic qualities are therefore becoming more and more well-liked as substitute therapies. These natural remedies offer a potential solution with fewer adverse effects, and they are increasingly being explored for their therapeutic benefits in managing diabetes. Despite the potential benefits of plant extracts and bioactive compounds, the body often struggles to effectively absorb many of these active substances. This is mostly caused by elements that together lower their bioavailability, such as quick elimination, restricted permeability, or poor solubility. As a result, the therapeutic effects of these compounds may be diminished, necessitating the development of strategies to enhance their absorption and prolong their action in the body [56]. Given that separated components and extracts often don't exhibit the similar level of efficacy as their Nanoencapsulations, the development of plant-based nanomedicines presents a promising strategy to conquer these challenges. Nanoencapsulation can improve the bio accessibility, stability and release of active compounds, enhancing their therapeutic potential for managing diabetes and other related conditions. By utilizing nanocarrier systems the effectiveness of plant-based anti-diabetic drugs can be significantly enhanced. These advanced delivery systems help overcome some of the limitations of traditional herbal formulations, such as poor bioavailability, rapid metabolism, and limited therapeutic

efficacy, thus improving the overall effectiveness and therapeutic outcomes of herbal treatments for diabetes [57].

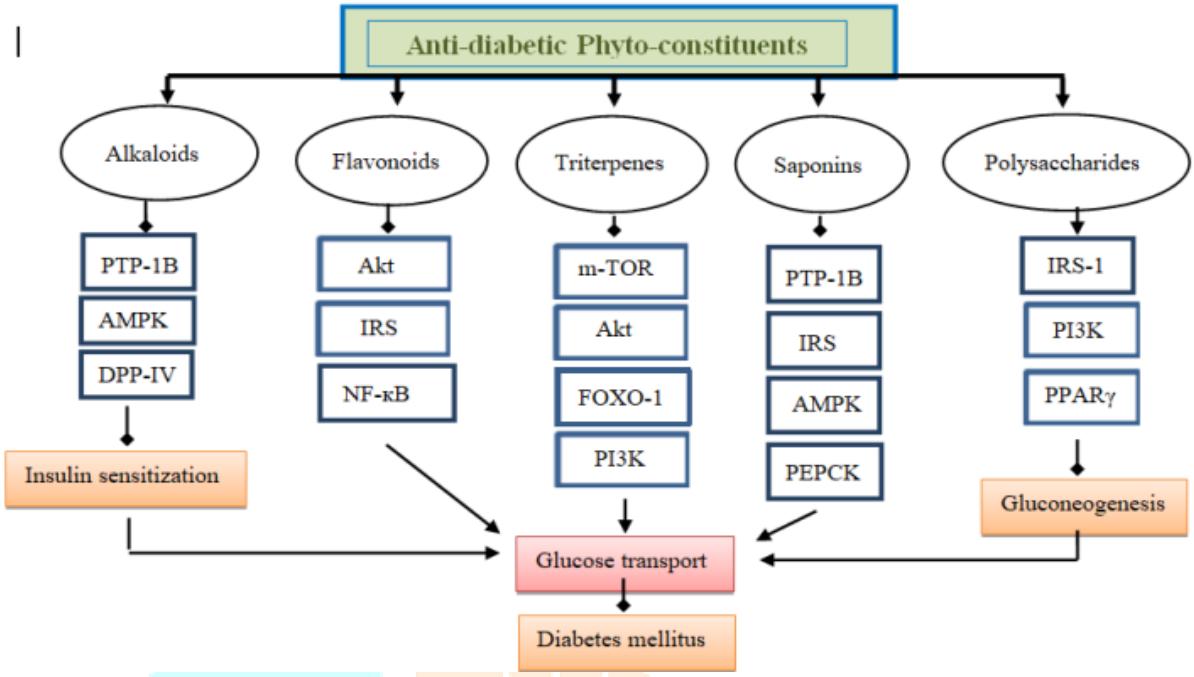

Fig 2: Anti-Diabetic Phyto-Constituent

Nano science and nanotechnology have advanced rapidly, offering a A wide range of applications across various fields. In particular, the medical and health sciences have greatly benefited from these innovations. Nanotechnology has enabled the development of more efficient drug delivery systems, improved diagnostic tools, and advanced therapeutic treatments. Its potential to manipulate materials at the molecular or atomic level allows for more precise and targeted interventions, enhancing the effectiveness and safety of medical treatments. The use of nanosized formulations in the medical has revolutionized drug delivery systems, achieving remarkable success over conventional formulations. By enhancing the biopharmaceutical characteristics of medicinal medicines, nanosized formulations can dramatically increase their clinical effectiveness, such as solubility and stability [51]. Additionally, they optimize pharmacokinetic profiles, ensuring more efficient absorption, distribution, metabolism, and excretion. These formulations also provide increased target specificity, enabling more precise delivery to affected areas while minimizing off-target effects. As a result, nanosized drug delivery systems hold enormous possibilities for improvement the safety and effectiveness of medical treatments. Novel drug delivery systems (NDDSs) are essential in advancing the therapeutic potential of drugs by addressing several key challenges in conventional drug delivery methods. These systems improve drug efficacy by enhancing bioavailability, ensuring more efficient absorption, and reducing toxicity. By controlling the release rate of the drug, NDDSs can maintain optimal drug levels over extended periods, reducing the need for frequent dosing. Additionally, they enable targeted delivery to specific sites in the body, improving the drug's effectiveness while minimizing adverse side effects [53]. As a result, NDDSs represent a promising approach to maximizing the therapeutic benefits of medications. Furthermore, NDDSs contribute to better patient compliance by minimizing the need for frequent administrations. These systems are designed to provide a controlled, sustained release of active ingredients over an extended period, thereby reducing the dosing frequency. This prolonged release mechanism helps ensure a consistent therapeutic effect, which not only enhances the efficacy of the treatment but also encourages patients to adhere more consistently to their prescribed medication regimen. Pharmaceutical firms are progressively integrating plant extracts into their innovative formulations because of the added advantages they provide. For example, plant extracts can address challenges such as mass dosing and absorption difficulties, which are common concerns about certain medications [55]. By utilizing plant-based components, these formulations can improve bioavailability and therapeutic effectiveness, making them a valuable option in modern drug development. Consequently, pharmaceutical companies are investigating the potential of plant extracts to create improved and more efficient methods of medication

administration. Chronic hyperglycaemia, these anti-diabetic medications are available as both single-agent and combination therapies. With the rising demand for effective, safe treatments that have minimal side effects and are cost-efficient, there is an increasing need for innovative solutions in diabetes management [56].

SYMPTOMS OF DIABETES MELLITUS

Feeling more thirsty than usual, feeling very hungry, losing weight, feeling tired and week, having blurry vision, fatigue, frequent urination, poor wound healing, yeast infections that keep coming back [58].

ANTI-DIABETIC

Anti diabetic is defined as the Drug that works to lower abnormally high glucose (sugar) level in the blood. All of them have shown a certain degree out anti-diabetic activity by different mechanism. There various herbal anti-diabetic remedies used in various traditional system of medicine prevailing around the world 90-95%diabetes type 2 [58].

The pharmacognosy of antidiabetic plants has significantly increased traction recently, motivated by the necessity of alternative and complementary therapies to manage diabetes mellitus. This review highlights key trends in the identification, mechanism of action, and clinical evidence surrounding the use of these botanical agents [53].

Mechanisms of Action

Recent studies have elucidated various mechanisms through which antidiabetic plants exert their effects. Many of these plants enhance insulin sensitivity, stimulate insulin secretion, and improve glucose metabolism. For instance, compounds such as flavonoids, terpenoids, and alkaloids have been shown to modulate key signaling pathways, including the AMP-activated protein kinase pathway, which is essential for maintaining energy balance. Additionally, some phytochemicals exhibit antioxidant properties, reducing oxidative stress, which is often elevated in diabetic patients [51].

The modulation of gut microbiota by certain antidiabetic plants has emerged as a significant area of research, suggesting that these plants may improve glycemic control by enhancing the gut barrier function and influencing metabolic pathways through microbial metabolites. Furthermore, the anti-inflammatory properties of many antidiabetic herbs contribute to reducing insulin resistance, highlighting the complex interplay between inflammation and metabolic dysregulation [48].

Clinical Evidence

The clinical evidence supporting the efficacy of various antidiabetic plants continues to grow. Randomized controlled trials (RCTs) and meta-analyses have demonstrated the benefits of specific herbal formulations in managing blood glucose levels, improving lipid profiles, and reducing complications associated with diabetes [59].

Moreover, the safety profiles of these herbal treatments are being increasingly documented, suggesting that many antidiabetic plants can be safely integrated into conventional treatment regimens. However, the variability in results due to differences in plant preparation, dosages, and population characteristics necessitates further standardized research [39].

Future Directions

As we move forward, the integration of pharmacognosy with modern pharmacology will be crucial in validating traditional knowledge and uncovering new therapeutic potentials. There is an urgent need for big-scale, multicentric clinical studies to confirm the efficacy and safety of these herbal treatments across diverse populations. Additionally, advancements in phytochemistry and molecular biology can aid in isolating active compounds, elucidating their mechanisms, and developing standardized extracts for clinical use [58].

The role of antidiabetic plants in personalized medicine also warrants exploration, as genetic and environmental factors may influence individual responses to these therapies. Incorporating traditional knowledge with cutting-edge research can pave the way for innovative treatment strategies that enhance patient outcomes in diabetes management [45].

CONCLUSION:

In conclusion, the pharmacognosy of antidiabetic plants is a dynamic and evolving field. By bridging traditional herbal practices with scientific inquiry, we can harness the potential of these natural products to provide effective, safe, and accessible treatment options for diabetes. As research continues to uncover the complexities of plant-based therapies, the future looks promising for integrating these agents into mainstream diabetes care, ultimately benefiting patients worldwide.

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