A Review on Antidiabetic Property of Mangrove Plants

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A thesis submitted to the School of Pharmacy in partial fulfillment of the requirements for the degree of School of Pharmacy (Hons.)

School of Pharmacy

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Declaration

It is hereby declared that,

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2. The thesis does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.

3. The thesis does not contain material which has been accepted, or submitted, for any other degree or diploma at a university or other institution.

4. I have acknowledged all main sources of help.

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Approval

The thesis titled “A Review on Antidiabetic Property of Mangrove Plants” submitted by Rashni Akter (19146082), of Spring,2019 has been accepted as satisfactory in partial fulfillment of the requirement for the degree of Bachelor of Pharmacy (Hons.) on September, 2023.

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Ethics Statement

This study does not involve any in vivo and in vitro human trial yet.

Abstract

At present, diabetes mellitus encompasses an extensive number of metabolic disorders characterized by chronic hyperglycemia, representing a significant global health concern. According to the mangrove plant it has many antidiabetics property which reduces the sugar level in the body. For this particular scenario, antioxidants assume a significant role in enhancing the condition of individuals with diabetes and minimizing the complication. In contrast, oxidative stress happens within the human body when there is an imbalance in how it produces of reactive oxygen species. We can review that mangrove plant has several phytochemicals derived antioxidant activity which minimizes the complication of diabetics and related to the oxidative stress. These compounds have shown promising potential in the treatment of diabetes and its related complexity, which are often linked to oxidative stress. Hence, the application of mangrove plants holds promise in efficiently handling the issues associated with diabetes and its associated difficulties. The present review investigates the correlation between oxidative stress and diabetes, along with the potential ofmangrove plants in mitigating the effects of diabetes and its accompanying issues connected with oxidative stress.

Keywords: Mangroves; antidiabetic; antioxidant; oxidative stress; metabolites

Dedication

Dedicated to my parents, teachers and friends.

Acknowledgement

First of all, I would like to express my gratitude to Almighty Allah for the continued blessings towards myself, because without Allah's blessings, it would not have happened. Secondly,I would like to give a special thanks to my supervisor, Dr. Farhana Alam Ripa, Associate Professor, School of Pharmacy, for her continuous support throughout the project. From the beginning until the end, her instructions, advice, and valuable moments gave me great support to complete my project. I would also like to express my gratitude towards our honourable dean and chairperson, Dr. Eva Rahman Kabir, School of Pharmacy, Brac University, for her excellent support and cooperation to complete the project. Finally, I am grateful for my family and friends, who have motivated and supported me throughout the review work and helped me complete it.

Table of Contents

List of Table:

2.List of Figures:

List of Acronyms:

AGEs *Advanced glycation end product.*

DPPH *2, 2-diphenylpicrylhydrazyl*

GLUT *Glucose transporter*

ROX *Rifamycin monooxygenases*

p38, MAPK, *Mitogen-Activated Protein*

KinasePI3k *Phosphoinositide 3-Kinase*

WHO World Health Organaization

Chapter01

1.1. General Introduction

Firstly, diabetes is a chronic metabolic disorder characterized by deficiencies in insulin secretion or function, leading to sustained high blood sugar levels and disturbances in the metabolism of carbohydrates, lipids, and proteins. Similarly,the classification of diabetes mellitus, as acknowledged by the World Health Organization (WHO), encompasses three distinct forms: type 1 diabetes (insulin-dependent), type 2 diabetes (non-insulin-dependent), and gestational diabetes. The pancreatic beta cells play a crucial role in maintaining glycemichomeostasis. The impact of glucotoxicity, lipotoxicity, inflammatory mediators, and incretin on the function and viability of pancreatic beta cells has been well-documented in academic literature. Moreover, it is widely believed that oxidative stress plays a significant role in the development and advancement of diabetes. Both type 1 and type 2 diabetes are characterized by elevated levels of free radicals and reduced antioxidant capacity. Diabetes is a prevalent medical condition that impacts populations in both developed and developing nations. According to a 2011 estimate by the World Health Organization (WHO), the global prevalence of diabetes is approximately 360 million individuals. There is a higher prevalenceof diabetes in economically disadvantaged countries, such as India. Based on data provided by the World Health Organization (WHO), it was observed that in the year 2002, theprevalence ofdiabetes in India reached 32 million individuals. Furthermore, projections indicate that the number of individuals affected by diabetes is expected to increase in the foreseeable future. Consequently, the management of diabetes has emerged as a prominent issue in contemporary times. In addition to insulin, a variety of glucose-lowering medicationshave been formulated, encompassing insulin secretagogues, insulin sensitizers, α-glucosidase inhibitors, peptide analogs, dipeptidyl peptidase-4 inhibitors, and glucagon-like peptide-1. In contrast synthetic oral hypoglycemic agents exhibit a notable array of adverse effects, such as hypoglycemia, increase in body mass, gastrointestinal distress, and feelings of nausea. diarrhea, liver complications, and cardiac impairment, among others. Consequently, there is asignificant demand for alternative therapy. Numerous botanical species have been utilized over an extended period of time as a valuable reservoir of potent pharmaceutical agents for the treatment of diabetes, with the belief that these herbal formulations are devoid of any adverse reactions. It is widely believed that over 400 plant species. There is an increasing worldwide inclination towards the identification of pharmacologically active antioxidant molecules with minimal side effects, specifically for their potential application in anti-diabetic therapy. Also, mangrove plants have historically been employed in pharmaceutical interventions have been developed to address a range of medical conditions, such as diabetes mellitus. Therefore, the potential antidiabetic properties of these plants, as well as their potential relationship with antioxidant activity, have not yet been established. Consequently, the present study highlights the association between oxidative stress and diabetes, along with the potential importance of mangrove plants in the mitigation of diabetes and its oxidative stress-related implications. Mangroves, which are unique plant communities found in tropical and subtropical regions, have the ability to flourish even in challenging conditions characterized by elevated salinity levels, excessive tidal activity, strong winds, high temperatures, and oxygen-deprived muddy soils. According to these organisms possess advanced morphological and physiological adaptations that enable them to thrive in harsh environmental conditions (Das et al. 2016). Additionally, they produce metabolites that exhibit distinctive biological activity and hold promise for therapeutic application(Karim.etal.2021)(Habib.et.al.2018).

1.1.1. Pathological pathways involved in diabetes

There are four principal metabolic pathways that exist that assume significant roles in the occurrence of cell damage induced by hyperglycemia and complications associated with diabetes. These pathways include: (a) increased polyol path-way flux; (b) increased advanced glycation end products (AGEs); (c) Activation of protein kinase C; and (d) increased hexosamine pathway flux (as depicted in Figure-1).According to Das et al. (2021)

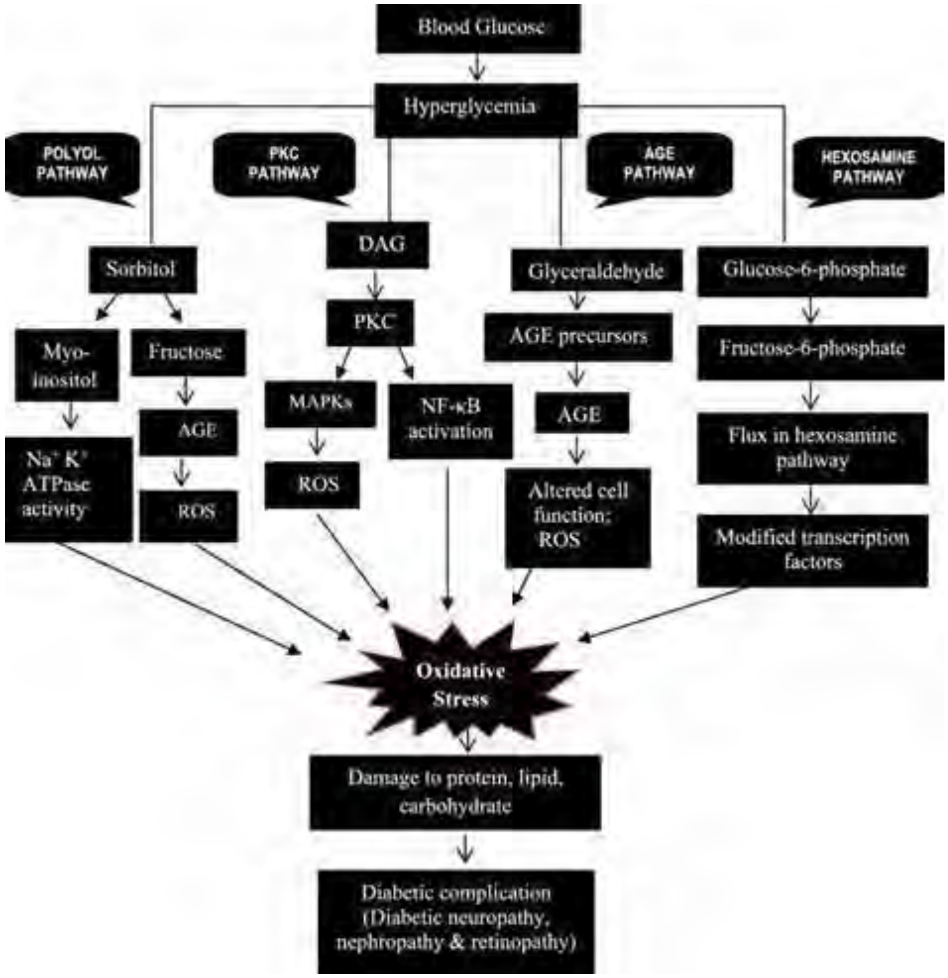

Figure 1. *Hyperglycaemia-induced reactive oxygen species (ROS) generation and diabetic- associated pathological complications. ↑: Stimulate. ↓: Inhibit(S. K. Das et al., 2016)*

1.1.2. Influence of oxidative stress on insulin signaling

The insulin signalling pathway, typically characterised by strict regulation, has been observed to be compromised under situations of oxidative stress, leading to the manifestation of insulin resistance. Activation of the NF-κβ pathway is facilitated through the phosphorylation of a serine kinase known as IkB kinase. This phosphorylation event has been observed to exert a detrimental impact on the normal insulin signalling pathway. The dephosphorylation of the insulin receptor substrate (IRS) by many stress signalling pathways, including p38, MAPK, and JNK/SAPK, hinders insulin signalling. (S. K. Das et al., 2016)

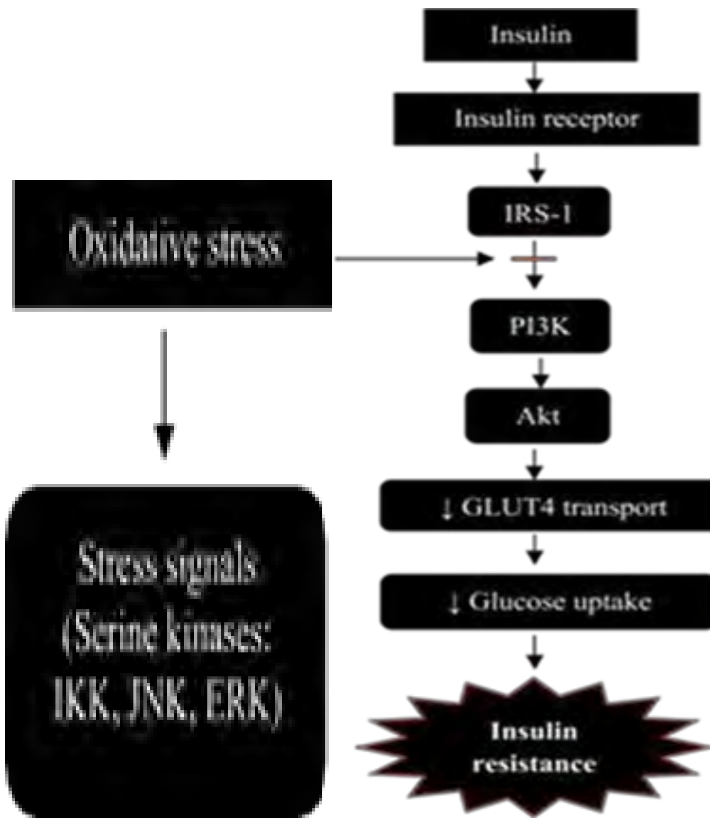

Fig-2. *Effects of oxidative stress on the insulin signalling pathway. ↑: Stimulate. ↓: Inhibit(S. K. Das et al., 2016).*

1.1.3. Oxidative Stress and Complications of Diabetes

A considerable body of evidence suggests that hyperglycemia plays a key role in the pathogenesis of several complications associated with diabetes, including nephropathy, retinopathy, neuropathy, as well as macro- and microvascular damage. The occurrence of complications associated with late- stage diabetes is heavily impacted by oxidative stress, which is a result of either increased production of reactive oxygen species (ROS) or inadequate removal of these species. In persons suffering from uncontrolled diabetes, there is a notable decrease in the levels of superoxide dismutase, an enzyme that plays a crucial role in the inactivation of the superoxide radical. Furthermore, there is a decrease in the concentrations of the antioxidants vitamin E and alpha-lipoic acid. Moreover, there is empirical evidence indicating a correlation between a deficiency of erythrocyte catalase, an enzyme responsible for the breakdown of hydrogenperoxide (H2O2), and an increased prevalence of diabete Despite the considerable progress made inunderstanding the underlying processes via which high blood sugar levels lead to oxidative stress and subsequent tissue damage, the options for effective therapy interventions to reduce or delay the occurrence of such damage are now limited(S. K. Das et al., 2016)

1.2. Diabetes Concern and the Use of Plants for its Treatment

Diabetes is a prevalent and complex health problem that has had a significant impact on the globalpopulation. The aforementioned ailment is a manifestation of a metabolic problem within the body'ssystems, namely caused by elevated levels of glucose in the bloodstream. The Rhizophora mucronata and Avicennia marina are plant species known for their antibacterial properties. These plants have been traditionally used for their potential to reduce glucose levels and enhance insulin production. First of all, diabetes is associated with disruptions in the metabolism. Furthermore, this disease may arise due to the body's inability to effectively respond to endogenously produced insulin. The bark of Rhizophora mucronata contains a substantial quantity of bioactive components, including glycosides, anthroquinone,

phenolic compounds, catechins, triterpenes, sugar, protein, and tannins. These chemicals have been found to be beneficial in the treatment and control of diabetes(Mahera et al., 2013). Avicennia marina possesses both ecological and economic advantages. Numerous components of the plant have been empirically demonstrated to possess ethnomedicinal properties, exhibiting potential therapeutic efficacy in the management of diverse ailments such as diabetes. Significantly, the pharmacological examinations conducted on Avicennia marina have demonstrated its antioxidant, anti-inflammatory, antiviral, antimicrobial, and antidiabetic properties. Therefore, as a result of this phenomenon, traditional medicine practitioners have been able to effectively employ the products derived from it in order to create pharmaceuticals containing biologically active phytochemicals(Heba.et.al.,2017).

1.3. Therapeutic activity of mangrove plants

The therapeutic attributes of mangrove have been utilized in the treatment of diverse health conditions. Secondary metabolites, including alkaloids, phenolics, saponins, flavonoids, and tannins, have been recognized for their substantial pharmacological, mutagenicity, and economic importance. (S. K. Das et al., 2016). Recent studies have identified distinct and innovative bioactive compounds from various species of mangrove, which fall into different active classes of secondary metabolites. These compounds have been found to exhibit a range of bioactivities, including antidiabetic properties (Encarnação et al., 2022).

Table 1. *Major phytoconstituents of mangrove plants exhibiting hypoglycaemic activities(Sk. al., 2016)(Eze.et.al.,2022)(Encarnação.et.al.,2022).*

Class of compound	Hypoglycaemic activity	Mangrove species	Major phytoconstituents.
Alkaloids	1. Inhibit alpha glucosidase. 2. The transport of glucose over the intestinal epithelium.	Bruguiera sp., X. granatum	Brugine, tropine and tropine esters of acetic, iosbutyric, ios valeric, propionic, n-butyric, 4-hydroxybenzoic acid, ethyl 3,4dihydroxybenzoate Das et al. (2021),
Polysaccharides	• ↑ Levels of serum insulin • ↓ Blood glucose levels • Improve tolerance of glucose.	S. alba	Complex polysaccharide(S. K. Das et al., 2016)
Flavonoids	1. Suppressed the glucose Level 2. ↓ Plasma cholesterol and triglycerides significantly 3. ↑ Hepatic glucokinase activity.	A. ilicifolius, Bruguiera sp., X. granatum.	Rutin, quercetin, kaempferol, catechin, epicatechin(Encarnação et al., 2022)
Saponins	1.Stimulates the release of insulin.	B. gymnor rhiza,B. seaxangul.	β-Sitosterol, β-amyrin, ursolic acid, α-amyrin, stigmasterol Nebula et al.(Eze et al., 2022)
Phenolic compounds	• ↑ The levels of serum insulin, • ↑ The sensitivity of tissues to insulin action	B. racemosa, Rhizophora sp.	Methyl 3,4,5- trihydroxy benzoate; 3,4,5- trimethoxy phenol 1-O-β-D-(6-galloyl)-glucopyranoside, gallic acid(S. K. Das et al., 2016)

Table:2- - Mangrove plants with reported antioxidant and antidiabetic activities(Eze.et.al.,2022).

Mangrove species	Family	Phytoconstituents	Antioxidant activities studied (A)	Antidiabetic mechanism (D)
A.corniculatum	Myrsinaceae	Flavonoids, tannins, saponins,	Phenolic content; reducing ability	1. Administered by direct stimulation of glucose uptake or mediated by enhanced insulin secretion; 2. High levels of glucose and glycosylated hemoglobin
A. ilicifolius	Acanthaceae	Flavonoids	OH radical, DPPH, ABTS scavenging	Regeneration of pancreatic β cells
A.marina	Avicenniaceae	Saponins	Catalase	1. Stimulation of β-cells release more insulin 2. Anti hypoglycemic activity
B. racemosa	Lecythidaceae	Flavonoids, tannins, saponins	DPPH scavenging, superoxide scavenging, FRAP	α-glucosidase and α-amylase. inhibitory properties.
R. mucronata	Rhizosphoraeae	Alkaloids, tannins, saponins, phenolic compunds.	SOD, LPO, NO and DPPH assays	1.Improves the level and action of insulin secretion; 2.Insulin-mimicking activity; 3.α-glucosidase Inhibitors.

1.3.1. Geographical location of manogrove plants in Bangladesh

Fig3- *Geographical location of mangrove plants in bangladesh sunderbunds*(*Banerjee et al., 2008*).

The Sunderbunds is an extensive region consisting of mangrove forests and saltwater wetlands located in the lower portion of the Padma (Ganges [Ganga])-Brahmaputra River delta. It spans over southeastern West Bengal state in India and southern Bangladesh. The geographical region under consideration spans a distance of approximately 160 miles (260 km) in an east-west direction along the Bay of Bengal, starting from the estuary of the Hugli River in India and extending to the western part of the Meghna River estuary in Bangladesh. Plants that have been recognized for their high phytochemical content and potential anti- diabetic effects provide significant promise for the effective management of diabetes mellitus in Bangladesh(Banerjee et al., 2008).

1.4. Medicinal use of mangrove plant:

According to review data from the World Health Organization (WHO), a significant majority of the global population, exceeding 80%, relies on the utilization of plants for medicinal purposes. Mangroves have been extensively employed for this specific objective. Mangrove plants are known to play a significant role in the treatment of various ailments such as fever, kidney stones, toothaches, sore throats, diarrhea, malaria, constipation, fungal infections, and other diseases. Acanthus ilicifolius, a species of mangrove plant, has been historically employed for the treatment of various ailments such as asthma, rheumatism, snake bites, paralysis, as well as for the prevention of tumor growth and progression of cancer. A recent review has clarified an extensive range of therapeutic characteristics exhibited by Avicennia species, which have demonstrated efficacy in addressing a multitude of diseases including HIV, cancer, diarrhea, hepatitis, diabetes, inflammation, oxidative stress-related disorders, and other associated conditions(S. K. Das et al., 2016). According to review data from the World Health Organization (WHO), a significant majority of The resin derived from Avicennia alba is employed in the management of contraception, ulceration, dermatological conditions, and neoplastic disorders. The utilization of the bark and seeds of A. alba for piscicidal purposes is observed. In the context of the Solomon Islands, the utilization of Bruguiera gymnorrhiza bark for the treatment of malaria and diarrhea, as well as the application of its leaves for burn treatment, has been observed. The stem of this plant is also employed for the treatment of viral fever, whereas its root and bark are utilized for the management of diabetes. Ceriops decandra is a plant species commonly employed in traditional medicine for the management of various ailments, including diabetes, diarrhea, dysentery, angina, wounds, and boils. Excoecaria agallocha has been historically employed for thetreatment of various ailments including sores, stings, ulcers, epilepsy, leprosy, paralysis, rheumatism,dermatitis, and conjunctivitis. The traditional application of Heritiera littoralis stem and seed decoction encompasses the treatment of dysentery, diarrhea, stomach discomfort, as well as mosquito control. Ipomoea pes-caprae is frequently employed for the treatment of jellyfish stings and as a means to alleviate malevolent entities during ceremonial ablutions. I. pes- caprae is utilized in various regions across the globefor the management of a range of conditions including diarrhea, constipation, diabetes, hypertension, arthritis, meningitis, renal ailments, hydrocephaly, and fatigue. The leaves of this plant are utilized for the alleviation of rheumatic pain and inflammation. The treatment of fever involves the utilization of a decoction derived from the leaves of Pluchea indica. The sap derived from the leaves of this plant is utilizedfor the therapeutic management of dysentery. The usage of a poultice derived from the plants of this botanical specimen is employed as an external therapeutic intervention for the management of wounds and ulcers (Habib et al. 2018).

1.4.1. Mangroves in traditional medicine

Folk medicine and therapy are a very significant aspect of traditional knowledge. The intergenerational transmission of traditional medical knowledge is prevalent, as rural inhabitants in remote areas persevere in utilizing these practises, so making a significant contribution to the sustainable preservation of civilization and its cultural heritage. The World Health Organisation (WHO) offers a comprehensive description of traditional medicine, which comprises a range of practises, tactics, knowledge, and benefits obtained from plant, animal, and microbial sources. Furthermore, this comprehensive approach encompasses spiritual therapies, physical techniques, and exercise, which can be utilized either alone or in conjunction to effectively address the treatment, diagnosis, prevention, or maintenance of well-being in relation to various conditions. Based on statistical data from the World Health Organisation in 2008,traditional medicine is primarily employed by indigenous or native populations, with a considerable segment of the populace in various Asian and African nations depending on traditional medicine as their primary means of accessing fundamental healthcare services. Furthermore, a considerable segment of the population residing in rural regions relies on indigenous plant species for therapeutic applications in the treatment and control of various health conditions. The application of mangrove plants in traditional ethnomedicine remains prevalent, with extracts obtained from many mangrove species exhibiting notable inhibitory effects against diseases that impact humans, animals, and plants. Mangrove species are commonly utilized in traditional folk medicine owing to their strong antioxidant capacity, which is attributed to the presence of phytochemical constituents. The application of bioactive compounds derived from mangroves is of great significance in enhancing human health and potentially contributing to the enhancement of animal health as well. The investigation of secondary metabolites derived from mangroves is being pursued as a viable solution to address the increasing need for creative medications, owing to their distinctive attributes such asnovelty, structural diversity, and cost-effectiveness.

1.4.2. Antidiabetic Activity of Mangrove Extracts and their Phytochemicals

Mangrove plants are widely recognized as a valuable reservoir of potent antidiabetic compounds and are reputed for their lack of adverse effects. Across the globe, the management of diabetes mellitus involves the utilization of over 400 plants (S. K. Das et al., 2016). These ecosystems endure challenging conditions such as elevated salinity levels, fluctuating tides, intense winds, elevated temperatures, and oxygen-deprived, muddy soils. Asia is widely recognized as the region with the highest level of mangrove species diversity, boasting a reported total of 44 distinct species(Elekofehinti, 2015).

1.4.3. Rationale of the project

A number of review articles have discussed the utilization of mangrove plants in traditional medicine, where they are believed to provide medicinal benefits for various ailments. For instance, those diagnosed with diabetes and the associated complications they may have. Mangrove plants provide antidiabetic properties and are strong in antioxidants. Mangrove plants live in soil-rich ecosystems and offer a range of benefits with reduced adverse effects and enhanced efficacy for individuals with diabetes. The substance of concern contains potent antidiabetic properties that effectively reduce the complications associated with diabetes and its related oxidative stress. The presence of several secondary metabolites is essential in the treatment of diabetes. However, in the future, the compound shows promise due to its reduced adverse effects and increased benefits for diabetes. The main goal of this project is to review the antidiabetic property of mangrove plant and find out why it is essential for diabetics and what are the future benefits.

1.4.4. Aim of this project :

In recent years, diabetes mellitus has emerged as a globally major subject of study. However, the term "antidiabetic property" refers to the characteristic or property of a substance or compound that has the ability to reduce or prevent the effects of diabetes .A comprehensive analysis of relevant papers was conducted, revealing that mangrove plants possess anti-diabetic properties that can effectively limit the impact of diabetes. Furthermore, it was shown that the use of mangrove plants in diabetes treatment is associated with minimal side effects and enhanced efficacy. The aim of this project is to inspect the future of mangrove plants in reducing diabetic complications.

1.4.5-Objective of the project

The objective of this project are:

1. To learn about how the antidiabetic properties of mangrove plants are beneficial for diabetics.
2. To give an insight into how the antidiabetic properties of mangrove plants can be potential candidates for drug delivery to diabetic patients and their complications.
3. To explore more about future aspects and challenges of the antidiabetic properties of mangrove plant mediated drug delivery.

1.4.5. Antidiabetic potential of phytochemicals; a mangrove plant perspective:

Unique chemical structures and diverse chemical classes of metabolites have been identified in mangroves and their associated mangal species(Tomar & Sisodia, 2014). The classes of compounds encompassed in this list are aliphatic alcohols, acids, amino acids, alkaloids, carbohydrates, carotenoids, hydrocarbons, free fatty acids (including polyunsaturated fatty acids), lipids, pheromones, phorbol esters, steroids, triterpenes and their glycosides, tannins, terpenes, phenolics, and compounds that are closely related to them(Ardalani.et.al.,.2021).

Chapter02: Important metabolites that reduces diabetes:

2.1. Alkaloid

Alkaloids exhibit antihyperglycemic effects by enhancing pancreatic insulin secretion from islet β-cells or by facilitating the transfer of blood glucose to peripheral tissues. A tissue is a soft, thin, and absorbent material typically used for personal hygiene purposes, such as wiping Previous studies have demonstrated the presence of alkaloids, including xylogranatinin, granatoin, acanthicifoline, and trigonellin, in mangrove plants such as Xylocarpus granatum and Acanthus sp(S.K. Das et al., 2016). The potential utility of innovative pharmacological drugs in alleviating insulin resistance for the prevention and treatment of diabetes is a subject of interest in current research and development. PTP-1B is an enzyme classified as a protein tyrosine phosphatase, which functions as a suppressor of the insulin signaling pathway. (Rafe, 2017).

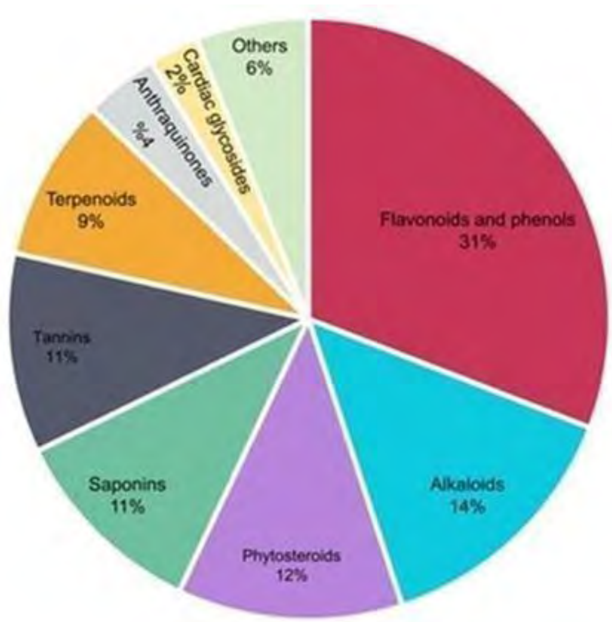

Fig 4-*The class of compounds with antidiabetic bioactivity in plant roots and rhizomes(S. K. Das et al., 2016).* -

2.1.1. Polysaccharide-

Polysaccharides exhibit antihyperglycemic properties by enhancing serum insulin levels, reducing blood glucose levels, and enhancing glucose tolerance. The presence of a complex polysaccharide molecule in the mangrove plant Sonneratia alba has been suggested as a potential explanation for its hypoglycemic property. The anti-diabetic properties of polysaccharides and complexes are primarily mediated through the following mechanisms: There are three main areas of focus in this study: (1) the enhancement of cellular dysfunction, (2) the inhibition of -amylase and-glucosidase activities, and (3) the targeting of signaling pathways to improve insulin action and glucose metabolism(S. K. Das et al., 2016).This heightenedattention is primarily attributed to their favorable characteristics, such as low toxicity and a diverse array of pharmacological effects. These entities consist of monosaccharide units that are joined together through glycosidic linkages. The assessment of the impacts of polysaccharides with anti-diabetic properties has become a prominent field of study (Ganesan & Xu, 2019**).**

2.1.2. Flavoniod

Flavonoids have been identified as potentially beneficial for alternative treatment of diabetes due to their ability to inhibit apoptosis of pancreatic beta cells, stimulate proliferation of these cells, enhance insulin secretion, and improve insulin activity.Mangrove plant species, namely Avicennia marina, X. granatum, and Bruguiera sexangula, have been identified as rich sources of hypoglycemic flavonoids, including quercetin, kaempferol, catechin, epicatechin, and rutin. Flavonoids exhibit a multitude of advantageous effects on metabolic disorders, including but not limited to cardiovascular disease, cancer, obesity, and diabetes. Existing literature has indicated that flavonoids potentially possess the capacity to contribute tothe mitigation and management of some viral illnesses, namely influenza. (A. Das et al., 2021). Additionally, they serve as antioxidants, regulating oxidative stress within the body by counteracting the impact of nitrogen and oxygen species, thereby mitigating the occurrence of diseases. The anti-diabetic effect of flavonoids contributes to the regulation of various physiological processes, including carbohydratedigestion, insulin signaling, insulin production, glucose absorption, and adipose deposition. They specifically target a variety of molecules that are involved in the regulation of different pathways. The interventions described involve many strategies to address the physiological processes related to diabetes. These strategies include promoting the growth of pancreatic beta cells, enhancing the production of insulin, preventing cell death, and regulating glucose metabolism in the liver to control high blood sugar levels. These interventions encompass the stimulation of T-cell proliferation, augmentation of insulin secretion, reduction of apoptosis, and management of hyperglycemia through the modulation of glucose metabolismin the liver (Raj et al., 2016).

2.1.3. Saponoid

Saponins encompass a class of glycosides that consist of triterpenoid and steroidal compounds. Some of these chemicals have demonstrated significant hypoglycemic effects. According to reports, the anti-diabeticeffect exhibited by the A. marina mangrove plant can be attributed to the presence of stigmasterol-3-O--D-galactopyranoside and -amyrin. In a similar vein, it was found that bartogenic acid exhibits inhibitory activity against -glucosidase in the mangrove plant Barringtonia racemosa. Mangrove plants, specifically A.marina and Sonneratia caseolaris, contain pentacyclic triterpenoids, including oleanolic acid, ursolic acid, and lupeol, which possess anti-diabetic properties(A. Das et al., 2021).This antihyperglycemic effect is believed to be due to the saponin's capacity to stimulate insulin secretion from the pancreas(Heinrich et al., 2021).

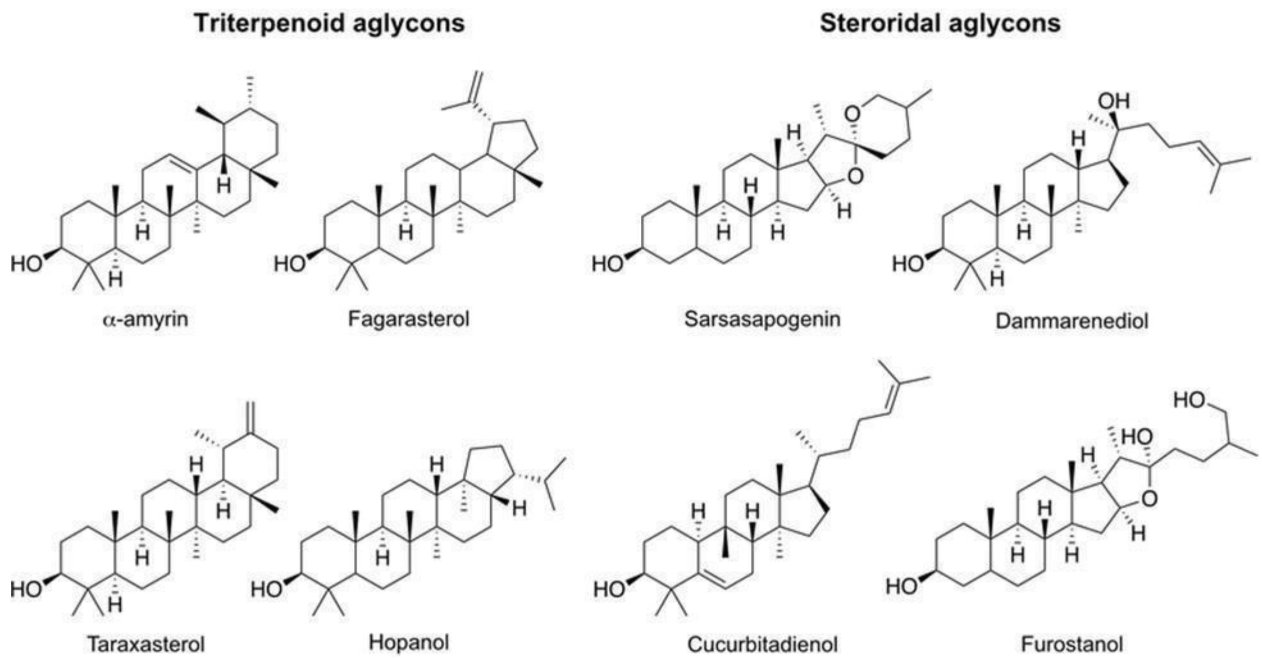

Fig 5-*Chemical structure of selected triterpenoid and steroidal aglycones of saponins present in the plant root system(Heinrich et al., 2021).*

2.1.4. phenolic compound-

The hypoglycemic activities of phenolic compounds can be attributed to several mechanisms, including the elevation of serum insulin levels, enhancement of tissue sensitivity to insulin, stimulation of glucose utilization enzymes, and inhibition of α- amylase activity. Mangrove plants, specifically B. racemosa, exhibit antidiabetic properties due to the presence of phenolic compounds, such as gallic acid. The effectsof phenol on diabetes vary. By inhibiting G6Pase, CGA reduces glucose production in the liver and acts as an insulin sensitizer to increase the effectiveness of insulin. Curcumin lowers AGE's in diabetes vialowering insulin resistance. The effects of resveratrol on glucose absorption and insulin secretion are enhanced. CGA's antioxidant activity is comparable to that of vitamin E, while ellagic acid may be even more powerful(S. K. Das et al., 2016).

2.1.5. Tannins

Tannins are known to have a significant impact on mitigating diabetic complications through their ability to decrease the formation of advanced glycation end products (AGEs) and oxidative stress. The families Avicenniaceae, Rhizophoraceae, and Sonneratiaceae are known for their abundant tannin content. Xylocarpus moluccensis, a type of mangrove, has been documented to contain a significant amount of non-hydrolysable tannins, specifically procyanidindecamer and procyanidinundecamer(Raj et al., 2016). These substances have been widely acknowledged for their potential benefits in cardiovascular protection, anti-inflammatory effects, anti-carcinogenic properties, and anti-mutagenic activities, among other recognized attributes. The protective effects of these substances are associated with their ability to: (a) function as scavengers of free radicals; (b) stimulate the activation of antioxidant enzymes. It has been observed that they possess the ability to augment glucose uptake by activating mediators within the insulin-signaling pathways, such as PI3k(Phosphoinositide 3-Kinase) and p38 MAPK (Mitogen-Activated Protein Kinase), as well as facilitating GLUT-4 translocation.(Ahangarpour et al., 2019).

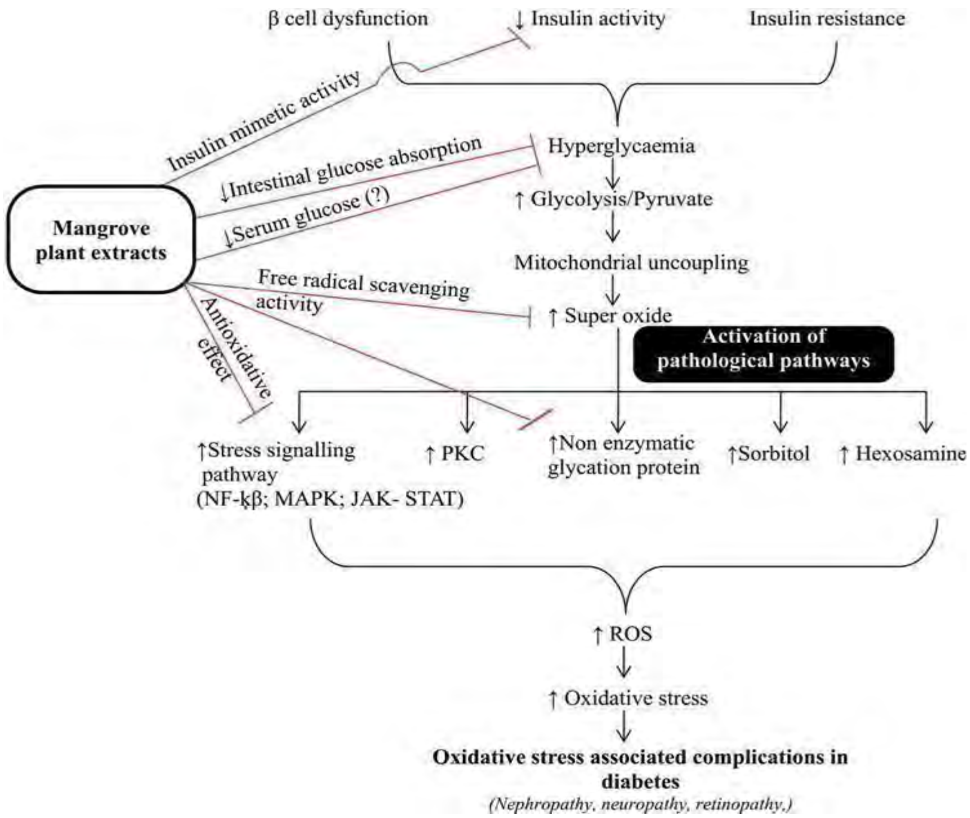

Figure 6- *Possible role of mangrove plants in the management of diabetes and its associated oxidativ).*

estress-mediated complications.↑: Stimulate. ↓: Inhibit(S. K. Das et al., 2016)

Chapter3
Methodology

A comprehensive literature review was conducted utilizing online databases such as CAS, Science Direct, and PubMed. Furthermore, the review conducted manual searches. Consulting scholarly literature in books and journals. In conducting this review, the data has been meticulously gathered through a rigorous process of systematically compiling information from various available sources. During writing process,information was properly paraphrased and cited. The in-text citation and the bibliography were generated by using Mendeley Desktop.

Some mangrove plants have antidiabetic property:

3.1.Avicennia corniculatum L:

Avicennia corniculatum L., commonly known as black mangrove, is a member of the Myrsinaceae family. The various components of the plant have historically been employed for the management of rheumatism, arthritis, inflammation, as well as for their antioxidant, free radical scavenging, and hepatoprotective properties. (Gurudeeban et al., 2012).

3.1.2. Acanthus ilicifolius:

Acanthus ilicifolius, a plant belonging to the Acanthaceae family, has garnered significant interest as a result of its diverse array of secondary metabolites and its long- standing utilization in the traditional medicinal practices of India and China. According to reports, this particular botanical specimen is classified as a mangrove plant. Mangroves are able to thrive in highly challenging environments characterized by fluctuating tidal patterns and high salinity levels. Therefore, these plants are regarded as abundant reservoirs of steroids, triterpenoids, saponins, flavonoids, alkaloids, and tannins (Mouafi et al., 2014).This review article aims to comprehensively discuss the recent advancements in the phytochemical and pharmacological properties of drugs. Throughout history, there is evidence of the utilization of this botanical specimen for the purpose of treating a range of maladies, including dyspepsia, paralysis, asthma, headache, rheumatism, skin problems, and diabetes. (Singh & Aeri, 2013).

3.1.3. A. marina :

A. marina is classified within the taxonomic family Avicenniaceae. The antihyperglycemic activity of the ethanolic leaf extracts of A. marina has been demonstrated in induced diabetes. Additionally, there was an observed increase in total haemoglobin (Hb), total protein, and serum insulin levels. The leaf extract of A. marina has been found to possess the ability to decrease the concentration of serum urea, indicating its potential to provide protection to essential organs such as the kidney, liver, and pancreas. (Aiyer, 2021). The current review was conducted with the aim of acquiring additional knowledge regarding the secondary metabolites of A. marina. In this review ,we present the isolation and structural elucidation of a sterol glucoside, as well as the identification of two triterpenoids. The sterol glucoside exhibited a moderate level of activity against the process of glycation(Mahera et al., 2013).

3.1.4. B. racemose:

B. racemosa is a perennial mangrove species classified within the taxonomic family Lecythidaceae. The bark and leaves of this plant have historically been utilized for their medicinal properties, specifically in relation to their anticancer, analgesic, antibacterial, anticolic, and antifungal effects and anti-diabetic.(Alam et al., 2022) (Ardalani et al., 2021).

3.1.5. Rhizophora sp:

The taxonomic classification of the mangrove genus Rhizophora places it within the family Rhizosphoraceae. Within the genus Rhizophora, there are 10 distinct species. Notably, three of these plants, specifically Rhizophora apiculata, Rhizophora annamalayana, and Rhizophora mucronata, have been extensively studied and found to have traits that can potentially mitigate the effects of diabetes. The root extracts of R. apiculata showed promising antihyperglycemic efficacy in experimental rats when administered at a dosage of 250 mg/kg. The ethanolic root extract of the plant exhibits antihyperglycemic activity, which can be ascribed to the presence of a variety of phytochemicals present in its chloroform and aqueous sub-fractions. By employing supplementary purification techniques, a comprehensive set of seven discrete chemical components were effectively extracted, specifically identified as lupeol, oleanolic acid, β-sitosterol, palmitic acid, β-sitosterol-β-D- glucoside, inositol, and pinitol(Das et al., 2016).

Chapter 04

4.1.Result

Upon reviewing several scholarly articles, it becomes evident that mangrove plants are the sole residents of soil-rich environments, as no other plant species have been observed to do well in such conditions.Likewise, it exhibits potent anti-diabetic characteristics. Nowadays, diabetes mellitus has emerged as a highly significant subject of concern. Certain forms of traditional medicine are employed for the treatment of individuals suffering from diabetes. However, it is important to note that these kinds of treatments can result in significant adverse effects. In contrast, several components of the mangrove plant are used to the mitigation of diabetes, as well as for the extraction of diverse secondary metabolites found within the plant. For instance, many classes of compounds such as terpenoids, saponins, steroids, tannins, flavonoids, and glycosides can be considered. Among the previously mentioned metabolites, there exists a subset that exhibits the capacity to diminish the generation of free radicals within individuals afflicted with diabetes. However, when the body experiences an imbalance in the production of reactive oxygen species, oxidative stress ensues, leading to various complications.

Chapter 5

5.1 Discussion:

The primary focus of our review was on the enhanced effectiveness of mangrove plants and their minimal adverse effects in the context of diabetes. Based on several examined publications, it is evident that mangrove plants are currently being used in traditional medicine, namely in the area of folklore medicine. This form of treatment has gained considerable popularity due to the significant impact it has demonstrated in managing diabetes. In recent times, there has been an increase in the prevalence of diabetes mellitus. However, the current treatment options have not been updated that include thepotential benefits of mangrove plants, which possess anti-diabetic properties and may offer a means to mitigate the effects of diabetes(Elekofehinti, 2015).The mangrove plant contains compounds that mostly exhibit therapeutic effects for individuals with diabetes. For instance, various classes of compoundssuch as terpenoids, saponins, steroids, glycosides, and polysaccharides can be considered. Likewise, it isevident from several sources of literature that diverse components of mangrove plants are employed in the management of diabetes. Additionally, there are several plant families that are predominantly usedin this particular context. The current status of the product's marketing remains uncertain until itundergoes more investigation, including in vivo and in vitro testing, after which it may potentially be approved for official use in the treatment of diabetes. Mangrove plants, which inhabit an ecologically challenging environment characterized by various stressors including salinity, high temperature, waterlogging, low oxygen, and limited light availability, have been found to possess a significant abundance of antioxidant compounds. The compounds encompassed in this category consist of various phytochemicals, namely cinnamic acids, coumarins, diterpenes, flavonoids, lignans, monoterpenes, phenyl-propanoids, tannins, and triterpenes(Eswaraiah et al., 2020). The investigation into the presence of antidiabetic phytoconstituents with enhanced antioxidant properties in mangrove plants has gained momentum. Based on the conducted review on mangrove plants and their potential antidiabetic properties, it has been proposed that these plants may manifest their antidiabetic effects through various mechanisms, including insulin mimetic activity, reduction of intestinal glucose absorption, decrease in advanced glycation end products (AGEs), and exertion of antioxidative effects, consequently mitigating diabetic conditions associated with oxidative stress.In subsequent periods, this particular chemical exhibits significant potential for the therapeutic intervention of patients afflicted with diabetes. (Encarnação et al., 2022).

Chapter 06

6.1 Conclusion

This review aims to provide valuable insights for scholars, scientists, and health professionals engaged in the field of pharmacology and therapeutics, specifically in the development of antidiabetic drugs. This review focuses on the examination of conventional botanical remedies utilized in the management of diabetes mellitus. There have been reports of various plant species exhibiting properties such as antidiabetic, anti-hyperglycemic, and hypoglycemic activities, as well as inhibition of α-amylase and α- glucosidase enzymes. The antidiabetic properties of plants are described to the combination of phytochemicals or individual constituents found in the extracts of the plants. The main phytochemicals that have been linked to antidiabetic activities encompass alkaloids, phenolic acids, flavonoids, glycosides, saponins, polysaccharides, and tannins. Moreover, the phytochemical content in plants is significantly altered by many different kinds of internal and external stimuli.These factors encompass genetic characteristics, the specific plant organs utilized, as well as the conditions under which the plants are cultivated, dried, and stored. Various stress factors, including unfavorable climatic conditions and plant diseases, also have an impact on the composition of phytochemicals acquired. However, despite this, these studies remain valuable in the pursuit of identifying a novel natural antidiabetic medication that holds significant potential. As previously mentioned, the current antidiabetic drugs available to a significant population of individuals have demonstrated low efficacy and safety, prompting a pressing need to address this prominent health concern and seek improved management strategies for diabetes. The significance of the anti-diabetic property of mangrove plants lies in their potential to offer increased efficacy and improved safety..(Heba et al., 2017).

6.2 Future work:

Mangrove plants, which inhabit an ecologically challenging environment characterized by various stressors including salinity, high temperature, waterlogging, low oxygen, and limited light availability, have been found to possess a significant abundance of antioxidant compounds. The compounds encompassed in this category consist of various phytochemicals, namely cinnamic acids, coumarins, diterpenes, flavonoids, lignans, monoterpenes, phenyl-propanoids, tannins, and triterpenes(Eswaraiah et al., 2020). The investigation into the presence of antidiabetic phytoconstituents with enhanced antioxidant properties in mangrove plants has gained momentum. Based on the conducted review on mangrove plants and their potential antidiabetic properties, it has been proposed that these plants may manifest their antidiabetic effects through various mechanisms, including insulin mimetic activity,reduction of intestinal glucose absorption, decrease in advanced glycation end products (AGEs), and exertion of antioxidative effects, consequently mitigating diabetic conditions associated with oxidative stress.In subsequent periods, this particular chemical exhibits significant potential for the therapeutic intervention of patients afflicted with diabetes(Encarnação.et.al.,2022).

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