



Received on 12 September 2025; received in revised form, 19 February 2026; accepted, 24 February 2026; published 01 March 2026

ANTIDIABETIC ACTIVITIES AND PHYTOCHEMICAL CONSTITUENTS OF SELECTED MEDICINAL PLANTS FROM *ETHIOPIAN FLORA*: A BRIEF REVIEW

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Keywords:

Diabetics, Efficacy, Ethnobotany, Phytochemical, Medicinal plants, Safety

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ABSTRACT: Background: Diabetes mellitus (DM) is a dangerous metabolic illness that causes blood glucose levels to rise unnaturally. This is brought on by problems with insulin secretion, which controls how the body uses glucose to make energy. The two main types of diabetes mellitus (DM) are Type 1 DM and Type 2 DM. Type 1 Diabetes Mellitus (T1DM), which is brought on by a complete or nearly complete lack of insulin, and Type 2 Diabetes Mellitus (T2DM), which is defined by insulin deficiency or insulin resistance. In order to control hyperglycemia for T2DM hyperglycemic drugs. Insulin therapy is also used as an alternative for patients who show allergic reactions to oral hyperglycemic drugs. The aim of this paper is to review phytochemical constituents and antidiabetic activities of selected medicinal plants (*Otistiga integrigolia*, *Moringa stenopetala*, *Sativa rabaudiana rabaudiana*, *Meriandra dianthera*, *indica*, *Momordica charantia*, *Allium sativum*, and *Ajuga remota*) from Ethiopian flora. **Methods:** This review article is intended to compile information already available on selected Ethiopian medicinal plants of active compounds and extracts they contain that are used to treat DM from their morphological sources. The information were gathered from published scientific papers, Theses, Books and Ethnobotany reports. Search terms such as diabetes and medicinal plants were used to gather information form Science direct, Google Scholar and Scopus. **Conclusion:** There are currently no proven effective treatments for controlling diabetes, and the prevalence of DM is increasing from time to time. The commercial oral hypoglycemic drugs have limitations. Some of the limitations are they are expensive and have serious adverse effects on patients' health making their use more difficult. In order to address the aforementioned concerns, it is crucial to concentrate on identifying safe and efficient remedies from the available medicinal plants. In order to discover drugs with improved antidiabetic activities, researchers are expected to carry out investigation on crude extracts and bioactive compounds isolated from medicinal plants.

INTRODUCTION: Diabetes mellitus (DM) is one of the most common endocrine metabolic disorders characterized by chronic hyperglycemia caused by varying degrees of insulin resistance, deficiency in insulin secretion, or both ¹. DM is not only a complex disease, but also a chronic metabolic

disorder having glycosuria and negative nitrogen balance as its main features and it occurs because of a decrease in insulin secretion by beta cells of the pancreas and poor response of insulin receptors to insulin ²⁻³.

Diabetic complications could be linked to alteration in the body's antioxidant defense system, increased oxidative stress, and dyslipidemia ⁴. Nearly 10.5% of the world population is affected with its prevalence increasing at an type 1 diabetes (T1DM). It is also known as insulin-dependent diabetes, and it happens due to autoimmune destruction of the pancreatic beta cells leading to



significantly reduced secretion of insulin⁵. It is a non-hereditary genetic condition that mainly affects the juvenile under thirty years of age. Type 2 diabetes (T2DM), also known as non-insulin-dependent diabetes, is the most common form of diabetes, with its prevalence rapidly rising worldwide⁶. It is a hereditary condition caused as a result of insulin resistance, insufficient insulin secretion, or a combination of both, largely affecting an older population⁷. Both forms of DM alter carbohydrate, protein, and fat metabolism. The effect of insulin resistance leads to high blood sugar levels by hindering the uptake and efficient use of glucose by most cells of the body⁸. The progression of the disease is accompanied by tissue or vascular damage resulting in severe complications, including retinopathy, diabetic neuropathy, cardiovascular, pulmonary, cerebral, and peripheral vascular diseases, ulcers, and thyroid gland disorders, leading to serious morbidity and mortality^{1,9-10}.

The most effective management of DM, demands an inter-professional approach involving both lifestyle modifications with diet and exercise and pharmacologic therapies as needed to meet individualized glycemic goals¹¹. Healthcare practitioners must encourage patients to combine lifestyle modifications with oral pharmacologic agents for optimal glycemic control, particularly T2DM as it progresses with continued loss of pancreatic beta-cell function and insulin production¹². The key defect in carbohydrate metabolism in diabetes results in extensive, multiorgan complications that eventually involve every system of the body¹³. It also is true that with the advancement of knowledge about the path physiology of DM, and better understanding of its development, this syndrome is now at the front line of research in molecular biology and immunology¹⁴. Because DM complications are serious health issue and can worsen with every passing day, there is need for an efficacious treatment for its management and prevention¹⁵. This is the failure of synthetic drugs and a question mark on authorities addressing the management of DM¹⁶. Many plant preparations are being prescribed by conventional healers and these preparations also are accepted by patients experiencing diabetes and many other illnesses throughout the world, especially in third-world countries¹⁷.

Therefore, a thorough scientific investigation or research about medicinal plants by chemical investigation, followed by pharmacological screening, is important¹⁸. Plant extracts and preparations have remarkable effectiveness in treating diabetes and its complication with less notable side effects¹⁹. Currently, there are numerous traditional medications in market, science still seeks the best medicine for the prevention and management DM. This review's goal was to compile existing research documents on Ethiopian flora's indigenous medicinal plants so that their specific anti-diabetic activities and mechanisms of action may be further explored.

Causes and Burden of DM: Being overweight or obese, having a sedentary lifestyle, unhealthy diet, chronic stress, poor sleep habits, smoking and excessive alcohol consumption are the known risk factors for both hypertension and diabetes. Although individual-level factors play a substantial role in developing hypertension and diabetes, several studies point out that ecological level factors are also important determinants²⁰. It's expected that DM will be the seventh leading cause of death by 2,030, accounting for 6.7 million fatalities (1 every 5s). Moreover, cost at least USD 966 billion in health expenditure in 2021, and this is a 316% increase over the last 15 years²¹. In Africa about USD 9.5 billion was spent on healthcare for people with diabetes in 2019²².

Globally, the prevalence of DM has intensified widely. According to the International Diabetes Federation (IDF), the estimated 463 million (9.3%) adults aged 20–79 years had diabetes in 2019. It is predicted that the number will increase to 578 million (10.2%) and 700 million (10.9%) in 2030 and 2045, respectively²². It is important to note that more than half (50.1%) of people with DM are unaware of their disease and most of them (84.3%) were found in low and middle-income countries. In Africa, nearly 60% of all people living with diabetes were undiagnosed²². By 2030 and 2045, there will be 28.6 million (47.5% increase), and 47.1 million (142.9% increase) adults aged 20–79 with diabetes, respectively, more than double the number in 2019 and the highest increase compared to other IDF regions, By 2,045, this number is expected to rise to 47 million people with diabetes and 110 million people with impaired glucose

tolerance, putting them at a high risk of developing T2DM²³. According to the 2017 IDF report, the prevalence of DM among adults aged 18–99 years was 4.8% and total diabetes-related death was 31,536. Moreover, about two-thirds of adults with DM has been reported to be undiagnosed in the African country²⁴.

There are different factors for the high rate of undiagnosed DM for many years, which includes lack of awareness in the general population and health care providers, poor health systems and slow onset of the symptoms. Late diagnosis and treatment of DM are associated with the increased occurrence of acute and chronic complications²⁵. Subsequently, this affects patients' quality of life, incurs additional costs to households, and overburdens health care systems. Thus, routine screening and early detections is a current global approach to mitigate the progression of DM²⁵⁻²⁷.

The high degree of hyperglycemia in patients with DM associates with macro vascular complications as coronary artery disease, peripheral arterial disease, stroke, and with micro vascular complications as diabetic nephropathy, neuropathy, and retinopathy. Uncontrolled hyperglycemia in patients with DM leads to no enzymatic glycation of proteins, glucose oxidation, and increases lipid per oxidation. All above mentioned biochemical alterations cause increase of reactive free radicals and thereby increase the oxidative stress²⁸. Currently, it becomes one of the leading public health problems and the cause of morbidity and death universally²⁹⁻³⁰.

Among the highly populated African nations that have the highest number of people with diabetes, include South Africa (4.6 million), Nigeria (2.7 million), the Democratic Republic of Congo (1.8 million), and Ethiopia (1.7' million). More than half (55.8%) of all 20–79-year-old adults with diabetes in the region live in one of these four countries. Studies in various parts of Ethiopia showed that the prevalence of diabetes varies from 0.3 to 7.0%. The IDF estimated that the total health expenditure due to diabetes in 2019 was USD 760 billion worldwide.

It is projected that expenditure will reach USD 825 billion by 2030 and USD 845 billion by 2045^{23, 31}.

According to the IDF, the prevalence of diabetes among Ethiopian adults is 3.2%³². T2DM is the most common form of diabetes (90%–95%) in sub-Saharan Africa³³.

T2DM is a chronic disease and patients may have difficulties, mental problems or stress as a result of efforts to comply with treatment guidelines. Studies have shown that depression as a common comorbid health problem among T2DM people who face significant challenges in accessing diagnosis and treatments contributing to high mortality and prevalence of complications in sub-Saharan Africa³⁴.

The prevalence of T2DM is expected to increase to 592 million adults worldwide in 2035 and 642 million adults by 2040³⁵⁻³⁶. The reports that studies on the prevalence of diabetes in Ethiopia documented prevalence estimates by age groups, sex, residence (urban or rural) and region other studies in Ethiopia reported the prevalence of DM to be in a range from 0.5% to 6.5% and also according to the national WHO STEPS survey of 2015, the prevalence of DM was 3.2%³⁷⁻⁴⁰.

Moreover, the prevalence of undiagnosed diabetes, those who are neither aware of raised blood sugar nor taking any anti-diabetic medications, was very high in Ethiopia⁴¹. Thus, this study aimed to review the *in-vivo* and *in-vitro* antidiabetic activity of selected medicinal plants used for diabetic management in Ethiopian traditional medicine.

Antidiabetic Drugs and Their Side Effects:

Available therapies currently in use for the treatment and management of DM include insulin and several oral hypoglycemic medications such as T2DM sulfonylureas. For instance glipizide (1), glyburide (2) glimepiride (3), Meglitinides like repaglinide (4) and nateglinide (5) Biguanides which is metformin (6) Thiazolidinediones such as rosiglitazone (7), pioglitazone (8), α -Glucosidase inhibitors like acarbose (9), miglitol, (10) and DPP inhibitors such as sitagliptin (11), saxagliptin (12), vildagliptin (13) and linagliptin (14). Despite the launch of metformin (6) and sulfonylurea about 50 years ago, no considerable lead has been achieved for better management of diabetes **Fig. 1**⁴²⁻⁴³.

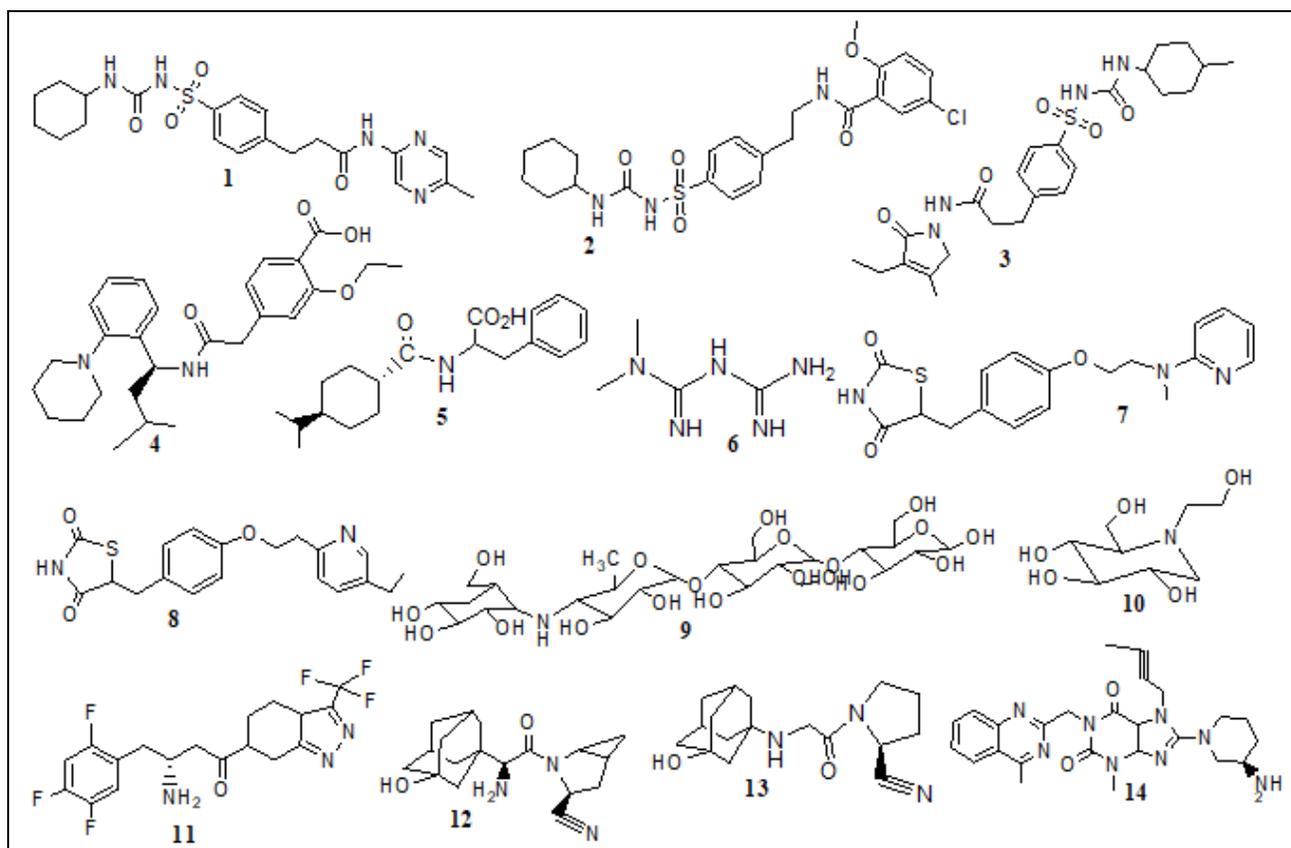


FIG. 1: THE CHEMICAL STRUCTURE OF COMPOUNDS (1-14) OF DRUGS USED TO TREAT DIABETES MELLITUS

Diabetes is a disease that is still not completely curable through currently available anti-diabetic drugs⁴⁴. However, these drugs, intended to boost insulin sensitivity and increase insulin secretion together with the reduction in circulatory plasma glucose levels by increasing glucose excretion or uptake in adipose tissue, are usually associated with many side effects. These include weight gain, hypoglycemia, gastrointestinal tract disturbances, liver injury, renal failure, hypersensitivity reactions, flatulence, diarrhea, and including hepatocellular injury, exacerbate renal diseases, blood dyscrasias, gastrointestinal irregularities, hypoglycemias, hypersensitivity reactions, weight gains, and lactic acidosis which decrease their effectiveness compliance rates and abdominal bloating^{1, 45-47}. The conventional and newer agents are still with their shortcomings, and successful treatment of diabetes is being a global challenge requiring further investigations. In fact, these medications are associated with unnecessary drug reactions or side effects⁴⁸. For instance, 3.9 and 32.7% severe and nonsevere hypoglycemic events were reported in 826 (2.8%) patients during their most recent year of sulfonylurea treatment,

respectively⁴⁹. Clearly, the weight gain associated with the use of thiazolidinediones (pioglitazone and rosiglitazone), sulphonylureas (glibenclamide), and insulin is also the major drawback for treating diabetes⁵⁰. Several drawbacks have been reported associated with the use of antihyperglycemic medications, such as decreasing effectiveness and increasing adverse effects and toxicities.

The reports showed that according to the findings, 56 (30.6%) of the 183 DM patients had various adverse effects. The most common negative effect, hypoglycemia, was identified (n=31), along with tingling, light-headedness, gastrointestinal problems including stomach pain and diarrhea, and other side effects like weariness, joint pain, and eye irritation. However, when patients were explained about symptoms of hypoglycemia, 49.7% (n = 91) of the patients reported occurrence of those symptoms. This indicated that 65.9% of patients were unaware of the characteristics of hypoglycemia and did not recognize the symptoms as unfavorable consequences. A research found that the primary medications causing hypoglycemia in T2DM patients were insulin and sulfonylurea⁵¹.

One of the major contributors of hypoglycemia is aging, and studies also showed that older T2DM patients are less likely to be aware of their disease. Additional risk factors for hypoglycemia include skipping meals, coronary artery disease, renal impairment, usage of insulin or sulphonyl urea, and a history of severe hypoglycemia. Insulin therapy is associated with weight gain and hypoglycemia and shows other adverse effects like local reactions such as swelling, erythema and lipodystrophy, allergy and edema⁵². The side effects of metformin (6) included metallic taste, diarrhea, nausea, vomiting, anorexia, and a range of other GI symptoms like bloating. These effects are often minor, temporary, and gastrointestinal (GI) in nature. Although hypoglycemia is not a side effect of metformin (6), it becomes more likely when it is combined with other medicinal substances. Because it reduces vitamin B12 absorption, prolonged usage of the drug results in a vitamin B12 deficit⁵³. In a comparison experiment, it was discovered that the combination of metformin (6) and glibenclamide caused more adverse events, such as weight gain, hypoglycemia, and GI side effects, than metformin plus glimepiride (3)⁵⁴.

Reports showed that other negative side effects associated with sulfonylureas include hyperinsulinemia, GI side symptoms such nausea, vomiting, and cholestatic jaundice, and dermatological side effects like rash, purpura, and itch. According to research, certain people who experience hypersensitivity responses, such as allergies to sulfonamide medicines, may also respond negatively to sulfonylureas⁵⁵. The incidence of hypoglycemia and weight gain may be decreased in meglitinides. According to a research, the medicine caused hypoglycemia to occur more frequently but less frequently in severe cases, and diarrhea to occur less frequently⁵⁶. Few patients receiving thiazolidinediones (TZDs) hypoglycemia has been reported to be a side effects, however, when glitazone and increased insulin dosage were combined, the risk of hypoglycemia was found to rise. Due to the rise in body weight and redistribution of adipose tissue from visceral to subcutaneous areas brought on by TZDs, peripheral edema may develop and congestive heart failure may worsen as well⁵⁷. The side effects seen during treatment may not have been exclusively attributable to the antidiabetic medicines; they may

also have been brought on by the administration of other medications, such as statins, an antihypertensive, and other medications like vitamins, cephalosporins, *etc.* Calcium channel blockers like amlodipine, angiotensin receptor blockers (ARB) like losartan, telmisartan, *etc.*, -blockers like metoprolol, ACE inhibitors like enalapril, ramipril, *etc.* Losartan, an ARB, has been linked to physical issues including diarrhea, muscular cramps, and back or leg discomfort in addition to adverse effects like weakness, lightheadedness, and dizziness. These adverse effects may be mistakenly thought to be the result of the antidiabetic medications. Calcium channel blockers' early vasodilating effects have been linked to side effects such headache, nausea, palpitations, and diarrhea⁵⁸. Although synthetic oral hypoglycemic drugs alongside insulin are the main route for controlling diabetes, they fail to reverse the course of its complications completely and further worsen it by the fact that they also demonstrate prominent side effects. This forms the main force for discovering alternative sources of antidiabetic agents⁵⁹.

Despite the significant progress made in the treatment of diabetes using oral antidiabetic agents in the past three decades, the results of treatment of diabetic patients are still far from perfect. Several disadvantages have been reported related to the use of those oral hypoglycemic agents, including drug resistance (reduction of efficiency), adverse effects, and even toxicity. For example, sulfonylureas lost their effectiveness after 6 years of treatment in approximately 44% of patients, whereas glucose-lowering drugs are reported to be not able to control hyperlipidemia⁶⁰.

Apart from the significance of the study in preserving indigenous knowledge about the use of plants, it is also essential for discovering novel antidiabetic drugs. Previously, medicinal plants have been documented from the region where the current study falls, especially in Ibadan⁶¹. The importance of indigenous knowledge about plants in treating different ailments among local communities has been affirmed in several studies⁶². The use of herbal medicines for the treatment of various health challenges continues to expand rapidly across the world. There is a tremendous surge in acceptance and public interest in natural

therapies both in developing and developed countries, with these herbal remedies being available not only in drug stores but also in food stores. Herbal medicinal products are the primary healthcare sources for the large population living in developing countries. India has a rich traditional system of medicine⁶³. In Ethiopia, there are few publications that collect *in-vivo* and *in-vitro* assessments of MP extracts for their potential as a road map for future clinical trials and other associated investigations.

Medicinal Plants to Treat Diabetes: There are some medicinal plants believed to treat diabetes, and scientific studies have reported certain MPs do contain antidiabetic properties, such as improved insulin sensitivity and hypoglycemic activities⁶⁴. This is often associated with their high level of phenolic compounds, flavonoids, terpenoids, alkaloids, and glycosides, which can improve insulin secretions as well as control blood glucose⁶⁵.

The reports showed that some of the compounds known to have beneficial effects on carbohydrate metabolism are quercetin (29), and betulinic acid (31) which are found in onion (*Allium cepa* L.) and (*Dillenia indica*), respectively⁶⁶. From time to time the use of traditional medicine throughout world increases due to the locally availability, easily accessible, simple to use and assumed to be safe⁶⁷. Plant-based formulations become the key players of all available treatments due to accessibility, affordability, and minimum adverse effects, particularly in rural areas⁶⁸.

The combined effects of biologically active constituents (such as polyphenols, carotenoids, and glucosinolates) also result in the potential valuable properties of each medicinal plants, and this can act as the first stage to understand their biological effects and beneficial activities⁶⁸. In developing nations, especially MPs are used in treating DM to overcome the economic burden of modern medicines⁶⁹. Several pharmaceuticals commonly used today are structurally derived from natural compounds that are found in traditional medicinal plants. For example, the anti-hyperglycemic drug called metformin (6), currently used to treat diabetes, can be traced back to the traditional use of *Galega officinalis* to treat diabetes⁷⁰.

Given that many medicinal plants are easily accessible, wide availability, and useful for the management of diabetes, many developing countries and a few wealthy countries use MPs to meet their healthcare needs⁷¹. In Ethiopia, there are several MPs used for the treatment of DM and a number of these were examined for their antihyperglycemic effect. About 80–90% of Ethiopians use medicinal plants as a primary form of health care⁷².

Different MP parts were used experimentally for antidiabetic effects in Ethiopia. Among these, leaves were the most commonly investigated medicinal plant part. Plant-based products which are rich in phytoconstituents such as flavonoids, coumarins, terpenoids, phenolic compounds, and other bioactive compounds have revealed the blood-glucose-lowering effect⁷³.

The eight MPs such as *Allium sativum* (garlic)⁷⁴, *Ajuga remota*, *Sativa rebaudiana*, *Otistiga integrigolia*, *Maringa stenopetala*⁷⁵, *Meriandra dianthera*⁷⁶, *Dillenia indica* and *Momordica charantia*⁷⁶, have been selected for this review as they are widely plant species in Ethiopian local communities used in traditional medicine to treat DM.

Description and Ethano Botanical uses of *Stevia rebaudiana*: *S. rebaudiana*, locally called yeshayketel (in Amharic), usually grow in semi-dry mountainous terrains, their habitats range from grasslands, forested mountain slopes, conifer forests, to sub-alpine vegetation. It is an herb of 80 - 180 cm tall with a life span of 3-5 years. It grows best in soil that is well drained but with reasonable water holding capacity and preferably with pH 5-7; alkaline soil should be avoided⁷⁷ **Fig. 2.**

S. rebaudiana is safe for diabetics, as it does not affect blood sugar levels, not have the neurological or renal side effects as other artificial sweeteners and also, this plant possess anti-fungal and anti-bacterial properties in addition to its other versatile uses, it can be safely used in herbal medicines, tonics for diabetic patients and in daily usage products such as mouthwashes and toothpastes, moreover mild *S. rebaudiana* leaf tea offers excellent relief for an upset stomach⁷⁸⁻⁸⁰.



FIG. 2: *STEVIA REBAUDIANA* PLANT⁷⁷

Description and Ethanobotanical uses of *Otistiga integrifolia*: *O. integrifolia* plant locally known as “Tinjut” in Amharic, belongs to the family Lamiaceae. It is endemic to Ethiopia in different parts of the country in the dry and moist agro climatic zones. The blade is bluish greyish-green, oblanceolate to lanceolate shaped, and reaches 2-9 cm long **Fig. 3**. The plant grows in the wild but is also cultivated in gardens. It grows on montane bush lands and wood lands over grazed slopes at altitudes ranging from 1,300 to 2,800 m. The plant is endemic to Ethiopia, Eritrea and Yemen⁸¹. In Ethiopian folk medicine, the leaves of the stated medicinal plant have been utilized to treat DM by the community. As cited by a study, several studies also confirmed the uses of *O. integrifolia* as having an ophthalmic, mosquito repellent, antimicrobial, anti-diabetic as well as antioxidant activities both in naturally as well as scientifically⁸²⁻⁸⁴.



FIG. 3: *OTOSTEGIA INTEGRIFOLIA* PLANT⁸⁵

Description and Ethanobotanical uses of *Moringa stenopetala*: *M. stenopetala* is commonly known as the African Moringa or cabbage tree, there are different local names in Ethiopia communities called Haleko’ in Gofa and Wolayta areas, ‘Shelagta’ in the Konso language, ‘Shiferaw’ in Amharic⁸⁶ **Fig. 4**. Over 5 million people depend on *M. stenopetala* as a vegetable source in southern Ethiopia⁸⁷. It is a deciduous tree in the flowering

plant genus *Moringa*, native to Kenya and Ethiopia. A drought-resistant species, it is characterized by its bottle-shaped edible leaves likened to cabbage, from which its common name is derived. *M. stenopetala* grown in Ethiopian Highlands, mainly in the Konso region, the Dirashe and Burji people in southern Ethiopia use it to relieve indigestion and for treating dysentery⁸⁸. Around Arba Minch, a town in southern Ethiopia, the decoction of leaflets and roots of *M. stenopetala* is used for treating malaria, diabetes, hypertension, asthma, common cold, wound, stomach problem, to expel retained placenta⁸⁹.

The different parts of this medicinal plant have locally been utilized by Ethiopian communities to manage diseases like malaria, hypertension, asthma, diabetes, stomach pain. Various literatures reports showed that the uses of this plant as anti malarial, antileishmanial and antifertility, hypertensive, antihypertensive, hypoglycemic, antimicrobial and antidiabetic effects⁹⁰.



FIG. 4: *MORINGA STENOPETALA* PLANT⁸⁶

Description and Ethanobotanical uses of *Meriandra dianthera*: *M. dianthera* (Roth.) locally known as “mesaguh” (Tigrigna) is a branched aromatic shrub which grows up to 2 m in height. It is native to the high plateau of Ethiopia, Eritrea, Yemen, and Saudi Arabia⁹¹ **Fig. 5**. *M. dianthera* has wider applications in the treatment of diabetes and other ailments in the traditional medical practices of the communities in the Central and Southern Zones of Eritrea. An ethnobotanical study in Saharti samire, Southern part of Tigray, Ethiopia showed the uses of this plant for management of hypertension and diarrhea⁹². The leaf extract of *M. dianthera* is widely used as a folk medicine for the treatment of malaria, diabetes, diarrhea, ascariasis, and hypertension⁹²⁻⁹³.



FIG. 5: MERIANDRA DIANTHERA PLANT⁹⁴

Description and Ethanobotanical uses of *Dillenia indica*: *D. indica*, commonly known as elephant apple. It is found in tropical and subtropical evergreen or rain forests altitude up to 2500ft. *D. indica* grows in areas where annual daytime temperatures are within 30-40°C, but can tolerate 7- 47°C Fig. 6. It prefers a mean annual rainfall in the range 3,000–4,000mm but tolerates 2000–5,500mm. Grows best in a rich, slightly acid soil. It prefers a well-drained sandy loam and sunny weather⁹⁵. The leaves and fruits of *D. indica* have been traditionally used to cure diseases like fever, constipation on, dysentery and stomach-ache⁹⁶. Leaves of *D. indica* are used as an astringent. Various dosage forms can also be made from the leaves like paste, poultice, decoction, powder which can be used in bone fracture, bleeding piles, skin diseases, body ache and breast cancer⁹⁷. The fruit is said to possess tonic laxative properties and used for relieving abdominal pain. The bark and leaves are use as astringent⁹⁸. Its fruit juice is also used as cardio tonic. Barks and leaves of the plant are used as laxative and astringent. Due to its various biological activities including anti-diabetic and anticancer properties making the plant is very important or valuable medicinal plant⁹⁹.



FIG. 6: DILLENIA INDICA PLANT¹⁰⁰

Description and Ethanobotanical uses of *Allium sativum*: *A. sativum* L. Fig. 7, commonly known as

garlic, locally called Nech shinkurt (in Amharic). It belongs to the family Amaryllidaceae¹⁰¹. The bulb is mostly used to treat ailments and the perennial herbaceous plant is large, with upright flowering stems that extend up to 1 m¹⁰². Its medical benefits have been documented in Sanskrit texts dating back about 5,000 years and it first appeared in traditional Chinese medicine at least 3,000 years ago^{101, 103}.

A. sativum have been used in traditional medicine of Iran and other countries for a long time¹⁰⁴. In the pre-antibiotic era, allicin (62) Fig. 7 can kill bacteria via the gas phase and was used to successfully treat many lung-pathogenic bacteria such as tuberculosis from crushed garlic preparations through breathing in the vapor¹⁰⁵. Garlic's promising therapeutic advantages in ethnomedicine include its application against hypertension, pneumonia, hair loss, snakebite, diabetes, wounds, cough, paralysis, scabies, malaria, hemorrhoids, carbuncles, heart diseases, asthma, pain, respiratory disorders, influenza, female infertility, etc. which are mainly attributed to its antidiabetic, antiatherosclerotic, antimicrobial, antihypertensive, anticancer, cardioprotective, diuretic, aphrodisiac, sedative, carminative, and antipyretic properties evidenced by various studies¹⁰⁶.



FIG. 7: THE ALLIUM SATIVUM PLANT¹⁰¹

Description and Ethanobotanical uses of *Momordica charantia*: *M. charantia* is a member of the Cucurbitaceae family. The plant makes green berry-like fruits that become yellow-orange when ripe and light or white-yellow monoic flowers Fig. 8, it is a terrestrial that stands out for its long, pubescent tendrils that are simple and lengthy as well as a slender, grooved, and green herbaceous stem¹⁰⁷. The actinomorphic venation pattern on the simple, alternating, membranous leaves has right lateral insertion. Moreover, their cross section is

obtuse-quadrangular¹⁰⁸. *M. charantia* used by tribal people for abortions, birth control, increasing milk flow, vaginal discharge, menstrual disorders, constipation, food, hyperglycemia, diabetes, jaundice, stones, kidney, liver, fever (malaria), eczema, gout, fat loss, hemorrhoids, hydrophobia, intestinal parasites, skin, pneumonia, leprosy, psoriasis, rheumatism, scabies, piles, snakebite, vegetables anthelmintic and purgative¹⁰⁹⁻¹¹⁰.



FIG. 8: THE MOMORDICA CHARANTIA PLANT¹⁰⁷

Description and Ethanobotanical uses of *Ajuga remota*: *A. remota* Benth is belongs to the Family Lamiaceae and in Ethiopia it is known by different local names such as Armaguusa (in afan oromo) and Akorarach (in Amharic) **Fig. 8**. It often lying on the ground and rooting at the nodes, covered with soft hairs, stems growing to 40 cm high. It occurs in different regions of Ethiopia at an altitude of 1600-2200 m. flowering from late August to October, honeybees collect pollen and nectar from the flowers¹¹¹. It has a very bitter taste, leaves moderately to densely hairy, grayish green, simple, and flowers pale blue, pale violet, light blue or white¹¹² **Fig. 9**. In the Ethiopian traditional medicine, the fresh or dried leaves of *A. remota* was infused with water and sometimes with Alcohol, locally called “Arekie”. The infusions are used as remedy to heal diseases such as diabetes, malaria, pain and fevers, toothache, hypertension, stomachache, and pneumonia etc¹¹³⁻¹¹⁵.



FIG. 9: THE AJUGA REMOTA PLANT¹¹¹

Evaluation of Antidiabetic Potential of Extract from the Selected Medicinal Plants: To make clear the status quo on antidiabetes of these medicinal plants, we performed a thorough literature review by using electronic databases. Specific keywords include “scientific name of species” and “diabetes” until 2021. The important parts of the species were searched about their antidiabetes including traditional use, in vitro assay, *in-vivo* animal studies, clinical trials, and antidiabetic constituents¹¹⁶.

Evaluation of Antidiabetic Activities of Extract from *Stevia rebaudiana*: The studies revealed that different concentrations of stevia extract had a good efficacy in controlling diabetes with an excellent control of random and fasting blood glucose level in diabetic rats at study period of 8 weeks. According to another study, stevia extract was found to contain some biomolecules that may sensitize the insulin receptor to insulin or stimulates the β -cells of islets of langerhans to release insulin which may finally lead to improvement of carbohydrate metabolizing enzymes towards the reestablishment of normal blood glucose level¹¹⁷. A similar study reports showed that the leaves extract of *S. rebaudiana* decreased the random and fasting blood glucose levels of rats by revitalizing the β -cells of pancreas thus reactivated the glycogen synthase system by improving insulin secretion and liver glycogen level¹¹⁸⁻¹²⁰. Another *in-vivo* experiments it has found that show *S. rebaudiana* increases glucose tolerance in diabetic rats by maintaining the blood glucose level¹²¹. According to the reports of stevioside (20) **Fig. 10** a natural sweetener isolated from leaves of *S. rebaudiana* which increases the insulin level by affecting the β -cells of the pancreas and lowers the blood sugar levels¹²². The reports also showed that the leaf extracts of Stevia lower random blood sugar levels, decreased fasting blood glucose level and glycosylated hemoglobin (5.32%) amount in streptozotocin-induced diabetic albino rats. An improved level of insulin and liver glycogen in diabetic samples has also been observed after eight weeks of treatments¹²³.

Evaluation of Antidiabetic Activities of Extract from *Otistiga integrigolia*: Reports showed that the leaf extract *O. integrigolia*, is a good natural anti-oxidant that can be used as health-promoting

agent for various disorders including DM⁸⁵. Another reports also showed that in the experiment, 80% *O. integrifolia* leaf extract induced hyperglycemic rats. The same study revealed, maximum anti-diabetic, hypoglycemic and oral glucose tolerance activities 200mg/kg in treated mice. Thus 200 mg/kg was the dose that lowered the high glucose level in streptozotocine-induced diabetic mice which is close to the normal range like the standard drug glibenclamide. With regard to safety and toxicity profile the methanolic leaf extract was found to show no mortality or any adverse side effects up on the experimental animals up to the dose of 500mg/kg¹²⁴.

Evaluation of Antidiabetic Activities of Extract from *Moringa stenopetala*: The crude aqueous/ethanol extract and fractions of the leaves of *M. stenopetala* have been reported to have both hypoglycemic and antihyperglycemic effects¹²⁵. Moreover, chronic administration of the n-butanol fraction of ethanol extract of leaves in alloxan-induced diabetic mice showed antihyperglycemic and antihyperlipidemic effects with wide margins of safety, indicating its potential for long term management of diabetes and dyslipidemia through enzyme inhibition mechanisms¹²⁶. According to the reports aqueous ethanol and n-butanol extracts of *M. stenopetala* leaves 500 mg/kg significantly decreased BGL ($P < 0.05$) in STZ-induced rat model after 14 days. The extracts also reported to lower postprandial BGL ($P < 0.001$) at 750 mg/kg dose¹²⁷.

The leaves extract of *M. stenopetala* also found to show significant ($P < 0.05$) decrease in BGL with dose-dependent manner in the same model. The findings indicated that the extracts of *M. stenopetala* produced potential antihyperglycemic effects due to various descriptions. It produced regeneration/proliferation of the pancreatic β -cells possibly due to the prevention of free radical formation¹²⁷⁻¹²⁸. In another investigation also done to describe the antiglycation effect of hydroalcoholic leaves of this plant extract in bovine serum albumin (BSA)/fructose method showed a significant (< 0.05) inhibited advanced glycation end products formation by $54.75 \pm 0.94\%$ at 2 mg/ml. Moreover, the extract was found to decrease concentration of fructosamine, formation of N ϵ -(carboxymethyl) lysine (CML), and the

extent of amyloid cross β -structure in fructose-induced BSA glycation test¹²⁹.

Evaluation of Antidiabetic Activities of Extract from *Meriandra dianthera*: A report showed that the antidiabetic activities of methanol leaf extracts of this medicinal plant by administering 200 and 400 mg/kg doses of the extract orally in diabetic induced experimental rats. The methanolic extract resulted in a dose-dependent lowering of FBG levels and the result exhibited very significant decreases ($P < 0.001$) in fasting blood glucose level by the end of the experimental day as compared to the diabetic control. The extract at 400 mg/kg concentration was found to produce significant antihyperglycemic effect which is comparable to standard drug.

An OGTT on normal rats also indicated that the hyperglycemia with glucose challenge was significantly brought down ($P < 0.001$) by the plant extract at 60 and 120 min relative to the negative control 130. The methanol leaf extract of *M. dianthera* also showed a fall in blood glucose after oral administration of the extract in normal rats¹³⁰. This might be attributed to the presence of hypoglycemic bioactive molecules like flavonoids, terpenoids, alkaloids or saponins contained within the leaf plant¹³⁰. Reports also showed that administration of metformin to diabetic rats resulted in increase in the body weight compared to diabetic control rats; this suggests that metformin treatment has positive effect on maintaining body weight. However, diabetic rats treated with plant extracts at doses of 200 and 400 mg/kg per body weight showed decrease in body weight but it was significant improvement as compared to the body weight of the diabetic control group. Moreover, the methanol extracts of *M. dianthera* showed significant change ($P < 0.05$) in body weight compared to the normal control group¹³¹.

Evaluation of Antidiabetic Activities of Extract from *Dillenia indica*: Literature reports showed *D. indica* produced significant attenuation in the glycemic status, lipid profile and level of antioxidant enzymes proving efficacy in diabetic nephropathy¹³². It has also been found to decrease in the glycemic condition, renal parameter, lipid profile and antioxidant enzymes level proving its efficacy in diabetic nephropathy. Reports also

showed *D. indica* ethyl acetate fraction shows prominent antidiabetic effect in experimental type-1 and type-2 diabetes models in rats¹³³. *D. indica* showed significant inhibition of AGEs formation *in-vitro*. *D. indica* produced significant attenuation in the glycemic status, lipid profile and level of antioxidant enzymes proving efficacy in diabetic nephropathy¹³⁴. Daily oral administration of *D. indica* methanol extract (250 and 500 mg/kg body weight) and glibenclamide (10mg/kg) showed beneficial effects on blood glucose level ($P < 0.001$) as well as improving kidney, liver functions and hyperlipidaemia due to diabetes as reported by¹³⁴⁻¹³⁵. Also alcoholic extract of *D. indica*, chromane (45) **Fig. 14**, isolated, which possessed antioxidant and antidiabetic activity and could be a therapeutic agent for regulating several pharmacological targets for management of diabetes¹³⁶.

Evaluation of Antidiabetic Activities of Extract from *Allium sativum*: Among different antidiabetic plants, *A. sativum* L. (garlic) is one of the main accepted herbs. Chemical analyses due to it is a main resource of sulfur holding compounds, predominantly S-alk-(en)yl-L-cysteine sulphoxides (Cs), being alliin the foremost one¹³⁷. Volatiles such as allicin and lipid-soluble sulphur compounds such as diallyl disulphide, diallyl sulphide, ajoene, dithiins, diallyl trisulphide attributed typical odour, taste, as well as biological and therapeutic properties to *A. sativum* L. It is used as an anti-diabetic mediator¹³⁸.

Reports showed that ability of *A. sativum* L. to trap glucose determines its antidiabetic efficacy. At certain intervals, the effects of extracts to prevent glucose diffusion into the external solution (I1:5, I2:10, I3:20, I4: 40g/L) were examined¹³⁹. 15 mL of a glucose and NaCl (0.15M) solution were added to a dialysis tube (6 cm–15 mm), and the amount of glucose that appeared in the external solution was calculated. A centrifuge tube holding 45mL of 0.15M NaCl and a sealed tube was used. At room temperature, the tube was put on an orbital shaker. The glucose oxidase kit technique was used to test glucose concentrations. Using the trapezoidal rule, incremental areas under the glucose curves (AUC) were determined¹⁴⁰. The highest control concentration of glucose movement out of the dialysis tube (18.2 mmol/L) in control was reached

at the conclusion of the research period. The passage of glucose across the membrane was restricted by *A. sativum* root extracts, and this action was dose-dependent. 20 g/L extracts considerably slowed down the membrane's ability to transport glucose, and the observed 12.4 mmol/L glucose levels reflected a 31.86% drop in overall glucose diffusion compared to the control ($p < 0.05$). In a similar vein, 40 g/L ginger showed a 42.30% decrease in glucose transport as compared to the control group, which had external glucose concentrations of 10.5 mmol/L ($p < 0.05$). *A. sativum* extracts at concentrations of 5 g/L (I1) and 10 g/L (I2) have negligible capacity to obstruct glucose transport. Average final glucose concentrations (mmol/L) in external solutions for I2 and I1 were 14.6 and 15.7, respectively¹⁴¹.

In comparison to the control, every extract reduced the amount of glucose that could cross the dialysis membrane. Reports also showed that the findings can be supported by a number of processes. Plant fibers have two effects on glucose: first, they make glucose more viscous and prevent it from diffusing, and second, they bind glucose and slow down its transit through membranes¹⁴². Despite the fact that the precise mechanisms through which *A. sativum* effected its hypoglycemic effects remain unclear. However, *A. sativum* fiber's capacity to slow absorption unquestionably has a significant impact on how carbohydrates are metabolized¹⁴³.

Evaluation of Antidiabetic Activities of Extract from *Momordica charantia*: According to various studies showed on animals have frequently demonstrated the hypoglycaemic effects of *M. charantia* seeds, fruit pulp, leaves, and the entire plant in normal animals. animal studies have repeatedly shown hypoglycaemic effects of the seeds, fruit pulp, leaves and whole plant of *M. charantia* in normal animals¹⁴⁴. For instance, *M. charantia* extract can increase insulin sensitivity and lipolysis in rats improve glucose tolerance, and reduce postprandial hyperglycemia¹⁴⁵⁻¹⁴⁶. Some studies also claimed that the hypoglycaemic effect of *M. charantia* was comparable with oral medications such as tolbutamide, chlorpropamide and glibenclamide¹⁴⁷. Activation of the AMP-activated protein kinase system and the role of α - and γ -peroxisome proliferator-activated receptors (PPAR α and PPAR γ), which are crucial in lipid and

glucose haemostasis and may reduce insulin resistance, are recurring themes in the abundant biochemical data that have illuminated potential mechanisms of the anti-diabetic actions of *M. charantia*¹⁴⁸. An earlier study on the development of diabetic cataracts demonstrated that blood sugar level-dependent cataract formation was slowed down by the consumption of bitter melon fruit extract in association with better glucose homeostasis¹⁴⁹. Different reports showed animal studies have repeatedly hypoglycaemic effects of the seeds, fruit pulp, leaves and whole plant part in normal animals¹⁵⁰⁻¹⁵². Clinical research on the hypoglycaemic effects of *M. charantia* has been few and inconsistent compared to animal trials. In 1956, Lakholia, a doctor, likely became the first to record the beneficial effects of bitter melon using himself as the subject¹⁵³.

Evaluation of Antidiabetic Activities of Extract from *Ajuga remota*: Different investigations revealed the antidiabetic activity of *A. remota* Benth in alloxan diabetic mice¹⁵⁴. The fasting mean BGL of alloxan-induced mice model treated with aqueous leaves extract 300 and 500 mg/kg and ethanol extract 300 and 500 mg/kg was reported to be reduced by 27.96%, 38.98%, 28.09%, and 28.25%, respectively (P<0.05)¹⁵⁴ and STZ-induced diabetic rats¹⁵⁵. Another investigation showed the hypoglycemic effect of this plant in alloxan-induced mice model. Aqueous extract of leaves 300 and 500 mg/kg decreased BGL by $27.83 \pm 2.96\%$ and $38.98 \pm 0.67\%$ (<0.0001), respectively. Seventy percent ethanol extract 300 and 500 mg/kg also caused a reduction of $27.94 \pm 1.92\%$ and $28.26 \pm 1.82\%$ (<0.05), respectively¹⁵⁶. According to reports, the ethanolic leaves extract of *A. remota* can lower blood sugar levels in a rat model of STZ-induced diabetes. On the 21st and 14th days of therapy, the doses of 200 and 400 mg/kg ethanol leaves extract substantially (P< 0.05) lowered fasting BGL on the 21st and 14th day of treatment, respectively. Steroids, phenols, flavonoids, tannins, saponins, diterpenoids, phytoecdysteroids, and glycosides were major secondary metabolites that were believed support the antidiabetic activities of this MP¹⁵⁷.

Phytochemical with Antidiabetic Activities of Medicinal Plants: Natural products are promising

lead compounds for discovering and also easily available, affordable and tolerable¹⁵⁸⁻¹⁵⁹. Bioactive compounds produced by plants, some of which have anti-diabetic properties, may be found in plants. Either a single component or a combination of phytochemicals are believed for the action. Alkaloids, phenolics, flavonoids, glycosides, saponins, polysaccharides, stilbenes, and tannins may be the primary phytochemicals with anti-diabetic effects¹⁶⁰. Phytochemical investigation of current review showed the presence of this component in most studied plants. Several animal studies reported a wide variation in composition between the extraction methods. Phytochemical compositions are also highly dependent on several endogenous and exogenous factors, environment, genetics, and plant part used, growing, drying, and storing conditions¹⁶¹.

Compounds Isolated from *Stivia rebaudiana* and Evaluation of Their Antidiabetic Activities: The reports showed that Centaureidin (15) is flavonoid having antiproliferative effects isolated from *S. rebaudiana*¹⁶². The flavonoid heteroside quercitrin (quercetin-3-O-rhamnoside) (16) was isolated from *S. rebaudiana* as documented in the anti-inflammatory activity Quercitrin (17), showing antidiabetic activity and Quercetin-3-O-B-DGlc (18) having anti-plasmodium in addition to antidiabetic activities of *S. rebaudiana*^{148, 163}. Others which are Apigenin-4-O-glucoside (19) and Xanthine (20) oxidase inhibition which having antioxidant activities¹⁶⁴ **Fig. 10.**

Isolation of glycosides such as, rebaudioside A (21), rebaudioside B (22), rebaudioside D (23) and Stevioside (24) has been reported for the leaves of this plant species¹⁶². So, it is relatively safe for human health, especially for people with diabetes. The therapeutic value of compound stevioside (26) shows that was that it can stimulate insulin secretion in the pancreas during the treatment of diabetic patients and reduce other carbohydrate metabolism disorders¹⁶⁵. Rebaudioside A (21) which are responsible for the typical sweet taste. Literature reports also showed that steviol glycosides possesses additional activities such as antioxidant, mutagenic and bactericidal, antiviral, gastro protective, and their effectiveness on renal function, blood pressure and blood glucose¹⁶⁶⁻¹⁶⁷.

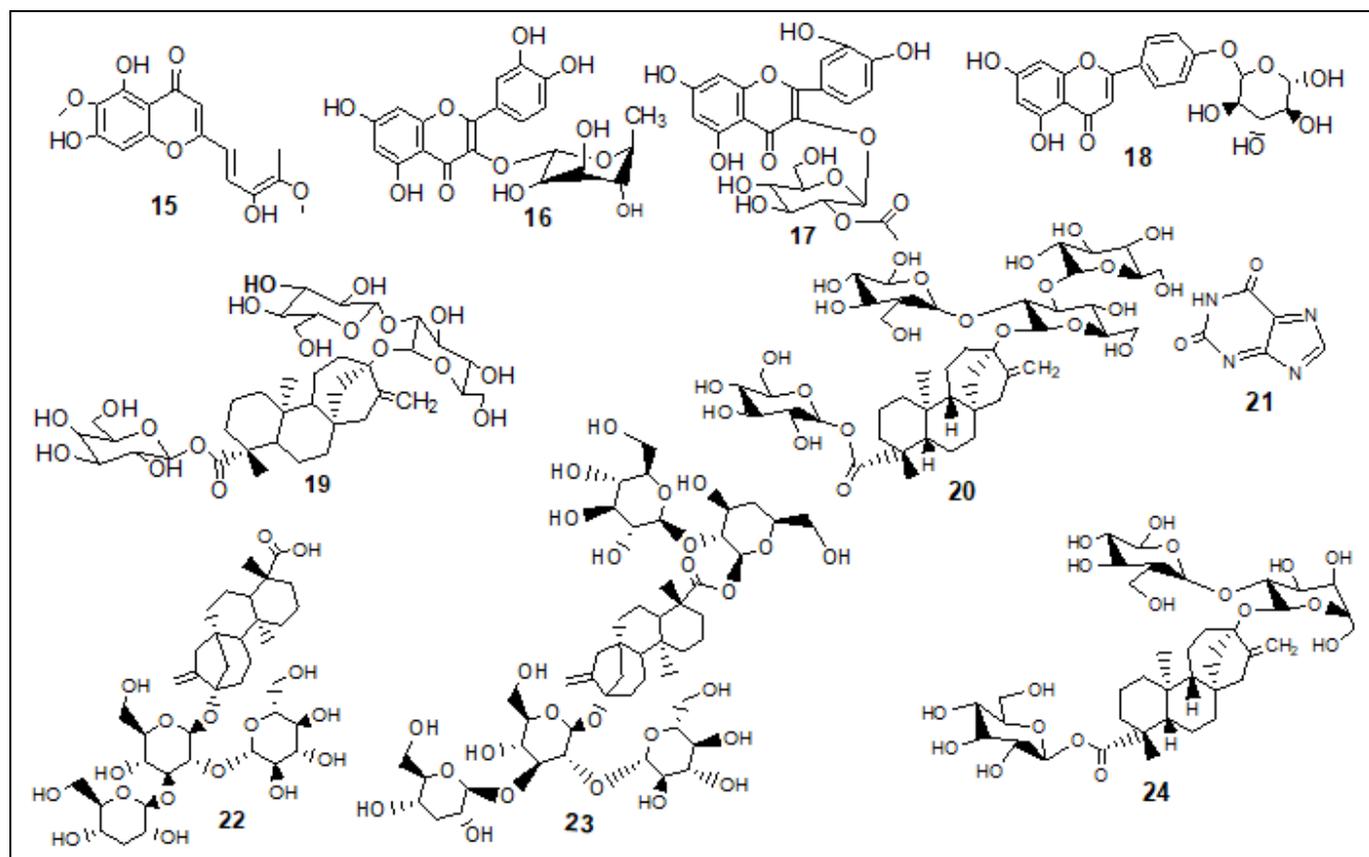


FIG. 10: THE CHEMICAL STRUCTURES OF COMPOUNDS (15-24) ISOLATED FROM *STIVIA REBAUDIANA*

Compounds Isolated from *Otostegia integrifolia* and Evaluation of Their Antidiabetic Activities:

The major component isolated includes (+)-axinyssene (25), pentatriacontane (26) and otostegindiol (27) ¹⁶⁸ Fig. 11. Chromatographic technique were used to detect the presence of

essential oil and chloroform extract of air-dried leaves of *O. integrifolia* of secondary metabolites such as alkaloid compound, dihydroedulan (28) and triterpene stigmasterol (29) reduced hyperglycemic effects and therefore could be used as a supplement in diets for diabetic patients ¹⁶⁸⁻¹⁶⁹ Fig. 11.

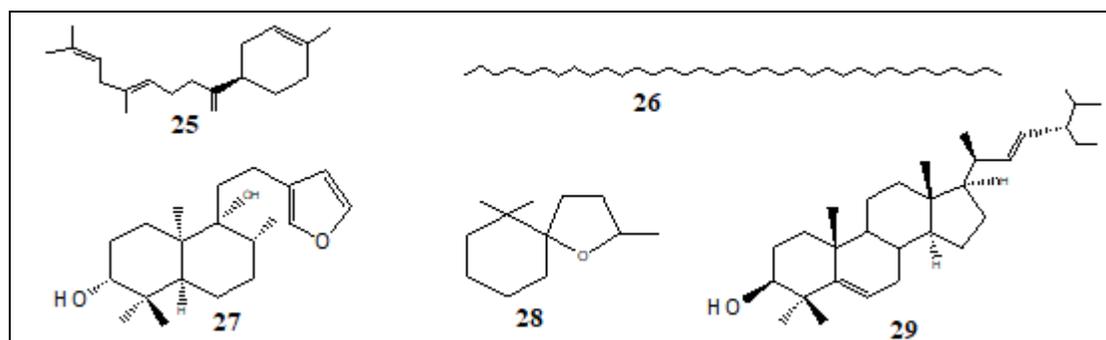


FIG. 11: THE CHEMICAL STRUCTURES OF COMPOUNDS (25-29) ISOLATED FROM *OTOSTEGIA INTEGRIFOLIA*

Compounds Isolated from *Moringa stenopetala* and Evaluation of their Antidiabetic Activities:

Phytochemical screening tests on the crude aqueous leaf extracts and butanol fraction of *Moringa stenopetala* detect the presence of alkaloids, saponins, polyphenols, flavonoids, coumarins, terpenoids, anthraquinones, tannins, phytosterols and cardiac glycosides and the presence of all the

secondary metabolites except saponins in 70% alcohol fractions ¹⁷⁰. Rutin (30), which is the marker component, was isolated from the leaves of *M. stenopetala* leaves ¹⁷¹ Fig. 12. The other four based on the literature reports physical properties and spectroscopic (IR and NMR) data the chemical structures of the compounds such as 4-acetylramnosyloxy-benzaldehyde (31) cholest-5-

en-3-ol (32), n-octacosane (33), palmitic acid (34), and oleic acid (35) which are isolated from acetone extract of root wood of *M. stenopetala* by produced the highest activity against *E. coli*¹⁷¹ and studies

showed that both rutin (30)¹⁷² and 5-cholestenone (32) have dietary additive with anti diabetic activities¹⁷³.

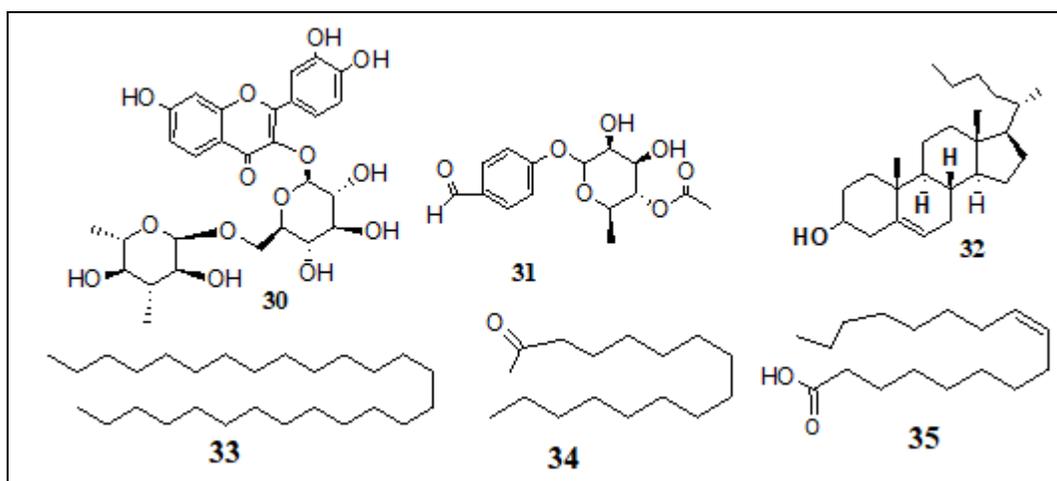


FIG. 12: THE CHEMICAL STRUCTURES OF COMPOUNDS (31-36) ISOLATED FROM *MORINGA STENOPETALA*

Compounds Isolated from *Meriandra dianthera* and Evaluation of their Antidiabetic Activities:

A total of 44 compounds, representing 89.2% of the total oil, could be identified. *M. dianthera* the essential oil was characterized by a high content of oxygenated monoterpenes (76.2%). Camphor (36) was the major constituent in the volatile oil followed by 1,8-cineole (37), camphene (38), borneol (39), lionene (40), camphenilone (41), P-Cymene (42) and Tricyclene (43) which are

isolated from the leaves part of *M. dianthera*¹³¹ **Fig. 13.** 1,8-Cineole (44) was studied for its anti-inflammatory activity by cell line method using murine lung alveolar macrophage¹⁷⁴. (36) was found to possess antidiabetic effects in alloxan-induced diabetic rats. Moreover, treatment of diabetic rats with camphor (36) was found to increase antioxidant capacity and reduces the oxidative stress markers in the liver, pancreas, and kidney tissues as compared to the diabetic rats¹⁷⁵.

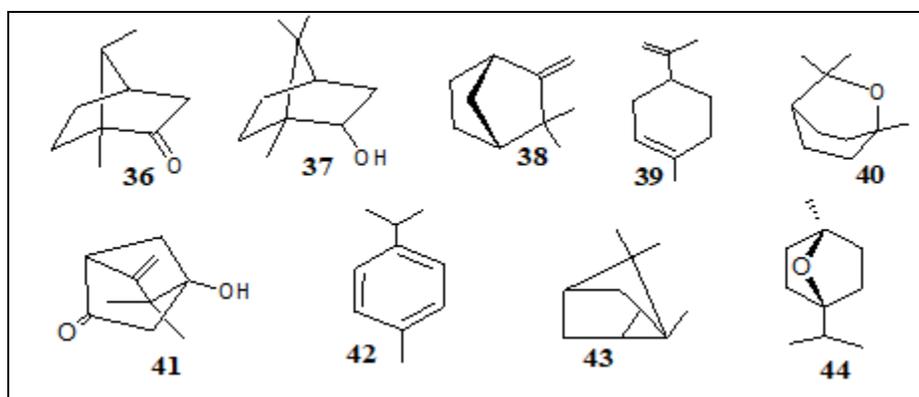


FIG. 13: THE CHEMICAL STRUCTURES OF COMPOUNDS (37-44) ISOLATED FROM *MERIANDRA DIANTHERA*

Compounds Isolated from *Dillenia indica* and Evaluation of their Antidiabetic Activities:

The reports showed that the ethanol extract of stem bark afforded two flavonoids viz., kaempferol quercetin (17) **Fig. 10** and glucoside (45) as well as a triterpenes derivative such as Lupeol (11) and betunaldehyde (46)¹⁷⁶. The reports revealed isolation of betulinic acid (47) and has been

described as a potential antidiabetic agent of interest for the T2DM¹⁷⁷. Leaves of *D. indica* found to contain flavonoids, triterpenoids, steroids, tannins; its petroleum ether extract afforded cycloartenone (48), n-hentriacontanol (49), sitosterol (50), and betulin (51)¹⁷⁸. Six antidiabetic compounds were isolated from the leaves *D. indica* such as, n-heptacosan-7-one (52), n-

nonatriacontan-18-one (53), quercetin (17), β sitosterol (54), stigmasterol (55), and stigmasteryl palmitate (56) **Fig. 14**¹⁷⁹⁻¹⁸⁰. The reports showed the presence others flavonoids such as dillenetin (57), 3,4,5,7-tetrahydroxy-3 -methoxyflavanone (58) and 3,5,7-trihydroxy-3,4 -dimethoxy-flavone (59) from *D. indica* The flavonoids of 3,5,7-

Trihydroxy-2-(4'-hydroxy-benzyl)-chroman-4-one (60) was obtained from the leaves part of *D. indica* L. quercetin (17) and Chroman (61) have antidiabetic activities 135-136,¹⁷⁶ **Fig. 14**. Several studies have described its effects on absorption and uptake of glucose, insulin resistance and insulin sensitivity^{135, 181-182}.

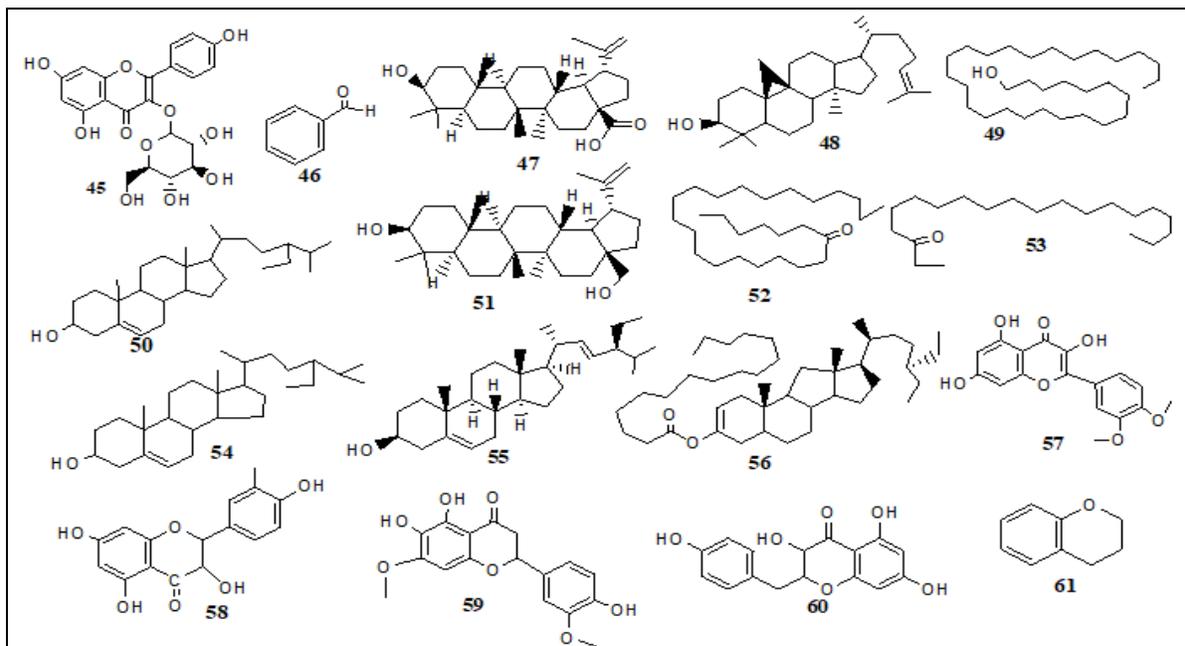


FIG. 14: THE CHEMICAL STRUCTURES OF COMPOUNDS (45-61) ISOLATED FROM *DILLENIA INDICA*

Compounds Isolated from *Allium sativum* And Evaluation of their Antidiabetic Activities: *A. sativum* bulbs are reported to have many bioactive compounds, many of which are sulfur-containing such as squallicin (62), aliin (63), ajoenes (E-ajoene (64), Z-ajoene (65), diallyl disulfide (66), diallyl sulfide (67), 3-vinyldithiin (68), diallyl disulfide (69)¹⁸³, S-allyl- cysteine (70), S-allylmercaptocysteine (71), and so on. These

constitute up to 82% of the total sulfur content in garlic¹⁸⁴. Caffeic acid (72)¹⁸⁵. Another molecules that include Diallyl tetrasulfide (73) and Allyl methyl trisulfide (74) and Quercetin (17) were obtained from *Allium sativum*¹⁸⁶ **Fig. 15**. Compound (72) has exhibited pharmacological, antioxidant¹⁸⁷, antiviral, anticancer¹⁸⁸, anti-inflammatory properties¹⁸⁹, and antidiabetic effect¹⁹⁰⁻¹⁹¹.

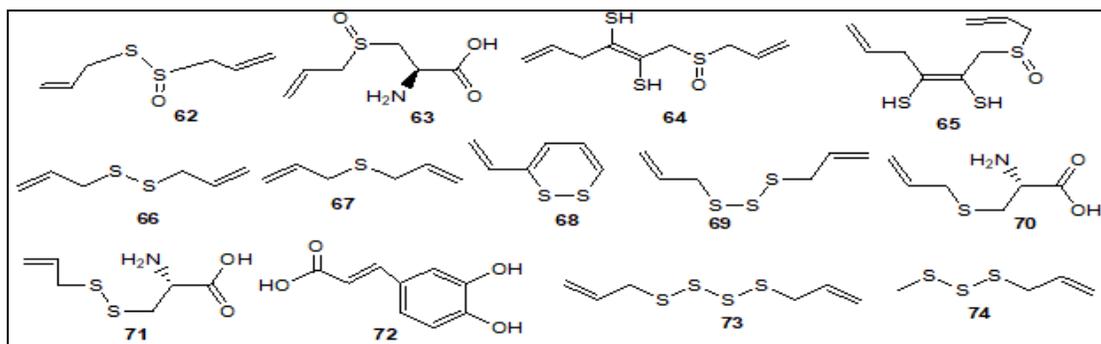


FIG. 15: THE CHEMICAL STRUCTURES OF COMPOUNDS (62-74) ISOLATED FROM *ALLIUM SATIVUM*

Compounds Isolated from *Momordica charantia* and Evaluation of their Antidiabetic Activities: From the literatures showed that secondary

metabolites of flavonoids such as myricetin (75); quercetin (17) has anti-diabetic activity, Kaempferol (76), Catechin (77)¹⁹².

Rutin (30) which have anti-diabetic potential 172, Phenolic compounds Caffeic acid (78) which antidiabetic effect 191, p-Coumaric acid (79) Ferulic acid (80) O-Coumaric acid (81), m-Coumaric acid (82) p-hydroxybenzoic acid (83) Gallic acid (84) Protocatechuic acid (85), Vanillic acid (86); Syringic acid (87); Gentic acid (88). Salicylic acid (89), Vanillin (90), Veratric acid (91), Naringenin (92), Homogentisic acid (93)¹⁹².

The Phenolic compounds of 4-Hydroxybenzoic acid (94), sinapinic acid (95), 2,4-bis (2-phenylpropan-2-yl) phenol (96), were isolated from the leaf and Stem part of the plant¹⁹³ **Fig. 16** some of the compounds have antidiabetic properties. For instance, Kaempferol (76), has been found to prevent the progression of “obesity–IR– β -cell apoptosis–diabetes–diabetic complications¹⁹⁴”.

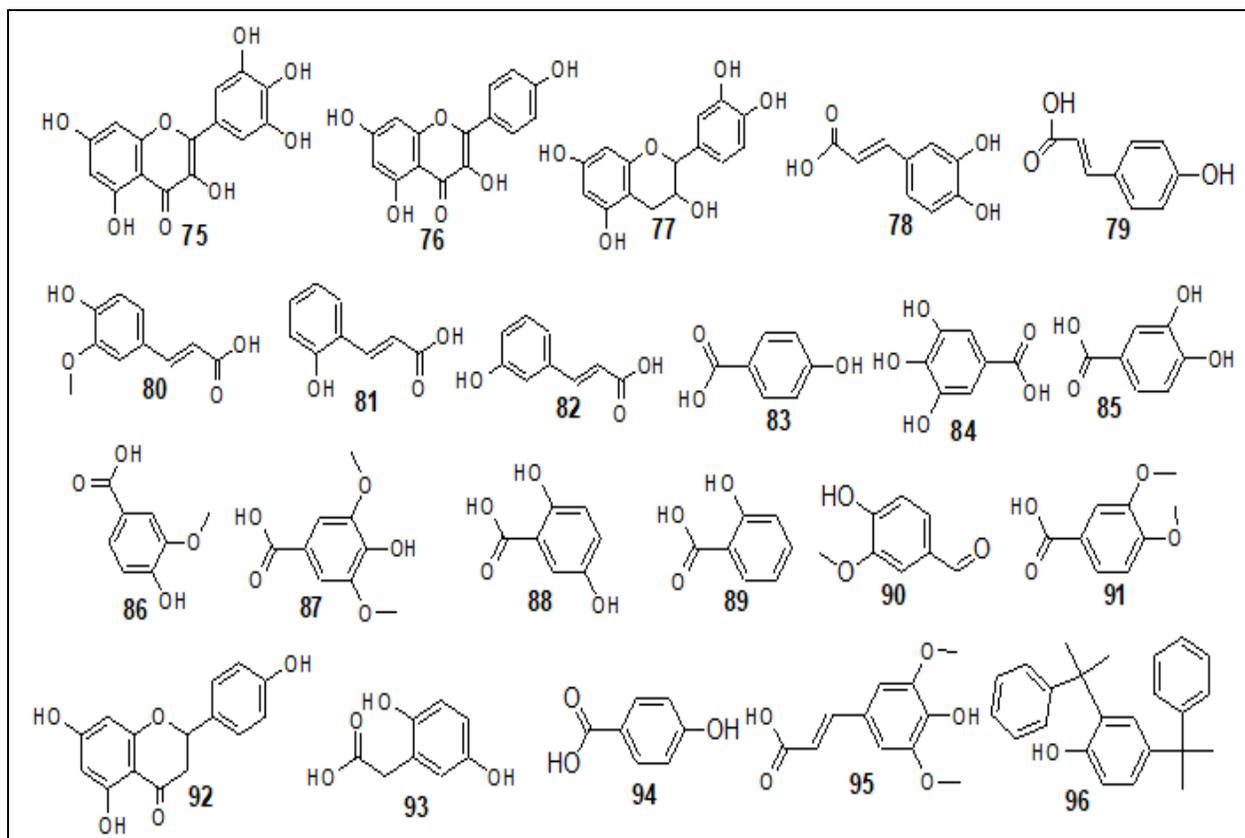


FIG. 16: THE CHEMICAL STRUCTURES OF COMPOUNDS (75-96) ISOLATED FROM *MOMORDICA CHARANTIA*

Compounds Isolated from *Ajuga remota* and Evaluation of their Antidiabetic Activities:

Phytochemical tests were carried out for the methanol extract of the plant using standard procedures.

Anthersneo-clerodanediterpene compounds namely Ajugarin I (97), Ajugarin II (98), and Ajugarin V (99) and clerodin (100) were, isolated and characterized from the leaves of *A. remota*. Bioactive compounds such as, ajugalactone (101), ergosterol-5, 8-endoperoxide and 8-O acetylharpagide (102) were also reported from this plant¹⁹⁵ **Fig. 17**.

Other compounds such as Myricetin 3-O-rutinoside 4'-O-rutinoside (103), Myricetin 3-O-rutinoside 3'-

O-rutinoside (104) and Isorhamnetin 3-O-rutinoside 7-O-rutinoside 4'-O- β -glucopyranoside (105) obtained from aerial part of *A. remota*¹⁹⁵ **Fig. 17**.

Flavonoids of epicatechin (106), tannin of catechin (77) **Fig. 16** and an alkaloid of vindoline (107) (were some of the documented compounds that were isolated from the plant with a potential to decrease the blood glucose level¹⁹⁶⁻¹⁹⁸).

Thus, the significant antidiabetic effect of the extracts of *A. remota* could be due to the presence of the above mentioned components in the extracts, which could act synergistically and/or independently to enhance the activity of glycolytic enzymes.

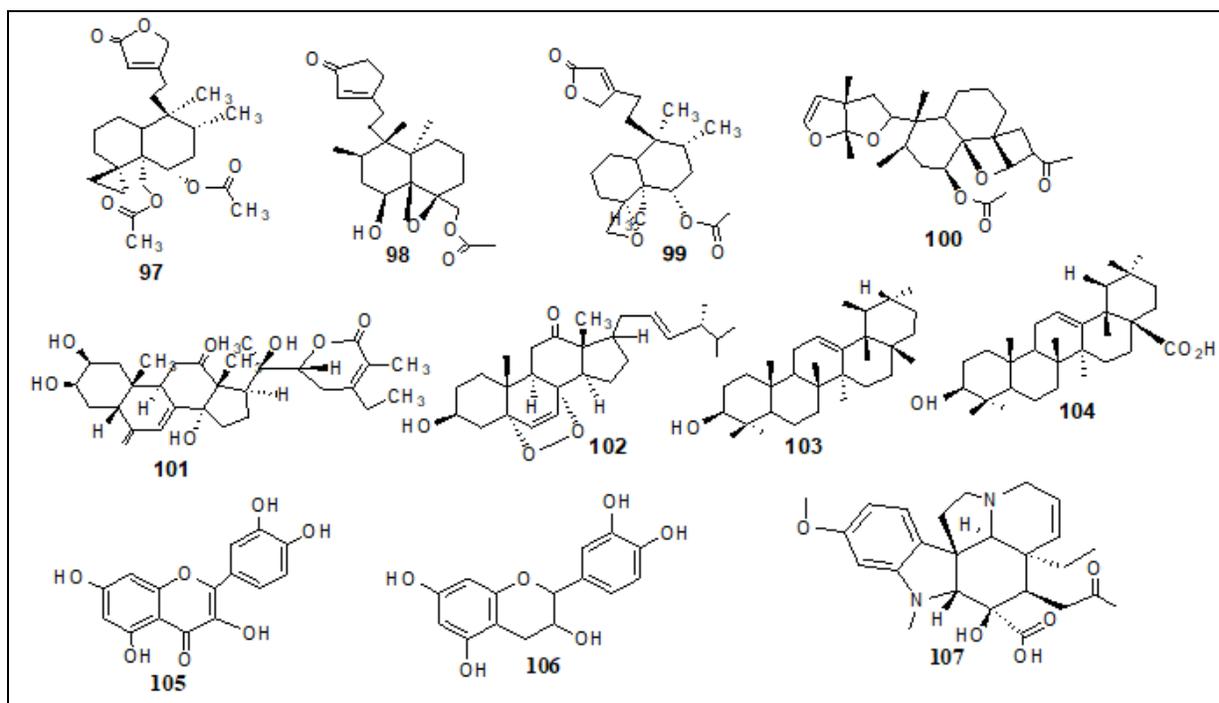


FIG. 17: THE CHEMICAL STRUCTURES COMPOUNDS (97-107) ISOLATED FROM *AJUGA REMOTA*

CONCLUSION: DM is a huge health, social, and economic burden because to its widespread occurrence, and it has been identified as a key factor in how patients', their families', and society's economies are affected. Desperate chronic problems including blindness, renal failure, and heart failure also result from unmanaged DM. Worldwide, the prevalence of DM is continuing to rise, and there are currently no proven effective medications for managing DM. The use of commercial oral hypoglycemic medications is becoming increasingly challenging because of their high prices and harmful side effects on the patient's health. In order to address the aforementioned issues, the search for efficient and secure medications from the accessible medicinal plants needs to be intensified.

In order to encourage or motivate interested researchers to find anti-diabetic prospective candidate pharmaceuticals from folk medicine that might cure or manage the patients and enable future self-reliance, it is also vital to document indigenous knowledge of medicinal plants. Moreover, herbal extracts can now be used with conventional medications for therapeutic purposes. Some plants include their own active components that help manage diabetic problems and blood sugar levels. A variety of animal models, including normoglycemic mice, mice given oral glucose,

mice induced with streptozotocin to become diabetic, and mice treated with alloxan to become diabetic, were used in Ethiopia to study the majority of medicinal plants with antidiabetic claims. The bulk of medicinal plants with antidiabetic claims were studied in Ethiopia using a range of animal models, including normoglycemic mice, mice given oral glucose, mice induced with streptozotocin to become diabetic, and mice treated with alloxan to become diabetic. The knowledge required to demonstrate the safety of the bioactive chemicals for the management of diabetes from Ethiopian medicinal plants is anticipated to be provided by this review.

In order to improve anti-diabetic activities, future research should concentrate on isolating and identifying bioactive components from medicinal plants. Ethiopian antidiabetic medicinal plant utilization is important for the future creation of new antidiabetic drugs. Finally, we suggest insuring future success in clinical research additional investigations on *in-vitro*, *in-vivo*, *ix-vivo*, and *in-silico* studies should be advised to confirm the anti-diabetic properties of crude extract and active isolated components from diverse medicinal plants.

ACKNOWLEDGEMENTS: The authors duly acknowledge Hawassa University and Vice

President for Research Technology Transfer (VPRTT) office of Hawassa University for the financial support to NS.

Authors also acknowledge Sathyabama Institute of Science and Technology, Jeppiaar Nagar, Rajiv Gandhi Road, Chennai- 600119, Tamilnadu, INDIA, for the support provided to NS to carry out laboratory experiments and all the necessary accommodations.

CONFLICTS OF INTEREST: The author declare no conflict of interest.

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How to cite this article:

Sintayehu N, Adane L, Swanalatha Y and Kumar CS: Antidiabetic activities and phytochemical constituents of selected medicinal plants from *Ethiopian flora*: a brief review. *Int J Pharm Sci & Res* 2026; 17(3): 824-47. doi: 10.13040/IJPSR.0975-8232.17(3).824-47.

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