1.1. Introduction

Natural products (NPs) have been used to combat human diseases for thousands of years; and therefore play a vital role in drug discovery and development (Thomford *et al.*, 2018). Most of the NPs with therapeutic efficacy are secondary metabolites. The underlying reason for NPs as sources of such a large proportion of existing drugs might be the similar interaction of NPs with biosynthetic enzymes and therapeutic targets (Nair and Jez, 2020). NPs provide greater structural diversity than standard combinatorial chemistry and thus they offer major opportunity for finding novel therapeutic leads that are active against a wide range of assay targets. Moreover, they contain higher numbers of chiral centers and greater stearic complexity than either synthetic drugs or combinatorial libraries. Generally, biologically active NPs with drug like properties are small molecules that are capable of being absorbed and metabolized by the body. In addition, the development costs of NPs as medicines are likely to be much lower than that of biotechnological products or compounds produced from combinatorial chemistry (Wright, 2019).

Plants are the basis of traditional medicine (TM) systems that have been used for thousands of years. The plant based TM system continue to play important role in healthcare and according to the report of World Health Organization (WHO), about 80% of the world's population rely mainly on TM for their primary health care. TM and ethnobotanical information have also played an important role in scientific research, particularly when the literature and field work data have been properly evaluated (Chaachouay *et al.*, 2019). A large number of plant derived NPs continue to be discovered on the basis of traditional or empirical local medical practices. Globally, about 80% of plant derived drugs have the same or related use as the plants from which they were derived and rest only 20% of plant derived drugs were discovered independently of medicinal folklore information. According to a report only 10% of the world's biodiversity has been tested for biological activity, still many more useful NPs are remains to be identified.

Plants are endowed with a variety of bioactive chemicals that may have a synergistic effect on plant biological activities. Thus, in order to identify safer drugs and synthesize pharmaceutically significant lead chemicals, it is essential to screen active substances and understand their chemical composition (Mariswamy *et al.*, 2011). With the emergence of several purification techniques and the isolation of pure compounds or phytochemicals, drug discovery might be facilitated. These compounds have been discovered to play a potential role in many pathway regulations and could be used as ligands for in silico drug design. Severel chromatography techniques, like column chromatography, thin layer chromatography, high performance liquid chromatography, flash chromatography and Sephadex chromatography have been used to separate bioactive substances for identification, quantification and characterization (Sasidharan *et al.*, 2011). Despite variations in the polarity of phytochemicals continue to pose a challenge for isolating pure compounds, several plant derived therapeutics NPs have been developed (Sheeja and Kuttan, 2007; Mukherjee *et al.*, 2007).

Recent trend of research based on bioactive plants to develop drugs for anticancer, antiviral, antiprotozoal, antidiabetic and cardiovascular diseases. The strategy for plant based NP drug discovery generally involves testing of plant extracts in appropriate in vitro assays (cytotoxicity/cytostatic or enzyme/target based), followed by bioassay-guided fractionation of the active extracts and isolation and purification of active constituents. Those constituents showing significant in vivo activity in appropriate animal models are considered as lead molecules which may be selected as candidates for preclinical development (Cragg *et al.*, 2005).

Several disease conditions are associated with increased production of free radicals through oxidation reduction mechanisms leading to oxidative stress to cause cellular damages (Ratnam *et al.*, 2006). To neutralize or balance the creation of free radicals, each individual is gifted with a sophisticated defense system that includes enzymes such as catalases, superoxide dismutase, glutathione peroxidase and glutathione reductase; or substances such as glutathione, vitamins E, C and others. Antioxidants are compounds that can counteract the negative effects of free radicals. Lowered levels of antioxidant on the other hand, result in the production of excessive free radicals, which can lead to a variety of diseases, including cancer, stroke, myocardial infarction, diabetes, septic and hemorrhagic shock, Alzheimer's and Parkinson's diseases (Tsao *et al.*, 2004; Pavelescu, 2015). Synthetic antioxidants such as butylated hydroxyl anisole, butylated hydroxyl toluene and others play a significant role in delaying or avoiding oxidative stress-related disorders, but they have a number of negative health effects (Sultana *et al.*, 2007).

Additionally, in current years, the incidence of deaths from infectious diseases has increased dramatically, as the reports on drug-resistant human pathogenic bacteria from throughout the world (Mahesh and Satish, 2008; Demiraslan and Uysal, 2016). Infectious disease management with plant-based antimicrobials has been proven to be successful in the past because unlike synthetic antimicrobials they generally lack the negative side effects. Furthermore, phytomedicines have a variety of effects in the body. *Hydrastis canadensis*, for example, not only has antimicrobial properties but also increases blood supply to the spleen, accelerating the discharge of mediators (Murray, 1995).

Diabetes mellitus (DM) is a global health problem affecting quite a number of people from all walks of life. In our country the current disease burden estimate is 25 million. According to ICMR report (2002), it is projected that by 2025 there would be 57 million diabetics in India, mainly those having Type-II diabetes. There appears to be a host of potential genetic, environmental and immunological risk factors that may be involved in the etiology and pathogenesis of these aberrations. Moreover, Type-II DM has been observed as a new epidemic among pediatric population and as in the adult population, Type-II DM in children and youth occurs as a result of insulin resistance coupled with relative β-cell failure. DM is still not completely curable by the present anti-diabetic agents. Insulin therapy is the only satisfactory approach in DM, even though it has several drawbacks like insulin resistance (Chen *et al.*, 2022), anorexia, brain atrophy and fatty liver in chronic treatment (Tsimihodimos *et al.*, 2018). DM is threatening because of the development of many severe secondary complications, including atherosclerosis, microangiopathy, renal dysfunction and failure, cardiac abnormalities, diabetic retinopathy and ocular disease (Shah *et al.,* 2021). TM is a fruitful source of future drugs to counteract insulin resistance, consistent with a resurgence of interest in drug discovery from NPs. For example, metformin is a biguanide derivative of guanide, originated from the plant Goat's Rue (*Galega officinalis*) as a structure-modified natural product to vastly improve its efficacy. A major advantage of TM is that they have been used to treat human diseases for many years and so there is considerable knowledge concerning in vivo efficacy and safety, two of the confounding problems facing other new chemical entities (Tan *et al*., 2008).

India is one of the twelve mega-biodiversity countries of the World having rich vegetation with a wide variety of plants with medicinal value with northeastern region being the biodiversity hotspot (Patrick, 2002; Saha *et al.,* 2011). The floristic wealth of north eastern region is nearly 43% of the country's total flora and good number of known and unknown medicinal plants are found in the forest of the Darjeeling district of West Bengal and the state of Sikkim, India (Mukherjee *et al.,* 2007). The tribal people of this region possess a great knowledge on the uses of medicinal plants for the treatment of various kinds of diseases, which includes wounds, diarrhea, dysentery, diabetes, jaundice and skin infection etc (Hussain *et al.,* 2008). Phytochemicals, such as phenolics, flavonoids and steroids have received a lot of attention in current years because of their antioxidative, antimutagenic, antidiabetic, antiallergenic, anti-inflammatory, antimicrobial, anticoagulant, antiproliferative, antitumor, antibacterial, antiviral and antiadhesive properties, as well as their potential to prevent neurodegenerative diseases, cardiovascular disorders and various forms of cancer (Kang *et al.,* 2006; Yoo *et al.,* 2018).

Darjeeling Himalaya is situated between 87°53′ East longitude and 28°10′ North longitude in India. The region though very small in area, is rich in floral diversity and density, many endemic elements and a number of species which have become rare, threatened or endangered (Chhetri *et al.,* 2005). The richness in medicinal plants is related to the richness in vegetation composition. The tribes of this Himalayan region (Nepalese, Lepchas and Bhutias) also have rich ethnomedicinal traditions for which a few literature are available (Bantawa and Rai, 2009). These literatures are the source for selecting the plants having various medicinal properties. Although, ethno-pharmacological studies have documented several of these plants with anti-diabetic activity, they have never been explored for developing antidiabetic agents.

Plant pre-fractionated libraries can be an effective strategy to identify the active principle due to following reasons: (i) the samples produced by the pre-fractionation approach are simpler mixtures and the final resolution of active components requires fewer purification steps. (ii) Interferences are reduced due to the fact that extremely polar and extremely non-polar components are separated from the bulk of the library samples and (iii) the relative concentration of minor components is increased over that in the crude, thereby enhancing the opportunity to uncover novel biologically active metabolites. Hence, the present investigation aimed at selection of plants with anti-diabetic potential on the basis of ethno-pharmacological studies and analyzing the plant/plant parts for phytochemicals, antimicrobial and antioxidant activities; and pre-fractionation of natural compounds from plant sample with potent antimicrobial and antioxidant activities, and further screening of the fractions for anti-diabetic potential by in vitro assay, and finally, in vivo activity of the active component in rat model system.

1.2. Objectives

1. Collection and identification of some ethnomedicinally important plants of Darjeeling Himalayan region.
2. Qualitative and quantitative phytochemical screening of the plant samples.
3. Determination of the antioxidant activities of plant samples.
4. Isolation and characterization of active compound(s) from plant samples having potent antimicrobial and antioxidant activities.
5. Performing in-vitro antidiabetic activities of active compound(s) from the selected plant samples.
6. To study the in-vivo antidiabetic activities of active compound(s) in the rat model system.

1.3. Review of literature

Plants have served as the primary source of energy (O_2, food, fabric and medications) for all kinds of life. Most crucially, plants are being studied as therapeutic agents since the dawn of civilization, some 60,000 years ago (Prasathkumar *et al.*, 2021). The great civilizations of the ancient Chinese, Indians and North Africans have provided documentary evidence of the same. The earliest account of the use of plants as medicine in India can be found in the Rig Veda, which dates from 3500 B.C. to 1800 B.C. Plants have always played an important part in primary health care, dating back to ancient times. Theophrastus, commonly regarded as the "Father of Botany," was a constant source of information that aided in plant identification. However, man did not become aware of the active elements of plants until the nineteenth century. The French scientists Caventou and Pelletier discovered quinine from *Cinchona* bark; morphine and codeine extraction from poppy; digoxin derived from *Digitalis* leaves; reserpine from *Rauwolfia* species; vinblastine and vincristine from *Catharanthus roseus* and so on. In addition, pharmacological research brought to the production of the first synthetic medication, 'aspirin', which was based on the natural chemical 'salicylic acid' (Sneader, 2000). For a long time, the value of natural phytochemicals declined as synthetic drug development took hold. Although, in recent decades, the search for natural medications has accelerated, as synthetic drugs have been linked to a slew of side effects. Taxol, etoposide and artemisinin were among the natural medications identified (Phillipson, 1999), piqueing interest in the usage of natural remedies as secure substitutes. Furthermore, the inclusion of many chemical compounds may have a synergistic or cumulative pharmacological impact, eliminating negative side effects associated with the usage of single xenobiotics (Tyler, 1999). NPs from plants have been the basis of traditional medicine system and it has been estimated by World Health Organization (WHO) that in both advanced and developing nations, 80–85% of the population depends on traditional medicine for their fundamental healthcare requirement and the major part of traditional therapy involves the use of plant extracts or their active principles (Elujoba *et al*., 2005; Ignacimuthu *et al*., 2006; Alves and Rosa, 2007).

Nature has provided us with all of the necessary components to maintain life on this Earth since the beginning of time. It has also proven to be an effective source of severel therapeutic herbs, from which a significant number of modern medications have been identified and successfully used to cure a variety of disorders. Chemical substances that provide health-promoting action on the human body have been known to confer therapeutic benefits. Despite the fact that ethnobotanical plants have been employed in conventional medicine since antiquity, they have been largely overlooked in modern times. However, numerous studies have been published on the effectiveness of certain ethnic plants as antiviral, antirheumatic, anticancer, antidiabetic, antiinflammation and antibacterial medicines. In this context, a brief assessment of the following topics linked to the current investigation has been assembled and presented: phytochemical screening of ethnobotanical plants, their role as antioxidative, antimicrobial and antidiabetic agents (Kumar *et al.,* 2021).

1.3.1. Phytochemical screening of plants

Plants contain bioactive, naturally produced substances known as phytochemicals that have been shown to produce particular physiological effects on humans (Saxena *et al.*, 2013). They help to protect plants from biotic and abiotic stressors, as well as contribute to their colour, scent and flavour. Individuals and societies have long been aware that phytochemicals play a vital role in their health. Several phytochemicals are recognized or identified; there is still some obscurity in their classification. Moreover, they have been categorized into primary and secondary metabolites. The primary metabolites include amino acids, proteins, sugars, nucleic acids, purines and pyrimidines, chlorophyll and others. The secondary metabolites include phenolics, alkaloids, terpenes, flavonoids, lignans, plant steroids, saponins and glucosides (Agidew, 2022). Phenolics are the most frequent and structurally variable plant phytoconstituents among the different secondary metabolites. The occurence of diverse bioactive substances in medicinal plants, as well as their importance to the welfare of individuals and communities, has piqued the interest of researchers all over the globe to investigate the plants' biological activities. Alkaloids, tannins, flavonoids and phenolic chemicals are the most essential bioactive elements of plants (Kang, 2014). A study was conducted by Edeoga *et al.,* (2005) to evaluate, analyze and estimate the percentage of crude phytochemical present in ten different medicinal plants, namely *Tridxa procumbens, Cleome rutidosperma, Euphrobia heterophylla, Emilia coccinea, Physcalis bransilensis, Richardia bransilensis, Scorparia dulcis, Sida acuta, Stachytarpheta cayennensis, Spigelia anthelmia* and widely utilized as natural remedy in South Eastern Nigeria. They found alkaloid and flavonoid in all of the samples, however tannin was only not found in *Sida acuta*. With the exception of *Tridxa procumbens*, all of the samples contained cardiac glycoside. Saponin was not found in *Euphrobia heterophylla* or *Sida acuta*, but it was found in all other samples. Only *Emilia coccinea, Physcalis bransilensis, Richardia bransilensis* and *Spigelia anthelmia* contained steriod. Phlobatannin was only found in the following plants: *Euphrobia heterophylla, Physcalis bransilensis, Scorparia dulcis, Spigelia anthelmia* and *Stachytarpheta cayennensis*. Terpenoid was not found in *Cleome rutidosperma, Scorparia dulcis, Spigelia anthelmia, Stachytarpheta cayennensis* or *Tridxa procumbens*, but was found in the other species. The quantitative estimation of these phytochemicals showed that *Sida acuta* had the greatest percentage crude output of alkaloids (1.04%) and flavonoid (0.98%). *Cleome rutido sperma* had the lowest alkaloid output (0.32%) but the highest tannin content (15.25%). Saponin (3.92%) was discovered to be highest in *Physcalis bransilensis,* while phenols were found to be negligible in the plants (0.20-0.04%).

A breif analysis of phytoconstituents of four Caesalpinaceae species was conducted by Awoyin *et al.,* (2007). In both water and ethanolic extracts of *Cnidoscolus aconitifolius,* eight major bioactive components were present in the dry leaf. Both extracts tested positive for three potent substances i.e. phenols, saponins and cardiac glycosides. Phlobatannin was found in the water extract, however alkaloids were found in the ethanolic extract. Both extracts were devoid of flavonoids, anthraquinones and mixed anthraquinones.

Phytochemical analysis on the ethyl acetate fraction of an ethanolic extract of *Pseudocedrella kotschyii* leaf was assessed by Musa *et al.*, (2008). They investigated flavonoids, glycosides and tannins as important chemical components. The extract included no alkaloids, saponins, cardiac glycosides or steroids. Qualitative analysis for phytochemicals in the leaf and root of four clinically essential plants e.g. *Acalypha indica*, *Cassia auriculata*, *Eclipta alba* and *Phyllanthus niruri* showed the presence of alkaloids, catechols, flavonoids, phenolic compounds, saponins and steroids in the root and leaf portions of *Acalypha indica*, but no anthroquinone, tannins or triterpenoids. *Cassia auriculata* root and leaf portions contained anthroquinone, alkaloids, flavonoids, phenolic compounds, saponins, steroids and tannins. The leaf and root of *Eclipta alba* contained phenolic chemicals, saponins, steroids, tannins and triterpenoids. *Phyllanthus niruri* root and leaf portions contained phenolic chemicals, anthroquinone, flavonoids, saponins, steroids, tannins and triterpenoids (Chitravadivu *et al.*, 2009).

The phytochemical analysis of leaf and stem of *Cardiospermum helicacabum* revealed a wide range of secondary metabolites (Viji and Murugesan, 2010). In all five solvent extracts of leaf and stem examined phenol, tannins and saponins were discovered in the highest concentrations, followed by steroids, sugars, flavonoids and terpenoids (Benzene and acetone). Leaf extracts in acetone and chloroform demonstrated greater inhibitory activity against *Salmonella typhi* and *Streptococcus subtilis*, respectively. Acetone extracts of the stem exhibited the strongest inhibitory effect on *Salmonella typhi*, whereas benzene extracts of the stem had an average inhibitory effect on *Escherichia coli*. In a separate investigation, the phytochemical contents of four plants *Clerodendrum viscosum, Moringa oleifera, Cinnamomum tamala* and *Scoparia dulcis* commonly utilized for various medical uses were compared. The active components revealed in these plants included alkaloids, tannin, saponin, terpenoid, flavonoid and cardic glycoside. *Clerodendrum viscosum*, *Cinnamomum tamala* and *Moringa oleifera* all had steroid, while laking in *Scoparia dulcis*. The experiment for quantifying phenols and ascorbic acids revealed that *Cinnamomum tamala* possessed the maximum concentration of phenol and ascorbic acids, whereas *Clerodendrum viscosum* possessed these substances in lowest concentration (Das and Chakraborty, 2011).

The phytoconstituents of leaf extracts of *Gymnema sylvestre*, *Phyllanthus amarus* and *Phyllanthus reticulatus* were assessed. In our country, these herbs are utilised ethnomedically as anti-diabetic medicines. The experiment was conducted using three distinct extracts: ethanol, methanol and water. In the water extract of *Phyllanthus amarus*, they found terpenoids, flavonoids, phenol, quinines and catechin, as well as steroids, tannins, phenol and quinones in the ethanolic extract and just tannins, phenol and quinones in the methanol extract. The water extracts of *Gymnema sylvestre* contained terpenoids, alkaloids, flavonoids, saponins, tannins and quinones, whereas the methanolic extracts contained terpenoids, alkaloids, saponins, tannins and quinones. Only alkaloids, tannins and quinones were found in the ethanolic extracts. *Phyllanthus reticulatus* water extracts contained flavonoids, phenol and quinones. Steroids, tannins, phenol and quinones were found in ethanolic extracts, while steroids, tannins, phenol and quinones were found in methanolic extracts (Gopinath *et al.*, 2012).

Medicinal plants of diverse families, including *Ficus religiosa, Citrus limonia, Phoenix dactylifera, Swertia chirata* and *Raphanus sativus*, were investigated to identify and correlate their existence with plant bioactivities. All the six plants had tannins and flavonoids. Additionally apart from *Phoenix dactylifera*, terpenoids were found in all of the plant samples. Saponins and steroids elsewhere were lacking from all plants apart from *Swertia chirata*, while phlobatannins were not detected from all plants apart from *Raphanus sativus*. Carbohydrates, glycosides and coumarins were also found in all of the plants studied, apart from *Phoenix dactylifera* and *Raphanus sativus*. Except for *Ficus religiosa, Phoenix dactylifera* and *Raphanus sativus,* all of the plants studied contained alkaloids. Proteins were only discovered in *Ficus religiosa* and *Swertia chirata*, but emodins, anthraquinones, anthocyanins and leucoanthocyanins were lacking in all six plants studied. They determined that *Swertia chirata* has the best medicinal potentiality because it contains the maximum types of phytochemicals, whereas *Phoenix dactylifera* has the lowest medicinal efficacy since it lacks the potential phytochemicals (Yadav *et al.*, 2014). Total phenolic and antioxidant tests on *Adenanthera pavonina* L. (family Mimosaceae) was conducted by Ghosh and Chowdhury (2015). Tribal people utilized the leaf and bark of this sample to treat a variety of maladies and disorders. For pharmacognostic examination of different portions of this plant, many criteria such as micromorphology, anatomy, phytochemical screening and physical constant were taken into account. Carbohydrates, proteins, alkaloids, glycosides, saponins, flavonoids, steroids, tannins and other compounds were detected in methanolic preparations of leaf and bark. Fenugreek (*Trigonella foenum-graecum* Linn.), an annual medicinal plant of family Fabaceae, is extensive used as TM. Extensive preclinical and clinical research has shown antibacterial, antifungal, anti-inflammatory, antiobesity and antioxidant pharmacological effects of fenugreek. The phytoconstituent analysis revealed the availability of alkaloids, steroids, polyphenols, flavonoids, saponins, carbohydrates, lipids, hydrocarbons and amino acids in the plant (Venkata *et al.,* 2017).

1.3.2. Antioxidant activity of plants

The primary mechanism behind a variety of human neurological illnesses, hyperglycemia, inflammation, viral infections, autoimmune disorders and digestive system problems appears to be cellular imparement or oxidative damage caused by free radicals or reactive oxygen species (ROS) (Bardawell *et al.*, 2018). Free radicals are produced as a result of regular pharmacological, environmental and other xenobiotic metabolism, as well as endogenous substances, particularly stress hormones (epinephrine and norepinephrine) (Das and Roychoudhury, 2014). According to accumulating research, ROS can be scavenged through chemoprevention using natural/synthetic antioxidant compounds. Antioxidants are compounds that counteract the effects of free radicals and they have long been utilized as primary health-protecting agents (Pham-Huy *et al.*, 2008). Synthetic antioxidants have been linked to a variety of negative effects, thus the quest for natural antioxidants, particularly from botanicals, has accelerated in recent years (Ahmad *et al.,* 2008). In a study by Shyur *et al.,* (2005), the antioxidative potential of twenty-six medicinal plant extracts were evaluated that are often used as traditional medicine in Taiwan. Between some of these plants *Ludwigia octavalvis, Vitis thunbergii, Rubus parvifolius, Lindernia anagallis* and *Zanthoxylum nitidum* were shown to have high DPPH activity, while *Ludwigia octavalvis, Vitis thunbergii, Prunella vulgaris, Saurauia oldhamii* and *Rubus parvifolius* had higher superoxide scavenging activity. *Ludwigia octavalvis* and *Bombax malabaricum* provided crutial defence against strand breakdown caused by UV irradiation H_2O_2 on ΨX174 super coiled DNA. In another research work, the total equivalent antioxidant capacity and phenolic content of twenty six popular spices ingredients from 12 different plants were assessed. Various spices with significant quantities of phenolic contents were found to correlation with having more antioxidant potential. Phenolic acids, phenolic diterpenes, flavonoids, volatile oils (e.g. aromatic compounds) and rosmarinic acid were among the phenolic elements found in the spice extracts, all of which were present in variable amounts. The total quivalent antioxidant capacity values and total phenolic content were found to have a strong positive linear relationship, indicating that phenolic substances in the evaluated spices may have dramatically increased their antioxidant activity (Shan *et al.,* 2005). The antioxidant and free radical scavenging activitiy of crude methanolic extracts of 12 commonly used Indian medicinal herbs were investigated by Aqil *et al.*, (2006). The extracts showed significant antioxidant and free radical scavenging action in varied degrees. The presence of phenolics, alkaloids, glycosides and tannins in the crude extracts was discovered by phytochemical analysis, which could explain the reported antioxidant effect. Total phenolic content and antioxidant capacity of 70 medicinal plant tinctures was investigated by Katalinic *et al.,* (2006). The in vitro antioxidant assay was evaluated using standard assays such as Ferric reducing antioxidant power (FRAP), DPPH radical scavenging activity and ABTS activity. Out of various medicinal plants, *Melissae folium* was found to have the highest concentration of phenolics as well as the highest antioxidant activity, implying that the antioxidant potentiality is linked to the quantity of phenolics in the plant sample.

The antioxidant potentiality of methanolic crude extracts of certain regularly used medicinal herbs was investigated by Khalaf *et al.,* (2008) and Rai *et al*., (2019). All methanolic fractions possessed substantial antioxidant capability which was found to be correlated with the presence of alkaloids, glucosides, tannins and flavonoids. In vitro antioxidant activity, total polyphenolic, flavonoid and flavonol content of petroleum ether, chloroform and methanolic extracts of *Limonia acidissima* Linn., leaf were investigated by Maleki *et al.,* (2008). According to the findings, the methanolic extract had a high concentration of total polyphenolics, total flavonoids and total flavonols, which could explain its increased antioxidative potentiality. The antioxidant activity of methanolic extracts of *Gmelina arborea* Roxb. (Verbaneceae) was investigated by Patil *et al.,* (2009). The extracts were shown to have strong antioxidant activity, which appeared to be connected to the phenolic content. The methanolic extract of plants commonly utilized as folk treatments by the tribes of the Attapady region was assessed for the antioxidant and radical scavenging activity (Sini *et al.,* 2011). When compared to other plants examined, *Cassia occidentalis, Clitoria ternatea, Trianthema decandra, Capparis zeylanica, Anisomeles malabarica* and *Plumbago zeylanica* all showed antioxidant potential, with *Trianthema decandra* having the greatest antioxidant potentiality. The results thus suggested medicinal potential of these plants.

The total phenolic and flavonoid content, as well as the antioxidative capacity of dried and powered leaf of *Tinospora cordifolia* were determined using different in vitro assays such as total reducing power, total antioxidant activity, lipid peroxidation inhibitory activity, DPPH radical scavenging activity and superoxide radical scavenging activity (Premanath and Lakshmidevi, 2010). Among all the solvent tested, the ethanol extract had the highest phenolic and flavonoid concentration, as well as antioxidant activity. The study concluded a relatively better extraction of active antioxidants in ethanol.

The antioxidant property of *Mucuna pruriens* Linn., was investigated by (Satheesh *et al.,* 2010). The antioxidant activity of the whole plant of *Mucana pruriens* in different solvents was tested by using in vitro DPPH (2, 2-diphenyl 1-picrylhydrazyl) radical scavenging activity, superoxide anion scavenging activity and iron chelating scavenging activity. The antioxidant and free radical scavenging activity of ethyl acetate and methanol extracts were found to be greater than those of the petroleum extract, which could be due to the presence of phenolic components in the former two extracts.

A similar study to assess the antioxidant capability and total phenolic content of 13 key medicinal plants was conducted by Narayanaswamy and Balakrishnan, (2011). The herbal extracts were prepared using solvents such as water and ethanol at a concentration of 5%. In all solvent systems, *Ocimum basillicum* leaf, *Alpina calcarata* leaf, *Jatropa multifida* flower, *Hyptis suaveolens* leaf, *Solanum indicum* leaf and *Clitorria ternate* leaf and flower showed increased DPPH radical scavenging activity. *Ocimum basillicum* and *Clitorria ternate* had the highest total phenolic contents. It was comcluded that the hydrogen donating ability of phenolics may be responsible for free radical scavenging function of medicinal plants.

One of the commercially available and most popular medicinal plants in the Himalayan region is *Withania somnifera* L., which is believed to have aphrodisiac property and can cure a variety of ailments. The antioxidant activity of *Withania somnifera* was investigated by Sharma *et al.,* (2013). They had taken the plant from two different habitats in Kullu, North-West Himalaya, namely forest and roadside, and found that the plants' antioxidant activity differed significantly among the habitats.

Traditional medicine has employed *Crataegus monogyna* (hawthorn) leaf, flower and berry to treat chronic heart failure, high blood pressure, arrhythmia and numerous digestive illnesses, as well as geriatric and antiarteriosclerosis therapy. The water and ethanol extracts of leaf, flower and fruit of hawthorn was analyzed for H_2O_2 radical scavenging and total antioxidant activity (Keser *et al.,* 2012). Both extracts were found to have significant antioxidant activity in the study.

The phytochemical composition and antioxidant potentiality of methanolic extract of dried leaf of four medicinally significant herbs was assessed by Soni and Sosa, (2013). The herbs were *Ocimum sanctum, Mentha spicata, Trigonella foenumgraecum, Spinacia oleracea* and one medicinally essential tree *Gmelina arborea* used in the regular diet. Tannins, phlobatannin, saponins, flavonoids, steroids and alkaloids were found through phytochemical investigation. The leaf extract of *Mentha spicata* displayed the greatest antioxidant and reducing activity among the examined plants, which could be attributable to its phenolic content.

Cichorium glandulosum has long been utilized in China to treat degenerative and chronic disorders. The research work by Yao *et al.,* (2013) reported the antioxidant activity, α-glucosidase and α-amylase inhibitory activity and chemical composition of flavonoids from *Cichorium glandulosum* seeds using HPLC-ESI/MS. The plant showed substantial antioxidative activity against DPPH, ABTS, hydroxyl radicals and superoxide anion in vitro, as well as inhibitory effect against α-amylase and α-glucosidase. In vivo treatment of rats with flavonoids (100, 200, 400 mg/kg) resulted in a promising reduction in malondialdehyde levels, whereas superoxide dismutase and glutathione levels were regained to nearly basic levels and catalase and glutathione peroxidase levels highly rised in comparison to the group of rats consumed CCl_4. Due to their antioxidant, anti-glucosidase and anti-amylase activity, *C. glandulosum* seeds may be given proper consideration as a food supplement or popular folk remedy.

Despite the fact that a large number of plants have been examined for antioxidant content, there are still considerable gaps in knowledge about various medicinal plants. The antioxidant property and phenolic substances of tropical plants from the Euphorbiaceae, Rubiaceae, Anacardiaceae, Scrophulariaceae and Poaceae families was examined by (Coulibaly *et al.,* 2014). The research on various crude extracts of seven plant species found that substantial concentrations of phenolics present with the highest amounts in *Feretia apodanthera* and highest antioxidant activity found in *Ozoroa insignis*. An in vitro investigation of the antioxidant, antibacterial and anti-diabetic effects of polyphenols from *Passiflora ligularis* Juss. fruit pulp was evaluated by Saravanan and Parimelazhagan, (2014). To test biological potency, the plant was extracted in various solvents, such as petroleum ether, chloroform, acetone and methanol. In comparison to other extracts, the acetone extract had the highest concentration of phenolics, tannin and flavonoid. The acetone extract also had the highest in vitro antioxidative activity, such as metal chelating activity, FRAP and free radical scavenging activity, such as DPPH•, ABTS•+, O2•, •OH and NO• scavenging activity. Similarly, the acetone extract exhibited the greatest dose-dependent antibacterial, α-amylase and α-glucosidase inhibitory activity. Gallic acid, caffeic acid, rutin, ellagic acid and kaempferol were found in varied amounts in the polyphenolic components after HPLC analysis. Eventually, a greater level of phenolic contents in the extract was correlated with more powerful antioxidant, antibacterial, α-amylase and α-glucosidase activity. Similarly, investigations conducted by Medini *et al.,* (2014) on several *Limonium delicatulum* extracts demonstrated that the plant has powerful antioxidant and antibacterial property. The ethanol extracts exhibited the greatest overall antioxidant activity when compared to the other solvents, acetone extracts had the highest capacity to scavenge free radicals and methanol extracts had the maximum suppression of β-carotene bleaching activity.

The antioxidant activity and total flavonoids content of aerial portions of *Ficus pyriformis* Hook. and Arn. (Moraceae) growing in Egypt was assessed by Ibraheim *et al.,* (2015). Various fractions of *Ficus pyriformis* were tested for their ability to scavenge free radicals after being fractionated on vacuum liquid chromatography (VLC) with organic solvents of various polarities such as n-hexane, dichloromethane, ethyl acetate and methanol. Methanol and ethyl acetate fractions had the maximum potency between the extracts, followed by dichloromethane and n-hexane fractions. Steroids, triterpenoids, flavonoids, tannins, carbohydrates and/or glycosides were discovered through phytochemical study. The antioxidant potentiality of the methanolic extract and entire extract of *Ficus pyriformis* aerial parts contained polyphenolic substances including flavonoids and tannins, which have been shown antioxidant property. Similar experiments were carried out on the aerial sections of *Teucrium barbeyanum* Aschers. and antioxidant activity as well as chemical constituents were reported. It was shown that fractions containing a greater percentage of polyphenols had significant antioxidant activity, implying that *Teucrium barbeyanum's* antioxidant activity is linked to the presence of these substances (Mohamed *et al.,* 2015).

The antioxidant potentiality of chloroform and ethanol fractions of four Indian medicinal plants like *Grewia asiatica, Caesalpinia bonducella, Syzygium samarangense* and *Asteracantha longifolia* was evaluated. The antioxidant capacity of these plant extracts varied dramatically (Madhura *et al.,* 2015). The four plant seeds of *Asteracantha longifolia* were found to have high antioxidant property. Siqun *et al.,* (2015) evaluated the antioxidant potentiality, anticancer impact and antiaging activity of proanthocyanidins extracted from *Kunlun chrysanthemum* flower (PKCF) found in Xinjiang. The principal component of *Kunlun chrysanthemum* in the Chinese market is dry tea, which entirely lacks refinery processing and is believed to have a variety of medical advantages. Both in vitro and in vivo analysis have demonstrated the exceptional antioxidant property, which is higher than that of vitamin C. In mice in vivo and in *Drosophila*, the extract was found to decrease malondialdehyde production while increasing superoxide dismutase activity. It has strong antitumor action, as it could suppress the proliferation of H22, Eca-109 and HeLa cancer cells at minimum doses, with IC_{50} values of 70.96 ± 0.05409 μg/ml, 260.4 ± 0.06887 μg/ml and 113.3 ± 0.08062 μg/ml, respectively. Because of its significant antioxidant capability, PCKF was proposed as a novel antioxidant to be used in food and pharmaceuticals. The antioxidant capability of several extracts of *Phoenix dactylifera* L., which has been used to cure a number of diseases in many conventional systems of drug in Southwest Asia and North Africa, were described by (Eddine *et al.,* 2015). The FRAP, superoxide radical scavenging (O_2) and DPPH radical scavenging capacity assays were used to determine the antioxidant activity of ethanol, methanol, hexane and chloroform fractions. The experiments found a pronounced positive relation between DPPH radical scavenging capacity of the extracts and phenolic content, as well as a substantial correlation between FRAP values and total proanthocyanidins content. Ethanol had stronger phenolics and antioxidative property than the other extracts, which was thought to be due to the existence of phenolics in the extracts. The hill-mango, *Commiphora caudata* Engl. (Syn. *Protium caudatum* Wight and Arn.), belonging to the Burseraceae family and blooms in the arid or moderate-evergreen habitats of South India. The plant has been seen to perform a variety of biological activity (Sivakumar *et al.,* 2009; Annu *et al.,* 2010). Reddy *et al.*, (2015) assessed in vitro experiments to study the chemical constituents, antibacterial and antioxidant property of *C. caudata* essential oils obtained from leaf and fruit to further investigate the therapeutic activity of the plant. The findings revealed the existence of fifteen chemicals in leaf oil and thirty substances in fruit oil and both the oil fraction showed significant antibacterial and antioxidant potentiality to differing levels.

The chemical compositions and antioxidant evaluation of the essential oils (EOs) obtained by hydrodistillation from the leaf and stem of *Indigofera spicata* Forssk (Fabaceae) grown in Nigeria have been studied by Adeleye *et al.,* (2021). Methanolic extract of *Xylocarpus moluccensis* was found to be significantly effective in scavenging DPPH and ferric reducing antioxidant activity was tested by Budiarso *et al.,* (2021). The phytochemical test of *Origanum vulgare* ethanol extract was showed some phytochemicals, such as a flavonoid, alkaloid, triterpenoid, steroid, essential oil, tannin, ethyl acetate and hexane. Additionally in vitro assay showed that *Origanum vulgare* extract has strong antioxidant activity with an IC_{50} value of 133.47 μg/ml (Rosmalena *et al.,* 2021). Flavonoid content and antioxidant potential of leaf extracts of *Passiflora setacea* was reported by Santos-Tierno *et al.,* (2022). Phytochemical analysis and antioxidant activity of *Cotinus coggygria* (Smoke tree) was evaluated. The amount of flavonoid in ethanol extract of *C. coggygria*, growing in Armenia, was 0.94%. In volatile oil of the plant leaf 22 compounds were identified and among them the Germacrene D, Linalool, formate, ά–Terpineol sesquiterpenes and diterpene alcohol were predominant. The essential oil of *Cotinus* leaf also showed antioxidant activity (Shaboyan *et al.*, 2021).

1.3.3. Antimicrobial activity of plants

Plants produce antimicrobial substances as part of their defensive strategy against pests and diseases, as is widely documented. Several researchers have published various research articles on extracting plant based antimicrobial chemicals and test against microorganisms in vitro with the goal of using them as a source of pharmaceuticals (Vaou *et al.,* 2021).

The disc diffusion method utilized to test the antibacterial activity of crude and methanol extracts of *Terminalia bellerica* dry fruit against nine human bacterial pathogens was evaluated by Elizabeth, (2005). Both of the crude and methanolic extracts were reduced the proliferation of the examined pathogens to varied degrees. Except for *Escherichia coli* and *Pseudomonas aeruginosa*, methanolic extract was more productive than crude extract against most of the microorganisms studied. Among the bacteria studied, *Staphylococcus aureus* was shown to be the most sensitive to both extracts, implying that *Terminalia bellerica* is a significant inhibitor of this pathogen. The minimal inhibitory concentrations (MICs) of crude extracts varied from 300 to >2400 g/ml, whereas MICs of methanolic extracts varied from 250 to >2000 g/ml, with the least

MIC value against *Staphylococcus aureus,* indicating that arid fruit of *Terminalia bellerica* has significant broad spectrum antibacterial action. Antibacterial activity of aqueous, ethanolic, methanolic and phenolic fractions derived from three Palestinian traditional medicinal plants, as well as their industrial oils, against ten pathogenic microbes was evaluated. In Palestine, sage, hyssop and madder have long been utilized as traditional remedy to cure a variety of disorders. The antimicrobial potentiality of plants was assessed and evaluated against *E. coli, Proteus mirabilis, Klebsiella pneumoniae, Enterobacter cloacae, Pseudomonas aeruginosa, Actinobacter haemolyticus, Enterococcus sp*. and *Candida albicans* extracted from UTI (urinary tract infections) patients, as well as *Salmonella typhi* and *Staphylococcus aureus* isolated from the stool of food poisoning patient. The sage and hyssop derived from the aqueous extracts were found to be productive against the majority of the bacteria have been tested. The phenolic extracts of sage and hyssop were found to be sensitive against *Staphylococcus aureus* and *Enterococcus sp*, respectively. Additionally the ethanolic extract of madder was more sensitive against *Escherichia coli*, but had no potency on the Gram positive bacteria. *Escherichia coli, Proteus mirabilis* and *Salmonella typhi* were not restricted by industrial oils of sage, hyssop or madder. *Staphylococcus aureus* was found to be the most vulnerable bacterium to maximum extracts of the three plants studied out of the ten studied bacteria. The findings support the traditional therapeutic usage of hyssop, sage and madder for the treatment of microbial diseases such as UTIs and foodborne disease caused by bacteria (El Astal *et al.*, 2005).

Bidens pilosa L., *Bixa orellana* L., *Cecropia peltata* L., *Cinchona officinalis* L., *Gliricidia sepium* H.B. and K, *Jacaranda mimosifolia* D. Don, *Justicia secunda* Vahl., *Piper pulchrum* C. DC, *Piper paniculata* L., and *Spilanthes americana* L. plants were assessed for antibacterial activity against five bacteria: *Staphylococcus aureus, Streptococcus β hemolyticus, Bacillus cereus, Pseudomonas aeruginosa* and *Escherichia coli*. and one yeast (*Candida albicans*) (Rojas *et al.*, 2006). The findings revealed that all of the plants tested were potent against three or more harmful bacteria, but impotent against *Streptococcus hemolyticus* or *Pseudomonas aeruginosa*. The study also revealed that *Bixa orellana* L., together with *Justicia secunda* Vahl. and *Piper pulchrum* C. DC, could be potential sources of novel antimicrobial compounds, promoting the utilization of traditional medicinal plants as antimicrobial substances. Agyare *et al.*, (2006) evaluated that both methanolic and petroleum ether extracts of the leaf and bark of *Nauclea latifolia, Bridelia atroviridis* and *Zanthoxylum gilletii* possessed antimicrobial activity when screened against six microbs, including *Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus, Bacillus subtilis, Candida albicans* and *Aspergillus niger*, but that methanolic extracts were more potent than petroleum ether.

Psidium guayava and *Mangifera indica* were reorted by Akinpelu and Onakoya, (2006) to determine their antibacterial property. In the South Western portion of Nigeria, these two plants are commonly utilized for herbal medicines to cure odontalgia, gastrointestinal issues, dynsentery, diarrhoea, painful gums and sore throats. Both plant extracts were found to be capable of reducing the proliferation of all fifteen various bacteria employed to variable degrees, although *Psidium guajava* was found to be more significant.

The antimicrobial property of 18 ethnobotanical plant extracts against nine bacterial strains (*Bacillus subtilis, Staphylococcus aureus, Staphylococcus epidermidis, Enterococcus faecalis, Escherichia coli, Klebsiella pneumonia, Pseudomonas aeruginosa, Ervinia sp*.) was investigated by Duraipandiyan *et al.,* (2006). Methanolic extracts of *Acalypha fruticosa, Peltophorum pterocarpum, Toddalia asiatica, Cassia auriculata, Punica granatum* and *Syzygium lineare* were shown to be most effective than the hexane extracts among the plants studied. Methanolic extracts of *Peltophorum pterocarpum* and *Punica granatum* have the significant antifungal efficacy against *Candida albicans* (Parveen *et al.*, 2010).

The extracts of *Bryophyllum pinnatum* and *Kalanchoe crenata* possessed midium antimicrobial property against gram-negative bacteria (*Escherichia coli, Pseudomonas aeruginosa, Klebsiella pneumoniae, Shigella flexneri, Salmonella paratyphi, Citrobactor sp*.) and gram-positive bacteria (*Staphylococcus aureus, Enterococcus faecalis, Bacillus subtilis*) was found by Odunayo *et al.,* (2007). In a related experiment conducted by Ushimaru *et al.,* (2007) to determine the in vitro antibacterial potentiality of different plant extracts i.e. *Allium sativum, Zingiber officinale, Caryophyllus aromaticus, Cymbopogon citratus, Mikania glomerata* and *Psidium guajava* against Gram-positive and Gram-negative bacterial pathogen obtained from human infections. The study revealed that all of the extracts showed different levels of antimicrobial activitiy. Out of those plants, *Caryophyllus aromaticus* showed the significant effect.

The antibacterial and antifungal property of several of the native plants in Mysore, including *Acacia nilotica, Sida cordifolia, Tinospora cordifolia, Ziziphus mauritiana* and *Withania somnifera* was tested by Mahesh and Satish, (2008). The study found that all sections of the plants were effective to varied degrees against bacterial and fungal pathogens. Likewise, Islam *et al.*, (2008) conducted a through investigation and reported the antibacterial property of various native flora of Bangladesh that tribal public in Chittagong had been using to cure infectious diseases. Only five plants, out of the total 16 plants i.e. *Mentha arvensis, Enhydra fluctuans, Blumea lacera, Chenopodium album* and *Glinus oppositifolius*, exhibited antibacterial action at various levels against *Shigella dysenteriae, Salmonella typhi, Salmonella paratyphi, Bacillus cerus, Bacillus subtilis, Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus, Vibrio cholera* and *Bacillus megaterium*. Furthermore, gram positive bacteria were more vulnerable to the crude extracts than gram negative bacteria and *Blumea lacera* might show more activity compared to the other plants.

The antibacterial activitiy of severel commonly used therapeutic flora such as *Ocimum sanctum*, *Origanum majorana*, *Cinnamomum zeylanicum*, and *Xanthoxylum armatum* against various bacterial pathoges such as *Bacillus subtilis, Bacillus cereus, Bacillus thuringiensis, Staphylococcus aureus, Pseudomonas sp., Proteus sp., Salmonella typhi, Escherichia coli, Shigella dysentriae* and *Klebsiella pneuminiae* were assessed. The results revealed that the effectiveness of these plants against bacterial pathogens varied significantly. Out of them *Origanum majorana* showed the most potent activity. Gram-positive bacteria have been found to be more vulnerable than gram-negative bacteria (Joshi *et al.*, 2009). The antibacterial and antioxidant capability of *Inula aucherana, Fumaria officinalis, Crocus sativus, Vicum album, Tribulus terestris, Polygonatum multiflorum, Alkanna tinctoria* and *Taraxacum officinale* against severel microorganisms was tested by Sengul *et al.*, (2009). Almost all of the plants exhibited varying degrees of antioxidant and antibacterial property. The potentiality of methanolic extracts was found to be higher than that of aqueous extracts. Because total phenolic concentration did not correspond with antioxidant ability, it was inferred that phenolic chemicals were not the primary cause of the extracts' antioxidant ability. Indeed, various additional phytochemicals, including as ascorbic acid, tocopherol and pigments, may be thought to contribute to total antioxidant activity in a synergistic way.

In additional research, the methanolic extract of *Oldenlandia umbellata* showed antibacterial ability against pathogens obtained from respiratory tract infections. The research revealed that both gram positive and gram negative bacteria may be efficiently restricted by the root and leaf of this plant. Seven distinct anthraquinones were found in the methanolic extract of the plant, with the 1-2- dihydroxy anthraquinone known as Alizarin being the most abundant. Plant based Alizarin and synthetic Alizarin were shown to be similarly potential to restrict the bacterial proliferation (Arun *et al.*, 2010).

The antifungal property of different medicinal plants, including *Andrographis paniculata, Valeriana jatamansi, Asparagus racemosus, Tinospora cordifolia, Coleus barbatus, Berberis aristata, Achyranthes aspera* and *Plantago depressa* against harmful fungus was tested by Mathur *et al.*, (2011). The research revealed that all of the plants showed varying levels of antifungal activity, with hydro-alcholic extracts being more powerful than hexane extracts. Hydro-alcoholic extracts of *Andrographis paniculata* and *Achyranthes aspera* were found to restrict efficiently the proliferation of *Aspergillus niger* and *Candida albicans*.

The antimicrobial potentiality of severel medicinal plants i.e. *Asphodelus tenuifolius, Asparagus racemosus, Balanites aegyptiaca, Cestrum diurnum, Cordia dichotoma, Eclipta alba, Murraya koenigii, Murraya koenigii, Peladium murex, Richinus communis* and *Trigonella foenum graecum* against bacterial pathogens obtained from oral cancer like *Staphylococcus aureus, Escherichia coli, Staphylococcus epidermidis, Pseudomonas aeruginosa, Klebsiella pneumonia, Proteus mirabilis, Proteus vulgaris* and the pathogenic fungus like *Candida albicans* and *Aspergillus fumigates* was investigated by Panghal *et al.*, (2011). The findings revealed that eight out of the ten medicinal plants studied had efficient antimicrobial ability against the majority of the bacteria, with *Pseudomonas aeruginosa* being the most vulnerable bacterium, suggesting that therapeutic plants could be used as a significant antimicrobial substance to restrict secondary infections in cancer patients. The antimicrobial property of chloroform: methanol (1:1) extracts of numerous *Helichrysum* species against three Gram-positive bacteria (*Bacillus cereus, Staphylococcus aureus* and *Staphylococcus epidermidis*), two Gram-negative bacteria (*Klebsiella* *pneumoniae* and *Pseudomonas aeruginosa*) and one fungus (*Cryptococcus neoformans*) was evaluated by Lourens *et al.*, (2011). At the similar concentration, seven out of those studied plants had minimum inhibitory concentrations of less than 0.1 mg/ml against *Bacillus cereus* and/or *Staphylococcus aureus*, and less than 25% growth for the Graham and MCF-7 cell lines.

The antibacterial and antifungal property of crude extracts of *Withania somnifera* fruit coat (calyx) in various solvents (hexane, petroleum ether, toluene, benzene, isopropyl alcohol, chloroform, ethyl acetate, acetone, ethanol, glacial acetic acid and water) against both plant and human pathogens like *Proteus merabilis, Klebsiella pnemoniae, Agrobacterium tumefaciens* (plant pathogen) and one fungus *Aspergillus niger* was investigated by Singariya *et al.,* (2012). The findings revealed that 9 out of 11 extracts were effeicient against bacterial and fungal proliferation, demonstrating *Withania somnifera's* vast range nature. The antibacterial activity of ethyl acetate, glacial acetic acid, isopropyl alcohol and chloroform extracts were the highest, while glacial acetic acid exhibited remarkable potency with a quite low MIC and MBC/MFC values that were equal to the standard medicines utilized (gentamycin and ketoconazole). The antibacterial activity of the genus *Murraya koenigii* (Mitha neem) leaf, one of the most often utilized aromatic substances in Indian cuisine was tested by Harish *et al.,* (2012). The herbs have been utilized as folk medicines for centuries and are said to have antibacterial, anti-inflammatory, anti-feedant and other properties (Dahanukar *et al.*, 2000). The study found that water, ethanol, chloroform and petroleum ether extracts possessed antimicrobial property against gram positive (*Staphylococcus aureus*) and gram negative (*Pseudomonas aeuriginosa*, *Escherichia coli, Klebsiella pneumonia* and *Salmonella typhi*) bacteria at different levels. These four extracts showed MIC ranging from 12.5 to 50.0 mg/ml, whereas the minimum bactericidal concentration (MBC) was from 50.0 to 100.0 mg/ml. The ethanolic extract, on the other hand, possessed the highest bactericidal impact compared to all of the extracts. *Murraya koenigii* considered as an antibiotic source due to the presence of carbazole alkaloids which was thought to be antibacterial substance. Antifungal potentiality of ethanolic, methanolic and distilled water extracts of *Blumea lacera* against *Aspergillus niger, Aspergillus oryzae, Aspergillus praraciticus*-456, *Aspergillus flavus* and *Aspergillus parasiticus* at different concentrations was investigated by Kagne *et al.*, (2012). The activity of ethanolic extract was higher when compared with the other extracts, which could be due to the chemical subtances such as oils present in the sample.

The antibacterial efficacy of *Rivea ornata* methanolic extract against bacterial strains i.e. *Bacillus subtilis, Staphylococcus aureus, Pseudomonas aeruginosa* and *Escherichia coli* were investigated by Sharma and Patel, (2013). The antibacterial efficacy of *Amaranthus spinosus, Orchis muscula* and *Solanum nigrum* against *Staphylococcus aureus, Streptococcus mutans, Bacillus subtilis, Bacillus amylolique faciens, Aspergillus fumigates* and *Escherichia coli* was evaluated. Methanol, acetone and hexane extracts of *Amaranthus spinosus, Solanum nigrum* and *Orchis muscula* showed antibacterial efficiency at different degrees. Although, methanolic extracts showed the best antibacterial activity when compared with the other extracts, whereas chloroform extract proved ineffective against the bacterial pathogens. Phytochemical research indicated the methanolic extracts possessed tannins and flavonoids but those are not present in chloroform extracts, which could have influenced to the superior antibacterial action of methanolic extracts, hence supporting the plants' traditional use (Thalwal *et al.*, 2013). The antioxidant, antibacterial and phytochemical property of various raw extracts of *Datura metel* accessible in the Sultanate of Oman, in various solvent i.e. hexane, ethyl acetate, chloroform, butanol and methanol was examined by Alabri *et al.*, (2014). All of the raw extracts of both arid and fresh leaf were shown to have different levels of antibacterial and antioxidant actions in the research. The methanolic extracts, on the other hand, were slightly more effective in reducing the proliferation of one gram positive (*Staphylococcus aureus*) and three gram negative bacteria (*Escherichia coli*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*). Phytochemical screening demonstrated the existence of alkaloid, flavonoid, saponin and tannin components in all raw extracts of both arid and fresh leaf, but no steroids and triterpenoid. Antioxidant and antibacterial actions may have been produced by the existance of phytochemicals such as tannins and flavonoids.

The antibacterial activity of the medicinal plant *Rhinacanthus nasutus* Linn., was conducted by Nanthakumar *et al.*, (2014). The study found that the aqueous and ethanolic extracts of *Rhinacanthus nasutus* showed antimicrobial potency against *Bacillus subtilis, Streptococcus faecalis, Salmonella paratyphi*, *Aspergillus flavus*, *Candida albicans*, *Trichoderma viride*, *Bacillus subtilis* and *Pencillium sp*. at different levels those are human pathogenic microbes. The aqueous extract, on the other hand, exhibited significant action against *Bacillus subtilis, Salmonella paratyphi, Candida albicans* and *Aspergillus flavus* than the ethanolic extracts, creating it a viable optional antimicrobial substence to inhibit the pathogens that developing infection. The antioxidant and antibacterial effects of several *Sonneratia alba* extracts in an another investigation was demonstrated by Haq *et al.*, (2014). The ethanolic and aqueous extract of this plant bark exhibited the potent antioxidative and antibacterial effects when compared with all of the other extracts. Maximum phenolic concentration in the sample, may have related to the potent biological properties. The phytochemical and antibacterial properties of several therapeutic floras against five bacterial pathogens that cause oral infections were tested by Gauniyal and Teotia, (2014). Nearly all of the plants investigated showed antibacterial action against *Streptococcus mutans, Enterococcus faecalis, Lactobacillus acidophilus, Candida albicans* and *Candida tropicalis*. Although, *Acacia nilotica, Citrus limon, Emblica officinalis, Juglans regia, Psidium guajava* L., and *Withania somnifera* were shown to be successfully suppress the microbial proliferation, while *Lannea coromandelica (Houtt) Merr* and *Rosa centifolia* were found to faintly restrict the microbial proliferation. Phytochemical screening showed alkaloids, glycosides, terpenoids, steroids, flavonoids, tannins, reducing sugars and saponins were found in nearly all of the tested plants, selecting these plants as viable source for the production of antimicrobial drugs against oral pathogens. Similarly, Tirupatirao *et al.*, (2014) assessed the antibacterial actions of different extracts i.e. water, methanol and petroleum ether of two therapeutic plants in our country, *Ocimum sanctum* and *Azadirachta indica*, against *Bacillus* *subtilis, Staphylococcus aureus, Escherichia coli, Micrococcus luteus* and *Pseudomonas aeruginosa*. Each and every extracts were capable to restrict the proliferation of the pathogens at different levels. On the other hand, the methanolic extract of *Azadirachta indica* and the water extract of *Ocimum sanctum* exhibited significant antibacterial efficacy compared to the petroleum ether extract.

The antibacterial potentiality of ethanolic fractions of sixteen folk medicinal plants in Nepal was tested against 13 pathological and 2 reference bacterial strains by Marasini *et al.*, (2015). The findings revealed that the plants showed antimicrobial activity at different levels. Among the selected plants, *Cynodon dactylon* considered as the most effective plant that reduce the proliferation of indeed the methicillin-resistant *Staphylococcus aureus*, imipenem-resistant *Pseudomonas aeruginosa*, multidrug-resistant *Salmonella typhi* and *Salmonella typhimurium*. Additionally, the ethanolic extracts of *Cinnamomum camphora, Curculigo orchioides* and *Curcuma longa* exhibited the greatest MIC values against *Strepcoccus pyogenes*, whereas the chloroform fraction of *Cynodon dactylon* showed the significant antibacterial effect against *Staphylococcus aureus*. *Cynodon dactylon*, *Cinnamomum camphora*, *Curculigo orchioides* and *Cucurma longa* extracts with MIC values less than 100 µg/ml could be thought as a substantial source of antibacterial drug against diseases caused by multi-drug resistence bacteria. The antibacterial efficacy of *Morus indica* leaf extract against *Staphylococcus aureus*, *Aspergillus niger* and *Penicillium* was evaluated by Chaitali *et al.*, (2015). The antibacterial and antifungal efficiency of the ethanolic and methanolic extracts was superior, which could be attributable to the existance of different additional metabolites in the leaf of *Mangifera indica*. Londhe *et al.*, (2015) found that leaf of *Ocimum tenuiflorum, Ocimum gratissimum* and *Ocimum kilimandscharicum* possessed antimicrobial action against *Bacillus cereus, Bacillus subtilis, Escherichia coli, Pseudomonas aeruginosa* and *Aspergillus niger*. Antimicrobial effect was found in all of the three *Ocimum* species at different levels. Although, *Ocimum kilimandscharicum* exhibited significant antibacterial action against *Bacillus cereus*, *Escherichia coli* and *Pseudomonas aeruginosa*, whereas *Ocimum gratissimum* leaf extract was efficient against *Aspergillus niger*. Reducing sugars, monosaccharides, hexose sugar, amino acids, tannins and phenolic compounds, citric, malic and tartaric acids were found in primary phytochemical screening.

Phytochemical analysis, antioxidant and anti-microbial activity of *Suaeda vermiculata* were evaluated. The n-hexane extract contained twenty four compounds with bornyl acetate, γ-elemene and phytol constituting 73.74 % of the extract. At a concentration of 10 mg/ml, the n-hexane extract inhibited DPPH-radicals with a 27% efficiency, which was less effective than the volatile oil's DPPH reactivity. Except for *Candida albicans*, which showed inhibition zone diameter values of 19 mm with MIC values at 5.2 mg/ml for the volatile oil while inhibition zone diameter values of 26 mm and MIC values at 4.7 mg/ml were observed for the n-hexane extract, thus the antimicrobial activity of n-hexane extract was relatively weaker than the volatile oil (Al-Omar *et al.*, 2021). Antioxidant and antimicrobial activity of methanolic leaf extract of *Aegle* *tamilnadensis* revealed the presence of phenols and flavonoids as major phytochemicals and it possessed significant antioxidant and antimicrobial activity against *Staphylococcus aureus* and *E. coli* (Chellakumar *et al.,* 2017). Antibacterial activity of leaf and seed extract of *Carica papaya* against *Pseudomonus aeruginosa* and *E. coli* assessed by Dagne *et al.,* (2021). They found seed with ethanol extract showed highest antibacterial activity against *Pseudomonus aeruginosa* whereas lowest inhibition was recorded from leaf ethanol crude extract against *E. coli*. In vitro antibacterial activity of *Psidium guajava* leaf extract against *Klebsiella pneumonia* was evaluated by Hackman *et al.,* (2020). The investigation revealed that the ethanolic extract of guava leaf had MIC and MBC of 6.25 mg/ml, both of which indicated strong antibacterial activity against the carbapenem-resistant *K. pneumoniae*. Because the guava leaf extract contains flavonoids and other antimicrobial phytochemicals, it may be responsible for the antibacterial activity of the extract from the leaf. The results of these initial laboratory investigations point to the potential for developing effective antibiotics to treat carbapenem-resistant systemic illnesses. Jude *et al.,* (2020) found various phytochemicals like alkaloids, flavonoids, tannins, terpenoids, cardiac glycosides and reducing sugar from methanol extract of *Garcinia Kola*. The extract also exhibit effective antimicrobial activity against four pathogenic bacteria e.g. *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumonia* and two fungus like *Candida albicans* and *Aspergillus niger*. Anti-bacterial activity of isolated compounds i.e. pyrethrin II, jasmolin I and cinerolone from *Chrysanthemum cinerariaefolium* against methicillin-resistant *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Shigella sonnei* was studied by Kosgei *et al.,* (2021). Phytochemical screening of methanol extract of *Curcuma longa* showed the presence of alkaloids, phenols, saponins, steroids, tannins, glycosides and flavonoids. This study was also carried out to assess the antimicrobial potential of the methanolic extract of *Curcuma longa* rhizome against seven clinical isolates including *Staphylococcus aureus, Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Candida albicans, Aspergillus flavus* and *Fusarium* species (Maduakor *et al.,* 2022). The stem bark of *Khaya grandifoliola* and its ethanol extract possessed tannins, alkaloids, saponins, reducing sugars, flavonoids, terpenoids and phenols, according to a preliminary phytochemical screening. Using the agar well diffusion method, the antibacterial activity of its ethanolic extract was assessed against *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Escherichia coli* and *Klebsiella pneumoniae*. DPPH radical scavenging activity and total antioxidant capacity of its ethanolic extract also assessed (Quartey *et al.,* 2020). Phytochemical composition of *Buchholzia coriacea* and *Psychotria microphylla* leaf extracts revealed to possess minerals, alkaloids, protein, terpenoids, phenols, flavonoids, glycosides, steroids, tannins and vitamins. These plant extracts also used to study antibacterial activity against bacterial isolates from the water bodies like *Aeromonas hydrophila*, *Escherichia coli* and *Vibrio cholera* (Ude *et al.,* 2021). Phytochemical composition of *Syzygium polyanthum* methanolic leaf extract consists of alkaloids, saponin, terpenoids and steroid. Additionally antibacterial activity was tested against four bacterial pathogens like *Staphyloccous aureus, Streptococcus pyogenes*, methicillin-resistant Staphylococcus aureus and *Klebsella pneumonia* was demonstrated by Wahab *et al.,* (2021).

The effectiveness of leaf extracts from several South African plant species (*Bucida buceras, Breonadia salicina, Harpephyllum caffrum, Olinia ventosa, Vangueria infausta and Xylotheca kraussiana*) against a variety of phytopathogenic fungi was examined (*Aspergillus niger, Aspergillus parasiticus, Colletotricum gloeosporioides, Penicillium janthinellum, P. expansum, Trichoderma harzianum* and *Fusarium oxysporum*). These plant infections, which include blue rot on stamens and postharvest disease in citrus, generated significant financial losses in the fruit business. 600 plant species were chosen and tested against two animal fungal diseases, among other things (*Candida albicans* and *Cryptococcus neoformans*) (Mahlo *et al.*, 2016).

1.3.4. Hypoglycemic activity of plants

Diabetes mellitus is a severe and fatal disorder characterized by increased blood glucose level caused by reduction of insulin production, insulin resistance and modified carbohydrate, lipid and protein metabolism which can contribute to additional difficulties such as chronic kidney failure, retinal damage, cardio-vascular and neuro-degenerative disorders (Tomic *et al.,* 2022). Apart from breakthroughs in diabetes management and awareness, the occurrence of disease and disease-related complications appears to be increasing at a serious rate. Various medicines are used to treat diabetes and oxidative stress has been linked to a variety of side effects, prompting a worldwide hunt for plants with therapeutic activity (Inas *et al.,* 2011). In this point of view, hypoglycemic efficiency of *Murraya koenigii* leaf water extract in normal and alloxan-induced diabetic rabbits was evaluated by Kesari *et al.,* (2005). The findings revealed that a single oral treatment of different dose contents (200, 300, and 400 mg/kg body weight (BW)) of the water extract was effective in decreasing blood sugar levels in both normal and diabetic rabbits. *Murraya koenigii* leaf have long been used as a spice for food essence and are considered as secure component to eat, thus they could be given as a supplement to other diabetic therapy such as dietary therapy and pharmacological therapy.

The research by Rao and Nammi's, (2006) backs up the traditional use of *Terminalia chebula* (Combretaceae) to cure diabetes. They used short and long term research procedures to assess the anti-diabetic and renal function-protecting effects of the chloroform extract of *Terminalia chebula* in STZ-induced diabetic rats. Administering the extracts orally to STZ-induced diabetic rats at dosages of 100, 200 and 300 mg/kg in a trial of brevity and (300 mg/kg) in a lenthy research (daily for 8 weeks) was demonstrated to considerably lower blood glucose levels and showed considerable renoprotective effect. The lowering of blood glucose by *Terminalia chebula* can be attributed to either enhanced insulin production from Islets β-cells or an additional pancreatic pathway; although, the pathway of renoprotection remains unknown. The impact of *Dorstenia picta* methanolic extract on blood glucose levels and a few biochemical parameters in normal and STZ-induced diabetic rats was studied by Florence *et al.,* (2007). The findings revealed that a combination of *Dorstenia picta* methanolic extract and insulin might arrest the loss of body weight, polyphagia and polydipsia. The extract, when given at doses of 75 mg/kg and 150 mg/kg, was found to decrease blood glucose levels in diabetic rats effectively by 53.88% and 81.96% ($p<0.01$). Additionally, serum cholesterol, triglycerides, plasma SGOT and SGPT levels were effectively reduce in both normal and diabetic rats, whereas creatinine and total protein level remain unchanged. According to the authors, administration with *Dorstenia picta* extract may enhance glucose homeostasis in STZ-induced diabetes by perhaps insulin related action and ameliorating kidney and liver functions. The hypoglycemic impact of *Anacardium occidentale* Linn., in STZ-induced diabetic rats in a comparable study was evaluated by Sokeng *et al.,* (2007). The experiment found that when methanolic extract administered orally at doses of 35, 175 and 250 mg/kg, after 3 h it lowered blood glucose levels in diabetic rats efficiently with highest decrease of 37 and 35% at doses 175 and 250 mg/kg, respectively. Repeat delivery of methanolic extracts and their fractions, as well as n-hexane, dichloromethane and ethyl acetate fractions, dramatically lowered blood glucose levels by 21-48%, as well as urine glucose levels. Hexane and ethyl acetate portions of the extracts had the strongest effects, which could be attributed to the plant's non-polar and polar hypoglycemic chemicals.

The in vitro anti-diabetic and antioxidant actions of *Cirsium japonicum* roots, was investigated by Jie *et al.,* (2008). In Korea, the herb has been utilized as an antihemorrhagic, antihypertensive and antihepatitis substence. The methanolic and aquoeus extracts of *Cirsium japonicum* roots showed antioxidant activity at different levels. The methanolic extract being more powerful when compared with aqueous extract. Although, methanolic extract possessed no α-glucosidase inhibitory action, the aqueous extract possessed medium inhibitory effect on α-glucosidase, despite the methanolic extract having higher phenolic and flavonoid substance. The antidiabetic efficacy of both the leaf and callus collected from *Aegle marmelos* leaf explants was assessed by Arumugama *et al.,* (2008). In STZ-induced diabetic rabbits, both the leaf and the callus were found to dramatically lower blood sugar levels. The methanolic extracts of the leaf and callus showed the highest anti-diabetic activity when compared with other extracts.

The anti-diabetic properties of the methanol extract of *Artanema sesamoides* Benth., in STZ-induced diabetic rats were investigated. The extract at doses of 200 and 400 mg/kg BW efficiently lowered fasting blood glucose levels while raising liver glycogen levels (25.84 ± 1.52 mg/ml) when compared to diabetes control (12.31 ± 0.63 mg/ml) ($P<0.001$). Moreover, there was a maximum decline in the serum SGOT, SGPT and alkaline phosphatase activity than that of diabetic rats. On the other hand, the extract exhibited cytoprotective action as validated by a considerable reduction in cholesterol and triglycerides contents, as well as a progress in the HDL/LDL ratio (Sengul *et al.,* 2009). In a similar study, Prasad *et al.,* (2009) tested the anti-diabetic effect of water leaf extracts of three medicinal plants i.e. *Murraya koenigii*, *Psidium guajava* and *Catharanthus roseus*, in diabetic albino rats induced by STZ. Single oral adminidtration of these extracts at dose of 500 mg/kg BW daily for 15 days were found to lower blood sugar levels ($p<0.001$) efficiently and raise body weight in regard to diabetes control after 15 days. Additionally, histological architecture that was changed during diabetic symptoms was regained in a way that was equivalent to the conventional drug glibenclamide, which is used to treat diabetes. Methanolic extract of *Vinca rosea* (*Catharanthus roseus*) showed anti-diabetic effect in alloxan-induced diabetic rats (Ahmed *et al.*, 2010). Nearly all plant components of *Vinca rosea* have been utilized to treat numerous ailments in the past and have been scientifically confirmed (Cowley and Bennet, 1928; Pillay *et al.*, 1959; Nammi *et al.*, 2003). Furthermore, in diabetic rats, the methanolic whole plant extract of *Vinca rosea* at a dose of 500 mg/kg BW showed considerable antihyperglycemic effect as well as improvements in body weight, lipid profile and pancreatic β-cell regeneration. Some β-cells might have survived after alloxan's action, allowing *Vinca rosea* extract to act on them and causing to generate insulin, resulting in the plant's antidiabetic function. Furthermore, histological tests revealed that *Vinca rosea* extracts repair the pancreas, proving its antihyperglycemic activity. Antidiabetic efficacy of *Ravenala madagascariensis* leaf revealed the n-Hexane, ethyl acetate, ethanol and water leaf extracts of this plant at a concentration of 50 g/l showed antidiabetic property in both at in vitro and in vivo system at different levels. The ethanolic and water extracts strongly inhibited the impact on glucose diffusion in vitro and both extracts showed considerable in vivo antidiabetic property; moreover, the ethanolic extract exhibited superior blood glucose reducing property than the water extract. As a result, the findings proved the utilization of this plant as traditional medicine to cure diabetes (Priyadarsini *et al.*, 2010).

The water extract of *Garcinia kola* seeds, when given orally at a concentration of 200 mg/kg BW to normal rats, it was able to considerably reduce ($p<0.05$) blood glucode levels, as well as efficiently boost ($p<0.05$) superoxide dismutase action. The catalase activity, on the other hand, was not significantly affected ($p>0.05$). As a result, the study demonstrated that *Garcinia kola*, which has long been used in Nigeria to optimise neurological alertness and sleeplessness, may also have hypoglycemic and antioxidative potentials (Omage *et al.*, 2011). The antioxidant action and in vitro alpha-amylase property of *Amaranthus spinosus* in alloxan-induced diabetic rats was evaluated. *Amaranthus spinosus* has commonly been utilized to treat a variety of illnesses (Vaidyaratanam, 1996; William D'ymock, 1976; Kirtikar and Basu, 1987). The findings revealed that the methanolic extract of *Amaranthus spinosus* could considerably suppress the α-amylase activity, lower the increased blood sugar levels, reduce malondialdehyde and recover glutathione and catalase levels, which might be related to the active compound(s) found in the plant extract. An experiment of the anti-diabetic potential of *Scoparia dulcis* in STZ-induced diabetes rat was conducted. The water extract of *Scoparia dulcis* at a concentration of 250 mg/kg BW/twice in daily basis resulted in a significant reduction in fasting blood sugar level, urine sugar, thiobarbituric acid reactive substances, reduced glutathione and glycogen level with a simultaneous gain in body weight (Das and Chakraborty, 2011).

In addition to in vivo antidiabetic study, an in vitro experiment based on inhibitory effect on enzymatic activity can be useful in understanding the mechanism of plant extracts in the treatment of diabetes (Kifle *et al.*, 2022). As a result, reduction of α-amylase and α-glucosidase has received a lot of attention since it may offer an approach to regulate blood sugar levels in type

2 diabetes people (Ali *et al.,* 2006). In this regard, the anti-hyperglycemic effect of *Caesalpinia digyna* root methanolic extract was investigated for in vitro α-amylase and α-glucosidase inhibitory activity. The extract reduced both α-amylase and α-glucosidase activity in varying degrees (Narkhade *et al.,* 2011). The flavanols found in the extract are thought to be responsible for the plant's α-amylase inhibitory property, whereas the α-glucosidase inhibitory action is related to the intestinal α-glucosidase inhibitory activity. As increased blood sugar level following meal is one of the most prominent characteristics of diabetes mellitus, pharmacological efforts aimed at reducing postprandial hyperglycemia by suppressing the action of α-amylase have been a primary focus in diabetes management. The leaf of *Thespesia populnea* was evaluated for in vitro α-amylase inhibitory action (Sangeetha and Vedasree, 2012). The findings revealed that all of the extracts utilized, including petroleum ether, chloroform, ethyl acetate and methanol, had different levels of α-amylase inhibitory action. Ethyl acetate and methanol fraction, on the other hand, showed significant inhibitory action while compared with other extracts. Additional research revealed that the inhibitors have proteinous structure. Overall, the research supports the folkoric usage of *Thespesia populnea* to lower oxidative stress and ameliorate postprandial hyperglycemia, hence assisting in the prevention of diabetic complications.

In a study the reducing impact of *Telfaira occidentalis* on α-amylase and α-glucosidase was analyzed and it was found that both unprocessed and blanched *Telfaira occidentalis* leaf extracts showed enzymatic inhibition at varying degrees, with unprocessed leaf extracts showing greater inhibition. The antioxidant potential of *Telfaira occidentalis* leaf, together with enzyme inhibitory action, could be a plausible explanation for its application in the treatment of type 2 diabetes (Oboh *et al.,* (2012). The different leaf extracts of *Carica papaya* L., such as ethyl acetate, alcohol and water extract raised the percentage inhibitory effect on α-amylase in varying degrees while also slowing the digestion of starch over time. The method by which *Carica papaya* exhibited its inhibitory function could be linked to its effect on carbohydrate binding domain of α-amylase leading to the break down of the internal α-1, 4 glucosidase links in starch, thus inhibiting postprandial hyperglycemia (Jiju *et al.,* 2013).

Cassia fistula Linn., has been commonly used to treat hematemesis, pruritus, intestinal problems, leucoderma, diabetes and as an antipyretic, analgesic and laxative (Bhakta *et al.,* 2001). Shrikant and Manjunath, (2013) have backed up the traditional assertion that *Cassia fistula* can help with diabetic treatment. They investigated the in vitro α-amylase inhibitory actions of the entire alcoholic bark fraction of *Cassia fistula*, as well as its ethyl acetate and butanol extracts. The ethyl acetate fraction showed the most substantial inhibitory effect. The existance of flavonoids in the ethyl acetate extract could be the cause of α-amylase inhibitory activity.

In vitro α-amylase and α-glucosidase inhibitory property of *Terminalia bellirica* bark were investigated by Mary and Gayathri, (2014). Its extracts in petroleum ether, chloroform and ethanol showed different degrees of α-amylase and glucosidase inhibition. However, the ethanolic fraction displayed significant inhibitory action, which could be related to the existence of additional metabolites in the sample. The in vitro α-amylase activity of petroleum ether, chloroform, ethyl acetate and methanol fractions of *Tinospora cordifolia* leaf was also reported by Shareef *et al.,* (2014). The ethyl acetate and methanol extracts possessed the most significant inhibitory efficacy. Both in vivo and in vitro antihyperglycemic potential of *Actinidia kolomikta* extracts was evaluated by Yuan *et al.,* (2014). Alcohol and aqueous extracts of both the root and leaf of this plant showed α-glucosidase inhibitory effect at varying levels. Moreover, water leaf extract inhibited α-glucosidase more effectively when compared with the other extracts. Additionally, the water extract was found to lower blood glucose levels without producing hypoglycemia, as well as control severel diabetes-related blood parameters like protein metabolism, lipid profile and liver functions, indicating that *Actinidia kolomikta* could be a viable and long-term resource for diabetes treatment. The methanolic bark extract of *Pseudovaria macrophylla* at doses of 200 and 400 mg/kg BW were able of reducing blood sugar levels in STZ-nicotinamide induced diabetic rats, as well as efficiently raising antioxidant enzymes, decreased glutathione, progressing serum insulin, C-peptide levels and reducing lipid peroxidation levels (Aditya *et al.,* 2014). Moreover, *Pseudovaria macrophylla* significantly decreased serum pro-inflammatory cytokines while efficiently restoring the shape of the islet and β-cells. Furthermore, increased expression of insulin protein, GLUT-1, GLUT-2 and GLUT-4 in pancreatic cells could be one of the pathways behind the plant extract's antihyperglycemic effect.

Folk remedies for diabetes treatment have been widely utilized around the world until date. Although advancements in diabetes management, rural and urban African communities still depend entirely on folk medicines. Severel Sudanese plants have been documented to have antidiabetic property. In this regard, the antidiabetic potential of *Mitragyna inremis, Nauclea latifolia, Randia nilotica, Tinospora bakis* and *Striga hermonthica* has been investigated. The experiment revealed that water extracts of *Tinospora bakis, Nauclea latifolia* and *Randia nilotica* at concentrations of 400 mg/kg BW could efficiently decrease blood sugar levels in diabetic rats at acute condition. Additionally, the plants water extracts exhibited a various potentiality to efficiently reduce total cholesterol, total triglycerides, LDL-Cholesterol, plasma SGOT, SGPT, urea and blood urea nitrogen, whereas enhance HDL-Cholesterol. Though, *Striga hermonthica* contained no antihyperglycemic effect on diabetic rats. As a result, the study backs up the utilization of these plants in Sudanese folk remedy (Maha *et al.,* 2015). The ethanolic leaf extract of *Phyllanthus amarus* was found to decrease blood glucose levels in alloxan-induced diabetic mice effectly (Shetti and Kaliwel, 2015). In another research, Gupta *et al.,* (2015) evaluated the antidiabetic activity of *Urginea indica* ethanolic bulb extract and they found that 1.5 g/kg BW dose when given orally, it efficiently decreased blood glucose, total cholesterol and triglyceride levels, while increase in HDL-cholesterol level in STZ-induced diabetic rats.

Antioxidant and α-glucosidase inhibitor screening of *Merremia peltata* was conducted by Af-idah *et al.,* (2021) revealed significant DPPH and total antioxidant activity in its stem methanolic extract. Additionally leaf and stem extract of *Merremia peltata* showed potential as α-glucosidase inhibitors for diabetic therapy. Dabie *et al.,* (2022) evaluated the α-amylase inhibitory property of *Anthocleista nobilis* leaf extract. The 70% ethanolic extract had significant α-amylase inhibitory property due to the presence of phytochemicals such as flavonoids, saponins, alkaloids, tannins and terpenoids. Phytochemical investigation revealed the presence of three compounds namely, α-spinasterol, palmitic acid and pheophorbide A-methyl esters were isolated from wild *Amaranthus cruentus* and these were tested for in vitro antidiabetic activity. *Amaranthus* extracts and isolated compounds showed strong α-glucosidase activity inhibition and mild α-amylase activity inhibition indicating that the compounds slow glucose absorption (Nkobole *et al.*, 2021). Phytochemical investigation of the methanol stem-bark extract of *Ficus capensis* revealed the presence of alkaloids, cardiac glycosides, flavonoids, saponins, tannins, steroids, phenols and triterpenes. Its effects on alloxan induced hyperglycaemia in wistar rats reported that its fractions at tested doses (100, 200 and 400 mg/kg BW) significantly decreased blood glucose level after 2, 4, 8, 16 and 24 h post administration when compared with diabetic control (Bashir *et al.*, 2020). Different solvents like boiling water, 50% ethanol and 100% dan ethanol were used to extract *Cosmos caudatus* (kenikir) leaf and it was repoted that 50% ethanol extract had highest phenolic, flavonoid content and significantly higher antioxidant and antidiabetic property than other solvent fractions (Firdaus *et al.*, 2021). Phytochemical screening of the *Salvia officinalis* leaf extracts revealed presence of flavanone, sterols, saponins, tannins, alkaloids and triterpenes. Aqueous leaf extract of *Salvia officinalis* showed significant hypoglycemic effect on alloxan-induced diabetic Swiss albino mice model while comparing with other extract like methanol, hexane and ethyl acetate (Mbiti *et al.*, 2020). Anti-diabetic activity of *Hylocereus polyrhizus* (red dragon fruit peel) ethanolic extract against diabetic rats reported that 74.88 mg/200 g BW dose had statistically similar antidiabetic effect when compared with standard drug glibenclamide (0.09 mg/200 mg BW dose) (Panjaitan *et al.*, 2021). In the Fokoue and Santchou subdivisions of the Menoua Division, West Cameroon and a total of 49 medicinal plant species representing 26 distinct botanical families were counted. For the treatment of diabetes, hypertension and cardiovascular diseases, plant species like *Allium sativum*, *Aloe vera*, *Asystasia sp*., *Cymbopogon citratus*, *Gouania sp*., *Persea americana*, *Sonchus oleraceus* and *Vernonia amygdalina* were thought to be quite helpful (Zhang *et al.*, 2022).

1.3.5. Effect of antidiabetic compounds isolated from plants

'Berberine' is an oral hypoglycemic compound isolated from *Coptis chinensis*, *Berberis amurense*, *Phellodendron amurense* and various other plants having anti-dyslipidemic and anti-obesity property. Several animal models have been used for extensive research on its metabolic activity in controlling blood glucose and lipids. Berberine is an AMP-activated protein kinase (AMPK) activator. Its insulin-independent hypoglycemia impact is linked to mitochondrial function inhibition, glycolysis promotion and AMPK pathway activation. Additionally, berberine might function as an inhibitor of α-glucosidase. This compound increases insulin sensitivity in newly diagnosed type 2 diabetic individuals, which lowers blood insulin levels. However, it may enhance insulin secretion in patients with impaired β-cell function by regenerating damaged islets (Yin *et al.*, 2012).

'Ellagic acid' extracted from *Emblica officinalis* having many therapeutic benefits. Treatment with ellagic acid for 16 weeks after diabetes onset dramatically reduced renal impairment and oxidative stress. It greatly reduced the activation of NF-κB in the kidneys and also dramatically reduced renal disease and reduced the expressions of fibronectin and transforming growth factor-beta in renal tissues. Interleukin-1 beta, IL-6 and tumour necrosis factor-alpha, three pro-inflammatory cytokines were all considerably lowered in serum by ellagic acid. In diabetic rats, this compound had a protective impact on the kidneys in part due to its ability to lower blood sugar levels. This effect was accompanied by a reduction in inflammatory responses through inhibiting the NF-κB pathway (Ahad *et al.,* 2014).

'Erianin' is a naturally occurring substance isolated from *Dendrobium chrysotoxum* Lindl., which prevented choroid-retinal endothelial RF/6A cells from migrating and forming tubes as a consequence of high glucose. In RF/6A and microglia BV-2 cells, erianin decreased high glucose-induced vascular endothelial growth factor (VEGF) production, hypoxia-inducible factor 1-alpha (HIF-1-alpha) translocation into nucleus and ERK1/2 activation. It also prevented VEGF-induced activation of VEGF receptor 2 (VEGFR2) and its downstream cRaf-MEK1/2-ERK1/2 and PI3K-AKT signaling pathways in RF/6A cells, as well as VEGF-induced angiogenesis in both vitro and in vivo. In addition, this compound decreased the enlarged retinal arteries, VEGF expression and microglia activation in mice with oxygen-induced retinopathy and STZ-induced hyperglycemia (Yu *et al.,* 2016).

'Resveratrol' is a phytoestrogen compound having many beneficial influences on diabetic organisms. When administered to hyperglycemic mice, resveratrol lowered blood sugar levels. This effect appeared to be primarily the result of enhanced intracellular glucose transport. This compound had also been shown to protect Islets beta cells in diabetis. The potential of resveratrol to lower insulin secretion was revealed in tests on pancreatic islets; this effect was confirmed in animals with hyperinsulinemia, where it lowered blood insulin levels. Additionally, this compound had recently been found to block cytokine function and minimize the oxidative damage to pancreatic tissue. Resveratrol may also enhanced insulin activity, according to studies on animals with insulin resistance. It enhanced insulin action through a variety of mechanisms, including decreased adiposity, altered gene expression and altered enzyme activity. These findings suggested that this compound may help to manage and prevent diabetes (Szkudelski and Szkudelska, 2011).

'Piceatannol' is a natural resveratrol-like analog that extracted from the seeds of the passion fruit *(Passiflora edulis).* The activation of sirtuin and AMP-activated protein kinase by resveratrol has led to speculation that it may be a substance that prevents metabolic disorders. Researchers examined the impact of piceatannol on mice that fed a high-fat diet. Their findings demonstrated that piceatannol had no impact on the body weight gain or visceral fat gain brought on by high-fat diets in mice; however it lowered fasting blood sugar levels. Model mice showed lower blood sugar levels after receiving a single dose of this compound. Thus it may be useful in the prevention of diabetes, according to the evidence (Uchida-Maruki *et al.,* 2015).