Harnessing Nature's Pharmacy: Biotechnology Advances in Medicinal Plant Research

Abstract

The integration of biotechnology into medicinal plant research has revolutionized the pharmaceutical industry, offering unprecedented opportunities for the development of novel therapeutics and healthcare solutions. By tapping into the vast biochemical diversity of plants, scientists have unlocked a treasure trove of potential drug candidates, many of which have been used in traditional medicine for centuries. Biotechnological tools such as genetic engineering, tissue culture, metabolomics, and bioinformatics have enabled the precise manipulation and optimization of plant-derived compounds, leading to the production of high-value pharmaceuticals with enhanced efficacy and safety profiles. Moreover, biotechnology facilitates sustainable practices by enabling the cultivation of medicinal plants under controlled conditions, reducing reliance on wild harvesting and alleviating pressure on endangered species. As our understanding of plant biology continues to deepen, the synergy between biotechnology and medicinal plant research holds tremendous promise for addressing global health challenges and improving patient outcomes.

Keywords: biotechnology, medicinal, genetic engineering, controlled

Introduction

According to estimates, between 70 and 80 percent of people throughout the world rely on traditional herbal remedies for their main medical treatment. In vitro regeneration and genetic transformation are two examples of the biotechnological technologies that have been implemented in order to improve the content of bioactive chemicals in medicinal plants [1]. It is possible to make use of these instruments in order to produce secondary metabolites by employing plants as bioreactors. Advances in tissue culture and genetic engineering methods, particularly transformation technology, have made it possible to produce medicines, nutraceuticals, and other useful chemicals in large quantities. These advancements have opened up new paths for the manufacturing of these substances [2].

Recent developments in the fields of molecular biology, enzymology, and fermentation technology of plant cell cultures have led researchers to hypothesize that these systems have the potential to become a potentially useful source of secondary metabolites. In contrast, transgenic plants are able to sustain steady levels of protein production without the need for any extra intervention [3]. This is because DNA alteration causes plants that are infected with an engineered virus to create huge quantities of substances that would otherwise be undesirable. The use of plant tissue culture on a large scale is an appealing alternative to the conventional techniques of planting because it provides a regulated supply of biochemical that is independent of the availability of plants [4].

The process of combinatorial biosynthesis, which involves the combination of genes from several microbes in order to produce unique and intriguing metabolites, has emerged as a new tool for the manufacture of innovative natural products as well as for the manufacturing of rare and expensive natural goods [5]. Additionally, it is anticipated that combinatorial biosynthetic techniques may produce intriguing alternatives in the not too distant future. Due to the complexity of hundreds of genes and the products they produce in living organisms, conventional expression profiling methodologies are designed for single gene analysis [6]. However, genome-wide expression analysis demands a high degree of automation because of the complexity of the genes and their products. DNA microarrays have been designed for the purpose of studying transcriptional patterns in physiological and pathological settings. This

has led to the discovery of novel genes and molecular markers that may be used for the diagnosis, prediction, or prognosis of certain states [7].

There is a large variety of bioactive chemicals that are essential for the biomaterial businesses that are found in medicinal plants, which are classified as green chemical factories. However, because to the tremendous economic importance of these plants, plant breeders frequently fail to take them into consideration. Plant scientists have devised speedier biotechnology-based techniques (BBMs) to protect and improve these vital yet neglected plants in order to compensate for this situation [8].
The first thing that has to be done is to tell people about endangered medicinal plants and raise awareness about them. Research such as the examination of material by Kakkar et al. concerning nomenclature, classification, endangerment, plant morphology, ploidy, secondary metabolites, drug pharmacokinetics, conservation, and omics-based computational studies in the Aconitum genus is one method that might be utilized to accomplish this goal [9].
The second phase is to investigate the genetic history of plants that are considered to be important medications. Complete chloroplast genome sequencing and phylogenetic analysis were utilized by Wei et al. in order to differentiate between three medicinal plants that are related to Gaoben. These plants are Ligusticum sinense, L. jeholense, and Conioselinum vaginatum. With regard to the identification of these Gaoben-related medicinal compounds, their approach was proven to be of great use [10].
The third phase includes raising the amount of bioactive chemicals that are very beneficial. One of the most typical ways to enhance secondary metabolites is by the use of elicitors, which may be carried out either in vitro or ex vitro. Using Aspergillus niger, methyl jasmonate (MeJA), and silver nanoparticles (AgNPs) as elicitors in hydroponic media [11]. published a procedure that was designed to enhance the amount of important secondary metabolites that Silybum marianum produces. For the purpose of determining the important parameters involved in the response to elicitation in cell suspension cultures of medicinal Bryophyllum [12]. proposed a model that was based on machine learning...
An great foundation for increasing the amount of useful bioactive components found in medicinal plants is provided by the combination of novel isolation techniques and breeding procedures that are based on biotechnology. Tests were carried out by Jang and colleagues in order to isolate high-purity ginseng exosomes. These tests demonstrated that the procedure that they had devised could be utilized for other valuable medicinal plants [13].

Tissue culture

The process of cultivating plant tissue involves the growth and multiplication of plant cells, tissues, and organs on prescribed solid or liquid medium in an environment that is both aseptic and regulated. The commercial technology is mostly based on micropropagation, which is a technique that allows for fast multiplication of cells from very small stem cuttings, axillary buds, somatic embryos, cell clumps in suspension cultures, and bioreactors. There are various steps that make up the process of micropropagation [14]. These stages include pre-propagation, the initiation of explants, the culturing of explants for proliferation, shooting, rooting, and hardening, and they are generally applicable in the process of large-scale plant multiplication [15].
The creation of identical pathogen-free plants for use in agriculture and forestry is accomplished by the use of micropropagation, which is a sophisticated biotechnological technology. Protocols for the cloning of some medicinal plants have been created, and protocols for in vitro blooming, in vitro fruiting, and successful micropropagation have been researched in Withania somnifera, a medicinal plant that is used to treat tumors [16]. These protocols involve the use of axillary buds implants. Using nodal explants that were obtained from mature trees, a methodology for fast micropropagation of Hoslundia opposita was

devised [17].
The automation of micropropagation in bioreactors has been proposed by a number of writers as a potential method for lowering the expenses associated with micropropagation. Bioreactors are vessels that are built for the purpose of cultivating huge quantities of cells, tissues, or organs in liquid medium [18]. There are two primary categories that may be distinguished between them: those in which the cultures are submerged in the medium in a partial or temporary manner, and those in which the cultures are submerged in the medium continually [19]. The propagation of plants through the use of bioreactors has the potential to enhance the rate of multiplication and growth of cultures while simultaneously lowering the amount of space, energy, and labour that is required for commercial micro propagation. The culture systems that are used in bioreactors may be divided into three primary categories: those that produce biomass, those that produce metabolites and enzymes, and those that are responsible for the biotransformation of exogenously introduced metabolites [20]. The employment of customized air-lift, bubble column, bioreactors, and temporary immersion systems for propagating shoots, bud-clusters, and somatic embryos has resulted in the development of clonal propagation methods that need less labour and are more cost-effective. It has been shown that roots grown in bioreactors have the ability to release medicinally active chemicals, including as anticancer medicines, into the liquid medium of the bioreactor [21]. These compounds may then be continually extracted for use in pharmaceutical formulations.
A technique known as in vitro technology for the creation of plant bioactive compounds involves the cultivation of plant cells, tissues, and organs under aseptic conditions, without regard to the influence of geographical and climatic contexts [22]. In the face of unfavourable conditions, such as the depletion of plant populations, the loss of genetic diversity, the degradation of habitat, and the extinction of species, this method provides an option for the production of significant bioactive metabolites [23]. The technique of plant tissue culture is a feasible biotechnological tool that can be used to produce bioactive chemicals that can be utilized in a variety of contexts and contribute to the conservation of biodiversity in a sustainable manner while also allowing for the rational exploitation of biodiversity [24]. Because of its independence from environmental factors, its capacity to maintain consistent product quality and yield, its ability to recover new synthesis routes from mutant cell lines, and its ability to reduce pressure on overexploited medicinal and economically important plants, plant cell culture has emerged as a dependable method for the mass production of plant material. It has also made major achievements in building on breakthroughs in plant science, and it offers a constant and consistent source of natural products [25]. Additionally, it allows for the production of bioactive secondary metabolites in regulated conditions. Increasing the use of genetic tools and gaining a better knowledge of the structure and control of pathways for secondary metabolism will offer the foundation for levels of product output that are acceptable to the commercial sector [26]. A resurgence in interest in large-scale plant cell culture technologies can be attributed to the combined factors of low product yields and supply difficulties associated with plant harvesting, as well as the greater availability of natural goods for medical uses. The amount of knowledge on the biosynthesis pathways of desirable phytochemicals in plants and cultures is frequently in its infancy. It is necessary to design methodologies that will allow for the development of information based on cellular and molecular levels [27].

Combinatorial Biosynthesis

The technique of mixing metabolic pathways in diverse organisms at the genetic level is known as combinatorial biosynthesis. This method involves the combination of genes from various microbes in order to produce novel and intriguing secondary metabolites for plants. From the perspective of the pharmaceutical industry, hydroxylations and glycosylations are

classified as highly beneficial bioconversions [30]. These bioconversions have the potential to produce novel medications and enhance current treatments by increasing their activity and decreasing their toxicity. The promise of combinatorial biosynthesis has been demonstrated by recent accomplishments in the biosynthesis of polyketides from microbes, particularly Streptomyces [31].

Pharmaceuticals such as podophyllotoxin and paclitaxel are examples of substances that can only be manufactured by isolating them from plants. An excellent illustration of combinatorial biosynthesis is the process by which the enzymes of one species are combined with the product of another species in order to produce the product that is necessary [32]. The class of natural products known as terpenoids is considered to be quite extensive and significant, since it contains over 30,000 distinct structures. A significant amount of importance is attached to the sesquiterpenoids from a pharmaceutical point of view. The mevalonate (MVA) pathway and the deoxyxylulose phosphate (DOXP) pathway are the two pathways that are utilized in the biosynthesis of terpenoids [33]. E. coli that harbors the DOXP route has recently been shown to express the MVA pathway, which has resulted in the effective manufacture of the terpenoids amorpha-4,11-diene and taxadiene. In the family Asteraceae, the plant Artemisia annua is the source of the antimalarial medicine artemisinin [34]. The manufacture of the substance through transgenic plants or the modification of the biosynthetic route in host cells that are less complicated are also potential alternatives.

Carotenoids are produced by microorganisms through a process known as combinatorial biosynthesis. Lycopene, ß-carotene, and astaxantin are all products of the modified Candida utilis that has been selected for their synthesis [35]. Additionally, the biosynthesis of the intermediate GGDP is necessary for the formation of carotenoids in a host (host). For endogenous terpenoid compounds, E. coli is responsible for the production of the C15 precursor FDP. In addition to the expression of the GGDP synthase gene gps from Archaeoglobus fulgidis, the expression of the CrtE gene, which codes for geranyl diphosphate synthase, from Erwinia sp., is responsible for catalyzing the formation of GGDP from FDP [36].

In addition to the alkaloids vincristine, vinblastine, ajmaline, and morphine, which are derived from plants, combinatorial biosynthesis has also been described for the antibiotics rebeccamycin and staurosporine, which are derived from Streptomyces albus. There are seventeen stages involved in the production of morphine in Papaver somniferum [37]. One of the most important intermediates, known as (S)-norcoclaurine, is produced by the condensation of dopamine and 4-hydroxyphenylacetaldehyde (4-HPAA). The enzyme that catalyzes the production of (S)-norcoclaurine synthase was recently isolated from Thalictrum flavum and cloned in E. coli [38].

It has been determined that codeinone reductase is responsible for the final step in the conversion of codeine to morphine. Additionally, the gene that is expressed in E. coli and insect cells has been identified. Vinblastine and vincristine, which are monoterpenoid indole alkaloids derived from Catharanthus roseus, are employed as anticancer medications [39].

Advances in nature medicine

Plant biotechnology is a prominent area of attention in the field of biotechnology, which is defined as the utilization of biological systems and organisms for the purpose of developing or producing useful goods. Numerous bioactive secondary metabolites are produced by plants. These metabolites find use in a wide range of sectors, including the pharmaceutical industry, the fragrance industry, the cosmetics industry, the agrochemical industry, and the food additives industry. All of these secondary bioactive substances can be classified into five primary categories: medicines (drugs), flavours, scents (fragrances), pigments (dyes), agrochemicals, cosmetics, and food additives [40].

Alternative methods for the production of essential metabolites can be obtained through the

use of the in vitro plant cell culture technique. These methods include callus, suspension, immobilized cells, and differentiated cultures. The process of cultivating cells as a dispersed cell culture from callus that has been suspended in liquid growth media results in the formation of suspension cultures [41]. As a result of their superior efficiency in comparison to entire plants, they are utilized extensively in the research that investigates the generation of bioactive secondary metabolites by plant cells. It is not possible for microbial cells or chemical synthesis to create the important therapeutic compounds, tastes, perfumes, and colorants that may be obtained through plant cell culture systems. These systems provide a potential renewable supply of these substances [42].

Plant tissue culture technology has the potential to be an alternative method for the bioproduction of phytoconstituents with therapeutic value. It may be appealing under certain circumstances, such as when cultivation is difficult, when cultivation takes a long period of time, when the yield of metabolites is low, when chemical synthesis is not achieved, or when there are technical issues. It is possible to regulate the biosynthetic pathway of plants by the utilization of biotechnological techniques. This allows for the enhancement or reduction of the synthesis of certain chemicals [43].

Because of the research that has been done in the field of plant tissue and organ culture technology, several bioactive metabolites that may be used in the development of novel therapies have been produced under certain conditions. It is possible to get bioactive compounds from microbial, algal, and vegetable sources. These compounds are utilized in a variety of applications, such as antioxidants, anti-inflammatory agents, anti-allergenic chemicals, and so on [44]. The use of Agrobacterium rhizogenes to perform genetic transformations on plants is a relatively new technique that has been developed to address challenges that are associated with cell suspension cultures. It has been discovered that hairy roots are appropriate for the formation of secondary metabolites because of their consistent and high productivity in culture conditions that do not include the exposure of hormones. The manipulation of metabolic pathways and the production of protein medicines like antibodies and protein hormones are both possible applications of recombinant DNA technology of various kinds [45].

The toxicity of secondary metabolites, their economically useful nature, and the protective function they play against insects, diseases, or animal foragers are the three factors that contribute to the relevance of secondary metabolites in the field of biotechnology [46]. The various goals that can be accomplished through the application of plant biotechnology include the production of useful biochemicals, the rapid multiplication of clonal lines, the elimination of viruses, the rapid development of homozygous lines, the production and recovery of hybrids that are difficult to produce, the conservation of germplasm, the modification of plants genetically, and the creation of genome maps and molecular markers to assist conventional breeding efforts [47].

Plants are an excellent source for the production of bioactive secondary metabolites, which are of significant economic importance since they are used in the production of pharmaceuticals, flavourings and perfumes, dyes and pigments, insecticides, and added ingredients to food. There have been recent developments in the fields of molecular biology, enzymology, and fermentation technology that have led to the hypothesis that these plant products may be isolated from the aseptic growth of plant cells, tissues, and organs [48].

Preparation of herbal medicine

Because of the bioactive phytochemicals that they contain, medicinal plants are extremely important in both the prevention and treatment of a wide range of ailments. These chemicals, which include alkaloids, phenols, flavonoids, glycosides, and saponins, possess a wide range of properties, including antispasmodic, antimalarial, analgesic, diuretic, antioxidant, anti-allergenic, antibacterial, antiviral, anticancer, antimalarial, anti-inflammatory, antifungal, and

plant defence properties [49]. The usage of medicinal herbs and herbal preparations is a time-honoured practice that has been passed down from generation to generation. In recent years, developments in contemporary therapeutics have prompted the utilization of these natural therapies for the purpose of various disease preventive and treatment modalities.

When it comes to the management of chronic diseases, herbal medicines are the complementary and alternative medicine (CAM) strategies that are utilized the most frequently all over the world [50]. Some of the most prevalent chronic diseases include diabetes mellitus (DM), hypertension (HT), hyperlipidemia (HL), osteoporosis, cardiovascular disease, chronic obstructive pulmonary disease (COPD), asthma, epilepsy, seizures, obesity, oral health problems, hepatitis C and HIV/AIDS, dementia, Alzheimer's, autoimmune, Parkinson's disease, schizophrenia, bipolar disorder, multiple sclerosis, and glaucoma [51].

It was discovered in a study that involved 217 patients that around 29% of patients utilized herbal medication, with the percentage of patients who used herbal medicine being substantially higher among females. It was shown that users of herbal medicine were less likely to take conventional medications. The herbs that were used the most commonly were lemon (39.6%) and garlic (11.1%) for HT, cinnamon (12.7%) for DM, and walnut (6.3%) for HL [52].

Numerous photochemical, also known as nutraceuticals, derived from medicinal plants, including omega-3-fatty acids, dietary fibres, vitamins, antioxidants, plant sterols, flavonoids, and nutraceutical photochemical, have been shown to have therapeutic effects on chronic illnesses and to function as chronic fighters. When it comes to the prevention and treatment of a variety of chronic diseases, these photochemical are a successful method since they are plentiful, less hazardous, and less expensive [53].

In conclusion, medicinal plants play a vital part in the prevention and treatment of a variety of diseases due to the bioactive phytochemicals that they contain as well as the many therapies that they offer that are both inexpensive and effective. It is possible for us to strive toward a future that is both healthier and more sustainable if we make these natural treatments a part of our everyday lives [54].

Two separate disorders that produce frequent urination and continual thirst are diabetes mellitus (DM) and diabetes insipidus (DI). Both of these illnesses are referred to as diabetes. In contrast to diabetes mellitus (DM), which is a chronic endocrine condition defined by raised plasma glucose concentrations due to inadequate insulin, diabetes mellitus (DI) is caused by insulin shortage or resistance, which ultimately leads in high blood glucose. Both of these disorders result in the need to urinate often and persistent thirst [55].

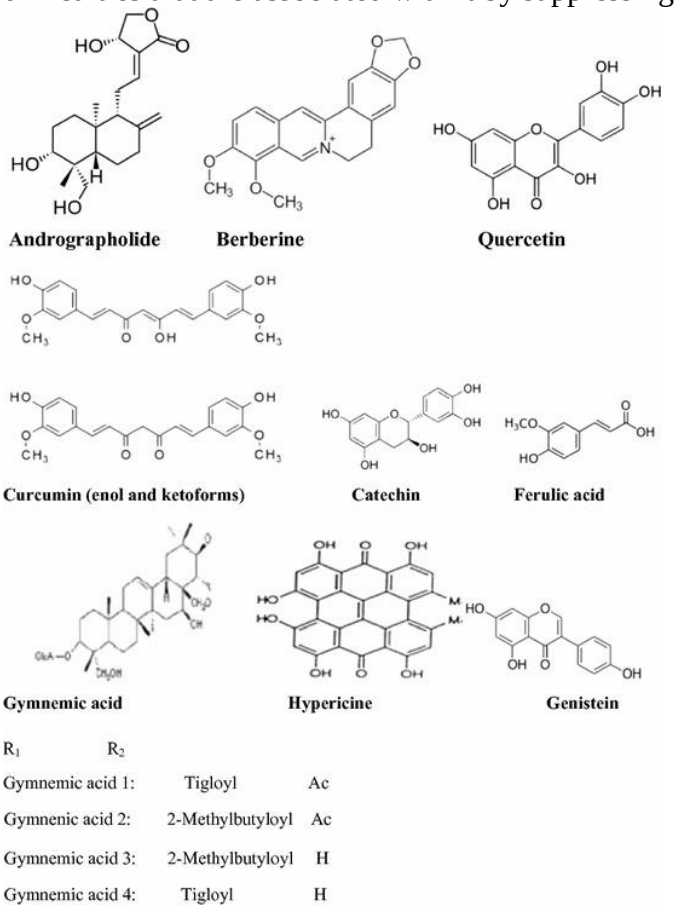
Central diabetes insipidus, nephrogenic diabetes insipidus, dipsogenic diabetes insipidus, and gestational diabetes insipidus are the four subtypes of this uncommon condition. Frequent urination is the most typical symptom of diarrhoea in children. Diabetes mellitus is classified as a non-communicable disease (NCD), which is a chronic endocrine illness that involves carbs, lipids, and proteins. Based on recommendations made by the National Institute for Clinical Excellence (NICE), target blood glucose level ranges are advised for both normal and diabetes blood sugar levels [56].

When it comes to the management of diabetes, a complete herbal medication therapeutic regimen provides a safe and effective support system for conventional therapy techniques. This, in conjunction with the monitoring of one's diet and the participation in physical activity, is an integrated approach to the management of type 2 diabetes. The development of type 2 diabetes is associated with the failure of β-cells, which is accompanied by resistance and obesity. Additionally, adipokines, hormones, and proteins are responsible for regulating sensitivity [57].

Hyperglycemia and glucose intolerance are two symptoms that are associated with diabetes,

which is a metabolic and endocrine illness that is caused by insulin resistance. Traditional Chinese and Indian medicine have recognized the efficacy of herbal medicines in the treatment and prevention of type 2 diabetes for a very long time. There is a rise in secondary consequences caused by the treatment medications that are now available. These complications include cardiovascular disease, renal failure, liver injury, dizziness, mental disorders, weight gain, and skin illnesses [58].

Sulfonylureas, metformin, and insulin-sensitizing glitazones are some of the most important therapeutic medicines for treating type 2 diabetes and the comorbidities that come along with it. Metformin and sulfonylureas are the primary medications used to prevent type 2 diabetes. Glitazones, on the other hand, bind to peroxisome proliferator-activated receptors (PPARs) and thereby lower inflammatory indicators [59]. An anti-inflammatory therapy known as salicylates, which inhibits IκB kinase (IKK) and reduces glucose levels by enhancing beta cell activity, together with nonsteroidal anti-inflammatory drugs (NSAIDs) and cyclooxygenase inhibitors, has the potential to enhance glucose-mediated macrosomia management. Researchers are actively looking for effective natural therapeutic targets that have fewer or no adverse effects, produced from bioactive molecules that are obtained from natural products. The goal of these molecules is to ameliorate insulin resistance and the difficulties that are associated with it by suppressing inflammatory signalling pathways [60].



	R_1	R_2
Gymnemic acid 1:	Tigloyl	Ac
Gymnenic acid 2:	2-Methylbutyloyl	Ac
Gymnemic acid 3:	2-Methylbutyloyl	H
Gymnemic acid 4:	Tigloyl	H

Fig 1. Ingredients for herbal medicine preparation

<u>Different compounds extract for herbal medicine</u>

A number of different mechanisms have been discovered by researchers that bioactive phytoconstituents can reduce hyperglycemic activity. Berberine, casuarine 6-O-α-glucoside, and calystegine B2 are examples of alkaloids that have the ability to block alpha glucosidase and in turn reduce the amount of glucose that is transported through the intestinal epithelium. In addition to being insulinotropic, substances containing imidazoline increase insulin secretion in a way that is reliant on glucose supply. Polysaccharides enhance glucose tolerance, lower blood glucose levels, and raise serum insulin levels. Polysaccharides also reduce blood glucose levels [61].

The levels of glucose are suppressed by flavonoids, which also considerably lower plasma cholesterol and triglycerides and boost the activity of hepatic glucokinase when they are present. Included in the category of flavonoids are the following: Bengalenoside flavonoids, cyanidin-3-galactoside, epigallocatechin gallate, genistein, hesperidin, naringin, prunin, kaempferitrin, kaempferol, kolaviron, leucodelphinidin, marsupsin, pterostilbene, quercetin, Rutin, shamimin, and leaves [62]. Dietary fibres have the ability to efficiently absorb glucose, slow down the diffusion of glucose, and block the activity of alpha-amylase, which may result in a reduction in the rate of glucose absorption and the concentration of postprandial blood glucose during the digestive process [63].

Terpenoids and steroids, such as α-amyrin acetate, andrographolide, 3 ω-acetoxy-16 c-hydroxybetulinic acid, bassic acid, charantin, christinin-A, colosolic acid, maslinic acid, corosolic acid, elatosides E, escins-IIA and IIB, forskolin, ginsenosides, gymnemic acid IV, momordin ic, β-sitosterol, and senegin derivatives, stimulate insulin release and related compounds [64]. Glycosides include Kalopanax pictus stem bark, jamboline/antimellin, myrciacitrins I and II, myrciaphenones A and B, neomyrtillin, pelargonidin 3-O-α-l rhamnoside, pseudoprototinosaponin AIII, prototinosaponin AIII, vitexin, isovitexin, and isorhamnetin 3-O-β-d-rutinoside, and miscellaneous compounds like allicin, bellidifolin, bakuchiol, curcuminoids, and ellagitannins [65].

In a nutshell, bioactive phytoconstituents are an essential component in the elimination of hyperglycemic activity in a variety of different aspects. Certain substances, such as alkaloids, polysaccharides, terpenoids and steroids, glycosides, and other compounds, are included in this category. These compounds, when incorporated into diets, have the potential to assist in the management of blood sugar levels, the improvement of glucose tolerance, and the promotion of general health [66].

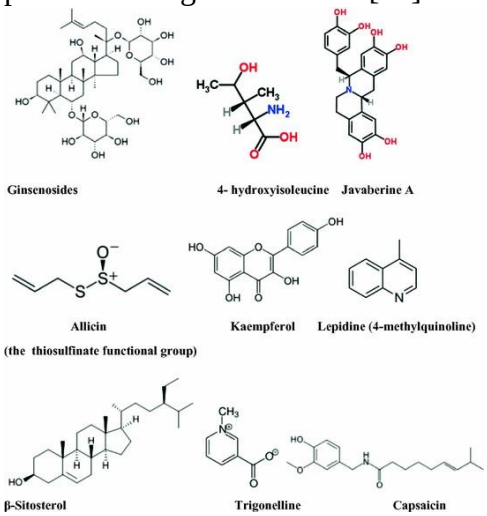


Fig 2. Different compounds extract for herbal medicine

It has been demonstrated that medicinal plants and the bioactive chemicals they contain have the ability to reduce blood glucose levels through a variety of processes. These mechanisms include insulin-mimicking action, increased β-cell regeneration, and glucose absorption. A number of phytoconstituents, including alkaloids, imidazoline compounds, polysaccharides, flavonoids, saponin, and bitter melon, have the ability to block alpha-glucosidase and reduce the amount of glucose that is transported through the intestinal epithelium. In addition to steroidal saponins, insulin-like peptides, alkaloids, and triterpenoids, bitter melon has a number of other components that have anti-diabetic properties [67].

A medical disease known as hypertension (HTN) is characterized by a high blood pressure in the arteries over an extended period of time. Systolic and diastolic pressure are the two components that make up blood pressure. Hypertension is often referred to as the "silent killer" due to the fact that it is asymptomatic and a significant contributor to cardiovascular morbidity and mortality figures [68]. The classification of hypertension in adults may differ, but at the age of around fifty, the systolic number becomes the most significant factor. It is possible for high blood pressure to cause arterial damage, aneurysm, and heart failure, blocked or burst blood vessels, decreased renal function, eyesight loss, loss of cognitive function, and metabolic syndrome. Hypertension can also lead to these complications [69]. The following are some of the warning indications that may indicate that your blood pressure is extremely high: chest pains, disorientation, headaches, ear noise or buzzing, irregular pulse, nosebleeds, fatigue, or changes in eyesight, etc. A high-salt diet, mental stress, alcohol, coffee, smoking, obesity, inactivity, birth control pills, heavy metal toxicity, and other factors are all potential causes of high blood pressure [70]. Individuals who have a blood pressure reading that is more than 130/80 mmHg and who also have diabetes or renal disease at the same time require further care. An extremely high rise (systolic values between 200 and 230 mmHg) in blood pressure during exercise is referred to as exercise hypertension. This elevation may be an indication that an individual is at risk for developing hypertension while they are at rest. In addition to being a significant cause of chronic kidney failure, persistent hypertension is also one of the risk factors for cardiovascular events such as strokes, heart attacks, heart failure, and arterial aneurysm. A moderate increase in arterial blood pressure is associated with a reduction in life expectancy [71].

Recent data suggests that hypertension and elevated blood pressure are on the rise, in part because of the rise in risk factors such as smoking, obesity, excessive alcohol use, social uneasiness and anxiety, and a lack of physical activity. Alterations to one's food and way of life, in addition to the use of medication, have the potential to enhance blood pressure control and reduce the health issues that are linked with it [72]. Alterations to one's food and way of life can assist improve blood pressure regulation and reduce the risk of related health concerns. Conventional antihypertensive are often accompanied with a number of adverse effects [73].

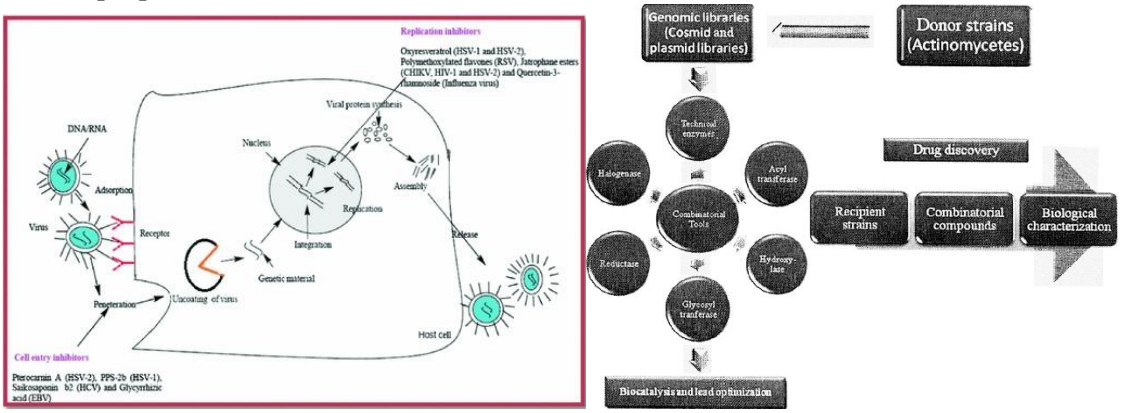


Fig 3. Drug discovery

Antihypertensive medications, which include calcium channel blockers, angiotensin II receptor antagonists, and angiotensin converting enzyme (ACE) inhibitors, are utilized in the treatment of hypertension. ACE inhibitors decrease the activity of angiotensin-converting enzyme (ACE), which is an enzyme responsible for the conversion of angiotensin I into angiotensin II, a powerful vasoconstrictor [74]. Calcium channel blockers, on the other hand, prevent calcium from entering muscle cells that are located in the walls of arteries. A few examples of these medications include captopril, enalapril, fosinopril, lisinopril, moexipril, perindopril, quinapril, ramipril, trandolapril, benazepril, and similar medications.
Azilsartan, candesartan, eprosartan, irbesartan, losartan, olmesartan, olmesartan medoxomil, telmisartan, valsartan, fimasartan, and other medications are examples of angiotensin II receptor antagonists [75]. These medications function by inhibiting the activation of angiotensin receptors. They may result in a variety of adverse effects, including but not limited to tiredness, headache, diarrhoea, constipation, skin rash, and edema. Herbs, on the other hand, do not result in any adverse effects such as a lack of strength, fatigue, sleepiness, impotence, cold hands and feet, depression, insomnia, irregular heartbeats, skin rash, dry mouth, dry cough, stuffy nose, headache, dizziness, puffiness around the eyes, constipation or diarrhoea, fever, and so on [76].
Because of their vast range of biological and therapeutic activity, variety, convenience of availability, greater safety margins, and lower cost compared to modern pharmaceuticals, herbal medicines have garnered increased interest in the treatment of hypertension. There has been a significant amount of study conducted in recent decades on local plants that have been shown to have antihypertensive medicinal properties. Some of these plants have been proven, while others have been refuted [77].

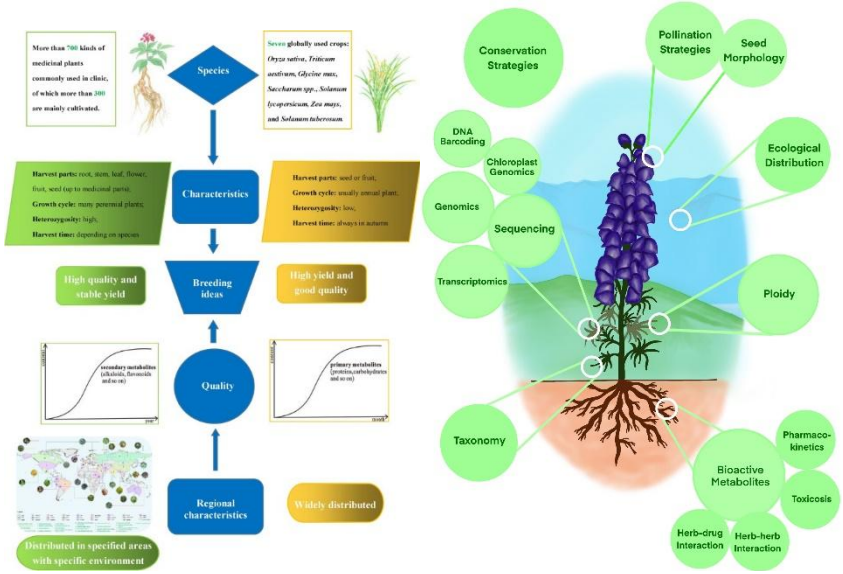


Fig 4. Antihypertensive medicinal properties

There are a number of medicinal plants that have been extensively researched and found to have hypotensive or antihypertensive effects, according to scientific research. There are some of these plants that have high levels of potassium, fibres, and bioactive chemicals that originate from secondary metabolic processes. A number of various plant sources, such as Stevia rebaudiana, Hippophae ramnoides, Fritillaria pugiensis, Evodia rutaecarpa, C. forskohlii, Peucedanum ostruthium, Salvia miltiorrhizae, Nandina domestica, Uncaria rhyncho, and others, were investigated by Ren-Ren et al. (2015) for their potential to reduce

hypertension [78].

Cancer treatments with herbal extracts

The condition known as cancer is defined by aberrant cell development, which takes place when the normal control system of the body ceases to function properly. Old cells do not die; rather, they replicate uncontrollably, resulting in the formation of new aberrant cells that have the potential to become a tumour [79]. The classification of cancer is based on the type of cell that is afflicted, and there are over 200 distinct varieties of cancer. Cancer can be treated in a variety of ways, with some patients responding better to surgical procedures, while others are more responsive to medication or radiation therapy [80]. According to the worldwide TNM system, there are five stages of cancer: stage 0 stands for the main tumour, stage II stands for lymph nodes, stage III is for distant metastases, and stage IV stands for widespread malignancy. Cancer that has metastasized throughout the body is referred to as being in the fourth stage. The metastases that are created by cancers often spread to certain organs, such as the liver, lungs, adrenal glands, brain, and bones. The symptoms that are caused by metastases differ depending on the location of the metastases [81].

In the past, medicinal plants have been utilized for the purpose of preventing and treating a broad range of ailments, including cancer, which continues to be one of the major causes of mortality around the globe [82]. Some bioactive components from these plants have been confirmed for their anticancer activities, such as curcumin from turmeric, genistein from soybean, EGCG from green tea polyphenols, resveratrol from grapes, sulforaphane from broccoli, isothiocyanates from cruciferous vegetables, silymarin from milk thistle, diallyl sulfide from garlic, lycopene from tomato, rosmarinic acid from rosemary, apigenin from parsley, gingerol from gingers, vitamin E from plant oil, boron-rich natural compound, hydroxytyrosol from virgin olive oil, phytoestrogens, etc [83].

There is now no treatment available for cancerous cancer; but, cancer chemoprevention using natural bioactive phytochemicals is a developing method that has the potential to prevent, hinder, postpone, or cure cancer [84]. Some of the bioactive components used as cancer chemopreventive include apiigenin, curcumin (diferuloylmethane), crocetin, cyanidin, Indole-3-carbinol (I3C), epigallocatechin gallate (EGCG), fisetin, genistein, gingerol, kaempferol, lycopene, phenyl isothiocyanate (PEITC), resveratrol, rosmarinic acid (RA), sulforaphane, triterpenoids, light-exposed mushrooms, vitamin D, and tocopherols [85]. Apigenin is a flavone that may be found in plants including parsley, celery, chamomile, and Moringa peregrina. It has been shown to have cytotoxic activity against breast cancer cell lines (MCF 7) and colon cell lines (HCT 116) [86]. For the treatment of colon cancer, breast cancer, lung metastases, and brain tumours, curcumin, which is a significant component of turmeric, has been the subject of research. A food colorant called crocetin, which is found in the dried stigmas of the plant, has the potential to be used as an agent in the development of a new anticancer medication that targets hepatocellular carcinoma [87]. In addition to its antioxidant and radical-scavenging properties, cyanidin, which is an extract of the pigment found in red berries, has the potential to lower the risk of developing cancer. Genistein, an isoflavone that may be found in a variety of plants, has antiangiogenic properties and has the potential to inhibit enzymes that govern cell division and cell survival, so preventing the uncontrolled cell proliferation that is linked with cancer [88]. The anticancer properties of gingerol, which is the active component of fresh ginger, have been investigated for their potential to inhibit the growth of malignancies in the pancreas, breast, colon, and ovary. Research has been conducted on the effects of kaempferol, a naturally occurring flavonol that has been extracted from a variety of foods and beverages, including tea, broccoli, witch-hazel, grapefruit, brussels sprouts, apples, and others [89]. Lycopene, a pigment that is brilliant red in colour and a phytochemical that may be found in tomatoes, red carrots, watermelons, and red papayas, possesses antioxidant activity and provides chemopreventive

benefits, particularly with regard to prostate cancer. Researchers have investigated the ability of phenyl isothiocyanate (PEITC) and sulforaphane derived from cruciferous vegetables to induce apoptosis in cell lines [90]. The results of these studies indicate that PEITC is particularly effective against melanoma. Resveratrol, a naturally occurring phenol that may be found in peanuts, red grape skin, and other fruits, has been shown to be effective in preventing cancer [91].

Rosmarinic acid, often known as RA, is a naturally occurring antioxidant that may be discovered in culinary spices and medicinal herbs. Lemon balm, peppermint, sage, thyme, oregano, and rosemary are some examples of these plants. Extracts of rosemary have been shown to have significant anti-inflammatory, anti-tumour, and anti-proliferation effects in a variety of in vitro and in vivo therapeutic applications [92]. Sulforaphane is an organosulfur chemical that may be derived from cruciferous vegetables. When a plant is damaged, the enzyme myrosinase in the gastrointestinal system converts glucoraphanin into sulforaphane. The cyclization of squalene, a triterpene hydrocarbon that is a precursor to all steroids, is the process by which plants produce triterpenoids through the process of biosynthesis [93]. There is a possibility that mushrooms that have been exposed to light are a great source of vitamin D, which has been linked to the development of breast cancer, colon cancer, ovarian cancer, and pancreatic cancer. Both tocopherols and tocotrienols, which are both fat-soluble antioxidants, have been shown to have antitumor effects due to their antioxidant capabilities. Vitamin E is a fat-soluble antioxidant that may be found in a wide variety of foods [94]. Vinblastine, vincristine, camptothecin derivatives, topotecan and irinotecan, etoposide, and paclitaxel are only some of the anticancer drugs that have been generated from plants. These molecules have been a significant source of various anticancer medications that have been used in clinical settings. According to their selective action against cancer-related molecular targets, a number of intriguing novel medicines are now in the process of being developed for clinical use. It is important to note that various bioactive substances have varying responses to various forms of cancer [95].

Alkaloids, which include vinblastine, vincristine, vindesine, and vinorelbine, are antimitotic and anti-microtubule medicines that are obtained from C. roseus. Camptothecin (CPT) is a topoisomerase inhibitor that is derived from Camptotheca acuminata. PPT is a non-alkaloid toxic lignan that is isolated from the roots and rhizomes of the polygonum peltatum plant. Docetaxel and paclitaxel are two chemotherapeutic medications that are derived from T. brevifolia, sometimes known as Pacific yew. Cell death is induced in Euphorbia peplus sap by the presence of ingenol mebutate. Breast cancer is treated with a medication called trastuzumab emtansine, also known as Kadcyla. This medication is an antibody that has been attached to a synthetic version of the cytotoxic principle of Maytenus ovatus [96].

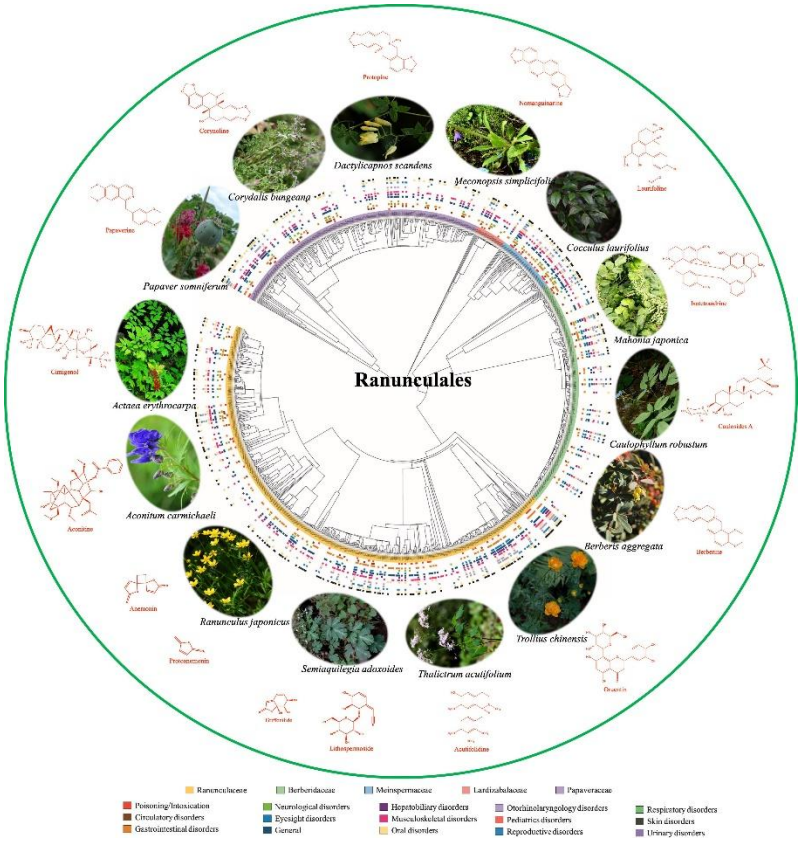


Fig 5. Cancer treatments with herbal extracts

Genetic engineering associated with herbal medicine

In many different types of crops, genetic transformation technology is a potent tool that may be used to produce plants with desired features. This technique holds the promise of overcoming agronomic and environmental issues that conventional breeding programs are unable to resolve. The introduction of foreign genes into plant cells and the subsequent regeneration of transgenic plants is accomplished by the use of Agrobacterium tumefaciens, a soil plant pathogenic bacterium. This is the approach that is utilized the most frequently. Through the delivery of a well-defined DNA segment, known as the transferred (T) DNA, of its tumor-inducing (Ti) plasmid into the host cell, this bacteria possesses the inherent capacity to alter its host without any external intervention [97].

The fast advancements in agricultural biotechnology may be attributed, in large part, to the development of effective regeneration and Agrobacterium-mediated transformation techniques that are suited for a variety of crop species. It is also possible to attain a similar level of success using medicinal plants, which may be utilized for the purpose of increasing the amount of secondary metabolites present. When compared to alternative techniques of transfection, agrobacterium-mediated gene transfer allows for the steady integration of specified DNA into the plant genome. This results in a reduced number of copy numbers, fewer rearrangements, and more stability of expression over the course of several generations [98].

Recent research has demonstrated that virus-based vectors may be utilized well for the creation of transgenic plants, and that non-Agrobacterium bacterial species can be utilized for the development of transgenic plants. This is the case for high transient expression of foreign proteins in transfected plants. Rhizobium sp. NGR234, Sinorhizobium meliloti, and Mesorhizobium loti are examples of non-Agrobacterium species that have the ability to genetically change a variety of plant species and plant tissues [99].

A modified shotgun is used in the process of particle bombardment, which was first developed in 1987. The goal of this technique is to accelerate tiny metal particles into plant cells at a velocity that is high enough to pierce the cell membrane. There are several kinds of plant materials that have been utilized as transformation targets. These include callus, cell suspension cultures, and structured tissues such immature embryos and meristems. Because of the relatively straightforward nature of this technology, it is a strong recommendation for potential application in the production of genetically modified plants in the future [100].
The development of transgenic therapeutic plants has been accomplished by a variety of techniques, such as electroporation, chloroplast transformation, and pathway engineering. In the process of electroporation, short pulses of high voltage electricity are used to produce transitory holes in the membrane of the host cell. These pores serve as pathways via which bare DNA may enter the host cell. The exposure of cell suspension protoplasts of the woody medicinal plant, Solatium dulumara, to a voltage ranging from 250 to 1250 V cm–1 for three consecutive pulses, each lasting 10-50 µs, resulted in the stimulation of the growth of protoplast-derived tissues [101]. These tissues displayed increased morphogenesis and required a shorter period of time in culture to exhibit this effect compared to tissues derived from untreated protoplasts. In addition, regenerated shoots were able to root more easily and had more extensive root systems than shoots that originated from protoplasts that had not been treated [102].
The process of chloroplast transformation includes the introduction of foreign genes into the genome of the chloroplast. This was initially accomplished in single-cell green algae, Chlamydomonas reinhardtii, tobacco plant, and more recently, Arabidopsis thaliana. With the help of the tobacco chloroplast genome, more than forty transgenes have been successfully integrated and expressed in order to bestow the agronomic features that are required or to produce large amounts of vaccination antibodies and biopharmaceuticals [103]. High levels of expression, non-affected by gene silencing, greater expression of bacterial genes than nuclei, and high levels of transgenic expression that ensure high pest mortality are some of the advantages of chloroplast transformation. There is also no possibility of the transgene being passed by pollen to plants, which is another advantage [104].
Another method of genetic manipulation is known as pathway engineering, and its primary objective is to enhance the generation of phytochemical ingredients that are active. To a large extent, however, the metabolic pathways that are responsible for the biosynthesis of active chemicals are not well known, and only a small number of genes that are responsible for important enzymatic or regulatory stages have been discovered [105]. The breadth and accuracy of manipulation through transgenesis will surely extend as a result of the application of new genomic methodologies and effective gene isolation methods to challenging secondary pathways in the metabolism of medicinal plants. This will provide the breeder with potentially superior material [106].
The application of biotechnology to abiotic stressors and other elements of agronomic performance has allowed for the engineering of agronomic features in medicinal plants. There have been descriptions of transgenic Atropa plants that are resistant to herbicides, pests, and diseases. Additionally, resistant biotypes can be utilized as a valuable source of germplasm for breeding purposes. Transgenesis will be of assistance in the breeding of types that are resistant to infections, particularly those that cause illnesses caused by fungi [107].

Conclusion

In conclusion, the advances in biotechnology have significantly revolutionized medicinal plant research, opening up new avenues for drug discovery, production, and understanding of plant biology. Through techniques such as genetic engineering, tissue culture, and metabolomics, scientists can now manipulate plant genomes to enhance desired traits, increase yields of bioactive compounds, and even develop entirely novel therapeutic agents.

This not only accelerates the pace of drug discovery but also offers solutions to challenges like plant conservation and sustainability. Furthermore, biotechnological tools enable the production of medicinal compounds in controlled environments, ensuring a consistent and reliable supply, which is particularly crucial for rare or endangered plant species. As we continue to delve deeper into the molecular mechanisms underlying plant biosynthesis and bioactivity, the potential for biotechnology to further advance medicinal plant research remains vast. However, ethical considerations, environmental impacts, and regulatory frameworks must be carefully navigated to ensure that these technologies are employed responsibly and sustainably for the betterment of human health and the environment.

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