# Medicinal Plants: A Rich Source of Bioactive Molecules Used in Drug Development 10

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**Abstract**

Medicinal plants are a rich repository of various biologically active molecules that have various pharmacological effects in mammals. The majority of the world's population (around 60–80%) still rely on the traditional medicinal method to treat common illnesses. In addition, finding a plant-derived antioxidant, which scavenges reactive oxygen species (ROS), has become a central focus of drug development research. The increment in oxidative stress and impaired cellular redox homeostasis due to elevated ROS lead to age-related diseases, including type 2 diabetes, cancer, and neurodegenerative disorders. Although drugs of plant extraction origin are available to prevent these age-related disorders, living cells have various defense mechanisms to prevent the harmful effects of ROS generation. Antioxidant enzymes neutralize free radicals and help the cell to overcome stress. Phytomolecules having antioxidative properties can help in stress modulation by scavenging ROS. This book chapter summarizes how bioactive molecules can be utilized as a tool for screening plant extract/ bioactive molecules of natural origin and advance our understanding of molecular mechanisms of drug action and diseases.

**Keywords**

Bioactive molecules · Antioxidant · Drug discovery

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## Abbreviations

| | |
|---|---|
| AD | Alzheimer's disease |
| *C. elegans* | *Caenorhabditis elegans* |
| HDL | High-density lipoprotein |
| LDL | Low-density lipoprotein |
| MAPs | Medicinal and aromatic plants |
| PD | Parkinson's disease |
| ROS | Reactive oxygen species |

## 10.1 Introduction

The reverse pharmacological consideration of conventional herbal medicine can be a better alternative and intelligent choice to systematically develop new, safer drugs (Patwardhan and Mashelkar 2009; Yuan et al. 2016). Since ancient times, medicinal and aromatic plants (MAPs) have been used as medicine. Medicinal herbs are a rich reservoir of huge bioactive molecules that are synthesized as "sidetracks" of the primary metabolism of crops (Petrovska 2012; Yuan et al. 2016). The majority of the world's population still relies on the traditional herbal medicine system for their primary health needs (Ekor 2014; Oyebode et al. 2016). There were more than 100 herbal prescriptions at the clinical stage (Atanasov et al. 2015; Chugh et al. 2018). More understanding of the side effects of synthetic drugs and the least side effects of plant-based medicines has led to the re-emergence of the demand for herbal products, which is expected to grow continuously by 2050 (Ekor 2014; Karimi et al. 2015; Welz et al. 2018). For decades, natural plant-derived medicines have developed to treat multiple human pathologies and ailments, including AIDS (Ji et al. 2009; Yin et al. 2013). Drug discovery strategies based on medicinal plant development and traditional herbal medicines are all of a sudden on the rise from the past decade. India accounts for approximately 1.6% of the ever-growing herbal industry (Gurib-Fakim 2006; Veeresham 2012; Ekor 2014). India has been a wealthy repository of maps and medicinal herbs used for multiple medical procedures since time immemorial in the Indian medical scheme (Pandey et al. 2013; Sen and Chakraborty 2017). Approximately 25,000 efficient herbal formulations are used by Indian rural groups to treat serious ailments. More than 7800 drug-manufacturing units in Indian consume a total of 2000 tons of herbs annually for the manufacturing of herbal medicines (Pandey et al. 2013; Sen and Chakraborty 2017). A tedious and expensive method to find robust and viable candidate herbs and their compounds is large-scale screening of traditionally used herbs. Successful completion of broad screening requires a better understanding of various approaches, and key past learning with correct future strategies is necessary (Leelananda and Lindert 2016; Harvey 2008; Atanasov et al. 2015; Yuan et al. 2016). The development of drugs of natural origin is currently limited to the discovery of new active molecules, but these traditional formulations need to be systematically evaluated to develop a better alternative to synthetic drugs (Pan et al.

2013; Li and Weng 2017). Hour-needed is a useful tool which consumes less time and cost. To this end, the model organisms like *C. elegans*, *D. melanogaster*, and *mice* emerged as an important tool for biomedical and toxicological research, especially for functional characterization of novel drug targets discovered using genomics technologies and for compound screens and broad-scale target validation (National Research Council 2000; Giacomotto and Ségalat 2010; Bulla and Cheng 2013).

## 10.2 Aging Impact on Health

Aging is a debilitating process that is associated with physiological deterioration (Kenyon 2010). It is characterized by a gradual deterioration that results in increased vulnerability to disease and death (Kenyon 2010). The rise in age was associated with the increased incidence of degenerative diseases such as diabetes, Alzheimer's disease (AD), and Parkinson's disease (PD) which are responsible for morbidity and higher socioeconomic costs (Blagosklonny and Hall 2009; Patrícia et al. 2017). The delay of aging and the avoidance of aging-related chronic disease pathogenesis are, therefore, an important part of the strategy to promote healthy aging (Topp et al. 2004; Shilsky et al. 2017). Chronic disease associated with aging and age is highly associated with high levels of stress and metabolic cellular load. Disrupting cellular homeostasis contributes to damages to DNA, lipids, and proteins that eventually decrease an organism's health and lifespan (Pomatto and Davies 2017; Srivastava 2017). Recent developments in gerontological research have resulted in the production of plant extracts and bioactive phytomolecules as a potential candidate for the management of age-related pathologies (Pant and Pandey 2015; Pohl and KongThoo Lin 2018). With the discovery of different cellular signaling pathways controlling aging and age-related diseases in many organisms, it appears targeting nutrient-sensing pathways and energy metabolism can prolong survival in living beings and preserve the vitality of later life (Kenyon 2010; Carmona and Michan 2016; Johnson 2018).

## 10.3 Medicinal Plants: An Age Source that Defies Bioactive Molecules

Medicinal plants is health-promoting influence has uncovered a gold mine of natural bioactive molecules (~1.00,000) (Zhang and Reddy 2018). The world is filled with a rich abundance of strength, medicinal plants. According to the active bioactive molecule, each plant is associated with its own unique therapeutic properties (Thomford et al. 2018; Koparde et al. 2019). Natural drug substances are stated to be vital in the modern medical system and have appreciable roles. By the existence of their bioactive molecules, their therapeutic function was justified. These are extremely useful as natural drugs because they possess disease-inhibiting properties, they contain less toxic and more stable natural bioactive compounds, and they integrate chemical or biological means of alteration and extraction of natural products into potent drugs (Ji et al. 2009; Zhang and Reddy 2018; Koparde et al. 2019). Bioactive molecules formed as sidetracks of the primary metabolic process of plants are typically found in various foods including fruits, vegetables, nuts, berries, and drinks. Fruits like grapes, pears, apples, berries, and cherries contain up to 200–300 mg of polyphenols per 100 g of fresh weight (Pandey and Rizvi 2009; Pant and Pandey 2015). In different plant species, more than 8000 polyphenolic compounds have been identified. Phytomolecules are groups of phenols, terpenes, indole/glucosinolates/sulfur compounds, organosulfides, betalains, enzyme inhibitors, and other organic acids (Tsao 2010; Upadhyay and Dixit 2015).

Such bioactive molecules play a significant role in the treatment of various human diseases and drug development due to their least side effects in comparison to their chemical counterparts (Pan et al. 2013; Tungmunnithum et al. 2018). Previous research on medicinal plants centered on the beneficial effect of phytomolecules as a dietary supplement, such as a source of vitamins (Vitamin A, E) or minerals (Nasri et al. 2014). Nevertheless, with advances in modern medical science and the discovery of various side effects of chemically synthesized medicines, biologists are looking for drugs from natural sources to treat various age-related neural diseases and others (Lublin and Link 2013; Durães et al. 2018). Various phytomolecules and plant extract are found to boost age-related pathologies for this reason (Pant and Pandey 2015). The ever-increasing geriatric population is of great concern to people worldwide, as it puts an immense socioeconomic burden on the world community. Hence, this hour is required to discover and improve antiaging medication with the least side effects. Antiaging work has boomed with increasing studies and articles on antiaging plant molecules. In *C. elegans*, several plant molecules and extracts are found to cause lifespan extension (Carretero et al. 2015; Pant and Pandey 2015). The higher homology of *C. elegans* model worth noting in human and higher mammals also extends the pharmacological use of antiaging phytomolecules in human (Pant and Pandey 2015; Tissenbaum 2015). It has been found that these bioactive molecules modulate cellular signaling pathways that control age-related disorders (Rea et al. 2018). Bioactive molecules can link fruit, herbs, vegetables, and health benefits (Pant and Pandey 2015). *Ginkgo biloba*, bananas, red wine, and tea extract, for example, are rich in flavonoids such as quercetin (Pant and Pandey 2015).

## 10.4 Phytochemicals as a Human Reality: Potential and Challenges for the Development of Drugs

It is a gift from God to find new herbal medicines for scientific research. A modern driving force for developing new drugs, biologically active metabolites derived from such products, which were led to drug success (Lahlou 2013; Thomford et al. 2018). Supplements to dietary habits play a crucial role in the everyday life of humans and also play an important role in improving human health. Most pharmaceutical compounds contain secondary plant metabolites which are critical to drug design (Katz and Meller 2014; Panche et al. 2016). Due to active bioactive molecules, each plant is known by its own unique therapeutic properties. Natural drug products are known to be important and have essential roles in the modern medicine system. Their therapeutic function was explained by their bioactive molecules (Veeresham 2012; Koparde et al. 2019). They are tremendously valuable as natural drugs because they possess disease-inhibiting properties; consist of simple, less harmful, and more powerful bioactive compounds; and combine chemical and biological means of modifying and converting natural products into effective drugs (Dias et al. 2012; Yuan et al. 2016). However, other considerations, such as environmental changes, varied geographical distribution, labor costs, and superior crop choice, should be taken care of by green plant developers to ensure adequate supply of the source material so that ample plants can assist the pharmaceutical industry in developing high-quality bioactive medicinal drugs (Atanasov et al. 2015; Koparde et al. 2019). Herbs, vegetables, and fruits have been used in many fields including medicine, food, flavoring, drinks, dyeing, repellents, fragrances, cosmetics, and other industrial applications. Such plants have been the basis for almost all-medicinal treatment and the use of synthetic drugs since the pre-historic period (Wang 2002; Kennedy and Wightman 2011). The medicinal benefit of these plants is correlated with their phytochemical elements, which perform different physiological behaviors on the human body (Pant and Pandey 2015). Alkaloids, tannins, flavonoids, and phenolic compounds are the most common of these elements. Several herbs have been reported to exhibit antioxidant activity, and polyphenols are a major potential source of antioxidant (Tungmunnithum et al. 2018). The benefit of these plants is linked to the secondary metabolites generated by the plants, because plants developed such secondary metabolites for the benefit of the plant itself as a protection against infection and injury; however secondary metabolites have beneficial effects on the human health and the potential to cure human diseases (Takshak and Agrawal 2019). Herbs in modern medicine have provided the very important life-saving medicines. But among the approximate 4 lakh plant species, only 6% were studied for their behavior, and not more than 20% of phytochemicals were studied (Atanasov et al. 2015; Yuan et al. 2016; Koparde et al. 2019). Therefore, to achieve the dreams of herbal drug discovery, there is a need to examine the various bioactive fractions and phytoanalysis and phytopharmacological assessment of herbal products.

## 10.5 Phytochemicals Can Enhance the Production of Antioxidants

The importance of the antioxidant components of plant materials in preserving health and protecting against coronary heart disease and cancer also raises interest among researchers, food producers, and consumers, as the step toward functional foods with unique health effects (Abuajah et al. 2015; Wilson et al. 2017). Phytochemicals can be present in a wide variety of foods, including fruits, vegetables, cereals, nuts, and cacao/chocolate, as well as soda, tea, coffee, and wine (Upadhyay and Dixit 2015). Polyphenolic compounds commonly distributed in higher plants have possible health benefits that are thought to be derived primarily from their antioxidant activity (Tungmunnithum et al. 2018). Antioxidant protection mechanism involves the exogenous and endogenous antioxidants. The main endogenous antioxidants are superoxide dismutase, glutathione peroxidase, catalase, and glutathione (Ighodaro and Akinloye 2018). ROS may also induce enzymes such as metalloproteinase collagenase, mucopolysaccharase hyaluronidase, and serine protease (elastase), contributing to invisible skin aging. Nevertheless, numerous in vitro scientific studies have shown that phytochemicals can diminish oxidant levels and thus inhibit collagenase and hyaluronidase tyrosinase enzymes (Garg 2017; Madan and Nanda 2018). Exogenous antioxidants include vitamins, carotenoids, and polyphenols, of which the diet is the primary source. There is growing evidence that polyphenols, as antioxidants, can protect cell constituents from oxidative damage and the risk of various degenerative diseases linked to oxidative stress (Pandey and Rizvi 2009). Table 10.1 included various bioactive extract of medicinal plants used in the treatment of various diseases/disorders.

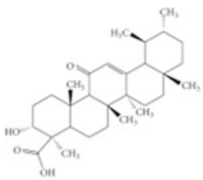
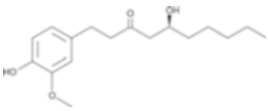
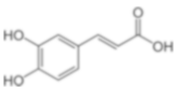
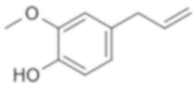
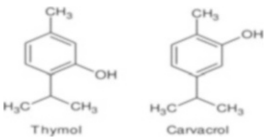
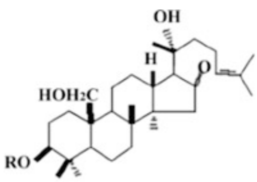
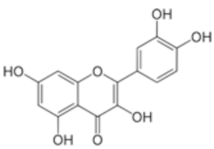
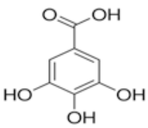
## 10.6 Polyphenols Uses in Human Healthspan and Lifespan

Several studies have shown that plant-derived bioactive compounds can postpone age-related declines and increase the lifespan and health of a variety of species (Argyropoulou et al. 2013; Leonov et al. 2015; Ergen et al. 2018). To prevent or slow down normal aging processes like cancer growth, one approach is to reduce stress such as shortening telomeres, non-telomeric DNA damage, and severe mitogenic signals (Shammas 2011; Bär and Blasco 2016). Several model organisms are concerned with the effect of exogenous antioxidants such as several phytomedicines on the aging process and age-related diseases (Pant and Pandey 2015).

### 10.6.1 Cardioprotective Effect

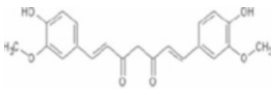
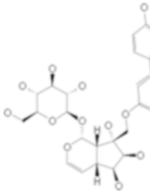
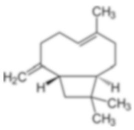
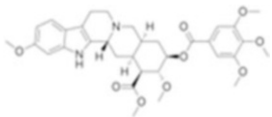
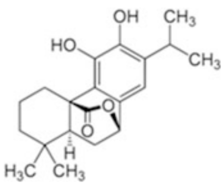
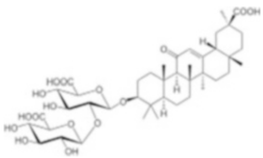
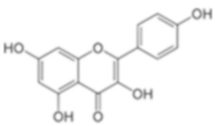
Polyphenols are powerful inhibitors of LDL oxidation, and this form of oxidation is seen as a key factor in the development of atherosclerosis. Antioxidant, antiplatelet, and anti-inflammatory behavior and improved HDL and endothelial function are many forms of defending polyphenols against cardiovascular diseases (Khurana et al. 2013; Cheng et al. 2017). The causal association between cardiovascular diseases (CVDs) and LDL oxidation is now well established. LDL particulate oxidation is closely associated with the risk of heart failure and myocardial infarction. Several studies have shown that many phytomolecules potentially inhibit LDL particle oxidation by chelating copper or directing free radical scavenging (Brites et al. 2017; Ahmad and Leake 2018).

**Table 10.1** Bioactive extract from medicinal plants used in the treatment of a various diseases/ disorders

| Natural drugs | Bioactive molecules | Therapeutics activity | References |
|---|---|---|---|
| *Himalaya Boswellia* | Boswellic acid<br> | Inflammation, healthy joints, immune-modulating | Siddiqui (2011) |
| *Zingiber officinale* (ginger) | 6-Gingerol<br> | Antifungal, antibacterial, anti-inflammatory, antidiabetic, nausea | Gunathilake and Rupasinghe (2015) |
| *Allium sativum* L. (garlic) | Caffeic acid<br><br>*S*-allyl cysteine | Antiaging, anticancer, hepatoprotective activity | Moutia et al. (2018) |
| *Ocimum sanctum* | Eugenol<br> | Bronchitis asthma, malaria, diarrhea, dysentery, skin diseases, arthritis, chronic fever | Garg and Sardana (2016) |
| *Origanum vulgare* (oregano) | Thymol, carvacrol<br> | Antibiotics, anti-allergies, tumors | Gutiérrez-Grijalva et al. (2018) |
| *Bacopa monnieri* | Bacosides<br> | Antiaging, neuroprotection | Singh et al. (2016) |
| *Emblica officinalis* (amla) | Quercetin,<br><br>Gallic acid,<br><br>Myricetin | Cardioprotective, gastroprotective, antidiarrheal, and neuroprotective properties | Bhandari and Kamdod (2012) |

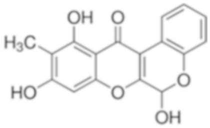
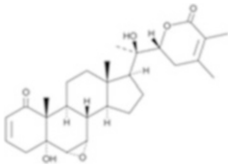
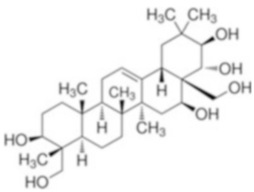
(continued)

**Table 10.1** (continued)

| Natural drugs | Bioactive molecules | Therapeutics activity | References |
|---|---|---|---|
| *Curcumin longa* (turmeric) | Curcumin  | Antiaging, neuroprotection | Panda et al. (2017) |
| *Premna integrifolia* | 4-hydroxy-E-globularinin  | Antiaging, skin disorders, asthma, diabetes | Mali (2016); Asthana et al. (2015) |
| *Ocimum basilicum* | Beta-caryophyllene  | Neuroprotective activity, antiaging | Asthana et al. (2015) |
| *Rauwolfia serpentina* | Reserpine  | Antiaging | Kaur (2018) |
| *Rosmarinus officinalis* L. (rosemary) | Carnosol  | Antiaging, anticancer | Kompelly et al. (2019) |
| *Glycyrrhiza glabra* | Licorice  | Antiaging, hepatitis, HIV, influenza, pain relief | Ishtiyaq et al. (2019) |
| *Ginkgo biloba* | Kaempferol  | Neuroprotection, antiaging | Luo (2001); Nuhu et al. (2017) |

(continued)

**Table 10.1** (continued)

| Natural drugs | Bioactive molecules | Therapeutics activity | References |
|---|---|---|---|
| *B. diffusa* | Boeravinone B   | Antiaging | Rathor and Pandey (2018); Akhter et al. (2019) |
| *Withania somnifera* | Withanolide A  | Antiaging, anticancer, neuroprotective | Verma and Kumar (2011); Mandal and Reddy (2017) |
| *Asparagus racemosus* | Shatavarin IV   | Antiaging, anti-parkinsonism | Singh and Geetanjali (2016); Selvaraj et al. (2019) |
| *Cinnamomum cassia* | Cinnacassosides | Antidiabetes, antiulcerogenic | Upadhyay (2017) |

## 10.6.2 Anticancer Effect

The impact of bioactive compounds on human cancer cell lines is most often protective and helps to minimize the number or growth of tumors. Some polyphenols including catechins, quercetin, isoflavones, lignans, flavanones, ellagic acid, red wine polyphenols, resveratrol, and curcumin have protective effects in some models, but their mechanisms of action have been found to be unique (Pandey and Rizvi 2009; Działo et al. 2016). Multiple mechanisms of action for the chemical prevention of polyphenols have been established, including estrogenic/antiestrogenic behavior, antiproliferation and initiation of cell cycle arrest or apoptosis, and oxidation prevention (Cipolletti et al. 2018). It has also been shown that theaflavins and thearubigins, the abundant polyphenols in black tea, possess significant anticancer properties (Pandey and Rizvi 2009). Some compounds inhibit all stages of cancer growth and have been shown to be active in most cancers, including lung, hair, breast, prostate, stomach, and colorectal cancer (Wang et al. 2012).

### 10.6.3 Antidiabetic Effect

Impairment of the glucose metabolism causes metabolic instability with the onset of hyperglycemia and then diabetes mellitus. There are two major diabetes categories: type 1 and type 2. Numerous studies document polyphenols' antidiabetic effects. Tea catechins are tested for their antidiabetic potential (Pandey and Rizvi 2009; Umeno et al. 2016). Polyphenols can affect glycemia through a variety of mechanisms, including inhibition or absorption of glucose in the intestine by peripheral tissues. A recent study showed that quercetin can help protect changes in patients with diabetes during oxidative stress. Several research papers have shown that by working at many levels, some polyphenols act as an effective antidiabetic agent. These molecules have shown decreased blood glucose, followed by significantly increased plasma insulin and a negative correlation between blood glucose and plasma insulin (Bahadoran et al. 2013; Mukhopadhyay and Prajapati 2015).

### 10.6.4 Antiaging Effect

Aging is associated with gradual degeneration of organ function in organism. This is due to excess amount of cellular ROS which can cause oxidative stress. A certain amount of oxidative damage occurs even under normal conditions, but the rate of this damage increases as the efficacy of antioxidant and repair mechanisms declines throughout aging process (Nita and Grzybowski 2016; Tan et al. 2018). Fruit and vegetable extracts with high flavonoids also exhibit high total antioxidant activity such as blueberries, strawberries, and lettuce (Pandey and Rizvi 2009).

### 10.6.5 Neuroprotective Effects

Oxidant inflammation and brain macromolecular damage are important factors in neurodegenerative diseases. Polyphenols are highly antioxidant in nature, and their use in neurological diseases can provide protection (Tan et al. 2018). Furthermore, the antioxidant function is also associated with the induction of antioxidant expression and detoxifying enzymes, particularly in the brain (Kurutas 2015).

## 10.7 Future Avenues in Herbal Drug Discovery

Phytochemistry or natural product phytoanalysis is the foundation and core of both the herbal and food industries of chemical science. Scientific research on medicinal plants in many developed countries is increasingly needed for an hour at various research institutes, universities, and pharmaceutical laboratories as well as in their clinics. Nearly all countries have their own herbal pharmaceutical copeias and make adjustments to new monographs and procedures from time to time to maintain their interest of herbal products that come from common people. India's Ayurvedic pharmacopeia includes many specific quality standards and techniques of isolation, separation, and spectroscopic identification of hundreds of common herbal medicines. Both research and advances on drug discovery have immense potential to exploit chemical and natural product varieties. Newly established techniques are fast-growing, with strong results in the discovery of natural drugs.

## 10.8 Conclusion

Nature's exceptional phenomenon is always a golden mark of completing the discovery of herbal medicines. In recent days, the majority of the prevalent diseases and metabolic disorders have been treated with natural medicines. The chemical constituents of the plant and the pharmacological screening will provide the basis for creating a lead molecule through the discovery of herbal medicines. A increasing interest in the production of herbal medicinal products which increases minimal side effects, there are better opportunities to explore medicinal and other biological properties of previously inaccessible natural products. Life was made possible or extended many years ago only because of natural herbs as per the literature references that can be obtained. In the new era of the twenty-first century, without herbal medicines or products obtained through the discovery of natural herbal drugs, no life on earth is possible.

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