



FOLKLORE MEDICINAL PLANTS USED AS ANTIAGEING AGENTS: A REVIEW

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ABSTRACT

Natural products play an essential role in prevention of ageing and therapy of various neurodegenerative diseases, and neuronal dysfunctions. Different studies suggest that natural products, such as polyphenolic and alkaloids compounds that isolated from plants potentially delayed the ageing processes, delayed neurodegeneration and also improve memory and cognitive function. Ethno pharmacological studies have provided information to identify potential new drugs from plant sources. Numerous plants have been used to delay the ageing processes and treat cognitive disorders. Anti-inflammatory and antioxidant activities of plants and isolated components from plants were used in improvement neuro-

inflammation, anxiety, convulsion, ageing etc. Medicinal plants have beneficial properties due to presence of various complex chemical substances for treatment of toxicity in the nervous system. The medicinal plants contain several phytochemicals such as vitamins, carotenoids, terpenoids, polyphenols, alkaloids, tannins, saponins, etc. These compounds have antioxidant activities, which can be used in the treatment of multiple ailments like diabetes, cancer, neurodegenerative disorders etc. Since phenolic compounds are capable of inhibiting free radicals, they can retard the ageing process. Ageing is an inevitable process for all living organisms in which the involvement of reactive oxygen species (ROS) and free radicals have been implicated. This review focuses on some medicinal plants and their bioactive compounds which can serve as anti-ageing agents.

KEYWORDS: Medicinal plants, ageing, phytochemicals, reactive oxygen species, neurodegeneration.

MEDICINAL PLANTS

Medicinal plants, also called **medicinal herbs**, have been discovered and used in traditional medicine practices since prehistoric times. Plants synthesise hundreds of chemical compounds for functions including defence against insects, fungi, diseases, and herbivorous mammals.

Numerous phytochemicals with potential or established biological activity have been identified. Medicinal plants are widely used in non-industrialized societies, mainly because they are readily available and cheaper than modern medicines. The annual global export value of 50,000 to 70,000 types of plants with suspected medicinal properties was estimated to be US\$2.2 billion in 2012, and in 2017, the potential global market for botanical extracts and medicines was estimated at several hundred billion dollars.^[1] In many countries, there is little regulation of traditional medicine, but the World Health Organization coordinates a network to encourage safe and rational usage. Medicinal plants face both general threats, such as climate change and habitat destruction, and the specific threat of over-collection to meet market demand.^[1]

A medicinal plant is a plant that is used to attempt to maintain health, to be administered for a specific condition, or both, whether in modern medicine or in traditional medicine.^{[2][3]} The Food and Agriculture Organization estimated in 2002 that over 50,000 medicinal plants are used across the world.^[4] The Royal Botanic Gardens, Kew more conservatively estimated in 2016 that 17,810 plant species have a medicinal use, out of some 30,000 plants for which a use of any kind is documented.^[5]

In modern medicine, around a quarter of the drugs prescribed to patients are derived from medicinal plants, and they are rigorously tested.^{[3][6]} In other systems of medicine, medicinal plants may constitute the majority of what are often informal attempted treatments, not tested scientifically.^[7] The World Health Organization estimates, without reliable data, that some 80 percent of the world's population depends mainly on traditional medicine (including but not limited to plants); perhaps some two billion people are largely reliant on medicinal plants.^{[3][6]} The use of plant-based materials including herbal or natural health products with supposed health benefits, is increasing in developed countries.^[8] This brings attendant risks of toxicity and other effects on human health, despite the safe image of herbal remedies.^[8] Herbal medicines have been in use since long before modern medicine existed; there was and often still is little or no knowledge of the pharmacological basis of their actions, if any, or of their

safety. The World Health Organization formulated a policy on traditional medicine in 1991, and since then has published guidelines for them, with a series of monographs on widely used herbal medicines.^{[9][10]}

Medicinal plants may provide three main kinds of benefit: health benefits to the people who consume them as medicines; financial benefits to people who harvest, process, and distribute them for sale; and society-wide benefits, such as job opportunities, taxation income, and a healthier labour force.^[3] However, development of plants or extracts having potential medicinal uses is blunted by weak scientific evidence, poor practices in the process of drug development, and insufficient financing.^[2]

All plants produce chemical compounds which give them an evolutionary advantage, such as defending against herbivores or, in the example of salicylic acid, as a hormone in plant defenses.^{[11][12]} These phytochemicals have potential for use as drugs, and the content and known pharmacological activity of these substances in medicinal plants is the scientific basis for their use in modern medicine, if scientifically confirmed.^[2] For instance, daffodils (*Narcissus*) contain nine groups of alkaloids including galantamine, licensed for use against Alzheimer's disease. The alkaloids are bitter-tasting and toxic, and concentrated in the parts of the plant such as the stem most likely to be eaten by herbivores; they may also protect against parasites.^[13-15]

PHYTOCHEMICALS IN MEDICINAL PLANTS

Phytochemicals, also known as phytonutrients, are natural non-essential chemical compounds found in plants (phyto is a Greek word meaning “plant”). They can occur in vegetables, grains, legumes, beans, fruits, herbs, nuts, roots, leaves and seeds. Phytochemicals are compounds that give plants their color, flavor, and smell. These compounds are thought to be largely responsible for the medicinal properties and health benefits of medicinal herbs. In addition, phytochemicals also include poisonous and toxic chemicals found in plants. These natural compounds are classified according to their chemical structure and to some extent functional properties. There are thousands of known phytochemicals and more are discovered every year. Phytochemicals present in plants protect from various diseases.

Modern knowledge of medicinal plants is being systematised in the Medicinal Plant Transcriptomics Database, which by 2011 provided a sequence reference for the transcriptome of some thirty species.^[16] The major classes of pharmacologically

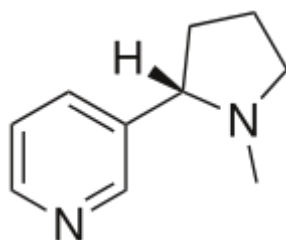
active phytochemicals are described below, with examples of medicinal plants that contain them.^{[10][17-19]}

Alkaloids

Alkaloids are bitter-tasting chemicals, very widespread in nature, and often toxic, found in many medicinal plants.^[20] There are several classes with different modes of action as drugs, both recreational and pharmaceutical. Medicines of different classes include atropine, scopolamine, and hyoscyamine (all from nightshade),^[21] the traditional medicine berberine (from plants such as Berberis and Mahonia), caffeine (Coffea), cocaine (Coca), ephedrine (Ephedra), morphine (opium poppy), nicotine (tobacco), reserpine (Rauwolfia serpentina), quinidine and quinine (Cinchona), vincamine (Vinca minor), and vincristine (Catharanthus roseus).^{[9][22]}



The opium poppy *Papaver somniferum* is the source of the alkaloids morphine and codeine.^[51]



The alkaloid nicotine from tobacco binds directly to the body's Nicotinic acetylcholine receptors, accounting for its pharmacological effects.^[23]



Deadly nightshade, *Atropa belladonna*, yields tropane alkaloids including atropine, scopolamine and hyoscyamine.^[21]

Glycosides

Anthraquinone glycosides are found in medicinal plants such as rhubarb, cascara, and Alexandrian senna.^{[24][25]} Plant-based laxatives made from such plants include senna,^[26] rhubarb^[27] and Aloe.^[19]

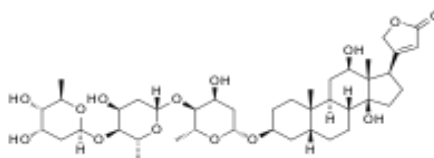
The cardiac glycosides are powerful drugs from medicinal plants including foxglove and lily of the valley. They include digoxin and digitoxin which support the beating of the heart, and act as diuretics.^[11]



Senna alexandrina, containing anthraquinone glycosides, has been used as a laxative for millennia.^[26]



The foxglove, *Digitalis purpurea*, contains digoxin, a cardiac glycoside. The plant was used on heart conditions long before the glycoside was identified.^{[3][28]}



Digoxin is used to treat atrial fibrillation, atrial flutter and sometimes heart failure.^[11]

Polyphenols

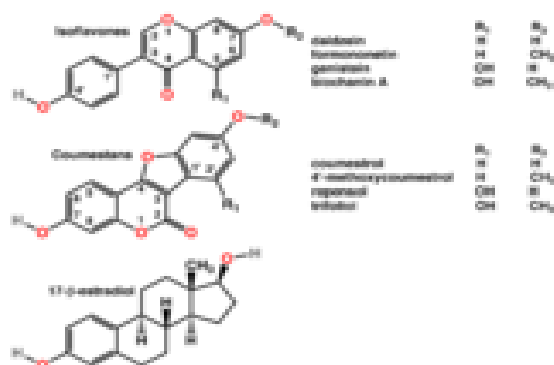
Polyphenols of several classes are widespread in plants, having diverse roles in defenses against plant diseases and predators.^[11] They include hormone-mimicking phytoestrogens and astringent tannins.^{[19][29]} Plants containing phytoestrogens have been administered for centuries for gynecological disorders, such as fertility, menstrual, and menopausal

problems.^[30] Among these plants are *Pueraria mirifica*,^[31] kudzu,^[32] angelica,^[33] fennel, and anise.^[34]

Many polyphenolic extracts, such as from grape seeds, olives or maritime pine bark, are sold as dietary supplements and cosmetics without proof or legal health claims for beneficial health effects.^[35] In Ayurveda, the astringent rind of the pomegranate, containing polyphenols called punicalagins, is used as a medicine.^[36]



Angelica, containing phytoestrogens, has long been used for gynaecological disorders.



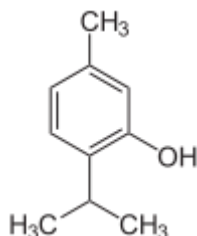
Polyphenols include phytoestrogens (top and middle), mimics of animal estrogen (bottom).^[37]

Terpenes

Terpenes and terpenoids of many kinds are found in a variety of medicinal plants^[38] and in resinous plants such as the conifers. They are strongly aromatic and serve to repel herbivores. Their scent makes them useful in essential oils, whether for perfumes such as rose and lavender, or for aromatherapy.^{[19][39][40]} Some have medicinal uses: for example, thymol is an antiseptic and was once used as a vermifuge (anti-worm medicine).^[41]



The essential oil of common thyme (*Thymus vulgaris*), contains the monoterpenthymol, an antiseptic and antifungal.^[41]



Thymol is one of many terpenes found in plants.^[41]

Approximately 80% of the population of developing countries relies on traditional medicines for their primary health care needs.^[42] Many plant products from medicinal herbs can use as treatment and prevent diseases. Natural plant compounds are showing a wide range of activities like anti-cancer, anti-inflammatory, and anti-ageing.^[43] The medicinal plants contain several phytochemicals such as vitamins, carotenoids, terpenoids, polyphenols, alkaloids, tannins, saponins, etc. These compounds have antioxidant activities, which can be used in the treatment of multiple ailments.^[42] Phenolic compounds are capable of inhibiting free radicals so, can retard the ageing process.

AGEING

Ageing is an inevitable process for all living organisms. Ageing is due to complicated biochemical processes in which the involvement of reactive oxygen species (ROS) and free radicals have been implicated. During this process reactive oxygen species generation is increased which leads to the activation of hyaluronidase, collagenase and elastase, which can further contribute to skin aging. Ageing causes pathogenesis of the skin.^[44] Based on increased life expectancy, it is estimated that there will be over 1.2 billion older adults (over 60 years old) worldwide in 2025.^[45] Older adults are more susceptible to different clinical conditions, such as tumors, neurodegenerative diseases and cardiovascular diseases. This is at least partially attributed to an age related increase in frailty and immunosenescence, and perhaps mitochondrial dysfunction.^[45-48] During this process reactive oxygen species

generation is increased. According to free radical theory, mitochondria were identified as responsible for the initiation of most of the free radical reactions occurring in the cells. It was also postulated that the life span is determined by the rate of free radical damage to the mitochondria.^[49] The increasing oxidative stress in aging seems to be a consequence of the imbalance between free radical production and antioxidant defenses with a higher production of the former.^[50] The identification of free radical reactions as promoters of the aging process implies that interventions aimed at limiting or inhibiting them should be able to reduce the rate of formation of aging changes with a consequent reduction of the aging rate and disease pathogenesis.^[51] Antioxidants from plants prevent the action of free radicals, so there is growing interest all over the world to identify the untapped reservoir of plants of medicinal importance. Maintenance of physical function in older adults is therefore a major public and clinical priority. In this regard the application of small natural compounds is a promising avenue of therapeutical intervention. It has been estimated that more than 50% of all the drugs in the world are natural products and their derivatives, and plant-based health remedies are promising.^[52-53] In these years, a number of small natural compounds have been discovered exhibiting possible anti-aging potential as exemplified by the elongation of lifespan in both invertebrate and vertebrate-based experimental models, and the amelioration of a wide spectrum of aging-related metabolic phenotypes. However, since a single plant contains widely diverse phytochemicals, the effects of using a whole plant as medicine are uncertain. Further, the phytochemical content and pharmacological actions, if any, of many plants having medicinal potential remain unassessed by rigorous scientific research to define efficacy and safety.

MEDICINAL PLANTS HAVING ANTI-AGEING PROPERTIES

Leguminosae family contains isoflavones such as genistein (4, 5, 7-trihydroxyisoflavone) and daidzein (4,7- dihydroxyisoflavone) which are phyto-estrogens. These compounds improve quality of the skin and reduce ageing.^[54] The isoflavones have a phenyl group attached to the 3-position as opposed to the 2- position found in flavones. An example of an isoflavone would be the genistein and daidzein already mentioned above.

Dioscorea villosa (Wild yam) and *Ruscus aculeatus* (butcher's broom) have diosgenin and ruscogenin (1-βhydroxydiosgenin), respectively. The diosgenin is converted to progesterone. Ruscogenin can be used for the inflammatory.

Trigonella foenum-graecum (Fenugreek) is another source of diosgenin. Plant oils extracted from seeds have fatty acids which can provide emolliency and skin protection against drying.

Luffa cylindrical has photoprotective effects. The seeds of this plant contain oil in which the fatty acids are stearic and linoleic acids are unsaturated fatty acids which have free radical scavenging properties.^[55-56]

Persea gratissima (Avocado) oil has shown great effect on the skin, regarding to repairing and calming effect. It may be due to the presence of phytosterols and other derivatives such as campesterol, stigmasterol, brassicasterol and tocopherols.^[57]

Another plant is *Hydrocotyle asiatica* in which one of its constituents is asiaticoside which works to stimulate skin repair and strengthen skin, hair, nails and connective tissue.^[58]

Gamma-linolenic acid from *Oenothera biennis* (evening primrose) oil can help persons with low metabolism of this material.^[59] It has an anti-inflammatory effect on the skin.^[60-61] This compound is found in other plant oils. such as *Borago officinalis* (borage oil) and rosehip oil.^[62]

Piper longum produce piperine which has antioxidant activity so, it is used in the cream against sunburn.^[63]

Glycine max or Soya contains β -sitosterol, daidzen and genistein, which are anti-inflammatory and cell regenerating.

Aesculus hippocastanum or horse chestnut (by producing esculin) has anti-inflammatory effects.^[64]

Resveratrol (3,5,4-trihydroxy-trans-stilbene) is a stilbenoid, a type of natural phenol, and a phytoalexin produced naturally by several plants when under attack by pathogens such as bacteria or fungi.^[65] In grapes, resveratrol is found primarily in the skin^[66] and in muscadine grapes also in the seeds. It is antioxidant, anti-inflammatory, anti-viral and protects against cancer, diabetes, alzheimer and other brain disorders.^[65]

The roots of *Pueraria mirifica* contain daidzein and genistein and some other fascinating steroids and hormonal materials.

Vitis vinifera (Grape seeds) show another group of compounds named procyanidins.^[67]

Terminalia chebula, contains ascorbic acid, gallic acid and ellagic acid, which scavenge free radicals.^[68]

Aloe barbadensis (Aloe vera) can protect skin against radiation.^[69] Kaempferol is a flavonol and show skin healing effects. This compound is found in *Calendula officinalis* (marigold), *Centella asiatica* (Indian pennywort) and *Echinacea purpurea* (purple coneflower).

Portulaca oleracea (Pigweed) has antiphlogistic (takes the heat out), antibacterial and antidiabetic effects and can use as refreshing agent.^[70-71] Flavones such as apigenin and luteolin^[72] show also anti-inflammatory effects.

Catechins, another flavonoids, can form procyanidins which are free-radical scavengers and anti-oxidants. Catechins and epicatechins can find in *Camelia sinensis* (green tea) or seeds of apple. *Hypericum perforatum* (St, john's wort) contains hypericin and pseudohypericin can recover inflammatory effects.^[73]

Scopolia japonica contains scopoletin which indicate anti-inflammatory activity. Materials found in *Borago officinalis* (Borage) can show this property.^[74]

Rutin found in the Graminae family and in *Fagopyrum esculentum* (buckwheat)^[75], *Anthriscus sylvestris*^[76] and *Ginkgo biloba*^[77] has antioxidant activity and protects cells against lipid peroxidation.

Ravichandran's group^[78] reported that The "Anti-Wrinkle cream" is a polyherbal formulation recommended for the management of skin wrinkling, and it contains the extracts of Aloe vera, *Papaver rhoeas*, *Vitis vinifera*, *Citrus limon*, *Solanum lycopersicum*, *Santalum album*, *Rubia cordifolia*, *Saussurea lappa*, *Lens culinaris*, *Symplocos racemosa*, *Amomum subulatum*, *Curcuma longa*, *Glycyrrhiza glabra*, *Valeriana wallichii*, *Vetiveria zizanoides* and oil of *Triticum sativum*.^[78-80]

CONCLUSION

In this review we intend to concentrate on different medicinal plants which showed anti-ageing properties. Plants and their constituents play their roles in delaying ageing processes. The medicinal plants contain several phytochemicals such as vitamins, carotenoids,

terpenoids, polyphenols, alkaloids, tannins, saponins, etc. These compounds have antioxidant activities, which can be used in the treatment of multiple ailments like diabetes, cancer, neurodegenerative disorders etc. Phenolic compounds are capable of inhibiting free radicals so, can retard the ageing process. Aging is an inevitable process for all living organisms. During this process reactive oxygen species generation is increased. According to free radical theory, mitochondria were identified as responsible for the initiation of most of the free radical reactions occurring in the cells. It was also postulated that the life span is determined by the rate of free radical damage to the mitochondria. The increasing oxidative stress in aging seems to be a consequence of the imbalance between free radical production and antioxidant defenses with a higher production of the former. The identification of free radical reactions as promoters of the aging process implies that interventions aimed at limiting or inhibiting them should be able to reduce the rate of formation of aging changes with a consequent reduction of the aging rate and disease pathogenesis. Antioxidants from plants prevent the action of free radicals, so there is growing interest all over the world to identify the untapped reservoir of plants of medicinal importance.

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