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Medicinal plants: Past traditions and hope of tomorrow

Al-Shimaa Saber Abd-elmegeed *, Heba saad Abd-alrahman, Asmaa Ahmed Mohamed and Basma Mohamed Ghaber

Department of Biology, College of science, Jazan University, P.O. Pox.114, Kingdom of Saudi Arabia, Jazan, 45142.

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Abstract

Medicinal plants have been used as a source of therapies since ancient times and its widespread use is described in the Vedas and the Bible. These plants play a critical role in the development of human cultures around the whole world. Medicinal Plants have been used for thousands of years to flavor and conserve food, to treat health disorders and to prevent diseases including epidemics. The knowledge of their healing properties has been transmitted over the centuries within and among human communities. Assurance of the safety and efficacy of medicinal plants and herbal products has now become a key issue in developing countries. Besides that, medicinal plants consider as a rich resources of ingredients which can be used in drug development and synthesis. Active compounds produced during secondary metabolism are usually responsible for the biological properties of plant species for treatment of various diseases. Currently, data on the antimicrobial, antioxidant and antitumor activity of numerous plants have been scientifically confirmed. Numerous studies have aimed to describe the chemical composition of these plant and the mechanisms involved in its biological activity.

Keywords: Medicinal Plants; Traditional Medicine; Phytomedicines; Antioxidant; Antitumor Potential

1. Introduction

Over the ages, people have depended on nature to provide them with basic necessities like food, clothing, shelter, transportation, fertilizer, fragrances, and, last but not least, medications. Plants serve as the basis for intricate traditional medical systems that have been used for thousands of years and are still developing new ways to treat patients. Although some of the therapeutic properties attributed to plants have proven to be erroneous, medicinal plant therapy is based on the empirical findings of hundreds and thousands of years [1].

2. Medicinal Plants – An Overview

All over the world, people depended on herbal medications for relief of disease before the advent of modern medicine [1]. The World Health Organization has estimated that 80% inhabitants of the world especially those of developing countries with ancient civilizations such as Egypt, India and China, rely chiefly on traditional medicines for their basic preventive and curative healthcare [2]. Herbal medicines are often used to provide first-line and basic health service to people living in remote and poor areas. Even in areas where modern medicine is available, the development and recognition of medicinal aids of these plants are on rise in both industrialized and developing nations.

The number of higher plant species on earth is about 250,000. It is estimated that 35,000 to 70,000 species have been used in some cultures for medicinal purposes because of their easy accessibility, low cost and their efficacy and safety in treatment of diseases [3]. Even today, plants are not only essential in health care, but form the best hope of source for safe future medicines, that it have proved their sole role in coping with a number of deadly diseases including cancer

* Corresponding author: Al-Shimaa Saber Abd-elmegeed

and the diseases associated with viral onslaught viz. Hepatitis, AIDS etc. A screening program was initiated by Leven *et al.,* (1979) that identified many anti-bacterial, anti-fungal, anti-viral, anti-parasitic and other pharmacologically active substance activities in higher plants [4,5]. In spite of the fact that we have now at our command a number of modern drugs, it is still genuinely urgent to discover and develop new therapeutic agents and the fight against diseases must be carried on relentlessly [6].

3. Traditional Use of Medicinal Plants

Traditional medicine is the total of the knowledge, skills and practices based on the theories, politics and experiences indigenous to different cultures used in the maintenance of health. In practice, traditional medicine refers to the following components: acupuncture (China), Ayurveda (India), Unani (Arabic countries), traditional birth attendant's medicine, herbal medicine, and various forms of indigenous medicine [7].

Knowledge of plants and healing have been closely linked from the time of human beings' earliest social and cultural groupings. The medicine man was usually an accomplished botanist, even in historical times, botany and medicine continued to be almost the same discipline until about 1500 CE, when they began to separate from their close association. Scripts about medicinal plants date back to almost 5000 years ago in India, China and Egypt, and at least 2500 years in Greece and Central Asia. According to some inscriptions, Egyptians and Chinese who used plants as medicine since more than 27 centuries BC were among the earliest human beings who did so [8,9].

4. Ancient Systems of Medicine

4.1. Traditional Indian Medicine

The word Ayurveda means the science of life that derived from 'Ayur', meaning life, and 'veda', meaning knowledge. It is an ancient system of health care and aims at positive health, which has been defined as a well-balanced metabolism coupled with a healthy state of being. Disease, according to Ayurveda, can arise from the body or mind due to external factors or intrinsic causes and its treatment consists of the healthy use of drugs, diet and certain practices [10]**.** Ayurveda is probably older than traditional Chinese medicine. The origin of Ayurveda is lost in prehistoric antiquity, but its characteristic concepts appear to have matured between 2500 and 500 BCE in ancient India. The earliest references to drugs and diseases can be found in the Rigveda and Atharvaveda, dating back to 2000 BCE. Atharvaveda, comprised of 6599 hymns and 700 prose lines, is considered as the forerunner of Ayurveda. The Samhitas or encyclopedia of medicine were written during the post vedic era and include 'Charak Samhita' (900 BCE), 'Sushruta Samhita' (600 BCE) and 'Ashtang Hridaya' (1000 CE). Later on, many more treatises were prepared and the use of medicinal plants is described in 'Nighantu Granthas' between the 7th and 16th centuries [11].

Ayurveda believes that the human body is formed of living and non-living environments including earth, water, fire, air and space. Illness is the consequence of imbalance between the various elements and it is the goal of treatment to restore this balance [12]**.** Ayurvedic drugs are also attracting much attention for diseases for which there are no drugs for treatment in modern medicine, such as metabolic and degenerative disorders.

4.2. Traditional Chinese Medicine

It has been in practice for more than 200 years and includes acupuncture, massage, breathing exercise and dietary therapy and its products were safe and effective for the treatment of many human diseases. Famous texts include the Yellow Emperor's Inner Classic (200 BCE to 100 CE), Divine Husband-man's Classic of Materia Medica (25-220 AD), and cold-induced disorders (220 AD). The most complete reference to Chinese herbal medicines is Chinese Materia Medica, published in 1977. It lists nearly 6000 drugs of which 480 are of plant origin. This ancient system of medicine is based on two separate theories about the natural laws that govern good health and durability which are in antagonism to each other, and the five elements "earth, metal, water, wood and fire" each of which is linked to the main organ systems of the body (spleen, lungs, kidney, liver and heart), respectively. It considers that an unbalanced diet, lifestyle or environment will disrupt the body balance, which in turn displays as symptoms of diseases [11,13,14]**.**

4.3. Traditional Arabic Medicine

The Babylonians, Assyrians and Sumerians consist of one of the oldest civilizations. Several medicinal plants were domesticated and are mentioned in civil laws carved on stone and commissioned by the King of Babylon (1700 BCE). The earliest written evidence of the use of medicinal plants for preparation of drugs has been found on a Sumerian clay slab in cuneiform date from about 2600 BC from Mesopotamia, among the materials that were used were oils of

Cupressus sempervirens (Cypress), Commiphora species (Myrrh), Papaver somniferum (Poppy juice), Glycyrrhiza glabra (Licorice) and Cedrus species (Cedarare) still used today for the cure of colds, coughs, inflammation and parasitic infections. The Arabs recognized drugstores in the eighth century, and the Persian pharmacist Avicenna described all Greco-Roman medicine in his book "Canon of Medicine" [15,16].

4.4. Traditional Egyptian Medicine

Egyptian medicine is some of the oldest ever documented from the 33rd century BC until the Persian invasion in 525 BC. The ancient Egyptian medical papyri documented several details about the way by which they practiced medicine as in Ebers papyrus, Edwin Smith papyrus, Kahun Papyrus, Ramesseum medical papyri, Hearst papyrus, London Medical Papyrus, Brugsch Papyrus, Carlsberg papyrus, Chester Beatty Medical Papyrus, Brooklyn Papyrus, Erman Papyrus, and Leiden Papyrus, these remedies included herbal remedies. The Papyrus Ebers which is the most famous encyclopedia, a 110 page scroll which rolls out to be about 20 meters long. Therefore, medicine has its origin in Egyptian or Nile Valley civilization [17]. The range of plants used by ancient Egyptians was very wide, they have used the whole plant, or its fruit, leaves, juice, or root. Uses of *Citrilus colocynthes, Senna alexandrina* and *Punica granatum* roots in large quantities are mentioned in the ancient Egyptian literature. These uses were later documented by the Greek physician Dioscorides (100 CE). Writings of the Greeks, such as Hippocrates (460–377 BCE) and Galen (130–200 CE) [18].

4.5. Traditional Greek Systems of Medicine

Ancient Greek people were also familiar with the medicinal properties of some medicinal plants, and Hippocrates, the founder of Greek medicine and Aristotle, pupil of Hippocrates, used medicinal plants for the treatment of diseases. After that, Theophrastus, a Greek scientist, founded the School of Medicinal Plants. Then, Pedanius Dioscorides (He lived in the first century A.D), a physician and surgeon in the years 75-45 BC, wrote an encyclopedia, called De Materia Medica, to describe 600 therapeutic medicinal plants in the form of a series of scientific studies on medicinal plants [19,20].

4.6. African, European and Other Traditional Systems of Medicine

Traditional African medicine is the oldest and perhaps the most diverse of all healthcare systems [21]. South America is also rich in biodiversity and diverse healing cultures. The famous book *De Materia Medica* by the Greek physician Dioscorides was the standard reference in Europe for more than 1000 years. The use of herbal teas prepared from *Humulus lupulus, Rosmarinum officinalis,* and *Valeriana officinalis* and decoctions is still very common in Europe [22].

5. Natural Antibiotic Properties of Plants and Phyto-chemicals

The term medicinal plant refers to a variety of plants that have medicinal properties. These plants are a rich source of compounds that can be used to develop drug synthesis. Plants are vital source of antimicrobial agents, most of them with effectiveness against fungi, yeasts, bacteria, insects, nematodes and other plants. The parts of medicinal plants that may be used are different types of seeds, root, leaf, fruit, skin, flowers or even the whole plant. The active compounds in most parts of the medicinal plants have direct or indirect therapeutic effects and are used as medicinal agents. These Phyto-chemicals are generally high value-low volume products and obtained from plant materials by steam distillation or by extraction with organic or aqueous solvents and classified as primary or secondary metabolites. Many secondary metabolites are often accumulated by plants in smaller quantities and used commercially as biologically active compounds (e.g. phenols, steroids, quinones, alkaloids, terpenoids, tannins and flavonoids) that are able to inhibit peptidoglycan synthesis, damage microbial membrane structures, modify bacterial membrane surface hydrophobicity [23,24]. To determine the chemical properties of such compounds, isolation of a substance in pure form using several separation methods and spectral characteristics are requirements for establishing its correct structure. Thus, medicinal plants are used in purified form in the preparation of drugs in different systems [25]. Structural novelty and new modes of action are common features of plant drugs which has been shown by anti-cancer agents like vinblastine and paclitaxel, cardiovascular agents like forskolin, anti-HIV agents like calanoid and anti-hyperlipidemic agents like guggulsterones [26].

6. Bioactive Molecules of Medicinal Plants

6.1. Phenolics and Polyphenols.

Natural polyphenols which present in medical plants have been reported to have anti-oxidant, anti-mutagenic, anti-bacterial, anti-viral, and anti-inflammatory activities. Medicinal plants rich in polyphenols can retard the oxidative degradation of lipids and improve the quality and nutritional value of food [27, 28]. The highest phenolic contents were found in Chinese toon bud, loosestrife, penile leaf, cowpea, and broccoli. In addition, Mediterranean diets are associated

with reduced risk of cardiovascular disease due to adequate intake of olive oil which contained high contents of polyphenols. The mechanisms which responsible for phenolic toxicity to microorganisms possibly through reaction with sulfhydryl groups or through more nonspecific interactions with the proteins [29].

6.1.1. Simple phenols and phenolic acids

It consist of a single substituted phenolic ring. Cinnamic and Caffeic acids are common representatives of a wide group of phenyl propane-derived compounds which are in the highest oxidation state. The common herbs tarragon and thyme both contain caffeic acid, which is effective against viruses, bacteria, and fungi. Catechol and pyrogallol both are hydroxylated phenols. Catechol has two 2OH groups, and pyrogallol has three. The site(s) and number of hydroxyl groups on the phenol group are thought to be related to their relative toxicity to micro-organisms. In addition, some authors have found that, more highly oxidized phenols are more inhibitory agents [30].

6.1.2. Quinones

Quinones are aromatic rings with two ketone substitutions. These compounds, being colored, are responsible for the browning reaction in cut or injured fruits and vegetables and are an intermediate in the melanin synthesis pathway in human skin. Vitamin K is a complex naphthoquinone. It's antihemorrhagic activity may be related to its ease of oxidation in body tissues. Quinones are known to complex irreversibly with nucleophilic amino acids in proteins, often leading to inactivation of the protein and loss of function. For that reason, the potential range of quinone antimicrobial effects is great [31].

Kazmi *et al.,* (1994) described an anthraquinone from *Cassia italica*, a Pakistani tree, which was bacteriostatic for *Bacillus anthracis*, *Corynebacterium pseudodiphthericum*, and *Pseudomonas aeruginosa* and bactericidal for *Pseudomonas pseudomalliae*. Hypericin, an anthraquinone from St. John's wort (*Hypericum perforatum*), has received much attention in the popular press lately as an antidepressant, and Duke reported in 1985 that it had general antimicrobial properties [32].

6.1.3. Flavones, flavonoids, and flavonols

Flavones are phenolic structures containing one carbonyl group. The addition of a 3-hydroxyl group yields a flavonol. Flavonoids are also hydroxylated phenolic substances but occur as a C_6-C_3 unit linked to an aromatic ring. Since they are known to be synthesized by plants in response to microbial infection, it should not be surprising that they have been found in vitro to be effective antimicrobial substances against a wide array of microorganisms and protection against inflammation, ulcers, hepatoxins, viruses, and tumors. Catechins, the most reduced form of flavonoid compounds, and have been extensively researched due to their occurrence in oolong green teas. These compounds inhibited *in vitro* *Vibrio cholerae*, *Streptococcus mutans*, *Shigella*, and other bacteria, possibly due to complexing activities described for quinones above. Flavonoids lacking hydroxyl groups on their b-rings are more active against microorganisms than are those with 2OH groups [33].

6.1.4. Tannins

They are divided into two groups, hydrolyzable and condensed tannins. Hydrolyzable tannins are based on gallic acid, usually as multiple esters with D-glucose, while the more numerous condensed tannins (often called proanthocyanidins) are derived from flavonoid monomers. Many human physiological activities, such as stimulation of phagocytic cells, host-mediated tumor activity, and a wide range of anti-infective actions, have been assigned to tannins. Their mode of antimicrobial action may be related to their ability to inactivate microbial adhesins, enzymes, cell envelope transport proteins, etc. Tannins in plants inhibit insect growth and disrupt digestive events in ruminal animals. Tannins are considered responsible for the antibiotic activity of methanolic extracts of the bark of *Terminalia alata* found in Nepal [34].

6.1.5. Coumarins

Coumarins are phenolic substances made of fused benzene and α-pyrone rings. They are responsible for the characteristic odor of hay. Their fame has come mainly from their anti-thrombotic, anti-inflammatory, and vasodilatory activities. Warfarin is a particularly well-known coumarin which is used as an oral anticoagulant and as a rodenticide. Coumarins are known to be highly toxic in rodents and therefore are treated with caution by the medical community. It appears that toxic coumarin derivatives may be safely excreted in the urine in humans. Hydroxycinnamic acids, related to coumarins, seem to be inhibitory to Gram-positive bacteria. Also, phytoalexins, hydroxylated derivatives of coumarins, are produced in carrots in response to fungal infection and can be presumed to have antifungal activity [35].

6.2. Terpenoids and Essential Oils

The fragrance of plants is carried in the so called quinta essentia, or essential oil fraction. These oils are secondary metabolites that are highly enriched in compounds based on an isoprene structure. They are called terpenes "$C_{10}H_{16}$". When the compounds contain additional elements, usually oxygen, they are termed terpenoids. Terpenoids are active against bacteria, fungi, viruses, and protozoa. In 1977, it was reported that 60% of essential oil derivatives examined to date were inhibitory to fungi while 30% inhibited bacteria [36,37].

Oil of basil was found to be as effective as 125 ppm chlorine in disinfecting lettuce leaves. Many essential nutrients, such as vitamin C, provitamins A and E, and several B vitamins, are found in chiles. A terpenoid constituent, capsaicin, has a wide range of biological activities in humans, affecting the nervous, cardiovascular, and digestive systems as well as finding use as an analgesic, capsaicin is also bactericidal to *Helicobacter pylori* [38].

6.3. Alkaloids

Heterocyclic nitrogen compounds are called alkaloids. The first medically useful example of an alkaloid was morphine, isolated from *Papaver somniferum*. Codeine and heroin are both derivatives of morphine. Diterpenoid alkaloids, commonly isolated from the plants of the Ranunculaceae or buttercup family are commonly found to have antimicrobial properties, Solamargine, a glycoalkaloid from the berries of *Solanum khasianum*, and other alkaloids may be useful against HIV infection. While alkaloids have been found to have microbiocidal effects against *Giardia* and *Entamoeba* species. Berberine is an important representative of the alkaloid group. It is potentially effective against trypanosomes and plasmodia [39].

6.4. Lectins and Polypeptides

Peptides which are inhibitory to microorganisms were first reported in 1942. They are often positively charged and contain disulfide bonds. Their mechanism of action may be the formation of ion channels in the microbial membrane or competitive inhibition of adhesion of microbial proteins to host polysaccharide receptors. Thionins are peptides commonly found in barley and wheat and consist of 47 amino acid residues. They are toxic to yeasts, Gram-negative and Gram-positive bacteria. Thionins from sugar beet are active against fungi but not bacteria. Fabatin, from fava beans inhibits *Escherichia coli*, *Pseudomonas aeruginosa*, and *Enterococcus hirae* but not *Candida* or *Saccharomyces* [39].

The larger lectin molecules, which include mannose-specific lectins from bitter melon, *Gelonium multiflorum* and jacalin are inhibitory to viral proliferation, probably by inhibiting viral interaction with critical host cell components [40].

6.5. Other Compounds

Gupta and Pandey, (2020) isolated a C_{17} polyacetylene compound from *Bupleurum salicifolium*, a plant native to the Canary islands, this compound was inhibitory to *Staphylococcus aureus* and *Bacillus subtilis* but not to Gram-negative bacteria or yeasts. The glycosides consist of various categories, the main groups of glycosides are cardiac glycosides, cyanogenic glycosides, glucosinolates, saponins and anthraquinone glycosides. Saponin compounds served as natural antibiotics, which help the body to fight infections and microbial invasion and inhibit cancer tumor growth in animals, particularly, lung and blood cancers, without killing normal cells. Saponins are the plant's immune system acting as an antibiotic to protect the plant against microbes and fungus [36].

In the early 1990s, researchers found that the monosaccharide fructose present in cranberry and blueberry juices competitively inhibited the adsorption of pathogenic *Escherichia coli* to urinary tract epithelial cells, acting as an analogue for mannose.

7. Medicinal Plants and Anti-oxidant Properties

An anti-oxidant can be defined as "any substance that when present in low concentration compared to that of an oxidisable substrate significantly delays or inhibits the oxidation of that substrate". It is well known that oxidant by-products of normal metabolism such as free radicals and reactive oxygen species (ROS) in excess can cause extensive damage to DNA, proteins, and lipids. Under stress, the body produces more ROS, such as superoxide anion and hydroxyl radical, which are highly reactive and potentially damaging transient chemical agents. These are continuously produced in the human body, as they are essential for energy supply, detoxification and immune function. Overproduction of free radicals and ROS causes oxidative stress leading to various degenerative diseases such as arthritis, asthma, mongolism, Parkinson's disease, cancer, cardiovascular disease, cataracts, immune system decline, and brain dysfunction. Human body has an inherent anti-oxidative mechanism and many of the biological functions such as the anti-mutagenic, anti-carcinogenic and anti-aging responses originate from this property [41]. There are various endogenous and exogenous

sources of anti-oxidants. The endogenous sources include anti-oxidant enzymes "superoxide dismutase, catalase, glutathione peroxidase, low-molecular weight anti-oxidants" and exogenous sources such as food sources and medicinal plants [42, 43]. Several synthetic anti-oxidants such as butylated hydroxytoluene are used currently, but may be unfortunate for chronic human consumption, as recent publications have mentioned their possible toxic properties for human health. Hence, the development of alternative anti-oxidants of natural origin has considerably increased for use in food and pharmaceutical products [44].

Studies on herbal plants, vegetables and fruits have indicated the presence of anti-oxidants such as phenolics, flavonoids, tannins, and proanthocyanidins. They are well known as radical scavengers, metal chelators, reducing agents, hydrogen donors and singlet oxygen quenchers. There were many experiments *in vitro* that reported that phenolics were usually major contributors of anti-oxidant capacities of plants. Rosmarinic acid, caffeic, chlorogenic, vanillic, p-hydroxybenzoic acid, and so on were identified to contribute to the anti-oxidant potential of tea by using DPPH and Nitric Oxide radical scavenging assays [45].

8. Medicinal Plants and Anti-tumor Activity

Cancer is one of the most life-threatening diseases, with more than 100 different types occurring due to some molecular changes within the cell. It is the third leading cause of death worldwide following cardiovascular and infectious diseases. The International Agency for Research on Cancer estimates, for 184 countries of the world revealed that there were 14.1 million new cancer cases, 8.2 million cancer deaths and 32.6 million people living with cancer (within 5 years of diagnosis) in 2012 worldwide. By 2030, it is predictable that there will be 26 million new cancer cases and 17 million cancer deaths per year [46].

Breast cancer is the most common form of cancer in women and accounts for 38.5% of all female cancers. About half (43.7%) of all breast cancers are detected in an advanced stage. Colon cancer is the second most common cause of cancer deaths and prostate cancer is the most often diagnosed cancer among men in the western countries, and ranks second to skin cancer, with an estimated 180,000 new cases and 37,000 deaths expected to occur by the American Cancer Society each year.

During the last decade, novel synthetic chemo-therapeutic agents currently in use clinically have not succeeded in fulfilling expectations despite the considerable cost of their development and its side effects. Therefore there is a constant demand to develop effective natural anti-carcinogens like plant-derived that would prevent, slow or reverse cancer development at various stages. At this time, more than 3000 plants worldwide have been reported to have anti-cancer properties. Worldwide, the incidence of plant-derived products for cancer treatment is from 10% to 40% with this rate reaching 50% in Asiatic patients. In Europe alone expenditure for anti-cancer herbal products is estimated to be 5 billion dollars per year [47].

The anti-cancer effects of polyphenols have been observed at mouth, stomach, duodenum, colon, liver, lung, mammary glands or skin. Many polyphenols, such as proanthocyanidins, flavonoid, resveratrol, tannins, epigallocatechin-3-gallate, gallic acid, and anthocyanin, have been tested and all of them showed protective effects in some models although their mechanisms of action were found to be different. Scientists therefore investigated the effects of proanthocyanidins *In vitro* on a highly metastatic mouse mammary carcinoma cell line and resulted in significant inhibition of cellular proliferation and viability and induction of apoptosis in 4T1 cells after exposed with proanthocyanidins. The effects of dietary proanthocyanidins were then examined by an *in vivo* model in which 4T1 cells were implanted subcutaneously in mice. Proanthocyanidins significantly inhibited the growth of the implanted 4T1 tumor cells. Moreover, the metastasis of tumor cells to the lungs was inhibited and the survival of the mice was improved [48]. Berries are rich in anthocyanins, which possess a broad spectrum of therapeutic and anti-carcinogenic properties. Six berry extracts were studied for anti-angiogenic properties and resulted in reduction of unwanted growth of blood vessels, which can lead to varicose veins and tumor formation. Recently, an exploratory meta-analysis of observational researches supported the hypothesis that green tea may have a protective effect against prostate cancer. The most abundant and bioactive components of green tea have shown to act as proteasome inhibitors and tumor cell death inducers [49].

9. Conclusion

There is a confidence that the solutions to all health problems can be found in nature, where 80% of people all over the world are only dependent on herbal medicines. The importance of traditional medicine has also been recognized by the World Health Organization (WHO) and has created strategies, guidelines and standards for botanical medicines. There is a promising future of medicinal plants as there are about 500,000 plants around the world, and most of them are not

yet investigated for their medical activities. These medicinal plants are the sources of therapy in the health systems worldwide, not only to treat diseases but also to prevent them and maintain health. The scientific study and identification of the phytochemicals and their effects can lead to the discovery of new therapeutic benefits and the production of nature-based products in the future. To realize this purpose, extensive research is essentially important to control the quality of raw drugs and the formulation to justify their use in the modern medicine system.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declares that there is no conflict of interest.

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