



PHYTOTHERAPY IN THE TREATMENT OF INFECTIOUS DISEASES

BY

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Abstract

Background: and Objectives: Medicinal herbs are widely used to treat infectious diseases, and a large number of the traditional remedies have recently been proven effective by science. Even though the processes underlying the majority of plant-derived medicines are not fully understood, the effectiveness of herbal medicine in treating infectious disorders shows that many plants have good effects in treating a variety of bacterial, fungal, viral, or parasitic infections. Modern methods for the isolation, purification, and characterization of active compounds have substantially benefited in the improvement of both in vitro and in vivo research. For use in clinical trials in the future, this stage is essential. This goal of this review includes some information about the use of herbal remedies in the treatment or prevention of infectious diseases

Materials and methods: Articles related to ethnopharmacological and chemotherapeutic studies on plants or natural products were collected from PubMed, Web of Science and Scopus, etc. using keywords related to chemotherapy, medicinal plants, and natural products, etc. products showing potential for chemotherapeutic effects have been identified from these medicinal plants.

Results: Many plant-based compounds, including quinine and artemisinin, have already been used successfully to treat infectious diseases that are extremely dangerous to human health. The main barriers to plant medicine's potential to heal are the plant-based products' inconsistent and unpredictable quality.

Conclusion: Despite the lack of clinical trials evaluating their effectiveness, the use of adult plant uses, gemmotherapy, phytotherapy, and embryonic stem cells should be reexamined as useful resources in the hunt for novel active compounds with extended antibacterial action.

Keywords: Phytotherapy, Gemmotherapy, Antibiotics, Infection, Herbal medicine

INTRODUCTION

Many medicinal plants have long been used in traditional medicine to treat infectious diseases (1). Traditional healers often combine mysterious spells with medicinal plants; their

family recipes and trade secrets are passed down with the recipes. Complicated rituals for collecting, preparing, applying, calculating dosages, and weaving plants into other unsaid stories about the nature of illness were all part of traditional therapeutic procedures. This entire information was



transmitted verbally. This review includes some information about the use of herbal remedies in the treatment or prevention of infectious diseases. Our knowledge of the use of herbal remedies in the treatment of infectious diseases has progressed faster than it has with the introduction of new antibiotics; yet, the emergence of drug-resistant strains demands the creation of novel therapeutic strategies. Since bacteria's genetic adaptation depends on more than just antibiotic exposure, it has become challenging to analyze the evolution of antibiotic resistance (2). These days, we often find ourselves at a loss when it comes to choosing an effective anti-infective medication for nosocomial infections (3). Without a fact, bacteria are always changing their defense systems, thus any freshly synthesized antibacterial agent will eventually become ineffective. Penicillin G's potent activity against *Streptococcus pyogenes* is the only one described, albeit there are a few notable outliers. Since the dawn of time, people have been afflicted with infections, which can range from mild UTIs to massive epidemics. They reportedly used the broadest variety of drugs for their treatment, including regional natural products and herbs (4). For instance, a recent study demonstrates that the well-known natural material honey has antibacterial activity against *Staphylococcus aureus* and *Streptococcus pyogenes* in vitro (5). Many drugs have also been discovered thanks to ethnobotanical leads. The plant known as *Filipendula ulmaria*, frequently referred to as the "queen of the meadow," is the source of aspirin, the most used anti-inflammatory and analgesic drug (6). This review does not seek to further the history of empirical antimicrobial therapy; rather, it seeks to recover the significant results of conventional medical prescriptions that have led to current medicines. The precise history of employing plants for healing has been lost since the dawn of humankind. Humans have always made an effort to understand and treat illnesses, and they have also made an effort to understand how humans and nature interact (7). It may be said that they approached sickness philosophically, seeking the causes and remedies in all things that symbolized life. Time was valued differently in the past, and people were more patient and thoughtful. They had the remarkable capacity to make connections between even the smallest details and were astute observers of their surroundings. How prehistoric humans devised therapeutic procedures without access to medical instruments or epidemiological resources is beyond our comprehension. First of all, compared to our times, the ancients traveled a great deal less and engaged in less substantial commodities trading, with the amazing exception of ocean voyagers (8). They were therefore forced to make their healing remedies from locally available materials. Plants—almost always wild plants—and animal products were undoubtedly used widely and generally with effectiveness. For several of them, outstanding investigations demonstrated their scientific value. Numerous medical experts claim that naturalistic or reductionist approaches—which distinguish allopathic medicine from complementary and alternative therapies—have gained traction. Recognizing the advantages of both strategies and taking use of opportunities in healthcare delivery has been approached from a more equitable perspective for some time

now (8). Although there are not many trustworthy studies on the efficacy of complementary and alternative medical practices at the moment, patients' positive perceptions of these therapies—even those of younger patients—will eventually force us to do a more in-depth investigation of this field (9). This review does not explore the superiority of different branches of herbal medicines over allopathic pharmaceutical products; it only addresses herbal therapies with proven antibacterial activity (10). The purpose of the review is to synthesize commercial plant products that have been demonstrated to have biological effect in infectious human diseases, rather than to be encyclopedic. Research publications on plant extracts with antibacterial activity have also been reviewed in an effort to find data that supports the use of plants in the treatment of infectious illnesses. Rather than trying to cover every herb and every infectious disease, this review is aimed at medical specialists, thus the plant products are organized in the following parts according to their clinical situations. Since the basic healing mechanisms of chemotherapy and phytotherapy differ, their applications for infectious conditions will be covered separately.

1. Plant-based medicine

Plant-based medicine or phytotherapy is one of the oldest, if not the oldest, methods of treating infectious diseases. Many countries have a long history of using herbal treatment (11). People who reside in countries where traditional medicine is extensively used are more likely to continue using these practices (12). Herbalists are trying to treat contemporary infectious diseases (such as HIV) in the modern day, although there is little evidence to support their efficacy or safety (13). Moreover, the addition of a seemingly innocuous plant product, like rose or pomegranate flowers, may be the cause of antibiotic treatment failure since certain plant relationships with antibiotics are antagonistic (14). Many lost legends concerning traditional medicine and the global interconnection of human lifestyles with plant life cycles exist, but this subject is too complex to discuss in this review (15). In phytotherapy, the entire plant or plant pieces processed using various methods are employed. Many plant products are accessible these days, such as essential oils, oils, tinctures, plant extracts, mother tinctures (TM), powders, suppositories, syrups, inhalants, and other combinations. Research has demonstrated the antibacterial qualities of some plants, but it has also hinted to a possible mode of action. *Juglans regia* (walnut) and *Camellia sinensis* (tea plant, tea shrub) interact in concert with several antimicrobial medications to suppress multiple-resistance bacteria (MDR), most likely by targeting the bacterial cell membrane (16).

2. Using medicinal plants to treat bacterial infections

For oral hygiene: There are many of herbal dentifrices and mouthwashes available in stores nowadays. People gravitate toward natural products, and dentists concur that using efficacious substitutes for prophylactics containing sodium fluoride or chlorhexidine is a good idea (17). Dental professionals' interest has led to the completion of numerous

clinical trials with encouraging outcomes. *Hydrastis canadensis* (goldenseal) and *Cymbopogon nardus* (citronella grass) are also effective against *Candida albicans* and *Staphylococcus aureus* biofilms on the maxillofacial silicone polymer, however washing with water and neutral soap revealed to be the most effective treatment against them (18). Juices from *Hippophae rhamnoides* (sea buckthorn) and *Ribes nigrum* (blackcurrant) have been shown to have anti-inflammatory and bacterial growth inhibitory properties, which may lower the risk of gingivitis and tooth decay (19). Positive results were shown when a paste containing *Myrtus communis* (myrtle) was evaluated for the treatment of recurrent aphthous stomatitis, an idiopathic oral illness (20).

Infections of the respiratory tract. Essential oils are frequently used to treat respiratory conditions (21). While efforts are made to precisely define active principles, the outcomes of precisely identifying a particular antibacterial component are not encouraging. Popular herbs such as *Urena lobata* (Caesarweed), *Rosmarinus officinalis* (rosemary), *Thymus vulgaris* (thyme), or *Primula veris* (primula root) have the ability to treat or prevent bacterial respiratory infections (22). The essential oil combinations of *Eucalyptus globulus* (eucalyptus), *Rosmarinus officinalis* (rosemary), *Daucus carota* (wild carrot), and *Cinnamomum zeylanicum* (cinnamon) are also useful in treating influenza infection and bacterial complications associated with influenza (23).

Urinary tract infections are common, particularly in women. Many plant formulations, such as the root of *Astragalus membranaceus* (Mongolian milkvetch), *Sophora flavescens* (shrubby sophora), *Lindera aggregata* (lindera) root, *Oldenlandia diffusa* (snake-needle grass), *Phellodendron amurense* (Amur cork tree), and *Desmodium styracifolium* (Guang Jing Qian Cao), have been used for centuries because of their antibacterial and anti-inflammatory properties (24). *Calluna vulgaris* (common heather) and *Vaccinium vitis-idaea* (lingonberry, cowberry, or bearberry) aqueous extracts either directly suppress or stop the formation of biofilms in the majority of uropathogenic strains (24).

Infections of the skin. Herbs are frequently used in cosmetology in a variety of forms to cure other hard-to-treat skin conditions (25). Acne is a chronic ailment that lowers quality of life; therapy is discouraging because of relapses and length of treatment, which frequently prompts doctors and patients to turn to herbal remedies. It is common practice to apply different plants or plant-drug mixtures topically. Numerous *in vitro* and *in vivo* studies that demonstrate the inhibition of specific bacterial species seen in cutaneous illnesses by plant and essential oil extracts lend credence to their antibacterial activity (26).

Intestinal infections. Unquestionably, *Vaccinium myrtillus*, or bilberry, is the primary plant species advised for diseases of the digestive system (27). Prickly pears, or *Punica granatum*, have been used to treat *Helicobacter pylori*-related gastritis (28). A clinical trial demonstrates the effectiveness of the Jiechang mixture, a traditional Chinese herb used in medicine, in treating infantile mycosis enteritis (29).

3. Use of medicinal plants in the cases of viral infections

The majority of herbal remedies that help with viral infections target respiratory conditions. Formulations for traditional Chinese herbal medicine (TCHM) are widely utilized and have a significant impact on viral infectious disorders such as respiratory syncytial virus infections (30). A lengthy list of plants is included in TCHM formulae, yet the underlying mechanism is still unknown. Remember that traditional Chinese medicine is deeper and more complex than the mere application of certain medicinal formulas because of its philosophical foundation (31). The greatest option for treating common colds and preventing influenza complications is most likely *Echinacea angustifolia*, often known as thin leaf *echinacea*, which is a versatile immunomodulator (32). Essential oils, commonly known as bacterial infections, can be used either singly or in various combinations to help avoid influenza-related problems. Treatment for infectious herpes simplex has become more challenging due to the rise of acyclovir-resistant clinical isolates and other recurring viral infections. The early stages of infection of acyclovir-sensitive and acyclovir-resistant clinical isolates of herpes simplex virus type 1 (HSV-1) have been demonstrated to be inhibited by the efficacy of bark (33).

4. Treatment of parasites with medicinal plants

(34). The resistance to parasite medicine reduces the efficacy of treatment for human parasitosis. Furthermore, certain parasite illnesses necessitate prolonged use of high-dose medications with significant side effects. Thus, it is not unexpected that scientists are looking into using plant treatments that have been shown to be beneficial in treating parasite diseases (35). Conventional herbal remedies for parasitosis rely on well-known herbs like ramson, garlic, or pumpkin seeds; nevertheless, intriguing research indicates that novel technologies can offer fresh perspectives on the management of parasitic illnesses (36). *Allium ursinum* TM (ramsons) aid in the removal of intestinal worms and promote digestion. As an alternative, suppositories could be advised in pediatrics. *Nigella sativa* L. seeds, also known as black cummin, fennel flower, and negrilla, have been used to treat a variety of clinical problems, including epilepsy, helminth infections, and oral malodor (37). A novel combination of highly antiparasitic chemical silver doped titanium dioxide nanoparticles (TiAgNps) and *Nigella sativa* L. essential oil is particularly effective on cutaneous Leishmaniasis (38). Promising results were reported in helminth infections. A recent *in vitro* study demonstrates that the reduction in the size, number, and weight of hydatid (*Echinococcus granulosus*) cysts is dependent upon a nano emulsion of *Zataria multiflora* (Shirazi thyme) essential oil (39). *Trichomonas vaginalis* is a protozoan that this kind of thyme is also effective against (39). Sweet wormwood, *Artemisia annua* L., can be used to treat acanthamoebiasis both locally and generally. It can also be used in combination with antibiotics to increase the survival rate of animals infected

with *Acanthamoeba* sp. in experiments (40). Even now, with efforts to create a vaccine that is commercially available and ongoing clinical trials, malaria remains a challenge for medical professionals (41). These days, plants are the primary source of antimalarial drugs (quinin, artemisinin, and the recently discovered lupane triterpenes) (42). Combining antimalarial drugs with curcuma oil has been shown to have beneficial effects since phytotherapy takes a holistic approach to treating disorders (42).

Numerous manufacturers have created a number of easier-to-administrate formulas, particularly for young people or the elderly. Vermicin is an antiparasitic mixture found in Romania that contains *Thymus vulgaris* (thyme, thymi herba), *Olea europaea* L. folium (olive leaf), dry extract of the rhizome of *Hydrastis canadensis* (goldenseal), berberine sulfate (an alkaloid derived from *Berberis aristata*) (43). Active ingredients can change the flavor of breast milk, so it is not advised for women who are nursing or pregnant owing to the potential consequences of stimulating uterine contractions. Ovidiu Bojor suggests a formulation called Giardinophyt, which includes extracts of *Chrysanthemum vulgare* (tansy), *Thymus vulgaris* (thyme, thymi herba), *Eugenia caryophyllata* (cloves), and propolis cera seeds (44). The manufacturer states that eliminating parasites is preferred in addition to having other advantageous benefits on the digestive tract. In order to avoid relapses, seven-day treatments are advised (45).

5. Gemmotherapy

Gemmotherapy is part of complementary and alternative medicine, being a form of herbal therapy which uses embryonic stem cell tissues of plants—inflorescences, buds, bark of the stalk, young branches of the spring plants, young roots, acorns, sap, seeds or bark of roots (46). Gemmotherapy, the youngest branch of herbal therapy, was developed by a group of homeopaths—Henry Pol, Max Tétou and O.A. Julian—and is characterized by a different approach to illness, health and life in general (47). Although this review is not dedicated to gemmotherapy, we cannot ignore its fundamental principles. The most important intriguing concept is that then prior to any treatment, it is essential to understand that symptoms are considered an expression of energetic status of a certain organ. Therefore, the efforts are directed to restoring the dynamic balance of the affected organs rather than simply treating the pathological symptoms; in other words—a holistic approach to human being and disease. Principle of preparation of the extracts used in gemmotherapy (48). The procedure involves two steps—the fresh harvested plants are first treated with alcohol, then a hydro-glycerin solution is added. In the first step, there is inhibition of enzymatic activity of the plant followed by further extraction and stabilization of active principles (49). The extracts are stored as concentrated glycerin macerate 1DH (dilution 1:10) in glass brown bottles at room temperature. The warranty period is 5 years (49).

Mechanism of action of the extracts used in gemmotherapy. The principles of gemmotherapy derived from the drainage concepts from homeopathy; for the very first time it was

named in France as “drainage therapy”. The main action of the extracts used in gemmotherapy is the rebalancing of cellular and tissue homeostasis, targeting the reticulohistiocytosis tissue (50). The most important characteristic of these products is their holistic activity, separated molecule do not have the same activity like the whole extract (51). Until now, we could not separate a certain molecule in order to accurately characterize its activity due to coordinated action of the active principles. The comprehensive studies about precise mechanism of action of extracts used in gemmotherapy are very rare, therefore, in my opinion, at this moment clinical observation is the most relevant way to validate gemmotherapy (46). Treatment regimen in gemmotherapy. There is not a standardized therapeutic regimen in gemmotherapy, but the glycerine macerate 1DH are usually administrated 40–50 drops/1–2 times/day diluted in 100 ml water (46). Fernando Piterà explained that this water dilution not only releases active principles, but triggers crucial electronic exchanges between the molecules (52). If a complementary regimen is recommended, 50–70 drops/once a day are recommended. The association of different glycerine macerate 1DH are often proposed. Usually the treatment lasts for a month and can be repeated after at least 2 weeks. Some authors do not recommend the mixtures and administration of more than one extracts at once, although therapeutic regimens often includes more than one extract (52). The main argument for avoiding mixtures is that of avoiding reactions between different active compounds that can cause inactivation or even the formation of toxic compounds. Since the scientific literature dedicated to gemmotherapy is so scant, recommendations on the application of gemmotherapy products to infectious diseases—bacterial infections, viral infections or parasitosis—are selected from the Fernando Piterà’s *Compendio di gemmotherapia clinica (Meristemoterapia) con indice clinico*, 3rd edition, Genova (53). Inflammatory response is a well-known feature of many infectious diseases, so most of the gemmotherapy regimens include *Ribes nigrum* (black currant) that reduces inflammation and stimulates and supports the adrenal glands. Also, *Juglans regia* (walnut) is considered to be the major stem cell plant-derived “antibiotic”. Note that embryonic plant cell stem tissues are unique in structure and composition therefore their properties and clinical applications differ from the adult plant (54).

6. Gemmotherapy in bacterial infections

Oral hygiene. The common and mild form of periodontal disease known as gingivitis and aphthous stomatitis are characterized by frequent recurrences and a lack of specialized therapy. With the adoration of *Alnus glutinosa* (alder), linked with *Vaccinium myrtillus* (bilberry), *Juglans regia* (walnut), *Ligustrum vulgare* (privet), and *Ulmus campestris* (elm), gemmotherapy may prove to be beneficial in preventing relapses of oral ulcers or gingivitis. *Abies pectinata* (silver fir), *Betula pubescens* (downy birch), or *Quercus pedunculata* (oak) may be recommended in cases of paradontosis (46).

Infections of the respiratory tract. According to Fernando Piterà, *Vitis vinifera*, or common grape vine, in combination with *Juglans regia* (walnut), *Ampelopsis veitchii* (peppervine), *Ribes nigrum* (black currant), and *Rosa canina* (dog rose), can lower the level of streptolysins and avert the complications of rheumatic fever in cases of recurrent tonsillitis and group A streptococcal pharyngitis (55). The clearance and spread of *Mycobacterium tuberculosis* in tuberculosis are significantly influenced by the immune response dynamics, with underlying immunological dysfunctions being directly linked to the disease's heterogeneity (56). The convalescence phase after tuberculosis is crucial for the recovery of the illness. *Prunus spinosa*, or blackthorn, is a wonderful tonic that boosts the immune system when combined with walnut and dog rose, *Juglans regia*, and gemmotherapy (57).

In urinary tract infections. According to Fernando Piterà, *Vaccinium vitis-idaea* (lingonberry, cowberry, or bearberry) and *Calluna vulgaris* (common heather) are the two most significant gemmotherapy products for urinary tract infections. *Calluna vulgaris* acts as a urinary tract disinfectant and diuretic. The young branches of the *Vaccinium vitis-idaea* spring plant contain urinary tract antiseptic, antimicrobial, and anti-inflammatory properties. Fernando Piterà suggests *Vaccinium vitis-idaea* (lingonberry, cowberry, or bearberry), *Calluna vulgaris* (common heather), and *Vaccinium myrtillus* (bilberry) for acute cystitis; for recurrent cystitis, *Juniperus*, *Calluna vulgaris*, and *Vaccinium vitis-idaea* are recommended (58).

Infections of the genitalia. A little, constantly green, and hazardous shrub, *Buxus sempervirens* (common box) gets its name from the compound cyclobuxine. Even though there is no specific treatment for it, the glycerine macerate 1DH of young branches of *Buxus sempervirens* (common boxwood), obtained in vegetative stage, and seems to alleviate the sequelae of syphilis. Although there are several causes of vaginosis, an imbalance in the vaginal microbiota is frequently linked to it (59). Along with *Calluna vulgaris* (common heather) and *Juglans regia* (walnut), *Rubus idaeus* (raspberry) has been shown to target the hypothalamic-pituitary-gonadal axis and help restore the homeostasis of the vaginal microbiota (59).

Digestive infections. *Vaccinium myrtillus* (bilberry) is strongly recommended in enteritis, diarrhea, dysentery and membranous colitis. *Juglans regia* (walnut) and *Vaccinium vitis-idaea* (lingonberry, cowberry or bearberry) could be associated (60).

Cutaneous-mucosal infections. Walnut, or *Juglans regia*, is advised for numerous cutaneous conditions, including blepharitis, mycosis, dermatoses, and acne. *Juglans regia* is associated with a number of noteworthy difficult illnesses, including infected wounds with *Buxus sempervirens* L. (boxwood); pustular acne; and furunculosis complicated by staphylococcal and streptococcal infection with *Ulmus campestris* (elm). Along with *Ficus carica*, or common fig, *Juglans regia* is useful in the treatment of superficial forms of

paranarium. The best combination for treating oral candidiasis is *Buxus sempervirens* L. (boxwood), *Ligustrum vulgare* (common privet), and *Rubus fruticosus* (blackberry) (61).

Gemmotherapy for viral illnesses. When treating viral respiratory infections, *ribes nigrum*, also known as black currant, is an essential tool. It can be linked to *Abies pectinata*, also known as the silver fir, and *Rosa canina*, also known as the dog rose, for the common cold; and to *Alnus glutinosa*, also known as alder, *Betula pubescens*, also known as downy birch, *Lonicera nigra*, also known as blackberry honeysuckle, or *Salix alba*, or white willow, when it comes to the flu, especially if fever and arthralgia are present (53). Herpes simplex relapses are avoided by combining *Juglans regia* (walnut) with *Acer camestris* (field maple), *Ulmus campestris* (elm), and *Rosa canina* (dog rose) (46). In cases of recurrent herpes simplex keratitis, *Acer camestris* and *Prunus spinosa*, often known as blackthorn, may be combined. Gemmotherapy provides a lengthy range of treatments for treating Epstein-Barr virus infectious mononucleosis, which is a prevalent viral infection affecting young people worldwide (62). *Alnus glutinosa* (alder), *Vitis vinifera* (common grape vine), *Juniperus communis* (common juniper), *Ribes nigrum* (black currant), *Betula pubescens* (downy birch), and *Juglans regia* (walnut). Because of its ability to promote hepatocyte regeneration, the root of the Radical Secale (rye) has a specific tropism for hepatic parenchyma. In cases of acute viral hepatitis, it is combined with *Zea mays* (corn), *Corylus avellana* (hazel), *Berberis vulgaris* (barberry), *Lonicera nigra* (blackberry honeysuckle), or *Rosmarinus officinalis* (rosemary) (62). Among the herbs used to treat chronic hepatitis are Radical Secale (rye) root, *Rosmarinus officinalis* (rosemary), *Berberis vulgaris* (barberry), *Corylus avellana* (hazel), *Juniperus communis* (common juniper), *Ribes nigrum* (black currant), and *Berberis vulgaris* (rosemary) (62). Keep in mind that *Rosmarinus officinalis* has a particular tropism for the biliary tract, adrenal glands, liver, cholecyst, and gonads, all of which aid in the regeneration of the liver. For both patients and doctors, the treatment of warts—common viral illnesses brought on by the human papilloma virus—is disappointing, but gemmotherapy provides some alternatives: Boxwood, *Thuja orientalis* (Chinese thuja), *Vitis vinifera* (common grape vine), *Rosa canina* (dog rose), *Juglans regia* (walnut), *Buxus sempervirens* L. (boxwood), and *Ficus carica* (fig) (63).

Gemmotherapy in cases of parasitism

Combining the commonly used phytotherapy plant *Buxus sempervirens* (common boxwood) with *Juglans regia* (walnut) and *Alnus incana* (gray alder) may prove to be a successful treatment for parasitoses (23).

Active ingredients found in therapeutic plants

There are two main barriers that impede efforts to determine the precise mechanisms of action and antibacterial impact of medicinal herbs. First, a number of elements work together to produce the antimicrobial effect; some of these factors are not directly antimicrobial but are crucial to attaining the therapeutic effect. Second, the active chemicals in the great majority of medicinal plants have effects other than

antibacterial ones, such as anti-inflammatory ones. Specifically, gemmotherapy has shown that every active ingredient in embryonic cell stem tissues acts in concert, making it pointless to try to split the overall impact (23). However, in order to obtain a pure molecule for further experimental testing and clinical trials, it is necessary to identify the therapeutically active elements (64). It is more difficult to trace the relationships between the active chemicals and their breakdown products than it is to isolate a pure component and figure out its structure (64). These days, precise protocols and extraction techniques are available for examining the physico-chemical characteristics of pure substances, but taking into account all potential interactions is far more difficult than that. Since healing is the outcome of a complex web of chemicals, it is frequently the case that the mode of action of plant-based products is poorly understood (65). The practical procedures for bioassaying the chain of reactions between the active chemicals are actually what are required. Accurately characterizing the active chemicals in plant products is the first step towards understanding their medicinal effect. Developments in nanotechnology are promising for the creation of plant-derived medicines that are more stable, efficacious, and controllable. The immediate use of nanoparticles in managing the adverse effects, such as toxicity, of certain medications used to treat infectious disorders is anticipated in the near future (65). Here are some quotes about plant-active chemicals. **1,8-cineole** (ethyl-dimethyl-(3 sulfopropylazanium) (C7H18NO3S+) (PubChem CID 448830) is found in many essential oils, for example, Eucalyptus globulus (eucalyptus) oil (66).

Anthocyanins (2-phenylchromenylium) (Cyanidin: C15H11O6Cl; Peonidin: C16H13O6Cl; Malvidin: C17H15O7Cl; Delphinidin: C15H11O7Cl; Petunidin: C16H13O7Cl; Pelargonidin: C15H11O5Cl or C15H11O+) (PubChem CID 448830) are found in *Vaccinium myrtillus* (bilberry). A recent study about intestinal accessibility and bioavailability show that the colon is a significant site for anthocyanins and their degradation products (67).

Arbutin ((2R,3S,4S,5R,6S)-2-(hydroxymethyl)-6-(4-hydroxyphenoxy)oxane-3,4,5-triol) (C12H16O7) (PubChem CID 440936) is found in plants from the families Ericaceae, Asteraceae, and Rosaceae. It explains the antiseptic properties, but its relation with microorganisms are not enough studied, notably the mutagenic effect of its metabolites hydroquinone (68).

Alliin (3-prop-2-enylsulfanylprop-1-ene) (C6H10OS2) (PubChem CID 65036) found in family Alliaceae, has a broad spectrum antimicrobial and immunomodulatory activity, along with many other beneficial effects for human health (69).

Artemisinin (C15H22O5) (PubChem CID 68826) is one of the most celebre semi-synthetic plant-derived compound used in infectious diseases. The discovery of artemisinin, the active compound of *Artemisia annua* (sweet wormwood) has brought new hope for medical community (40). The

emergence of artemisinin-resistant *Plasmodium falciparum* explains the critical need to identify new antimalarials (69). Hope comes again from herbal compounds—a recent paper describe lupane triterpenes, originated from *Buxus sempervirens* (common boxwood), as being the next antimalarials (40).

Benzoic acid (C7H6O2) (PubChem CID 243), found in the fruits of *Vaccinium vitis-idaea* (lingonberry, cowberry or bearberry), has antiseptic effect which explains the preservation of jam (70).

Curcumin ((1E,6E)-1,7-bis(4-hydroxy-3-methoxyphenyl)hepta-1,6-diene-3,5-dione) (C21H20O6) (PubChem CID 969516), an active compound extracted from aromatic *Curcuma aromatica* (wild turmeric), is not only a powerful antioxidant, anti-inflammatory and anticancer ingredient but also has antiparasitic activity, in vitro studies showed antimalarial, antileishmanial and antitrypanosomal activity (71).

Essential oils are ethereal oils consisting of complex mixture of many volatile compounds. Even if research on their mechanism of action is lacking, their antimicrobial efficacy is demonstrated by the results of their use in infectious diseases (72).

Quinine ((R)-[(2S, 4S, 5R)-5-ethenyl-1-azabicyclo [2.2.2] octan-2-yl]-(6-methoxyquinolin-4-yl) methanol) (C20H24O2N2 or C20H24N2O2) (PubChem CID 3034034) originates from *Cinchona*. It was for decades the main cure in malaria, other active compounds of plant origin demonstrated their value (73).

Resveratrol (5-[(E)-2-(4-hydroxyphenyl) ethenyl] benzene-1,3-diol) (C14H12O3) (PubChem CID 445154) is best known for its antioxidant properties, but also has antimicrobial activity (73).

Thymoquinone (2-methyl-5-propan-2-ylcyclohexa-2,5-diene-1,4-dione) (C10H12O2) (PubChem CID 1028) is the main active compound of *Nigella sativa* L. seeds essential oil. It has not only an anti-inflammatory effect, but it is a versatile immunomodulator, novel mechanisms being recently discovered (74). The role in activation cellular immunity, by stimulating CD4+ T lymphocytes and production of γ -interferon, explain the positive results of *Nigella sativa* L. seeds essential oil in viral infections (74).

7. Phytotherapy and gemmotherapy's limitations

The primary drawback of phytotherapy and gemmotherapy, as with any other conventional therapeutic approach, is the absence of treatment standardization (53). The majority of doctors do not even think of herbs as an alternative to antibiotics because of this, which contributes to the low credibility around the efficacy of medicinal plants (75). They are essentially correct. Is there anyone brave enough to use thyme essential oil alone to treat their own acute pneumonia? However, the abuse of antibiotics is a significant contributing cause to the emergence of multidrug-resistant bacteria.

Antibiotics were frequently claimed by patients, even for simple common colds. Fortunately, general health laws restrict the empirical use of antibiotics. The identification and isolation of biologically active chemicals has been the subject of numerous studies recently; this is the first step towards the development of novel medications with a standardized mechanism of action. Standardizing treatment protocols will undoubtedly result from learning more about the pharmacology of active substances produced from plants (75). Health care providers are more comfortable using approved medications since they are used to exact treatment regimens than they are using plant extracts with unknown compositions. It is important to understand that in the fields of phytotherapy and gemmotherapy, skilled practitioners are needed to prescribe a brief treatment plan tailored to the individual patient's pathology for a particular infection (76). The consistency of plant products' composition is another significant drawback; different suppliers may provide products with distinct qualities. In order to create quality control protocols, researchers are interested in the analytical characterisation and authentication of active substances. Once more, the number of considerations that must be made makes this stage extremely difficult. For the purpose of authenticating single plant ingredients and mixed plant products, respectively, DNA barcoding and metabarcoding have been proposed (76). Variations in clinical trial results are primarily caused by inadequate characterisation of plant materials. The International Food Standard, Community Herbal Monograph, German Homeopathic Pharmacopeia, or other globally recognized quality standards are examples of verified production processes that establish a plant product's credibility (77). The primary challenge in the production of plant-based products is the inherent genetic diversity seen in plant species. Because of the raw material's place of origin, a product made using the certified manufacturing technique from the same source may differ. Environmental factors have a significant impact on plant quality, with pollution being one such factor. Third, only a specific geographic region has access to high-quality plant species, especially exotic ones (78). The interest in the extensive cultivation of medicinal plants stems from the fact that only ancient people relied exclusively on wild herbs for treatment. Simultaneously, the availability of high-quality medicinal plants is greatly influenced by a number of other factors, including plant species and environmental factors (79). Environmental pollution is an issue that seems to be getting worse all the time, and there doesn't seem to be any hope for a workable solution. The environment in which plants grow is the first factor that influences the quality of a final product, even if we are unable to alter it. Lastly, no comprehensive clinical trials have been conducted to assess the side effects and efficacy of phytotherapy and gemmotherapy for infectious illnesses (80). Standardized tests and guidelines for comparing experimental data are necessary for evaluating the antimicrobial efficacy of plant products. While the Clinical and Laboratory Standards Institute (CLSI) and the European Committee on Antimicrobial Susceptibility Testing (EUCAST) (www.eucast.org) have provided standards for antibiotics and

antifungals, there are no consistent procedures for testing plant products (80). The least inhibitory concentration (MIC) of pure active substances might be readily determined, but testing plant extracts or essential oils requires other techniques (81).

Discussion

Before engaging in further discussion, conclusive proof regarding the efficacy of herbal products in treating infectious disorders should be provided. Unquestionably, several plant species have developed antibacterial compounds as part of their natural fight against diseases. Plant defense mechanisms differ significantly from human defense mechanisms, and plant diseases and human pathogens are undoubtedly not the same (82). However, these variations shouldn't be used as justification for dismissing plants' ability to treat some viral disorders. On the other hand, one should not disregard the proven antibacterial properties of some plants and abandon the use of traditional medication regimens. But Youyou Tu, a pharmacologist at the Chinese Academy of Chinese Medical Sciences in Beijing and 2015 Nobel Prize winner, discovered artemisinin, which prevented millions of deaths. This is one of the most recent scientific confirmations of the value of plants in treating infectious diseases (83). It appears that breaking into the natural products market is not too difficult, given the wide variety of affordable and more expensive over-the-counter herbal products available. People are more likely to try something that is affordable, easily accessible, and appears to have no negative impacts. A professional advertisement ensures the suppliers' success (84). Where is the source of this confidence regarding herbal products? We can only speculate that the primary cause is the fact that we frequently employ plants in our daily lives to make tea, spices, or even just soft drinks like lemonade, mint water, and so forth. We can assume that there is nothing wrong with the administration of herbal items such, for example, essential thyme oil since hot tea with lemon and honey is usually always helpful in treating the flu. At first glance, there doesn't seem to be anything wrong, but standardization is the primary issue with herbal product therapy. Not only do we mean to standardize dosages, but we also mean, in particular, to standardize the treatment regimen in cases where two or more herbal items are suggested. It is interesting to notice that when multiple plants are incorporated in a treatment regimen, combined herbal medicines are offered as an easier substitute. It should be obvious to all sensible people that mixing substances will always change their individual effects. Since the effect of a herbal product is derived from the tiny interactions between its molecules, mixing different plants at random can potentially negate its medicinal effect (84). This is because herbal products are inherently mixed. We are now unable to comprehend the complexity of the network generated in a receiver that contains multiple plant species due to the paucity of reliable studies on plant interactions. The Food and Drug Administration (FDA) has not assessed most plant products, and the absence of conclusive research on the safety of some herbs—like elderberry and echinacea—suggests that they shouldn't be used to treat pregnant women or other risk groups

(85). Natural goods are frequently thought of as miracle cures, but new research indicates that they should be utilized cautiously in the lack of reliable proof of their efficacy (86). Plant-derived medications, however, can be particularly helpful in some therapeutic settings, such as simplex hepatic infections, which are illnesses with recurrent episodes, or infections like the flu or tuberculosis, where immune modulation is necessary for full recovery. Parasitic infections are among the most prevalent infections in pediatrics and geriatrics, particularly in nurseries and daycare facilities. Given the high rate of relapses in these types of care facilities, plants may offer significant therapeutic and preventive benefits. These days, we can analyze herbal products using methods that break them down into their constituent parts. However, the physico-chemical analysis of all plant components, in my opinion, does not address the fundamental question of whether or not it will ever be possible to create synthetic antimicrobial compounds that function similarly to those found in nature. It's similar to trying to isolate the sounds of each instrument when listening to a symphony. According to Fernando Piterà, this method ignores the fact that each natural component's actions are essentially dependent on the plant as a whole. He refers to a plant as a biological entity with internal dynamics, or a "phyto-complex." This is actually the gemmotherapy doctrine. It could be argued that traditional research techniques are inappropriate for use in phytotherapy or gemmotherapy clinical trials. Complementary medicine experts contend that finding research techniques that match the standards of traditional medicine is not insurmountable (86). It is not hyperbolic to recall the title of a well-known Goya engraving, "El sueño de la razón produce monstruos" (literally, "The sleep of reason produces monsters"). Reason becomes even more crucial when determining if a treatment plan will be successful or unsuccessful. Healthcare professionals are aware of the repercussions of using the incorrect therapeutic regimen to treat infectious infections. Long-term effects include antibiotic resistance and the dissemination of these genes not only in clinical wards but also in the surrounding environment if the immediate result is therapeutic failure (87).

Conclusion

Different geographic regions have different traditional herbal therapy plans directly impacted by the local flora. Herbal medicine is based on folklore, with few references to pertinent bibliographies. People feel more comfortable using plant products in nations where there is a long history of plant healing. Nevertheless, the present antimicrobial resistance trend has persuaded several research teams to focus their efforts on choosing and standardizing plant remedies that can help treat or prevent infectious diseases. When it comes to goods suggested for infectious disorders, embryonic stem cells are frequently employed in numerous organotropic ways, with a greater emphasis on immunomodulation than on true antimicrobial drugs. Furthermore, the properties of embryonic stem cells differ from those of mature plants. The benefits of several plant-based or plant-derived medications in the treatment of infectious diseases support reevaluating their

therapeutic potential. Just two factors motivate the careful planning of in vitro and in vivo experiments aimed at determining the antibacterial activity of plants: the growth of bacteria, viruses, or parasites resistant to different medications, as well as the toxicity of synthetic pharmaceuticals. The medicinal potential of the plant is yet so vastly untapped that there may be concealed evidence of both novel plant applications and the mechanisms of action lurking beneath these traits.

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