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REVIEW RESEARCH

Review on the production of effective plant biopolymers in reducing microbial infections

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Abstract

One of the most important problems from the past to the present is deadly opportunistic disease in developing countries, which leads to increase mortality in the world. Microbial pathogens such as fungi, bacteria, parasites, and viruses can cause these deadly opportunistic infections. Herbal medicines in the form of nanoparticles, nanocapsules, and biocompatible polymers, and liposomes can be effective in reducing mortality from these infections. Also due to the excessive use of antibiotics, microbial resistance is expanding day to day. On the other hand, indigenous, cheapness, availability, and rich source of effective herbal substances have made these compounds have many applications in biomedical fields. The aqueous extract, essential oil, and active ingredients of various parts of plants such as bark, stems, leaves, fruits, and seeds are used in the treatment of infectious diseases. This article provides information about medicinal plants that have antibacterial properties and are used to treat microbial infections. It is hoped that using this method can reduce and treat microbial infections to some extent.

Keywords: Medicine plants, Microbial infections, Biopolymers, Nanocapsules, Nanoparticles

Introduction

Today, The emergence of microbial resistance is considered an important concern in human health worldwide and there is one of the most important challenges of the World Health Organization. It has been predicted microbial resistance due to the death of 10 million people until 2050(1). Pathogens such as *Staphylococcus aureus, Ecoli, Klebsiella pneumonia, Acinetobacter baumanni, Pseudomonas aeruginosa, Salmonella spp, Shigella, Vibrio cholerea, Candida albicans* are known as the most important cause of drug-resistant in the world. Bacterial and fungal agents with biofilm formation on intravascular equipment and urine catheters lead to infection and even death. According to the results of studies and prevention of deterioration patients and their death, It's so necessary to leading off these infections with little attention and observe of prevention principles (3). Nosocomial pathogens such as *Pseudomonas aeruginosa,* have resistance to antimicrobial agents and disinfectants such as ammonium hexachlorophene, soaps, and iodine solutions (4,5). The need for simple nutrition, multiple virulence factors, and the most importantly, resistance to a wide range of antimicrobials makes this organism a dangerous pathogen (6). This pathogen is also wound causing agent in patients with hospitalized burns (5).In addition, in recent years, the widespread use of antibiotics has made these bacteria resistant to broad-spectrum antibiotics from different groups of antibiotics. The growing use of biocides in health products, which began in the mid-1990s and continues this day, has exacerbated the concerns of microbiologists and health professionals (7). Today, plant metabolites are the best resource and have the appropriate capacity for controlling and reduction of microorganisms (8).

The ideal antimicrobial medicine, which has selective toxicity, means the medicine is harmful to the organism but does not damage host cells. Toxicity is often selective relative and not absolute. It means the drug concentration that the host cell can tolerance but harm to infection organism. Selective toxicity may be the result of the action of a receptor required to bind to the drug, or it may result from the inhibition of biochemical events that are critical to the organism and not to the host cell(9). For decreasing microbial toxicity, there is some research about the potential from antimicrobial ingredients with the route of plant for control and treatment pathogenicity agents, and on the other hand, it can be a good alternative for antibiotics (10,11).

Medicinal plants in the world

Medicines plants have an essential role as traditional medicine in the treatment of a wide range of diseases and form the basis of traditional medicine. It is used to prevent and treat diseases. It is estimated that 8% of the population in developing countries use herbal medicines in health care. It is common to use herbal medicines in India, China, and southeast countries for the treatment of diseases (12).In China 30-50% of the medications, including herbal and traditional medicine(13). In recent years, Indian herbal medicines also have a high potential for the production of medicinal care. This country has a rich resource of plants with the medicinal base for treatment and prescription of medicines9
14,15). Indian traditional medicine uses herbal medicine as powder, syrup, and emulsion. For example, mango crust that is one of the Indian native fruits contains polyphenols whose main substance is mangiferin. This substance has a scientific name *C-glucosylxanthone1,3,6,7-tetrahydroxyxanthone-C2-β-D-glucoside* has the antimicrobial on microorganisms of *Bacillus, Staphylococcus aureus, Ecoli, Salmonella spp, Klebsiella pneumoniae* (16,17).

In countries of Ghana, Nigeria, and Zambia herbal medicines are used as the first treatment for children with malaria fever(18). Egypt is also known as one of the largest sources of herbal plants in the world due to its Mediterranean climate. So that in the region of Florida it accounts for about 52.5% of the 2085 species recorded in Egypt (19). According to studies, with the increase of antibiotic medications, urinary tract infections caused by drug-resistant pathogens is increasing. The use of leaf extracts, fruits seeds of plants in the treatment of urinary tract infections has a great effect on reducing these infections and their symptoms. Researchers have also studied the effects of herbal medicines on Urinary tract infection caused by

Ecoli و*Enterococcus* و *Klebsiella spp*(20). Using herbal medicines for anti-inflammatory and antiviral infections from the past. According to the researcher's results, in China traditional medicine,ه *Prunella vulgaris*, contains different biological agents included triterpen, phenol agents that have anti-inflammatory and antiviral effects, Also it is effective in the treatment of cancer. This plant has immunosuppressive activity and can also be effective against the AIDS virus. Further studies on the effect of this plant on viral infections such as herpes simplex indicate that this plant may have similar effects on COVID-19 viral infection (21).

The use of medicinal plants is also used in the treatment of wounds and skin infections with anti-inflammatory and antimicrobial properties. In different cultures of non-Western societies, about 30% of herbal plants are used to treat skin infections (23,24). Pakistan has a rich source of flowers and herbal plants that are the use of herbals in home remedies has long been common this country, In third world countries such as Pakistan, where infections diseases are more prevent, the use of herbal plants has played an important role in reducing these diseases, so herbal plants are widely used in this country due to their low cost and high effectiveness (24,25).

In this study, a review of different types of medicinal plants rich areas of these plants extracted as a source of antimicrobial medicines.

Medicinal plants biopolymers

The most important field for the production of nanomaterials for medical purposes and other fields (agriculture, electronics, food) is based on nanotechnology (26). With the spread of various infectious diseases, researchers and pharmaceutical companies are looking to develop and discover new types of antibiotics against pathogens. Nanomaterials can be used as a new type of antibiotic due to their high potential, levels, and volume (27). Biopolymers, or biopolymers, are polymers that exist in nature in various forms. Many large-scale commercial biopolymers are also produced by humans. These natural raw materials are biodegradable in the permanent production cycle and have a wide variety of applications as absorbable materials for bioplastic (28) .

These substances are easily broken down into smaller units by the activity of microorganisms such as fungi and bacteria. Fundamental Solution for the Release and Elimination of Drug-Resistant Strains Since 1980, there has been a dramatic increase in the production of nano-based drug products. Identified nanoparticles include nanocrystals, liposomes, and lipid nanoparticles, metal-based particle-based nanoparticles, and proteins (29). Medicinal plants are the best candidate for inhibition of antibiotic-resistant infections of bacteria, the advantages of which are low production costs, and no environmental problems. Medicinal plants with many secondary metabolites are the active ingredients of many drugs. As a result, these plants can be considered as one of the most important sources of drugs with new antibacterial and antifungal effects that in many diseases are used.

Today, there are many reports about the encapsulation of medicinal and herbal substances in polymer-carriers by different methods. By loading the drugs in nanocapsules, the bioavailability and stability of the drugs in the biological environment can be increased and with a low dose of the extract, slow, continuous, and targeted release of the drug can be provided on-site (30). Different methods are used to encapsulate plant materials in polymeric carriers to achieve the desired size of the drug system, which largely depends on the type of application. The average size of nanocapsules is in the range of 500-100 nm, which the microemulsion method is one of the best and most widely used methods for the synthesis of drug systems with capsule size (31). But there are still questions that hopefully in the future nanoparticles can be used to control diseases without their toxic effects. In this section, the study of medicinal plants and their properties on various microorganisms such as gram-positive and gram-negative bacteria that have the greatest effect on these microorganisms, methods, and materials used to extract them, and the percentage of use of different parts of the plant (Table 1) It is also possible to use different parts of plants such as bark, stems, leaves, fruits and seeds in the treatment of infectious diseases.

Table 1. Microorganism, methods, and solvents are described in the text.

Gram positive Bacteria: Bacillus cereus, Bacillus pumilus, Bacillus subtilis, Staphylococcus, Micrococcus, Listeria, Streptococcus, Cocci, Lactobacillus and Enterococcus faecalis.
Gram negative Bacteria: Enterobacter, Escherichia coli, Pantoeaagglomerans Proteus, Shigella, Pseudomonas aeruginosa, Serratia, Vibrio, Klebsiella, Salmonella, Yersinia , and Citrobacte.
Fungal species: Trichophytonmentagrophytes, Candidakrusei, Candida albicans, Candida glabrata, Candidakrusei, Aspergillus, A. flavus, A. niger, Curvularia sp., Fusarium sp., Rhizopussp and Candidaparapsilosis
Viruses : Monkeypoxvirus, respiratorysyncytial virus, HIV-1, hepatitis B virus, and herpes simplex virus type 1, Vaccinia virus, human parainfluenza virus, type 3 (HPIV-3), Herpes simplex virus type 1 and type 2 (HSV-1 and HSV-2), tacaribe virus (TCRV), hepatitis B virus (HBV), Coxsackie virus B3, and influenza virus
Method Used: Agar well diffusion, Agar disk diffusion, Agar ditch diffusion, Tube diffusion, Bauer disc diffusion, Broth dilution, Micro dilution, Liquid, dilution and Serial dilution
Solvent Used : Methanol, n-Hexane, Aqueous, Chloroform, Ethyl Acetate, Benzene, Petroleum Ether, Acetone, Ethanolic, Dichloromethane, Dimethyl Sulphoxide and Diethyl Ether

Figure 1. Frequency of use of different parts of medicinal plants in the whole world

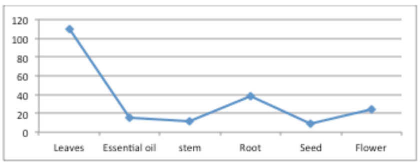
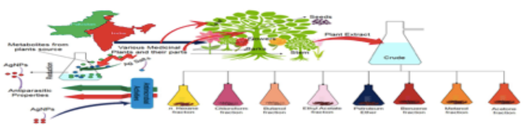


Figure 2. View of different parts of medicinal plants synthesized with silver particles



Anti-microbial effects of medicinal plants

Today, with the increasing use of antibiotics, drug resistance to infectious diseases is expanding. One of the reasons for bacterial resistance is the formation of biofilm structures. In recent years, the importance of biofilms in causing disease, the spread of microbial resistance, and the side effects of antibiotics have led researchers to use natural compounds such as plant extracts to obtain new antimicrobial compounds, especially in the form of microbial biofilms. Biofilm-borne pathogens in hospitals are replaced on hospital equipment such as catheters, artificial heart valves, artificial joints, and are an important cause of nosocomial infections in hospitalized patients (32). The *Cassandra L* study, conducted at the Florida Research Center in the United States, examined the effect of medicinal plant extracts in southern Italy on the growth and biofilm formation of methicillin-resistant *Staphylococcus aureus (MRSA*) strains (22). A study in China used 30 species of medicinal plants native to the region to treat infections *(MRSA*) (33-35). With the increasing use of antibiotics, urinary tract infections caused by drug-resistant pathogens are increasing. The use of leaf extracts, fruits, seeds of plants in the treatment of urinary tract infections has a great effect on reducing these infections. The use of plant extracts in combination with milk, honey, fruit juice, and black pepper is also used (20). According to Girish and Satish's study, the effect of three main plants on gram-positive bacteria *Bacillus* and gram-negative bacteria *Pseudomonas aeruginosa*, *Ecoli,* and *Salmonella* (36). Nair et al. have investigated the effect of 9 plants on 6 bacterial strains *Pseudomonas testosteroni, Staphylococcus epidermitis, Klebsiella pneumoniae, Bacillus subtilis, Proteus, Micrococcus (37).* In Pakistan, the effects of ten medicinal plants used for therapeutic purposes have been studied (24).

Medicinal plants effects on Covid

According to studies conducted in recent years, a Chinese plant called *Lianhuaqingwen* is a mixture of 11 species of medicinal and mineral plants called *gypsum* and *menthol* that have antiviral properties of *SARS-Cov*. In traditional Chinese medicine, this plant is used to treat fever, cough, Used for influenza, bronchitis, pneumonia, and measles (38). The use of medicinal plants in India such as black tea and golden tea, black pepper, dried ginger, and raisins is used to strengthen the immune system and a mixture of these plants can be effective in preventing and reducing the effects of *Covid* disease (18). The use of medicinal plants is effective in strengthening the immune system in preventing people from getting this disease. One of these plants is anise or Roman anise. Anise seed extract, in addition to having antiviral effects, can stimulate the immune system to reduce the risk of people suffering from a variety of diseases, including viral diseases, so this plant can be considered as one of the main options. Researchers should pay attention to the prevention of treatment of viral diseases, including coronary heart disease (39-41). A medicinal plant called asparagus is also considered an antiviral plant due to its steroidal saponins (42). *Rhubarb* is also an

important source of a phytochemical compound called anthraquinone, and it has been found in traditional plants in China that anthraquinones have antiviral properties. The extract of this plant can be effective in inhibiting the activity of *SARS-Co V* virus (43).
Also, the use of a fruit called *Noni*, scientifically called *Morinda citrifolia*, may be effective in preventing infectious diseases such as corona, which is also called cashew berry, because it strengthens the immune system and helps treat infections. And when it ripes. The use of Noni in traditional medicine has been common for more than 2000 years and it has been used to treat infections due to its properties in strengthening the immune system (44, 45). Use of onions, garlic, kiwi, pineapple, papaya, pomegranate, watermelon, black pepper, neem, black *myrobalan*, *guduchi*, *shatavary*, nutmeg *(jaiphal*), and peppermint Antioxidant and antimicrobial properties are effective in strengthening the immune system and preventing infectious diseases(45-47). Studies have also shown that ginger has a similar effect to the cytokine interferon-beta (β-INF) in the treatment of viral respiratory infections (48).

The decreased yield of medicinal plants

The emergence of strains that are resistant to several antibiotics is another problem and challenge. *MRSA* strains, strains that produce various beta-lactamase enzymes such as Metallobetalactamase (*MBL*), carbapenemase (*KPC*), and *AmpC*, have been implicated in the development of resistant infections and even herbal medicines. The prevalence of these genes encoding these enzymes is spreading rapidly among different gram-negatives. This is seen not only in the genus *Pseudomonas aeruginosa*, but also in other bacteria of the *Enterobacteriaceae* family. Because this group of chromosomal genes of beta-lactamase enzymes can be found in genera such as *Ecoli, Enterobacter, Acinetobacter, Klebsiella pneumoniae*. This is especially true when the first strains carrying this gene group were first observed in *Klebsiella pneumoniae,* and in a short time, this resistance spread to other genera of this family. In this study, in total, about 40% of the isolates obtained contained all beta-lactamase genes, which is shown by the study of Rafeei et al. (49) Drugs derived from natural products are usually secondary metabolites and their derivatives. As a result of screening the phytochemicals of various plants, several bioactive compounds such as alkaloids, tannins, flavonoids, glycosides, and saponins have been identified. A large number of phytochemicals belonging to several chemical classes have shown significant inhibitory effects on different types of microorganisms.

Biopolymer properties of medicinal plants and funguses

One of the most important roles of biopolymers in plant extracts is to increase their stability at target sites. Ginger, for example, has many antimicrobial properties, but its extract can not be stabilized in the blood. Encapsulation of ginger in the nanoliposome improves its biological activity and increases the stability of ginger in the blood (50). In medical applications, the use of non-inflammatory and non-toxic coating agents such as collagen, peptides, and biopolymers. The combination of these nanoparticles with other nanomaterials with antibacterial properties such as graphene oxide increases their synergistic effects and ultimately provides better and more effective antibiotic properties. It has recently been shown that titanium dioxide nanoparticles (Tio2 NPs) have a wide range of antimicrobial activity against various microorganisms such as gram-negative and gram-positive bacteria, fungi, and even drug-resistant microorganisms. Most importantly, Tio2-based nanocomposites are environmentally friendly and have a non-contact biocidal activity. Therefore, it is not necessary to release potentially toxic nanoparticles into the environment to achieve disinfection ability. The study of antibacterial activity of Tio2 nanoparticles in a study showed the potential of these nanoparticles in inhibiting the growth of *Ecoli* and *Staphylococcus aureus* strains. The effective properties of Tio2 nanoparticles offer a promising prospect for the serious use of these compounds as alternative antibiotics, disinfectants, and bio preservatives in the food industry (51).
However, biopolymers are also very good candidates for the production of antimicrobial

nanomaterials. In particular, positively charged chitosan can interact with the negative charge on cell membranes, causing changes in cell wall permeability and ultimately leakage of intracellular compounds. However, parameters such as molecular weight, degree of deacetylation, and positive charge content of these polysaccharides strongly affect their antibacterial activity. Today, many studies have been performed to chemically modify chitosan with sulfonate groups or type IV ammonium groups and to integrate antibacterial enzymes with chitosan granules or nanoparticles to increase their antimicrobial activity. Findings from a study by Wardani and Sudjarwo show that chitosan nanoparticles have good potential in inhibiting the growth of Mycobacterium tuberculosis and can be effective in the successful treatment of tuberculosis (52). In general, nanomaterials exhibit a wide range of antimicrobial activity against gram-positive and gram-negative bacteria, mycobacteria, and fungi. The antibacterial activity of nanoparticles varies depending on their type. The mechanisms of nanoparticle toxicity are not clearly defined and require further in-depth studies. However, different theories for the antimicrobial activity of different nano Nanocapsules Nanocapsules are one of the new methods to increase the physical stability of bioactive compounds, protection of these compounds against adverse environmental factors, and the interaction effects of food compounds. This method involves the manipulation of atoms and molecules, which leads to the creation of nanoscale structures that also preserve their properties(53).

Nanocapsule

Nanocapsules are used as a new technology in the packaging of small amounts of active materials using techniques such as nanocomposites, nano emulsification, nanostructures, and finally to provide a useful end product that involves controlled release of the nucleus. Nanocapsule compounds have higher biological activity due to their smaller cell size. This method is also used to protect active compounds against environmental factors such as oxygen, light, moisture, and pH (54). One type of nanostructure is liposomes. Liposomes in small, hollow vesicles have one or more bilayer lipid membranes in the center of which is a fluid nucleus and can trap active substances in their internal space. Nanocapsules are protected by liposomes from bioactive substances against digestion in the gastrointestinal tract, increasing the rate of gastrointestinal absorption, which ultimately increases their bioavailability and biological activity (55, 56).particles have been proposed (53).

Use of silver nanoparticles

Among different types of nanoparticles, silver particles are used in medical research as antibacterial (57), antifungal (58) and viral (59), and parasitic (60) (57). (61-61).

Local medicinal plants of Iran

So far, about 30,000 plant species are known in the world, of which Iran's share is about 8,000 species. Currently, about 2300 species of medicinal plants have been identified in the country. Medicinal plants, on the other hand, account for one-third of the medicines used in human societies. In Laripour et al., The effect of garlic allicin on macrophage nitric oxide production in Candida albicans in immunocompromised patients with candidiasis was investigated (78). Some medicinal plants that exist in different regions of Iran are listed in Table 2 (79, 80).

Table 2. Medicinal plants in different regions of Iran

Part used	Efficacy	Extract	Scientific Name
Root, Rhizome	Burn Wound, Antibacterial, Anti-inflammatory	Emulsion	*Arnebia euchroma(Royle.) Johnston*
Leaves	Treatment of indigestion, rheumatism	Inhaled	*Kelussia odoratissima Mozaf*
Leaves	Skin wound, Gastrointestinal diseases	Emulsion	*Myrtus communis L*
Leaves,Flower	Anti-cough, Antibacterial	Inhaled	*Salvia hydrangea DC*
Leaves ,Flower	Anti-cough, Antibacterial	Inhaled	*Satureja bachtiarica Bung*
Leaves, Flower	Painkiller, Antibacterial	Inhaled	*Thymus daenensis Celak*

Types of medicinal forms of plants:

Aqueous extract Brewed

To prepare brewed plant extract, plant material is imported into water that is above 90 degrees Celsius according to the particle size. Then place the container containing the plant material on the steam bath and keep it at this temperature while stirring frequently, and then strain it hot. Boiling water is poured on the filtered plant residue until the total volume of the resulting liquid reaches the previously determined weight (81). Infusion: To prepare the medicine in this way, moisten a part of the chopped plant material in a mortar with 3 to 5 parts of water several times and then mix it with the rest of the water that is boiling and then on a snail while Frequent stirring keeps at temperatures above 90 ° C. One of the disadvantages of this method is the activity of enzymes remaining in the plant, which cause changes in the content of plant constituents, including the breakdown of glycosides. In addition, the living microorganisms found on the plant easily enter the cold extract and are eventually transferred to the drug. All of these cause more instability of the aqueous extracts. Dry extracts are plant extracts that are obtained by concentrating and drying liquid extracts under mild conditions. When preparing dry extracts, percolation is generally terminated when 3 to 4 parts of the extract have been prepared from one part of plant material or the desired amount of solvent has been used in the instructions. Due to the complex composition of the extracts, the freezing point of most of them is low, so they soften at relatively low temperatures, so they should be kept cold and powdered in a cool environment with refrigerated equipment. Otherwise, cold extracts get wet quickly at normal room temperature due to the absorption of air moisture. Hydroalcoholic First, different parts of the plant are dried and pulverized. The powders obtained are soaked in alcohol with different percentages and smoothed. The alcoholic extract obtained by vacuum distillation is concentrated and decoded with chloroform to remove chlorophyll, fats, and proteins, and the resulting aqueous phase is dried under appropriate conditions (82). Alcoholic solvents including ethanol, methanol, dimethyl sulfoxide. Can be used.

Essential oils of medicinal plants

Plant essential oils are one of the potential sources of antibacterial compounds and have beneficial and effective properties. The composition of plant essential oils varies according to the geographical area of growth of these plants, plant variety, age of the plant when preparing the essential oil, drying method, and extraction of essential oil. Many studies have been done on the antibacterial and fungal effects of various plant essential oils (83).

Properties of curcumin

Curcumin is the biologically active compound of turmeric and has therapeutic properties and antioxidant, anti-cancer, anti-inflammatory, and liver protection properties. Curcumin is the active ingredient in the rhizome of Curcuma langa. Its chemical name is diferuloylmethane (Figure 2). Curcumin is well soluble in ethanol, methanol, acetone, and dimethyl sulfoxide and does not dissolve in acidic solutions. There are several ways to increase the effectiveness of curcumin, one of which is to make a special nanoparticle carrier (dendrosome). Polyester nanoparticles are suitable for curcumin, which is hydrophobic and water-insoluble (85).

Antimicrobial properties of thymol

Thymol (5-methyl-2-isopropyl phenol) is a substance derived from the plant Thymus and (thyme), which is obtained in the form of aromatic alcohol. (Figure 3) Various medicinal products are obtained from Thymus vulgaris. Due to its antiseptic effect, thymol can be effective in intestinal diseases or poisoning, dysentery, and cholera (as prevention). Thymol can be used in combination with chlorhexidine to inhibit oral bacteria. Thymol in thyme oil can be used in skin antifungal compounds, dental formulations (86). Thymol can be used to prevent the growth of bacteria and fungi in powder form. Lotions and ointments can be used. Thyme phenolic essential oil has antibacterial, antifungal, and antioxidant properties (87). It reduces the enzymatic activity of bacterial cells and alters or destroys the bacterial intracellular membrane. According to studies, it acts on gram-positive and gram-negative bacteria such as streptococci and selenomonads. Thymol is used as a hydroalcoholic extract (88).

Figure 2. Curcumin chemical structure

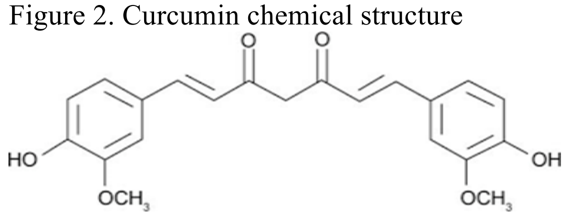
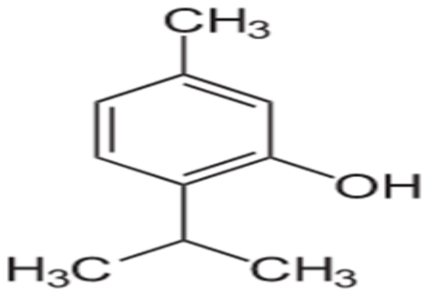


Figure 3. The chemical structure of the thymol



According to the World Health Organization, 80% of people in developed countries use herbs to treat disease. This leads to a more detailed study of the effectiveness of medicinal plants and their safety. Plants with antimicrobial effects on various microorganisms inhibit the growth of bacteria. Therefore, with further research, herbs can be used as a suitable alternative to antibiotics in the treatment of diseases.

Conflict of interest

Author declares no conflict of interest.

References:

1. Brooks L UHS, Chan B,Sistrom M. Quantifying the Evolutionary Conservation of Genes Encoding Multidrug Efflux Pumps in the ESKAPE Pathogens To Identify

Antimicrobial Drug Targets American society for microbiology. 2018;3(3):18-24.

2. Brooks LE, Ul-Hasan S, Chan BK, Sistrom MJ. Quantifying the evolutionary conservation of genes encoding multidrug efflux pumps in the ESKAPE pathogens to identify antimicrobial drug targets. Msystems. 2018;3(3).

3. Larypoor M, farsad, Evaluation of the incidence of nosocomial infections in one of the hospitals of Qom province, Journal of Iran medical microbiology,2011,5(3), 7-17

4. Kramer A, Schwebke I, Kampf G. How long do nosocomial pathogens persist on inanimate surfaces? A systematic review. BMC infectious diseases. 2006;6(1):1-8.

5. Jahantigh M, Tahmasbi H, Bakaeiyan M. Antibiotic Resistance Pattern of Pseudomonas aeruginosa Strains Isolated from Burn Patients. medical journal of mashhad university of medical sciences. 2019;62(5):1121-31.

6. Zahedani S, Jahantigh M, Amini Y. Determining a pattern for antibiotic resistance in clinical isolations of pseudomonas aeruginosa. Tehran University Medical Journal. 2018;76(8):517-22.

7. Coast J, Smith RD, Millar MR. Superbugs: should antimicrobial resistance be included as a cost in economic evaluation? Health economics. 1996;5(3):217-26.

8. Samoilova Z, Smirnova G, Muzyka N, Oktyabrsky O. Medicinal plant extracts variously modulate susceptibility of Escherichia coli to different antibiotics. Microbiological research. 2014;169(4):307-13.

9. Wu G, Wu H, Fan X, Zhao R, Li X, Wang S, et al. Selective toxicity of antimicrobial peptide S-thanatin on bacteria. Peptides. 2010 9//;31(9):1669-73.

10. Dandela R MD, Cravatt B,Rayo J,Meijler M. Proteome-wide mapping of PQS-interacting proteins in Pseudomonas aeruginosa. The Royal Society of Chemistry. 2018;9:2290-4.

11. Khan SU, Anjum SI, Ansari MJ, Khan MHU, Kamal S, Rahman K, et al. Antimicrobial potentials of medicinal plant's extract and their derived silver nanoparticles: A focus on honey bee pathogen. Saudi journal of biological sciences. 2019;26(7):1815-34.

12. Malesh B, Satish S. Antimicrobial Activity of some important medicinal plant against plant and human pathogen. World Journal of Agriculture Sciences. 2008;4(5):839-43.

13. Qin S, Li J, Chen H-H, Zhao G-Z, Zhu W-Y, Jiang C-L, et al. Isolation, diversity, and antimicrobial activity of rare actinobacteria from medicinal plants of tropical rain forests in Xishuangbanna, China. Applied and environmental microbiology. 2009;75(19):6176-86.

14. Sakthi S, Saranraj P, Geetha M. Antibacterial evaluation and phytochemical screening of Datura metel leaf extracts against bacterial pathogens. International Journal Pharm Biol Arch. 2011;2(4):1130-6.

15. Abat JK, Kumar S, Mohanty A. Ethnomedicinal, phytochemical and ethnopharmacological aspects of four medicinal plants of Malvaceae used in Indian traditional medicines: a review. Medicines. 2017;4(4):75.

16. Nandagopal B, Sankar S, Ramamurthy M, Sathish S, Sridharan G. Could the products of Indian medicinal plants be the next alternative for the treatment of infections? Indian journal of medical microbiology. 2011 Apr-Jun;29(2):93-101. PubMed PMID: 21654101. Epub 2011/06/10. eng.

17. Kirtikar KR, Basu BD. Indian Medicinal Plants. Indian Medicinal Plants. 1918.

18. Karou D, Nadembega WM, Ouattara L, Ilboudo DP, Canini A, Nikiéma JB, et al. African ethnopharmacology and new drug discovery. Medicinal and Aromatic Plant Science and Biotechnology. 2007;1(1):61-9.

19. Rahman SMA, Abd-Ellatif SA, Deraz SF, Khalil AA. Antibacterial activity of some wild medicinal plants collected from western Mediterranean coast, Egypt: Natural alternatives for infectious disease treatment. African Journal of Biotechnology. 2011;10(52):10733-43.

20. Shaheen G, Akram M, Jabeen F, Ali Shah SM, Munir N, Daniyal M, et al. Therapeutic potential of medicinal plants for the management of urinary tract infection: A

systematic review. Clinical and experimental pharmacology & physiology. 2019 Jul;46(7):613-24. PubMed PMID: 30932202. Epub 2019/04/02. eng.
21. Shahzad F, Anderson D, Najafzadeh M. The Antiviral, Anti-Inflammatory Effects of Natural Medicinal Herbs and Mushrooms and SARS-CoV-2 Infection. Nutrients. 2020 Aug 25;12(9). PubMed PMID: 32854262. Pubmed Central PMCID: PMC7551890. Epub 2020/08/29. eng.
22. Quave CL, Plano LR, Pantuso T, Bennett BC. Effects of extracts from Italian medicinal plants on planktonic growth, biofilm formation and adherence of methicillin-resistant Staphylococcus aureus. Journal of ethnopharmacology. 2008;118(3):418-28.
23. Grierson D, Afolayan A. Antibacterial activity of some indigenous plants used for the treatment of wounds in the Eastern Cape, South Africa. Journal of Ethnopharmacology. 1999;66(1):103-6.
24. Walter C, Shinwari ZK, Afzal I, Malik RN. Antibacterial activity in herbal products used in Pakistan. Pak J Bot. 2011;43:155-62.
25. Shinwari ZK. Medicinal plants research in Pakistan. Journal of medicinal plants research. 2010;4(3):161-76.
26. Ahluwalia V, Elumalai S, Kumar V, Kumar S, Sangwan RS. Nano silver particle synthesis using Swertia paniculata herbal extract and its antimicrobial activity. Microbial pathogenesis. 2018;114:402-8.
27. Rai M, Ingle A. Role of nanotechnology in agriculture with special reference to management of insect pests. Applied microbiology and biotechnology. 2012;94(2):287-93.
28. Ling S, Chen W, Fan Y, Zheng K, Jin K, Yu H, et al. Biopolymer nanofibrils: Structure, modeling, preparation, and applications. Progress in polymer science. 2018;85:1-56.
29. Shanmuganathan R, Edison T, LewisOscar F, Kumar P, Shanmugam S, Pugazhendhi A. Chitosan nanopolymers: An overview of drug delivery against cancer. International journal of biological macromolecules. 2019 Jun 1;130:727-36. PubMed PMID: 30771392. Epub 2019/02/17. eng.
30. Syafiq R, Sapuan S, Zuhri M, Ilyas R, Nazrin A, Sherwani S, et al. Antimicrobial activities of starch-based biopolymers and biocomposites incorporated with plant essential oils: A review. Polymers. 2020;12(10):2403.
31. Slager J, Domb AJ. Biopolymer stereocomplexes. Advanced drug delivery reviews. 2003;55(4):549-83.
32. Zahedani SS, Tahmasebi H, Jahantigh M. Coexistence of Virulence Factors and Efflux Pump Genes in Clinical Isolates of <i>Pseudomonas aeruginosa</i>: Analysis of Biofilm-Forming Strains from Iran. International Journal of Microbiology. 2021 2021/05/21;2021:5557361.
33. Zuo G-Y, Zhang X-J, Yang C-X, Han J, Wang G-C, Bian Z-Q. Evaluation of traditional Chinese medicinal plants for anti-MRSA activity with reference to the treatment record of infectious diseases. Molecules. 2012;17(3):2955-67.
34. Tohidpour A, Sattari M, Omidbaigi R, Yadegar A, Nazemi J. Antibacterial effect of essential oils from two medicinal plants against Methicillin-resistant Staphylococcus aureus (MRSA). Phytomedicine. 2010;17(2):142-5.
35. Okwu MU, Olley M, Akpoka AO, Izevbuwa OE. Methicillin-resistant Staphylococcus aureus (MRSA) and anti-MRSA activities of extracts of some medicinal plants: A brief review. AIMS microbiology. 2019;5(2):117.
36. Girish H, Satish S. Antibacterial activity of important medicinal plants on human pathogenic bacteria-a comparative analysis. World Applied Sciences Journal. 2008;5(3):267-71.
37. NAIR R, KALARIYA T, Chanda S. Antibacterial activity of some selected Indian medicinal flora. Turkish Journal of biology. 2005;29(1):41-7.
38. Hu K, Guan W-j, Bi Y, Zhang W, Li L, Zhang B, et al. Efficacy and safety of Lianhuaqingwen capsules, a repurposed Chinese herb, in patients with coronavirus disease 2019: A multicenter, prospective, randomized controlled trial. Phytomedicine. 2021;85:153242.
39. Shahrajabian MH, Sun W, Cheng Q. Survey on Chemical Constituent, Traditional and Modern Pharmaceutical and Health Benefits of Chinese Star Anise, a Treasure from the East. Pharmacognosy Communications. 2021;11(1).

40. Gamaleldin MM, NASHAT SM. COVID-19 treatment modalities. 2020.
41. Yang Y, Islam MS, Wang J, Li Y, Chen X. Traditional Chinese medicine in the treatment of patients infected with 2019-new coronavirus (SARS-CoV-2): a review and perspective. International journal of biological sciences. 2020;16(10):1708.
42. Huo X, Dai Y, Yang T, Zhang Y, Li M, Xu X. Decreased erythrocyte CD44 and CD58 expression link e-waste Pb toxicity to changes in erythrocyte immunity in preschool children. Science of the Total Environment. 2019;664:690-7.
43. Gangal N, Nagle V, Pawar Y, Dasgupta S. Reconsidering Traditional Medicinal Plants to Combat COVID-19. AIJR Preprints. 2020;34:1-6.
44. Almeida-Souza F, Taniwaki NN, Amaral ACF, Souza CdSFd, Calabrese KdS, Abreu-Silva AL. Ultrastructural changes and death of Leishmania infantum promastigotes induced by Morinda citrifolia Linn. fruit (Noni) juice treatment. Evidence-Based Complementary and Alternative Medicine. 2016;2016.
45. Dussossoy E, Bichon F, Bony E, Portet K, Brat P, Vaillant F, et al. Pulmonary anti-inflammatory effects and spasmolytic properties of Costa Rican noni juice (Morinda citrifolia L.). Journal of ethnopharmacology. 2016;192:264-72.
46. Batiha GE-S, Alqahtani A, Ojo OA, Shaheen HM, Wasef L, Elzeiny M, et al. Biological properties, bioactive constituents, and pharmacokinetics of some Capsicum spp. and capsaicinoids. International journal of molecular sciences. 2020;21(15):5179.
47. Mao Q-Q, Xu X-Y, Cao S-Y, Gan R-Y, Corke H, Li H-B. Bioactive compounds and bioactivities of ginger (Zingiber officinale Roscoe). Foods. 2019;8(6):185.
48. Wang J, Prinz RA, Liu X, Xu X. In Vitro and In Vivo Antiviral Activity of Gingerenone A on Influenza A Virus Is Mediated by Targeting Janus Kinase 2. Viruses. 2020;12(10):1141.
49. Rafiee R, Eftekhar F, Tabatabaei SA, Tehrani DM. Prevalence of extended-spectrum and metallo β-lactamase production in AmpC β-lactamase producing Pseudomonas aeruginosa isolates from burns. Jundishapur journal of microbiology. 2014;7(9).
50. El-Baroty GS, Abd El-Baky H, Farag RS, Saleh MA. Characterization of antioxidant and antimicrobial compounds of cinnamon and ginger essential oils. African journal of biochemistry research. 2010;4(6):167-74.
51. Malmir S, Karbalaei A, Pourmadadi M, Hamedi J, Yazdian F, Navaee M. Antibacterial properties of a bacterial cellulose CQD-TiO2 nanocomposite. Carbohydrate polymers. 2020;234:115835.
52. Giftania W, Mahmiah, Sri Agus S. In vitro Antibacterial Activity of Chitosan Nanoparticles against Mycobacterium tuberculosis. Pharmacognosy Journal. 2018;10(1).
53. Hussain I, Singh NB, Singh A, Singh H, Singh SC. Green synthesis of nanoparticles and its potential application. Biotechnology Letters. 2016 2016/04/01;38(4):545-60.
54. Sinha-Ray S, Sahu R, Yarin A. Nano-encapsulated smart tunable phase change materials. Soft Matter. 2011;7(19):8823-7.
55. Bozzuto G, Molinari A. Liposomes as nanomedical devices. International journal of nanomedicine. 2015;10:975.
56. Vazquez-Guillamet MC, Vazquez R, Micek ST, Kollef MH. Predicting resistance to piperacillin-tazobactam, cefepime and meropenem in septic patients with bloodstream infection due to Gram-negative bacteria. Clinical Infectious Diseases. 2017;65(10):1607-14.
57. Tanvir F, Yaqub A, Tanvir S, Anderson WA. Poly-L-arginine coated silver nanoprisms and their anti-bacterial properties. Nanomaterials. 2017;7(10):296.
58. Sre PR, Reka M, Poovazhagi R, Kumar MA, Murugesan K. Antibacterial and cytotoxic effect of biologically synthesized silver nanoparticles using aqueous root extract of Erythrina indica lam. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy. 2015;135:1137-44.
59. Villeret B, Dieu A, Straube M, Solhonne B, Miklavc P, Hamadi S, et al. Silver nanoparticles impair retinoic acid-inducible gene I-mediated mitochondrial antiviral immunity by blocking the autophagic flux in lung epithelial cells. ACS nano. 2018;12(2):1188-202.
60. Fayaz AM, Ao Z, Girilal M, Chen L, Xiao X, Kalaichelvan P, et al. Inactivation of microbial infectiousness by silver

nanoparticles-coated condom: a new approach to inhibit HIV-and HSV-transmitted infection. International journal of nanomedicine. 2012;7:5007.
61. Murugan K, Senthilkumar B, Senbagam D, Al-Sohaibani S. Biosynthesis of silver nanoparticles using Acacia leucophloea extract and their antibacterial activity. International Journal of Nanomedicine. 2014;9:2431.
62. Nithya Deva Krupa A, Raghavan V. Biosynthesis of silver nanoparticles using Aegle marmelos (Bael) fruit extract and its application to prevent adhesion of bacteria: a strategy to control microfouling. Bioinorganic chemistry and applications. 2014;2014.
63. Joseph S, Mathew B. Microwave assisted biosynthesis of silver nanoparticles using the rhizome extract of Alpinia galanga and evaluation of their catalytic and antimicrobial activities. Journal of Nanoparticles. 2014;2014.
64. Gurunathan S, Han JW, Kwon D-N, Kim J-H. Enhanced antibacterial and anti-biofilm activities of silver nanoparticles against Gram-negative and Gram-positive bacteria. Nanoscale research letters. 2014;9(1):1-17.
65. Raghunandan D, Mahesh BD, Basavaraja S, Balaji S, Manjunath S, Venkataraman A. Microwave-assisted rapid extracellular synthesis of stable bio-functionalized silver nanoparticles from guava (Psidium guajava) leaf extract. Journal of Nanoparticle Research. 2011;13(5):2021-8.
66. Gogoi N, Babu PJ, Mahanta C, Bora U. Green synthesis and characterization of silver nanoparticles using alcoholic flower extract of Nyctanthes arbortristis and in vitro investigation of their antibacterial and cytotoxic activities. Materials Science and Engineering: C. 2015;46:463-9.
67. Vilas V, Philip D, Mathew J. Catalytically and biologically active silver nanoparticles synthesized using essential oil. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy. 2014;132:743-50.
68. Mubayi A, Chatterji S, Rai PM, Watal G. Evidence based green synthesis of nanoparticles. Adv Mat Lett. 2012;3(6):519-25.
69. Ajitha B, Reddy YAK, Reddy PS. Green synthesis and characterization of silver nanoparticles using Lantana camara leaf extract. Materials science and engineering: C. 2015;49:373-81.
70. Praba PS, Vasantha V, Jeyasundari J, Jacob YBA. Synthesis of plant-mediated silver nanoparticles using ficus microcarpa leaf extract and evaluation of their antibacterial activities. European Chemical Bulletin. 2015;4(1-3):117-20.
71. Patil SV, Borase HP, Patil CD, Salunke BK. Biosynthesis of silver nanoparticles using latex from few euphorbian plants and their antimicrobial potential. Applied biochemistry and biotechnology. 2012;167(4):776-90.
72. Muniyappan N, Nagarajan N. Green synthesis of silver nanoparticles with Dalbergia spinosa leaves and their applications in biological and catalytic activities. Process biochemistry. 2014;49(6):1054-61.
73. Vankar PS, Shukla D. Biosynthesis of silver nanoparticles using lemon leaves extract and its application for antimicrobial finish on fabric. Applied Nanoscience. 2012;2(2):163-8.
74. Abdel-Aziz MS, Shaheen MS, El-Nekeety AA, Abdel-Wahhab MA. Antioxidant and antibacterial activity of silver nanoparticles biosynthesized using Chenopodium murale leaf extract. Journal of Saudi Chemical Society. 2014;18(4):356-63.
75. Jeeva K, Thiyagarajan M, Elangovan V, Geetha N, Venkatachalam P. Caesalpinia coriaria leaf extracts mediated biosynthesis of metallic silver nanoparticles and their antibacterial activity against clinically isolated pathogens. Industrial Crops and Products. 2014;52:714-20.
76. Panneerselvam C, Ponarulselvam S, Murugan K. Potential anti-plasmodial activity of synthesized silver nanoparticle using Andrographis paniculata Nees (Acanthaceae). Arch Appl Sci Res. 2011;3(6):208-17.
77. Ponarulselvam S, Panneerselvam C, Murugan K, Aarthi N, Kalimuthu K, Thangamani S. Synthesis of silver nanoparticles using leaves of Catharanthus roseus Linn. G. Don and their antiplasmodial activities. Asian Pacific journal of tropical biomedicine. 2012;2(7):574-80.
78. Soltani Maryam LM, Akhavan sepahi Abas,Pirali hamedani Morteza. The effect of garlic allicin on macrophage nitric oxide production against Candida albicans. Journal of clinical plants. 2009;7(29):164-200.

79. Ghasemi PA, Jahanbazi P, Enteshari S, Malekpoor F, Hamedi B. Antimicrobial activity of some Iranian medicinal plants. Archives of Biological Sciences. 2010;62(3):633-41.
80. Haddad MHF, Mahbodfar H, Zamani Z, Ramazani A. Antimalarial evaluation of selected medicinal plant extracts used in Iranian traditional medicine. Iranian Journal of Basic Medical Sciences. 2017;20(4):415.
81. Dorman H, Peltoketo A, Hiltunen R, Tikkanen M. Characterisation of the antioxidant properties of de-odourised aqueous extracts from selected Lamiaceae herbs. Food chemistry. 2003;83(2):255-62.
82. Sundaram E, Reddy P, Singh K. Effect of alcoholic extracts of Indian medicinal plants on the altered enzymatic activities of diabetic rats. Indian Journal of Pharmaceutical Sciences. 2009 Sep 2009;71(5):594-8. PubMed PMID: 869944893. English.
83. Jafari B, Ebadi A, Aghdam BM, Hassanzade Z. Antibacterial activities of lemon grass methanol extract and essence on pathogenic bacteria. American-Eurasian J Agric and Environ Sci. 2012;2:1042-6.
84. Menon VP, Sudheer AR. Antioxidant and anti-inflammatory properties of curcumin. The molecular targets and therapeutic uses of curcumin in health and disease. 2007:105-25.
85. Maheshwari RK, Singh AK, Gaddipati J, Srimal RC. Multiple biological activities of curcumin: a short review. Life sciences. 2006;78(18):2081-7.
86. Khan IA, Abourashed EA. Leung's encyclopedia of common natural ingredients: used in food, drugs and cosmetics: John Wiley & Sons; 2011.
87. Malik M, Sattar A, Khan S. Essential oils of the species of Labiatae Part III. Studies on the essential oil of Zataria multiflora. Pakistan Journal of Scientific and Industrial Research (Pakistan). 1987.
88. Evans JD, Martin SA. Effects of thymol on ruminal microorganisms. Current microbiology. 2000;41(5):336-40.