

A Study Based on Analysis of Plant Products as Antimicrobials

Dr. Ravi Bala Goyal

Senior Lecturer,

Department of Zoology Government College, Gangapurcity, Rajasthan

ABSTRACT- *In recent years, the usage of an interest in medications and dietary supplements made from plants has increased. Researchers in the fields of ethnopharmacology, botany, microbiology, and natural product chemistry are scouring the planet for phytochemicals and "leads" that might be used to treat infectious diseases. Despite the fact that 25 to 50% of today's medications come from plants, none of them are employed as antimicrobials. Western medicine is attempting to replicate the effectiveness of traditional healers who have employed plants for a long time to prevent or treat infectious diseases. Secondary metabolites that have been shown to have antimicrobial activities in vitro include tannins, terpenoids, alkaloids, and flavonoids, which are abundant in plants.*

This review aims to provide an overview of the present state of botanical screening initiatives and in vivo tests of their efficacy and safety. Additionally discussed are the structure and antibacterial qualities of phytochemicals. Clinicians must take into account the effects of patients using these botanical preparations for self-medication because many of these substances are already available as unregulated botanical preparations and public use of them is growing quickly.

Keywords- *Antimicrobials, microbiology, metabolites, terpenoids, etc*

I. INTRODUCTION-

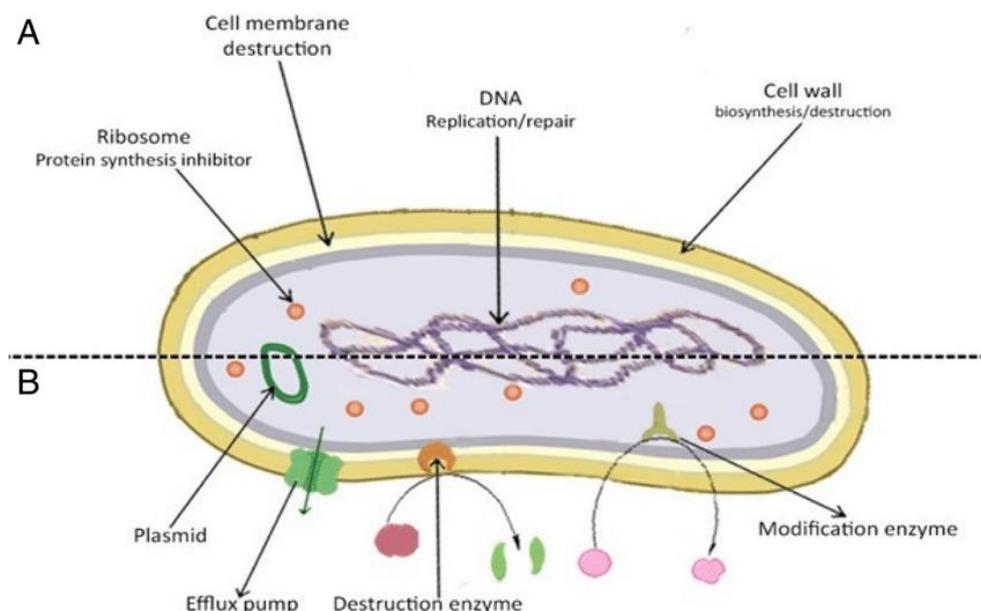
In tropical nations, infectious diseases are responsible for around half of all fatalities. Despite advancements in the study of microbiology and its management, epidemics caused by drug-resistant germs and the appearance of previously unidentified disease-causing microbes represent serious threats to public health in developed countries. The fast development of microbial resistance to conventional antibiotics has caused major concern in the management of infectious diseases. Numerous research have recently been conducted in an effort to identify potentially effective ways to solve these issues. Different modes of action have been used by phytochemicals to potentially combat both susceptible and resistant diseases. In this overview, we've outlined the primary ways that bacteria get resistant to antibiotics and talked about how phytochemicals from several chemical classes may be able to break this resistance. Several of them have demonstrated in vitro synergistic effects when coupled with conventional antibiotics in addition to having direct antibacterial properties. Given these details, it is reasonable to conclude that phytochemicals are a valuable source of bioactive substances with strong antibacterial properties.

Plants have historically been a strong source of anti-infectives; emetine, quinine, and berberine continue to be powerful weapons in the war against microbial illnesses. Plant-based medications known as phytomedicines have showed considerable promise in the treatment of infectious diseases that are difficult to treat, such as opportunistic AIDS infections. Many different microorganisms have been found to be resistant to protoberberines and related alkaloids, picralima-type indole alkaloids, and garcinia biflavonones, which are present in plants used in traditional African medicine. To demonstrate the huge potential of anti-infective compounds from higher plants, the profiles of well-known medications such as *Hydrastis canadensis* (goldenseal), *Garcinia kola* (bitter kola), *Polygonum* sp., and *Aframomum melegueta* (grains of paradise) will be employed. There will be a review of more recent medications such *Xylopiya aethiopyca*, *Araliopsis tabouensis*, *Cryptolepis sanguinolenta*, *Chasmanthera dependens*, and *Nauclea* species.

INFECTIOUS DISEASE- Infectious diseases are the leading cause of death worldwide, accounting for over half of all fatalities in tropical nations. These statistics in developing countries may not be shocking, but it may be unexpected to learn that industrialized nations like the United States are experiencing an increase in infectious illness mortality rates. Infection-related deaths, which were the fifth-leading cause of mortality in 1981, rose to the third spot in 1992. According to estimates, 8% of all deaths have an infectious disease as the primary factor. Given that it was formerly thought that infectious diseases would be completely eradicated by the year 2000, this is concerning. The rises are related to higher rates of HIV/AIDS and respiratory tract infections. Increased antibiotic resistance in nosocomial and community-acquired illnesses are other contributing causes. The age range of 25-44 year olds is also experiencing the most notable growth. These unfavorable health trends necessitate innovative treatment and prevention measures as well as a rekindled

interest in infectious illness within the medical and public health communities. The CDC outlines proposed remedies as a multifaceted strategy that involves prevention (such as vaccination), enhanced monitoring, and the development of novel treatments. This final option would also include the creation of fresh antibiotics.

MECHANISMS OF ANTIBACTERIAL ACTIVITY AND RESISTANCE- An agent's antibacterial action is mostly attributed to two processes, which involve interfering chemically with the production or operation of essential bacterium components and/or evading the established antibacterial resistance mechanisms. These pathways are depicted in Figure 1, and as can be seen, there are numerous targets for the antibacterial drugs. Through a number of strategies, the bacteria may demonstrate resistance to antibacterial medicines. Some types of bacteria have an intrinsic resistance to one or more antimicrobial agent classes. In these situations, every strain of that bacterial species displays resistance to every antibiotic class member. The development of bacterial resistance, in which initially susceptible bacterial populations develop resistance to the antibacterial treatment, is a serious concern. Knowing the mechanisms of antibacterial resistance, which mainly include the activation of the efflux pump, the destruction of antibacterial agents through the use of destruction enzymes, the modification of antibiotics through the use of modifying enzymes, and the alteration of target structures in the bacterium that have lower affinity for antibacterial recognition, is therefore one of the key factors in finding solutions for slowing the development of antibiotic-resistant bacteria. It should be mentioned that antibacterial agent resistance might relate to a single type of mechanism or a combination of various types. Plasmids, which operate as the genetic material and may be independently duplicated and transmitted across bacterial cells and species, are the fundamental method for propagating antibiotic resistance among bacterial populations. The following includes distinct discussions of each of these mechanisms.



HISTORICAL USE- Historically, plants have provided a source of inspiration for novel drug compounds, as plant derived medicines have made large contributions to human health and well-being. Their role is two fold in the development of new drugs:

- (1) They may become the base for the development of a medicine, a natural blueprint for the development of new drugs, or;
- (2) A phytomedicine to be used for the treatment of disease.

There are many examples of medications made from plants. Below is a selection of examples, including several that are considered anti-infective. Since many years ago, abscesses caused by the propagation of *Escherichia histolytica* infections have been treated with the isoquinoline alkaloid emetine, which is found in the subterranean portion of *Cephaelis ipecacuanha* and kindred species. Quinine is a significant medication with a long history of use that is derived from plants. The bark of the *Cinchona* tree contains this alkaloid naturally. In addition to continuing to be helpful in the treatment of malaria, it can also be used to ease nighttime leg cramps. At the moment, quinine analogs like chloroquine are the most often prescribed medications. Antimalarial medications with novel modes of action are needed since some types of malarial parasites have developed resistance to quinines. Some higher plants have significantly impacted fields other than anti-infectives, like cancer treatments. The antileukemic alkaloids vinblastine and vincristine, both of which were derived from the Madagascan periwinkle (*Catharanthus roseus* syn. *Vinca roseus*), are two early examples. Other anti-cancer

medications include taxol, homoharringtonine, and several camptothecin derivatives. For instance, papaverine, a popular benzylisoquinoline alkaloid, has been demonstrated to have a strong inhibitory effect on the reproduction of a number of viruses, including CMV, measles, and HIV. Most recently, the tropical liana *Ancistrocladus korupensis* from the Cameroonian rainforest was found to have three new atropisomeric naphthylisoquinoline alkaloid dimers, michellamines A, B, and C. The three substances demonstrated anti-HIV activity, with michellamine B being the strongest and most prevalent of the group. In vitro, the cytopathic effects of HIV-1 and HIV-2 on the human lymphoblastoid target cell could be completely inhibited by these substances. Phytomedicine Development and the Ethnomedicinal Approach Typically, the earliest generation of plant medications consisted of straightforward botanicals that were used in a very raw state. On the basis of empirical evidence of their clinical application by traditional societies from various areas of the world, a number of potent medicines that are utilized in their natural condition, such as cinchona, opium, belladonna, and aloe, were chosen as therapeutic agents. A second generation of plant-based medicines developed after the industrial revolution, focused on the scientific processing of plant extracts to separate "their active constituents." Pure molecules made up the second-generation phytopharmaceutical drugs, some of which were much more pharmacologically potent than their synthetic equivalents. Quinine from *Cinchona*, reserpine from *Rauvolfia*, and more recently taxol from *Taxus* species were notable instances. Only the source of these substances set them apart from manufactured medicinal medicines. They developed and were evaluated using the same process as other pharmacological medicines. Pharmaceuticals are typically developed in the following order: identification of active lead molecules, thorough biological assays, formulation of dosage forms, and several phases of clinical studies to establish the drug's safety, efficacy, and pharmacokinetic profile. Clinical trials may reveal potential interactions with food and other medicines. A top-bottom strategy is typically used in the creation of "Third Generation" phytotherapeutic drugs. This entails first performing a clinical review of the therapeutic approaches and treatment modalities utilized by conventional practitioners or by the general public as folk medicine. Animal investigations on acute and chronic toxicity are conducted after this evaluation. Cytotoxicity tests should be included in research where appropriate. Conducting in-depth pharmacological/biochemical investigations would only be necessary if the substance has a satisfactory safety index. The dosage forms' formulation and test manufacture are set up to resemble how the herb is typically used. When creating the final dosage form, significant consideration is paid to the end product's stability. This is a special combination of the experimental studies used to demonstrate the efficacy and safety of second generation separated pure chemicals with the empiricism of the older first generation botanicals. By separating the 'active molecules' from plant extracts, a number of pharmaceutical companies are working to generate medications from natural products.

PRESENT USE OF PLANTS AS ANTIMICROBIALS-According to estimates, 50% of current Western medications contain plant ingredients or are based on them. Many of the commercially successful medications used in contemporary medicine were first used in undeveloped forms in conventional or folk medicine, or for other uses that revealed potential biological activity. The main advantages of using plant-derived medications are that they are generally safer than synthetic equivalents, have significant therapeutic benefits, and are more cost-effective than other forms of therapy. Therapeutic Advantage Microbial sources are used extensively in the exploration and application of natural compounds as antimicrobials. Later discoveries of antibiotics including streptomycin, aureomycin 459, and chloromycetin were made possible thanks to the discovery of penicillin. Higher plants have also served as a source of antibiotics, even though soil microbes or fungi manufacture the majority of the therapeutically utilized antibiotics. Lichens' bacteriostatic and antifungicidal qualities, allinine's antibiotic characteristics in *Allium sativum* (garlic), or berberines' antimicrobial activities in goldenseal are a few examples of these. Antimicrobials derived from plants are a big untapped source of potential drugs. There needs to be ongoing research into plant-based antimicrobials. Antimicrobials derived from plants have a great deal of medicinal promise. They effectively treat infectious infections while also minimizing a number of the adverse effects sometimes connected to synthetic antimicrobials. They are powerful but delicate. Numerous plants exhibit tropisms toward particular bodily organs or systems. Phytomedicines typically have a variety of physiological effects. They frequently take activities that go beyond simply treating a disease's symptoms. *Hydrastis canadensis* is an illustration of this. Along with having antibacterial properties, *hydrastis* also improves blood flow to the spleen, which helps it function at its best and produce mediating substances. Economic Advantage There has been a resurgence of interest in natural products all across the world. These factors include consumer dissatisfaction with conventional medicine, consumer beliefs that natural products are superior, legal changes allowing structure-function claims, which leads to more permissive advertising, the aging of the baby boomer generation, and widespread concerns about the cost of healthcare. To meet consumer demand, many previously wildcrafted plants will need to be domestically cultivated. This gives several chances for the industry's agricultural cultivation. The analysis of the herbal goods industry provides a market-based depiction of the demand for plant-based antimicrobials.

PROMISE-MAKING ANTI-INFECTIVE PLANT SPECIES- Our organizations have placed a strong emphasis on medication discovery using data from ethnomedicine, or the "Third Generation Approach." This approach varies in that the chemical makeup and safety of the extracts are established prior to formulation into dosage forms, but the clinical evaluation in humans occurs before the particular active components are identified. The herb also has antihepatotoxic and anti-diabetic properties. Aframomum is used as a purgative, galactagogue, anthelmintic, hemostatic agent, measles and leprosy remedy, as well as for excessive lactation and postpartum hemorrhage. The ingredients are essential oils like paradol, shagaol, and gingerol. Schistosomes can be effectively treated with antibiotic and antifungal agents, according to studies.

The herb is used medicinally as a carminative, a cough suppressant, a postpartum tonic, and a breastfeeding aid. Dysentery, biliousness, bronchitis, and stomach discomfort are additional applications. To treat headaches and neuralgia, it is also applied externally as a poultice. Lemon grass and it are combined for feminine hygiene. Copper, manganese, and zinc concentrations are high. Xylopic acid and diterpenic acid are important components. The fruit's extract has been found in trials to have antibacterial activity against both gram positive and negative bacteria. Despite the fact that it hasn't been proven to work against *E. coli* Additionally, xylopic acid has shown efficacy against *Candida albicans*. On the west coast of Africa, a shrub known as *Cryptolepis sanguinolenta* Lindl. Schltr. (Periplocaceae) grows in tropical rainforests and deciduous belt forests. The eastern and southern halves of the continent are home to related species. Fever is the main medical condition it is used to treat. It treats urinary tract infections, particularly *Candida* infections. Other use include inflammatory disorders, malaria, hypertension, microbiological infections, stomachaches, and colic.

The Ways In Which Antibacterial Agents Work

Protein production in bacteria

Initiation, elongation, and termination of protein building by the bacterial ribosome include a sizable number of molecular processes. Therefore, a successful strategy to fight bacterial infections is to decrease protein synthesis by specifically targeting the ribosomal subunits. This specific method is used by significant types of antibiotics like macrolides, tetracyclines, minoglycosides, and oxazolidinones to exhibit antibacterial activity.

Biosynthesis of cell walls

Antibacterial drugs have successfully targeted the layer of the bacterial cell wall, which is made up of a network of peptide and glycan strands that are covalently bonded to one another and can offer greater mechanical resistance to osmotic lysis. Transglycosylases and transpeptidases, two different family enzymes whose functions have already been discussed, play crucial roles in the creation of this layer.

Preventing the production of nucleic acids

The enzyme known as DNA gyrase is known to carry out DNA replication as well as the supercoiling and uncoiling of bacterial DNA. Gyrase might be thought of as a good target for antibacterial agents and antibiotics include nalidixic acid, as well as fluoroquinolones such as ciprofloxacin because it is necessary for synthesis, replication, repair, and transcription processes.

Breaking down of the bacterial membrane

Numerous antibiotics, including polymyxins, can bind to the lipid A portion of lipopolysaccharide and subsequently modify its structural makeup by phospholipid exchange, leading to an osmotic imbalance and ultimately to the fast death of bacteria. The degradation of bacterial cell membranes has been documented for a very long time, and it has even been linked to other chemical substances such local anesthetics or disinfectants. The loss of permeability, the leakage of internal components, and even the coagulation of cytoplasm might result from the destruction of a cell's exterior membrane, cytoplasmic membrane, and energy metabolism.

Plant-based substances

Although many nations have already legalized the use of synthetic antimicrobial agents, many researchers are interested in the use of natural substances that are derived from microorganisms, animals, or plants. When it comes to combating the development of antibiotic resistance in bacterial pathogens, these substances have shown encouraging outcomes. The chemicals produced from plants have shown the most promise for use in battling bacterial infections of all the choices. A large class of chemical substances that have been discovered naturally in plants are referred to as plant-derived chemicals. These substances are widely present, and their antioxidant, antibacterial, and antifungal properties have proven to be advantageous. By making older antibiotics more potent, they can restore their therapeutic use and, as a result, prevent the emergence of resistance. Some of the plants and/or plant components which containing antimicrobial activities and are commercially available to consumers are listed in Table 1.

Table 1. some of plant products with antimicrobial activity

COMMON NAME	SCIENTIFIC NAME	COMPOUND	ACTIVE AGAINST	DOSAGE FORM
BARBERRY	<i>Berberis vulgaris</i>	Berberine	Bacteria, protozoa	Soft gel 1000 mg
BLACK PEPPER	<i>Piper nigrum</i>	piperine	Fungi, Lactobacillus, Micrococcus, E. coli, E. Faecalis	
BURDOCK	<i>Arctium lappa</i>		Bacteria, Fungi, viruses	Capsule 475 mg
CARAWAY	<i>Carum carvi</i>		Bacteria, Fungi, viruses	Capsule 1000 mg
CASCARA SAGRADA	<i>Rhamnus purshiana</i>	Tannins	Bacteria, Fungi, viruses	Capsule 425, 450 mg
CHAMOMILE	<i>Matricaria chamomilla</i>	Anthemic acid	M. tuberculosis, S. typhimurium, S. aureus	
CLOVE	<i>Syzygium aromaticum</i>	Eugenol	General	Capsule 500 mg
CRANBERRY	<i>Vaccinium spp</i>	Fructose	Bacteria	Capsule 500 mg
EUCALYPTUS	<i>Eucalyptus globulus</i>	Tannin	Bacteria, viruses	Inhaler and tablet
GARLIC	<i>Allium sativum</i>	Allicin, ajoene	General	Tablet
GOLDENSEAL	<i>Hydrastis canadensis</i>	Berberine, hydrastine	Bacteria, Giardia duodenale, Trypanosomes	Solution, 500 mg per dosage
GREEN TEA	<i>Camellia sinensis</i>	Catechin	General	
LICORICE	<i>Glycyrrhiza glabra</i>	Glabrol	S. aureus, M. tuberculosis	Capsule 450 mg
OAK	<i>Quercus rubra</i>	Tannins		Capsule 500, 650 mg
ONION	<i>Allium cepa</i>	Quercetin		
OREGON GRAPE	<i>Mahonia aquifolia</i>	Allicin	Bacteria, Candida	
SENNA ST. JOHN'S WORT	<i>Hypericum perforatum</i>	Berberine	Plasmodium	Capsule 500 mg
THYME	<i>Thymus vulgaris</i>	Hypericin, others	Trypanosomes, general	Table 450 mg
TURMERIC	<i>Curcuma longa</i>	Caffeic acid	General	
		Thymo	Viruses, bacteria, fungi	Capsule 450 mg
		Tannins		
		Curcumin, Turmeric	Bacteria, protozoa	
		oi		

Table 2. The strongest plant antimicrobial compounds reported in recent years

Class of naturally compound	Compound	Conc.	Mechanisms of action	Active against	Findings	References
Alkaloids	Reserpine	100 mg/L	Efflux pump inhibitor	Staphylococcus sp., Streptococcus sp. And Micrococcus sp	Reducing the (MIC) of antibiotics	In vitro mode
	Piperine	100µg/mL	Efflux pump inhibitor	Methicillin resistant Staphylococcus aureus (MRSA) and Staphylococcus aureus		In vitro mode
	Berberine	4Mm	Cell division inhibitor, Protein and DNA synthesis inhibitor	Escherichia coli		In vitro mode
	Chanoclavine		Efflux pump inhibitor	E. coli	Reducing the MIC of tetracycline up to 16-folds	
	Salasodine	32µg/mL	Destruction of bacterial membrane	C. albicans	Potent fungicidal activity	In vitro model
	Conessine	20mg/L	Efflux pump inhibitor	Pseudomonas aeruginosa	Active against RND family pump	
	Evocarpine	5mg/mL		Mycobacterium tuberculosis		
	Tomatidine		ATP synthase inhibitor	Listeria, Bacillus and Staphylococcus spp		In vitro model
	Lysergo		Efflux pump inhibito	E. coli	Lowering the dose of antibiotics	
	Organosulfu	Allicin		Sulfhydryl-dependent enzyme inhibitor, DNA and protein	Staphylococcus epidermidis, P. aeruginosa, Streptococcus agalactiae	In the gas phase active against antibiotic resistant strains

A Study Based on Analysis of Plant Products as Antimicrobials

			synthesis inhibitor		
Ajoene			Sulfhydryl-dependent enzyme inhibitor	Campylobacter jejuni, Streptoproteus, Staphylococcus and E. coli	Zone inhibition method • More potent than allicin
Sulforaphane			Destruction of bacterial membrane, ATP synthase inhibitor, DNA and protein synthesis inhibitor	E. coli	Did not destroy the membrane integrity directly
Berteroin	Range of 1 – 16 µg/m			Helicobacter pylori	
Hirsutin	Range of 8 – 16 µg/mL			P. aeruginosa and Bacillus cereus	Having antifungal and antimicrobial activities.
Alyssin				H. pylori	
Erysolin	Range of 4 – 32 µg/mL			H. pylori	
Allyl isothiocyanate, Benzyl isothiocyanate and Phenethyl isothiocyanate				Bacillus subtilis, S. aureus, S. epidermidis, Enterococcus faecalis, Salmonella typhimurium, Enterobacter aerogenes, Enterobacter cloacae, and E. coli	Show antibacterial activity against foodborne and esistant pathogens. AITC was the major ITC in the stem and leaf of R. sativus
Phenolic compounds					
Resveratrol	0.064, 0.313 mg/mL		Efflux pump inhibitor	Mycobacterium smegmatis, Campylobacter jejuni	Reduced MIC value of antibacterial agent against resistant strain
Baicalein	64, 128, 64 µg/mL		Efflux pump inhibitor	M. smegmatis, MRSA, C. albicans	Reduced MIC value of antibacterial agent against resistant strain
Biochanin A	256 µg/mL, no inhibitory effect, 12 Mm		Efflux pump inhibitor	M. smegmatis, MRSA, Chlamydia spp.	Reduced MIC value of antibacterial agent against resistant strain
Formononetin	256 µg/mL		Efflux pump inhibitor	M. smegmatis	Reduced MIC value of antibacterial agent against resistant strain
Luteolin	32 µg/mL		Efflux pump inhibitor	Mycobacteria spp	Reduced MIC value of antibacterial agent against resistant strain
Kaempfero	125, 128-256 µg/mL		Efflux pump inhibitor	MRSA, C. albicans	Reduced MIC value of antibacterial agent against resistant strain
			Rigidifying bacterial membrane	E. coli	Reduced MIC value of antibacterial agent against resistant strain
Kaempferol rhamnoside	1.56 µg/mL		Efflux pump inhibitor	S.aureus	
Myricetin	32 µg/mL		Efflux pump inhibitor	M. smegmatis	Increased antimicrobial activity of ciprofloxacin
Rhamentin	19-75 µg/mL		Efflux pump inhibitor	S. aureus	
Quercetin	75 µg/mL		Efflux pump inhibitor	S. aureus	
	48.5 and 19.9µM			H. pylori and E. coli	

A Study Based on Analysis of Plant Products as Antimicrobials

Chrysosplenol-D	25 µg/mL	Efflux pump inhibitor	S. aureus	Inhibited NorA EP in the presence of subinhibitory concentrations of berberine
Chrysopentin	6.25 µg/mL	Efflux pump inhibitor	S. aureus	Inhibited NorA EP in the presence of subinhibitory concentrations of berberine
Silybin		Efflux pump inhibitor	S. aureus	
Biochanin A	10 µg/mL	Efflux pump inhibitor	S. aureus	Reduced the expression of NorA protein
Genistein	10 µg/mL	Efflux pump inhibitor	S. aureus	
Orobo	10 µg/mL	Efflux pump inhibitor	S. aureus	
4',6'-Dihydroxy-3',5'-dimethyl-2'-methoxychalcone	10 µg/mL	Efflux pump inhibitor	S. aureus	duced MIC of erythromycin from 0.4 to 0.1 µg/mL
4-phenoxy-4'-dimethylamino ethoxychalcone	9 µM	Efflux pump inhibitor	S. aureus	Equipotent to reserpine
4-dimethylamino-4'-dimethylamino ethoxychalcone	7.7 µM	Efflux pump inhibitor	S. aureus	Equipotent to reserpine
Bergamottin epoxide	35.7 µg/mL	Efflux pump inhibitor	MRSA	Resulted in the 20-fold reduction in MIC value of norfloxacin
5,7-dihydroxy-6-(2-methylbutanoyl)-8-(3-methylbut-2-enyl)-4-phenyl-2-H-chromen-2-one	8 µg/mL	Efflux pump inhibitor	MRSA	
5,7-dihydroxy-8-(2-methylbutanoyl)-6-(3-methylbut-2-enyl)-4-phenyl-2-H-chromen-2-one	8 µg/mL	Efflux pump inhibitor	MRSA	
Epigallocatechin gallate	1-10 µM	DNA gyrase	-	
	200 µM	Beta-ketoacyl-[acyl carrier protein] reductase (FabG)	E. coli	
	64 µg/mL	Inhibition of dihydrofolate reductase	Stenotrophomonas maltophilia	
Chebulinic acid		DNA gyrase	M. tuberculosis	In silico
3-p-Trans-coumaroyl-2-hydroxyquinic acid	2.5-10 µg/mL	Damage to the cytoplasmic membrane	S. aureus	Active against eleven food-borne pathogens
p-Coumaric acid		Damage to the cytoplasmic membrane	Oenococcus oeni and Lactobacillus hilgardii	
Apigenin	132.7 and 163.0 µM	d-Alanine:d-alanine ligase	H. pylori and E. coli	Reverse inhibitor and competitive with ATP
Sophoraflavanone B	15.6-31.25 256 µg/mL	Direct interaction with peptidoglycan	MRSA	-
Naringenin	256 µg/mL	Beta-Ketoacyl acyl carrier protein synthase	E. faecalis	Showed activity against vancomycin resistance E. faecalis

A Study Based on Analysis of Plant Products as Antimicrobials

			(KAS) III		
	Eriodictyol	256 µg/mL	Beta-Ketoacyl acyl carrier protein synthase (KAS) III	<i>E. faecalis</i>	Shown activity against vancomycin resistance <i>E. faecalis</i>
	Taxifolin	128 µg/mL	Beta-Ketoacyl acyl carrier protein synthase (KAS) III	<i>E. faecalis</i>	Shown activity against vancomycin resistance <i>E. faecalis</i>
	Sakuranetin	2.2 µM	Fabz	<i>H. pylori</i>	
	3,6-Dihydroxyflavone	16-32 µM	Beta-Ketoacyl acyl carrier protein synthase (KAS) III and I	<i>E. coli</i>	High binding affinity with KAS III
	Curcumin	13.8 µg/mL	Sortase A	<i>S. aureus</i>	No growth inhibitory activity
		25-100 µM	Leaky membrane	<i>S. aureus</i> and <i>E. coli</i>	Broad spectrum activity
	Morin	39.37 and 8.54 µM	Sortase A and B	<i>S. aureus</i>	No growth inhibitory activity
	4',7,8-trihydroxyl-2-isoflavene	0.85 µM	Urease inhibitor	<i>H. pylori</i>	20-fold lower than acetohydroxamic acid
Coumarin	Aegelinol	16 µg/mL	DNA gyrase inhibitor	<i>Salmonella enterica</i> serovar Typhi, <i>Enterobacter aerogenes</i> , <i>Enterobacter cloacae</i> , <i>S. aureus</i>	Higher activity against Gram-negative bacteria than Gram-positive ones particularly <i>Salmonella thypii</i>
		Dose dependent inhibition between 5 and 25 µg/mL		<i>H. pylori</i>	
	Agasyllin	32 µg/mL	DNA gyrase inhibitor	<i>S. enterica</i> serovar Typhi, <i>E. aerogenes</i> , <i>E. cloacae</i> , <i>S. aureus</i>	Higher activity against Gram-negative bacteria than Gram-positive ones particularly <i>Salmonella thypii</i>
		Dose dependent inhibition between 5 and 25 µg/mL		<i>H. pylori</i>	
	4'-seneciioiloxysthol	5µg/mL	DNA gyrase inhibitor	<i>B. subtilis</i>	6-fold more active against <i>B. subtilis</i> ATCC 9372 than that of xanthotoxin
	Osthole	125 µg/mL	DNA gyrase inhibitor	<i>B. subtilis</i> , <i>S. aureus</i> , <i>K. pneumoniae</i> , MSSA	-
	Asphodelin A 4'-O-β-D-glucoside	Range of 128–1024 µg/mL	DNA gyrase inhibitor	<i>S. aureus</i> , <i>E. coli</i> , <i>P. aeruginosa</i> , <i>C. albicans</i> , <i>Botrytis cinerea</i>	-
	Asphodelin A	ange of 4–128 µg/mL	DNA gyrase inhibitor	<i>S. aureus</i> , <i>E. coli</i> , <i>P. aeruginosa</i> , <i>C. albicans</i> , <i>B. cinerea</i>	-
	Clorobiocin	-	DNA gyrase inhibitor	-	noviosyl sugar moiety is essential for biological activity mutations at Arg136 of GyrB in <i>E. coli</i> results in coumarin-resistant
	Novobiocin	-	DNA gyrase inhibitor	-	noviosyl sugar moiety is essential for biological activity

				mutations at Arg136 of GyrB in <i>E. coli</i> results in coumarin-resistant
Coumermycin A1	-	DNA gyrase inhibitor	-	noviosyl sugar moiety is essential for biological activity
Bergamottin epoxide	-	Efflux pump inhibitor	MSRA	mutations at Arg136 of GyrB in <i>E. coli</i> results in coumarin-resistant
6-Geranyl coumarin	No inhibitory effect	Efflux pump inhibitor	<i>S. aureus</i>	20-fold reduction in the MIC value of norfloxacin against MRSA
Galbanic acid	No inhibitory effect	Efflux pump inhibitor	MDR clinical isolates of <i>S. aureus</i>	Reduced the MIC for tetracycline and norfloxacin by 2 times
				Reduced MIC range of ciprofloxacin and tetracycline from 10-80 µg/ml to 2.5-5 µg/ml

Perspectives and conclusions

Numerous studies have found that medicinal plants are particularly successful in treating infectious disorders. The plants have a lot of potential as a source of cutting-edge antibacterial compounds. They are inexpensive, easily accessible, and nearly without any negative side effects. Phytochemicals, which are molecules made from plants, have even been used to treat a variety of infectious diseases and have displayed intriguing antibacterial efficacy against a number of human infections. Some of these substances exhibit both inherent antibacterial activity and activities that reduce the need for antibiotics.

In conclusion, because of the qualities of herbal-based treatments, people have been paying more attention in recent years. To ensure the mechanism of action and the safety of antimicrobial phytochemicals, more studies must yet be done.

Challenges and the future in view

The main difficulty in creating new phytochemicals has been translating in vitro research into in vivo tests, and then into human clinical trials. The issue is particularly serious when it comes to natural antimicrobial agents because various aspects, such as tissue penetration, maximum plasma concentration, and bioavailability, might impact their efficacy. For instance, hepatic enzymes quickly glucuronidate phenolic natural compounds, which has a significant impact on their tissue penetration and maximum plasma levels. The successful treatment of microbial infections has been seriously threatened by the emergence of antibiotic-resistant bacteria. To date, a new strategy to tackle antibiotic resistance is urgently needed. In the coming years, bioactive products will likely be discovered using phytochemicals, which exhibit a variety of chemical structures and methods of action. However, further research must be done to determine the precise pathways as well as the pharmacodynamic and pharmacokinetic characteristics of the compounds.

REFERENCES

- [1]. Spratt BG. Resistance to antibiotics mediated by target alterations. *Science*. 1994;264(5157):388–93.
- [2]. Song MD, Wachi M, Doi M, Ishino F, Matsuhashi M. Evolution of an inducible penicillin-target protein in methicillin-resistant *Staphylococcus aureus* by gene fusion. *FEBS Lett*. 1987;221(1):167–71.
- [3]. Khan IA, Mirza ZM, Kumar A, Verma V, Qazi GN. Piperine, a phytochemical potentiator of ciprofloxacin against *Staphylococcus aureus*. *Antimicrob Agents Chemother*. 2006;50(2):810–2.
- [4]. Yi ZB, Yan Y, Liang YZ, Bao Z. Evaluation of the antimicrobial mode of berberine by LC/ESI-MS combined with principal component analysis. *J Pharm Biomed Anal*. 2007;44(1):301–4.
- [5]. Lin CM, Preston JF 3rd, Wei CI. Antibacterial mechanism of allyl isothiocyanate. *J Food Prot*. 2000;63(6):727–34.
- [6]. Kuete V, Wansi JD, Mbaveng AT, Kana Sop MM, Tadjong AT, Beng VP, et al. Antimicrobial activity of the methanolic extract and compounds from *Teclea afzelii* (Rutaceae). *S Afr J Bot*. 2008;74(4):572–6.
- [7]. Siddiqui BS, Ali ST, Rizwani GH, Begum S, Tauseef S, Ahmad A. Antimicrobial activity of the methanolic bark extract of *Holarhena pubescens* (Buch. Ham), its fractions and the pure compound conessine. *Nat Prod Res*. 2012;26(11):987–92.
- [8]. Alhanout K, Malesinki S, Vidal N, Peyrot V, Rolain JM, Brunel JM. New insights into the antibacterial mechanism of action of squalamine. *J Antimicrob Chemother*. 2010;65(8):1688–93.
- [9]. Rehman F, Mairaj S. Antimicrobial studies of allicin and ajoene. *Int J Pharm Bio Sci*. 2013;4(2):1095–105.
- [10]. Dufour V, Stahl M, Baysse C. The antibacterial properties of isothiocyanates. *Microbiology*. 2015;161(Pt 2):229–43.
- [11]. Farhadi F, Khameneh B, Iranshahi M, Iranshahi M. Antibacterial activity of flavonoids and their structure–activity relationship: An update review. *Phytother Res*. 2019;33(1):13–40.

- [12]. Ramezani M, Fazli-Bazzaz BS, Saghafi-Khadem F, Dabaghian A. Antimicrobial activity of four Artemisia species of Iran. *Fitoterapia*. 2004;75(2):201–3.
- [13]. Morel C, Stermitz FR, Tegos G, Lewis K. Isoflavones as potentiators of antibacterial activity. *J Agric Food Chem*. 2003;51(19):5677–9.
- [14]. Duan F, Li X, Cai S, Xin G, Wang Y, Du D, et al. Haloemodin as novel antibacterial agent inhibiting DNA gyrase and bacterial topoisomerase I. *J Med Chem*. 2014;57(9):3707–14.