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Antimicrobial properties of natural products and their application in pharmacognosy

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Abstract : Both the food business and consumers are paying close attention to the usage of natural antibacterial agents in food. There are two main causes for this. First, a class of microorganisms known as foodborne pathogens has dramatically increased as a result of the abuse and improper management of antibiotics. These bacteria are not only resistant to medicines but also more tolerant of various food processing and preservation techniques. Furthermore, researchers are becoming more interested in the creation and application of natural compounds in food due to growing public knowledge of the possible health risks associated with synthetic preservatives vs the advantages of natural additives. This has forced the food sector to search for substitute preservatives that can improve food quality and safety. The antibacterial capabilities of compounds obtained from natural sources can be applied to food safety, as they can combat a wide variety of foodborne diseases. This article examines the antibacterial properties of many natural substances, such as bacteria, algae, mushrooms, plants, and animals, as well as their possible application in food systems.

IndexTerms **- Natural antimicrobials, Pharmacognosy, Drug discovery, Phytochemicals, Secondary metabolites.**

I. INTRODUCTION

Given their ability to prevent infectious diseases and save millions of lives, antibiotics are among the most significant discoveries of the 20th century. Since the use and abuse of antibiotics has increased over time, microbes have developed acquired antimicrobial resistance (AMR) to numerous medications as a result of strong selection pressure. Both inside and outside of healthcare facilities, human-to-human contact is the main method by which antimicrobial resistance (AMR) is acquired and transmitted. Veterinarians and agricultural workers are included in the group representing animal health, and ecologists and wildlife experts are represented in the group representing environmental issues. For thousands of years, people have used natural products to treat various illnesses and ailments. They have been included into traditional oils, potions, cures, and medications. In addition, they have been employed in the preparation of food and drinks. Natural goods include, among others, aspirin, penicillin, amrubicin hydrochloride, and a natural ether. In particular, natural products have been crucial in the search for new drugs to treat infectious and cancerous disorders. Additionally, they have contributed to various therapeutic domains such as multiple sclerosis and cardiovascular illnesses. The study of natural materials utilized in drug discovery, including microorganisms, plants, and animals, is known as pharmacognosy. The study of drugs, drug compounds, or potential drugs' physical, chemical, biological, and biochemical characteristics is part of it. Identifying natural drug sources, determining morphological characteristics, planning the cultivation of medicinal plants, assessing crude natural drugs for quality control, and assessing the pharmacology of crude extracts and active constituents are just a few of the many tasks that fall under the umbrella of pharmacognosy. Botany and plant chemistry, which both have their roots in older scientific investigations on medicinal plants, are strongly associated with pharmacognosy. Drug prototypes and new drug development can benefit from pharmacognosy. Additionally, it can support the efficacy and safety of dietary supplements and nutraceuticals—products made with natural substances including vitamins, minerals, and herbs.

II. DIVERSITY OF NATURAL PRODUCTS WITH ANTIMICROBIAL ACTIVITY:

Anything created by life is considered a natural product in the broadest sense. Examples of such materials are biotic (such as wood, silk), bio-based (such as bioplastics, cornstarch), bodily fluids (such as milk, plant exudates), and other natural materials (such as dirt, coal).Natural products can be categorized based on their source, biological function, or metabolic process. There are between 300,000 and 400,000 recognized natural product molecules, depending on the sources.Alkaloids are abundant in nature as natural compounds. Owing to the gravity of drug resistance in bacteria, alkaloids' antibacterial effect has drawn a lot of attention lately. The bacteriostatic effects of pyridine alkaloids, indole alkaloids, steroidal alkaloids, and other alkaloids are the subject of this study. Of these, isoquinoline alkaloids and indole alkaloids are the principal classes of substances with antibacterial activity.

1. Alkaloids

Alkaloids are heterocyclic nitrogen molecules with extremely varied chemical structures that have antibacterial, analgesic, and spasmodic properties. Specifically, numerous research studies have demonstrated that these substances frequently have a notable impact on the management of various infections. While quinine, an alkaloid, is well-known for its antiprotozoal activity against the malarial parasite, indoquinoline alkaloids have been shown to exhibit activity against yeast and Gram-negative bacteria. The majority of alkaloids work by inhibiting EP. The isoquinoline alkaloid berberine is an efficient DNA intercalator that is active in a variety of microorganisms and targets RNA polymerase, gyrase, and topoisomerase IV as well as nucleic acid. It accumulates in cells driven by the membrane potential. As a result, berberine increases the permeability of bacterial membranes, disrupting the structure of the membrane.

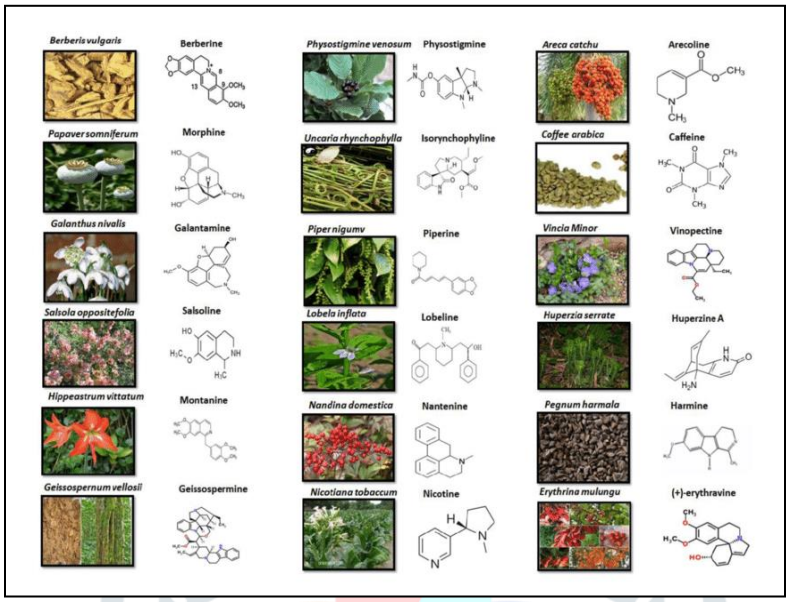

Fig 1 Alkaloids- Secondary Metabolite & their Sources

2. Flavonoids :

Many plants, fruits, vegetables, and leaves contain phytochemicals called flavonoids, which may have uses in medical chemistry. Many health advantages are associated with flavonoids, such as their antiviral, anticancer, and antioxidant qualities. Plants, fruits, and seeds contain large amounts of flavonoids, which are secondary metabolites that give them their distinctive color, flavor, and scent. Flavonoids have a wide range of roles in plants, including controlling cell division, drawing pollinating insects, and providing defense against biotic and abiotic stressors.

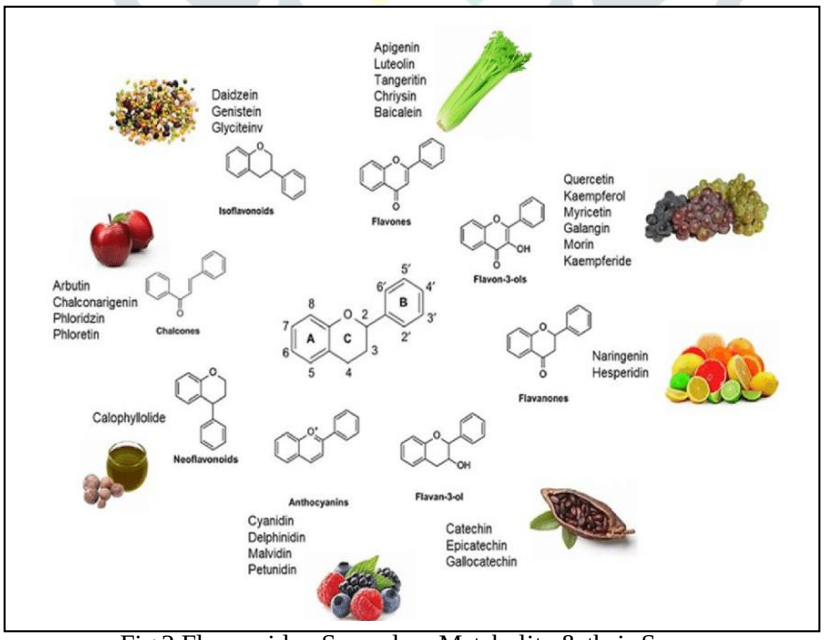

Fig 2 Flavonoids - Secondary Metabolite & their Sources

3. Essential oils:

Concentrated plant extracts are called essential oils. These are fragrant compounds that plants employ to draw pollinators and defend themselves against invaders and pests.

Essential oils are used in many products, including:

- Perfumes
- Cosmetics
- Soaps
- Air fresheners

- Food and drink flavoring
- Incense and household cleaning products

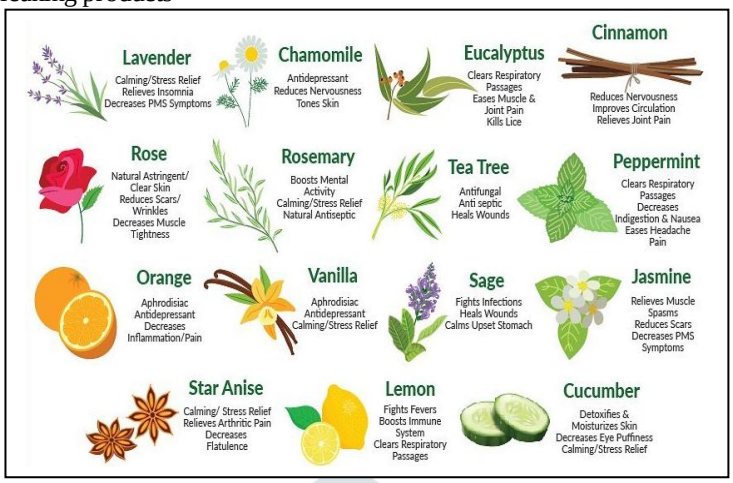

Fig 3 Essential Oils & their Sources

Additionally, essential oils are employed in aromatherapy, an alternative medicine that links the antimicrobial, antiviral, antifungal, and antibacterial properties of aromatic molecules to health benefits. Numerous studies have examined the antibacterial properties of various plant extracts. Numerous plants have been shown to treat gastrointestinal issues, respiratory conditions, skin infections, and urinary tract infections. It has been possible to isolate cytotoxic chemicals from the Vismia species. There have also been prior reports of the essential oil's antibacterial properties and the use of refined eugenol from Ocimum gratissimum to treat conjunctivitis, pneumonia, and diarrhea. The World Health Organization states that the greatest source for a wide range of medications is medicinal plants. These data help to both validate and quantify the significance of natural product screening.

III. Mechanism of Antimicrobial Action:

In both industrialized and developing nations, bacterial infections are thought to be one of the major causes of human sickness. Over time, pathogens change and develop resistance to previously identified antibiotics. 700,000 of the two million persons that contract different types of bacteria every year throughout the world pass away as a result of bacterial resistance.For example, in Europe and the United States, methicillin-resistant Staphylococcus aureus is responsible for 50,000 deaths every year. Around 480,000 persons in developing nations contracted antibiotic-resistant Mycobacterium TB at the same time in 2013.

Bacterial resistance to conventional antimicrobial treatments is explained by a number of processes, and around 20,000 resistant genes have been found in bacteria. The first known cases of antibiotic resistance were linked to the E. coli, Shigella, and Salmonella bacteria in the 1950s. It took two decades to identify this growing issue, though, as multiple examples of penicillin, tetracycline, and chloramphenicol resistance were documented in the 1970s. Seldom were the suggested mechanisms of bacterial resistance put to the test in a clinical setting. It's unclear if every microbe has a unique mechanism or if multiple bacteria use a similar process to develop resistance.

IV. Mechanism of Bacterial Resistance against Antimicrobial Agents

Bacteria can develop resistance to drugs by a single mechanism or by combining many mechanisms. In order to determine a potential target for future effective medication, it is imperative to comprehend the mechanisms underlying resistance. The details of each of the aforementioned mechanisms will be covered in more detail below.

1. Efflux Pump

The antibiotic must penetrate the bacterial cell at a sufficient concentration and remain there for a significant amount of time in order to produce antibacterial activity. Through the efflux pump mechanism, many MDR bacteria resist antibiotics. Located in the cytoplasmic membrane, efflux pumps are proteinaceous transporters that control the internal environment of bacteria. Together with antibiotics, they help bacteria eliminate toxins. For the first time, the efflux pump was found to be the root cause of tetracycline-resistant E. coli. But it was recently thought to be a significant contributor to resistance.

2. Alteration of Membrane Permeability

A characteristic of gram-negative bacteria is their outer membrane (OM), which serves as an extra barrier against pathogenic substances. The proteins called porins are found in the outer membrane of bacteria, and they have the ability to create pores filled with water that regulate the flow of various substances and nutrients across the membrane. They are among the potential targets that antibacterial agents may have. It was discovered that E. coli had porins. They can be divided into particular and nonspecific categories according to their activities. Porins that selectively absorb maltose, maltodextrin, and Fep A specific for iron complexes are more selective for certain chemicals, such Lam B. Conversely, nonspecific or general porins are connected to bacterial resistance to antimicrobial drugs and have a role in membrane permeability.

3. Destruction of Antibiotics

Enzymes linked to the creation of bacterial cell walls, nucleic acids, and metabolites are collectively referred to as bacterial enzymes. As part of their mechanism, certain antimicrobial drugs target these enzymes directly. Therefore, structural alterations or modification of the antibiotic-affected structural elements such as methyltransferases' alteration of ribosomes—may enable bacteria to withstand antibiotics.

4. Alteration of the Binding Site

By altering their target site in a way that reduces the antimicrobial agent's binding affinity, bacteria can become resistant to antibiotics. Methylation of the target site, a peptidyl transferase enzyme, significantly reduces the binding interaction between erythromycin and other drugs. Moreover, Staphylococci developed resistance to oxacillin and methicillin due to mutations in penicillin-binding proteins (PBPs). In order to counteract the effects of antibiotics, vancomycin-resistant enterococci (VRE) convert the targeted enzyme's amide linkage into an ester linkage, which reduces the antibiotic's binding affinity by a factor of 1000.

Application in Pharmacognosy:

1. There isn't a concern with drug resistance to other medications, multidrug resistance (MDR), or antibiotic resistance.
2. A wider range of activities.
3. Less adverse effects when taken as directed.
4. Widely accessible in the natural world.
5. Less costly or inexpensive but still efficient.
6. Using these medications for self-medication is a typical practice.
7. Human testing on a number of natural antimicrobials has already produced encouraging results.

High-quality herbal medicinal products are made by starting with pure, fully authenticated raw ingredients that are rich in bioactive components. Since many external factors might affect these qualities, it is crucial for success to apply best practices and optimized processes during the growth/cultivation, harvest/collection, and postharvest processing stages.

V. THE ROLE OF NATURAL PRODUCTS IN MODERN DRUG DISCOVERY.

Natural goods, mostly derived from plants, minerals, animals, etc., are frequently utilized to cure a wide range of illnesses. Records exist that demonstrate how these compounds were used medicinally by people thousands of years before to the birth of Christ. For many centuries, the primary sources of medicines were medicinal plants and microbes. There are numerous instances of plant-derived extracts and/or chemicals that have been extracted from plants and are currently being employed extensively in the treatment of numerous serious illnesses. Marijuana (Cannabis sativa) and poppies (Papaver somnniferum), to mention only two, have been utilized for up to 4,000 years.

Standardization and quality control:

For herbal products to be safe, effective, and repeatable, their quality and standardization must be maintained (Rahath Kubra et al., 2016). Strict quality control procedures are necessary to safeguard customers' health and safety (Deutch et al., 2019). Potential dangers like adulteration, contamination, and the inclusion of dangerous ingredients can be reduced by putting strict testing and quality assurance procedures in place, guaranteeing that the herbal medicine products are safe to consume.

Challenges and future perspective:

The literature has a large number of studies on the systemic delivery of antimicrobial medications. On the other hand, site-specific medication delivery, undesirable side effects, and even possible toxicity present numerous difficulties. Investigating novel strategies for the delivery of active ingredients with antibacterial qualities is required to address them. As a result, the main focus of this issue will be on novel antimicrobial application delivery systems, with a particular emphasis on topical and targeted distribution. Applications for antimicrobials include the healing of wounds, the treatment of respiratory, ear, skin, and urinary tract infections, as well as the prevention and management of periodontal diseases and tooth decay. Antimicrobial principles can be released through a variety of systems, including gels, hydrogels, emulsions, and micro- and nanoparticles (capsules, liposomes, spheres).

Since the oral route is the least invasive delivery method and complies with cost-containment rules in most industrialized nations, it is often accepted as the preferred mode of administration for patients. This encourages the shift of cancer treatment away from hospital-based settings. When taken orally, medications may be intended to act locally or systemically within the gastrointestinal tract. Drugs intended to have a systemic effect are anticipated to enter the bloodstream after oral administration by passing through the intestinal or stomach lining epithelium, and depending on their enzymatic stability, they will subsequently undergo first-pass metabolism by the liver. Although novel drug-delivery strategies are being explored to extend this delivery route to larger molecules, such as peptides and proteins, the oral route has historically been mostly utilized to transport tiny molecules with a molecular weight of less than 500 g/mol. The solubility and stability of small molecules in intestinal medium, as well as their permeability across the intestinal membrane, are the three primary factors that determine their bioavailability following oral administration. Based on the solubility and permeability of the medications, four groups of drugs are identified by the Biopharmaceutical Classification System. According to estimates, 90% of molecules' oral distribution was hampered by their Insoluble nature in intestinal fluid. Four main issues are linked to poor oral medication bioavailability and are enumerated restricted drug absorption and enzymatic drug breakdown (e.g., big molecules) in the GI tract; low drug solubility; poor permeability; poor stability; the requirement for tailored therapy administration to specific GI tract regions where cancer is localized. The creation of formulations that can improve drug permeability and solubility, the application of creative nanocarriers to facilitate better intestinal epithelial crossing, and the creation of site-specific delivery systems are the primary approaches devised to solve those difficulties.

VI. CONCLUSION:

A fresh hope for addressing the grave risks posed by mounting evidence of antibiotic resistance is medicinal plant antibacterial activity. Consequently, the identification and isolation of novel bioactive chemicals from medicinal plants—which have not yet received enough research—is urgently needed. These substances' great diversity has demonstrated their therapeutic potential as antimicrobials and as modulators of antimicrobial resistance.It is difficult to utilize novel bioactive chemicals to their full potential. It is crucial to stress that in order to ensure the selection of potent and safe antibacterial plant-derived compounds, comprehensive in vitro and in vivo testing must be carried out. Exploiting the possible antagonistic or synergistic effects of chemicals within and amongst medicinal plant extracts is another significant problem. It is clear that as biotechnology develops, we will be able to delve deeper into the chemical makeup of therapeutic plants and create increasingly complex methods for the extraction, fractionation, and identification of bioactive compounds—which are distinguished by a variety of chemical structures and modes of action.

Standardizing extraction and in vitro testing procedures would be helpful in order to make the search process more methodical and make it easier to comprehend the results. Furthermore, reference models have not yet been utilized in the investigation of pl ant extract mixtures; subsequent research will ascertain their suitability for this methodology. Priority should be given to research on the extracts' methods of action, interactions with antibiotics and other therapeutic plants or chemicals, and pharmacokinetic and pharmacodynamic profiles.It is anticipated that this review and the primary difficulties found In this sector would be beneficial in the use of more effective, successful, and simple techniques to enable the employment of novel therapeutic medicinal plants against microorganisms more rapidly.

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