Eurasian Journal of Analytical Chemistry
ISSN: 1306-3057 OPEN ACCESS 2024 19 (1): 408-414

A Review on Exploring the Synthetic Derivatives of Herbal Active Constituents Used in Anti-microbial Activity.

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Abstract: -
Herbal plants produce many varieties of phytochemicals, many of which humans have utilized for their therapeutic benefits. Since the development of powerful and efficient synthetic antimicrobial agents, microbial infections can now be prevented and treated using them, Several naturally occurring chemicals produced from bacteria, plants, animals, marine species, and other sources are now being studied for antimicrobial characteristics, This review focuses on synthetic derivatives of herbal active constituents and their potential to enhance antimicrobial activity. The increasing incidence of drug-resistant pathogens raises an urgent need to identify and isolate new bioactive compounds from medicinal plants using standardized modern synthetic procedures, These natural antimicrobial chemical compounds extracted from different sources have been demonstrated to be effective against a variety of diseases. Overall, the synthesis of herbal derivatives represents a valuable strategy for advancing antimicrobial therapies and addressing the urgent need for effective treatments against resistant pathogens.

Keywords: Medicinal plants; bioactive compounds; antimicrobial activity.

Introduction: -

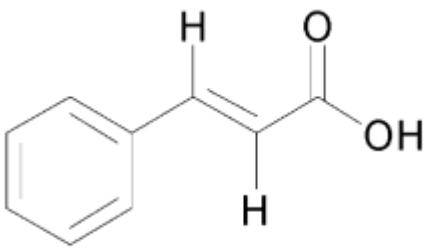
At the beginning of human civilization, people have employed the beneficial characteristics of the various phytochemicals that plants generate. (1) Synthetic derivatives of active constituents from herbal plants are often developed to enhance their antimicrobial activity or to overcome the limitations of natural compounds. These derivatives can include modified versions of compounds like alkaloids, flavonoids, terpenoids, and others. Herbal plants have long been a source of medicinal compounds with antimicrobial properties, but their natural forms often come with limitations such as low potency, poor solubility, or undesirable side effects. (3) By chemically modifying these compounds, researchers aim to create derivatives with enhanced antimicrobial activity, improved stability, and better pharmacokinetic properties. (4) However, their clinical application can be limited by factors like inadequate bioavailability, rapid metabolism, or adverse effects. Synthetic derivatives are designed to address these issues by optimising the chemical structure of the original compound. (5) Modification of active chemical constituents using synthetic mechanisms has a better effect on various diseases.

Involved Herbal Plants and their Synthetic Derivatives: -

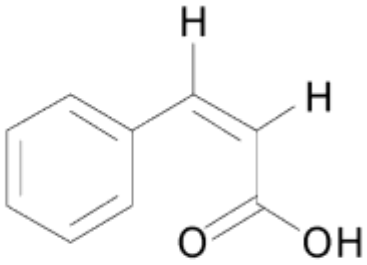
Sr.no.	Herbal plants	Synthetic Derivatives of Active chemical constituents
1.	Cinnamon	I. Cinnamic acid II. Cinnamaldehyde
2.	Clove	I. Eugenol
3.	Lemon	I. Benzothiazole II. Benzoxazole
4.	Black pepper	I. Piperine
5.	Onion	I. Allicin II. Quercetin
6.	Turmeric	I. Curcumin
7.	Barberry	I. Berberine
8.	Henna	I. Gallic acid

1) Cinnamon: Cinnamon has synthetic derivatives like Cinnamic acid and Cinnamaldehyde.

I. Cinnamic Acid (fig.1): - A class of aromatic carboxylic acids (C6-C3) found naturally in the family of plants are called Cinnamic acids. They are created by the same chemical reaction that produces lignin, a polymeric substance that gives plant cell walls mechanical strength. [5], The majority of Gram-positive and Gram-negative bacterial species were weakly inhibited by cinnamic acid (6).



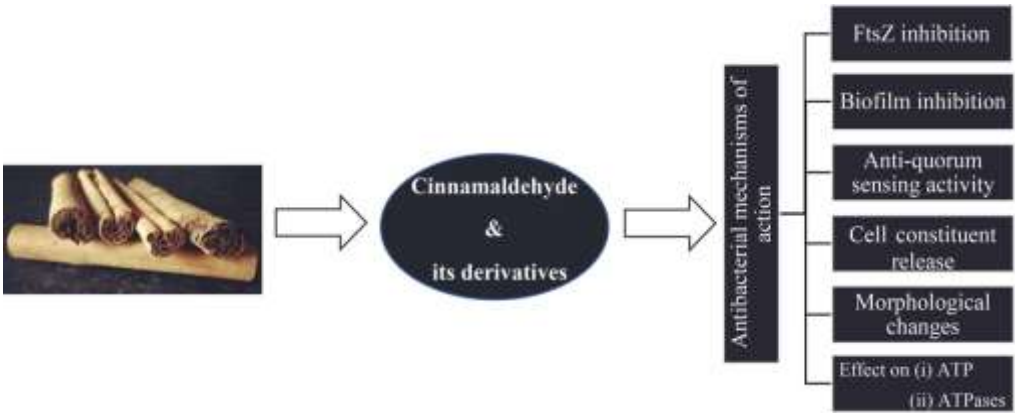
Trans –Cinnamic acid



Cis-Cinnamic acid

Fig.1 Cinnamic acid

II. Cinnamaldehyde: - There has been a revival of interest in the development of natural antibacterial agents, and trans-cinnamaldehyde is one naturally occurring compound that has drawn a lot of attention recently. Several species of Cinnamomum contain significant amounts of (E)-cinnamaldehyde in their bark (7). It has been found that trans-cinnamaldehyde exhibits strong antibacterial activity (8)



2) Clove: - clove has a synthetic derivative like Eugenol.

I. Eugenol: - The aromatic phenolic component eugenol gives the clove plant its antibacterial properties. After eugenol (fig.2) was extracted from cloves through stem distillation(11), it was evaluated for antimicrobial activity against Staphylococcus aureus. Of the three compounds examined, oxide-eugenol was the most potent antimicrobial agents.

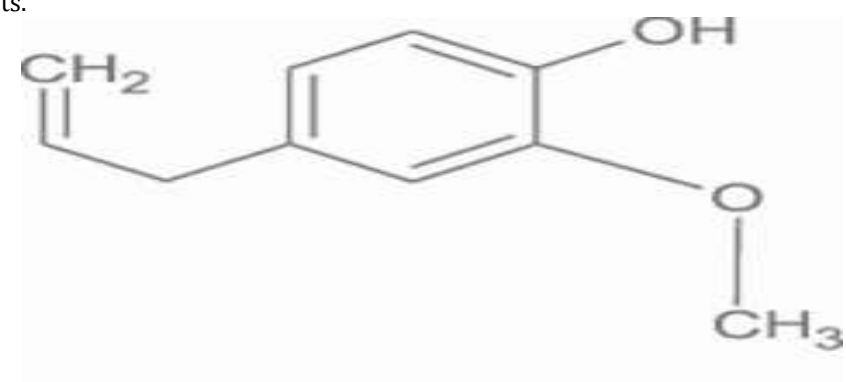


Fig.2 Eugenol

2) Lemon: - Utilizing lemon juice as a natural and environmentally friendly catalyst, 2-aminothiophenol or 2-aminophenol has been reacted with a range of aryl aldehydes to produce benzothiazole and benzoxazole derivatives in good - excellent yields. (12)

I. Benzothiazole: - A Schiff series of benzothiazoles is an effective antimicrobial agent. The foundation for benzothiazole derivatives was created. The generated compounds were clarified using spectrum data and elemental analysis. Every synthetic molecule received testing to determine its antimicrobial activity. (13,14)

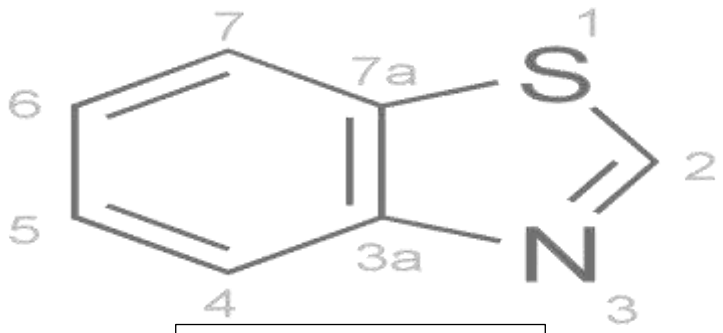


Fig.3 Benzothaizole

II. Benzoxazole (fig.4) :- calcimycin, cezomycin, routeennocin, and other naturally occurring molecules with antimicrobial action were the first synthetic substances with benzoxazole that indicated potential antimicrobial activity. (15,16)

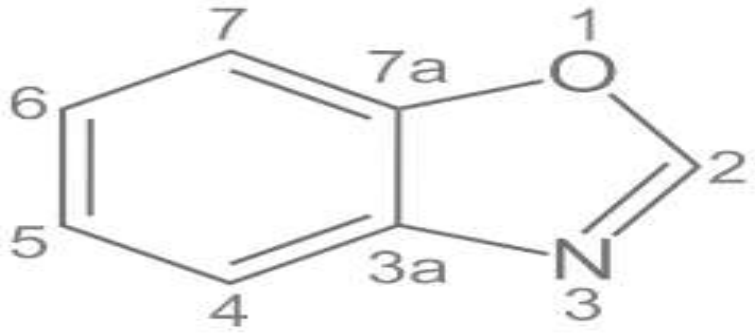


Fig.4 benzoxazole

3) Black pepper:- the primary toxic ingredient in pepper Peppercorns' main alkaloid, **piperine**, is responsible for the distinctive scent and spicy flavor of black pepper.(18)(19)

I. Piperine:- An alkaloid amide derived from pepper, is the cause of its biological activity, Piperine derivatives show influential antimicrobial properties in different mediums. (20), the major components and essential oils of black pepper showed good antimicrobial activity for Escherichia coli and Staphylococcus aureus [22,23].

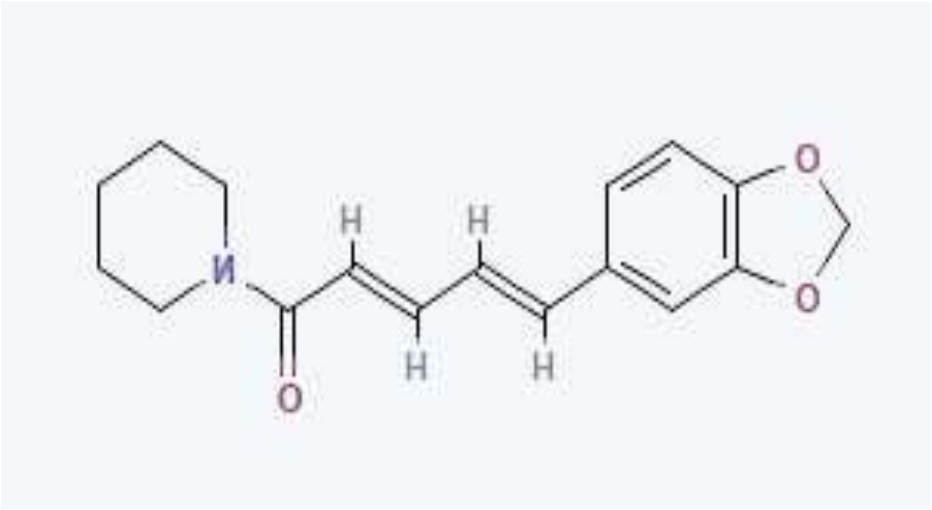


Fig.5. Piperine

4) Onion:- Allicin, quercetin, fisetin, and other substances are abundant in onions (24), and they also contain a variety of phytochemicals, such as polysaccharides, phenolic compounds, organosulfur compounds, and saponins.. (25)

I. Allicin:- Allicin shows broad antimicrobial activity in the low micromolar range, target both Gram-positive and Gram-negative bacteria, including strains resistant to antimicrobial agents, as well as fungi. Allicin can inactivate vital enzymes by its reaction with thiol groups. (26)

Fig.6. Allicin

II. Quercetin:- Quercetin (fig 7) was an antibiotic with a broad spectrum that not only suppresses bacteria well but also exhibits an effective inhibitory effect on fungi, based on studies. (27)

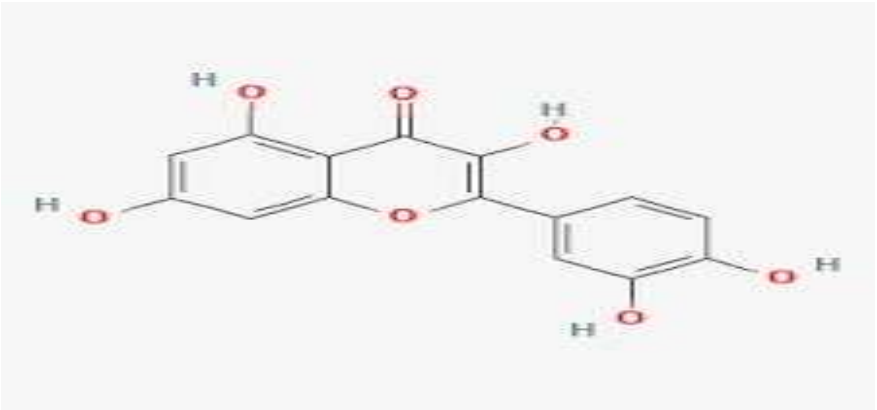


Fig.6. Quercetin

5) Turmeric:- Three to six percent of turmeric is made up of polyphenolic substances
called curcuminoids, which are a combination of curcumin, demethoxycurcumin, and bisdemethoxycurcumin. Curcuminoids are important substances that have a variety of biologicaeffects. (28)

I. Curcumin: - Many in vitro studies show that curcumin has antimicrobial properties towards both Gram-positive and Gram-negative bacteria [29, 30]. Curcumin's antimicrobial effects are caused by a multitude of atomic routes. (31)

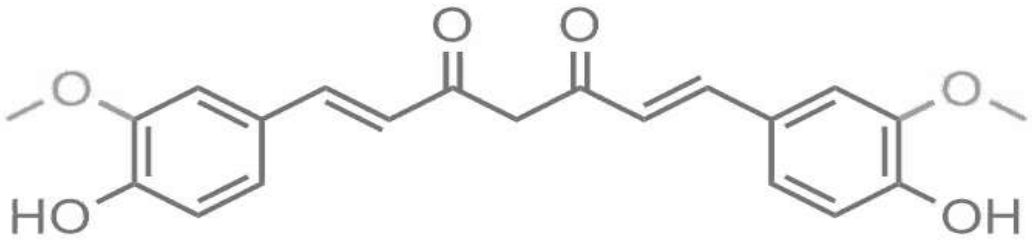


Fig.7. Curcumin

6) Barberry: - The plant's chemical composition suggests that isoquinoline alkaloids including palmatine, berberine, and berbamine, are its most significant constituents. Among the protoberberine alkaloids found naturally, berberine is one of the most studied. (32,33)

I. Berberine: - These plants berberine extract showed strong antibacterial action against fungal viruses, bacteria, protozoa, and yeasts [34, 35, 36]. Both in vivo and in vitro, berberine exhibits minimal toxicity and mutagenicity to human cells.. (37,38)

8) Henna: - Extracts from henna leaves exhibit antimicrobial activity against the microorganisms that cause common skin diseases (41), In addition to gallic acid, mucilage, and trace amounts of alkaloids, henna leaves are rich in lawsone (43,44), a pigment molecule, and naphthoquinone compounds. Alcoholic and oily henna extracts show the actions of the antibiotics frequently used in clinical practice. (45)

I. Gallic acid(fig.8): -A certain type of phenolic acid has been shown to have antimicrobial properties against a range of bacteria (46,47), including Pseudomonas strains. It also increases the potency of other antimicrobial medications (48). It has two functional groups in the gallic acid molecule: hydroxyl groups and carboxylic acid groups (49,50).

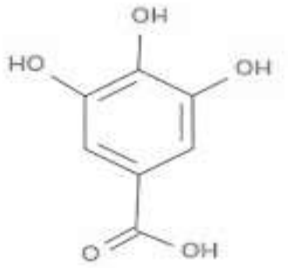


Fig.8. Gallic acid

Conclusion: -

The exploration of synthetic derivatives of herbal active constituents presents a promising avenue in the development of new antimicrobial agents. Herbal compounds, with their diverse chemical structures and biological activities, offer a valuable foundation for designing novel derivatives with enhanced potency, stability, and selectivity against resistant microbial strains. The review highlights that while natural products have been effective in traditional medicine, the synthetic modification of these molecules can address limitations such as poor bioavailability, low solubility, and rapid degradation, thereby increasing their clinical potential. The successful synthesis and evaluation of these derivatives in various studies underscore their potential as a new class of antimicrobial agents. However, further research is necessary to optimize these derivatives, assess their safety profiles, and conduct rigorous clinical trials to fully establish their therapeutic efficacy. The continued integration of natural product chemistry with synthetic approaches holds great promise for overcoming current challenges in antimicrobial resistance and contributing to the development of more effective and sustainable antimicrobial therapies.

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