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BIOEFFICACY AND SYNERGISTIC ACTIVITY OF MEDICINAL PLANTS AGAINST SELECTED MICROORGANISMS- A REVIEW

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Abstract* :** Use of medicinal plants with anti-microbial characteristics seems sensible and can be used as alternative approach to combat with microbial resistance to antibiotics and the prevalence of adverse effects. The present study- was designed to evaluate the phytochemicals of ***Tinospora cordifolia **(Giloy),** ***Glycorrhiza glabra*** **(Mulethi),** ***Cinnamomum verum*** **(Cinnamon),** ***Zingiber officinale*** (**Ginger**) extracts and their antibacterial potency against laboratory ***Salmonella paratyphi A, Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa***. The qualitative analysis is very essential to identify the phytochemical constituent present in plants. The medicinal value of plants is due to the presence of particular bioactive constituents which can be easily accessed by standard methods. Nowadays, researchers are in search of some novel antimicrobial molecules which have a broad spectrum of activity against both Gram-negative and Gram-positive bacteria without having many or any side effects. Agar Well diffusion method is used to test antimicrobial activity of all plant extract prepared in different solvents methanol, ethanol, chloroform, and distilled water against pathogenic bacteria.Apart from these, each plant extract was mixed in equal proportion and same procedure was followed to study their synergistic effect.To overcome such problems, synergistic approach can be applied to reduce the dose of antibiotics and to enhance the effectiveness within the combination of different plant extracts. Different nanoparticles will be synthesized via biological to study their synergistic effects with the combination of different plant extract and antibiotics. This review is emphasis on bio-efficacy of selected plants which works as strong pillar to the upcoming researches.

Key words: Phytochemical; Synergistic effect; Antibiotic; Antibacterial, Plant extract

1. Introduction:

Use of medicinal plants with anti-microbial characteristics seems sensible and can be used as alternative approach to combat with microbial resistance to antibiotics and the prevalence of adverse effects. The present study- was designed to evaluate the phytochemicals of ***Tinospora cordifolia*** **(Giloy),** ***Glycorrhiza glabra*** **(Mulethi),** ***Cinnamomum verum*** **(Cinnamon),** ***Zingiber officinale*** (**Ginger**) extracts and their antibacterial potency against laboratory microorganisms. The classification of selected plants is given below:-

Tinospora cordifolia
Kingdom- Plantae
Class- Magnoliopsida,
Order- Ranunculales,
Family- Menispermaceae,
Genus- Tinospora
Glycyrrhiza glabra
Kingdom- Plantae
Division- Magnoliophyta

Class- Magnoliopsida
Order-Fabels
Family- Leguminosae
Genus-Glycyrrhiza

Cinnamomum verum
Kingdom-Plantae
Division- Magnoliophyta
Class- Magnoliopsida
Order- Laurales
Family- Lauraceae
Genus-Cinnamomum

Zingiber officinale
Kingdom-Plantae
Division- Magnoliophyta
Class- Magnoliopsida
Order- Zingiberales
Family-Zingiberaceae
Genus- Zingiber

Ayurvedic science of medicine is based on the principle that prevention is better than cure. Ayurveda is an ancient science that has many remedies based on naturally occurring substances. These Ayurvedic supplements are concocted using herbs, natural extracts, and a variety of plants that have positive effects in treating various disorders. This use of naturally occurring elements gives Ayurveda an edge as holistic healing system.The concepts of universal interconnectedness, the body's constitution (prakriti), and life forces (doshas) are the primary basis of Ayurvedic medicine. Goals of treatment aid theperson by eliminating impurities, reducing symptoms, increasing resistance to disease, reducing worry, and increasing harmony in life.World Health Organization (WHO) estimated that 80 percent of people worldwide rely on herbal medicines for some aspect of their primary health care needs. According to WHO, around 21,000 plant species have the potential for being used as medicinal plants.

1.1 Medicinal plants: Properties and Applications

Several plant extracts from different plant parts have been broadly investigated through many experiments to understand their capacity in balancing microbial medication tolerance and these reference studies will give promising direction to forthcoming experimental studies on the inversion of antimicrobial resistance.Antibiotics were considered a magic bullet that selectively targeted microbes that were responsible for disease causation, but at the same time would not affect the host. Fleming was the first who cautioned about the potential resistance to penicillin if used too little or for a too short period of treatment. To overcome such problems, synergistic approach can be applied to reduce the dose of antibiotics and to enhance the effectiveness within the combination of different plant extracts (**Upadhyay *et al*., 2022**).

The quantitative analysis is very essential to identify the phytochemical constituent present in plants. The medicinal value of plants is due to the presence of particular bioactive constituents which can be easily assessed by standard methods include Saponin, Alkaloids, Phenolic Compounds, Tannin, Glycoside, Coumarins, Phytosterols (Salkowski's test). Quantitative analysis of phytochemicals methods includesTotal Phenolic Content, Total Flavonoid Content,Total Alkaloid Content, Total Protein, Free Amino Acid, Total Carbohydrate **(Tiwari *et al*., 2016).**

Agar Well diffusion method is used to test antimicrobial activity of all plant extract prepared in different solvents like methanol, ethanol, chloroform and distilled water against pathogenic bacteria.

In synergistic effect, two or more drugs/plant extracts/antibiotics that individually produce overtly similar effects will sometimes display greatly enhanced effects when given in combination. When the combined effect is greater than that predicted by their individual potencies, the combination is said to be synergistic**.** Recently, plant antimicrobials have been found to be synergistic enhancers in that though they may not have any antimicrobial properties alone, but when they are taken concurrently with standard drugs they enhance the effect of that drug (**Hübsch *et al*., 2014).**

The exogenous antioxidants are mainly derived from food and medicinal plants, such as fruits, vegetables, cereals, mushrooms, beverages, flowers, spices and traditional medicinal herbs (**Zhang *et al.*, 2016**). Normally, antioxidant system occurring in human body can scavenge these radicals, which would keep the balance between oxidation and anti-oxidation. The increment of intake of exogenous antioxidants from different sources like medicinal plants would ameliorate the damage caused by oxidative stress through inhibiting the initiation or propagation of oxidative chain reaction, acting as free radical scavengers, quenchers of singlet oxygen and reducing agents (**Li *et al*., 2015; Xu *et al*., 2017**).

2. Review of the literature

2.1 Phytochemical Profiling and Antimicrobial Study of Plant Extract

Juariah *et al.*, 2023 assessed the antibacterial activity and inhibition mechanism of red ginger extract as an inhibitor of pathogenic bacterial infection. Red ginger ethanol extract can inhibit the growth of *Salmonela thypi*, *Staphylococcus epidermidis*, and *Streptococcus mutans* at a concentration of 500µg/mL, while *Pseudomonas aeruginosa* at a concentration of 250 µg/mL. Further observation of bacterial cell leakage showed that the higher the red ginger ethanol extracts concentration, the higher the bacterial cell leakage. Based on SEM results, the quantity of *S. thypi*, *S. epidermidis*, and *S. mutans* after treatment with red ginger ethanol extract decreased and the cell wall became wrinkled and destroyed.

Al Mousawi *et al.*, 2022 collected plant samples from Babylon governorate, Iraq. Various extracts and chemical compounds were obtained and the antimicrobial effects of *G. glabra* was assessed against *Staphylococcus aureus*, *Escherishia coli*, *Pseudomonas aeruginosa* and *Candida albicans* using agar well diffusion method and concentration range of 500-3000mg/mL. All tested isolates were sensitive to both extracts at concentration of 3000 mg/ml. *S. aureus* and *E. coli* showed higher sensitivity; maximum effective inhibition for *G. glabra* aqueous extract was found against *S.aureus*, whereby the minimum inhibition was recorded against *P. aeruginosa*. Regarding *G. glabra* alcoholic extracts, the highest effect was noticed against *P. aeruginosa*, while the lowest effect was noticed on *C.albicans*.

Yousfi *et al.*, 2021 determined the antimicrobial potential of ginger root extracts against *Escherichia coli*, *Pseudomonas aeruginosa, Staphylococcus aureus, Enterobacter aerogenes and Klebsiella pneumonia*. Antimicrobial activity of ginger root extracts at various concentrations revealed that *E. coli* had the lowest concentration (1.2 mg/ml) in 20 mg/ml while the highest concentration (9.1 mg/ml) was observed for *S. aureus* in 75 mg/ml. Phytochemical screening of the ginger root extracts revealed the presence of all the tested secondary metabolites (saponins, tannin, flavonoids, glycoside, terpenoids and alkaloids).

Agarwal *et al.*, 2019 assessed the antimicrobial activity of different concentrations of commercially available *T. Cordifolia* powder ethanolic extract against *Streptococcus mutans*. The maximum antibacterial activity of *T. cordifolia* was observed with a volume of 40µl at 2% concentration with a zone of inhibition of 19 mm. A 30µl volume of 0.2% chlorhexidine showed a zone of inhibition of 28 mm, and no zone of inhibition was observed with dimethylformamide.

2.2 Synergistic effect

Cava-Roda *et al.*, 2021 investigated effects of vanillin, clove and cinnamon bark extracts individually and in combination against *Listeria monocytogenes* and *Escherichia coli* O157:H7. Vanillin exhibited the lowest antimicrobial activity (MIC of 3002 ppm against *L. monocytogenes* and 2795 ppm against *E. coli* O157:H7), while clove and cinnamon bark EOs exhibited the highest antimicrobial activity (402–404 against *L. monocytogenes* and 778–721 against *E. coli* O157:H7). The combination of the EOs of cinnamon bark/clove and cinnamon bark/cinnamon leaves showed additive effect against *L. monocytogenes* but indifferent effect against *E. coli* O157:H7. For *L. monocytogenes*, the best inhibitory effects were achieved by cinnamon bark EO (85 ppm)/vanillin (910 ppm) and clove EO (121 ppm)/vanillin (691 ppm) combinations. For *E. coli*, the inhibitory effects of clove EO (104 ppm)/vanillin (1006 ppm) and cinnamon leaves EO (118 ppm)/vanillin (979 ppm) combinations were noteworthy.

Rezvani *et al.*, 2017 investigated the effect of Iranian honey, cinnamon and their combination against *Streptococcus mutans* bacteria. Nine experimental solutions were examined in this study, including two types of honey (pasteurized and sterilized), two types of cinnamon extract(dissolved in distilled water or dimethyl sulfoxide) and five different mixtures of cinnamon in honey (prepared by admixing 1%–5% w/w of cinnamon extract into 99%–95% w/w of honey, respectively). Meanwhile, each of mentioned agents was considered as the first solution while it was diluted into seven serially two-fold dilutions (from 1:2 to 1:128 v/v). The highest zone of inhibition was recorded for the mixtures of honey and cinnamon while all the subgroups containing 95%–99% v/v of honey were in the same range ($P < 0.01$). The MIC for both honey solutions were obtained as 500 mg/mL whereas it was 50 mg/mL for both cinnamon solutions. Moreover, the MIC related to all honey/cinnamon mixtures were 200 mg/ml.

2.3 Antioxidant study

Kim *et al.*, 2021 evaluate the antioxidant properties of *Glycyrrhiza uralensis* DGC, DGD, and IsoA via FRAP assay. The highest FRAP values were obtained for DGC (1,169 ± 43 μM) and DGD (1,135 ± 16 μM) at a concentration of 1 mM, followed by IsoA (337 ± 46 μM). In the FRAP assay, DGC dose-dependently exhibited strong antioxidant activity and a similar level of activity was observed for DGD. IsoA also exhibited increased FRAP at a concentration between 0.2-1 mM, showing 3-5 fold weaker activity compared to that of DGC or DGD. Therefore, the reducing power of IsoA was the lowest among the compounds tested**.** DGC possesses the most potent antioxidant activity, suggesting it has protective effects against chronic diseases caused by reactive oxygen species as well as potential as an antioxidant food additive.

Shahid *et al.*, 2018 investigated the antioxidant potential of cinnamon extract. The resultant extract was analyzed for its antioxidant activity through total phenolic content (TPC), free radical scavenging activity (DPPH assay) and total antioxidant activity was measured by ferric reducing antioxidant power (FRAP) test. Researchers concluded the ferric reducing antioxidant power (FRAP) values of cinnamon extract were as 355.01 ± 8.34 gallic acid equivalent per gram (mg GAE/g), 90.18 ± 2.12 (%) and 132.82 ± 3.12 (μmol/g), respectively.

3. Conclusion

We concluded that as the concentration of plant extract increases, the zone of inhibition was also found to be increased. Synergistic effect was also revels the potency of plant extract which can be used to lower down the antibiotic dosage and can get rid of the side effects of antibiotics. As per the synergistic studies, results reveals the increased antibacterial efficiency when potential plant extract and potential antibiotic was combined in 1:1 ratio for all the organisms except *Salmonella paratyphi A.* Such kind of studies have been proved to lower down the use of antibiotics which further reduce the side effects caused due to antibiotics and lower chances of antibiotic resistance. There is lots of evidence suggesting that medicinal plants are very effective in the treatment of infectious diseases. The plants hold great promise as a source of novel antimicrobial agents. They are readily available, cheap and also, almost; do not have any side effects. However, many studies still need to be conducted to ensure the mechanism of action and also the safety of antimicrobial phytochemicals.

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