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Review Paper

A review on effect of different plant extract against multidrug resistant bacteria

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Abstract

Multidrug resistance in bacteria is current problem for which many researches are conducted to find a solution. There are different resistance mechanisms which the bacteria's have been adopting like mutation, by passing the target, efflux pumps etc. Herbal medicine has now drawn attention of world. Use of plant extracts against the bacterial infection could possibly reduce the antibiotic resistance which is mostly prevailing at present. Aloe Vera, Ginger, Garlic etc. have shown significant antibacterial activity against the multidrug resistant bacteria. In most of the studies Disk diffusion method was seen as the most commonly used method in finding the susceptibility of the extracts followed by determining the extracts Minimum inhibitory concentration. This is a review on resistance mechanism adopted by bacteria, and plant extract which have shown significant activity against the gram negative and gram positive bacteria.

Keywords: Multidrug resistance, antibacterial activity, plant extracts.

Introduction

Multi drug resistance in the pathogenic bacteria is the extremely important issue in the present scenario that must be addressed. Drug Resistance is a condition wherein the bacteria resists the action of drug which in normal grounds used to kill the bacteria or stop the further growth of it[1]. Resistance to the antibiotics could be even because of the more antibiotics prescription by physician at the primary care centre[2]. Multi drug resistant Acinetobacter baumannii is the most commonly observed organism among the health care workers[3].

Several medicinal plants and plant extracts have screened to check for its potency of antimicrobial activity as there is increase in failure of chemotherapeutic agents[4]. Antimicrobials of plant origin have good therapeutic value. They also reduce the side effects which are usually seen with synthetic antimicrobial agents. The beneficial effects of plant extract is because of many secondary metabolites (alkaloids, steroids, flavonoids, phenol compounds, tanins etc) present[5].

There are many plants which have shown antimicrobial activity against the Multidrug resistant bacteria. According to a report by World Health Organization there is an estimation that 65-80% of the world healthcare follow traditional method of medication[6]. Multidrug resistant bacteria cause urinary tract infections; respiratory tract infection. Many multidrug resistant bacteria have also been isolated from wound infection. I would like to discuss about few plant extracts which have shown noticeable activity against multidrug resistance bacteria and methods followed in finding Antibacterial susceptibility.

Mechanism of resistance

There are different mechanisms seen in the bacteria that results in the resistance:

Mutational alteration of the target protein: Resistance mechanism through mutation makes the target protein less susceptible to the agent. Fluoroquinolone resistance is mostly due to mutations in the target enzymes, DNA topoisomerases. Resistance conferred by *erm* gene also attributes to the target modification. They produce the methylation of adenine at position 2058 of the 50S rRNA, causing resistance to macrolides (erythromycin and many others), lincosamide, and streptogramin of group B, the MLS phenotype[7].

Enzymatic inactivation of drug: It is a mechanism expressed by bacteria usually against Aminoglycosides and β-Lactams. Aminoglycoside acetyl transferase and Aminoglycoside phosphorylase are the enzymes, source of which is the bacteria. They are involved in modifying Aminoglycosides. β-Lactamases are enzymes which are coded by a plasmid gene and they act against β-Lactams. There are several β-Lactamases identified like TEM enzymes, Amp-C[7].

Possesion of a gene: In case of Methicillin Resistant Staphylococcus aureus resistance towards β-Lactams is because of acquisition of mecA gene which codes for Penicillin binding protein 2a. This has very low affinity towards β-Lactam antibiotics[8].

Sidestepping of the target: Vancomycin, will bind to a substrate and not the enzyme while. It was thought that

resistance to this antibiotic was difficult to generate but present situation has changed. There is emergence of vancomycin resistant enterococcus. D-Ala-D-Ala is the end of the pentapeptide to which vancomycin binds but in resistant strain it will be replaced by an ester structure, D-Ala-D-lactic acid, which is not bound by vancomycin[7].

Preventing drug access to targets: There are different mechanisms by which drug accesses are prevented to the target. There could be local inhibition of drug access by plasmid coded Qnr protein, Drug specific efflux pumps related to tetracycline resistance protein Tet A in gram negative bacteria, or it could be non specific inhibition of drug access[7].

Plant parts used

Different parts of the plant have been used against the Multidrug resistant strains in the invitro studies. The plant parts which are usually used are leaves, fruits, bark, seeds and flowers or crude plant extracts are used[9-11].

Plant extracts against the multidrug resistant gram negative bacteria

The activity of Acacia nilotica, Terminalia arjuna, Eucalyptus globulus, Syzygium aromaticum and Cinnamomum zeylanicum tested against Escherichia coli, Klebsiella pneumonia and Candida albicans isolated from the community acquired and nosocomial acquired infection showed that ethanolic extract of three plants were effective in the following order Acacia nilotica > cinnamomum zeylanicum > Syzgium aromaticum[12]. Aqueous extract of Ripened fruits of Phyllanthus emblica Linn and roots of Aegle marmolos has displayed antibacterial activity with MIC of 200µg/ml and in contrast no zone of inhibition was seen around wells loaded with the extracts of Garcinia cambogia, Myristica fragrans, Cinnamomum tamala, Pimenta dioica, Piper longum, Premna latifolia and Ixora coccinea[13]. Aloe vera are found to have most wide spectrum of activity and uses. They have antiseptic, antiviral and healing properties[14]. Aloe vera has shown 80% susceptibility rate when compared with the antibiotic which are commonly used against. The susceptibility rate amongst the bacteria showed that Escherichia coli > Klebsiella sp. > Pseudomonas sp. with 46.7% > 16.7% > 6.7% respectively and Proteus sp. and Citrobacter sp. is found to have 3.3% susceptibility. These results indicate that as Aloe vera is an easily available plant, further studies regarding its effectiveness and safety in using should be made. This could be used as an alternative to antibiotics in treating the infections by these multidrug resistant bacteria[15]. Butea monosperma Lam. is a traditional plant which is used for treating the inflammatory diseases. In a study done on different extracts of its leaf it was seen that it has action on 12 different multi drug resistant bacteria. The most important enteropathogens when observed have shown following results. Among the gram negative bacteria tested lowest MIC value was 0.52mg/ml and this was observed in cold leaf extract with acetone against the Citrobacter sp. and Chromobacterium violaceum, cold leaf extract with petroleum ether against Pseudomonas aeruginosa, and on contrary both cold and hot leaf extract with methanol has given same MIC value of 0.52mg/ml[16].

Clove oil has more antibacterial activity followed by Eucalyptus oil as per a comparative study[17]. Garlic and ginger extracts have shown good antibacterial activity against the clinically isolated drug resistant bacteria[18]. It is mentioned in a review article on pomegranate that pomegranate peel extract at 250µg/ml was most effective at inhibiting antibiotic resistant strains of Salmonella Typhimurium[19]. Pomegranate is also proved to have resistance modifying agent against Acinetobacter baumannii in combination with novobiocin[20].

Plant extract against the multidrug resistant gram positive bacteria

Psidium guajava leaf extracts against 4 multidrug resistant staphylococcus aureus strains has noticeable antibacterial results with different MIC values. Cellular toxicity study of methanol extract using human erythrocytes showed no haemolysis at the concentration of 4mg/ml [21]. 2,3-dihydroxybenzoic acid component of the fruit Flacoutia Inermis have shown antibacterial activity. The authors mentions that 2,3-dihydroxy benzoic acid component has been shown to have anti oxidant character, but there study gives an additional information about its activity against the multi drug resistant bacteria[22]. Out of the three plants Taxus baccata, Phyllanthus debilis and Plectranthus amboinicus in the comparative study of their ethanol extract it has been found that the ethanolic extract of Phyllanthus debilis (MIC range 80-300µg/ml) has most potent broad spectrum activity against the tested multidrug resistance resistant bacteria. Phyllanthus debilis showed MIC of 80µg/ml and Taxus baccata showed the MIC of 200µg/ml against the methicillin resistant staphylococcus aureus strains[23]. Out of the 47 Enterococcus faecalis isolated from 100 different clinical specimens Aegles maromoles, Aristolochia indica and Ocimum canum were the plant which were tested against these multidrug resistant strain. Ethanolic extract of the Aristolochia indica showed strong activity[24]. In the research by Mustafa Oskay[11] out of the 19 plants tested against the multidrug resistant bacteria methicillin resistant staphylococcus aureus has shown most susceptibility to 17 plants ethanolic extracts with 26mm zone diameter with Cornus sanguinea and Streptococcus pneumoniae being sensitive to 14 plant extracts, and Streptococcus pyogenes being sensitive 13 plant extract. The leaf extract of Butea monosperma Lam. has shown antibacterial activity against Enterococcus sp., methicillin resistant staphylococcus aureus and the vancomycin resistant staphylococcus aureus and in addition the hot aqueous extract against Enterococcus sp. has shown the highest inhibition zone of 21mm[16]. Synergistic activity determination of Ocimum sanctum leaf extract and antibiotics on methicillin resistant Staphylococcus aureus strain is demonstrated[35]. Gram positive bacteria were more sensitive than Gram negative bacteria when the susceptibility was checked with garlic and

ginger extracts[18]. Phytochemical compounds of ethanol extracts of neem, tulasi and aloe vera has significant antimicrobial activity against the strain of methicillin resistant staphylococcus aureus[25].

Different methods used to check the antibacterial susceptibility

A suspension of selected bacterial strains is made and adjusted approximately to 0.5 Mc Farland[26-28]. Lawn culture of the organism is done on the Mulleur Hinton agar with a sterile swab. Agar surfaces are bored using a sterile borer and known amount of plant extract are poured in to the wells[25,29,30]. Plates are incubated overnight and the zone of inhibition is observed. The other method seen is instead of wells, filter paper discs are impregnated with the predetermined amount of plant extract[31-33].

Conclusion

Antimicrobial activity of many plants has drawn the attention of many scientists. Traditional medication using plants is present from centuries but a controlled clinical trial is found to be non many[34]. Many invitro studies are being done and has ended in good results. Mostly disk diffusion method is seen to be commonly employed in doing the susceptibility testing. More phytochemical analysis is required. It should be subjected to animal and human studies. The toxicity, effectiveness and dosage of the drug should be investigated.

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