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Opinion

Medicinal Plants: A New Hope against Microbial Resistance

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Increasing microbial resistance is a universal problem. Suboptimal conditions of living in developing world is a major contributing factor to enhanced microbial resistance at global level. Nosocomial, water borne, health care systems, poor hygiene and food products particularly meats are factors responsible for conferring microbial resistance. Modern science has made it feasible to understand, microbes, their resistance pattern and alternative approaches to control them. Plant derived antimicrobials (PDAms) offers new hope to deal with development of resistance. Pharmacologists are developing new antibiotic drugs of plant origin to treat and control various infections. In addition, research suggest that the combinations of PDAms and the synergistic compounds work efficiently on resistant strains ensuring no further resistance development. Moreover; world community is in need to put concerted efforts on poor countries to control antimicrobial resistance. In this regard, plant-derived antimicrobials in combination with antibiotics might suggest a cost-effective approach to deal with global antimicrobial resistance.

Microbes are most important life forms on earth and make 50 % of total living biomass. There is a huge difference between pathogenic and non-pathogenic microbes. Though this a fact that microbes exchange genetic material via plasmids thus conferring their pathogenicity to non-pathogenic ones [1]. In this way, various infectious diseases are transmitted in humans and animals. Antibiotics, also known as antimicrobials are chemical substances, toxic for most of the life forms and used to treat infections. However, repetitive and overuse use of antibiotics, uncontrolled migration of infected individuals to community and improper monitoring of health care units migration [2], are the major concerns in developing resistance microbes [3]. Furthermore, use of antimicrobial substances in veterinary unit as food additives is causing antimicrobial resistance (AMRs) in zoonotics, spreading to humans via food chain [2].

Microbes get resistant against most of the commercially available and newly developed antibiotics very rapidly due to presence of plasmids. Both gram positive and gram negative bacteria have ability to transfer plasmid through a natural way of horizontal gene transfer called as conjugation [4]. One set example is the transfer of plasmid in between *Vibrio fluvialis* and *Vibrio cholerae* conferring resistance to *V. fluvialis* [5]. Likewise, *Pseudomonas aeruginosa* and *Acinetobacter baumannii* are resistant to almost every antibiotic including the carbanems [6]. Surveillance practices including knowledge of invasive bacterial species, their presence in certain geographic area in general and monitoring-sampling techniques of pathogenic microbial isolates in particular are need to be administered properly. In developing countries of South East Asia, Western and Central Africa, India and Pakistan sudden outbreak of various infectious pandemic diseases is associated with the AMR development. Nosocomial infections, improper disposal of medical waste, misused antibiotics, drug abuse, poor hygiene are the major factors contributing to AMR [7].

The increasing antimicrobial resistance urge need to explore new horizons of drug development. Traditional medical practitioners had known the medicinal values of plants [8]. Plants have ability to produce great variety of secondary metabolites including aromatic compounds e.g. alkaloids, glycosides, terpenoids, saponins, steroids, flavonoids, tannins, quinones and coumarins [9]. Secondary metabolites of specific plant's is used to treat and control the infections globally e.g. Coumarins is specific for *Staphylococcus aureus* and ineffective on Gram-negative bacteria. PDA_m substances are plant-derived antimicrobials that are valuable due to their antibiotic activity [10]. Antimicrobial potential of PDA_ms is variable on the basis of dose ranging from 100 to 1,000 µg ml^{-1} for the minimum inhibitory concentration (MIC). In general, PDA_ms (mostly secondary metabolites) are phenol derivatives, sufficiently able to control microbes by reducing pH, increasing membrane permeability, altering efflux pumping.

In studies carried out by our group, methanolic, ethanolic and water extracts of several plants species viz., *Cinnamum zeylanicum, Acacia nilotica, Adhatoda vasica, Syzygium aromaticum, Aloe vera, Althaea officinalis, Cordia latifolia, Emblica officinalis, Eugenia caryophyllata, Glycyrrhiza glabra, Hyssopus officinalis, Lawsonia inermis, Linum usitatissimum, Malva sylvestris, Matricaria chamomilla, Mentha piperita, Moringa oleifera, Morus alba, Ocimum basilicum, Onosma bracteatum, Origanum vulgare, Pimpinella anisum, Piper longum, Saussurea lappa, Sisymbrium irio, Syzygium cumini, Thymus vulgaris, Viola odorata, Vitis vinifera, Zingiber officinale, Ziziphus jujube* were assayed for their antimicrobial activity on most of the common MDRs viz., *Staphylococcus aureus, Pseudomonas aeruginosa, Klebsiella pneumonia, E. coli*. Though plants exhibited generalized activity against a range of infectious microbes, however, their target specificity shouldn't be ignored due to unknown mechanism. A generalized mechanism of PDA_ms on microbes might be due to the contribution of a range of factors including efflux pumping on MDRs: increasing permeability and reduce selection pressure [11]. Plants also produce antimicrobial peptides (AMPs) as defensins against infections. These are small basic peptides, with characteristic 3D folding pattern, stabilized by eight disulfide linked cysteines. AMPS have also been suggested to support treatment outcome without conferring resistance [12].

Plant antimicrobials have been suggested to have amplified effect in combinations with other amphipathic compounds. Synergistic effect of plant origin compounds and efflux pump inhibitor (EPI) along with altering outer membrane permeability of multi drug resistant (MDR) bacteria has been a very successful strategy to combat resistance in microbial pathogenesis. Studies by Liaqat., *et al*. [13] reported another example of synergistic effect of toxic fungal metabolite such as patulin (mycotoxin produced by a variety of molds, in particular, *Aspergillus* and *Penicillium* and *Byssochlamys*.), in combination with EDTA to control dental unit water line biofilm formation by bacteria. Detailed mechanism of PDA_ms on MDR *S. aureus* has been reported in study by Gibbons [14].

In brief, ethno-pharmacology offers a wide scope with detailed discussion on AMR and alternating drug system. The science community throughout world is busy on putting endless efforts on developing new, effective and safe drugs. A lot of research potential exists in developing new plant-derived synergistic compounds capable of enhancing the activity of PDA_ms.

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