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Review Article

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Medicinal Plants Speak Bioactive Secondary Melabolites

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ABSTRACT

Traditional medicinal plants as potential sources of phytochemicals are known to have diverse biological activities (antibacterial, antifungal and anticancer). In recent year, plant-derived secondary metabolic compounds become easily accessible and economically available sources for the treatment of many different infection due to increase of multi drug resistant bacteria. This study will be discussed the antimicrobial activity of secondary metabolites that inhibit highly active pathogenic bacteria (B.subtilis, E.coli, P.aeruginosa, S.aureus) from different parts (stem, leaves, bark and root) of medicinal plants. An antimicrobial is as agent that kills microorganisms or stops their growth and can be classified according to their function. Some bio-active natural compounds such as terpenoids (Menthol) gives the plant odor, other (Quinone and Tannins) are responsible for plant pigment. Many compounds are responsible for plant flavor (Capasaicin from chilli peppers). Ocimum gratissimum and Toddalia asiatica were examined for antimicrobial activity against methicillin-resistant S. aureus and P. aeruginosa. Morphine alkaloids are pain relievers that are used as narcotics. Catecin (flavonoids) from Camelia sinesis inactivated cholera toxin in Vibrio cholerae. Eugeneol is a terpenoid that is considered against both fungi and bacteria.

Key words: *Vibrio cholera, Bacteria, Fungi, Antibacterial, Antifungal and Anticancer*

INTRODUCTION

Plants have been used for medicinal purposes long before prehistoric period. Indigenous cultures such as Rome, Egypt, Iran, Africa and America used herbs over 4000 years as "herbal medicine" for development of health care in their daily life. Traditional medical systems such as Unani, Ayurveda and Chinese Medicine were used large number of plant materials as a source of medicines systematically. According to WHO, around 21,000 plant species have the potential being used as "medicinal plants". Treatment with medicinal plants, which have ethnomedicinal importance is very safe, high efficiency and low cost due to the rich source of active ingredients which can be used in drag development through the World. It is estimated that there are 250,000 to 500,000 plants on Earth[4].

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A relatively small percentage (1to 10%) of these are used as food by both humans and other animal species. 12,000 active compounds are known to science; some of them (20 to 25%) were used as drugs in modern medicine such chemicals derived from plants. Infectious disease are one of the main cause of morbidity and mortality worldwide. Now-a-days many infections are caused by multi-resistant microorganisms resulting in difficult to treat infectious disease and increases in healthcare cost. Nature is a generous source of compounds with the potential to treat infectious disease. Natural substances with high antimicrobial activity, this study will be highlighted the bioactive secondary compounds from medicinal plants.

HISTORICAL BACKGROUND: In 1924, Gartia and Dath considered the discovery of naturally derived actinomycetin from strains of Actinomycetes and some soil microorganisms that has given us a number of antibiotics since 1940. In 1928 (28th September, morning of Friday), Scottish Scientist named Alexder Fleming was discovered "Penicillin" one of the first clinically effective antimicrobial substances as antibiotic which was derived from a type of mould, *Penicillum notatum (*blue-green*)* that controls against bacterial infections. Fleming noticed that a petri dish was containing with lawn of bacterial colonies (*Staphylococcus aureus*) which failed to grow the visible area that had been accidentally contaminated by fungal growth culture. Bacterial growth was inhibited around the mould. He concluded that mould released a substance that suppress the bacterial growth. He isolated the mold and purified form of the drug which was available for therapeutic agents that is successful treatment of bacterial infectious disease in human. The several kinds of penicillin synthesized by various species of the mold *Penicillum spp.* The naturally occurring Penicillin G (benzyl penecillin) and Penicillin V (phenoxymethyl penicillin), are still used clinically. In 1943 (19th October) Streptomycin, the first antibiotic drug found to treat a number of bacterial infections (pulmonary tuberculosis) was isolated a soil-based actinobacteria named *Streptomyces griseus* by Albert Schatz, a Ph.D student in the laboratory of Selman Abraham Waksman at Rutgers University. End of 1943, he and his mentor Waksman had successfully purified "Streptomycin" that is a more powerful antibiotic for infections resistant to Fleming's penicillin. In 1952, Waksman was awarded the Nobel Prize in Medicine in recognition "for his discovery of streptomycin, the first antibiotic active against tuberculosis". In 1962, the bark of Pacific yew tree were collected by researchers from United States (Department of Agriculture). The National Cancer Institute (NCI) was started a screening of plant extracts as the natural products that might cure Cancer. *Taxus brevifolia*, the Pacific yew (North-East) tree was used stem bark extracts that using tumor system models in vivo and tumor cell lines in vitro. Unfortunately, only a few of these substances was shown cytotoxic activity against in carcinosarcoma (rats) and leukemia in mice. Natural compounds have proved the pharmacological interest to reach the clinical trials. In 1965, identification and purification of the extracts most active component was isolated pure form Paclitaxel, also known by its trade name "Taxol" is the World's first billion-dollar anti-cancer drug. Taxol is one of the most promising drugs in the treatment of overian cancer and breast cancers. Many effective drugs were originated from plant parts (stem, root, bark and leaf) such as Atropine, Ephedrine, Digoxin, Morphine, Quinine, Reserpine and Tubocuramine[7].

SECONDARY METABOLITES FROM PLANTS: Secondary metabolic compounds exhibit many biological activities. These include antimicrobial, antifungal, anticancer and anti-inflammatory activities. Plants have almost limitless ability to synthesize aromatic substances, most of which are phenols or their oxygen-substituted derivatives. Most are secondary metabolites, of which at least 12,000 have been isolated, a number estimated to be less than 10% of the total. Medicinal plants are rich in a numerous variety of secondary metabolites with biological activities such as alkaloids, flavonoids,

quinones, tannins, phenol, terpenoids, essential oil[12]. An antimicrobial is as agent that kills microorganisms or stops their growth and can be classified according to their function. Some bio-active natural compounds such as terpenoids (Menthol) gives the plants odor, other (quinones and tannins) are responsible for plant pigment. Many compounds are responsible for plant flavor (terpenoid, capsaicin from chilli peppers) and a few of the same herbs and species used by humans for useful medicinal compounds.

PHENOL AND PHENOLIC COMPOUNDS: Phenolic compounds are widely distributed in plants, where they protect the plants from microbial infections. They have potential antioxidative properties but are also potent antiinfectives[20]. Some of the simplest bioactive phytochemicals consist of a single substitute phenolic ring. The common herb thyme and tarragon contains caffeic acids, common a wide group of phenylpropane-derived compounds which is effective against viruses, bacteria and fungi. Catechol and pyrogallol both are hydroxylated phenols, shown to be toxic to microorganisms. Eugenol is a well-characterized representative found in clove oil. It is considered bacteriostatic against both fungi and bacteria.

Flavonoids: They are a large group of aromatic compounds. It founds in many common edible part such as fruit, vegetables, nuts, seeds. The basic structural feature of flavonoid compounds is 2- phenyl-benzopyrane or flavane nucleus, consisting of two benzene rings linked through a hetericyclic pyrane ring. Flavones are phenolic structures containing one carbonyl group. Flavonoids are also hydroxylated phenolic substanes but occur as C_6-C_3 unit linked to an aromatic ring. Catechin are included among the flavan-3-ols or flavanols. It presents in particularly in oolong green tree (*Camelia sinesis*). The catecin inactivated cholera toxin in *Vibrio cholerae.* Flavones and their derivatives represent an antibacterial therapeutics possibility to disrupt the bacterial envelopes.

Quinones: Quinones (aromatic rings with two ketone substitution), ubiquitous in nature, are significant group of secondary metabolites with potential antimicrobial properties. These compounds are being colored (brown) in injured fruits and vegetables or melanin synthesis in human skin through oxidation and reduction reaction. The individual redox potential of the particular quinone-hydroquinone pair is very important in many biological systems such as ubiquinone (coenzyme Q) plays in mammalian electron transport systems, napthoquinine (Vitamin K) shows anti-hemorrhagic activity (tyrosine) in body tissue. Anthraquinone had a large spectrum of antimycobacterial activity which forms stable complex with free radicals irreversibly and nucleophilic amino acids in microbial proteins determining inactivation and loss of their functional proteins (bacteria). Hypericin, an anthroquinone from *Hypericum perforatum* had general antimicrobial activity (antidepressant). Rhein, an anthroquinone from Senna (*Cassia angustifolia*) has antimicrobial activity against *Staphylococcus aureus.* Cassia italic, a Pakistani tree shown bacteriostatic for *Bacillus anthracis*, *Cornybacterium pseudodipthericum and Pseudomonas aeruginosa* and bacteriocidal for *Pseudomonas pseudomalliae*.

Tannin: Tannins are polymeric phenolic substances found in every plant parts (barks, wood, leaves, fruits and roots) characterized by antifungal and antibacterial activity[21]. Their molecular weights range from 500 to 3,000[8]. They are divided into two groups (hydrolysable and condensed). Hydrolyzable tannins are based on gallic acid, usually as multiple esters with D-glucose. Condensed tannins (proanthocyanidins) are derived from flavonoids monomer. Tannins can be toxic to filamentous fungi, yeast and bacteria[22]. Condensed tannins have been determined to blind cell walls of ruminal bacteria, preventing growth and protease activity[10].

Coumarins: Coumarins are phenolic compounds with fused benzene and pyrone (α) groups. They are responsible for the characteristics odor of hay. 1300 had been

identified[9]. It has antithrombotic[23], anti-inflammatory[16] and vasodialatory[14] activities. Warfarin is a particularly well-known coumarin which is used both as an oral anticoagulant and interestingly, as a rodenticide. It also may have antiviral effects.

ALKALOIDS: Alkaloids are heterocyclic nitrogen compounds characterized by different antimicrobial activities. The first medically useful example of an alkaloid was morphine, isolated in 1805 from opium poppy (*Papaver somniferum*). Codeine and heroin are both derivatives of morphine. Barberine, isoquinoline alkaloid presents in roots, stem barks of Barberry (*Barberis vulgaris*) is potentially effective against bacteria, fungi, protozoa (*Trypanosomes*) and viruses (*Plasmodia*). Solamargine, a glycoalkoid from the berries of *Solanum khasianum* and other alkaloids may be useful against HIV infection[19] as well as intestine infections associated with AIDS. It have been found micro-biocidal effects (including against *Giardia* and *Entamoeba*).

TERPENOIDS AND ESSENTIAL OILS: Secondary metabolites that are highly enriched of potent compounds based on the isoprene structure which is responsible for fragrance of plants. The number of isoprene units can identify the many different molecules. Tarpenes are the largest group of natural compound. Monoterpenes are formed when five-carbon isoprene units are joined, having a molecular structure of $C_{10}H_{16}$ and they occur as diterprene, triterprene and tetraterprene (C_{20}, C_{30}, and C_{40}) as well as hemiterprenes (C_5) and sequiterpenes (C_{15}). When the compounds contain additional elements, usually oxygen, they are termed terpenoids that are synthesized from acetate units. Essential oil are made of monoterprenes or sequiterprenes. Menthol, terpenoid occurs from peppermint (*Mentha piperita*). It active against bacteria, fungi, viruses and protozoa.

Name	Secondary Metabolites	Nature	Activity
Betel pepper *Piper betel*	Catechols	Phenol	General
Thyme *Thymus Vulgaris*	Caffeic Acid	Phenolic compounds	Virsus, bacteria, fungi
Tarragon *Artemisia dracunculus*	Caffeic Acid	”	Viruses, *helminthis*
Clove *Syzygium aromaticum*	Eugenol	Terpenoid	General
Green Tea *Camellia sinensis*	Catechin	Flavonoid	General (*Shigella, Vibrio, S.mutans*)
Tree bard *Podocarpus nagi*	Totarol	Flavonol	*P. acnes*, other gram positive bacteria
Legume(West Africa) *Millettia thonningii*	Alpinumisoflavone	Flavone	*Schistosoma*
Senna *Cassia angustifolia*	Rhein	Anthraquinone	*S. aureus*
St. John’s wort *Hypericum perforatum*	Hypericiin	”	General
Henna *Lawsonia inermis*	Gallic acid	Phenolic acid	*S.aureus*
Chamomile *Matricaria chamomilla*	Anthemic acid	”	*M. tuberculosis, S.typhimurium, S.aureus*
Lemon balm *Melissa officinalis*	Tannin	Polyphenols	Viruses
Sainfoin *Onobrychis viciifolia*	Tannin	”	Ruminal bacteria
Woodruff *Gallium odoratum*	Coumarin	Phenolic compound	General
Eucalyptus *Eucalyptus globulus*	Tannin	Polyphenol	Bacteria, viruses
Cascara sagrada *Rhamnus purshina*	Tannin	”	Viruses, bacteria, fungi
Barberry *Berberies vulgaris*	Berberine	Alkaloid	Bacteria, protozoa
Black pepper *Piper nigrum*	Piperine	”	Fungi, *Lactobacillus, Micrococcus, E.coli, E.faecalis*
Golden seal *Hydrastis canadensis*	Berberine	”	Bacteria, *Giardia duodenale, Trypanosomes, Plasmodia*
Rauvolfia Chandra *Rauvolfia serpentina*	Reserpine	”	General

BIOLOGICAL ACTIVITY OF PLANT DERIVED SECONDARY METABOLIC COMPOUNDS

Name	Secondary Metabolites	Nature	Activity
Gory lily *Gloriosa superba*	Colchicine	Alkaloid	General
Coca *Erythroxylum coca*	Cocaine	Alkaloid	Gram-negative and Gram-positive cocci
Opium poppy *Papaver somniferum*	Morphine	”	General
Peppermint *Mentha piperita*	Menthol	Terpenoid	General
Chili peppers *Capsicum annuum*	Capsaicin	Terpenoid	Bacteria
Basil *Ocimum basilicum*	Essential oil	”	*Salmonella*, bacteria
Gotu kola *Centella asiatica*	Asiatocoside	Terpenoid	*M.lapre*
Turmeric *Curcuma longa*	Curcumin	”	Bacteria, protozoa
Allspice *Pimenta dioica*	Eugenol	Essential oil	General
Betel pepper *Piper betel*	Eugenol	”	”
Fava bean *Vicia faba*	Fabatin	Peptides	Bacteria
Wheat *Triticum aestivum*	Thionin	”	”
Papaya *Carcica papaya*	Papain	Latex(Mixture of terpenoids, organic acid and alkaloid)	General
Cranberry *Vaccinium spp*	Fructose	Sugar (Monosaccharide)	Bacteria (*E.coli*)
Olive oil *Olea europaea*	Hexanal	Aldehyye	General
Onoin *Allium cepa*	Allicin	Sulfoxide	Bacteria, Candida
Pasque-flower *Anemone pulsatilla*	Anemonins	Lactone	Bacteria
Mountain tobacco *Arnica Montana*	Helanins	”	General
Aloe *Aloe barbadensis*	Latex	Complex mixture	*Corynebacterium, Salmonella, Streptococcus, S.aureus*
Garic *Allium sativum*	Allicin	Sulfoxoide	Genaral
Apple *Malus sylvestris*	Phloretin	Flavonoid derivatives	”

Chile peppers are a food item that uses for flavor of food which constituent, capsaicin has a wide range of biological activities in humans, affecting the nervous, cardiovascular and digestive system as well as analgesic. Betulinic acid, one of several terpenoids have been shown to inhibit HIV. Essential oil (terpenoids) of Basil (*Ocimum bacilicum*) was found effective in disinfecting lettuce leaves. Food Scientist have been found essential oil as terpenoids of plants to be useful in the control of *Listeria monocytogenes.*

LECTINS AND POLYPEPTIDES: Peptides which are inhibitory to microorganisms were first reported in 1942. They are positively charged with disulfide bond. Thionins are peptides commonly found in barley and wheat which consists of 47 amino acid residues that

are toxic to yeast, gram-positive and gram-negative bacteria. Thionins, AX1 and AX2 from sugar beet are active against fungi but not bacteria. Fabatin, a newly identified 47 residues of peptide from fava beans, appears to be structurally related to thionins from grains and inhibits *P. aeruginosa*, *E.coli* and *Enterrococcus hirae* but not *Saccharomyces or Candida.* The larger lectin molecules, which include mannose-specific lectins from several plants, MAP 30 from bitter melon, GAP31 from *Gelonium multiforum* and jacalin are inhibitory to viral proliferation (HIV, cytomegaloviruses) by inhibiting viral interaction with critical host cell components.

CONCLUSION

The increasing of drug-resistant microorganisms observed in recent years and traditional used of healthy plants as medicine in several countries from plant derived natural products as an important source of antimicrobial compounds. Many different phytochemicals of medicinal plants were characterized by inhibitory of microbial world (viruses, bacteria, fungi, yeast and protozoa). Healthy plant produces a variety of compounds, mainly secondary metabolites that can possess different antimicrobial activities. Different plants have been shown to different quantities of secondary metabolites which exhibits biological activities. Several secondary metabolites are highly potent with biological activities due to their richness of phytochemicals which had higher zone of inhibitions than an antibiotic that are promising activities for these specific compound. The novel secondary metabolites with different antimicrobial activities have been identified and purified. The newly arising compound have been searching for further investigation of novel compound. The novel natural compound can help to treat the infectious disease that have increased of multi-drug resistance bacteria to commercially available antibiotics. They could provide alternative pathway of medicinal treatment, especially in developing countries where people may not have access to maintain proper healthcare in their daily life.

FUTURE PERSPECTIVE:

Scientist have investigated on different plant that shows antimicrobial activity of secondary metabolites against multidrug resistance bacteria. The study should be performed on biological activities of healthy plants from different climatic zones. These antimicrobial properties are important for pharmacological, agricultural and medical uses. The spread of drug-resistant microorganisms is a big threat to successful therapy of microbial infectious disease. Future study should be identified and isolated the bioactive natural compounds from medicinal plants. The potential component of different secondary metabolites will be eliminated the multidrug resistance microorganisms of different infectious disease. It would be advantageous standardized method for development of plant derived phytochemicals which acts against prevention and treatment of infectious disease.

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