Flora of Kashmir with Antimicrobial Activity: A Review

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ABSTRACT
Plants are the source of large amount of drugs comprising to different groups such as antispasmodics, emetics, anti-cancer, antimicrobials etc. A large number of the plants are claimed to possess the antibiotic properties in the traditional system and are also used extensively by the tribal people worldwide. It is now believed that nature has given the cure of every disease in one way or another. Plants have been known to relieve various diseases in Ayurveda. Therefore, the researchers today are emphasizing on evaluation and characterization of various plants and plant constituents against a number of diseases based on their traditional claims of the plants given in Ayurveda. In this present review, an attempt has been made to give an overview of certain bioactive compounds which may have the antimicrobial activity.

Keywords: Medicinal plants; Antimicrobial activity, Kashmir, Antimicrobials

INTRODUCTION
Microbial diseases remain among the principal causes of poor livestock performance, thus, making the farmers to go for modern day antibiotics. One of the most powerful and successful achievements of modern science and technology for the control of infectious diseases is the discovery and development of antibiotics. Antibiotics such as avoparcin, bacitracin, lincomycin, penicillin-G, procaine, chlorotetracycline and virginiamycin promote growth because of an effect on the micro flora in the gastrointestinal tract (De Man, 1975). However, the rate of resistance of pathogenic microorganisms to conventionally used antimicrobial agents is increasing with an alarming frequency. Antimicrobial resistance in zoonotic enteropathogens including Salmonella, Escherichia coli and Enterococi in food animals is of special concern to human health because these bacteria are likely to transfer from the food chain to humans (Endtz et al., 1991). In addition to this problem antibiotics are sometimes associated with adverse side effects on the host, which include hypersensitivity, depletion of beneficial gut and mucosal microorganisms, immunosuppression and allergic reactions (Al-Jabri, 2005). This situation has forced scientists to search for new antimicrobial substances from various sources as novel antimicrobial chemotherapeutic agents. Hence much attention has been paid recently to the biologically active compounds derived from plants used in herbal medicine (Lone et al., 2013). Plants produce a diverse range of bioactive molecules, making them rich source of different types of medicines. The most important of these bioactive compounds are alkaloids, flavonoids, tannins and phenolic compounds which are the important raw materials for drug production. Most plants contain several compounds with antimicrobial properties for protection against aggressor agents, especially microorganisms (Silva et al., 2010). Plants with possible antimicrobial activity need to be tested against some microbes to confirm the activity.

MEDICINAL PLANTS IN KASHMIR VALLEY SCREENED FOR ANTIMICROBIAL ACTIVITY: Kashmir Valley has a rich flora of medicinal plants and is at the vanguard of the organic farming movement. There are traditional ways of using some plants such as Artemisia absinthium (Tethwen), Allium sativum (Rohun), Achillea millifolium (Pehl-ghasa), Nepeta cataria (Gande-soi) etc. as antibiotics. The valley harbors a rich and unique flora of medicinal plants being distinct from those in the rest of the country and other parts of the world. Owing to its very rich variety of medicinal plants, Kashmir has been a favorable place for local “Hakims” to practice Unani System of Medicine (Dar et al., 2002). Thus, Kashmir valley has provided ample opportunity for sustaining the Unani system of medicine during onslaught of western system. In Kashmir, traditional health care systems are based mostly on the use of medicinal plants, the knowledge that has been acquired and developed over a long period of time through experimentation and passed from one generation to next mainly by word of mouth. Kaul (1997) has listed 111 medicinal plants from Kashmir and Ladakh. Author has also mentioned about healing properties of 291 species of medicinal plants from these regions which have microbial activities. Some of the most important medicinal plants of Kashmir are Artemisia spp., Arnebia benthamii, Allium cepa L., Allium sativum, Plantago lanceolata, Datura stramonium, Inula racemosa, Cannabis sativa L., Podophyllum hexandrum, Hyoscyamus niger, Nepeta cataria, Urtica dioica Linn etc. The medicinal use of these plants by the nomadic and migratory tribes like Gujjars and Bakerwals is an established fact. The
Phytochemicals are non-nutritive plant chemicals that have protective or disease preventive properties. There are more than thousand known phytochemicals produced from plants which help them to protect from various stresses. Major groups of antimicrobial phytochemicals found in plants are:

1. Alkaloids
Alkaloids are Heterocyclic nitrogen compounds. The first medically useful alkaloid was morphine, isolated in 1805 from Papaver somniferum (opium poppy) (Fessenden and Fessenden, 1982). Diterpenoid alkaloids, Isolated from the plants of the Ranunculaceae family, are commonly found to have antimicrobial properties. Faizi et al., 2003 isolated three new alkaloids Pendulamine A, pendulamine B and penduline along with stigma sterol 3-O-beta-D-glucoside, allantoin, the known diterpenoid kolanovic acid and the azulfuorene alkaloid isour sine from root extract of Polyalthia longifolia. Compound pendulamine A and pendulamine B were found to be active antimicrobial agents. Likewise erysotrine, erysodine, syringaresinol, vanillic acid, erythrina alkaloid, (+)-10, 11-dioxoerysotrine isolated from Erythrina latissima by Wanjala et al., 2002 have strong antimicrobial activities. Ahamd et al., 1993 have reported antimicrobial activity of liriodenine an alkaloid from Guatteria multivenia root against both bacteria and Candida albicans. Other known alkaloids from this plant with weak antimicrobial properties are liriodenine, lysicamine, lanuginosine, guadiscine and O-methyl pallidine.

2. Flavones, Flavonoids and Flavonols
Flavones are phenolic structures containing one carbonyl group. These are hydroxlated phenolic substances that occur as C6–C3 units linked to an aromatic ring. Flavonoids are known to be synthesized by plants in response to microbial infection (Dixon et al., 2005) and are effective anti-microbial substances against a wide array of micro-organisms. Antimicrobial flavonoids have been reported from Erythrina latissima (Wanjala et al., 2002). Compounds of Caesalpinia pulcherrima with anti-viral activities were derived from the flavonoid of quercetin (Chiang et al., 2003). Moreover, the flavonoids, acacetin-7-O-beta-D-galactopyranoside of Crysanthemum morifolium was found to be active as towards HIV (Hu et al., 1994). A wide variety of flavonoids, sesquiterpenoid alcohols, triterpenoids and quinic acid caffeates product from plants may also be useful as antimicrobials (Hu et al., 1997). The activity is probably due to their ability to form a complex with extra-cellular and soluble proteins, which then binds to bacterial cell wall. 

3. Polyphenols and Phenolics
Some of the simplest bioactive phytochemicals consist of a single substituted phenolic ring. Cinnamic and caffeic acids are common representatives of a wide group of phenyl-propane derived compounds that are in the highest oxidation state. The common traditional medicinal plants have such compounds that are effective against bacteria (Brantner et al., 1996). Phenolic compounds possessing a C3 side chain at a lower level of oxidation and containing no oxygen are classified as an essential oil and reported as anti-microbials. Phenols are toxic to microorganisms because of the sites and numbers of hydroxyl groups on the phenol groups, which is all related to their relative toxicity to microorganisms. There is evidence that highly oxidized phenols possess inhibitory action (Ur and Dunleavy, 1975). The mechanism responsible for phenolic toxicity to microorganism includes enzyme inhibition by the oxidized compounds, possibly through reaction with sulphydryl groups or through more non-specific interactions with proteins (Mason and Wasserman, 1987).

4. Essential oils and Terpenoids
The anti-microbial properties of aromatic volatile oils from medicinal, as well as other edible plants have been recognized since antiquity. These oils possess a broad spectrum of anti-microbial activities attributed to the high content of phenolic derivatives such as carvacrol and thymol. Essential oils consist of secondary metabolites which are highly enriched in compounds based on an isoprene structure as terpenes and occur as diterpenes, triterpenes, tetraterpenes as well as hemiterpenes and sesquiterpenes. When the compounds contain additional elements, usually oxygen, they are termed as terpenes. Terpenenes or terpenoids are active against bacteria (Ahamd et al., 1993). Nearly, 60% of all essential oil derivatives possess inhibitory effects upon fungi while 39% inhibited bacteria (Chaurasia and Vyas, 1997).

5. Polypeptides
Polypeptides can be grouped into two major classes: anti-microbial proteins and a wide variety of non-protein compounds. Their distribution is often tissue specific (Price et al., 1987) and they are usually found in cells located at the external layers of plant tissues, thus suggesting that these compounds would be the first
line of defense against a pathogen attack. Peptides that are inhibitory to micro-organisms were first reported in 1942. Peptides called cathelicidins represent an important native component of innate host defense in mice and provide protection against necrotic skin infection caused by Streptococcus (Nizet et al., 2001). The broad spectrum activity displayed by anti-microbial peptides is considered a chemical condom against HIV infection and Herpes simplex virus (Yasin et al., 2001).

6. Tannins
Tannins are a group of polymeric phenolic substances capable of tanning leather or precipitating gelatin from solutions, the property known as astringency. They are found in almost every plant parts: bark, leaf, root, wood and fruit. They form two groups, hydrolysable and condensed tannins based on Gallic acid. The first group is usually found as multiple esters with D-glucose, while the more numerous condensed tannins are derived from flavonoid monomers. The anti-microbial activities of tannins are well documented. The growth of many fungi, yeasts, bacteria and viruses are inhibited by tannins. Their anti-microbial properties seemed to be associated with the hydrolysis of an ester linkage between Gallic acid and polyolhydrolyzed after the ripening of many edible fruits. Tannins in these fruits thus serve as a natural defense mechanism against microbial infections. The anti-microbial property of tannic acid can also be used in food processing to increase the shelf-life of certain foods. Tannin components of epicatechin and catechin (Vaccinium vitis-idaea L.) showed strong anti-microbial activity against bacteria and fungi. Such anti-microbial activity could potentially be used as a possible alternative for the treatment of periodontal diseases (Ho et al., 2001).

<table>
<thead>
<tr>
<th>Plant (Family)</th>
<th>Local name</th>
<th>Test Strains</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arnebia benthamii (Boraginaceae)</td>
<td>Kahzaban</td>
<td><em>E. coli</em>, <em>P. aeruginosa</em>, <em>K. pneumonia</em>, <em>S. typhimurium</em>, <em>C. albicans</em>, <em>C. kruesie</em></td>
<td>Shamim et al., 2015</td>
</tr>
<tr>
<td>Rumex dentatus (Polygonaceae)</td>
<td>Abuj</td>
<td><em>S. flexneri</em>, <em>K. pneumonia</em>, <em>E. coli</em>, <em>A. versicolor</em></td>
<td>Nisa et al., 2013</td>
</tr>
<tr>
<td>Nepeta cataria (Lamiaceae)</td>
<td>Gande soi</td>
<td><em>S. aureus</em>, <em>K. pneumoniae</em>, <em>P. aeruginosa</em>, <em>B. subtilis</em></td>
<td>Bandh et al., 2011</td>
</tr>
<tr>
<td>Euphorbia helioscopia (Euphorbiaceae)</td>
<td>Guer sochal</td>
<td><em>Escherichia coli</em>, <em>Pseudomonas multocida</em>, <em>S. aureus</em>, <em>K. pneumoniae</em>, <em>C. albicans</em></td>
<td>Lone et al., 2013</td>
</tr>
<tr>
<td>Euryale ferox</td>
<td></td>
<td><em>S. aureus</em>, <em>P. aeruginosa</em>, <em>C. kruesie</em>, <em>S. flexneri</em></td>
<td>Paray et al., 2010</td>
</tr>
<tr>
<td>Euphorbia wallichii (Euphorbiaceae)</td>
<td>Guri-dud</td>
<td><em>S. aureus</em>, <em>P. multocida</em>, <em>P. aeruginosa</em>, <em>A. flavus</em>, <em>C. kruesie</em></td>
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<tr>
<td>Fumaria Indica (Fumariaceae)</td>
<td>Shahtar</td>
<td><em>E. coli</em>, <em>S. aureus</em>, <em>P. multocida</em>, <em>P. aeruginosa</em>, <em>C. albicans</em>, <em>C. kruesie</em></td>
<td>Khan et al., 2014</td>
</tr>
<tr>
<td>Iris kashmiriana (Iridaceae)</td>
<td>Mazar Mund</td>
<td><em>E. coli</em>, <em>S. aureus</em>, <em>P. multocida</em></td>
<td>Khan, 2015</td>
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CONCLUSION
This review sums up the medicinal plants of Kashmir screened for antimicrobial activity along with the major class of secondary metabolites responsible for their activity. It can be useful for scientists and researchers to carry out further studies on isolation and identification of active compounds that can be formulated into antimicrobial drugs.

REFERENCES