Evidence Based Antibacterial Potentials of Medicinal Plants and Herbs Countering Bacterial Pathogens Especially in the Era of Emerging Drug Resistance: An Integrated Update

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Abstract: Owing to rising incidences of antimicrobial resistance against various chemotherapeutic and antimicrobial agents, the treatment of bacterial infections requires special consideration that may otherwise lead to grave prognosis. Simultaneously, evolution of many a Multiple Drug Resistant (MDR) bacterial strains have further aggravated the present situation. In this scenario, scrutinizing for some alternative yet effective antibacterial therapeutics like herbs, nutritional immunomodulators, bacteriophages, avian egg antibodies and others have become need of the day. Herbs have been a valuable source of medication in virtually all cultures and societies worldwide due to their important antimicrobial principles and phytoconstituents and wider therapeutic potentials. As various extracts of herbs and medicinal plants are being reported with antibacterial activities, much effort should be made in their identification, studying biologically active ingredients, efficacy and potency testing and scientific validation for their significant and practical multi-beneficial uses. The present review elaborates the potential role and applications of several herbs in treating bacterial infections and various types of bacterial diseases for safeguarding health of humans and their companion animals. It highlights the salient beneficial applications of traditional herbs and novel phytomedicines, from ancient periods to modern usages. Due emphasis has been given regarding scientific approaches to be followed and future perspectives with a vision to counter the emerging antimicrobial resistance. The review will certainly promote and popularize herbs as alternatives to conventional antimicrobials, particularly in the event of emerging MDR bacterial infections. Global usages of herbs as alternative and complementary medicines to various antimicrobials would lead not only to safeguard health issues and obtain optimum production from animals but will also ensure the public health issues including of food safety concerns viz., antibiotic residual effects in animal products (milk, meat) and zoonotic threats.

Key words: medicinal plants, herbs, phytoconstituents, biological activity, pharmacological principles, bacterial pathogens, antibiotic resistance, multiple drug resistance, antibacterial effects, treatment, herbal therapy

INTRODUCTION

Initiation and development of a bacterial infection in an animal requires a three dimensional interaction between bacterial agents, environment and the immune status of the animal (Rahal et al., 2014a). A bacterial disease can be initiated only when pathogenic bacteria comes in contact with a susceptible host in a disease favouring...
environment (Engering et al., 2013; Kuehn and Kesty, 2005; Jelsbak et al., 2012). The environment plays a crucial role in modulating the virulence of the pathogens as well as reducing the host defence (Martinez and Baquero, 2002; Rahal et al., 2014a) and thus increases the susceptibility of the host towards various pathogens. A pathogenic agent can enter the animal body via various possible routes of exposure (Kumar et al., 2011; Dhamu et al., 2014; Verma et al., 2014a) but the immune system of host can certainly phagocytise the pathogen (e.g., by secreting chemical factors) and thus checks the disease progress. Moreover, alterations in the microenvironment such as abrasions, wound, malnutrition, pathophysiological conditions may further facilitate the disease development (Madenspacher et al., 2013).

For development of a disease, immune status of the animals and human population is an important issue. A susceptible host population can favour even a mild pathogen to produce an epidemic form of disease while immunocompetent population can resist even highly pathogenic microbial strains. The immune status of the animals depends on a number of environmental variables for its fluctuations (Rahal et al., 2014a). Animals with immunocompromised lungs usually show higher incidences of pathophysiology due to leukotoxins and lipopolysaccharide exposures (Panayotova-Penecheva and Alexandrov, 2010). Both these toxins act as chemotactic factors for inflammatory cells and promote inflammation and severe damage in the lung tissues. In immature animals, such outbreaks may take an acute form but with high mortality rates. Both these mechanisms of initiation of inflammation as well as cellular damage are pharmacologically well understood and can be counteracted with the use of phytoconstituents of herbs and plants (Rahal et al., 2009, 2014a,b).

Even today, due to high cost of effective antibiotics and the predicament of antibiotic resistance microbial strains worldwide, about 60-85% of the population of developing world relies either on herbal or on indigenous forms of Complementary and Alternative Medicines (CAM) medicines for their various general health related issues and countering several diseases/disorders (Kochhar, 1981; Okeke et al., 1999; Ernst, 2000; Archna et al., 2011; Umashanker and Shruti, 2011; Mahima et al., 2012; Tiwari et al., 2012, 2013a, b; Yamey et al., 2013; Midirullah et al., 2014). Herbal plants have been used as a source of valuable medication in virtually all cultures worldwide due to presence of important antimicrobial principles, immunomodulatory activities, maintenance of general health, precious therapeutic properties and healing potentials; thus ensure prevention and cure for several diseases and disorders of humans and animals (Baqar, 1995; Rios and Reece, 2005; Mahima et al., 2012; Rahal et al., 2014b). The healing properties of these medicinal plants and herbs were well accepted by our ancestors and nowadays also being scientifically proven as well (Sharma et al., 2014). Extracts or phytoconstituents derived from various parts of medicinal plants for prevention and cure of several diseases provide therapeutic modalities with broad spectrum antimicrobial activities against various pathogenic microorganisms (Suck, 1989; Gilani and Atta-ur-Rahman, 2005; Khan et al., 2006; Cyetayo and Cyetayo, 2006; Sudhakar et al., 2006; Kumar et al., 2013a, Vashney et al., 2012; Bhatia et al., 2013a, Sharma et al., 2014). In last few decades, there has been an upsurge in demand and delivery of various herbal products for multifaceted health benefits. In first world country like the United States, herbal remedies still continue as dietary supplements. A variety of herbal therapies have stood the test of time because of their efficacy and potency in the treatment of various bacterial infections with a few having scientific evidences of significant usefulness (Blumenthal et al., 1998; Bisset and Wicht, 2001, Mahima et al., 2012; Tiwari et al., 2012; Rahal et al., 2014b).

Currently, the focus on herbal therapy is not only in third world developing countries but also in developed countries. The studies regarding their assessment of risks and benefits, identifying pharmacologically active components/principles and biological activities; scientific validation and revealing ethnomedical values are going on worldwide with regards to thousands of herbs and their extracts, preparations and products which altogether would play vital role in perpetuating, propagating, popularizing and promoting the wider usages of drugs/medicines based on herbs. Active research on various aspects of herbs is being carried out in Nigeria, Rawanda, Maltese Islands, India, Cuba, Eastern part of African subcontinent, China, European countries, middle east, mediterranean and other countries (Odebiyi and Sofowora, 1978; Lanfranco, 1992; Vlister et al., 1995; Faby et al., 1998; Barrett et al., 1999; Blatt et al., 2002; Cano and Volpato, 2004; Arora and Kaur, 2007; Basha and Sudarsham, 2011; Mizaei-Aghsaghali, 2012; Mahima et al., 2012; Midirullah et al., 2014).

Improper diagnosis of any microbial infection leads to untargeted therapy and indiscriminate use of allopathic drugs, giving way to the emergence of antimicrobial drug resistant pathogens (Kumar et al., 2010; Tiwari et al., 2013a). Thus, due to exhaustive and indiscriminate use of antibacterials the phenomena of antibacterial therapy failure or ineffectiveness has evolved many drug resistant
pathogens. Amongst these, multidrug resistant pathogenic microorganisms are the concealed enemies to the mankind and animals (Tiwari et al., 2013a). The development of antimicrobial resistance among the bacteria is an important issue for treatment of infectious diseases in man as well as animals. Although, there is progress in research and development of new and improved salts of antimicrobial agents but the bacteria are developing resistances to these antibiotics at a higher pace from it. Antibiotic sensitivity testing of the currently available bacterial agents, isolated from different cases of infections, revealed resistant strains even against multiple drugs (Okeke et al., 1999; Levy, 2002; Alp, 2007; Tiwari et al., 2013a).

Nowadays, various risks factors have been identified which interfere in maintaining a sound health and predispose to several diseases and disorders/ailments, thus increasing the sufferings of both humans and animals. Some of these comprise of various stresses, immune pressures, environmental changes especially the global warming effects; increasing population, changing life styles and food habits and biodiversity changes. Common health problems being flared up due to these predisposing factors in humans are diabetes, blood pressure, heart ailments, arthritis, organ failures, increased incidences of tumors/cancers, immunodepression and obesity. Apart from these, both infectious and non-infectious diseases/disorders are showing an ever increasing trend both in humans and their companion animals along with threats of zoonotic pathogens and even pandemics (Taylor et al., 2001; Jones et al., 2008; Myers and Patz, 2009; Dhma et al., 2013a; Tiwari et al., 2013a; Dhma et al., 2014; Verma et al., 2014a, b).

In the present scenario of increasing emergence of drug resistance on behalf of continuously evolving resistant microbial pathogens; injudicious use of antimicrobials especially the antibiotics, residual toxic effects of drugs in food and in lieu of emerging and re-emerging pathogenic strains, many novel and safer therapeutic modalities are being explored. These approaches include a combination of immunological, biotechnological and molecular methods. Some of these comprise of bacteriophages, enzyme inhibitors, virophages, mycopephages, apoptins, cytokines, monoclonal antibodies, egg yolk antibodies, stem cells, si-RNA, nanomedicines, nutritional immunomodulation, probiotics, antioxidants, panchgavya elements, phytonutrients, fruits and vegetables and herbal remedies; which altogether could be of great help in curbing emerging and evolving pathogenic threats and zoonotic concerns (Natesan et al., 2006; Chah et al., 2006; Chakravarthi and Balaji, 2010; Shirley et al., 2011; Gokulakrishnan et al., 2012; Dhma et al., 2008, 2013c, d, e, f; 2014; Amarpal et al., 2013; Mahima et al., 2012, 2013a, b; Tiwari et al., 2012, 2013b, 2014a, b, c; Karthik et al., 2014; Rahal et al., 2014b). Out of all these alternative and novel therapies, traditional homeopathic and ayurvedic/herbal therapies are again gaining much momentum and particularly the herbal therapy is attaining wide popularity and spreading up with a good pace (Mahima et al., 2012; Dhma et al., 2013b).

Medicinal plants and herbs, the ancient period magical chemotherapeutic drugs and natural treasure to prevent or cure various diseases and ailments are very interesting and play crucial role in safeguarding various health related issues (Farnsworth et al., 1985; Ernst, 2000; Krishnan, 2006; Zampini et al., 2009; Umashanker and Shruti, 2011; Mitraei-Aghsaghal, 2012; Mahima et al., 2012; Dhma et al., 2013e, f; Kumar et al., 2013a; Tiwari et al., 2012, 2013b, 2014d, e). Nowadays, herbal remedies are also getting popularity in providing a viable and safer alternative to prevent and treat cancers (Wargovich et al., 2001; Agarwal et al., 2011; Mahima et al., 2012; Tiwari et al., 2012, Dhma et al., 2013f; Yarney et al., 2013). Being a valuable treasure of natural medicines, these are gaining much attention with their demand increasing day by day; owing to having several advantages over other medicinal systems including of allopathy. These possess multi-dimensional health benefits and show high utility in alternative and complementary medicinal systems as effective prophylactic and therapeutic regimen. Herbs also help in maintenance and boosting of general health condition, serve as general tonics and have wider practical applications at global level. Though variations in morphology, phytoconstituents, active principles and genetic make occur but altogether the wonder world of herbs forms a bunch of safer (show lesser or no side effects), cheaper/cost-effective and easily available nature’s medicines (Dhar et al., 2006; Kumar et al., 2007; Mahima et al., 2012). Such valuable therapeutic alternatives need to be explored fully, tested, standardized, validated and finally be used optimally for the cause of mankind.

Many studies have been performed at various places to know the exact therapeutic mechanisms and sensitivity patterns of herbal products against specific food-borne pathogens and bacterial agent of various infections/ailments in different species of animals (cattle, buffalo, goat, horse, camel, dog and avian species) (Rota et al., 2004; Kumar et al., 2010, 2011, 2013a; Aderetutu et al., 2011; Mahima et al., 2012; Vashney et al., 2012; Bhatia et al., 2013a; Sharma et al., 2014). Many developed as well as developing nations including India are rich source of plants used for medicinal purposes.
(2500 species of plants found) and exponential growth has been observed in the application of herbal medicines while treating bacterial infection. In India, a long list of medicinal plants and herbs have been reported to possess high utility against several diseases and disorders including of cancers and tumours and act as potent antimicrobial agents. These medicinal plants are available in the treasuries of herbal medicines such as Ashwagandha, Amla, Tulsi, Heeng, Arjuna, Aloe vera, Garlic, Turmeric, Ginger, Giloy, Shatavari, Neem, Guduchi, Pipali, Kiwifruit, Tut, Kamala, Tea tree, Palashlata, Kokilaksha etc., (Archana et al., 2011; Umashanker and Shruti, 2011; Mizaai-Aghsaghali, 2012; Mahima et al., 2012; Dhami et al., 2013f; Kumar et al., 2013b, 2013c; Yakout et al., 2013; Midrarullah et al., 2014; Tiwari et al., 2012, 2013b, 2014d, e). These are being used for human and animal health benefits since long back and are reported to have a therapeutic role in curing superficial wounds and other disease conditions due to bacteria (Faagali et al., 1997; Parekh and Chanda, 2007a, b; Mahima et al., 2012; Tiwari et al., 2013b, Rahal et al., 2014b). Moreover, an array of herbal remedies is in constant use as folk medicines used by the various tribal communities of India and other countries both orally and topically against various bacterial agents including of multi-drug resistant bacteria. Some of the best known examples of such plants/herbs are Calotropis procera, Acacia nilotica, Cassia fistula, Tridax procumbens, Hypericum japonicum, Trigonella foenum-graecum, Heliotropium indicum, Argemone mexicana, Termesia chebulica, Terminelia balsarica, Plumbago zeylanica, Chlorophyllum borivium, Moringa oleifera, Acalypha indica, Hypericum papuanum, Hypericum perforatum, Cissus quadrangularis, Ocimum gratissimum, Ocimum sanctum, Ageratum conyzoides, Soncus asper and many others (Shafiqur et al., 2007; Kumar et al., 2011; Mahima et al., 2012; Vashney et al., 2012; Bhatia et al., 2013a, b; Upadhya et al., 2013, Sharma et al., 2014).

The traditional system of medicines is supposed to evolve around 60,000 years ago, incorporating usage of plants and herbs for therapeutic purposes. However, lacking of proper documentation has restricted the use of herbal healers in the urban society even though their ethnobotanical prospection and ethnopharmacological aspects are well proven (Rigat et al., 2009; Chakraborty and Pal, 2012; Rahal et al., 2014b). The emergence of drug resistance as well as modern developments in therapeutic field have revived the use of traditional medicines and the plant-based remedies as potential source of therapeutic aids in health systems all over the world for both humans and animals (Macfay and Cline, 1990; Rios and Recio, 2005; Mahima et al., 2012). Apart from treating infectious and systemic diseases, topical botanical/herbal application is equally effective against specific conditions of ear infections, wounds, burns and skin irritations. Topical applications like pulifs/bandages of herbs and various sprays have advantage of being easy to apply, these gives soothing effects and immediate relief from superficial infections, burns, skin irritations and wounds due to bacterial etiology (Bowler et al., 2001; Tiwari et al., 2013b; Arun et al., 2013). Interestingly, 65% of the population of the world has incorporated methodology of medicinal agents involving plants into their primary health care modality as per the World Health Organization (WHO) and today, the plants/herbs constitute 25% of all the drugs prescribed (Farnsworth et al., 1985; Raskin and Ripoll, 2004; Mahima et al., 2012, Rahal et al., 2014b). The use of herbal medicine has proved positive upshot, being very encouraging and has a strong potential to be widely used in traditional health care around the globe (Farnsworth and Bingel, 1977; Newall et al., 1996; Ramalivahan, et al., 2010).

The present manuscript is a very exhaustive and comprehensive compilation well supported with evidence based updated information narrating the potential role and useful applications of several medicinal plants and herbs in treating and combating important bacterial pathogens and various types of bacterial diseases. It systematically covers most of the salient beneficial antibacterial applications of traditional herbs and novel phytomedicines, from ancient periods to modern usages. A special focus has also been given to various important phytocomstituents present in various herbs, their biological activities and pharmacological principles, mechanism of actions along with useful antibacterial effects with classical examples. Due emphasis has been made regarding current scientific approaches and advancements along with future perspectives of herbal remedies with a vision to counter the emerging problem of antimicrobial resistance by exploring rich heritage of medicinal herbs found in nature. The review will certainly help in promoting and popularizing medicinal plants and herbs as potent alternatives to conventional antimicrobials, particularly in the event of emerging MDR bacterial infections. It will be highly useful for researchers, biologists, pharmacists, medical and veterinary professionals, drug and pharmaceutical industries, animal sector (livestock and poultry industry), medicinal practitioners and the common man too. Global usages of herbs as alternative and complementary medicines to various antimicrobials could also help obtain optimum production from animals apart from protecting health of
both animals and humans. It can also take care of various public health concerns associated with food safety issues viz., antibiotic residual effects in animal products (milk, meat) and zoonotic threats which would altogether help in safeguarding health of humans and their companion animals in a holistic way.

IMPORTANT BACTERIAL PATHOGENS AND EMERGING ANTIBIOTIC RESISTANCE

Important bacterial diseases affecting animals and thereby affecting the socio-economic status of any country include anthrax (Bacillus anthracis); haemorrhagic septicaemia (Pasteurella multocida); Brucellosis (Brucella abortus, B. melitensis); tuberculosis (Mycobacterium bovis); Johne’s disease (Mycobacterium avium subsp. paratuberculosis); listeriosis (Listeria monocytogenes); leptospirosis (Leptospira); campylobacteriosis (Campylobacter spp.); glanders (Burkholderia mallei); swine erysipelas (Erysipelothrix rhhuysopathiae); actinomycosis (Actinomyces bovis); actinobacillosis (Actinobacillus lignieresii), black quarter, mastitis and others (Jones et al., 2008; Deb et al., 2013; Dham et al., 2013b, 2014; Singh et al., 2014; Verma et al., 2014a, b). Important bacterial diseases of poultry are bacillary white diarrhea (Salmonella pullorum); fowl typhoid (Salmonella gallinarum); fowl cholera (Pasteurella multocida); Escherichia coli infections; infectious coryza (Haemophilus paragallinarum); tuberculosis (M. avium complex); chronic respiratory disease (Mycoplasma gallisepticum); avian sriphraeiosis (Borreia anatrcina) and psittacosis (Chlamyophilla psittaci) (Saif et al., 2003; Kataria et al., 2005; Kabir, 2010; Dham et al., 2011, 2013b, 2014). Important infectious diseases affecting humans include tuberculosis (M. tuberculosis); Plague (Yersinia pestis); campylobacteriosis; salmonellosis; E. coli infections; mud fever (Leptospira); whooping cough (Bordetella pertussis); Ornithosis (Chlamydia psittaci); sore throat (Streptococcus sp.); Staphylococcus (Staphylococcus aureus); tetanus (Clostridium tetani) and others. Apart from these, several zoonotic bacterial diseases pose significant public health concerns viz., anthrax (Bacillus anthracis); plague (Yersinia pestis); glanders (B. mallei); Lyme disease (Borreilla burgdorferi); tuberculosis (M. bovis); salmonellosis (Salmonella sp.); campylobacteriosis (Campylobacter jejuni); colibacillosis (E. coli); leptospirosis (Leptospira); listeriosis (Listeria monocytogenes); chlamydiosis/psittacosis (Chlamyophila psittaci); Q fever (Coxella burnetii); tularacemia (Francisella tularensis) and botulism (Clostridium botulinum) (King, 2004; Kahn et al., 2007; Wolfe et al., 2007; Myers and Putz, 2009; Cascio et al., 2011; Verma et al., 2012, 2014a, b; Dham et al., 2013b, g, h, i, j, k, 2014).

Interaction of bacterial pathogens and human or animal host is a continuous process. A series of events including the interactions of virulence attributes of bacterial pathogens and protective mechanism of host cellular system occur before the onset of any infection or disease. Proper balance of both is thus essentially required to keep host healthy and free from infections. Pathogenic microorganisms (viruses, bacteria, fungi) are the concealed enemies of animals and mankind and can enter through various routes including air, water and food and are well known for their zoonotic concerns (Dham et al., 2013g, 2014; Verma et al., 2014a). Among these, bacterial agents are very prevalent viz., Staphylococcus species (S. aureus, S. albus, S. citrurs, S. intermedus), Streptococcus sp., Bacillus coli, B. pyocyaneus, E. coli, Salmonella sp., Pseudomonas, Klebsiella, Aeromonas, Proteus sp., multi-drug resistant Acinetobacter and Proteus sp. and many others as narrated above (Miyasaki et al., 2010; Pratheepa et al., 2010, Tiwari et al., 2013a; Verma et al., 2014a). Bacterial infections are typically caused by colonizing normal flora under certain circumstances and also by antibiotic resistant bacteria such as MRSA (Methicillin Resistant S. aureus), CA-MRSA (Community Acquired Methicillin Resistant S. aureus), VREF (Vancomycin Resistant Enterococcus faecalis) and other drug resistance bacteria. Superficial infections are primarily caused by aerobic micro-organism such as Staphylococcus, Streptococcus (Flesh eating bacteria), Vibrio or Aeromonas species, Corynebacteria sp., Pseudomonas aeruginosa, Pasteurella multocida, Erysipelothrix species but deeper areas may also be infected with anaerobic pathogens such as Bacteroides and Clostridium species. Bacterial skin infections which are common in small animal and veterinary practice, most frequently involve Staphylococcus intermedus apart from E. coli and Proteus sp., S. intermedus which is a normal resident in the nasal cavity, oropharynx and the perianal region of animals. It can be a transient resident in other sites especially during trauma and is probably transferred to these sites from the oral and anal mucosa during grooming. P. multocida is another principal microbial agent especially found in subcutaneous abscesses in cats. Many other pathogens play crucial role in different disease initiations and applications of herbal preparations not only help in preventing their ill effects but also cure animals from many of such ailments (Mahma et al., 2012; Tiwari et al., 2012; Mizaci-Aghasghali, 2012;
Midrurullah et al., 2014). Gram negative bacteria are generally the secondary invaders which are controlled by therapy effective against *Staphylococcus Pseudomonas* is difficult to eliminate and requires specific therapy (Yah et al., 2004). Enteric or diarrheal infections are another quandary of major public health concerns in developing countries adding to the death toll of many million patients and other economic losses annually. Enteric bacteria mainly of *Salmonella* sp., *E. coli*, *Campylobacter* sp., *Shigella* sp., *Proteus* sp., *Klebsiella* sp., *Arcobacter* sp., *L. monocytogenes*, *Clostridium perfringens*, *Cl. botulinum*, *Yersinia enterocolitica*, *Pseudomonas* sp., *S. pneumoniae*, *S. agalactiae*, *Mycoplasma* sp., *Vibrio cholerae*, *Bacillus cereus* and *S. aureus* act as major etiological agents of sporadic as well as epidemic diarrhea (Rani and Khullar, 2004; Akins, 2005; Anbumani et al., 2006; Miyasaka et al., 2010; Pratheepa et al., 2010; Dhama et al., 2013g).

Due to emerging drug resistant bacterial strains, nowadays many bacterial diseases do not respond to prescribed antibiotic treatments options and thus infectious diseases caused by various bacterial pathogens are flaring up and becoming uncontrollable (Tiwari et al., 2013a). The most common antibiotic-resistant organisms include *E. coli*, *Salmonella*, *Shigella*, *Klebsiella*, *Proteus*, *Vibrio cholerae* *Campylobacter* sp., *Enterococci* and others. Of these, few pathogens have become Multidrug Resistant (MDR) in nature viz., *Methicillin-Resistant Staphylococcus aureus* (MRSA), Vancomycin-Resistant Enterococci (VRE) among Gram positive bacteria; *Klebsiella pneumoniae* Carbapenemase (KPC), Extended-spectrum β-lactamase (ESBLs) producing Gram-negative bacteria; *S. enteritica* serovar Typhimurium DT 104 (ACSSuT-phenotype); Imipenem-resistant or MDR organisms *Acinetobacter baumanii*, *A. baumannii*, *Pseudomonas aeruginosa*, *Bacteroides* sp.; Cildamycin-resistant *Clostridium difficile*, Streptomycin-resistant *Thermus thermophilus*; *E. coli* resistant to multiple fluoroquinolone; *Mycobacterium tuberculosis* revealing resistance to isoniazid, rifampin (Levy and Marshall, 2004; Tiwari et al., 2013a; WHO, 2013). MDR, Extremely drug-resistant (XDR) strains and/or Totally Drug Resistant (TDR) strains include *Staphylococcus aureus*, *tuberculosis bacterium* and *Pseudomonas aeruginosa*. Thus many antibiotics like penicillin, methicillin, tetracycline, erythromycin, fluoroquinolone, kanamycin, chloramphenicol, cefatxime, isoniazid, rifampin etc., are not having much values in treating bacterial diseases effectively as they were of high use in earlier times (Tiwari et al., 2013a). Some specific drugs/antibiotics viz., DDT, diclofenac, paracetamol, aspirin, analgin, furazolidone, piperazone, nitrofurazone, penicillin as skin or eye ointments, tetracycline as liquid oral preparation of drug and many other drug combinations have been banned in many countries. It is because of their side effects, residual toxicity and related food safety concerns. Also, the use of penicillin, sulphonamides and many other drugs has raised public health and industrial issues. The resistant bacteria in animals can be transmitted to humans via consumption of improper/undercooked contaminated meat, milk or eggs, close or direct contact with animals or through the environment and thus poses significant food safety concerns and public health issues. Altogether, the ever emerging issue of antibiotic resistance has posed an alarming public health threat worldwide and increased the global worries, for which purpose solutions are being thought of including of finding alternative and complemenary therapeutic modalities (Byarugaba, 2004; Levy and Marshall, 2004; Zhang et al., 2006; Amirov, 2009; Yeh et al., 2009; Mahima et al., 2012; Dhama et al., 2013c; Tiwari et al., 2013a; WHO, 2013).

**HERBAL REMEDIES TO COUNTER BACTERIAL INFECTIONS**

The plant world is an immense store of pharmacologically active chemical compounds which exist as secondary phytoconstituents. The beneficial medicinal effects of plant materials typically result from the combinations of secondary products present in the plant. The medicinal actions of plants are unique to particular plant species or a related group (Archanas et al., 2011; Umashanker and Shruti, 2011; Mahima et al., 2012; Midrurullah et al., 2014; Rahal et al., 2014b). This concept is consistent with the fact that the combinations of secondary products in a particular plant are often taxonomically distinct. The secondary products can have a variety of functions in plants at the cellular level as plant growth regulators, modulators of gene expression, in signal transduction and also have protective actions in relation to abiotic stresses (Rahal et al., 2014c). So, it is likely that their ecological function may have some bearing on potential medicinal effects for humans and animals as well. Since, ancient times, antimicrobial activity of indigenous herbs and their essential oils have been exploited to promote human and animal health (Shelef, 1983; Zaika, 1988; Beuchet and Golden, 1989; Juven et al., 1994; Chang, 1995; Archanas et al., 2011; Sant’Ana, 2011; Mizaee-Aghsaghali, 2012; Midurullah et al., 2014). For the last one decade, many a medicinal plant extracts have
been developed and proposed for use in human and animal food as natural antimicrobials (Del Campo et al., 2000; Hsieh, 2000; Hsieh et al., 2001; Mahima et al., 2012; Rahal et al., 2014b). In the role of secondary products as defense chemicals, many phytoconstituents remain as a mixture of chemicals having additive or synergistic effects at multiple target sites. These phytoconstituents not only ensure effectiveness against a wide range of pathogens but also decrease the chances of these micro-organisms to develop resistance or immune evasion mechanisms (Rahal et al., 2014c). Such non-nutrient phytochemicals today form an important component of our routine feeding menu as vegetable or fruits and yet go unnoticed (Mahima et al., 2013a, b; Rahal et al., 2014b). With an increasing focus on the health care management using natural products, these plants and their constituents are increasingly being recognized as potential health promoters. These have been found useful in reducing the risks of various infectious and systemic diseases including of cardiovascular diseases, blood pressure problems, atherosclerosis; ameliorating various stresses and help maintain a sound health (Mahima et al., 2012; Rahal and Kumar, 2014).

**Antibacterial mechanisms of medicinal plants and herbs:** The antibacterial activities of herbs are multi fold and depend upon the phytoconstituents, concentration of phytoconstituents/phytochemicals and bioactive principles and their synergistic as well as antagonistic actions (Archana et al., 2011; Umashanker and Shruti, 2011; Miziaei-Aghsaghal, 2012; Mahima et al., 2012; Midrarullah et al., 2014). These phytochemicals include flavonoids, steroids, β-carotene, anthocyanins, anthraquinones, glycosides, coumarins, alkaloids, saponins, tannins, phenolic acids alkaloids, gallic acid and others (Kwon et al., 2000; Miyazaki et al., 2005; Islam, 2008; Pochapski et al., 2011; Sandhya et al., 2011; Mahima et al., 2012; Bhatia et al., 2013b; Kumar et al., 2013c; Sharma et al., 2014). Various mechanisms of action and antibacterial abilities of herbal remedies relies on their several beneficial properties viz., immunomodulatory nature with enhancement of both humoral and cell mediated immunity as well ameliorating stress and immunosuppression; cytokine regulation; anti-inflammatory, antioxidative and inhibiting pathogens by a variety of pathways (Archana et al., 2011; Miziaei-Aghsaghal, 2012; Mahima et al., 2012; Midrarullah et al., 2014; Rahal et al., 2014b). Many herbs have anti-oxidative potential by counteracting free radicals or metabolites produced during various biochemical pathways (Barreto et al., 2007; Moraes et al., 2010; Rufino et al., 2009, 2010; Rahal et al., 2014c). A vast number of herbal plants show anti-inflammatory action by selective inhibition of cyclooxygenase-2, 5-lipoxygenase, glutathione S-transferase and thus inhibiting the prostaglandin biosynthesis. Several herbs decreases the production of of inflammatory agents (histamine, bradykinin, serotonin), enhance activity of cortisol and augments blood circulation which help removing bacterial toxins out of the body (Nahrstedt et al., 2006; Rahal et al., 2014c). Certain plants contain vitamin C and carotenoids which have been found to augment both humoral and cell-mediated immune function, thereby reducing risk of infectious by enhancing the antigenic surveillance of the immune system (Bendich, 1989; Henson et al., 1991; Ringer et al., 1991; Mahima et al., 2012). Immunomodulation of most of herbal extracts are governed by cytokine regulation as well as anti-inflammatory properties (Wildfeuer and Mayerhofer, 1994; Bhatia et al., 2013b; Kumar et al., 2013c; Dhama et al., 2013e; Sharma et al., 2014). Certain plants facilitate proliferation of CD4 T-helper and B type immune cells. Others have been found beneficial in blocking bacterial adherence to different body cells thus help preventing the infection, blocking NF-κB pathway and the metagenic responses in infected cells; causing damage to cell membrane with loss of electrolytes and intracellular contents leading to bacteria death; downregulating the synthesis of LasA protease, LasB elastase and AHL molecules which inhibits the bacterial pathogenesis phenomenon by quorum sensing (Ruberto et al., 2000; Joc et al., 2004; Lee et al., 2006; Choi, 2008; Akram et al., 2010; Kang and Min, 2012; Yoo et al., 2012; Diao et al., 2014). Steroidal alkaloids and steroidal lactones present in herbs enhance engulfing activity of macrophages, increases the activity of white blood cells and other immune cells which in turn enhances their antimicrobial potentials (Gunning, 1999; Govindarajan et al., 2005; Owais et al., 2005; Tiwari et al., 2014d). All these factors decide the ultimate effect on host and pathogens and remedial effects of various herbs. Such mechanisms of actions, nature of phytoconstituents and potential antibacterial role/applications of many well established herbs and medicinal plants have been briefly enlisted in Table 1 and depicted in Fig. 1.

Alternative/traditional medicines are becoming progressively more popular and worth to overcome many multi-resistant organisms like as seen with potent efficacy of herbal extracts against multi-drug resistant Acinetobacter baumannii (Miyazaki et al., 2010; Vashney et al., 2012; Sharma et al., 2014). Such activities of plant extracts are mainly observed due to the presence of saponin, tannins, alkaloids, anthraquinone and cardiac
<table>
<thead>
<tr>
<th>Scientific name</th>
<th>Common name</th>
<th>Pharmacologically Active phytoconstituents</th>
<th>Biochemical class</th>
<th>Type of extracts</th>
<th>Antibacterial activity against</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Acorus calamus</em></td>
<td>Bach, sweet flag, calamus, vasa manju</td>
<td>Beta-arumone, eugenol</td>
<td>Phenylpropanoids</td>
<td>Crude methanolic extracts; 1,2-dimethyl-lindoline, linalool, linalene, acid methyl ester, (E)-phytol, polysaccharides, alkaloids, saponins, organic acid</td>
<td><em>S. albus</em>, <em>B. subtilis</em>, <em>S. typhimurium</em>, <em>S. dysenteriae</em>, <em>E. coli</em>, <em>S. aureus</em>, <em>Bacillus subtilis</em>, <em>E. coli</em></td>
<td>Phengpischarit et al. (2005)</td>
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<tr>
<td><em>Allium sativum</em></td>
<td>Garlic, laun, dasan, veili Poondu</td>
<td>Organosulfur compounds</td>
<td>Methanolic and aqueous extracts</td>
<td><em>Bacillus cereus</em>, <em>Staphylococcus aureus</em></td>
<td>Martinez and Baquer (2002), Grace et al. (2008), Alemdar and Aghashti (2009), Ashiban et al. (2012), Misra et al. (2009), Malabahyan et al. (2013), Vidyalakshmi and Ananthi (2013)</td>
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<tr>
<td><em>Aloe vera</em></td>
<td>Guarpatta, Ghurita kumara, Star cactus, Barbados, Kutrazhai</td>
<td>Lates, Glucomannan, acemannan, mannose derivatives, hemicellulose, carboxypeptidase, salicylate, Alom, 7-Coumaric acid, aldopentose, calcium oxalate</td>
<td>Complex mixture of polysaccharides and hydrocyanic acid</td>
<td>Aqueous, ethanol and methanolic extracts</td>
<td><em>Corynebacterium</em>, <em>Salmonella</em>, <em>Streptococcus</em>, <em>S. aureus</em></td>
<td>El-Chaghaby et al. (2014)</td>
</tr>
<tr>
<td><em>Andrographis paniculata</em></td>
<td>Charita, kalmegh</td>
<td>Androgrophiolide, deoxy andrographolide, tannins, andrographolide, flavonoids and saponins</td>
<td>Diterpene lactones</td>
<td>Aqueous, ethanol and methanolic extracts</td>
<td><em>Bacillus cereus</em>, <em>Staphylococcus aureus</em></td>
<td>El-Chaghaby et al. (2014)</td>
</tr>
<tr>
<td><em>Arumona squamosa</em></td>
<td>Siphal, custard apple, sugar apple</td>
<td>Squamosamide, acetogenin</td>
<td>Polyketide natural products</td>
<td>Acetone, boiling water, methanol and ethanolic extracts from the leaves</td>
<td><em>B. cereus</em>, <em>B. subtilis</em>, <em>S. aureus</em>, <em>P. aeruginosa</em>, <em>E. coli</em></td>
<td>Balachandran et al. (2012), Teyeb et al. (2012)</td>
</tr>
<tr>
<td><em>Astragalus membranaceus</em></td>
<td>Astragalus</td>
<td>Astragalosides, Liquiritigenin, calyosin, calystegin 7-O-D-glucoside, formononetin, formononetin 7-O-δ-D-glucoside (6), daidzein, daidzin 7-O-δ-D-glucoside, methylisoflavone, isomucronulat</td>
<td>Triterpenoids, saponins flavonoids</td>
<td>Methanolic and aqueous extracts from the roots</td>
<td><em>E. coli</em>, <em>S. enteritidis</em>, <em>Streptococcus sp.</em></td>
<td>Balachandran et al. (2012), Teyeb et al. (2012)</td>
</tr>
<tr>
<td><em>Azadirachta indica</em></td>
<td>Neem, holy tree, vembu</td>
<td>Azadirachtin, nimbin, gedunin, gallic acid, catechin, NS-II peptidoglycan</td>
<td>Limonoid group, Phenolic acid, tannins</td>
<td>Aqueous, methanolic and ethanolic extracts from seed, neem oil, dried root</td>
<td><em>Campylobacter jejuni</em>, <em>E. coli</em>, <em>K. pneumoniae</em>, <em>P. aeruginosa</em>, <em>S. typhi</em></td>
<td>Jeun et al. (2007), El-Mahmood et al. (2016), Koona and Budina (2011), Tiwari et al. (2014)</td>
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<tr>
<td><em>Brassica campestris</em></td>
<td>Mustard, sarsaun</td>
<td>Glucosinolates and steroids</td>
<td>Goiogenous glycosides</td>
<td>Ethanol, petroleum ether, methanolic, ethyl acetate extracts from root, stem and leaves</td>
<td><em>S. aureus</em>, <em>B. cereus</em>, <em>P. aeruginosa</em>, <em>E. coli</em>, <em>Staphylococcus epidermidis</em></td>
<td>Agrawal et al. (2013)</td>
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<tr>
<td><em>Calotropis gigantea</em></td>
<td>Akanda</td>
<td>Calatropin, gigantin, 2,4-bis(1,1-dimethylpropyl)-, Methyl tetradecanoate, Bicyclo[3.1.1]heptane, 2,6,6-trimethyl-, (16,25,58), Hecatadecanoic acid</td>
<td>Cardiac glycoside, phenols, alkaloids, tannin, quinines</td>
<td>Methanolic extract and its chloroform and petroleum ether fraction from the root bark</td>
<td><em>Sarcina lutea</em>, <em>Bacillus megaterium</em>, <em>P. aeruginosa</em>, <em>B. subtilis</em> and <em>Staphylococcus</em></td>
<td>Alam et al. (2008), Anitha et al. (2014)</td>
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<tr>
<td>Scientific name</td>
<td>Common name</td>
<td>Pharmacologically Active phytoconstituents</td>
<td>Biochemical class</td>
<td>Type of extracts</td>
<td>Antibacterial activity against</td>
<td>References</td>
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<tr>
<td>Camellia sinensis</td>
<td>Green tea</td>
<td>Catechin</td>
<td>Flavonoid</td>
<td>Methanolic and aqueous extracts from seeds and leaves</td>
<td>Shigella sp., Vibrio sp., S. mutans, S. aureus</td>
<td>Matsubara et al. (2003)</td>
</tr>
<tr>
<td>Cassia angustifolia</td>
<td>Senna</td>
<td>Rhein</td>
<td>Anthraquinone</td>
<td>Aqueous extracts from leaves and roots</td>
<td>B. subtilis, E. coli, S. aureus</td>
<td>Kroupashree et al. (2008)</td>
</tr>
<tr>
<td>Catharanthus roseus</td>
<td>Periwinkle, nityakalyani, sadabahar, burnamasi, ushurthali</td>
<td>Vinblastine, vincristine, raubicine, reserpine, serpentine</td>
<td>Alkaloids</td>
<td>Ethanol, methanolic extracts from leaf, stem, flower and root</td>
<td>B. subtilis, E. coli, S. aureus, S. pyogenes, P. aeruginos</td>
<td>Goyal et al. (2008), Govindasamy and Srinivasan (2012)</td>
</tr>
<tr>
<td>Curcuma longa</td>
<td>Turmeric, haldi, Indian saffron, yellow ginger</td>
<td>Zingiberene, curcumin, α and β-turmerone</td>
<td>Monocyclic sesquiterpen</td>
<td>Ethyl acetate, methanol and water extracts</td>
<td>Staphylococcus sp., Klebsiella sp., E.coli, Streptococcus sp., Pseudomonas sp., Salmonella sp., Vibrio sp</td>
<td>Kim et al. (2005), Fazaeli et al. (2012)</td>
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<tr>
<td>Datura alba</td>
<td>Vellamuttai, kaladhatu</td>
<td>Hyoscyamine, hyoscine, meteloidine</td>
<td>Tropane alkaloid</td>
<td>Ethanolic extract from leaves</td>
<td></td>
<td>Qureshi et al. (2011)</td>
</tr>
<tr>
<td>Echinacea purpurea</td>
<td>Indian comb, purple coneflower</td>
<td>Alkaloids, echinacoside, arabinogalactan, caffeic acid, chloric acid</td>
<td>Natural phenols</td>
<td>Aqueous and ethanolic extracts of leaves</td>
<td>E. coli, K. pneumonia, S. aureus</td>
<td>Gunning (1999)</td>
</tr>
<tr>
<td>Foeniculum vulgare</td>
<td>Fennel, finocchio, saunf</td>
<td>Anethole, essential oils, trans-anethole, estragole</td>
<td>Pherylpropene</td>
<td>Essential oil obtained from seeds</td>
<td>Staphylococcus albus, B. subtilis, S. Typhimurium, Shigella dysenteriae, E. coli</td>
<td>Roberto et al. (2000), Diao et al. (2014)</td>
</tr>
<tr>
<td>Glycyrrhiza glabra</td>
<td>Liquorice</td>
<td>Glycyrrhizic acid, glibridin, sterine</td>
<td>Isoflavonoid</td>
<td>Ethanol, methanolic extracts from leaves and root extracts</td>
<td>B. subtilis, Enterococcus faecalis, K. pneumonia, P. aeruginosa, S. aureus, E. coli</td>
<td>Irani et al. (2010), Sedghshian et al. (2012)</td>
</tr>
<tr>
<td>Hydrastis canadensis</td>
<td>Goldenseal</td>
<td>Berberine, Hydrastine</td>
<td>Alkaloids</td>
<td>Methanolic and aqueous extracts from leaves and root extracts</td>
<td>M tuberculosis, B. subtilis, S. aureus, E. coli, Proteus vulgaris</td>
<td>Gentry et al. (1998), Sujana et al. (2013)</td>
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<tr>
<td>Mentha piperita</td>
<td>Peppermint</td>
<td>Menthol</td>
<td>Terpenoid</td>
<td>Ethanol, methanol, ethyl acetate, chloroform, hexane and petroleum ether extracts from the leaves</td>
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<tr>
<td>Scientific name</td>
<td>Common name</td>
<td>Pharmacologically Active phytoconstituents</td>
<td>Biochemical class</td>
<td>Type of extracts</td>
<td>Antibacterial activity against bacterial strains</td>
<td>References</td>
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<tr>
<td><em>Olea europaea</em></td>
<td>Olive oil</td>
<td>Hecanal, caffic acid, verbascoside, oleuropein, luteolin 7-O-glucoside, rutin, apigenin 7-O-glucoside, luteolin 4-O-glucoside</td>
<td>Aldehyde</td>
<td>Methanolic, ethanolic and aqueous extracts</td>
<td><em>Porphyromonas gingivalis, Actinobacillus actinomycetemcomitans, Propionibacterium acnes,</em> methicillin-resistant <em>S. aureus, B. subtilis, E. coli, S. marcescens</em></td>
<td>Lee et al. (2006), Choi (2008), Rathi et al. (2012), Usman et al. (2012)</td>
</tr>
<tr>
<td><em>Panax ginseng</em></td>
<td>Ginseng</td>
<td>Ginsenosides Panaxadiol, panaxatriols Ginsan</td>
<td>Steroid glycosides Saponins Acidic polysaccharide</td>
<td>Aqueous, ethanolic and chloroform extracts from the roots</td>
<td><em>P. aeruginosa, S. aureus, B. subtilis,</em> Micrococcus luteus, E. coli</td>
<td>Reddy et al. (2003), Singh et al. (2011)</td>
</tr>
<tr>
<td><em>Pieroliza kurroa</em></td>
<td>Kutakai, kuru</td>
<td>Kutkin, picroside I, lutinose, picroside, vanillic acid, D-mannitol, androside, apocynin, phenolic compounds, sterols, cucurbatins</td>
<td>Triterpenoids and iridoid glycosides</td>
<td>Methanolic and aqueous extracts from rhizomes</td>
<td><em>P. aeruginosa, S. aureus, B. subtilis,</em> Micrococcus luteus, E. coli</td>
<td>歩 (2012), Usman et al. (2012)</td>
</tr>
<tr>
<td><em>Piper longum</em></td>
<td>Pipali, Indian long pepper</td>
<td>Piperine, piperlongumine, pellitorine</td>
<td>Alkaloid</td>
<td>Ethyl acetate fraction</td>
<td><em>Mycobacterium tuberculosis, Bacillus subtilis,</em> S. aureus</td>
<td>Reddy et al. (2003), Singh et al. (2011)</td>
</tr>
<tr>
<td><em>Rosmarinus officinalis</em></td>
<td>Rosemary</td>
<td>Essential oil, rosmarinic acid, carnosic acid, carnosol, 12-methoxy-trans-carnosic acid, ursoic acid, oleanolic acid</td>
<td>Abietane, diterpenes</td>
<td>Ethanol, methanol and aqueous extracts from leaves</td>
<td><em>Salmonella Typhimurium</em></td>
<td>Bernardes et al. (2010)</td>
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<td><em>Salviae Montana</em></td>
<td>Savory</td>
<td>Carvacrol</td>
<td>Terpenoid</td>
<td>Aqueous, ethanolic extracts and essential oil</td>
<td><em>P. multocida, E. coli, B. subtilis, S. aureus</em></td>
<td>Zabair et al. (2011), Parasansari et al. (2012)</td>
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<tr>
<td><em>Solanum nigrum</em></td>
<td>Black nightshade, wonderberry, namathakali</td>
<td>Solasodine</td>
<td>Glyco-alkaloids</td>
<td>Ethanol and methanolic extracts of stem, berries and whole plant</td>
<td><em>P. multocida, E. coli, B. subtilis, S. aureus</em></td>
<td>Zabair et al. (2011), Parasansari et al. (2012)</td>
</tr>
<tr>
<td>Scientific name</td>
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<tr>
<td>Syzygium aromaticum</td>
<td>Caryophyllus, kiramba</td>
<td>Eugenol, eugenol acetate, 4 and 6-caryophyllene</td>
<td>Phenylpropanoids</td>
<td>Aqueous, ethanolic and methanolic extracts from whole clove</td>
<td>S. aureus, P. aeruginosa, E. coli</td>
<td>Pandey and Singh (2011)</td>
</tr>
<tr>
<td>Taxus brevifolia</td>
<td>Yew</td>
<td>(+)-thujadene, 4-(4'-hydroxyphenyl)-butan-2-one, 4-(4'-hydroxyphenyl)-trans-but-3-en-2-one</td>
<td>Complex mixture</td>
<td>Ethanolic extracts of heartwood and leaves</td>
<td>S. typhimurium, P. syringae, B. subtilis</td>
<td>Reddy et al. (2001), Erode et al. and Sener (2001)</td>
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<td>Terminalis arjuna</td>
<td>Arjun tree, neer maruthulu, kola, white Manuhah</td>
<td>Arjunic acid, arjunanin, β-stilbesterol, tannins</td>
<td>Triterpenoids</td>
<td>Methanolic and aqeous extracts stem bark and leaves</td>
<td>Methicillin-resistant Staphylococcus aureus</td>
<td>Sato et al. (1997), Chaudhari and Mengi (2006)</td>
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<td>Tinospora cardifolia</td>
<td>Gily, guduchi, amrita</td>
<td>Tinosporone, tinosporic acid, berberine, giloin</td>
<td>Alkaloids, diterpenoids, flavonoid, lignins</td>
<td>Aqueous, ethanol and chloroform extracts from the stem</td>
<td>S. aureus, Enterobacter faecalis, Serratia marcescens, E. coli, P. vulgaris, S. typhi</td>
<td>Jayachandran et al. (2003), Nagaprashanthi et al. (2012)</td>
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<tr>
<td>Uncaria tomentosa</td>
<td>Cats claw</td>
<td>Ochinine C, 5'-hydroxycoumarin A, dihydrocondraflavone B, pentacylic and tetracyclic oxindoles</td>
<td>Flavonoids</td>
<td>Ethanolic and aqueous extracts from leaves and root extracts</td>
<td>E. faecalis, S. aureus, Candida albicans</td>
<td>Cahnana-Vasquez et al. (2007), Herrera et al. (2010)</td>
</tr>
<tr>
<td>Vaccinium spp.</td>
<td>Blueberry</td>
<td>Fructose</td>
<td>Monosaccharide</td>
<td>Aqueous, ethanolic and methanolic extracts</td>
<td>E. coli</td>
<td>Ofek et al. (1996)</td>
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<td>Withania somnifera</td>
<td>Ashwagandhula, winter cherry, Indian Ginseng</td>
<td>Withanolides, Withaferin A</td>
<td>Steroidal alkaloids and lactones</td>
<td>Methanolic and ethanolic extracts from dried root and leaves</td>
<td>E. coli, S. enteritidis, Shigella, Campylobacter, P. aeruginosa, S. typhimurium</td>
<td>Owais et al. (2005), Tiwari et al. (2014)</td>
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<tr>
<td>Zingiber officinale</td>
<td>Ginger, adak</td>
<td>Citral, curcumin, Dehydrozingerone</td>
<td>Sesquiterpene</td>
<td>Ethanolic and aqueous extracts from rhizomes</td>
<td>Multi-drug resistant bacteria such as S. aureus, P. aeruginosa</td>
<td>Azu et al. (2007),</td>
</tr>
</tbody>
</table>
Fig. 1: Overview of the mechanism of actions and potential antibacterial role/applications of herbs

glycosides; suggesting possible antimicrobial effects with marked bacteriostatic but not bactericidal effect (Azu et al., 2007; Sharma et al., 2014). Similarly, many plant and herb species have been analyzed for phytochemical substances and their antibacterial activities (Mahima et al., 2012; Tiwari et al., 2012, 2014a, b). Berberine, a natural isoquinoline present in a number of plants viz., Coptis chinensis, Berberis vulgaris, Berberis lyceum and Hydrastis canadensis has been found to be active against S. aureus in vitro with Minimum Inhibitory Concentration (MIC) of 25.0 mg mL\(^{-1}\); which can be further potentiated by bioflavonoids. This antibacterial effect appears to be due to inhibition of a Multidrug Resistance (MDR) pump of S. aureus (Chi et al., 1991; Gentry et al., 1998; Haq et al., 1999; Stemitz et al., 2002). Another well known medicinal herb, Artemisia annua has been employed for assessing the presence of inhibitors of bacterial MDR resistance pumps. Flavones (chrysoplenol-D and chrysoplenein) from the plant possess weak growth inhibitory action which can be enhanced along with berberine (Stemitz et al., 2000). A petroleum ether extract of the aerial parts of Hypericum perforatum (St. John’s wort) has been found to be active against Gram positive bacteria especially MRSA. Hyperforin, a phloroglucon derivative, has got an excellent antimicrobial activity with a MIC value of 1.0 μg mL\(^{-1}\) against MRSA hyperforin (Reichling et al., 2001). Plants such as Aloe arborescens, A. striata and Psidium guajava possess significant antibacterial activities against strains of Salmonella, Shigella, Escherichia, Staphylococcus, Pseudomonas and Enterococcus. This reflect credence of their use in ethnomedicine against Multidrug Resistance (MDR) enteric pathogens; especially against S. enterica serotype Typhi followed by S. enterica serotype Typhimurium strains exhibiting Extended-Spectrum Beta-Lactamases (ESBLs) (Parekh and Chanda, 2007a; Bisi-Johnson et al., 2012). Similarly, different herbal and plant preparations play vital role in the prevention and cure of disease development mechanism (Mahima et al., 2012). The role and useful applications of herbal constituents against bacterial pathogens is multifaceted. The herbs may either influence the pathogenicity of the pathogen, improve the immune status of the host or may even modulate the microenvironment of the disease production site.
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Herbs affecting virulence of bacterial pathogens: Thymol and carvacrol (active ingredients that are present in thyme) produce their antibacterial action by penetration into the Gram negative bacteria (Helander et al., 1998). Juven et al. (1994) postulated that the ingredients which are actively present in thyme bind to the amine as well as hydroxylamine group of the membrane protein of bacteria resulting in lysis of bacterial cell. Examples of medicinal plants having activity against E. coli include essential oils extracted from anise (Pimpinella anisum), angelica (Angelica sinensis), basil (Ocimum basilicum), carrot (Daucus carota); celery (Apium graveolens), cardamom (Elettaria cardamomum), coriander (Coriandrum sativum), dill weed (Anethum graveolens), fennel (Foeniculum vulgare), oregano (Origanum vulgare), parsley (Petroselinum crispum) and rosemary (Rosmarinus officinalis); as tested during in vitro studies (Elgayyar et al., 2001; Mahady, 2005; Sharma et al., 2014).

In Asia, plants like Cassia tora, Calendula officinalis as well as Momordica charantia are well known for their wide range of antibacterial activities. In India, they have been used as folk remedy as decoctions as well as infusions. These herbs have been subjected to successive extraction using various solvents in order to evaluate their antibacterial activity against both Gram positive as well as Gram negative organisms (Bhatia et al., 2013a; Upadhyay et al., 2013, Sharma et al., 2014). S. aureus has shown an increasing pattern of development of resistance against the common antibacterial agents that are available at present (Upadhyay et al., 2013). The aqueous extracts of the seeds of Cassia tora as well as M. charantia and flowers of C. officinalis have been found to possess better antibacterial activity against bacteria in comparison to the petroleum ether/methanolic or ethanolic extracts (Christopher, 2005; Roopashree et al., 2008).

Herbs modulating the host factors: Any impairment in antioxidant defence mechanism of the host facilitates the instigation and growth of the micro-organisms (Nathan and Shiloh, 2000). The phagocytic killing, the primary defence system of the host, indicates a microbicidal role of Reactive Oxygen Species (ROS) and Reactive Nitrogen Species (RNS) (Halliwell and Gutteridge, 2007). These free radicals are produced from macrophages and neutrophils to combat the invading microbes. However, reactive species can also injure the host tissues (immunopathological changes) as well as observed during chronic inflammations leading to extensive tissue damage with a subsequent burst in oxidative stress (Serci and Fairen, 2009; Rahal et al., 2014c). The multicomponent flavoprotein NADPH oxidase which play vital role in inflammatory processes by catalyzing the production of superoxide anion radical (O2•−) and ROS, leads to cellular damage. This cellular damage in general leads to altered immune response to microbes and ultimately altered susceptibility to bacterial, viral and parasitic infections (Puertollano et al., 2011). There are many herbs which have counter active metabolites to act against free radicals directly or by modifying many biochemical pathways, indirectly. Like certain photochemicals have been found to augment both humoral and cell-mediated immune function. Vitamin C and carotenoids have beneficial effects on immune function, thereby reducing risk of infectious by enhancing the antigenic surveillance of the immune system (Bendich, 1989; Henson et al., 1991; Ringer et al., 1991). Steroidal alkaloids and steroidal lactones of Ashwagandha root, the Indian ginseng, have been found to enhance engulfing power of macrophages and other immune cells which in turn enhances the antimicrobial properties of this plant against organism like Salmonella (Govindarajan et al., 2005; Owas et al., 2005; Tiwari et al., 2014d). Vaccinium macrocarpon (Cranberry) when taken as a juice or administered as a concentrated tablet form helps interfere with adherence of bacteria to the lining of bladder and thus can prevent the infection. At a dose of 4-32 ounces a day of V. macrocarpon juice, prevention of bacterial adherence has been reported (www.herbcy.com). Centella asiatica, a very important medicinal herb belonging to the family Umbelliferae (Apiceae) and commonly known as Mandukparni or Indian pennywort or Jalbhrami, has been used in Indian Ayurvedic medicine system for several years; being listed in the historic ‘Sushruta Samhita’. The herb is also known as “miracle elixirs of life” and its extracts are recommended in the treatment of various skin conditions such as leprosy, lupus, varicose ulcers, eczema, psoriasis along with its wound healing properties (Chandra and Purohit, 1980; Zheng and Qin, 2007; Dash et al., 2011; Upadhyay et al., 2013).

Herbs affecting macro and microenvironment of disease: The inception of a bacterial disease in a tissue depends on several factors of both bacteria and host. Oxidative stress is a normal biochemical and physiological phenomenon. Under normal conditions, the physiologically important intracellular levels of ROS are maintained at low levels by various enzyme systems participating in the in vivo redox homeostasis. Increased oxidative stress is a prerequisite for the production of a disease (Rahal et al., 2014c). Oxidative stress is also a
biodmark for the stress in a tissue. The ROS produced in the tissues cause direct damage to macromolecules of the cell, such as lipids, nucleic acids and proteins (Pechan et al., 2003), with polyunsaturated fatty acids as one of the favored oxidation targets. DNA bases may also undergo oxidation and cause mutations and deletions in both nuclear and mitochondrial DNA. Mitochondrial DNA is equally prone to oxidative damage due to its close proximity to a ROS origin and deficient repair capacity. These oxidative modifications thus lead to functional changes in both enzymatic as well as structural proteins, thereby producing a substantial physiological impact. Similarly, redox modulation of transcription factors may modify the gene expression (Rahal et al., 2014c).

**Herbs in wound healing process:** Application of herbs and herbal preparations on wounds and other skin ailments is commonly used all over the world and these are supposed to be boon for the cure of skin and wound conditions (Pawar and Toppo, 2012, Tiwari et al., 2013a, b, 2014e). *Elaeis guineensis* of Arecaceae family is widely used in conventional medicine in African countries and in other parts of globe. Leaf extract of *E. guineensis* has potent wound healing capacity and is famous for its antioxidant, antibacterial and antifungal properties which help in preparation of a potent antimicrobial natural ointment (Chong et al., 2008). Similarly, oleic acid obtained from *Androdera diffusa* has wound healing potentials (Moura-Letts et al., 2006). *Lonicera japonica*, a widely used traditional Chinese medicinal plant, also possess wound healing capacity as evidenced by its greater tissue regeneration effects on fibroblasts and angiogenesis and wound contraction; thus help to accelerate wound repair by anti-inflammatory properties of the medicinal plant.

Similarly, *Acalypha indica* extract has shown to affect the process of dermal wound healing by its antioxidative potential. *A. indica* contains four glycosides namely mauritianin, chlororin, nicotiflorin, biorobin and many other phytochemical constituents like flavonoids, acetylhamide, alkaloids and glycosides (Nahrstedt et al., 2006). Furthermore, *L. japonica* has significant antimicrobial activity against *S. aureus*, *S. epidermidis*, *E. coli*, Candida albicans and *C. tropicalis*. Other prominent herbs identified for reducing the inflammatory processes include Achillea millefolium (yarrow), Allium sativum (garlic), Convallaria majalis (lily of the valley), Crataegus laevigata (hawthorn), Cynara scolymus (globe artichoke), Gingko biloba (gingko) and Viburnum opulus (cramp bark). *Drymis brasiliensis* Miers (Casca-d’anta) is an antinflammatory spice (Lago et al., 2010). Echinacea angustifolia and *E. pallida* have antiseptic properties due to complex mixtures of secondary plant metabolites like phenylpropanes and terpenes which have made these plants as most widely used herb *E. pallida* as well as *E. angustifolia* and *E. pallida* show immunostimulatory property and increases the activity of the white blood cells. Hence, they are used for prevention as well as for treatment of viral, bacterial and fungal infections particularly and have been found useful in treating cases of chronic arthritis and upper respiratory tract infections (Gunning, 1999).

One of the most extensively researched medicinal plants is garlic (*Zingiber officinale*) which has potent antibacterial action due to alliin which has inhibitory effects (multiple) on various enzyme systems that are thiol dependent. A range of potencies have been shown by individual constituents like garlic oil and garlic powder during in vitro studies against enteric bacteria in human including *Helicobacter pylori*. It has been found that against certain strains of *H. pylori*, garlic and omeprazole have synergistic effects but their concurrent administration is not much effective (Boon and Smith, 1999; McNulty et al., 2001; Ross et al., 2001). Garlic contains ajene which exhibit antifungal and antidermatophytic activity. Aqueous extract of garlic is effectual against 90% of the dermatophytes and is capable of inhibiting a wide range of fungi in cases of ringworm infections (Agarwal, 1996).

Extracts of cinnamon in vitro have been found to have inhibitory effect on the growth as well as urease activity of a number of strains of *H. pylori* and thus have encouraged a number of researchers for conducting clinical trials. It has been suggested that the eradication of this particular organism can be achieved by the use of higher concentrations of cinnamon on a regimen by combined use of antibiotic as well as herbal therapy along with it (Tabak et al., 1999; Nir et al., 2000). Geosyzygum is a crude extract from the fruit of *Evodia rutaecarpa* (a Chinese herbal medicine) which is having antibacterial activity in vitro against *H. pylori*. The two active components in this herb include 1-methyl-2-[(Z)-8-tridecenyl]-4-(1H)-quinolone and 1-methyl-2-[(Z)-7-tridecenyl]-4-(1H)-quinolones. The Minimum Inhibitory Concentration (MIC) of these compounds against reference strains as well as *H. pylori* clinically isolated has been found to be similar to the MIC of amoxicillin as well as clarithromycin. Similarly, the urease activity of *H. pylori* is inhibited by the tea (Camellia sp.) as well as rosemary (*Rosmarinus officinalis*) (Matsubara et al., 2003).

*Ipomoea batatas*, popularly known as Sweet Potato (SP), has been effectively used in herbal medicine to treat
inflammatory as well as infectious oral, viral and microbial diseases. It contains different effective active principles like flavonoids, triterpenes/steroids, β-carotene, anthocyanins, caffeoyl quinic acid derivatives, anthraquinones, coumarins, alkaloids, saponins, tannins and phenolic acids that promote the process of curing the infection (Kwon et al., 2000; Miyazaki et al., 2005; Islam, 2008; Pochapski et al., 2011; Sandhya et al., 2011). The bark of plant Carallia brachvata Merrill, belonging to Rhizophoraceae family, has been found effective in the treatment of itching, cuts and wounds, oral ulcers. Elephandopus scaber, belonging to family Astereaceae, contains sesquiterpene, lactones, deoxyelephantopin, isodeoxyelephantopin, scabertopin, epifriedelinc, lupeol and stigmastanol. These plant extract promotes the wound healing when applied on the surfaces of wounds. Leaf paste of Myrsinaceae member Embelia ribes cures the wounds due to cation of quinone derivative embelin, an alkaloid christembine and a volatile oil vilangin. Hibiscus rosa sinensis (Malvaceae) is a herb used to rejuvenate the inflamed skin and in the treatment of wounds. Jasminum auriculatum and Jasminum grandiflorum, member of Oleaceae, contains lupeol and jasminol which has remarkable effects on wounds (Deshpande and Upadaya, 1967; Kumari et al., 2013). When extract of leaves of J. auriculatum is applied over the wounds in the form of jelly, beneficial effects have been observed in the form of endorse wound healing. Lycopodium serratum, member of family Lycopodiaceae, is the plant especially useful in the treatment of burns, sores, cuts and wounds. A thick paste of this plant prepared by boiling in water has widely been used by the tribes for treating wounds. Rafflesia hasseltii buds and flowers extracts are very effective in accelerating the wound healing process (Chandra and Purohit, 1980; Chopra et al., 1981; Kumari et al., 2013). Honey in combination with Azadirachata indica (neem) bark decoction can be used for the treatment of chronic wounds (Chandra and Purohit, 1980; Kelmanson et al., 2000; Srivasan et al., 2001; Abu-Shanab et al., 2004; Mohanasundari et al., 2007; Vasu and Singaracharya, 2008; Kwakman et al., 2008; Raja et al., 2011; Daoli, 2012; Goulakrishnan et al., 2012, Kumari et al., 2013; Tiwari et al., 2013b, 2014e).

There are certain other plants that contain several active components like saponin and alkaloids; fatty acids and sterols, amino acids and amino glycosides which are essentially effective in the treatment of various bacterial infections. Melaleuca alternifolia oil, popularly known as tea tree oil, is used topically for treatment of bacterial and fungal infections. Tea tree oil has shown in vitro activity against microorganisms such as Propionibacterium acnes, S. aureus, MRSA, E. coli, C. albicans, Trichophyton mentagrophytes and T. rubrum. Extracts from Derris elliptica, D. indica and D. trifoliata, Cinnamon, Citrus aurantifolia and C. aurantium (Rutaceae), Punica granatum (Punicaceae), Phyllanthus acidus (Euphorbiaceae); Crescenta cygote (Bignoniaceae); Rosmarinus officinalis (Lamiaceae); Urena lobata (Malvaceae); Cimicifuga sp.; Terminalia chebula, T. bellerica; Ocimum sanctum, Acacia nilotica and Tamarindus indica (Caesalpiniiaceae) possess strong in vitro antibacterial activity against many bacteria agents. These plant extracts have shown activity against Helicobacter pylori, E. coli, Pseudomonas sp., Proteus sp., Bacillus sp., Streptococcus sp., Klebsiella sp. and S. aureus (Binutu and Lajubutu, 1994; Takenaka et al., 1997; Nir et al., 2000; Mazumder et al., 2001; Khan et al., 2006; Melendez and Capriles, 2006, Kumar et al., 2011; Vashney et al., 2012; Bhatla et al., 2013a, Sharma et al., 2014).

Leaf extract of Aegle marmelos, member of family Rutaceae, exerts immune response in freshwater fish, Cyprinus carpio (Cyprinidae), to enhance the disease resistance against Aeromonas hydrophila infection (Pratheepa et al., 2010; Laphookheo et al., 2011). Leaves of Siam weed (Chromolaena odorata) possesses antibacterial properties against aerobic bacterial isolates of wound infections as these contain phenolic compounds (Phan et al., 2001; Oyetayo and Oyetayo, 2006). Examples include: Aegle marmelos, Allamanda catharica, Allium sativum, Datura alba (Qureshi et al., 2011), Dendrophthoe falcata, Flabella paniculata, Flavera trinervia, Mimosa pudica (Zhang et al., 2011), Morinda citrifolia and Moringa oleifera (Sharma, 2010).

Oxidative stress and altered immune function: The correlation between oxidative stress and immune function of the body is beyond doubts. The skilled phagocytes cells (macrophages, neutrophils, eosinophils) possess an enzyme, the nicotinamide adenine dinucleotide phosphate (NADPH) oxidase (Hampton et al., 1998; Babior, 1999), which is responsible for the production of ROS following an immune challenge. The host defense mechanism uses the lethal effects of ROS and RNS in the killing pathogens. At the commencement of an immune response, phagocytes increase their oxygen demand by 10-20 folds via, process of respiratory burst. The nascent oxygen generated by this enzyme serves as the starting material for the production of an array of reactive species. Production of other powerful pro-oxidants, such as hydrogen peroxide (H2O2), hypochlorous acid (HOCl), peroxynitrite (ONOO−) and possibly hydroxyl (OH•) and
ozone (O₃) by these cells have also been reported. Although, these highly reactive endogenous metabolites damage all the the bacterial cells non-specifically, they can also injure the host tissues (Rice-Evans and Gopinathan, 1995). Cashewnut, (Anacardium occidentale) is an antioxidant and is used in indigenous system for immunomodulation purposes (Barreto et al., 2007; Morais et al., 2010; Rufino et al., 2009, 2010).

Increased production of Nitric Oxide (NO) has been documented in dengue and in monocyte cultures infected with different types of viral infections and has role in inflammation and in the relationship between oxidative stress and immunomodulation (Valero et al., 2013). Increased level of stress leads to activation of hypothamic-pituitary-adrenal axis and indirectly the release of endogenous antistress hormone, cortisol. The herb may act by its anti-inflammatory activity thus reduces the oxidative stress in the target tissue and ultimately facilitates the system against the pathogenic bacteria. Immunomodulation of most of herbal extracts are governed by cytokine regulation. Up and down regulation of cytokine governs immunomodulation as well as anti-inflammatory activities (Wildfeuer and Mayerhofer, 1994; Dhama et al., 2013a; Bhatia et al., 2013b, Sharma et al., 2014).

**IMPORTANT HERBS AND THEIR VITAL ROLES/APPLICATIONS AGAINST BACTERIAL PATHOGENS**

**Tulsi (Ocimum sanctum or Holy Basil):** Ocimum is a household remedy throughout tropical and semitropical region of India and other Asian countries. Different parts of tulsi are traditionally utilized in the Ayurveda and Siddha systems of medicine for treatment of several ailments (Kumar et al., 2013c). The phytoconstituents of *Ocimum sanctum* is complex and include: Eugenol and urosolic acid; alkaloids and flavonoids; tannins and carbohydrates. The antibacterial activities of the plant is well proven against a wide variety of Gram positive and Gram negative bacteria including enteric organisms viz., *E. coli*, *Pseudomonas aeruginosa*, *Proteus mirabilis*, *Klebsiella aerogenes*, *Shigella dysenteriae*, *Salmonella Typhimurium*, *Vibrio cholerae* and *S. aureus* (Bhatia et al., 2013a, 2011, 2013c). Equally are susceptible the fungi and viruses (including fish pathogens) indicating versatility of its anti-infective properties. Methanolic extracts and aqueous suspension of leaves and seeds oil of tulsi, all bear immunomodulatory properties. The leaves of the plant can induce cytokine secretion. The fixed oil and linolenic acid of tulsi possess good analgesic, antipyretic as well as anti-inflammatory activities (Bhatia et al., 2013b; Kumar et al., 2013c).

**Black cohosh (Cimicifuga racemosa):** Black cohosh has a long history of use in traditional medicine since 18th century (Rahal et al., 2013). It has been used to relieve pre-menstrual symptoms, dysmenorrhea and discomfort of menopause. In homeopathy, preparations of *C. racemosa* have been used for treating discomfort in late pregnancy, labor pains, headache and depression. It is an effective ecofriendly drug for the management of abortions, prolapse as well as post-parturient care in large animals. The black roots of *C. racemosa* contain 15-20% amorphous resinous substance, cimicifugin and racemosin. Also the herb contains triterpene constituents, actein, cimigenol, cimicifugoside and 27-deoxyacetylecetol and the glycoside, 27-deoxyacteine (27-deoxyacetylecetol-O-D-xylpyranoside). The anti-inflammatory potential of the alcoholic extract of *C. racemosa* has been scientifically proven (Rathore et al., 2012). The constituents, acteaalactone, cimicifugic acid and fukinolic acid display an antioxidant activity (Nunthakorn et al., 2006, 2007).

**Cinnamon (Cinnamomum cassia):** Essential oils of *Cinnamon* have been found to possess antimicrobial properties against *B. cereus* (Kalemba and Kunioka, 2003; Valero and Salmeron, 2003) and *H. Pylori* (Tabak et al., 1999). A blend of cinnamon and nisin accelerated the death of *S. typhimurium* and *E. coli* O157:H7 in apple juice, thereby increasing its safety and shelf life (Yuste and Fung, 2004). An equal volume mixture of extracts of chive (*Allium tuberosum*), cinnamon and corni fructus (*Coriaceae officinalis*) has been found to possess a good antimicrobial spectrum in orange juice, pork and milk against common foodborne microorganisms; thereby increases their stability to heat, pH and storage (Mau et al., 2001). The cinnamon extract was well tolerated and side effects were minimal (Nir et al., 2000). A hydroethanolic extract of cinnamon bark inhibits the activity of bacterial endotoxin (Azumi et al., 1997) and growth of fluconazole resistant Candida sp. which cause an emerging illness. Cinnamaldehyde (CNA, 1), 2-hydroxycinnamaldehyde (2-CNA), coumarin (2) and cinnamyl acetate have been identified as chief antibacterial pytoconstituents of the essential oil of cinnamon (Choi et al., 2001; Sharma, 2010).

**Curcuma longa (Turmeric):** Curcuma longa, a perennial herb, is a member of the Zingiberaceae family. The roots form an important ingredient of Chinese and Ayurvedic
systems of medicine. The rhizomes of *C. longa* possess a large inventory of monoterpenoids, sesquiterpenoids and curcuminooids (Tang and Eisenbrand, 1992; Fang et al., 2003), which show antibacterial, anti-inflammatory as well as antineoplastic activities. Curcuminooids, which are basically bioflavonoid compounds, exhibit a variety of beneficial therapeutic and preventive health effects (Joe et al., 2004). Curcumin is the principal curcuminoid along with desmethoxycurcumin and bis-desmethylcurcumin, the other two curcuminooids (Akram et al., 2010). Insecticidal activity of the turmeric rhizome has also been reported (Chander et al., 1991, 1992). Curcumin has antioxidant, anti-inflammatory, antiviral and antifungal actions (Akram et al., 2010). Curcumin blocks NF-κB and the motogenic response in *H. pylori* infected epithelial cells and carries thrombogenic therapeutic potential. It acts as an inhibitor for cyclooxygenase, 5-lipoygenase and glutathione S-transferase. In addition to this, turmeric has been found to reduce the release of inflammation-inducing histamine, increase and prolongs the action of cortisol and improves circulation; thus increases the flushing toxins out of the body. Curcumin facilitates proliferation of CD4+ T-helper and B type immune cells.

Turmeric acts as a cholangogue, stimulating bile production, thus increases the digestion of fats and eliminating toxins from the liver. Wound healing and detoxifying properties of turmeric curcumin have also received considerable attention (Joe et al., 2004). The ethyl acetate extract of *C. longa* has demonstrated an excellent antibacterial activity against MRSA at a concentration of 0.125-2 mg mL\(^{-1}\) (Kim et al., 2005). A study by Limtrakul et al. (2004) using RT-PCR showed that all three curcuminooids isolated from *C. longa rhizomes* inhibit expression of MDR-1 gene. The oleoresin (second fraction of the turmeric oil) contains ar-tumerone, tumerone and curcione and has been proven antibacterial against *B. cereus*, *B. subtilis*, *B. coagulans*, *E. coli*, *S. aureus* and *P. aeruginosa* (Negi et al., 1999).

**Piper nigrum (Black pepper):** Both aqueous and ethanol extracts of black pepper inhibit the growth of penicillin G resistant strain of *S. aureus* (Dorman and Deans, 2000). The extracts from *Piper longum* contain pharmacological molecules piperlonguminine, piperine and pellitorine which exhibit significant antibacterial activity against Gram positive bacteria and moderate activity against Gram negative bacteria (Reddy et al., 2001). Piperine, [1-[5-[1,3-benzodioxol-5-yl]-1-oxo-2,4, pentadienyl] piperidine, a pungent alkaloid present in *P. nigrum* enhances the bioavailability of various structurally and therapeutically diverse drugs. Perhaps, it forms non-polar complexes with drug molecules and increases their permeability across the barriers (Khajuria et al., 1998). The *Piper longum* fruit extracts have also shown significant anti-mycobacterial activity against MDR *Mycobacterium tuberculosis* (Singh et al., 2011). Along with potent antimicrobial activity, black pepper is used to treat asthma, chronic indigestion, colic toxins, obesity, sinus congestion, fever, intermittent fever, cold extremities, colic, gastric ailsments and diarrhea (Khajuria et al., 1998; Rahal et al., 2014b).

**Syzygium aromaticum (Clove) (Syn-Caryophyllus aromaticum, Eugenia aromatic, Eugenia caryophyllus, Eugenia caryophyllata):** The aqueous and methanolic extract from whole clove is being efficiently used as an antimicrobial agent against food spoilage bacteria and food borne pathogens (*S. aureus, P. aeruginosa, E. coli*). The bread with a maximal of 1% clove extract is acceptable for human consumption (Pandey and Singh, 2011; Saeed et al., 2013). Essential oils of clove possess antimicrobial properties (Kalaeb and Kunicka, 2003) against four Gram positive bacteria such as *Brochothrix thermosphacta, Carnobacterium piscicola, Lactobacillus curvatus* and *Lactobacillus* and Gram negative bacteria such as *P. fluorescens* and *Serratia liquefaciens, E. coli, L. monocytogenes* and *S. enterica* (Friedman et al., 2002). Its antimicrobial properties are utilized in meat industry. A positive relationship has been established between the inhibitory effect of essential oils and the presence of eugenol and cinnamaldehyde (Ouattara et al., 1997). Crude methanolic extract inhibits gram-negative anaerobic pathogens, including *Porphyromonas gingivalis* and *Prevotella intermedia.* Eight pharmacologically active principles (5,7-dihydroxy-2-methylchromone 8-C-beta-D-glucopyranoside, biflorin, kaempferol, rhamnucitin, myricetin, gallic acid, ellagic acid and oleanolic acid) have been identified following chromatographic fractionation of clove oil. The bioflavonoid, kaempferol and myricetin also show potent growth-inhibitory activity against the periodontal bacteria, *Porphyromous gingivalis* and *P. intermedia* (Cai and Wu, 1996). Clove and clove oils are used in day today's life as potent anti-bacterial, anti-inflammatory and analgesic agents (Rahal et al., 2014b).

**Thymus vulgaris (Thyme):** The oil of thyme is a naturally occurring antibacterial, antifungal and antioxidant agent when used topically due to which it is gaining popularity (Vemogepal and Venugopal, 1995; Nagarawa et al., 1996; Caelli et al., 2000; Dursun et al., 2003; Akins, 2005; Carson et al., 2006; Shenefelt, 2011). Thyme has a broad antibacterial spectrum against both Gram positive and
Gram negative bacteria with a highly sensitivity against the former group (Nevas et al., 2004). Thymol and carvacrol are active constituents of ethanolic extract of thyme. The essential oil of thyme has been found to have strong inhibition activity against S. sonnei, B. subtilis, L. monocytogenes S. enterica, C. jejunii and E. coli O157:H7 (Fan and Chen, 2001; Friedman et al., 2002). The aqueous extract of thyme on the other hand was found to have significant inhibitory effects on the growth of H. pylori (Tabak et al., 1999). Thymol decreases the viable count of S. typhimurium and S. sonnei in vitro (Juven et al. 1994). Carvacrol shows a dose-dependent inhibition of B. cereus (Ulloe et al., 2000). The MIC was as low as 0.03% (v/v) thyme oil against C. albicans and E. coli (Hammer et al., 1999). The activity of thyme was modulated by alterations in pH and sodium chloride concentration of the medium (Bagamboula et al., 2003). The bacteriostatic and bactericidal properties of essential oil of thyme were evident against the non-toxigenic strain of E. coli O157:H7 in a broad temperature range. Lecithin weakened the antibacterial properties (Burk and Reinders, 2003). Thyme showed highest inhibitory potential against Aeromonas hydrophila compared to other psychrotrophic food-borne bacteria such as A. hydrophila, L. monocytogenes and Y. enterocolitica in in vitro conditions.

Zingiber officinale (Ginger): Z. officinale possess antimicrobial action against both Gram positive and Gram negative microorganisms (Martin et al., 2001; Srinivasan et al., 2001). It has potent anti-inflammatory, analgesic, antipyretic and antimicrobial activities. Methanolic extract of the dried powdered ginger rhizome contains 6-, 8-, 10-gingerol and 6-shogocnil which inhibited growth of different strains of H. pylori in vitro with a MIC of 6.25-50 μg mL⁻¹. Higher antibacterial efficacy has been shown by ginerols of the crude extract against H. pylori with an MIC range of 0.78-12.5 μg mL⁻¹ showed significant activity against the CagA⁺ strains (Mahady, 2005). Antibacterial activity has also been reported against the pathogens like S. aureus, S. pyogenes, S. pneumoniae and H. influenzae. The MIC and MBC values of various ginger extracts ranged from 0.0003-0.7 μg mL⁻¹ and 0.135-2.04 μg mL⁻¹, highlighting its therapeutic value (Akoachere et al., 2002).

Aloe vera: Aloe vera is obtained from the mucilaginous part of the centre of the leaf. Worldwide several studies have been suggested that Aloe vera, or Aloe vera gel has wide array of utility against various health-related disorders when applied orally and/or topically. The Aloe vera gel contains sugars, amino acids, vitamins A, B, C, E, enzymes, polysaccharides and minerals. Several reports have also shown encouraging role of Aloe vera in the management of both acute and chronic infected burn wounds (Raina et al., 2008). B-sitosterol, aecmanman and glycoprotein constituents of Aloe vera have therapeutic potentials. The antimicrobial potential of Aloe vera juice has been proved against a range of clinically relevant bacteria during in vitro studies. The various Gram positive bacteria (Mycobacterium smegmatis, S. aureus, MRSA, Enterobacter cloacae, E. bovis, E. faecalis, Micrococcus luteus and Bacillus sphaericus); Gram negative bacteria (P. aeruginosa, K. pneumoniae, E. coli, Shigella flexneri and Salmonella typhimurium) and fungi (Candida albicans) were found susceptible to Aloe vera juice. Furthermore, Aloe vera extract has antimicrobial activity against M. smegmatis, E. faecalis, M. luteus and B. sphaericus. Aloe vera juice can effectively be used in cosmetics and food industry as it has inhibitory effects against pathogenic bacteria causing food poisoning, especially the Gram-positive bacteria (Habib et al., 2007; Grace et al., 2008; Alemdar and Aagaoglu, 2009; Rahal et al., 2014b).

Withania somnifera (Ashwagandha): Ashwagandha has been found to show remarkable antibacterial properties, owing to its glycoprotein glycowithanolides, withaferin and withanolides (Tiwari et al., 2014d). Antibacterial activities have been demonstrated against various bacterial pathogens viz., Neisseria gonorrhoea, E. coli, Salmonella, Bordetella pertussis, Pseudomonas fluorescens, P. aeruginosa, Bacillus subtilis, L. monocytogenes, Clostridium michiganensis subsp. Michiganensis and Staph. aureus (Akinyemi et al., 2004; Owais et al., 2005; Girish et al., 2006; Teixeira et al., 2006; Kulkarni et al., 2007; Kambizi and Afolayan, 2008; Mehrotra et al., 2011; Sundaram et al., 2011; El-Boshy et al., 2013). Ashwagandha has also been found useful to counter even Multidrug Resistant (MDR) strains of few bacteria like of methicillin-resistant Staph. aureus (Mehrotra et al., 2011).

Azadirachta indica (Neem): Neem leaves and oil possesses proven beneficial effects on several skin conditions and bacterial infections (Drabu et al., 2012; Tiwari et al., 2014e). The methanol extract from the leaves of Azadirachta indica has the highest antibacterial activity followed by the hexane, methanol, chloroform extracts from it (Koono and Budida, 2011). The water and hexane extracts from the seeds of A. indica inhibits the growth of Gram positive more strongly than Gram negative bacteria. Neem leaf extracts and oil have been demonstrated to posses wide antibacterial activity
against various pathogens viz., *E. coli*, *Pseudomonas aeruginosa*, *Aeromonas hydrophila*, *B. cereus*, *B. pumilus*, *S. aureus*, *S. typhi*, *K. pneumoniae*, *Proteus* sp., *P. vulgaris*, *Vibrio* sp., *S. dysenteriae*, *Enterococcus faecalis*, *Streptococcus* sp. (*S. mutans*, *S. mitis*, *S. sanguis*, *S. salivarius*), *M. tuberculosis* and *Yersinia enterocolitica* (SairRam et al., 2000, Biswas et al., 2002; Parekh and Chanda, 2007b; Prashant et al., 2007; Anyaehie, 2009; Dhayanithi et al., 2010; Mehrotra et al., 2010; Samiento et al., 2011; Maragathavalli et al., 2012; Vinoth et al., 2012; Chava et al., 2012; Harjai et al., 2013; Rosaline et al., 2013; Tiwari et al., 2014e). Antibacterial potential of leaf extract of neem has been proven against methicillin-resistant *S. aureus* (Samiento et al., 2011). The hexane extracts from the seeds produces larger zones of growth inhibition diameter, lower MIC and MBC values when compared to aqueous extracts (El-Mahmood et al., 2010). Moreover, it has been reported that the neem oil has low MIC against *S. aureus*, *S. typhi*, *E. coli* and *P. aeruginosa*. *In vitro* studies have also shown the antibacterial activity of neem oil and which indicated that 92% *S. pyogenes*, *P. aeruginosa*, *Proteus* sp. and *E. coli* are susceptible to it (Jahan et al., 2007). Irodin A, recovered from leaves of neem, acts as a potent anti-malarial agent (WHO, 2008; Anyaehie, 2009). The bark and oil of this plant have antituberculosis (*M. tuberculosis*) and anti-leprosy properties (Subramanian and Lakshmanan, 1996; Tiwari et al., 2014e). Neem oil show antipulmonary actions while chewing its twigs help control dental tartar and caries (Prashant et al., 2007; Elavaraus et al., 2012). Recently, Kumar et al. (2013b) indicated the utility of neem preparations for treating endometritis in cattle.

*Morinda citrifolia* (Noni plant): *M. citrifolia* has been used by Polynesians for more than 2000 years for the treatment of various conditions and was commonly known as Noni plant (Chan-Blanco et al., 2006; Singh, 2012). Acubin, L-asperuloside and alizarin are the major bioactive molecules isolated from the noni fruit and scopoletin, anthraquinone compounds are obtained chiefly from noni roots. Various extracts from the fruits and leaves have shown potent antibacterial activities against *S. aureus*, *P. aeruginosa*, *B. subtilis*, *Vibrio algimlyticus*, *E. coli*, *P. morgari*, *Salmonella typhosa*, *S. schottmuelleri*, *S. montevideo*, *Lactobacillus lactis*, *S. thermophilus* and *Shigella paradys*. Noni is mainly used for the treatment of broken bones, bruises, sores and wounds, colds, fevers, skin infections and other bacteria induced ailments (Dittmar, 1993; Selvam et al., 2009; Usha et al., 2010; Natheer et al., 2012). A coumarin compound, scopoletin, has also been isolated from noni plant which inhibits the growth of *E. coli* and also helps to heal stomach ulcer by inhibiting the bacteria *H. pylori*. Murray et al. (2008) had observed similar *in vitro* effectiveness of noni juice along with chlororhexidine gluconate and sodium hypochlorite (NaOCl) to remove the smear layer of *E. faecalis* from the canal walls of endodontically instrumented teeth. The antibacterial activity of iridoids (deacetyl asperulosidic acid and asperulosidic acid) in *M. citrifolia* fruits against *C. albicans*, *E. coli* and *S. aureus* has been evaluated recently by West et al. (2012). Moreover, *M. citrifolia* leaf extract has shown anti-tubercular activity and can effectively kills 89% of *M. tuberculosis* compared to anti-TB drug rifampicin which kills 97% of bacteria at the similar dose concentrations. Various bioactive components like cycloartenol, E-phytol, beta-sitosterol, stigmasterol, ketosteroids stigmasta-4-en-3-one, campesta-5,7,22-trien-3beta-ol and stigmasta-4-22-dien-3-one were isolated from hexane fraction from noni and which are responsible for the pronounced antitubercular activity of noni (Saludes et al., 2002; West et al., 2012).

*Areca catechu*: Leaves, buds, shoots, husks and roots of *Areca catechu* are of medicinal values. Antibacterial and growth inhibitory effects of areca leaves have been seen against *B. cereus*, *P. fluorescens*, *Streptococcus mutans*, *S. salivarius*, *S. mitis*, *Lactobacillus acidophilus*, *C. albicans* and *Prevotella intermedia*. Active principles include alkaloids like arecoline and arecaine, catechin, tannins, gallic acid, fat, gum etc. (Lalithakumari and Sirsi, 1965; Samappito et al., 2012).

*Berberis lyceum*: *Berberis lyceum*, a member of family Berberidaceae is a shrub distributed in the temperate and subtropical parts of Asia, Europe and America. The plant contains flavonoids and alkaloids including berberine, tannins, saponins and triterpenoids. The principal alkaloid, berberine, is present in the rhizomes and used in the preparation of drugs for treating leprosy cholera, diarrhoea, dysentery and eye problems. It is also recommended orally for treating bacterial dysentery. However, its combination with Glycyrrhiza species abolishes its therapeutic effect (Hong et al., 2005; Irshad et al., 2013).

*Carallia brachiata* (Karalla): *Carallia brachiata* belongs to family Rhizophoraceae and is an evergreen decorative tree. It has been used against stomatitis, throat inflammation and for treating oral ulcers. The bark of the tree contains steroids, triterpenoids, phenols, carbohydrates, fixed oils, fats, proanthocyanidins...
(carallidin, mahuannin A, para-hydroxy benzoic acid, tannins, flavonoids) and glyceroglycolipids. The extract has shown antibacterial efficacy against both Gram positive and Gram negative bacteria like Micrococcus luteus, B. subtilis, S. aureus, E. coli, Proteus vulgaris and S. Typhi (Krishnaveni et al., 2009; Neelharika et al., 2010; Abraham and Thomas, 2013).

**Centella asiatica:** *Centella asiatica* is a perennial creeping herb of the family Umbelliferae that grows in moist areas of many tropical and subtropical countries. *C. asiatica* is the source of active constituents viz., saponins, asiaticoside, triterpenoids, madecassoside, madecassic acid, asiatic acid, triterpenoids, sitosterol, glucose, rhamnose and stigmasterol. Others include fatty acids consisting of glycerides of palmitic acid, linoleic acid, stearic acid, linolenic acid and vitamins like ascorbic acid along with minerals like calcium, iron and phosphate. Different extracts of *C. asiatica* have been found very effective in inhibiting the growth of four pathogenic bacteria viz., P. vulgaris, S. aureus, B. subtilis and E. coli and two fungal strains of *A. niger* and *C. albicans*. The plant has a promising scope to be developed as a novel broad spectrum antibacterial and antifungal herbal formulation due to potent fungicidal, antibacterial, antioxidant and anticancerous properties (Chandra and Purohit, 1980; Zheng and Qin, 2007; Gohil et al., 2010; Dash et al., 2011).

**Pyrostegia venusta (Ker Gawl.):** *Pyrostegia venusta* Miens is member of Bignoniaceae and is an ornamental tree cultivated in tropics of South America. Various parts of this plant show antioxidant, antimicrobial, antiviral, antibacterial, hepatoprotective, anti-inflammatory, spasmylytic, antirheumatic, anti-angiogenic, antitumor, anti-inflammatory, immunomodulatory and wound healing potentials. The plant contains phytochemicals such as iridoid glucosides, naphthoquinones, alkaloids, flavones, triterpenes, polyphenols, tannins, allo-tannic acid, oleanolic acid, seed oils, glycoside bellericin, acacetin-7-O-β-glucopyranoside and β-sitosterol. It has been found to be effective against diarrhea, cough, respiratory disorders and skin infections such as leukoderma, vitiligo and many bacterial and fungal pathogens. The various pathogens against which *P. venusta* has been tried include B. subtilis, S. epidermidis, S. pyogenes, S. aureus, Micrococcus luteus, Enterobacter aerogenes, E. coli, S. typhi, P. aeruginosa, Aspergillus niger, C. albicans and C. tropicalis (Ferreira et al., 2000; Roy et al., 2011, 2012; Mostafa et al., 2013).

**Peperonia galoides (Silver bush):** It is commonly called as tuna congona, congona grande or shiny bush. The herb is enriched with ethnomedical uses as anti-inflammatory, anti-oxidant, diuretic, antibacterial and analgesic. Plant is enriched with many components of medicinal importance, having the potential be be be used in the treatment of several health disorders viz., Parkinson’s disease, Alzheimer’s disease, headache, cancer, cardiovascular disorders, renal disorders, inflammation, abscesses, acne, boils, colic, fatigue, gout, rheumatic pain; as well as utility against various bacterial and viral infections. It possesses various alkaloids, tannins, grifolins, grifolic acid, resins, piperogalin, steroids, essential oils, phenols and carbohydrates responsible for broad spectrum antimicrobial activity against a range of pathogens viz., S. aureus, S. epidermidis, B. subtilis, E. coli, P. aeruginosa, K. pneumoniae, S. Typhi, C. albicans, Penicillium notatum, A. niger and Rhizopus stolon (Bojo et al., 1994; Mahiou et al., 1995; Aziba et al., 2001; Olayede et al., 2011).

**Panax ginseng:** Ginseng contains many phytochemical compounds such as tetracyclic triterpenoid saponins (ginsenosides), polyphenolic compounds, polyacetylenes and acidic polysaccharides. It exhibits anti-bacterial capacity by inhibiting survival mechanisms of pathogens. Ginseng extracts have been found to repress the synthesis of LasA protease, LasB elastase and AHL molecules; hence inhibits the pathogenesis mechanism of *P. aeruginosa* by phenomenon of quorum sensing. Similarly, pectin-type polysaccharides of *P. ginseng* as PG-F2, acidic heteroglycans and PG-HMW act against Porphyromonas gingivalis, Actinobacillus actinomycetemcomitans, Propionibacterium acnes, S. aureus, methicillin-resistant S. aureus, B. subtilis, E. coli, Serratia marcescens, H. pylori and many viruses including of influenza, Human Immune Deficiency Virus (HIV) and rota virus (Lee et al., 2006; Choi, 2008; Kang and Min, 2012; Yoo et al., 2012).

**Plantago major:** Popularly known as way bread, *Plantago major* is a perennial herb of the Plantaginaceae family which grows abundantly beside paths, roadsides and as a weed in crops. The genus name *Plantago* has been derived from a Latin word “planta”, meaning as sole of the foot. The plant has been extensively used in folklore medicine since long back because of its antitubercular, anti-malarial, anti-infective, anti-inflammatory, anti-oxidative and anti-tumor activities. The inhibitory effects of the herb have been scientific validated against
Cryptococcus, Franciscella, Listeria, Mycobacteria, many herpes and adenoviral infections, influenza and viral hepatitis (Chiang et al., 2002; Oto et al., 2011). Leaf extract of *P. major* contains phenolic compounds, organic acid groups, essential fatty acids, flavonoids, oleic acid, ferulic acid, ursoic acid, carotenes and terpenoids (Samuelsen, 2000; Turel et al., 2009; Nazarizadeh et al., 2013). Mechanism behind the anti-inflammatory action is the selective inhibition of cyclooxygenase-2 by ursoic acid thus inhibiting the prostaglandin biosynthesis. Acetone extract of *P. major* leaves has shown effective actions against *B. cereus, B. subtilis, S. aureus, S. epidermidis, E. coli, K. pneumoniae, P. aeruginosa, P. mirabilis, S. enteritidis, C. albicans* and *C. tropicalis*. Soluble pectin polysaccharide (PMI) of *P. major* leaves showed prophylactically protective effects against systemic *S. pneumoniae* infections (Metiner et al., 2012). *Scrophularia nodosa* (Figwort): *Scrophularia nodosa* is a flowering herb belonging to family Scrophulariaceae. It contains biologically active compounds like phenylethanoids, acylated iridoid glycosides, phenylpropanoids, flavonoids, iridoids, iridoid glycosides and terpenoids. *S. nodosa* crude extract possess significant antibacterial, antifungal, antiprotozoal, anti-tumor, anti-inflammatory and diuretic activities and have been used in the treatment of wounds, psychological, nervous and gastrointestinal disorders (Stevenson et al., 2002; Ahmad et al., 2012).

**Tamarindus indica** (Tamarind tree): Tamarind has been known as a medicinal plant due to its antimicrobial, antibacterial, antifungal and antiseptic properties. Tamarind leaves show broad spectrum of antimicrobial activity that can be attributed to its phytoconstituents like flavonoids, xyloglucan, benzyl benzoate, limonene, hexadecanol, pentadecanol and other polyphenols metabolites. Theses phytoconstituents have shown antibacterial and antifungal activities against *B. subtilis, E. faecalis, S. aureus, E. coli, S. Typhimurium, P. aeruginosa* and *C. albicans* (Pino et al., 2004; Muthu et al., 2005; Doughari, 2006; Escalona-Arranz et al., 2010).

**Vitis vinifera**: *Vitis* is affluent source of potentially bioactive polyphenols as resveratrol, flavonoids, flavonols and stilbenes. Leaves of *Vitis* are especially rich in total phenols and their extracts have useful antioxidant and antimicrobial activities. The antibacterial and antifungal activities of the extracts has been tested against *S. aureus, B. cereus, E. coli, Campylobacter jejuni, Salmonella infantis, P. aeruginosa, C. albicans, C. parapsilosis* and *C. krusei* (Thimothe et al., 2007; Katalinic et al., 2013; Oliveira et al., 2013).

**Stephania glabra**: The ethanolic extract of *Stephania glabra* has active principals against both Gram positive and Gram negative bacteria such as *S. mutans, S. epidermidis, E. coli, K. pneumoniae* with MIC of 50 µg mL⁻¹ (Semwal et al., 2009). By realizing these benefits, *S. glabra* has been long used in folklore medicine for the treatment of pyrexia, inflammatory conditions, hyperglycemia, asthma, tuberculosis, dysentery, intestinal disturbances, cancers and sleep disturbances. The tetrahydroberberine alkaloid called as 8-(4′-methoxybenzyl)-xypoline has been isolated from the ethanolic extract of its tubers and which showed antibacterial activity against *E. coli, P. aeruginosa, S. typhi* and *S. aureus* with Inhibition Zone Diameter (IZD) of 8-19 mm at MIC of 25-100 µg/mL (Semwal et al., 2012).

**Calotropis gigantea** (Akanda): The methanol extract and its chloroform fraction from the root bark of Akanda have demonstrated antibacterial activity against *Sarcina lutea, P. aeruginosa* and *Bacillus megaterium*. In addition, its petroleum ether fraction showed inhibitory activity against *Shigella sonnei* and *B. subtilis*. The ethyl acetate fraction of *Calotropis gigantea* also showed antibacterial activity against *E. coli* and *P. aeruginosa* (Alam et al., 2008). Anitha et al. (2014) also evaluated the antibacterial effect of *C. gigantea* latex extract against wide variety of pathogenic bacteria such as *S. aureus, Enterococcus faecalis, E. coli, K. pneumoniae* and *P. mirabilis*. The methanolic and ethanolic extracts have shown enhanced and wide spectrum of antimicrobial activity as compared to other extracts of the same plant. Hot aqueous and hot hydro methanolic extracts of *C. procera* also revealed mild to moderate dose dependent antibacterial activity against *S. aureus, E. coli, K. pneumoniae* and *P. mirabilis* (Sharma, 2010).

**Nelumbo nucifera**: Both the white and pink flowers of *Nelumbo nucifera* extracts have shown significant antibacterial activity in a concentration dependent manner. The flowers showed maximal efficacy against *S. aureus, E. coli* and *B. subtilis* and moderate effectiveness against *P. aeruginosa* and *K. pneumoniae*. Variation and concentration in pytoconstituents like flavonoids, tannins and alkaloids alter antimicrobial
activity of individual plant extracts. Such variation might occur within the same species with minor differences. Further, colour variations of flowers revealed differences not only in antibacterial activity but also in the level of activity of *Nelumbo*. The hydro ethanolic extract of white flowers showed significant antibacterial activity as compared to pink flower extracts. The white flower extract exhibited lowest MIC against both Gram positive and Gram negative bacteria as compared to pink flowers. Moreover, Gram negative bacteria were found more amenable to antibacterial activity of these flower extracts than the Gram positive bacteria (Brindha and Arthi, 2010).

*Lantana indica* Roxb and *Lantana camara*: The methanolic and aqueous extracts of the leaves from *Lantana indica* Roxb exhibit strong antibacterial against Gram positive bacteria such as *B. subtilis*, *S. aureus*, *Streptococcus pyogenes* as well as Gram negative bacteria such as *E. coli*, *P. vulgaris* and *K. pneumoniae*. The ethyl acetate extract showed moderate activity against *S. Typhi* and *P. aeruginosa* (Venkataswamy et al., 2010). The chemical constituents of essential oil from the fresh leaves of *Lantana* are davanone, α-humulene, β-caryophyllene, bicyclogermacrene and sabine. These bioactive compounds showed significant antibacterial activity against *B. cereus*, *S. aureus*, *B. subtilis* and *E. coli* (Saikia and Sahoo, 2011).

*Jatropha curcas*: The ethanolic and methanolic extracts of *Jatropha curcas* possess broad spectrum antibacterial activities. The extracts have lower potency for *K. pneumoniae* in comparison to other bacteria. The methanolic extract on the other hand showed significant antibacterial activity (MIC 0.5-10 mg mL⁻¹) than the ethanolic extract (MIC 0.5-6.25 mg mL⁻¹). This activity may be due to the presence of soluble phenolic and polyphenolic compounds (Igbinosa et al., 2009).

*Psidium guajava* L. (*Guava*): The antibacterial compound mainly found in guava are reducing sugar, alkaloids, saponins, tannins, phlobatannins, terpenoids and poly phenols. The crude aqueous and methanol extract from the leaf and bark of guava possess strong antibacterial activity against MDR *Vibrio cholerae*. The *in vitro* MIC for the crude aqueous and methanolic extract is 1,250 and 850 µg mL⁻¹, respectively. These concentrations were bactericidal against 10⁷ CFU mL⁻¹ of *V. cholera*. The antimicrobial activity of guava has other advantage of being stable at 100°C for 15-20 min, indicating the nonprotein nature of the active component (Rahim et al., 2010). The ethanol and hot water extracts possess less antibacterial activity compared to methanolic and ethyl acetate extracts (Pandey and Shweta, 2011).

*Ficus carica* L. (*Mulberry tree*): *Ficus carica* belongs to the family Moraceae which is one of the oldest fruits in the world and widely used for various diseases. It has been used as an anti-inflammatory agent ulcers and eruptions as well as digestion promoter. The methanolic extract of *F. carica* leaves have antimicrobial activity against MRSA (MIC 2.5-20 mg mL⁻¹) isolated from clinical samples. The methanolic extract also shows synergistic activity in combination with oxacillin or ampicillin and induces a more rapid decrease in the concentration of bacteria. The antibacterial effect has been suggested to act in a dose dependent manner against common bacterial pathogens (Lee and Cha, 2010; Al-Yousuf, 2012).

*Solanum nigrum*: The methanolic extract and different fractions (ethyl acetate, n-butanol, chloroform and n-hexane) of *Solanum nigrum* leaves possess antimicrobial activity against *S. aureus*, *Pasteurella multocida*, *E. coli* and *B. subtilis* (Zubair et al., 2011). Likewise, the ethanolic and methanolic extracts from stem, berries and whole plant of *S. nigrum* inhibits the growth of *B. subtilis*, *E. coli*, *K. pneumoniae* and *P. aeruginosa*. The methanolic extract generally shows higher antibacterial activity than the ethanolic extracts. Furthermore, the extracts of the whole plant have been reported to possess anti-bacterial activity (Parameswari et al., 2012).

*Glycyrrhiza glabra* (*Licorice*) and *Uncaria tomentosa* (*Cat's claw*): *G. glabra* and *U. tomentosa* extract show good antibacterial activity against oral pathogens such as *S. aureus* *E. faecalis* and *C. albicans*, suggesting their possible role to control dental caries and endodontic infections (Ceauhuana-Vasquez et al., 2007; Herrera et al., 2010; Sedighinia et al., 2012). The ethanolic and aqueous extracts from leaves and root extracts of licorice show dose dependent antibacterial activity against *B. subtilis*, *E. faecalis*, *S. aureus*, *K. pneumoniae*, *P. aeruginosa* and *E. coli*. Moreover, the ethanolic extract of the leaves is better against Gram positive bacteria (Irani et al., 2010).

*Brassica campestris*: The ethanolic, petroleum ether, methanol and ethyl acetate extracts from root, stem and leaves of *B. campestris* plant show excellent antibacterial activity against many Gram positive bacteria such as *S. aureus*, *S. epidermidis*, *B. cereus* and Gram negative
bacteria such as *P. aeruginosa* and *E. coli*. Although, benzene and chloroform extracts have antibacterial potential but these effects are least as compared to other alcoholic extracts (Agrawal et al., 2013).

**Picrorhiza kurrooa**: The crude extract of Rhizome of *P. kurrooa* has been used for long as traditional medicine to treat various gastrointestinal diseases especially diarrheal infections as well as skin and urinary tract infections. The rhizome contains various bioactive phytochemical constituents which includes phenolic compounds, sterols, eucarbitacins (triterpenoids) and iridoid glycosides (picroside I and kutkoside). Most of these compounds are extracted mainly as methanolic extracts and have significant antibacterial activity against *P. aeruginosa* and *S. aureus* and moderate effects against *Micrococcus luteus*, *E. coli* and *B. subtilis* (Rathhee et al., 2012; Usman et al., 2012).

**Actinidia macroasperma**: The hydrodistillate of leaf oil from *A. macroasperma* has shown variety of pharmacological activities against leprosy and cancers in cats. Its leaf oil contains high amount of monoterpenes. The major active components include the linalool, linalenic acid methylester, (E)-phytol and 1, 2-dimethyl-lindoline. Studies have shown that the oil has mild antibacterial activity against *S. aureus* and *B. subtilis* and significant activity against Gram-negative bacteria such as *E. coli* (Lu et al., 2007, 2012; Lau et al., 2012).

**Astragalus membranaceus** and *A. gombiformis*: *A. membranaceus* belongs to family Fabaceae and is commonly used to treat a wide variety of infections. The root contains various alkaloids, saponins, terpenoids, flavonoids and cardiac glycosides. Both the methanolic and ethanolic extracts from dried root show significant in vitro antibacterial activity against both Gram positive and Gram negative bacteria especially diarrhea causing pathogens (Balachandar et al., 2012). The methanolic extract from the leaves of wild *A. gombiformis* Pomel have been shown to exert antibacterial activity against *S. typhimurium* and *P. aeruginosa* (Teyeb et al., 2012).

**Emblica officinalis** (Amla) and **Coriandrum sativum** (Coriander): The aqueous extract from the fruit pulp of *E. officinalis* and *C. sativum* showed significant level of antibacterial activity against 345 bacterial isolates belonging to 6 different genera of especially those of Gram negative type (Saeed and Tariq, 2007). The methanolic extract of *E. officinalis* revealed higher antibacterial activity in comparison to leaf and stem extracts of *O. sanctum* (Vijayalakshmi et al., 2007). Recently, ethanolic and aqueous-ethanolic extracts of Coriander have shown variable antibacterial activity against *B. subtilis*, *S. aureus*, *E. coli*, *P. aeruginosa*, *P. vulgaris*, *K. pneumonia* and *L. monocytogenes* (Yakout et al., 2013).

**Catharanthus roseus**: *C. roseus* contains many phytochemical constituents such as reducing sugar, soluble sugar, amino acids, protein, total chlorophyll, lipids, ortho-dihydroxyphenols and phenol (Govindasamy and Srinivasan, 2012). The ethanolic and methanolic extract showed excellent antibacterial activity against *S. aureus*, *B. subtilis*, *E. coli*, *S. typhi* and *P. aeruginosa*. Maximal antibacterial activity has been observed against *S. aureus* at a concentration of 100 mg mL⁻¹ from its leaf extract (Goyal et al., 2008).

**Foeniculum vulgare** (Common fennel) and **Crithmum maritimum** (Marine fennel): Fennel is commonly used as a culinary spice for preservation of food spoilage. The main antioxidant compounds isolated from fennel are the essential oils which have significant antibacterial activity. Trans-anethole and estragole are the major components which show the antibacterial activity against the food-borne pathogens. These compounds inhibit the growth of the Gram positive bacteria such as *B. subtilis* and *S. albus*. They also exhibit antibacterial activity against Gram negative bacteria such as *S. typhimurium*, *Shigella dysenteriae* and *E. coli*. The essential oils are more active against *S. dysenteriae* as compared to other bacteria. The possible mechanism of action of the essential oil is by causing damage to cell membranes, resulting in leakage of electrolytes and losses of intracellular contents (Ruberto et al., 2000; Diao et al., 2014).

**Alternanthera sessilis**: *A. sessilis*, a member of family Amaranthaceae, is known for its antioxidant, hepatoprotective properties and antimicrobial activities along with wound healing potentials. The plant leaves contain active molecules such as A- and β-spiranosters, β-sitosterol and stigmasterol and have been used effectively in the treatment of cuts, wounds and skin diseases. The methanol extracts of *A. sessilis* leaves revealed antimicrobial potential against *E. coli* (Ryan, 1992; Shyamala et al., 2005; Lin et al., 1994; Jalalpur et al., 2008).
**Andrographis paniculata:** *A. paniculata* belongs to family Acanthaceae, is an annual herb distributed in Sri Lanka and many parts of India. It is enriched with medicinal properties of antimalarial, antidiarrhoeal, antihypertensive, antipyretic, antithrombotic, choleretic, immunostimulant and anti-inflammatory activities. The ethanol extract of plant is a potent growth inhibitor of both Gram negative and Gram positive bacteria especially *B. cereus* and *S. aureus*. The antibacterial properties of the plant may be attributed to the actions of tannins, andrographolide, flavonoids and saponins (Mishra et al., 2009; Malahubban et al., 2013; Vidyalakshmi and Ananthi, 2013).

**Angelica acutiloba** (Japanese Dong Quai): *A. acutiloba* is used mainly for treating gynecological disorders. Also, Arabinoxylans obtained from *Angelica acutiloba* plant, have immunomodulatory and antiviral effect in animals (Kiyohara et al., 1981; Kumazawa et al., 1982; Enriquez et al., 1995; Liu et al., 2011).

**Taxus baccata** (Yew): The active compound isolated from *Taxus baccata*, (-)-rhododendrol, is active against *Pseudomonas syringae* and *S. Typhimurium*. The other two compounds obtained from the same plant include 4(4’-hydroxyphenyl)-butan-2-one and 4(4’-hydroxyphenyl)-trans-but-3-en-2-one which exhibit antibacterial activity against *P. syringae* and *B. sphaericus* (Erdemoglu and Sener, 2001; Reddy et al., 2001).

**Allium cepa** (Onions) and **A. sativum** (Garlic): The ethanolic extracts from the cloves of *A. sativum* show antibacterial activity against MDR pathogens responsible for nosocomial infection (Karupiah and Rajaram, 2012). The ethanolic and aqueous extracts from the bulbs of *A. cepa* have been found to have antibacterial action against the common causes of urinary tract infections, *P. aeruginosa* and *S. aureus*, especially those isolated from high vaginal swabs (Azu et al., 2007).

**Annona squamosa**: The bacterial inhibition of the extracts from the leaves of *A. squamosa* is positively correlated with their phenolic contents. The acetone, boiling water, methanol and ethanolic extracts of *A. squamosa* showed low to moderate antibacterial activity in comparison to standard antibacterial drugs (El-Chaghaby et al., 2011).

**Acorus calamus**: The crude methanol extracts from rhizomes of *A. calamus* have significant antimicrobial activities against filamentous fungi and a low degree of activity against bacteria (MIC 5-10 mg mL⁻¹) (Phongpaichit et al., 2005).

**Tinospora cordifolia** (Guduchi/Amruta): It is an extensively used herbal plant in folk Ayurvedic medicine and rasayanas to enhance the immune system and body resistance against infections. The ethanolic extract has been found to show significant antibacterial activity against Gram positive bacteria such as *S. aureus*, *E. coli*, *Serratia marcescens* and Gram negative bacteria such as *E. coli*, *P. vulgaris* and *S. typhi* (Jeyachandran et al., 2003; Nagaprashanthi et al., 2012).

**Woodfordia fruticosa**: The methanolic and ethanolic extract from dried leaves of *W. fruticosa* exhibit excellent antibacterial activity against both Gram positive and Gram negative bacteria including *E. coli*, *Bacillus subtilis*, *P. aeruginosa*, *Salmonella paratyphi*, *Salmonella typhimurium*, *Shigella sonnei*, *K. pneumoniae*, *S. aureus* and *P. vulgaris* (Chougale et al., 2009; Kumar et al., 2013d).

**Betula utilis**: The methanol extract of *B. utilis* possess significant antibacterial activity against both Gram positive and Gram negative bacteria as compared to its aqueous and ethanolic extracts. However, its petroleum ether and chloroform extracts did not have any significant antibacterial activity (Kumaraswamy et al., 2008).

**Terminalia arjuna**, *T. Bellerica* and *T. chebula*: These are commonly used herbal preparations in traditional medicinal system of India. Different preparations of their leaves, stem, bark and seeds are used either as aqeous, ethanolic, methanolic or hydromethanolic extracts. These have been proven antibacterial activities. Tannins as antimicrobial constituents have been purified from *T. chebula* Retz which are effective against MRSA infection. Moreover, aqueous and hydromethanolic extracts have been reported to have antibacterial activity against bacterial pathogens isolated from the cases of bovines mastitis (Sato et al., 1997; Chaudhari and Mengi, 2006; Vashney et al., 2012).

**Capsicum minimum**: This particular plant along with other peppers both strengths and improves digestion as well as lesser the chance of bacterial infections due to unsanitary food as well as water consumption practices (Grubben and Denton, 2004).

**Arnebia densiflora**: The genus *A. densiflora*, member of family Boraginaceae, contain allamnin derivatives,
namely β, β-dimethylacyralkannin, tenacyralkannin and isovalerylalkannin, α-methyl-n-butyralkannin, naphthoquinones and shikonin, which are known for their potential antibacterial, anti-inflammatory and wound healing properties (Kosger et al., 2009).

Agathosma betulina (Buchu): The leaves of this plant have an effective antimicrobial as well as anti-inflammatory potential. ‘Buchu’ oil is obtained from this plant is among most renowned botanical assets of South Africa (Posthumus et al., 1996; Lis-Balchin et al., 2001; Moolla et al., 2007).

Laurus nobilis (Bay Leaf): Bay leaf oil exhibits bactericidal effect against S. enterica and E. coli (Friedman et al., 2002). The activity may be attributed due to the presence of essential oils extracted from bay leaf (Raharivelomanana et al., 1989; Rahman et al., 2008).

Acylphypha indica: A. indica contains flavonoids, acalyphamide, alkaloids and glycosides which exerts antibacterial efficacy by inhibiting pathogens like E. coli and V. cholerae (Nahlstedt et al., 2006; Krishnaraj et al., 2010).

Herbal antimicrobial as feed additives: The exact mechanism by which antibacterial agents improve growth performance is not known, however, several theories have been proposed to explain their beneficial effects:

- Because they reduce the thickness of small intestinal epithelium and nutrients are more efficiently absorbed from the intestinal lumen (Boyd and Edward, 1967; Fuller et al., 1984)
- Nutrients are spared because the number of competing microorganisms is reduced (Eysen, 1962)
- The different microorganisms responsible for subclinical infections are either reduced or eliminated completely (Barnes et al., 1978)
- There is a reduction in production of the growth-depressing toxins or metabolites by intestinal microflora (Dang et al., 1960)

Literature supports that the use of herbal preparations not only act as dietary supplements but also as agents to avert or control various bacterial infections especially enteric, respiratory or systemic infections. Organic extracts of many herbal preparations are available in Indian market viz., Triphala churna, Hareetaki churna, Dashmula churna, Manjistadi churna, Sukhsarak churna, Ajmodadi churna, Shivkshar pachan churna, Mahasudarshan churna, Swadist virechon churna and Pipramool churna. These were tested for their antibacterial potential against enteric bacterial pathogens such as E. coli, S. aureus, E. aerogenes, P. aeruginosa, B. subtilis, K. pneumoniae, S. typhi, S. epidermidis, S. Typhimurium and P. vulgaris, respectively. Result revealed potent antibacterial activity of Triphala churna, Hareetaki churna, Dashmula churna against S. epidermidis, P. vulgaris, S. aureus, E. coli, P. aeruginosa and S. typhi (Anesini and Perez, 1993; Tambekar et al., 2007; Tambekar and Dhikar, 2011).

OTHER CONVENTIONAL/TRADITIONAL AND EMERGING ANTIBACTERIAL THERAPEUTICS

The Complementary and Alternative Medicine (CAM) system includes long standing remedies passed on to generations to be practiced by common people such as herbal, Ayurveda, Siddha, Iranian, Unani, Islamic, Chinese, Acupuncture, Vietnamese and African health care practices all over the globe. Historical evidences suggest that in ancient times, honey, wine, vinegar, turmeric, indigenous herbs and dietary therapies were very successfully used for the management of wound. Some parts of plants can be used as a part of diet to support and hasten the healing process such as turmeric in lukewarm milk and citrus fruits to yield vitamins. These plants thus boost the formation of healthy granulation tissue network. At the time of war, commonly available materials like for treating gunshot wounds were boiling oil, egg yolk, turpentine, yogurt, oil from tea leaves, honey, palm oil and thin peelsings of potato which have been used as therapeutic agents. The use of honey in infected wound management has even been described in the holy books like Bible and the Quran. The first documentary proof of the use of honey as a natural remedy in wound management is well documented in 2000 BC old Egypt literature (Tiwari et al., 2013b). Being viscous and hypertonic in nature honey shows effective antiseptic as well as anti-inflammatory action. Also, because of hyperosmolarity of honey, it absorbs the exudates from the wound and enhances the healing process (Yusof et al., 2007; Tiwari et al., 2013b). Furthermore, honey is rich in antibacterial, antifungal and anti-inflammatory properties especially against S. aureus, coagulase negative staphylococci, community-acquired MRSA, E. coli O157:H7 and S. typhimurium infections. The antibacterial properties are mainly due to the multifarious interaction of the various components of honey viz. hydrogen peroxide, bee defensin-1 and methylglyoxal. Moreover, concentrated and medical grade honey has greater anti-bacterial action (Badawy et al.,
2004; Kwakman et al., 2008; Moussa et al., 2012). In recent years, researchers have also revived their interest in panchgavya element of cow urine for the treatment of various diseases and disorders viz., rheumatoid arthritis, bacteriological infections, tuberculosis, chicken pox, hepatitis, leucorrhoea, leprosy and many others (Dhama et al., 2013d). Studies revealed that cow urine can kill a number of drug resistant bacteria and viruses. Owe to its medicinal properties, cow urine has been granted U.S. Patents (No. 6896907 and 6,410,059), particularly for its use along with antibiotics for the control of bacterial infection and as a bioenhancer of anti-tuberculous drugs (Dhama et al., 2013d; Randhawa, 2010). Apart from these, in the current era of emerging drug resistance, various other novel and emerging antibacterial therapeutic regimens are emerging nowadays viz., bacteriophages, enzybiotics, avian egg antibodies, probiotics, immunomodulators, nutritional elements (Dhama et al., 2008, 2013c, d; Tiwari et al., 2014a, c). To overcome with hurdles of evolving microbial resistance these various alternative and novel therapies are opening new avenues to fight against various bacterial pathogens.

CONCLUSION AND FUTURE PERSPECTIVES

Encountering a bacterial infection is a routine part of the human and animal life. New treatment modalities are constantly sprouting with the advances in medicinal science. Use of various herbs and traditional medicine is safe as well as economical in the present scenario of escalating health care cost. Emergence of MDR microorganisms and a decrease in efficacy of allopathic medicines has driven health care professionals and practitioners to revisit the old ancient healing methods of traditional and alternative medicines. Hence, an abreast is required to dig out as much as possible from the treasure of nature in order to shore up the good health among the advancements in various therapeutic regimens for getting desired protection from several diseases and ailments. A thorough reviewing is therefore mandatory in order to observe and describe and at the same time investigate and validate experimentally the various indigenous drugs along with better understanding of their biological and pharmacological properties. In the safety class rating there is great variation in case of herbal therapy. Many of them are though biologically more active they have the concurrent disadvantages of being toxic as well which must be viewed very carefully regarding dose standardization and extraction procedures. Every phytoconstituent has its pharmacological activity that varies with concentration and presence of another phytoconstituent. Synergistic as well as antagonistic action of phytoconstituents may be beneficial or harmful as toxicity of phytoconstituents at higher concentrations is well documented. Moreover, various pharmacological activities of individual phytoconstituents or their combinations are yet to be established. At the same time a much needed emphasis is required on traditional remedies and new therapeutic approaches. However, at every point a full detailed and well organised and scientifically proved facts based on molecular mechanisms and clinical trials are required in order to avoid the popularized bias towards the important medical sector. Herbal therapy acts thus as a much cheaper, safer and most widely accepted concept of humanity throughout globe, possessing multi-dimensional health benefits. However, traditional medicinal plants require exhaustive scientific validation as well as standardization and safety evaluation before they can be accepted for commercialization. In the present scenario of emerging MDR, herbal therapy is opening new avenues to prevail over superbugs also. Last but not the least, in the field of antibacterials, herbal therapy has immense scope of development for which modern methodology must be employed by new investigations in addition to clinical studies on animals as well as humans. In the current era of “One World One Health One Medicine Concept”, these efforts would altogether pave a way to develop novel broad spectrum antibacterial herbal formulations out of the natural resources for safeguarding several health issues of humans as well as their companion animals.

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