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PRIMARY ARTICLE

Herbal Product Based Remedies Against Microbial Infections And Resistance

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ABSTRACT

Many disease causing microorganisms have developed resistance against drugs, thus causing a challenge for the treatment of infectious diseases. The increase in antimicrobial resistance of various pathogens and the reduced number of available drugs with their decreased efficacy, reduced life span directed to the search of new therapeutic substitutes. Phytochemical derived from herbal plants have a great potential against microbial infections and the medicines derived from plants are now considered safer in contrast to synthetic drugs for use. Medicinal plants are now evaluated against various drug resistant microorganisms. Antibiotic activity can be enhanced by plant derived drugs by decreasing virulence or by reversing drug resistance. In the present review we focus on the herbal plants as a source of bioactive components and their therapeutic properties which may substitute antibiotic based therapy and may be helpful to prevent and cure infections.

KEY WORDS: Infection, Herbal, Antimicrobials, Resistance

1. INTRODUCTION

Infectious diseases comprise clinically evident illness resulting from the infection, presence and growth of pathogen biological agents in an individual host organism. Emerging infectious diseases has emerged as a big challenge that has increased the rate of morbidity and mortality. Bacterial diseases are one of the major threats to human health, for example, tuberculosis which is a cause of deaths all around the world; diarrheal diseases caused by food and waterborne bacteria like *Salmonella* and *Campylobacter;* and the diseases caused by *Streptococcus* etc. Dengue fever is also one of the important arbovirus infections. Many infectious diseases have been recently encountered like SARS, Avian Influenza, Chandipura fever and Nipah virus.

Medicinal plants are being utilized by the human beings to fight diseases from the beginning of the civilization. The use of herbal drugs for treating various diseases has attracted lot of attention due to the emergence of multiple drug resistant pathogens that cause infectious diseases. The discoveries of antibiotics as chemotherapeutic agents lead to the eventual elimination of infectious diseases, but the microorganisms gained resistance because of the over use of the antibiotics. This increasing antimicrobial resistance of microorganisms has become a therapeutic problem and hence, there is a continuing need for new solutions. Also, the people are becoming aware of the side-effects due to over prescription and misuse of antibiotics. Besides increased drug resistance, high-dose and prolonged antimicrobial therapy can eliminate helpful bacterial flora and predispose people to infection (Carson and Riley, 2003; Guarner and Malagelada, 2003). Diarrhea is a common adverse effect of antibiotics, which can lead to loss of essential vitamins and minerals, especially vitamin K, magnesium, and zinc (Briend, 1988; Brunser, 1977; Fontaine, 1996; Guerrant,

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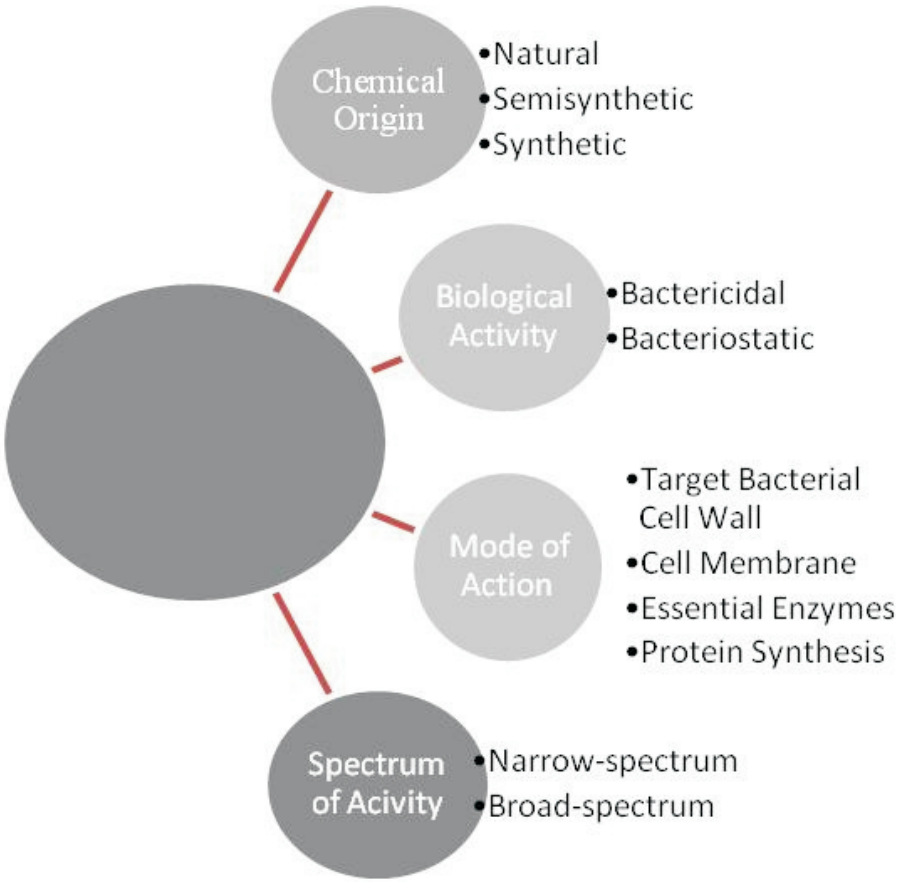
2000). Autoimmune disease, vitamin deficiencies, seizures, decreased platelets, allergic shock, kidney injury, drug/drug interaction, and death are the other harmful consequences of antibiotic therapy (Roden, 2004). Thus, the researchers are forced to search new antimicrobial substance from various sources including herbal plants (Bansod and Rai, 2008). The plant-derived drugs have been reported to be safe and without side-effects making them a better alternative to synthetic drugs. The antimicrobial property of herbal plants is due to the secondary metabolites like tannins, flavanoids and essential oils.

Many diseases have become difficult to treat due to the emergence of antibiotic resistant organisms, which include HIV, *E.coli , enterococci, staphylococci, Salmonella, Campylobacter*, fungi *Candida* and many more. The growing problem of microbial resistance and uncertainty in the use of antibiotics has lead to various actions like development of new drugs, understanding the mechanism of resistance and controlled use of antibiotics. Biomolecules derived from plants are one of the substitutes for controlling the pathogens that are antibiotic resistant (Raghavendra, 2006). Hence, there is an emphasis on studies for the use of plants as therapeutic agents especially for the control of antibiotic resistant microbes.

2.CONVENTIONAL THERAPIES AGAINST INFECTIONS

The mortality rate due to infectious diseases has decreased substantially due to the development and use of antibiotics. Antibiotics also called as “magic drugs” are being used from many decades until now for the treatment of infectious diseases caused by various pathogens. The life span of antibiotics has greatly decreased due to the resistance of microorganisms against them in addition to the declined rate of introduction of new agents against infections. The antibiotic penicillin was isolated from Penicillium spp. by Alexander Fleming in 1929 and it became one of the most famous drugs. Since then many antibiotics have been developed for the treatment of diseases.



The increasing Gram-positive infections, including those because of resistant bacteria, have sparked renewed interest in novel antibiotics. One of the novel lipopeptide antibiotic is daptomycin which have bactericidal activity *in vitro* against all clinically relevant Gram-positive bacteria like glycopeptide intermediately susceptible *Staphylococcus aureus* (GISA), vancomycin-resistant *enterococci* (VRE), methicillin-resistant *Staphylococcus aureus* (MRSA), coagulase-negative *staphylococci* (CNS) and penicillin-resistant *Streptococcus pneumoniae* (PRSP), for which there are very few therapeutic alternatives (Kotra, 2000; Tally and DeBruin, 2000; Barry et al., 2001;Carpenter and Chambers, 2004). Daptomycin presents rapid, concentration-dependent killing and a comparatively long-lasting concentration-dependent post-antibiotic effect *in vitro* (Hanberger et al., 1991; Bush et al., 1989). Spontaneous achievement of resistance to daptomycin occurs unusually (Kaatz et al., 1990; Oliver et al., 1998). One of the other synthetic antibiotic is Linezolid which is used for the treatment of serious infections caused by Gram-positive bacteria that are resistant to several other antibiotics including *streptococci*, vancomycin-resistant *enterococci* (VRE), and methicillin-resistant *Staphylococcus aureus* (MRSA) (Diekema and Jones, 2001; Kaplan et al., 2003).

Ketoconazole, triazoles fluconazole, itraconazole, voriconazole, and posaconazole are the antifungal agents which are available for use against fungal infections (Nagappan and Deresinski, 2007; Johnson and Kauffman, 2003; Kale and Johnson, 2005). The triazole antifungal agent posaconazole is having activity against *Candida* and *Cryptococcus* species, some endemic fungi and many molds (Mellinghoff et al., 2002; Pitisuttithum, 2005). Posaconazole has been approved for the treatment of oropharyngeal candidiasis (Schering-Plough., 2006), including infections refractory to itraconazole and/or fluconazole by the US Food and Drug Administration (USFDA) and also as prophylaxis for invasive *Aspergillus* and *Candida* infections in patients. Limited clinical practice suggests efficacy for the *Zygomycetes* infection treatment and as rescue therapy for patients with invasive coccidioidomycosis and aspergillosis (Ide et al., 2004). Low toxicity and oral administration are the advantages of azole over amphotericin B and is thus advantageous over the echinocandin antifungal agents (Vazquez and Sobel, 2006). Table 1 is showing some commonly used antibiotics along with their MIC range.

Resistance to conventional antibacterial therapies has lead to the development of various alternative strategies like phage therapy, resistance-modifying agents, bacteriocins, chelation of micronutrients, vaccination, biotherapy and probiotics etc.

In phage therapy viruses called phages are used to infect bacteria for the treatment of bacterial infections (Abedon and Calendar, 2005; Mattey and Spencer, 2008). Lytic phage therapy is an alternative approach to conventional antibiotics which shows that phages can be successful in fighting infections which are caused by a variety of pathogens in humans (Westwater et al., 2003). Problems associated with phage include speedy clearance of phage by the filtering organs of the reticuloendothelial system spleen and liver (Molenaar et al., 2002), phage specificity for bacteria, development of bacterial resistance to phages and phage-neutralizing antibodies. Resistance-modifying agents are the compounds that modify resistance to common antibacterials (Gillor et al., 2004). Development of resistance-modifying agents is one of the strategies to address bacterial drug resistance like some resistance-modifying agents may inhibit multidrug resistance mechanisms, such as drug efflux from the cell, thus increasing the susceptibility of bacteria to an antibacterial. The main targets include the efflux inhibitor Phe-Arg-β-naphthylamide, Beta-lactamase inhibitors (such as clavulanic acid and sulbactam). Another possible alternatives to conventional antibacterial compounds is bacteriocins which are peptides that are more readily engineered than small.

Table 1.Antibiotics with their mode of action and MIC range.

Antibiotic	Mode of action/ Target site	MIC range	Reference
Amoxicillin	Disrupt the synthesis of the peptidoglycan layer of bacterial cell walls.	0.032–64 mg/L	Glupczynski, 1993
Clarithromycin	Inhibit protein synthesis	0.0176–0.5 mg/L	Glupczynski, 1993
Kanamycin	Inhibit protein synthesis	0.5–64 mg/L	Glupczynski, 1993
Metronidazole	Produces toxic free radicals which disrupt DNA and proteins.	1–32 mg/L	Glupczynski, 1993
Lansoprazole	Proton pump inhibitor	1–4 mg/L	Glupczynski, 1993
Cefacrol	Inhibit cell wall synthesis	0.25–128 mg/L	Glupczynski, 1993
Clindamycin	Inhibit protein synthesis	1– 128 mg/L	Glupczynski, 1993
Fosfomycin	Inhibits bacterial cell wall biogenesis	2–64 mg/L	Glupczynski, 1993
Levo?oxacin	Inhibit the bacterial DNA gyrase or the topoisomerase IV enzyme, thereby inhibiting DNA replication and transcription.	0.25–64 mg/L	Glupczynski, 1993
Minocycline	Inhibit the binding of aminoacyl-tRNA to the mRNA-ribosome complex. They do so by binding to the 30S ribosomal subunit in the mRNA translation complex.	0.125–2 mg/L	Glupczynski, 1993
Daptomycin	Disrupt bacterial cell membrane function inhibiting protein, DNA, RNA synthesis.	=0.12–8 mg/L	Streit et al., 2004
Linezolid	Inhibit protein synthesis	1–8 µg/ml	Laura et al., 2003
Ketoconazole	Inhibiting the enzyme cytochrome P450.	0.03-1 mg/ml	Barchiesi et al., 1999
Fluconazole	Inhibits the fungal cytochrome P450 enzyme 14α-demethylase.	0.25–64 µg/ml	Sanati et al., 1997
Itraconazole	inhibits the fungal -mediated synthesis of ergosterol	=1–16 mg/L	Jevitt et al., 2003
Voriconazole	inhibits the fungal -mediated synthesis of ergosterol	0.003–4µg/ml	Sanati et al., 1997
Posaconazole	inhibits the fungal -mediated synthesis of ergosterol	=0.015–8 µg/ml	Lortholary et al., 2007
Amphotericin B	Cellular toxicity by binding to ergosterol	0.032–16 µg/ml	Peyron et al., 2001

molecules. Small-molecule bacteriocins like microcins and lantibiotics are similar to the classic antibiotics; colicin-like bacteriocins possess a narrow spectrum. The spread of pathogens can also be restricted by chelation of micronutrients that are essential for bacterial growth, for example, development of iron chelators aim to reduce iron availability specifically to bacterial pathogens (Brock et al., 2006). In biotherapy organisms like protozoa are involved to consume the bacterial pathogens (Nacar and Nacar, 2008). Probiotics consist of a live culture of bacteria as competing symbionts that inhibit or interfere with colonization by microbial pathogens. Various vaccines have also been developed to fight against infections. Immunoregulatory cytokines, hematopoiesis-stimulating factors and monoclonal antibodies can also be utilized against infections due to

antibiotic-resistant bacteria (Chopra et al., 1996).

3. RESISTANCE TO ANTIBIOTICS

The development of antibiotic-resistant strains of microbial pathogens has produced a problem in treatment of infectious diseases. Resistance in microorganisms arise due to two mechanisms i.e. mutation and acquisition. Various biochemical processes are engaged that produces antibiotic resistance by, altering the drug target, keeping antibiotics out of the cell or hindering the antibiotic. The escalating use of antibiotics in humans, animals, and agriculture has resulted in many microorganisms developing resistance to these powerful drugs. All major groups of pathogens like bacteria, viruses, fungi, and parasites can become resistant to antimicrobials. Due to the emergence of antimicrobial resistant pathogens, many diseases have become difficult to treat like malaria caused by parasite *Plasmodium falciparum*; respiratory infections such as tuberculosis and influenza; fungal infections caused by Candida; infections causd by HIV and other viruses; infections caused by bacteria such as *staphylococci, enterococci*, and *Escherichia coli*; ; foodborne pathogens such as *Salmonella* and *Campylobacter*; and sexually transmitted organisms such as *Neisseria gonorrhoeae*. Typhoid fever is no longer treated with chloramphenicol due to resistance developed against the drug. Another example is XDR TB which is a less common form of multidrug-resistant TB and it has become resistant to all the drugs used against MDR TB including the best two antibiotics isonicotinylhydrazine (INH) and Rifampicin (RIF) (Espinal, 2003; Gandhi et al., 2006; Goldman, 2007). In Asia a novel variant of swine flu has emerged with a genetic adaptation giving some resistance to the two main drugs used to tackle this disease i.e. Roche's Tamiflu and GlaxoSmithKline's Relenza (Hirschler, 2011). Gonorrhoea which once used to respond significantly to penicillin; now resists treatment with penicillin and various other antimicrobials like ciprofloxacin (Handsfield et al., 2005). Multi-resistant strains of commonly encountered bacteria are the major cause for most of the hospital-associated infections.

Before the approval of antibacterials for clinical use they are screened for any negative effects on humans or other mammals and then are generally regarded as safe and most are well-tolerated (Slama et al., 2005). Conversely, some antibacterials have been related with a range of adverse effects that range from fever and nausea to major allergic reactions, including photodermatitis , anaphylaxis and diarrhea. Antibacterial-resistant bacteria have emerged mainly due to inappropriate antibacterial treatment and overuse of antibiotics. Self prescription of antibacterials, failure to take the complete prescribed course of the antibacterial, incorrect dosage and administration, or failure to rest for sufficient recovery, use as growth promoters in agriculture are additional examples of misuse (Larson, 2007). Antibacterials like penicillin and erythromycin, have been coupled with emerging antibacterial resistance since the 1950s due to their overuse (Hawkey, 2008).

Antibacterial-resistant strains and species which are also termed as "superbugs", add to the emergence of diseases which were once well-controlled such as NDM-1 is a recently recognized enzyme conveying bacterial resistance to a broad range of beta-lactam antibacterials. It has been stated by the United Kingdom Health Protection Agency that "most isolates with NDM-1 enzyme are resistant to all standard intravenous antibiotics for treatment of severe infections." On January 12, 2011, Richard Horton, the editor of The Lancet, apologized and acknowledged that naming a superbug after New Delhi was an “error” (Sinha, 2011). After this, Ajai R. Singh, editor of Mens Sana Monographs, demanded that such 'geographic names giving' be abandoned and replaced by 'scientific names giving' and also proposed changing NDM-1 to PCM Plasmid-encoding Carbapenem-resistant Metallo-beta-Lactamase (Singh, 2011). Generation of b-lactam resistance has also been comprehensively studied in Enterobacter. b-lactam resistance is likely to be caused by use of cefoxitin and third-generation cephalosporins. Thus, these mutants are generally resistant to both third-generation cephalosporins and penicillins. Pathogens which are initially sensitive to cephalosporins during the treatment show failure to the cephalosporin treatment due to the

selection of highly resistant mutants (Yates, 1999).

4.HERBAL PRODUCT BASED THERAPY

Many plant species have been found to have antimicrobial activity and thus are used as medicinal herbs. These medicinal plants are used in the treatment of wide variety of infections and diseases like respiratory infections, cutaneous infections, gastrointestinal disorders and urinary tract infections. In twentieth century the drug industry was dominated by the synthetic chemistry, as a result of which synthetic molecules replaced the natural extracts. Modern medicine undoubtedly offers an unmatched opportunity to relieve symptoms and save lives in extreme conditions. Revival of interest in herbal medicines is because of the decreasing efficacy of the antibiotics which were once universally effective against serious infections. Many pathogenic microorganisms have developed resistance against the antibiotics which has resulted as a global challenge for the treatment of infectious disease. Another fact is that over thousands of years we have evolved along with plants which have made plant-based remedies to be easily digested and utilized in our system.

The growing presence of antibiotics in food, water and soil and the use of antibiotics in veterinary practices have contributed to the increasing problem of antibiotic resistance (Moshirfar et al., 2006). Many isolates of *Escherichia coli* and *Staphylococcus aureus* are found to be resistant to ampicillin, amoxicillin, tetracycline and trimethoprimsulfamethoxazole (Aibinu and Adenipekun, 2004).

Herbal medicines consist of mixture of one or more plant materials as their active components. The active compounds are utilized both by humans and animals as an important part of their diet. The plant materials include leaves, flowers, fruits, roots, wood, seeds, bark, rhizomes, resins, gum and essential oils. The active components of herbal medicines include phenols, alkaloids, saponins, tannins, anthraquinones, cardiac glycosides, cyanogenic glycosides, terpenes, terpenoids and flavonoids etc. (Harborne, 1973; Okwu, 2004) and these are also termed as secondary metabolites as they are formed metabolic processes of the plants. These components are the precursors for the synthesis of the drugs (Sofowora, 1993). The chemically active constituents interact in a complex way to give therapeutic effects. The working of medicinal herb in its natural form cannot be explained by dividing it into its constituents. The herb as a whole is more worth than sum of its constituents. The medicine derived from herbal plants can either be used in natural form or by isolating their active constituents. Antimicrobials derived from plants have great therapeutic potential, are effective and gentle. The whole specimens are more potential than that in the powder form due to change in tissue arrangements and pattern found in untreated plant samples because of plant cell wall damage during preparation (Metcalfe and Chalk, 1950; Metcalfe, 1954).

A large number of modern drugs have been isolated from herbal plants. About 80% of the world's inhabitants depend on traditional medicine for their health care and thus, the plant-based medicines play an important role in treatment of diseases (Owolabi et al., 2007). The medicinal plants have gained attention due to their increasing use in industries for development of drugs and faith in herbal medicines due to low side-effects than other synthetic antimicrobial compounds. The candidates for the development of new drugs are the substances that have low or no toxicity to host cell and can inhibit or kill the pathogens. The medicinal plants helps in development of drugs by either becoming the base for drugs or as phytomedicine (Iwu et al, 1999).

Medicinal plants have many beneficial effects due to additional action of various chemical compounds that act at single or multiple target sites associated with a physiological process in contrast to synthetic drugs which are based upon single chemicals. The additional pharmacological effects can be advantageous by removing the side effects linked with the high proportion of a single xenobiotic compound in the body (Tyler, 1999). The effectiveness of Phytomedicines is due to the underlying pharmacological effects (Kaufman et al., 1999).

Antioxidant, antifungal, antibacterial and antipyretic effects of medicinal plants are due to the presence of active compounds in them (Adesokan et al, 2008). The increased demand of herbal medicines has produced a high

pressure on the wild population of medicinal plants due to over-harvesting. Many plant species are found in narrow geographical range, have low population densities and slow growth rate (Nautiyal et.al, 2002).

A study shows that oils of *Cymbopogon martini, Eucalyptus globulus* and *Cinnamomum zylenicum* demonstrated the maximum antimycotic activity against human pathogenic *Aspergillus fumigatus* and A. Niger as compared to control (miconazole nitrate), followed by other oils ranging fom moderate to low activity (Bansod and Rai, 2008). Agarwal et. al. in 2007 found that four oils eucalyptus, peppermint, gingergrass and clove showed biofilm reduction significantly against the biofilm forming *Candida albicans strain* (CA I) isolated from clinical samples. Extracts of black pepper (*Piper Nigrum*) and turmeric (*Curcuma Longa*) in three solvents had also been evaluated for their antibacterial and antifungal activity (Pundir and Jain, 2010).

In vitro laboratory studies of honey have shown activity against TB, *H. pylori*, skin ulcers, and colitis (Boyanova et al., 2003; Dobrowolski et al., 1991; Grange and Davey, 1990). *Aframomum melegueta* has many medicinal uses including antimicrobial and antifungal activity, used in aphrodisiac, measles, and leprosy, purgative, galactogogue and anthelmintic (Iwu, 1993). Gingerol, shagaol, paradol are the key constituents. Bromelain is effective against *E.coli* and is proposed as a digestive aid and also shows immuno modulatory properties (Engwerda et al., 2001).

Cranberry juice is effective against bacterial urinary tract infections (Fleet, 1994; Kontiokari et al., 2001). *Martynia annua* L. has shown to be highly active against *Serratia marcescens* followed by *Pseudomonas aeruginosa* (Sermakkani and Thangapandian, 2010).Oregano oil has strong antibacterial properties (Dadalioglu and Evrendilek, 2004) and has been used for the treatment of jaundice, chronic inflammation, dysentery and respiratory infections. Thyme, an essential herbal oil inhibit many strains of *E. coli*, including *E. coli* 0157:H7 (Marino et al., 1999) and is effective in preventing the growth of listeria (Faleiro et al., 2005). Ginger has been found to inhibit gram-positive and gram-negative bacteria (Chrubasik et al., 2005; Mascolo et al., 1989; Thongson et al. 2004). Bactericidal activity is seen *in vitro* against *Escherichia coli, Salmonella typhi* and *Proteus vulgaris* (gram negative strains) and *Staphylococcus aureus* and *Corynebacterium diphtheria* (gram positive strains) by the alcoholic extract of dry nuts of *Semecarpus anacardium* (Bhallatak) (Nair and Bhide, 1996). Cryptolepis sanguinolenta Lindl. Schltr. is used for the treatment of fevers, urinary tract infections, especially Candida. The active components present in *Cryptolepis sanguinolenta* Lindl. Schltr. are indo quinoline alkaloids. Studies show inhibitory effect against gram negative bacteria, yeast (Silva et al., 1996) and also show its bactericidal activity. *In vitro* study shows activity against bacteria *E.coli, C. coli, C. jejuni, Pseudomonous*, *Salmonella, Shigella, Staphylococcus, Streptococcus*, and *Vibrio* and some activity against *Candida* (Sawer et al., 1995).

In traditional systems of medicine, different parts of *Ocimum sanctum* Linn (known as Tulsi) has been used as traditional medicine for the treatment of diarrhea, malaria, dysentery, insect bite, arthritis, skin diseases, bronchitis, bronchial asthma, painful eye diseases, chronic fever etc. The *Ocimum sanctum* L. also possess antimicrobial, antifertility, hepatoprotective, analgesic, anticancer, antidiabetic, antifungal, antimicrobial, cardioprotective, antispasmodic, adaptogenic, antiemetic, and diaphoretic actions (Prakash and Gupta, 2005). The active constituent present in *Ocimum sanctum* L. is eugenol (l-hydroxy-2-methoxy-4-allylbenzene) which is a phenolic compound and is largely responsible for the therapeutic potentials of Tulsi. Ursolic acid, a major constituents of the Tulsi leaves reduces spermatogenesis and causes a decrease in sperm counts because of its anti-estrogenic effect (Rajeshwari, 1992). Ethanol extract of the aerial parts of *Sida acuta Burm.* F. (Malvaceae) shows activity against *Staphylococcus aureus, Bacillus subtilis and Streptococcus faecalis* (Oboh et al., 2007). *Garcinia kola* is purgative, antiparasitic, antiviral and antimicrobial. It is used in the treatment of throat infections, to prevent and relieve colic, bronchitis, cure head or chest colds, relieve cough, treatment of liver disorders and as a chewing stick (Iwu, 1993). The major phytochemicals include

biflavonoids, xanthones and benzophenones mainly attributed to benzophenone, flavanones (Iwu, 1993).

The fruit extracts of *Xylopia aethiopica* (Ethiopian Pepper) has shown antimicrobial against gram positive and negative bacteria, but not effective against *E. coli* (Iwu, 1993). Major constituents are diterpenic and xylopic acid. Xylopic acid present in the plant shows activity against *Candida albicans* (Boakye-Yiadom et al., 1977). The major constituents of *Nauclea latifolia* Smith are indole-quinolizidine alkaloids, sapponins and glycoalkaloids and it is used in septic mouth and malaria, as a tonic and fever medicine, dental caries, toothaches, diarrhea and dysentery (Lamidi et al., 1995). There are studies by Iwu in 1993 shows that the root has antibacterial activity against gram positive and negative bacteria and antifungal activity. It is most efficient against *Corynebacterium diphtheria*, *Streptobacillis sp., Neisseria sp.*, *Pseudomonas aeruginosa, Streptococcus sp., Salmonella sp.* (Deeni and Hussain, 1991).

Table 2. Plants with antimicrobial activity, their active component and target microbe

Plant Name	Active Component	Target microbe	Reference
Adhatoda vasica Nees (Acanthaceae)	Bromohexane, ambroxol	Gram positive and Gram negative bacteria	Grange and Snell, 1996
Allium sativum	Allicin, ajoene, sulfoxide and sulphated terpenoids, ethanolic extract	Multi drug resistant *S.aureus, S.paratyphi, S.dysenteriae, E.coli, M.tuberculosis*	Hannan et al., 2011; Naganawa et al., 1996; San-blas et al., 1993; Ahmad and Beg, 2001
Vaccinium spp. (Blueberry)	Fructose	*E.coli*	Ofek et al., 1996
Aloe barbadensis, Aloe vera	Latex	*Corynebacterium, Salmonella, Streptococcus, S.aureus*	Martinez et al.,1996
Malus sylvestris (apple)	Phloretin	General	Hunter and Hull, 1993
Garcinia mangostana	alphamangostin	vancomycin-resistant enterococci (VRE)	Sakagami et al., 2005
Caesalpinia Coriaria	Methanolic extracts	*Klebsiella pneumoniae*	Mohana et al., 2008
Psidium guajava	Methanolic extracts	MDR *Staphylococcus aureus*	Anas et al., 2008
Commiphora molmol and Boswellia papyrifera	Methanolic extracts	methicillin-resistant *Staphylococcus aureus* (MRSA)	Abdallah et al., 2009
Centratherum punctatum	Methanolic and ethyl acetate extracts	MDR-*Acinetobacter baumannii*	Pawar and Arumugam, 2011
Pelargonium sidoides	Ethanolic extracts	*Aspergillus niger*	Mativandlela et al., 2006
Thonningia sanguinea	Aqueous extract	ESBL-producing *E.coli*	N'guessan et al., 2007
Acacia nilotica, Cinnamomum zeylanicum and *Syzygium aromaticum*	Ethanolic extracts	*Escherichia coli, Klebsiella pneumoniae* and *Candida albicans*	Khan et al., 2009
Cinnamomum cassia	Ethanolic extract	multi-drug resistant *Pseudomonas aeruginosa*	Sharma et al., 2009
Prosopis juliflora	Alkaloid fraction	*Acinetobacter*	Singh et al., 2011
Rabdosia trichocarpa	Trichorabdal A (Terpene)	*Helicobacter pylori*	Kadota et al., 1997
Aegle marmelos	Essential oil (Terpenoid)	Fungi	Rana et al., 1997
Ocimum basilicum	Essential oil (Terpenoid)	*Salmonella*, bacteria	Wan et al., 1998
Hydrastis canadensis	Berberine, hydrastine (Alkaloids)	Bacteria, *Giardia duodenale*, trypanosomes	Freiburghaus et al., 1996
Podocarpus nagi	Totarol (Flavonol)	*P. acnes, other gram-positive bacteria*	Kubo et al., 1994

Piper nigrum	Alkaloid	Fungi, *Lactobacillus, Micrococcus, E. coli, E. faecalis*	Ghoshal et al., 1996
Onobrychis viciifolia	Tannins (Polyphenols)	*Ruminal bacteria*	Jones et al., 1994
Petalostemum	Petalostemumol (Flavonol)	Bacteria, fungi	Hufford et al., 1993
Allium cepa	Allicin (Sulfoxide)	Bacteria, *Candida*	Vohora et al., 1973
Olea europaea	Hexanal (Aldehyde)	General	Kubo et al., 1995
Anacardium pulsatilla	Salicylic acids (Polyphenols)	*P. acnes*, Bacteria, fungi	Himejima and Kubo, 1991.
Matricaria chamomilla	Anthemic acid (Phenolic acid)	*M. tuberculosis, S. typhimurium, S. aureus*, helminths	Bose, 1958; Hamburger and Hostettmann, 1991; Scheel, 1972
Mahonia aquifolia	Berberine (Alkaloid)	*Plasmodium* Trypansomes, general	Omulokoli et al., 1997
Capsicum annuum	Capsaicin (Terpenoid)	Bacteria	Cichewicz and Thorpe, 1996; Jones and Luchsinger, 1986.
Curcuma longa	Curcumin Turmeric oil (Terpenoids)	Bacteria, protozoa	Apisariyakul et al., 1995
Millettia thonningii	Alpinumisoflavone (Flavone)	*Schistosoma*	Perrett et al., 1995
Carum carvi	Coumarins	Bacteria, fungi, viruses	Berkada, 1978; Hamburger and Hostettmann, 1991

5. IMPORTANT ANTIMICROBIAL BIOACTIVE COMPOUNDS DERIVED FROM PLANTS

The antimicrobial property of medicinal plants is due to the phytochemicals synthesized by plants, most of which are secondary metabolites. Many drugs are derived from these chemicals with an advantage of low side-effect and broad range of antibiotics. Phytochemicals act as a natural defence system for host plants and provide aroma, colour, and flavour.

Some of the phytochemical compounds present in medicinal plants are as follows:

5.1 Alkaloids

Alkaloids are basic natural products present primarily in many plants which are usually colourless. Alkaioids are among the most capable and therapeutically significant plant substances (Okwu, 2005). Morphine isolated from opium poppy *Papaver somniferum* in 1805 was the first medically used alkaloid (Fessenden & Fessenden. 1982). Quinine is a bitter tasting alkaloid extracted from bark of a cinchona tree (*C. succirubra*) and used in the treatment of unusually resistant strains of malaria. Diterpenoid alkaloids are found to have antimicrobial properties (Omulokoli, 1997) which are isolated from the plants of the Ranunculaceae (Jones & Luchsinger, 1986, Atta-ur-Rahman & Choudhary, 1995). Alkaloids have microbiocidal effects including against Giardia and Entamoeba species (Ghoshal et al., 1996), the major antidiarrheal effect of alkaloids is probably due to their effects on transit time in the small intestine. Berberine which is a highly aromatic planar quaternary alkaloids is effective against trypanosomes (Freiburghaus et al., 1996) and plasmodia (Omulokoli et al., 1997) due to its to intercalate with DNA(Phillipson and O'Neill, 1987). *Araliopsis tabouensis* is used in the treatment of sexually transmitted diseases, gonorrhoea (Irvine, 1961). The main components are alkaloids. Fish in 1976 isolated seven alkaloids from the root and stem bark. Solamargine is a

glycoalkaloid isolated from the berries of *Solanum khasianum*, and other alkaloids may be useful against HIV infection (McMahon et al., 1995; Sethi, 1979) as well as intestinal infections associated with AIDS (Mendoza et al., 1997).

5.2 Flavonoids

Flavonoids are 15-carbon compounds which are highly water-soluble super antioxidants and free radical scavengers, which prevent oxidative cell damage and have strong anti-cancer properties. Flavonoid compounds show inhibitory properties against multiple viruses. Several studies have recognized the effectiveness of flavonoids such as glycyrrhizin (from licorice) (Watanbe et al., 1996), swertifrancheside (Pengsuparp et al., 1995), and chrysin (Critchfield et al., 1996) against HIV. In a study it was found that flavone derivatives show inhibitory effect on respiratory syncytial virus (RSV) (Barnard et al., 1993; Kaul et al., 1985). A summary provided by Kaul et al. (1985) on modes of action of naringin, quercetin, catechin and hesperetin in in-vitro cell culture monolayers showed that there was no inhibitory effect of naringin on herpes simplex virus type 1 (HSV-1), parainfluenza virus type 3, poliovirus type 1, or RSV, while the other three flavonoids were effective. Intracellular replication of all four viruses was inhibited by hesperetin; infectivity was inhibited by catechin but not intracellular replication of RSV and HSV-1; and quercetin was universally effective in the reduction of infectivity. Teas contain a mixture of catechin compounds and exerted antimicrobial activity (Toda et al., 1989). Catechins inhibit *in vitro Vibrio cholerae* O1 (Borris, 1996), *Streptococcus mutans* (Batista et al., 1994, Sakanaka et al., 1989, Sakanaka et al., 1992, Tsuchiya et al., 1994), *Shigella* (Vijaya et al., 1995), and other bacteria and microorganisms (Sakanaka et al., 1992; Thomson, 1978). Galangin (3,5,7 trihydroxyflavone) shows activity against wide range of fungi(Afolayan and Meyer, 1997), gram-positive bacteria and viruses like HSV-1 and Coxsackie B virus type 1 (Meyer et al., 1997). Flavonoids, having antimicrobial activity have been recently reported which include quercetin 3'-Oglucoside, rutin (Abou-Donia et al., 2008), coumestrol, genistein and daidzein (Redko et al., 2007), morin (Rattanachaikunsopon and Phumkhachorn, 2007) etc.

5.3 Phenolics and Polyphenols

Phenols are a group of aromatic chemical compounds characterized by a hydroxyl (OH) group attached directly to an aromatic ring with weakly acidic properties. The presence of phenols is considered to be potentially toxic to the growth and development of pathogens (Okwu, 2004). Two hydroxylated phenols Catechol and pyrogallol are found to be toxic to microorganisms. Increased hydroxylation results in increased toxicity, thus the sites and number of hydroxyl groups on the phenol group are related to their relative toxicity to microorganisms (Geissman, 1963). In addition, some authors have found that more highly oxidized phenols are more inhibitory (Scalbert, 1991; Urs & Dunleavy, 1975). Phenolic toxicity to microorganisms is thought to be because of enzyme inhibition by the oxidized compounds, possibly through reaction with sulfhydryl groups or through more nonspecific interactions with the proteins (Mason & Wasserman, 1987). Phenolic compounds possessing a C3 side chain at a lower level of oxidation and containing no oxygen are classified as essential oils and often cited as antimicrobial as well. Eugenol is a well-characterized representative found in clove oil. Eugenol is considered active against both fungi (Duke, 1985) and bacteria (Thomson, 1978). Caffeic acid is found in tarragon and thyme and is effective against fungi (Duke, 1985), viruses (Wild, 1994) and bacteria (Brantner and Grein, 1994).

5.4 Quinones

Quinones are aromatic rings with two ketone substitutions which are highly reactive and are ubiquitous in nature. Quinones are known to complex irreversibly with nucleophilic amino acids in proteins (Stern et al., 1996), often leading to inactivation of the protein and loss of function and also as a source of stable free radicals due to which the potential range of quinone antimicrobial effects is great. Surface-exposed adhesins, cell wall polypeptides, and membrane-bound enzymes are the probable targets in the microbial cell. Quinones may also render substrates unavailable to the microorganism. As with all plant derived antimicrobials, the possible toxic effects of quinones must be thoroughly examined. Kazmi et al. (1994)

described an anthraquinone from *Cassia italica*, a Pakistani tree, which was bacteriostatic for *Bacillus anthracis, Corynebacterium pseudodiphthericum, and Pseudomonas aeruginosa and* bactericidal for *Pseudomonas pseudomalliae*. Hypercin is an anthroquinone, which is an example of quinine obtained from St. John's wort (*Hypericum perforatum*) has received much attention as an antidepressant, antiviral and also have several antimicrobial properties (Duke, 1985).

5.5 Terpenoids and Essential Oils

Essential oils or terpenes are secondary metabolites which are highly enriched in compounds based on an isoprene structure. Terpenoids are formed when the compounds contain additional elements, generally oxygen. Methanol, camphor, farnesol and artemisin are some of the common terpenoids. The mode of action of these compounds is not fully known but is thought to involve lipophilic compounds for membrane disruption. Purple prairie clover produce a terpenoid called petalostemumol, which shows very good inhibitory activity against *Bacillus subtilis* and *Staphylococcus aureus* and lesser activity against gram-negative bacteria and *Candida albicans* (Hufford et al., 1993). Artemisin and its derivative a-arteether are used as antimalarials (Vishwakarma, 1990). Terpenoids are active against viruses (Fujioka and Kashiwada, 1994; Hasegawa et al., 1994; Xu et al., 1996), bacteria (Amaral et al., 1998; Barre et al., 1997; Habtemariam, 1993;Tassou,1995), fungi (Ayafor et al.,1994; Rao et al., 1993; Suresh, 1997) and protozoa (Ghoshal, 1996; Vishwakarma, 1990). Trichorabdal A, a diterpene from a Japanese herb has been found to directly inhibit H. pylori (Kadota et al., 1997). The triterpenoid betulinic acid have been shown to inhibit HIV. Terpenoids present in essential oils are found to be useful in the control of *Listeria monocytogenes* (Aureli et al., 1992). Capsaicin, affects the cardiovascular, nervous, and digestive systems (Virus and Gebhart, 1979) and can be used as analgesic (Cordell and Araujo, 1993) but it may favour growth of *Candida albicans*. It is also effective against H.pylori (Jones et al., 1997). Another hot-tasting diterpene, aframodial, a diterpene from a Cameroonian spice, is an antifungal (Ayafor et al., 1994) with a broad-spectrum.

5.4 Tannins

"Tannins" are a group of polymeric phenolic substances with a property known as astringency i.e. capable of tanning leather or precipitating gelatin from solution (Harborne, 1973). They are found in almost all plant parts such as bark, wood, leaves, fruits, and roots (Scalbert, 1991). They are categorized as hydrolyzable and condensed tannins. Cure and prevention of various diseases was suggested by the consumption of tannin-containing beverages, especially green teas and red wines (Serafini et al., 1994) due to which this compound gained a lot of attention. The antimicrobial properties of tannins were studied by Scalbert (1991) and according to him tannins can be toxic to bacteria, filamentous fungi and yeasts. Condensed tannins prevents growth and protease activity of ruminal bacteria by binding to its cell wall (Jones et al., 1994). Studies have shown tannins to be inhibitory to viral reverse transcriptases (Kaul et al., 1985; Nonaka et al., 1990). Tannins bind to proteins and carbohydrates resulting in decrease in digestibility of these macromolecules and thus microbial growth inhibition (Nwogu et al., 2008; Butler, 1988). Astringent properties of tannins have been reported on mucous membranes (Egunyomi et al., 2009). Tannins have also been assigned various human physiological activities like host mediated tumor activity, stimulation of phagocytic cell and a broad range of anti infective actions (Haslam, 1996).

6. CONCLUSION

Antimicrobial worth of medicinal plants has been studied by various researchers and experiments show the inhibitory effect of several phytochemicals on almost all type of microorganisms in vitro. Thus, plants are found to be an important source for the development of safe and economic therapeutic agents for the treatment of various diseases. More studies should be done on these phytochemicals subjected to animals and humans More of these compounds should be subjected to animal and human studies to verify their effectiveness including toxicity studies and their effect on beneficial normal microbiota. Modern drugs can be derived from plant crude extracts showing medical application after investigation of

its bioactivity and toxicity. An extensive research and development work should be undertaken on these herbal plants showing promising activity in the area of antimicrobial agents.

7. REFERENCES

Abdallah, E.M., Khalid, A.E., Ibrahim, N. (2009). Antibacterial activity of oleo-gum resins of *Commiphora molmol* and *Boswellia papyrifera* against methicillin-resistant *Staphylococcus aureus* (MRSA). Scientific Research and Essay, 4, 351 – 356.

Abedon, S.T., Calendar, R.L., ed. (2005). The Bacteriophages.

Abou-Donia, A.H., Toaima, S.M., Hammoda, H.M., Shawky, E., Kinoshita, E., Takayama, H. (2008). Phytochemical and biological investigation of *Hymenocallis littoralis* SALISB. Chem Biodivers, 5, 332-340.

Adesokan, A.A., Yakubu, M.T., Owoyele, B.V., Akanji, M.A., Soladoye, A.O., Lawal, O.K. (2008).Effect of administration of aqueous and ethanolic extracts of *Enantia chlorantha* stem bark on brewer's yeast-induced pyresis in rats. African J. of Biochemistry Research. 2, 165-169.

Afolayan, A.J., Meyer, J.J.M. (1997). The antimicrobial activity of 3,5,7-trihydroxyflavone isolated from the shoots of *Helichrysum aureonitens*. Ethnopharmacol, 57, 177-8.

Agarwal, V., Lal, P., Pruthi. V. (2007). Prevention of *Candida albicans* biofilm by plant oils. Mycopathologia,165, 13-19.

Ahmad, I., Beg, A.Z. (2001). J. Ethnopharmacol, 74, 113-123.

Aibinu, I., Adenipekun, E.O. (2004). Emergence of quinolone resistance amongst *Escherichia coli* strains isolated from clinical infections in some Lagos state hospitals, in Nigeria. Nig. J. Health. Biomed. Sci., 3, 73-78.

Amaral, J.A., Ekins, A., Richards, S.R., Knowles, R. (1998). Effect of selected monoterpenes on methane oxidation, denitrification, and aerobic metabolism by bacteria in pure culture. Appl. Environ. Microbiol., 64, 520–525.

Anas, K., Jayasree, P.R., Vijayakumar, T., Kumar, P.R.M. (2008). *In vitro* antibacterial activity of *Psidium guajava* Linn. leaf extract on clinical isolates of multidrug resistant *Staphylococcus aureus*. Indian J. Of Experimental Biology, 46, 41-46.

Apisariyakul, A., Vanittanakom, N., Buddhasukh, D. (1995). Antifungal activity of turmeric oil extracted from *Curcuma longa* (Zingiberaceae). J. Ethnopharmacol., 49, 163–169.

Atta-ur-Rahman, Choudhary, M.I. (1995). Diterpenoid and steroidal alkaloids. Nat. Prod. Rep., 12, 361–379.

Aureli, P., Costantini, A., Zolea, S. (1992). Antimicrobial activity of some plant essential oils against *Listeria monocytogenes*. J. Food Prot., 55, 344–348.

Ayafor, J.F., Tchuendem, M.H.K., Nyasse, B. (1994). Novel bioactive diterpenoids from *Aframomum aulacocarpos*. J. Nat. Prod., 57, 917–923.

Bansod, S., Rai, M. (2008). Antifungal activity of essential oils from Indian medicinal plants against human pathogenic *Aspergillus fumigatus* and *A. Niger*. World J. of Med. Sciences. 3, 81-88.

Barchiesi, F., Tortorano, A.M., Francesco, L.F.D., Cogliati, M., Scalise, G., Viviani, M.A. (1999). In-vitro activity of five antifungal agents against uncommon clinical isolates of *Candida spp*. J. Antimicrob. Chemother., 43, 295-299.

Barnard, D.L., Huffman, J.H., Meyerson, L.R., Sidwell, R.W. (1993). Mode of inhibition of respiratory syncytial virus by a plant flavonoid. Chemotherapy, 39, 212–217.

Barre, J.T., Bowden, B.F., Coll, J.C., Jesus, J., Fuente, V.E., Janairo, G.C., Ragasa, C.Y. (1997). A bioactive triterpene from *Lantana camara*. Phytochemistry, 45, 321–324.

Barry, A.L., Fuchs, P.C., Brown, S.D. (2001). *In vitro* activities of daptomycin against 2,789 clinical isolates from 11 North American medical centers. Antimicrob. Agents Chemother., 45, 1919-1922.

Batista, O., Duarte, A., Nascimento, J., Simones, M.F. (1994). Structure and antimicrobial activity of diterpenes from the roots of *Plectranthus hereroensis*. J. Nat. Prod., 57, 858–861.

Berkada, B. (1978). Preliminary report on warfarin for the treatment of herpes simplex. J. Irish Coll. Phys. Surg., 22(Suppl.), 56.

Boakye-Yiadom, K., Fiagbe, N., Ayim, S. (1977). Antimicrobial properties of some West African medicinal plants IV. Antimicrobial activity of xylopic acid and other constituents of the fruits of *Xylopia aethiopica* (Annonaceae). Lloydia, 40, 543–545.

Borris, R.P. (1996). Natural products research: perspectives from a major pharmaceutical company. J Ethnopharmacol., 51, 29-38.
Bose, P.K. (1958). On some biochemical properties of natural coumarins. J. Indian Chem. Soc., 58, 367–375.
Boyanova, L., Derejian, S., Koumanova, R., Katsarov, N., Gergova, G., Mitov, I., Nikolov, R., Krastev, Z. (2003). Inhibition of *Helicobacter pylori* growth in vitro by *Bulgarian propolis*: preliminary report. J. Med. Microbiol., 52, 417-419.
Brantner, A., Grein, E. (1994). Antibacterial activity of plant extracts used externally in traditional medicine. J. Ethnopharmacol., 44, 35-40.
Briend, A. (1988). Vitamin A and diarrhoea: reducing the riskfi Dialogue on Diarrhoea online, 33, 4-5.
Brock, J.H., Liceaga, J., Kontoghiorghes, G.J. (2006). The effect of synthetic iron chelators on bacterial growth in human serum. FEMS Microbiology Letters, 47 (1), 55–60.
Brunser, O. (1977). Effects of malnutrition on intestinal structure and function in children. Clin. Gastroenterol., 6, 341-53.
Bush, L.M., Boscia, J.A., Wendeler, M., Pitsakis, P.G., Kaye, D. (1989). In vitro postantibiotic effect of daptomycin (LY146032) against Enterococcus faecalis and methicillin-susceptible and methicillin-resistant *Staphylococcus* aureus strains. Antimicrobial Agents and Chemotherapy, 33, 1198-2000.
Butler, L.G. (1989). Effects of Condensed Tannins on Animal Nutrition. In: Hemingway, R.W. and Karchesy, J.J. (eds.). Chemistry and significance of condensed tannins. Plenum Press, N.Y.
Carpenter, C.F., Chambers, H.F. (2004). Daptomycin: another novel agent for treating infections due to drug-resistant Gram-positive pathogens. Clin. Infect. Dis., 38, 994-1000.
Carson, C.F., Riley, T.V. (2003). Non-antibiotic therapies for infectious diseases. Commun Dis Intell., 27(suppl), S143-S146.
Chopra, I., Hodgson, J., Metcalf, B., Poste, G. (1996). New approaches to the control of infections caused by antibiotic-resistant bacteria. An industry perspective. JAMA 275, 401–403.
Chrubasik, S., Pittler, M.H., Roufogalis, B.D. (2005). *Zingiberis rhizoma*: a comprehensive review on the ginger effect and efficacy profiles. Phytomedicine, 12, 684-701.
Cichewicz, R.H., Thorpe, P.A. (1996). The antimicrobial properties of chile peppers (Capsicum species) and their uses in Mayan medicine. J.Ethnopharmacol., 52, 61–70.
Cordell, G.A., Araujo, O.E. (1993). Capsaicin: identification, nomenclature, and pharmacotherapy. Ann. Pharmacother., 27, 330–336.
Critchfield, J.W., Butera, S.T., Folks, T.M. (1996). Inhibition of HIV activation in latently infected cells by flavonoid compounds. AIDS Res. Hum. Retroviruses, 12, 39-46.
Dadalioglu, I., Evrendilek, G.A. (2004). Chemical compositions and antibacterial effects of essential oils of Turkish oregano, bay laurel, Spanish lavender, and fennel on common foodborne pathogens. J Agric Food Chem., 52, 8255-8260.
Deeni, Y., Hussain, H. (1991). Screening for antimicrobial activity and for alkaloids of *Nauclea latifolia*. J. Ethnopharmacol., 35, 91–96.
Diekema, D.J., Jones, R.N. (2001). Oxazolidinone antibiotics. Lancet, 358, 1975–1982.
Dobrowolski, J.W., Vohora, S.B., Sharma, K., Shah, S.A., Naqvi, S.A., Dandiya, P.C. (1991). Antibacterial, antifungal, antiamoebic, anti-inflammatory and antipyretic studies on propolis bee products. J Ethnopharmacol., 35, 77-82.
Duke, J.A. (1985). Handbook of medicinal herbs. CRC Press, Inc., Boca Raton, Fla.
Egunyomi, A., Moody, J.O., Eletu, O.M. (2009). Antisickling activities of two ethnomedicinal plant recipes used for the management of sickle cell anaemia in Ibadan, Nigeria. African J. of Biotechnology, 8, 020-025.
Engwerda, C.R., Andrew, D., Ladhams, A., Mynott, T.L. (2001). Bromelain modulates T cell and B cell immune responses *in vitro* and in vivo. Cell Immunol., 210, 66-75.
Espinal, M.A. (2003). The global situation of MDR-TB.Tuberculosis, 83, 44–51.
Faleiro, L., Miguel, G., Gomes, S., Costa, L., Venâncio, F., Teixeira, A., Figueiredo, A.C., Barroso, J.G., Pedro, L.G. (2005). Antibacterial and antioxidant activities of essential oils isolated from Thymbra capitata L (Car.) and Origanum vulgare L. J. Agric. Food Chem., 53, 8162-8168.
Fessenden, R.J., Fessenden, J.S. (1982). Organic chemistry, 2nd ed. Willard Grant Press, Boston, Mass.
Fish, F., Meshal, I., Waterman, P. (1976). Minor alkaloids of Araliopsis tabouensis.

Planta Med., 29, 310–317.
Fleet, J.C. (1994). New support for a folk remedy: cranberry juice reduces bacteriuria and pyuria in elderly women. Nutr Rev., 52, 168-70.
Fontaine, O. (1996). Dealing with diarrhoea. Child Health Dialogue, 3-4, 5.
Freiburghaus, F., Kaminsky, R., Nkunya, M.H.H., Brun, R. (1996). Evaluation of African medicinal plants for their in vitro trypanocidal activity. J. Ethnopharmacol., 55, 1-11.
Fujioka, T., Kashiwada, Y. (1994). Anti-AIDS agents. 11. Betulinic acid and platanic acid as anti-HIV principles from Syzigium clavifiorum, and the anti-HIV activity of structurally related triterpenoids. J. Nat. Prod., 57, 243–247,
Gandhi, N.R., Moll, A., Sturm, A.W., Pawinski, R., Govender, T., Lalloo, U., Zeller, K., Andrews, J., Friedland, G. (2006). Extensively drug-resistant tuberculosis as a cause of death in patients co-infected with tuberculosis and HIV in a rural area of South Africa. Lancet, 368, 1575–1580.
Geissman, T. A. (1963). Flavonoid compounds, tannins, lignins and related compounds. In: Florkin, M., Stotz, E. H. (ed.). Pyrrole pigments, isoprenoid compounds and phenolic plant constituents, vol. 9. Elsevier, New York, pp: 265.
Ghoshal, S., Krishna Prasad, B.N., Lakshmi, V. (1996). Antiamoebic activity of Piper longum fruits against Entamoeba histolytica in vitro and in vivo. J. Ethnopharmacol., 50, 167–170.
Gillor, O., Kirkup, B.C., Riley, M.A. (2004). Colicins and microcins: the next generation antimicrobials. Adv. Appl. Microbiol. 54, 129–46.
Glupczynski, Y. (1993). In vitro susceptibility testing of Helicobacter pylori to antimicrobial agents: basis for treatment or microbiologists' obsessionfi Int. J. of Med. Microbiology, Virology, Parasitology & Infectious Diseases, 280, 227–38.
Goldman, R.C., Plumley, K.V., Laughon, B.E. (2007). The evolution of extensively drug resistant tuberculosis (XDR-TB): history, status and issues for global control. Infect. Disord. Drug Targets, 7, 73–91.
Grange, J. M., Davey, R.W. (1990). Antibacterial properties of propolis (bee glue). J. R. Soc. Med., 83, 159-60.
Grange, J.M., Snell, N.J., (1996). Activity of bromhexine and ambroxol, semi-synthetic derivatives of vasicine from the Indian shrub Adhatoda vasica against Mycobacterium tuberculosis in vitro. J. Ethnopharmacol., 50, 49-53.
Guarner, F., Malagelada, J.R. (2003). Gut flora in health and disease. Lancet, 361, 512-519.
Guerrant, R.L., Lima, A.A., Davidson, F. (2000). Micronutrients and infection: interactions and implications with enteric and other infections and future priorities. J. Infect. Dis., 182(suppl 1), 134-8.
Habtemariam, S., Gray, A.I., Waterman, P.G. (1993). A new antibacterial sesquiterpene from Premna oligotricha. J. Nat. Prod., 56, 140–143.
Hamburger, H., Hostettmann, K. (1991). The link between phytochemistry and medicine. Phytochemistry, 30, 3864–3874.
Hanberger, H., Nilsson, L.E., Maller, R., Isaksson, B. (1991). Pharmacodynamics of daptomycin and vancomycin on Enterococcus faecalis and Staphylococcus aureus demonstrated by studies of initial killing and postantibiotic effect and influence of Ca2+ and albumin on these drugs. Antimicrobial Agents and Chemotherapy, 35, 1710-1716.
Handsfield, H., Spalintg, P., Mandell, L.G., Benneth, E.J., Dolin, R. (2005). Neisseria gonorrhoeae. In: (Eds). Principles and practice of infectious diseases.6th ed. Elsiver Inc. Philadelphia, USA, 2514-2526.
Hannan, A., Ikram-Ullah, M., Usman, M., et al. (2011). Antimycobacterial activity of Garlic (Allum Sativum) against multi-drug resistant and non-multi-drug resistant Mycobacterium tuberculosis. Pak. J. Pharm. Sci., 24, 81-85.
Harborne, J.B. (1973). Phytochemical methods, London. Chapman and Hall, Ltd. pp. 49-188.
Hasegawa, H., Matsumiya, S., Uchiyama, M., Kurokawa, T., Inouye, Y., Kasai, R., Ishibashi, S., Yamasaki, K. (1994). Inhibitory effect of some triterpenoid saponins on glucose transport in tumor cells and its application to in vitro cytotoxic and antiviral activities. Planta Med., 6, 240–243.
Haslam, E. (1996). Natural polyphenols (vegetable tannins) as drugs: possible modes of action. J. Nat. Prod., 59, 205-15.
Hawkey, P.M. (2008). The growing burden of antimicrobial resistance. J. Antimicrob. Chemother. 62 Suppl 1, i1–9.
Himejima, M., Kubo, I. (1991). Antibacterial agents from the cashew

Anacardium occidentale. J. Agric. Food Chem., 39, 418–421.
Hirschler, B. (2011-06-10). Swine flu starting to show resistance to drugs. Reuters.
Hufford, C.D., Jia, Y., Croom, E.M., Muhammed, I.Jr., Okunade, A.L., Clark, A.M., Rogers, R.D. (1993). Antimicrobial compounds from Petalostemum purpureum. J. Nat. Prod., 56, 1878–1889.
Hunter, M.D., Hull, L.A. (1993). Variation in concentrations of phloridzin and phloretin in apple foliage. Phytochemistry, 34, 1251–1254.
Ide, L., Buysschaert, I., Demuynck, H., De Man, R., Verlinde, A., De Laere, E., Surmont, I. (2004). Zygomycosis in neutropenic patients with past Aspergillus infection: a role for posaconazolefi Clin. Microbiol. Infect., 10, 862–863.
Irvine, F. (1961). Woody plants of Ghana. Oxford Univ. Press, London. pp. 48-50.
Iwu, M. (1993). Handbook of African medicinal plants. CRC Press, Boca Raton, FL.
Iwu, M.M., Duncan, A.R., Okunji, C.O. (1999). New Antimicrobials of Plant Origin. J. Janick (ed.), ASHS Press, Alexandria, VA.
Jevitt, L.A., Smith, A.J., Williams, P.P., Raney, P.M., McGowan Jr., J.E., Tenover, F.C. (2003). In Vitro Activities of Daptomycin, Linezolid, and Quinupristin-Dalfopristin against a Challenge Panel of Staphylococci and Enterococci, Including Vancomycin-Intermediate Staphylococcus aureus and Vancomycin-Resistant Enterococcus faecium. Microb. Drug Resist., 9, 389-93.
Johnson, L.B., Kauffman, C.A. (2003). Voriconazole: a new triazole antifungal agent. Clin. Infect. Dis., 36, 630–637.
Jones Jr., S.B., Luchsinger, A.E. (1986). Plant systematics. McGraw- Hill Book Co., New York, N.Y.
Jones, G.A., McAllister, T.A., Muir, A.D., Cheng, K.J. (1994). Effects of sainfoin (Onobrychis viciifolia scop.) condensed tannins on growth and proteolysis by four strains of ruminal bacteria. Appl. Environ. Microbiol., 60, 1374–1378.
Jones, N.L., Shabib, S., Sherman, P.M. (1997). Capsaicin as an inhibitor of the growth of the gastric pathogen Helicobacter pylori. FEMS Microbiol. Lett., 146, 223–227.
Kaatz, G.W., Seo, S.M., Reddy, V.N., Bailey, E.M., Rybak, M.J. (1990). Daptomycin compared with teicoplanin and vancomycin for therapy of experimental Staphylococcus aureus endocarditis. Antimicrobial Agents and Chemotherapy, 34, 2081-2085.
Kadota, S., Basnet, P., Ishii, E., Tamura, T., Namba, T. (1997). Antibacterial activity of trichorabdal from Rabdosia trichocarpa against Helicobacter pylori. Zentbl. Bakteriol., 286, 63–67.
Kale, P., Johnson, L.B. (2005). Second-generation azole antifungal agents. Drugs Today (Barc), 41, 91–105.
Kaplan, S.L., Deville, J.G., Yogev, R., Morfin M.R., Wu, E., Adler, S. et al. (2003). Linezolid versus vancomycin for treatment of resistant Gram-positive infections in children. Pediatr. Infect. Dis. J., 22, 677–686.
Kaufman, P.B., Cseke, L.J., Warber, S., Duke, J.A., Brielmann, H.L. (1999). Natural Products from Plants. CRC Press, Boca Raton, FL.
Kaul, T.N., Middletown, E. Jr., Ogra, P.L. (1985). Antiviral effect of flavonoids on human viruses. J. Med. Virol., 15, 71-9.
Kazmi, M.H., Malik, A., Hameed, S., Akhtar, N., Ali, S.N. (1994). An anthraquinone derivative from Cassia italica. Phytochemistry, 36, 761-3.
Khan, R., Islam, B., Akram, M., Shakil, S., Ahmad, A., Ali, S.M., Siddiqui, M., Khan, A.U. (2009). Antimicrobial Activity of Five Herbal Extracts Against Multi-Drug Resistant (MDR) Strains of Bacteria and Fungus of Clinical Origin. Molecules, 14, 586-597.
Kontiokari, T., Sundqvist, K., Nuutinen, M., Pokka, T., Koskela, M., Uhari, M. (2001). Randomised trial of cranberry-lingonberry juice and Lactobacillus GG drink for the prevention of urinary tract infections in women. BMJ, 322, 1571.
Kotra, L.P. (2000). Daptomycin. Current Opinion in Anti-Infective Investigational Drugs, 2, 185-205.
Kubo, A., Lunde, C.S., Kubo, I. (1995). Antimicrobial activity of the olive oil flavor compounds. J. Agric. Food Chem., 43, 1629–1633.
Kubo, I., Muroi, H., Kubo, A. (1994). Naturally occurring anti-acne agents. J. Nat. Prod., 57, 9–17.
Lamidi, M., Ollivier, E., Faure, R., Debrauwer, L., Nze-Ekekang, L., Balansard, G. (1995). Quinovic acid glycosides from Nauclea diderichii. Planta Med., 61,280–281.
Larson, E. (2007). Community factors in the development of antibiotic resistance. Annu Rev Public Health, 28, 435–447.
Lortholary, O., Dannaoui1, E., Raoux, D., Hoinard, D., Datry, A., Paugam, A., Poirot, J., Lacroix, C., Dromer, F., the

YEASTS Group (2007). In Vitro Susceptibility to Posaconazole of 1,903 Yeast Isolates Recovered in France from 2003 to 2006 and Tested by the Method of the European Committee on Antimicrobial Susceptibility Testing. Antimicrob. Agents Chemother., 51, 3378-3380.

Marino, M., Bersani, C., Comi, G. (1999). Antimicrobial activity of the essential oils of Thymus vulgaris L. measured using a bioimpedometric method. J Food Prot., 62, 1017-23.

Martinez, M.J., Betancourt, J., Alonso-Gonzalez, N., Jauregui, A. (1996). Screening of some Cuban medicinal plants for antimicrobial activity. J. Ethnopharmacol., 52, 171–174.

Mascolo, N., Jain, R., Jain, S.C., Capasso, F. (1989). Ethnopharmacologic investigation of ginger (Zingiber officinale). J. Ethnopharmacol., 27, 129-140.

Mason, T.L., Wasserman, B.P. (1987). Inactivation of red beet beta-glucan synthase by native and oxidized phenolic compounds. Phytochemistry, 26, 2197-2202.

Mativandlela, S.P.N., Lall, N., Meyer, J.J.M. (2006). Antibacterial, antifungal and antitubercular activity of (the roots of) Pelargonium reniforme (CURT) and Pelargonium sidoides (DC) (Geraniaceae) root extracts. South African J. of Botany, 72, 232-237.

Mattey, M., Spencer, J. (December 2008). Bacteriophage therapy--cooked goose or phoenix risingfi Curr. Opin. Biotechnol. 19 (6), 608–12.

McMahon, J.B., Currens, M.J., Gulakowski, R.J., Buckheit, R.W.J., Lackman-Smith, C., Hallock, Y.F., Boyd, M.R. (1995). Michellamine B, a novel plant alkaloid, inhibits human immunodeficiency virus-induced cell killing by at least two distinct mechanisms. Antimicrob. Agents Chemother., 39, 484–488.

Mellinghoff, I.K., Winston, D.J., Mukwaya, G., Schiller, G.J. (2002). Treatment of Scedosporium apioseprmum brain abscess with posaconazole. Clin. Infect. Dis., 34, 1648–50.

Mendoza, L., Wilkens, M., Urzua, A. (1997). Antimicrobial study of the resinous exudates and of diterpenoids and flavonoids isolated from some Chilean Pseudognaphalium (Asteraceae). J. Ethnopharmacol., 58, 85–88.

Metcalfe, C.R. (1954). Recent work on the systematic anatomy of the Monocotyledons (with special reference to investigation of the Jodrell Lab. at Kew), Kew Bulletin, pp. 523-532.

Metcalfe, C.R., Chalk, L. (1950). Anatomy of the Dicotyledons. Oxford at the Clarendon Press. UK. 1, 147-152.

Meyer, J.J.M., Afolayan, A.J., Taylor, M.B., Erasmus, D. (1997). Antiviral activity of galangin from the aerial parts of Helichrysum aureonitens. J. Ethnopharmacol., 56, 165-169.

Mohana, D.C., Satish, S., Raveesha, K.A. (2008). Antibacterial evaluation of some plant extracts against some human pathogenic bacteria. Advances in Biological Research, 2, 49-55.

Molenaar, T.J.M., Michon, I., De Haas, S.A.M., Van Berkel, T.J.C., Kuiper, J., Biessen, E.A.L. (2002). Uptake and processing of modified bacteriophage M13 in mice: implications for phage display. Virology, 293, 182–191.

Moshirfar, M., Mirzaian, G., Feiz, V., Kang, P.C. (2006). Fourth generation fluoroquinolone-resistant bacterial keratitis after refractive surgery. J. Cataract Refract Surg., 32, 515-8.

N'guessan, J.D., Dinzedi, M.R., Guessennd, N., Coulibaly, A., Dosso, M., Djaman, A.J., Guede-Guina, F. (2007). Antibacterial activity of the aqueous extract of Thonningia sanguinea against Extended Spectrum-β-Lactamases (ESBL) producing Escherichia coli and Klebsiella pneumoniae strains. Tropical J. of Pharmaceutical Research, 6, 779-783.

Nacar, A., Nacar, E. (2008). Phagotrophic protozoa: A new weapon against pathogensfi Medical Hypotheses, 70 (1), 141–142.

Naganawa, R., Iwata, N., Ishikawa, K., Fucada, H., Fujino, T., Suzuki, A. (1996). Inhibition of microbial growth by ajoene, a sulfur-containing compound derived from garlic. Appl. Environ. Microbiol., 59, 4238-4242.

Nagappan, V., Deresinski, S. (2007). Posaconazole: A Broad-Spectrum Triazole Antifungal Agent. Clin. Infect. Dis., 45, 1610–1617.

Nair, A., Bhide, S.V. (1996). Antimicrobial properties of different parts of Semecarpus anacardium. Indian Drugs, 33, 323-8.

Nautiyal, S., Maikhuri, R.K., Rao, K.S., Semwal, R.L., Saxena, K. G. (2002). Agroecosystem function around a Himalayan Biosphere Reserve. J. Environ. Syst., 29, 71-100.

Nonaka, G.I., Nishioka, I., Nishizawa, M., Yamagishi, T., Kashiwada, Y., Dutschman, G.E., Bodner, A.J., Kilkuskie, R.E., Cheng, Y.C., Lee, K.H. (1990). Anti-AIDS agents. 2: Inhibitory effects of tannins on HIV reverse transcriptase and HIV replication in H9 lymphocyte cells. J. Nat. Prod., 53, 587–595.

Nwogu, L.A., Igwe, C.U., Emejulu, A.A. (2008). Effects of Landolphia owariensis leaf extract on the liver function profile and haemoglobin concentration of albino rats. Afr. J. Biochem. Res., 2, 240-242.

Oboh, I.E., Akerele, J.O., Obasuyi, O. (2007). Antimicrobial activity of the ethanol extract of the aerial parts of sida acuta burm.f. (malvaceae). Tropical J. of Pharmaceutical Research, 6, 809-813.

Ofek, I., Goldhar, J., Sharon, N. (1996). Anti-Escherichia coli adhesion activity of cranberry and blueberry juices. Adv. Exp. Med. Biol., 408, 179–183.

Okwu, D.E. (2004). Phytochemicals and vitamin content of indigenous species of South Eastern Nigeria. J. of Sustainable Agric. and Environment, 6, 30-37.

Okwu, D.E. (2005). Phytochemicals, vitamins and mineral content of two Nigerian plants. Int. J. of Molecular Medicine and Advance Sciences, 1, 375-381.

Oliver, N., Andrew, T., Silverman, J.A., Li, T. (1998). In vitro studies on resistance of lipopeptide antibiotic daptomycin. In Program and Abstracts of the Thirty-eighth Interscience Conference on Antimicrobial Agents And Chemotherapy, San Diego, CA, 1998. Abstract F-117,p.262. American Society for Microbiology, Washington, DC.

Omulokoli, E., Khan, B., Chhabra, S.C. (1997). Antiplasmodial activity of four Kenyan medicinal plants. J. Ethnopharmacol., 56, 133-7.

Owolabi, J., Omogbai, E.K.I., Obasuyi, O. (2007). Antifungal and antibacterial activities of the ethanolic and aqueous extract of Kigelia africana (Bignoniaceae) stem bark. Afr. J. Biotechnol., 6, 882-85.

Pawar, N.K., Arumugam, N. (2011). Leaf extract of Centratherum punctatum exhibits antimicrobial, antioxidant and anti proliferative properties. Asian J. of pharmaceutical and clinical research, 4, 71-76.

Pengsuparp, T., Cai, L., Constant, H., Fong, H.H., Lin, L.Z., Kinghorn, A.D., Pezzuto, J.M., Cordell, G.A., Ingolfsdóttir, K., Wagner, H. (1995). Mechanistic evaluation of new plant-derived compounds that inhibit HIV-1 reverse transcriptase. J. Nat. Prod., 58, 1024-31.

Perrett, S., Whitfield, P.J., Sanderson, L., Bartlett, A. (1995). The plant molluscicide Millettia thonningii (Leguminosae) as a topical antischistosomal agent. J. Ethnopharmacol., 47, 49–54.

Peyron, F., Favel,A., Michel-Nguyen, A., Gilly, M., Regli, P., Bolmstrom, A. (2001). Improved Detection of Amphotericin B-Resistant Isolates of Candida lusitaniae by Etest. J. Clin. Microbiol., 39, 339–342.

Phillipson, J.D., O'Neill, M.J. (1987). New leads to the treatment of protozoal infections based on natural product molecules. Acta. Pharm. Nord., 1, 131-44.

Pitisuttithum, P., Negroni, R., Graybill, J.R., et al. (2005). Activity of posaconazole in the treatment of central nervous system fungal infections. J. Antimicrob. Chemother., 56, 745–55.

Prakash, P., Gupta, N. (2005). Therapeutic uses of Ocimum Sanctum Linn (Tulsi) with a note on eugenol and its pharmacological actions: a short review. Indian J. Physiol. Pharmacol., 49, 125–131.

Pundir, R.K., Jain, P., 2010. Comparative studies on the antimicrobial activity of black pepper (Piper nigrum) and turmeric (Curcuma longa) extracts. International Journal of Applied Biology and Pharmaceutical Technology,1, 492-501.

Raghavendra, M.P., Satish, S., Raveesha, K.A. (2006). Phytochemical analysis and antibacterial activity of Oxalis corniculata; a known medicinal plant. Myscience, 1, 72-78.

Rajeshwari, S. (1992).Ocimum sanctum. The Indian home remedy. In: Current Medical Scene.

Rana, B.K., Singh, U.P., Taneja, V. (1997). Antifungal activity and kinetics of inhibition by essential oil isolated from leaves of Aegle marmelos. J. Ethnopharmacol., 57, 29–34.

Rao, K.V., Sreeramulu, K., Gunasekar, D., Ramesh, D. (1993). Two new sesquiterpene lactones from Ceiba pentandra. J. Nat. Prod., 56, 2041–2045

Rattanachaikunsopon, P., Phumkhachorn, P. (2007). Bacteriostatic effect of flavonoids isolated from leaves of Psidium guajava on fish pathogens. Fitoterapia, 78, 434-436.

Redko, F., Clavin, M.L., Weber, D., Ranea, F., Anke, T., Martino, V. (2007). Antimicrobial isoflavonoids from Erythrina crista galli infected with Phomopsis sp. Z. Naturforsch [C], 62, 164-168.

Roden, D.M. (2004). Principles of clinical

pharmacology. In: Kasper DL, Braunwald E, et al., eds. Harrison's Principles of Internal Medicine . 16th ed. New York , NY : McGraw-Hill.
Rybak, M.J., Hershberger, E., Moldovan, T., Grucz, R.G. (2000). In vitro activities of daptomycin, vancomycin, linezolidand quinupristin-dalfopristin against staphylococci and enterococci, including vancomycin-intermediate and -resistant strains. Antimicrobial Agents and Chemotherapy, 44, 1062-1066.
Sakagami, Y., Iinuma, M., Piyasena, K.G.N.P., Dharmaratne, H.R.W. (2005). Antibacterial activity of alpha-mangostin against vancomycin resistant Enterococci (VRE) and synergism with antibiotics. 12, 203-208.
Sakanaka, S., Kim, M., Taniguchi, M., Yamamoto, T. (1989). Antibacterial substances in Japanese green tea extract against Streptococcus mutans, a cariogenic bacterium. Agric. Biol. Chem., 53, 2307–2311.
Sakanaka, S., Shimura, N., Aizawa, M., Kim, M., Yamamoto, T. (1992). Preventive effect of green tea polyphenols against dental caries in conventional rats. Biosci. Biotechnol. Biochem., 56, 592–594.
Sanati, H., Belanger, P., Fratti, R., Ghannoum, M. (1997). A New Triazole, Voriconazole (UK-109,496), Blocks Sterol Biosynthesis in Candida albicans and Candida krusei. Antimicrobial agents and chemotherapy, 41, 2492–2496.
San-blas, G., Marino, I., San-blas, F., apitz-Castro, R. (1993). Effect of ajoene on dimorphism of Paracoccidioides brasiliensis. J. Med. Vet. Mycol., 31, 133-141.
Sawer, I., Berry, M., Brown, M., Ford, J. (1995). The effect of Cryptolepine on the morphology and survival of Eschericia coli, Candida albicans and Saccharomyces cerevisiae. J. Appl. Bacteriol., 79, 314–321.
Scalbert, A. (1991). Antimicrobial properties of tannins. Phytochemistry, 30, 3875–3883.
Scheel, L.D. (1972). The biological action of the coumarins. Microbiol. Toxins, 8, 47–66.
Schering-Plough. (23 October 2006). Schering-Plough announces FDA approval of NOXAFIL(R) (posaconazole) for treatment of oropharyngeal candidiasis (OPC) [news release]. Summit, NJ: Schering-Plough.
Serafini, M., Ghiselli, A., Ferro-Luzzi, A. (1994). Red wine, tea and anti-oxidants. Lancet, 344, 626.
Sermakkani, M., Thangapandian, V., 2010. Phytochemical and antibacterial activity of Martynia annua L. against the different pathogenic bacteria. Journal of Herbal Medicine and Toxicology, 4 (2), 221-224
Sethi, M.L. (1979). Inhibition of reverse transcriptase activity by benzophenanthridine alkaloids. J. Nat. Prod., 42, 187–196.
Sharma, A., Chandraker, S., Patel, V.K., Ramteke, P. (2009). Antibacterial activity of medicinal plants against pathogens causing complicated urinary tract infections. Indian J. of pharmaceutical sciences, 71, 136-139.
Silva, O., Duarte, A., Cabrita, J., Pimentel, M., Diniz, A., Gomes, E. (1996). Antimicrobial activity of Guinea-Bissau traditional remedies. J. Ethnopharmacol., 50, 55–59.
Singh, A.R. (2011). Science, names giving and names calling: Change NDM-1 to PCM. Mens Sana Monographs, 9, 294-319.
Singh, S., Swapnil, Verma, S.K. (2011). Antibacterial properties of Alkaloid rich fractions obtained from various parts of Prosopis juliflora . Int. J. of Pharma Sciences and Research, 2, 114-120.
Sinha, K. (2011). Lancet says sorry for 'Delhi bug'. The Times of India.
Slama, T.G., Amin, A., Brunton, S.A. et al. (2005). A clinician's guide to the appropriate and accurate use of antibiotics: the Council for Appropriate and Rational Antibiotic Therapy (CARAT) criteria. Am. J. Med., 118 Suppl 7A, 1S–6S.
Sofowara, A. (1993). Medicinal plants and Traditional medicine in Africa. Spectrum Books Ltd., Ibadan, Nigeria. pp. 289.
Stern, J.L., Hagerman, A.E., Steinberg, Mason, P.K. (1996). Phlorotannin-protein interactions. J. Chem. Ecol., 22, 1887-99.
Streit, J.M., Jones, R.N., Sader, H.S. (2004). Daptomycin activity and spectrum: a worldwide sample of 6737 clinical Gram-positive organisms. J. Antimicrob. Chemother., 53, 669-674
Suresh, B., Sriram, S., Dhanaraj, S.A., Elango, K., Chinnaswamy, K. (1997). Anticandidal activity of Santolina chamaecyparissus volatile oil. J. Ethnopharmacol., 55, 151–159.
Tally, F.P., DeBruin, M.F. (2000). Development of Daptomycin for Gram-positive Infections. J. Antimicrob. Chemother, 46, 523-526.
Tassou, C.C., Drosinos, E.H., Nychas,

G.J.E. (1995). Effects of essential oil from mint (Mentha piperita) on Salmonella enteritidis and Listeria monocytogenes in model food systems at 4° and 10°C. J. Appl. Bacteriol., 78, 593–600.
Thomson, W.A.R., (ed.) (1978). Medicines from the Earth. McGraw-Hill Book Co., Maidenhead, United Kingdom.
Thongson, C., Davidson, P.M., Mahakarnchanakul, W., Weiss, J. (2004). Antimicrobial activity of ultrasound-assisted solvent-extracted spices. Lett. Appl. Microbiol., 39, 401-6.
Toda, M., Okubo, S., Ikigai, H., Suzuki, T., Suzuki, Y., Hara, Y., Shimamura, T. (1992). The protective activity of tea catechins against experimental infection by Vibrio cholerae O1. Microbiol. Immunol., 36, 999–1001.
Tsuchiya, H., Sato, M., Iinuma, M., Yokoyama, J., Ohyama, M., Tanaka, T., Takase, I., Namikawa, I. (1994). Inhibition of the growth of cariogenic bacteria in vitro by plant flavanones. Experientia, 50, 846–849.
Tyler, V.E. (1999). Phytomedicines: back to the future. J Nat. Prod., 62, 1589–1592.
Urs, N.V.R.R., Dunleavy, J.M. (1975). Enhancement of the bactericidal activity of a peroxidase system by phenolic compounds (Xanthomonas phaseoli var. sojensis, soybeans). Phytopathology, 65, 686–690.
Vazquez, J.A., Sobel, J.D. (2006). Anidulafungin: a novel echinocandin. Clin. Infect. Dis., 43, 215–22.
Vijaya, K., Ananthan, S., Nalini, R. (1995). Antibacterial effect of theaflavin, polyphenon 60 (Camellia sinensis) and Euphorbia hirta on Shigella spp. a cell culture study. J Ethnopharmacol., 49, 115-118.
Virus, R.M., Gebhart, G.F. (1979). Pharmacologic actions of capsaicin: apparent involvement of substance P and serotonin. Life Sci. 25, 1273–1284.
Vishwakarma, R. A. (1990). Stereoselective synthesis of a-arteether from artemisinin. J. Nat. Prod., 53, 216–217.
Vohora, S.B., Rizwan, M., Khan, J.A. (1973). Medicinal uses of common Indian vegetables. Planta Med., 23, 381–393.
Wan, J., Wilcock, A., Coventry, M.J. (1998). The effect of essential oils of basil on the growth of Aeromonas hydrophila and Pseudomonas fluorescens. J. Appl. Microbiol., 84, 152–158.
Watanbe, H., Miyaji, C., Makino, M., Abo, T. (1996). Therapeutic effects of glycyrrhizin in mice infected with LP-BM5 murine retrovirus and mechanisms involved in the prevention of disease progression. Biotherapy, 9, 209-20.
Westwater, C., Kasman, L.M., Schofield, D.A, Werner, P.A., Dolan, J.W., Schmidt, M.G., Norris, J.S. (2003). Use of genetically engineered phage to deliver antimicrobial agents to bacteria: an alternative therapy for treatment of bacterial infections. Antimicrobial Agents and Chemotherapy, 47, 1301–1307.
Wild, R. (ed.) (1994). The complete book of natural and medicinal cures. Rodale Press, Inc., Emmaus, Pa.
Xu, H.X., Zeng, F.Q., Wan, M., Sim, K.Y. (1996). Anti-HIV triterpene acids from Geum japonicum. J. Nat. Prod., 59, 643–645.
Yates, R.R. (1999). New Intervention Strategies for Reducing Antibiotic Resistance. Chest, 115, 24S-27S.