



# IJRASET

International Journal For Research in  
Applied Science and Engineering Technology



---

# INTERNATIONAL JOURNAL FOR RESEARCH

IN APPLIED SCIENCE & ENGINEERING TECHNOLOGY

---

**Volume: 5      Issue: XII      Month of publication: December 2017**

**DOI:**

**[www.ijraset.com](http://www.ijraset.com)**

**Call:  08813907089**

**E-mail ID: [ijraset@gmail.com](mailto:ijraset@gmail.com)**

# Phytomolecules as Sources of New Antimicrobials and Drug Resistance Modifying Agents

Sonali Gangwar<sup>1</sup>, D.V.Rai<sup>2</sup>, Maya Datt Joshi<sup>3</sup>

<sup>1</sup>Asistant Professor, Center for Biological Engineering, Shobhit University, Gangoh, Saharanpur U.P (India)

<sup>2</sup>Professor, Center for Biological Engineering Shobhit University, Gangoh, Saharanpur, U.P (India)

<sup>3</sup>Asistant Professor Department of Biotechnology, Shobhit University, NH-58 Modipuram, Meerut, U.P (India)

**Abstract:** *Plants contain a number of active compounds that are responsible for various biological activities and play an important role as constituents of medicine. It is also reported that phytochemicals, which are known as secondary metabolites from plants act in a synergistic manner along with other antibacterial agents. This makes phytochemical products and plant extracts as useful resistance-modifying agents. The therapeutic utility of these products, however, remains to be clinically proven. Antibiotics are very effective for treatment of number of infectious diseases. Traditional methods of antibiotic discovery have failed to keep pace with the evolution of antimicrobial resistance. Antimicrobial resistance (AMR) is the ability of a microorganism (like bacteria, viruses, and some parasites) to stop an antimicrobial (such as antibiotics, antiviral and anti malarials) agent from working against it. As a result, standard treatments become ineffective, infections persist and spread to others. Therefore, new strategies to control bacterial infections and to inhibit the resistance development are highly desirable. This strategy will provide away to accomplish the urgent need to find out some alternatives to overcome the problems of multidrug resistance. One approach is the use of combination of plant extracts with antibiotics. Many studies indicated that efficacy of antimicrobial agents can be improved by combining them with plant extracts. Interaction of plant extract with antibiotics leads to a novel strategy to treat infectious diseases.*

**Keywords:** *Antimicrobial resistance, Phytomolecules, Resistance-modifying agents, infectious diseases.*

## I. INTRODUCTION

Human Infectious diseases caused by bacteria, fungi and virus affect millions of people worldwide. Today, infectious diseases account for one-third of all deaths in the world. World Health Organization estimates that approximately 50,000 people die each day throughout the world from infectious diseases (WHO, 2002). Microbes are existing in earth since million years ago, being one of the oldest creatures in this planet. These microbes were already known since the time when humans are subjected to antibiotics produced from other microorganisms such as *Penicillium notatum*, as example. These microbes produce antibiotic resistant mechanisms, naturally (Opalet al, 2000). So, it is not surprising that the microbes have developed resistance in the modern era against our synthetic and semi-synthetic antibiotics. The discovery of antibiotics was an essential part in combating bacterial infections that once ravaged humankind. Different antibiotics exercise their inhibitory activity on different pathogenic organisms. The development and spread of resistance to currently available antibiotics is a worldwide concern. (Chanda&Rakholiya, 2011) The increasing phenomenon of acquisition of resistance among microorganisms to antimicrobial drugs is attributed to the indiscriminate and improper use of current antimicrobial drugs. Today, clinically important bacteria are characterized not only by single drug resistance but also by multiple antibiotic resistances, the legacy of past decades of antimicrobial use and misuse. Drug resistance presents an ever increasing global health threat that involves all major microbial pathogens and antimicrobial drugs. These resistant micro-organisms are difficult to treat and are responsible for a variety of infectious diseases. The rate of emergence of antibiotic resistant bacteria is not matched by the rate of development of new antibiotics to combat them. (Chanda&Rakholiya, 2011) Recently, the global problem of dramatic development of bacterial resistance to synthetic antibiotics has led researchers to consider the use of other natural products with antibiotic actions e.g. medicinal plants. Interestingly, traditional medicine (including herbal medicine) is currently considered as a rapidly growing health system worldwide, it remains widespread and increasing very fast in developed countries (WHO 2002). These medicinal plants could be effective alternative source for many therapeutics, particularly after the recent dramatic failures of antibiotics against multi-drug resistant micro organisms. This review focus on new phytochemicals that can be combined with antibiotics in the treatment of drug resistant infections. This may prove to be an alternative for overcoming the problem of resistance in bacteria. Crude extracts of medicinal plants stand out as veritable sources of potential resistance modifying agents.

## II. THEORY

### A. Development of antimicrobial resistance

Antimicrobial resistance is an immense and serious global challenge and could endanger the lives of future generations. The phenomenon of antibiotic resistance was anticipated by Alexander Fleming since the discovery of penicillin in 1940s (Levy, 2002). Scientists know that when antibiotics are used incorrectly, the target bacteria will directly adapt and develop resistance. Then, with its rapid multiplication, bacteria pass resistant genes through plasmid exchange, leading to an increased prevalence of multi-drug resistant in factions. Many factors such as whether the antibiotic is a concentration or time-dependent killing agent, its effects against the population of bacteria and its duration of the serum concentration in patient may prove to be the effective treatment strategy for the resistant microbes (Coates *et al*, 2002).

### B. Occurrence of multi-drug resistant microorganisms

At present most clinical isolates of *S. aureus*, *S. Pyogenes*, *Mycobacterium tuberculosis* are considered as highly resistant to most commercially known antibiotics (Sbnda and Okoh, 2007).

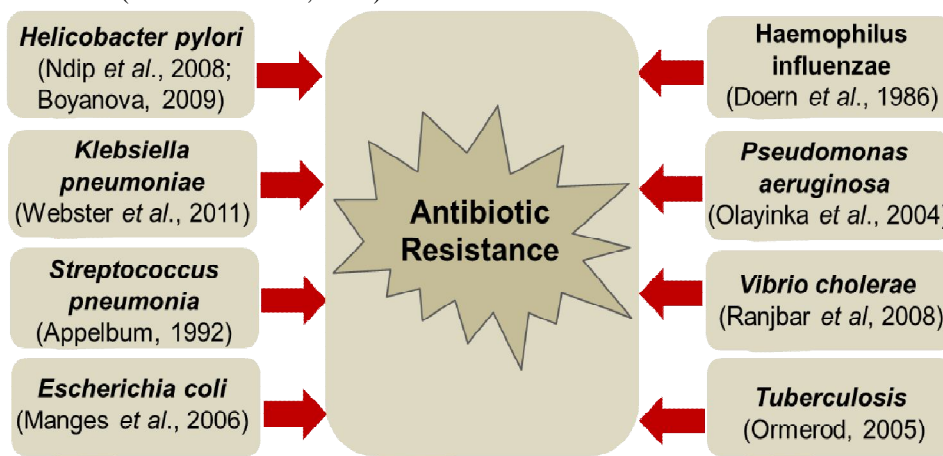


Figure 1: Antibiotic Resistant Microorganisms

In the last decades, prevalence and outbreaks of the multi-drug resistant bacterial strains have been increasingly documented throughout the world. The Figure 1 provides the information about the microbes that have developed antibiotic resistance till date. The use of antibiotics in veterinary practices and the growing presence of antibiotics in water, soil and food are contributed to the problem of antibiotic resistance (Moshirfare *et al.* 2006). Regretfully, quantitative data regarding the clinical implications of resistance are lacking for many common infections (Metlay and Singer, 2002).

### C. Phytomolecules As A Antimicrobial agents

Medicinal plants are known to produce certain bioactive molecules which react with organisms in the environment, inhibiting bacterial or fungal growth and protect the human body against pathogens (Yano *et al.* 2006, Wojdyloet *al.* 2007). Antimicrobial properties in plants are attributed to the presence of active compounds e.g., quinones, phenols, alkaloids, flavonoids, terpenoids, essential oil, tannins, lignans, glucosinolates and some secondary metabolites (see Table 1 for example)(Lewis and Ausubet *al.*, 2006; Cowan, 1999; Twari 2004).

Table 1: Examples of some plant derived compounds with antimicrobial value.

S. No.	Name of Plants	Antimicrobials	Microbes treated	Refe.
1	Acacia nilotica	Terpenoids, flavanoid, Saponins, Tannins	<i>S. viridians</i> , <i>S. aureus</i> , <i>E. coli</i> , <i>B. subtilis</i> , <i>Shigellasonnei</i> , Multidrug Resistance <i>E. coli</i> , <i>C. albican</i> , <i>K. pneumoniae</i>	Banso 2009, Riazet al. 2011,
2	Allium cepa	Flavanoid, Polyphenol	Multidrug Resistance <i>Pseudomonas aeruginosa</i> , <i>S.</i>	Adesinoet al. 2011.

			Typhi, E. coli	
3	Allium sativum	Organosulphur compounds (Phenolic compounds), Allicin	Campylobacter jejuni, Multidrug Resistance E. coli, C. albican, Entamoeba histolytica, Giardia lamblia	Luet al. 1999. Ankriet al. 1999
4	Angelica lucida L.	Coumarins	S. viridians, S. mutans	Widelski, et al. 2009
5	Chelidonium majus	Glycoprotein	B. cereus, Staphylococcus spp.	Janovska et al. 2003
6	Cinnamomum spp.	Cinnamaldehyde (essential oil)	Legionella pneumophila Multidrug Resistance E. coli, C. albican, K. pneumoniae	Changet al. 2008
7	Cirsium hypoleucum	Flavones	Multidrug Resistance K. pneumoniae	Ozceliket al. 2008
8	Curcuma longa	Curcuminoid (A phenolic compound), turmerone, curcumin, turmeric oil	S. typhi, E. coli, S. aureus, B. cereus, B. subtilis, Ps. aeruginosa, B. coagulans, A. niger, P. digitatum, Antifungal and antiviral activity	Gul, P.; Bakht 2015
9	Cymbopogon citratus	Essential oil	C. albicans, Aspergillus flavus, A. parasiticus	Ragaso 2008
10	Galium fissurense	Flavones	Multidrug Resistance K. pneumoniae	Ozceliket al. 2008
11	Hypericum perforatum	Hypericin (anthraquinone)	Methicillin Resistant Staphylococcus aureus and Methicillin sensitive Staphylococcus	Dadgar et al 2006
12	Lawsonia inermis	Quinones	Multidrug Resistance Pseudomonas aeruginosa	Habbalet al. 2011
13	Medicago sativa	Saponins, Canavanine	Enterococcus faecium, S. aureus, Antifungal	Aliahmadi et al. 2012
14	Mentha longifolia	Essential oil	Multidrug Resistance Staphylococcus aureus	Aliet al. 2015
15	Ocimum basilicum	Essential oil	Multidrug Resistance Staphylococcus aureus, S. Typhi, Aeromonas hydrophila, Pseudomonas spp.	Wanet al. 1998
16	Onobrychis sativa	AMPs (antimicrobial peptides)	E. faecium, S. aureus	Aliahmadi et al. 2012
17	Origanum vulgare	Essential oil	B. subtilis, B. cereus, Multidrug Resistance S. aureus	Falcoet al. 2013
18	Piper longum	Piperine, Saponin, alkaloid	Multidrug Resistance B. subtilis, Shigella sonnei	Kumaret al. 2013

19	Raphanussativum	RsAFP2 (Antifungal peptide)	C. albicans	Aertset al. 2009
20	Rhazyastricta	Alkaloids and Non alkaloids	Multidrug ResistanceE. coli, K. pneumoniae (Extended Spectrum Beta Lactamase), E. faecium(Vancomycin Resistant Enterococci)	Khanet al. 2016
21	Rosmarinusofficinalis	Essential oil	Streptococcusmutans	Falcoet al. 2013
22	Sanguisorbaofficinalis	Alkaloids, antimicrobial peptides	Ps. aeruginosa, E. coli	Janovskaet al. 2003
23	Sorghum spp.	Tannins	S.aureus, S. typhimurium, A. niger, A. flavus, S. cerevisiae	Moneimet al. 2007
24	. Stephaniaglabra	Alkaloids	S. aureus, S. mutans, Microsporungypseum, M. canis and Trichophytonrubrum	Semwal, D.K.; Rawat 2009
25	Syzygiumaromaticum	Essential oil	Eugenol Streptococcus mutans, S. aureus, Lactobacillus acidophilus, Candida albicansandSaccharomyces cerevisiae, Multidrug ResistanceE. coli, K. pneumoniae	Kumaret al. 2013
26	Vetiveriaziznioides	Vetivone (vetiver oil)	Enterobacter spp.	Srivastavaet al. 2007
27	Viscum album	Flavones	Multidrug ResistanceK. pneumoniae	Ozceliket al. 2008
28	Zingiberofficinale	Gingerol	E. coli, Enterobacter spp., P. aeruginosa, Proteus spp., Klebsiella spp., S. aureus and Bacillus spp.	Adesino,et al. 2011, Karuppiahet al.2012

#### D. *Phytomolecules AS resistance Modifying Agents*

During 1990's, approximately 80% of all remedies were produced from roots barks and leaves of plants (McChesney *et al.* 2007). Even after the antibiotic era and till now, many effective drugs traded globally were from plant origin such as Atropine, Ephedrine, Digoxin, Morphine, Reserpine and Tubocurarine (Gilani and Atta-ur-Rahman, 2005). Here, there is a correlation between the plant extract of antimicrobial activity and its major secondary metabolites. Accordingly, since times immemorial, plants have been resisting the continuous attacks of microorganisms (Parasites, fungi, Bacteria and Viruses) by producing endless secondary metabolites. On the other side, micro-organisms have continued trying to invade these plants by breaking down as many secondary metabolites as much as possible. According to this everlasting battle, plant kingdom develops a vast number of biochemical defense compounds. In a similar way, the conflict between humans and pathogenic microorganisms continues endlessly. As people develop new drugs to fight the disease, those microorganisms develop new ways to strengthen themselves and live longer. However, plants are able to develop new, faster and natural antimicrobials and then man-made remedies (Farnsworth *et al.* 1985). As antimicrobials are based on ethno-botanical data, considerable number of studies have been conducted on the antimicrobial activity of medicinal plants and showed promising potency against multi-drug resistant microorganisms after the current antibiotics failed to eliminate them. Many studies have indicated that a broad range of plant extracts may act against bacterial resistance mechanisms (Schelzet *et al.* 2010). The majority of these have now been focused on combinations between plant extracts and antibiotics in order to screen for resistance modifying agents (Sibinda and Okoh, 2007). The following sections will

focus on combinatorial activities of plant extracts and products with antibiotics, mainly due to a resistance-modifying action. Table 2 shows some promising plants having antimicrobial activity against multidrug resistant strain.

Table 2: Synergism between phytochemical product and antibiotics due to resistance modifying activity.

S.No.	Phytochemical product	Plant source	Antibiotic potentiated	Mechanisms of action	Refe.
1	Carnosic acid	Rosmarinus officinalis	Tetracycline Erythromycin	MDR efflux pumps inhibition	Oluwatuyiet al. 2004, Stavriet al. 2007, Gibbonset al. 2003.
2	Carnosol				
3	Reserpine	Rauwolfiaserpentina	Fluoroquinolones Tetracycline	MDR efflux pumps inhibition	Gibbons andUdo, 2000, Stavriet al. 2007, Gibbonset al. 2003, Marquez 2005, Markhamet al. 1999, Schmitz 1998.
4	Totarol	Chamaecyparisonotkatensis	Norfloxacin Tetracycline Erythromycin Methicillin	NorA inhibition Interference with PBP2a expression	Smithet al. 2007, Simoeset al. 2009, Nicolsonet al. 1999. Gibbons 2007.
5	Diterpene 416				
5	Berberine	Berberis spp.	Ampicillin Oxacillin	Intercalation into DNA; Increase membrane Permeability	Simoes et al 2009, Stermitz et al 2000, Lewis et al 2007, Yuet al.2005
7	5*-methoxy-hydnocarpin	Berberis spp.	Berberine Others (e.g. norfloxacin)	NorA inhibition	Guzet al. 2000, Stavriet al. 2007, Gibbons et al. 2003, Tegoset al. 2002.
8	pheophorbide a				
9	Ferruginol	Chamaecyparislawsoneana	Norfloxacin Erythromycin Oxacillin Tetracycline	EtBr efflux inhibition	SibandaandOkoh 2007, Smithet al. 2007.
10	5-Epispiferol				
11	Catechingallate	Camellia sinensis	$\beta$ -lactams Norfloxacin Carbapenems Tetracycline	b-lactamases inhibition; PBP2a synthesis inhibition; Reaction with peptidoglycan; EtBr efflux inhibition; TetK inhibition	Shibataet al. 2005, Marquez 2005, Zhaoet al. 2005, Yamet al. 1998, Hu et al. 2002, Roccaro and Enea 2004.
12	Epicatechingallate				
13	Epigallocatechingallate				

14	Methyl-1a-acetoxy-7a-14a-dihydroxy-8,15-isopimaradien-18-oate	Lycopuseuropaeus Piper nigrum	Tetracycline Erythromycin	MDR efflux pumps inhibition	Gibbonset al. 2003.
15	Methyl-1a,14a-diacetoxy-7a-hydroxy-8,15-isopimaradien-18-oate				
16	Piperine	Piper longum	Ciprofloxacin	EtBr efflux inhibition	Jinet al. 2011,Khanet al. 2006.
17	Thymol	Thymus vulgaris	Several	Increase membrane permeability	Helanderet al. 1998, Simoeset al. 2009, Lambertet al. 2001, Zhanget al.2011, Palaniappan and Holley2010
18	Carvacrol				
19	Baicalein	Scutellaria species	Tetracycline b-lactams Gentamicin Ciprofloxacin	Inhibition of PBP2a; Reaction with the peptidoglycan; NorA inhibition	Chanet al. 2011, Wagner and Ulrich-Merzenich 2009, Fujitaet al. 2005.
20	2,6-dimethyl-4-phenyl-pyridine-3,5-dicarboxylic acid diethyl ester	Jatrophaelliptica	Ciprofloxacin Norfloxacin	NorA inhibition	SibandaandOkoh 2007, Marquezet al. 2005.
21	Ethyl gallate	Caesalpiniaspinosa	$\beta$ -lactams	Restriction of substrate diffusion for PBPs	Shibataet al. 2005.
22	Cinnamaldehyde	Cinnamomumzeylanicum	Clindamycin	CdeA inhibition	Shahverdiet al. 2007
23	Gallic acid	Berry extracts	Tetracycline	Increase membrane permeability	Jayaramanet al. 2010, Nohynek et al. 2006, Saavedraet al. 2010.
24	Xanthohumol	Humuluslupulus	Polymyxin B sulphate Tobramycin Ciprofloxacin	Increase membrane permeability	Zahinet al. 2010,Natarajanet al.2008.
25	Lupulon				

26	Tellimagrandin I	Rosa canina L.	$\beta$ -lactams	Inactivation of PBP <sub>s</sub> , particularly PBP <sub>2a</sub>	Shiotaet al. 2002, Shiota, et al. 2004.
27	Rugosin B				
28	Corilagin	Arctostaphylosuva-ursi	$\beta$ -lactams Cefmetazole	Inhibition of PBP <sub>2a</sub> activity or Production	Shimizu et al. 2001, Shiota et al. 2004.
29	Myricetin	Widespread among plants including tea, berries, fruits, vegetables and medicinal herbs	Cefmetazole Amoxicillin/ clavulanate Ampicillin/ sublactam Cefoxitin	DNA B helicase inhibition	Hemaiswarya et al. 2008, Linet et al. 2005.
30	Allicin	Allium sativum	Cefazolin	RNA synthesis inhibition; Interaction with important thiolcontaining Enzymes	Hemaiswarya et al. 2008, Cai et al. 2007, Abascal and E. Yarnell 2002, Ankri and D. Mirelman 1999.
31	Silybin	Silybummarianum	Ampicillin Oxacillin	MDR efflux pumps inhibition	Stermitzet et al. 2000, Kanget et al. 2011.
32	The polyacylated	Geranium caespitosum	Berberine Ciprofloxacin Norfloxacin Rhein	MDR efflux pumps inhibition	Stavriet et al. 2007, Tegoset et al. 2002, Stermitzet et al. 2003.
33	Neohesperidoses				
34	Chrysosplenol D	Artemisia annua	Artemisinin Berberine Norfloxacin	MDR efflux pump inhibition	Stavriet et al. 2007.
35	Chrysoplenetin				
36	Chalcone	Daleaversicolor	Berberine Erythromycin Tetracycline	NorA inhibition	Zdzis 2007, Belofsky et al. 2004.
37	4',5'-O-dicaffeoylquinic acid	Artemisia absinthium	Berberine	MFS family efflux systems inhibition	Fiamegoset et al. 2011.
38	Genistein	Lupinusargenteus	Fluroquinolones Berberine Norfloxacin	MDR efflux pump inhibition	Morelet et al. 2003.
39	Orobol				
40	Biochanin A				



### III. CONCLUSION

The quest for solutions to the global problem of antibiotic resistance in pathogenic bacteria has often focused on the isolation and characterization of new antimicrobial compounds from a variety of sources including medicinal plants. Continuous efforts are being made to explore the plant kingdom in order to find wonder drugs that could save human life from harmful microbial and viral infections. Medicinal plants are very effective in the treatment of many infectious diseases. The mechanisms of bacterial resistance have exposed that active efflux plays a significant role in the development of bacterial acquired and intrinsic resistance. Overcoming efflux has therefore been seen as an attractive alternative to avoiding the problem. Bacterial efflux pump inhibitors (phytochemicals) have since been isolated from some plants. The combination of such MDR inhibitors (phytochemicals) with antibiotics *in vitro* has shown that the activities of some antibiotics can be dramatically increased even against antibiotic resistant strains of bacteria. The large varieties of compounds produced by plants have proved to have therapeutic potentials as antimicrobials and as resistance modifiers. The Indian biosphere that is gifted with the highest biodiversity of plant species promises to be a potential source of therapeutically useful compounds especially from the perspective of their potentials in combination with antimicrobial chemotherapy which should form the subject of further extensive study.

### REFERENCES

- [1] Abascal K. and Yarnell E. Herbs and drug resistance. Potential of botanical in drug-resistant microbes. *Altern. Complementary Ther.*, 2002; 8:237–241.
- [2] Adesino GO. Antibacterial activity of fresh juices of *Allium cepa* and *Zingiber officinale* against multidrug resistant bacteria. *Int. J. Pharm. Biol. Sci.* 2011; 2:289–295.
- [3] Aerts AM., The antifungal plant defensin RsAFP2 from radish induces apoptosis in a metacaspase independent way in *Candida albicans*. *FEBS Lett.* 2009; 583: 2513–2516.
- [4] Al-Ali K., Antibacterial activity of four herbal extract against methicillin resistant bacterial strains isolated from patient in Almadinah hospitals, Saudi Arabia. *Int. J. Acad. Sci. Res.* 2015; 3: 34–40.
- [5] Aliahmadi A., Identification and primary characterization of a plant antimicrobial peptide with remarkable inhibitory effects against antibiotic resistant bacteria. *Afr. J. Biotechnol.* 2012; 11: 9672–9676.
- [6] Ankri S., and Mirelman D., Antimicrobial properties of allicin from garlic. *Microbes Infect.* 1999; 1: 125–129.
- [7] Appelbaum PC. Antimicrobial resistance in *Streptococcus pneumoniae*: an overview. *Clin Infect Dis.* 1992; 15:77-83
- [8] Marquez B., Multidrug resistance reversal agent from *Jatropha elliptica*. *Phytochemistry*, 2005, 66, 1804–1811.
- [9] Banso A. Phytochemical and antibacterial investigation of bark extracts of *Acacia nilotica*. *J. Med. Plants Res.* 2009; 3: 82–85.
- [10] Belofsky G., Phenolic metabolites of *Dalea versicolor* that enhance. *J. Nat. Prod.*, 2004; 67: 481–484.
- [11] Cai Y., Antibacterial activity of allicin alone and in combination with beta. *J. Antibiot.*, 2007; 60:335–338.
- [12] Chan BCL., Studies in Natural Products Chemistry. *J. Ethnopharmacol.*, 2011; 137:767–773.
- [13] Chanda, S., & Rakholiya, K. Combination Therapy: Synergism Between Natural Plant Extracts And Antibiotics Against Infectious Diseases. *Science Against Microbial Pathogens: Communicating Current Research And Technological Advances*, 2011; 520–529.
- [14] Chang C., Antibacterial activities of plant essential oils against *Legionella pneumophila*. *Water Res.* 2008; 42:278–286.
- [15] Coates A., The future challenges facing the development of new antimicrobial drugs. *Nature reviews.* 2002; 1: 895-910.
- [16] Cowan MM. Plant products as antimicrobial agents, *Clinical Microbiol. Review.* 1999; 12: (4): 564-582.
- [17] Dadgar T., Antibacterial activity of certain Iranian medicinal plants against methicillin resistant and methicillin sensitive *Staphylococcus aureus*. *Asian J. Plant Sci.* 2006; 5:861–866.
- [18] Doern GV., Prevalence of antimicrobial resistance among clinical isolates of *Haemophilus influenzae*: a collaborative study. *Diagn Microbiol Infect Dis.* 1986; 4:95-107.
- [19] Falco ED., Chemical composition and biological activity of essential oils of *Origanum vulgare* L. subsp. *vulgare* L. under different growth conditions. *Molecules.* 2013; 18:14948–14960.
- [20] Fiamegos YC., Antimicrobial and efflux pump inhibitory activity of caffeoylquinic acids. *PLoS One.* 2011; 6:1–12.
- [21] Gibbons S., and Udo EE. The effect of reserpine, a modulator of multidrug efflux pumps, on the phytother. *Res.*, 2000; 14:139–140.
- [22] Gibbons S., A novel inhibitor of multidrug efflux pumps in *Staphylococcus aureus*. *J. Antimicrob. Chemother.* 2003; 51: 13–17.
- [23] Gilani AH. and Atta-ur-Rahman: Trends in ethnopharmacology. *J. Ethnopharmacol.* 2005; 100: 43-49.
- [24] Gul, P.; Bakht, J. Antimicrobial activity of turmeric extract and its potential use in food industry. *J. Food Sci. Technol.* 2015, 52, 2272–2279.
- [25] Guz NR., Flavonolignan and flavone inhibitors of a *Staphylococcus aureus* multidrug resistance pump: structure-activity relationships. *J. Med. Chem.*, 2000; 44: 261–268.
- [26] Habbal O., Antibacterial activity of *Lawsonia inermis* Linn (Henna) against *Pseudomonas aeruginosa*. *Asian Pac. J. Trop. Biomed.* 2011; 1:173–176.
- [27] Hemaiswarya S., Synergism between natural products and antibiotics against. *Phytomedicine*, 2008; 15:639–652.
- [28] Hu ZQ., Inhibition of Penicillinase by Epigallocatechin Gallate Resulting in Restoration of Antibacterial Activity of Penicillin against Penicillinase-Producing *Staphylococcus aureus*. *Antimicrob. Agents Chemother.* 2002; 46:558–560.
- [29] Janovska D., Screening for antimicrobial activity of some medicinal plants species of traditional Chinese medicine. *Czech J. Food Sci.* 2003; 21:107–110.
- [30] Jayaraman P., Activity and interactions of antibiotic and phytochemical combinations. *Int. J. Biol. Sci.*, 2010, 6, 556–568.
- [31] Jin J., Biotechnology of Bioactive Compounds: Sources and Applications. *J. Med. Microbiol.*, 2011; 60: 223–229.
- [32] Kang HK. Kim HY. Synergistic effects between silibinin and antibiotics on methicillin-resistant *Staphylococcus aureus*. *Chin. Biotechnol. J.*, 2011; 6:1397–1408.

- [33] Karuppiah P., Rajaram S. Antibacterial effect of *Allium sativum* cloves and *Zingiberofficinale* rhizomes against multiple drug resistant chemical pathogens. *Asian Pac. J. Trop. Biomed.*2012; 2: 597–601.
- [34] Khan IA., Piperine, a phytochemical potentiator of ciprofloxacin against, *Antimicrob. Agents Chemother.*, 2006;50:810–812.
- [35] Khan R., Antibacterial activities of *Rhazyastricta* leaf extracts against multidrug resistant human pathogens. *Biotechnol.Equip.* 2016; 30:1016–1025.
- [36] Kumar V., Antibiotic resistance reversal of multiple drug resistant bacteria using *Piper longum* fruit extract. *J. Appl. Pharm. Sci.*2013; 3: 112–116.
- [37] Lewis K. and Ausubel, FM. Prospects for plant-derived antibacterials.*Nat.Biotechnol.*2006; 24: 1504–1507.
- [38] Lin RD., Chin YP. and Lee MH. Antimicrobial activity of antibiotics in combination with natural *Phytother.Res.*, 2005; 19: 612–617.
- [39] Lu X., Investigating antibacterial effects of garlic (*Allium sativum*) concentrate and garlic-derived organosulfur compounds on *Campylobacter jejuni* by using Fourier transform infrared spectroscopy, Raman spectroscopy, and electron microscopy. *Appl. Environ. Microbiol.*2011; 77:5257–5269.
- [40] M. Fujita, Remarkable synergies between baicalein and tetracycline, and ..*Microbiol.Immunol.*, 2005, 49, 391–396.
- [41] M. Simoes, R. N. Bennett and E. A. S. Rosa, Characterization of the Action of Selected Essential Nat. Prod. Rep., 2009;26:746–757.
- [42] Manges AR., The changing prevalence of drug-resistant *Escherichia coli* clonal groups in a community: evidence for community outbreaks of urinary tract infections. *Epidemiol Infect.* 2006; 134(2):425–431.
- [43] Markham PN., Multiple novel inhibitors of the NorA multidrug transporter *Antimicrob. Agents Chemother.*, 1999;43:2404–2408.
- [44] Marquez B., Biochimie, Bacterial efflux systems and efflux pumps inhibitors, *Biochimie*,2005; 87:1137–1147.
- [45] McChesney JD., Venkataraman SK., and Henri JT. Plant natural products: Back to the future or into extinction, *J. of Phytochem.*2007; 68: 2015–2022.
- [46] Metlay J., Antimicrobial Drug Resistance, Regulation, and Research Emerging.*Infectious Diseases.* 2006; 12 (2): 183–190.
- [47] Moneim A., Quantitative determination of tannin content in some sorghum cultivars and evaluation of its antimicrobial activity. *Res. J. Microbiol.* 2007; 2:284–288.
- [48] Morel C., Isoflavones as potentiators of antibacterial activity. *J. Agric. Food Chem.* 2003; 51: 5677–5679.
- [49] Moshirfar M., Fourth generation fluoroquinolone-resistant bacterial keratitis after refractive surgery. *J Cataract Refract Surg.* 2006; 32(3):515–8.
- [50] Natarajan PS., Positive antibacterial c.action between hop (*Humulus lupulus*) *Phytochemistry*, 2008;15:194–201.
- [51] Ndiip RN., *Helicobacter pylori* isolates recovered from gastric biopsies of patients with gastro–duodenal pathologies in Cameroon: current status of antibiogram. *Trop. Med. Inter. Health.* 2008; 13: 848–854.
- [52] Nicolson K., Evans G. and PWO’ Toole, Potentiation of methicillin activity against methicillin-resistant *Staphylo-coccus aureus* by diterpenes, *FEMS Microbiol. Lett.*,1999; 179: 233–239.
- [53] Nohynek LJ., Plants as sources of new antimicrobials and resistance-modifying *Nutr. Cancer*, 2006; 54:18–32.
- [54] Olayinka AT., Onile BA. and Olayinka BO. Prevalence of multidrug resistant (MDR) *Pseudomonas aeruginosa* isolates in surgical units of Ahmadu Bello University Teaching Hospital, Zaria Nigeria: An indication for effective control measures. *Annals of African Medicine.* 2004; 3(1): 13– 16.
- [55] Oluwatuyi M., Kaatz GW., and Gibbons S. Antibacterial and resistance modifying activity of *Rosmarinus officinalis*. *Phytochemistry*, 2004; 65:3249–3254.
- [56] Opal SM, Mayer K and Medeiros A, Mechanisms of Bacterial Antibiotic Resistance. *Principles and Practice of Infectious ieseases* 5th ed. Ch. 16 (eds. Mandell, G. L., Bennett, J. & Dolin, R.). Churchill Livingstone, Philadelphia, USA.2000; 236–253.
- [57] Ormerod LP., Multidrug-resistant tuberculosis (MDRTB): epidemiology, prevention and treatment. *British Medical Bulletin.*2005; 73 and 74: 17–24.
- [58] Ozelcik B., Antimicrobial Activity of Flavonoids against Extended-Spectrum Beta Lactamase (ESBL)-Producing *Klebsiella pneumoniae*. *Trop J. Pharm. Res.* 2008; 7: 1151–1157.
- [59] Palaniappan K. and Holley RA. Use of natural antimicrobials to increase antibiotic susceptibility of *Int. J. Food Microbiol.*, 2010; 140:164–168.
- [60] R. J. W. Lambert, A study of the minimum inhibitory concentration and mode. *J. Appl. Microbiol.*, 2001; 91: 453–462.
- [61] Ragaso CY., Antimicrobial and Cytotoxic terpenoid from *Cymbopogon citratus* *Stapf. Philipp. Sci.*2008; 45:111–122.
- [62] Ranjbar M., High prevalence of multidrug-resistant strains of *Vibrio cholerae*, in a cholera outbreak in Tehran–Iran, during June–September 2008. *Tropical Doctor.* 2010; 40 (4):214–216.
- [63] Riaz S., Antibacterial and cytotoxic activities of *Acacia nilotica* L (Mimosaceae) methanol extract against extended spectrum beta lactamase producing *E. coli* and *Klebsiella* species. *Trop. J. Pharm. Res.* 2011; 10: 785–791.
- [64] Roccaro AS., Epigallocatechin-gallate enhances the activity of tetracycline in *Antimicrob. Agents Chemother.* 2004;48:1968–1973.
- [65] Saavedra MJ., Antimicrobial activity of phenolics and glucosinolate hydrolysis. *Med. Chem.*, 2010; 6:174–183.
- [66] Schelz Z., A Source of Complementary Therapeutics, ed. D. Chattopadhyay, Research Signpost, 1st edn, 2010; 6: 179–201.
- [67] Schmitz FJ., Real-Time PCR Assay for Detection of Fluoroquinolone Resistance, *J. Antimicrob. Chemother.*, 1998; 42: 807–810.
- [68] Semwal DK., Rawat U. Antimicrobial hasubanalactam alkaloid from *Stephaniaglabra*. *Planta Med.* 2009; 75: 378–380.
- [69] Shahverdi AR., Trans-cinnamaldehyde from *Cinnamomum zeylanicum* bark. *J. Food Sci.*, 2007; 72:S055–S058.
- [70] Shibata H., intensifiers of beta-lactam susceptibility in methicillin, *Antimicrob. Agents Chemother.*, 2005; 49:549–555.
- [71] Shimizu M., Marked potentiation of activity of beta-lactams against methicillin. *Antimicrob. Agents Chemother.* 2001;45: 3198– 3201.
- [72] Shiota S., Restoration of effectiveness of  $\beta$ -lactams on methicillin-resistant FEMS Microbiology Letters, 2000, 185, 135–138.
- [73] Shiota S., Mechanisms of action of corilagin and tellimagrandin I that remarkably *Microbiol.Immunol.*, 2004;48:67–73.
- [74] Shibata H., Alkyl gallates, intensifiers of beta-lactam susceptibility in methicillin. *Antimicrob. Agents Chemother.*, 2005, 49, 549–555.
- [75] Sibanda T., and Okoh AI., The challenges of overcoming antibiotic resistance: Plant extracts as potential sources of antimicrobial and resistance modifying agents. *African Journal of Biotechnology.* 2007; 6 (25): 2886–2896.
- [76] Simoes M., Bennett RN. and Rosa EAS. Understanding antimicrobial activities of phytochemicals against *Nat. Prod. Rep.*, 2009; 26:746–757.
- [77] Smith E., Antibacterials and modulators of bacterial resistance from the, *Phytochemistry*, 2007;68:210–217.
- [78] Srivastava J., Chandra H., Singh N. Allelopathic response of *Vetiveria zizanioides* (L.) Nash on members of *Enterobacteriaceae* and *Pseudomonas* spp. *Environmentalist* 2007;27: 253–260.
- [79] Stavri M., Piddock LJV., and Gibbons S. Bacterial efflux pump inhibitors from natural sources. *J. Antimicrob. Chemother.* 2007;59:1247–1260.
- [80] Stermitz FR., Polyacylated neohesperidosides from *Geranium caespitosum*. *Med. Chem. Lett.*, 2003;13:1915–1918.
- [81] Stermitz, F. R. 5'-Methoxyhydronecarpin-D and pheophorbide A: *Berberis*. *J. Nat. Prod.*, 2000, 63, 1146–1149.



- [82] Tegos G., Multidrug Pump Inhibitors Uncover Remarkable Activity. *Antimicrob. Agents Chemother.* 2002; 46:3133–3141.
- [83] Tiwar S., and Singh A. Toxic and sub-lethal effects of oleandrin on biochemical parameters of freshwater air breathing murrel, *Chant punctatus* (Bloch.). *Indian J Exp. Biolo.* 2004; 42:413–418.
- [84] Wagner H. and Ulrich-Merzenich G. Synergy research: approaching a new generation. *Phytomedicine*, 2009, 16, 97–110.
- [85] Wan J., Wilcock A., Coventry MJ. The effect of essential oil of basil on the growth of *Aeromonas hydrophila* and *Pseudomonas fluorescens*. *J. Appl. Microbiol.* 1998; 84: 152–158.
- [86] Webster DP., Young BC. and Morton R. Impact of a clonal outbreak of extended-spectrum  $\beta$ -lactamase-producing *Klebsiella pneumoniae* in the development and evolution of bloodstream infections by *K. pneumoniae* and *Escherichia coli*. *J. Antimicrob. Chemother.* 2011; Jun 21.
- [87] WHO: WHO traditional medicine strategy 2002-2005. World health report, World Health Organization, 2002b; Geneva. Levy SB: From tragedy the antibiotic era is born. In: Levy SB, ed. *The Antibiotic Paradox: How the Misuse of Antibiotics Destroys Their Curative Powers*, 2nd ed. Cambridge, MA: Perseus Publishing. 2002; 1–14.
- [88] WHO: WHO traditional medicine strategy 2002-2005. World health report, World Health Organization, 2002b; Geneva.
- [89] Widelski J., Antibacterial Activities. *Molecules*. 2009; 14: 2729–2734.
- [90] Wojdylo A., Oszmianski J. and Czemerys R. Antioxidant activity and phenolic compounds in 32 selected herbs. *Food Chemistry*. 2007; 105: 940–949.
- [91] Yam TS. the effect of a component of tea (*Camellia sinensis*) on methicillin. *J. Antimicrob. Chemother.*, 1998, 42, 211–216.
- [92] Yano Y., Antimicrobial effect of spices and herbs on *Vibrio parahaemolyticus*. *Int. J. of Food Microbiol.* 2006; 111: 6–11.
- [93] Yu HH., Antimicrobial activity of berberine alone and in combination. *J. Med. Food*, 2005, 8, 454–461.
- [94] Zahin M., *Ethnomedicine: a source of complementary therapeutics*, ed. D. Chattopadhyay, Research Signpost, 1st edn, 2010; 5:149–178.
- [95] Zdzislaw N., Eur. A review of anti-infective and anti-inflammatory chalcones. *J. Med. Chem.*, 2007; 42:125–137
- [96] Zhang D. Synergistic effects and physiological responses of selected bacterial. *Foodborne Pathog. Dis.*, 2011; 8: 1055–1062.
- [97] Zhao WH., Mechanism of synergy between epigallocatechingallate and  $\beta$ -lactams against methicillin-resistant *Staphylococcus aureus*. *Antimicrob. Agents Chemother.*, 2001; 45:1737–1742.



10.22214/IJRASET



45.98



IMPACT FACTOR:  
7.129



IMPACT FACTOR:  
7.429



# INTERNATIONAL JOURNAL FOR RESEARCH

IN APPLIED SCIENCE & ENGINEERING TECHNOLOGY

Call : 08813907089  (24\*7 Support on Whatsapp)