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Medicinal plants as source of antibacterial agents to counter *Klebsiella pneumoniae*

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ABSTRACT

Several antibiotics are in use to treat different diseases caused by human pathogenic microorganisms. It is being observed that the invented medicines are not much effective in treatment, as the infection causing microbes are becoming resistant and modifying themselves into multidrug resistant strains. To fight against these human pathogens there is a need of introduction of new antibiotics. The synthetic derivatives or synthetic antibiotics are effective but unsafe for use and the results are not satisfactory due the resistance building capacity of the microbes. At the same time, the side effects and adverse reactions caused by these multispectrum antibiotics are not ignorable**.** Due to these reasons plant derived compounds or phytomedicines having antimicrobial action are needed to be evaluated, introduced and implemented through clinical and biological trials. Here we present the information about some plants which are reported to be antimicrobial in nature and act against human pathogens. The efficacy of their antimicrobial action needs to be evaluated for their biological functions. To be concise, our review is limited to the plants showing antimicrobial efficacy against *Klebsiella pnuemoniae*. For the present work we have focused on essential oil yielding plants which are known to be more useful to fight against this pathogen. A total of 90 plants species are reviewed, among them 14 are essential oil yielding plants. The plants which are able to inhibit the growth of the *K. pneumoniae* are enlisted and their details of the study such as family it belongs, parts used, microbial strain number used in the study, extractant and the standard antibiotic used to compare the effect are tabulated in detail to have a complete analysis of the information from the recent work. The essential yielding plants are tabulated separately.

INTRODUCTION

We are witnesses to an era where globalization and advancement in science is going on side by side with population increase. Infectious diseases are one of the leading causes of morbidity and mortality worldwide, especially in developing countries (Zeigler, 2005; Yala *et al.*, 2001). Bacteria, in general, possess the genetic ability to acquire and transmit resistance to therapeutic agents. Following the massive use of antibiotics in human therapy, bacteria have developed several resistance mechanisms including the efflux of antibiotics (Yala *et al.*, 2001). Several mechanisms have been proposed, such as target site modification, expression of the efflux pumps, and metabolic inactivation, which contribute to the drug resistance in MDR bacteria (Hooper, 2001).

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According to World health organization (WHO) more than 80% of the world population relies on traditional medicine for their primary health care needs (Vashist and Jindal, 2012).

Not today, but from the ancient days itself, our ancestors depended on the plants for cure and medication. They have used several plants and their parts as treatment for different diseases. Plant based natural products traditionally known to combat microbial infections are expected to play a big role in this regard (Cowan, 1999).

Flavonoids isolated from natural dietary sources were also investigated in combination with antibiotics as a strategy against ESBL (Extended-Spectrum Beta-lactamase) producing clinical isolates of *Klebsiella pneumoniae* (Lin *et al.*, 2005). Oregano essential oil, given in combination with fluoroquinolones, was found to enhance the activity of the drugs against ESBL-producing Escherichia coli (Si *et al.*, 2008).

Similar enhancement of antimicrobial activity in combination with plant derived terpenoids has been reported by Shahverdi et al. (2004) and Alimirzaee et al. (2009).

A BRIEF INTRODUCTION ON *Klebsiella pneumoniae*

Biology of *K. pneumoniae*

Klebsiella pneumoniae is widely distributed in nature, found abundantly in soil and water. Klebsiella pneumonia is a Proteobacterian, included in Enterobacteriaceae. It is a Gram-negative bacterium, Cylindrical in shape and rod like. It is of about 2 microns in length and 0.5 microns in diameter (Fig 1). Its cells have a thick coat of slime or extracellular polysaccharide which is called a "capsule". The thickness of the capsule is approximately 160 nm in *K. pneumoniae*. The capsule protects the cells from desiccation, and may also protect them from phagocytosis when they are in an animal host. The structural genomics information of *K. pnuemoniae* can be read from the bioinformatics website http://kp.life.nthu.edu.tw/. *K. pneumoniae* has three subspecies with homologous DNAs but different biochemical reactions: *K. pneumoniae* subsp pneumoniae, *K. pneumoniae* subsp ozaenae, and *K. pneumoniae* subsp rhinoscleromatis. The characteristic biochemical reactions of these are:

- *K. pneumoniae* is lactose fermenting, H_2S- and indole negative, has a positive Voges Proskauer (VP) reaction, is capable of growth in KCN and uses citrate as a sole carbon source, and is incapable of growth at 10ºC.
- The other two subspecies (*ozaenae* and *rhinoscleromatis*) are indole negative with a negative VP reaction.
- *K. oxytoca*, which is one of the other species of the genus, is indole positive, has a positive VP reaction, and is able to grow at 10ºC

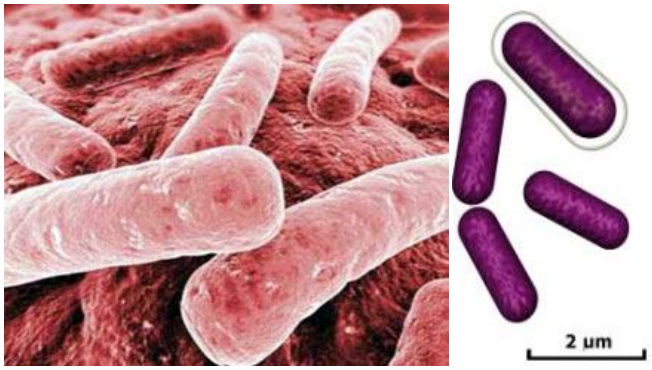

Fig. 1: Structure of *Klebsiella pnuemoniae.*

Pathology of *K. pneumoniae*

It was recognized over 100 years ago as a cause of community acquired pneumonia and is the opportunistic pathogen that can cause pneumonia, urinary tract infections, and bacteremia (Wu *et al.*, 2012). Although the incidence of community acquired pneumonia caused by *K. pneumoniae* decreased for few years, but in humans with some immune related and other health problems such as diabetes mellitus, there is a health risk as the *K. pneumoniae* can cause an acute primary infection that result in lobar pneumonia. It is a common health care associated infectious agent which causes several infections, of which, the urinary tract, bloodstream, pneumonia and intra abdominal infections have become enormously common. Community acquired primary pyogenic liver abscess (PLA) caused by *K. pneumonia* is an emerging disease receiving increasing attention since past 20 years. Patients with this infection can present with or without septic metastatic complications (Keynan and Rubinstein, 2007). It is also involved in surgical site infections, peritonitis, pyogenic liver abscess, thoracic empyema and psoas muscle abscess (Chang *et al.*, 2005; Maltezou *et al.*, 2009). *K. pneumoniae* has become a common cause of community acquired bacterial meningitis in adults in Taiwan, in the absence of liver abscess or other fecal infection. Most cases have been reported from Taiwan and studies revealed that *K. pneumoniae* was the predominant serotype causing liver abscess (Chuang *et al.*, 2006). The entity has also been described in other parts of Asia, North America and Europe (Chuang *et al.*, 2006; Ko *et al.*, 2002; Rahimian *et al.*, 2004; Fang *et al.*, 2005).

These Gram negative bacteria, such as *K. pneumonia* and *Escherichia coli* are proved to be the cause of bacterial endophthalmitis in North America and in East Asia. Among these cases, *Klebsiella* spp is the most common etiologic agent followed by *E. coli* (Jackson *et al.*, 2003; Wong, 2000), hence becoming the major cause of endogenous endophthalmitis. The resulting inflammation may progress within days and lead to decreased vision, loss of light perception or enucleation despite systemic antibiotics treatment or surgical interventions such as intravitreal antibiotic injections or vitrectomy (Jackson *et al.*, 2003; Yoon *et al.*, 2003). These bacteriae and their components such as lipopolysaccharide (LPS) carry pathogen associated molecular patterns. Recognition of LPS leads to the rapid activation of intracellular signaling pathways, resulting in the release of pro-inflammatory mediators in mammalian phagocytic cells (Heumann and Roger, 2002). Retinal pigment epithelium (RPE) cells have an important role in different pathologic processes of the retina such as age related macular degeneration, diabetic retinopathy or inherited pathologies (Cai *et al.*, 2000; Lutty *et al.*, 1999; Hamel et. al., 1998; Morimura *et al.*, 1998).

K. pneumoniae, were rarely reported as the monomicrobial cause (Gradon, 1996; Marra and Hotaling, 1996; Parhiscar and Har-El, 2001; Methieu *et al.*, 1995; Sethi and Stanley, 1991). However, several studies of Fascial space infections (FSI) in Taiwan showed that *K. pneumoniae* was not an uncommon pathogen for the disease (Wang *et al.*, 2002; Hsiao and Chao, 1996; Chu *et al.*, 1991; Yuan *et al.*, 1997; Ho and Hsu, 1994; Juang *et al.*, 1989). FSIs of head and neck are of either odontogenic or oropharyngeal origin and extend to potential fascial spaces of the lower part of the head and upper portion of the neck (Margo *et al.*, 1994). Infections of these spaces may intercommunicate with one another and thus potentiate the extension and complication of the disease (Lu *et al.*, 1997). Although rare, life threatening complications such as airway obstruction, intracranial or pleuropulmonary extension, and

haematogenous dissemination or other metastatic foci clearly indicate the potentially serious nature of these infections (Jang *et al.,* 1993).

Medication for *K. pneumoniae* infections

Infections with Gram negative bacteria are of imminent concern as they are more difficult to treat and visual outcome is poor. *K. pneumoniae* are major nosocomial pathogens producing extended spectrum betalactamase (ESBL). ESBL producers are usually susceptible only to carbapenems, and these drugs have been the treatment of choice for severe infections by ESBL-producer *K. pneumoniae* (Paterson and Bonomo, 2005). More recently, the emergence of carbapenemase producing *K. pneumoniae* (KPC) has severely challenged antimicrobial therapy, since it confers a high level of resistance to all β-lactams and distinct levels of resistance to carbapenems (Nordmann *et al.,* 2009). As *K. pneumoniae* is one of the most common nosocomial pathogens, its ability to produce extended spectrum β-lactamases (ESBLs) has caused great concern worldwide (Falagas *et al.,* 2007; Nordmann *et al.,* 2009). Carbapenem resistance among *K. pneumoniae*, which first emerged a decade ago, continues to spread (Jacoby and Munoz-Price, 2005; MacKenzie *et al.,* 1997; Livermore, 2002; Walsh *et al.,* 2005), and is a cause of major concern**.**

They can efficiently hydrolyse penicillins, all cephalosporins, monobactams, carbapenems, and even β-lactamase inhibitors (Papp-Wallace *et al.,* 2010). Many bacteria with these enzymes remain susceptible to colistin, tigecycline and one or more aminoglycoside, but some are resistant even to these drugs. Moreover, only a few drugs are in development against KPC-positive bacteria (Munoz-Price *et al.,* 2013). The ESBL producers can also develop co-resistance to other classes of antimicrobial agents, such as fluoroquinolones, cotrimoxazole and aminoglycosides. Howerver, a recent study showed its inhibition by Fosfomycin, an antibiotic used in the treatment of UTI related infections (Liu *et al.,* 2011)**.**

Epidiomology of the species is discussed (Montgomerie, 1979) and the comparison to its genomics study relating to antibiotics resistance is extensively studied and has revealed its resistance capacity

So, there is an urgent need of introducing new, effective antibiotics with lower side effect, such as natural antibiotic derived from plants. Aggressive treatments and analysis with these natural antibiotics are required to prevent its further spreading.

PLANTS SUPPRESSING THE SURVIVAL OF *K. pneumoniae*

Nature has been a source of medicinal agents for thousands of years and an impressive number of modern drugs have been isolated from natural sources. This plant based, traditional medicine system continues to play an essential role in health care, with about 80% of the world's inhabitants relying mainly on traditional medicines for their primary health care (Owolabi *et al.,* 2007). According to World Health Organization, medicinal plants would be the best source to obtain a variety of drugs (Doughari *et al.,* 2008).

Numerous studies demonstrated that medicinal plants are sources of nutrient and non-nutrient compounds, many of which display antioxidant and antimicrobial properties which can protect the human body against both cellular oxidation reactions and pathogens. Thus, it is important to characterize the different types of medicinal plants for their antioxidant and antimicrobial potentials, and such plants should be investigated to better understand their properties, safety and efficacy (Nascimento *et al.,* 2000). The use of medicinal plants as a source for relief from illness can be traced back over five millennia, to written documents of the early civilization in China, India and the north east (Mahesh and Satish, 2008). The potential of higher plants as a source for new drugs is still largely unexplored. Among the estimated 2,50,000- 5,00,000 plant species, only a small percentage have been investigated phytochemically and the fraction submitted to biological or pharmacological screening. Compounds of natural or synthetic origin have been the source of innumerable therapeutic agents (Mahesh and Satish, 2008; Kroschwitz *et al.,* 1992). Medicinal plants are rich sources of antimicrobial agents. A wide range of medicinal plants are used to get different rasayanas which possess different medicinal properties against various microbes (Vashist and Jindal, 2012). Long before mankind discovered the existence of microbes, the idea that certain plants had healing potential, indeed, that they contained what we would currently characterize as antimicrobial principles, was well accepted. Still these traditional medicines are included as part of the habitual treatment of various maladies to treat common infectious diseases (Doughari *et al.,* 2012).

In recent years, research on medicinal plants has attracted a lot of attentions globally. Large body of evidence has accumulated to demonstrate the promising potential of Medicinal Plants used in various traditional, complementary and alternate systems of treatment of human diseases. Plants are rich in a wide variety of secondary metabolites such as tannins terpenoids, alkaloids, flavonoids, etc, which have been found in vitro to have antimicrobial properties (Dahanukar et. al., 2000; Cowan, 1999). Clinical microbiologists have two reasons to be interested in the topic of antimicrobial plant extracts. First, it is very likely that these phytochemicals will find their way into the arsenal of antimicrobial drugs prescribed by the physicians; several are already being tested on humans. Scientists realize that the effective life span of any antibiotic is limited, so new sources, especially plant sources are also being investigated. Second, the public is becoming increasingly aware of the problems with the over prescription and misuse of traditional antibiotics. In addition many people are interested in having more autonomy over their medical care. A multitude of plants compounds (often of unreliable purity) is readily available over the counter from herbal suppliers and national food stores and the self medication with these substances is a common practice to certain extent (Cowan, 1999). In this review we had studied some recent publications to enlist some of the flora which are useful to inhibit the growth of the pathogen, *K.*

pnuemoniae. 90 plants belonging to 51 families are enlisted in Alphabetical order of the plant name (Table 1). Plant parts such as bark, leaves, roots, fruits were used to extract active components against the organism. Mostly the leaves were used. Solvents such as Methanol, Water, Chloroform, Ethanol, etc., were used to prepare the extracts. The results were compared with standard antibiotics.

PLANT ESSENTIAL OILS AS GROWTH INHIBITORS OF *K. pneumoniae*

The spread of drug resistant pathogens is one of the most serious threats to successful treatment of microbial diseases. Down the ages, essential oils and other extracts of plants have evoked interest as sources of natural products. They have been screened for their potential uses as alternative remedies for the treatment of many infectious diseases (Tepe *et al.,* 2004). World Health Organization (WHO) noted that majority of the world's population depends on traditional medicine for primary healthcare. Medicinal and aromatic plants are widely used as medicine and constitute a major source of natural organic compounds.

Plant essential oils and extracts have been used for many thousands of years (Jones, 1996), in food preservation and aromatherapy (Buttner *et al.,* 1996); fragrance industries (Van de Braak and Leijten, 1996); pharmaceuticals, alternative medicine and natural therapies (Reynolds, 1996; Lis-Balchin M, Deans, 1997)**.**

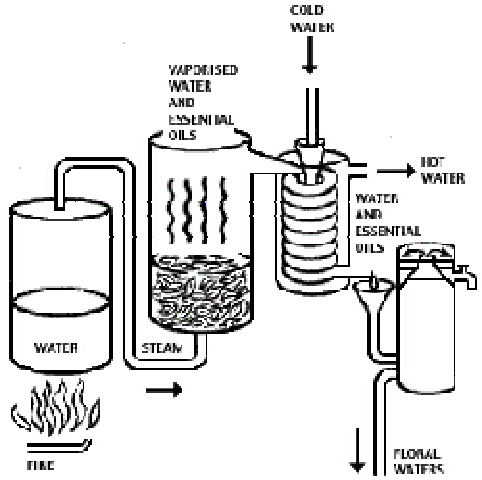

Fig. 2: Extraction of essential oils from plant parts using traditional steam vapor method.

Plants have an almost limitless ability to synthesize aromatic substances. Essential oils (also called volatile oils) are aromatic oily liquids obtained from plant materials (flowers, buds, seeds, leaves, twigs, bark, herbs, wood, fruits and roots) (see traditional essential oil extraction Fig 2). They can be obtained by expression, fermentation or extraction but the method of steam distillation is most commonly used for commercial production. An estimated 3000 different types of essential oils are known, of which 300 are commercially important in fragrance market (Van de Braak and Leijten, 1996). Essential oils are complex mixtures comprising many single compounds. Chemically they are derived from terpenes and their oxygenated compounds. Each of these constituents contributes to the beneficial or adverse effects. Essential oils have been shown to possess antibacterial, antifungal, antiviral insecticidal and antioxidant properties (Burt, 2004; Kordali *et al.,* 2005). Essential oil extracts of various plants have been reported to have inhibitory effects against diverse types of microorganisms including gram-positive bacteria, gram-negative bacteria, fungi and viruses. Many of these plant extracts contain organic chemicals inhibitory for particular microorganisms (Horne *et al.,* 2001).

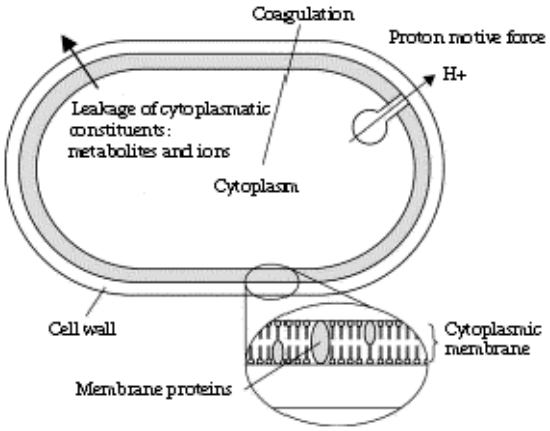

Fig. 3: Sites of action of natural compounds on bacterial cells (Source: Silva and Fernandes Júnior, 2010).

Essential oils such as aniseed, calamus, camphor, cedar-wood, cinnamon, citronella, clove, eucalyptus, geranium, lavender, lemon, lemongrass, lime, mint, nutmeg, orange, palmarosa, rosemary, basil, vetiver and wintergreen have been traditionally used by people for various purposes in different parts of the world. Cinnamon, clove and rosemary oils have shown antibacterial and antifungal activity (Ouattara et. al., 1997); cinnamon oil also possesses antidiabetic property. Anti-inflammatory activity has been found in basil (Singh and Majumdar, 1999). Lemon and rosemary oils possess antioxidant property (Calabrese *et al.,* 1999; Aruoma *et al.,* 1996). Peppermint and orange oils have shown anticancer activity (Kumar *et al.,* 2004; Arias and Ramon-Laca, 2005). Citronella oil has shown inhibitory effect on biodegrading and storage contaminating fungi (De Billerbeck *et al.,* 2001). Lime oil has shown immunomodulatory effect in humans (Arias and Ramon-Laca, 2005). Lavender oil has shown antibacterial and antifungal activity; it was also found to be effective to treat burns and insect bites (Cavanagh and Wilkinson, 2002).

The antimicrobial activity of many essential oils has been previously reviewed and classified as strong, medium or weak (Zaika, 1988). Essential oils are a rich source of biologically active compounds. There has been an increased interest in looking at antimicrobial properties of extracts from aromatic plants particularly essential oils (Milhau *et al.,* 1997). Therefore, it is reasonable to expect a variety of plant compounds in these oils with specific as well as general antimicrobial activity and antibiotic potential (Darokar *et al.,* 1998). An important

characteristic of essential oils and their components is their hydrophobicity, which enables them to partition the lipids of the bacterial cell membrane and mitochondria, disturbing the cell structures and rendering them more permeable (Knobloch *et al.*, 1986). Extensive leakage from bacterial cells or the exit of critical molecules and ions leads to death (Denyer *et al.*, 1991).

The study revealed different essential oils from plants; 14 essential yielding plants are able to inhibit the growth of the *K. pnuemoniae* (Table 2; Fig 4). The chemical composition of the essential oils from these plants is enlisted in the Table 3. The structures of essential oil compounds from *Allium rotundum, Bupleurum falcatum,* etc are shown in the Fig 5.

Fig. 4: Essential oil yielding plants showing inhibitory effects on the *K. pneumonia.*

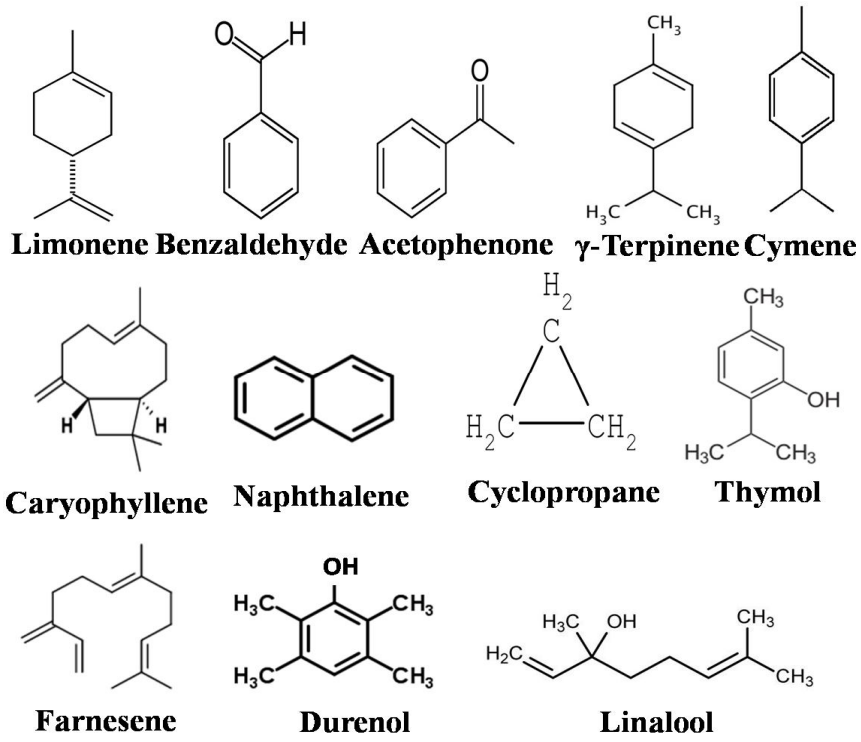

Fig. 5: Chemical structures of chemical compounds present in plant essential oils showing inhibition of the growth of *K. pnuemoniae*.

Table. 1: Plants with antimicrobial efficacy towards *K. pnuemoniae*.

S. No.	Plant name	Family	Plant part	Solvent	Strain	Antibiotic Used	Reference
1.	*Acacia mearnsii* De Wild.	Mimosaceae	bark	Methanol	ATCC 10031	Tetracycline	Olajuyigbe et al., 2012
2.	*Acacia nilotica* L	Mimosaceae	leaves	Methanol	_	Doxycycline	Mahmood et al., 2012
3.	*Acalypa indica*	Euphobiaceae	Leaves	Methanol	MTCC 3384	Chloramphenicol	Arutselvi et al., 2012
4.	*Achyranthes aspera*	Amaranthaceae	Leaves	Methanol	_	Ciprofloxacin	Doss et al., 2012
5.	*Adathoda vasica*	Acanthaceae	Leaves	Methanol	MTCC 3384	Chloramphenicol	Arutselvi et al., 2012
6.	*Adhatoda vasica*	Acanthaceae	leaves	Methanol	_	Streptomycin	Singh et al., 2012a
7.	*Adiantum capillus-veneris* L.	Polypodiaceae	aerial parts	Water and Methanol	_	-	Mahboubi et al., 2012
8.	*Aegle marmelos*	Rutaceae	Fruit	Ethyl acetate, Methanol	ATCC 20063	_	Maharjan et al., 2012
9.	*Aerva javanica*	Amaranthaceae	Whole plant	Ethyl Acetate, Chloroform Fraction, Aqueous Fraction, Crude Fraction, n-Hexane	ATCC 700603	_	Mufti et al., 2012
10.	*Albizia lebbeck* L	Mimosaceae	leaves	Methanol	_	Doxycycline	Mahmood et al., 2012
11.	*Allium cepa*	Liliaceae	fresh bulbs	–	*K24*	Ciprofloxacin	Stephen et al., 2012
12.	*Allium rotundum*	Liliaceae	flower	Methanol	PTCC 1290	Valinomycine, Gentamicine and Cholramphenicol	Dehpour et al., 2012
13.	*Annona squamosa* L	Annonaceae	seeds	Petroleum ether, Methanol, Chloroform	–	Streptomycin	Aher et al., 2012
14.	*Argemone mexicana*	Papaveraceae	Leaves	Methanol	_	Ciprofloxacin	Doss et al., 2012
15.	*Argemone mexicana*	Papaveraceae	leaves	Methanol	_	Streptomycin	Singh et al., 2012a

16.	*Asclepias curassavica* Linn.	Asclepiadaceae	roots	Chloroform, Acetone, Ethanol and Water	MTCC 109	Streptomycin	Kurdekar et al., 2012
17.	*Astragalus atropilosulus* (Hochst.) Bunge subsp. Abyssinicus (Hochst.) J. B. Gillett	Fabaceae	leaves	Acetone, Ethanol, Methanol, 1/1 Ethanol/Methanol, 1/1 Ethanol/Acetone,1/1 Acetone/Methanol, Hot water	_	Gentamicin	Sulaiman et al., 2012
18.	*Azadiracta indica*	Meliaceae	Leaves	Methanol	MTCC 3384	Chloramphenicol	Arutselvi et al., 2012
19.	*Barleria lupulina*	Acanthaceae	Leaves	Methanol	_	Ciprofloxacin	Doss et al., 2012
20.	*Begonia floccifera* Bedd.	Begoniaceae	Fresh flowers	Phenol, Tannins, Xanthoproteins, Steroids, Tannins, Steroids, Phytosterols, Triterpenoids, Sapogenins, Coumarins and Carbohydrates	_	Amikacin	Jeeva and Antonisamy, 2012
21.	*Berberis asiatica*	Berberidaceae	leaves	Methanol	_	Streptomycin	Singh et al., 2012a
22.	*Brassica oleracea* L.	Brassicaceae		Ethanolic	_	_	Paul et al., 2012
23.	*Bridelia retusa* (Linn.) Spreng.	Euphobiaceae	Bark	Chloroform, Acetone, Ethanol and Water	MTCC 109	Streptomycin	Kurdekar et al., 2012
24.	*Bupleurum falcatum*	Apiaceae	flowers	_	PTCC-1053	Ciprofloxacin, Gentamicin	Hadi et al., 2012
25.	*Cannabis sps*	Cannabaceae	_	Aqueous	_	Ceftazidime, Carbencillin, Ceftizoxime, Amikacin, Cefotaxime, Ofloxacin, Gentamicin, Amoxicillin, Ciprofloxacin, Cephalexin, Chloramphenicol, Tetracycline	Singh et al., 2012b
26.	*Capparis spinosa* L.	Capparidaceae	flowers	Methanol	ATCC 10031	-	Mahboubi et al., 2012
27.	*Carica papaya*	Caricaceae	seeds	_	KP55; K2; K24	Ciprofloxacin	Stephen et al., 2012
28.	*Cassia fistula*	Caesalpiniaceae	leaves	Methanol	_	Streptomycin	Singh et al., 2012a
29.	*Cenchrus ciliaris*	Poaceae	Whole Plant	Methanol	_	Ciprofloxacin	Doss et al., 2012
30.	*Cinnamomum cecidodaphne*	Lauraceae	Fruits	_	MTCC 4030	Ciprofloxacin	Bharti et al., 2012
31.	*Cinnamomum zeylanicum*	Lauraceae	leaves	_	PTCC-1053	Ciprofloxacin, Gentamicin	Hadi et al.,2012
32.	*Coccinia grandis*	Cucurbitaceae	Leaves	Methanol	_	Ciprofloxacin	Doss et al., 2012
33.	*Cola acuminate*	Malvaceae	fruits	_	ATCC 11296; KP55; K24	Ciprofloxacin	Stephen et al., 2012
34.	*Coriandrum sativum* (L.)	Apiaceae	fruits	-	_	Ampicillin, Tetracycline, Kannamycin	Suganya et al., 2012
35.	*Coriandrum sativum*	Apiaceae	Seeds	_	MTCC 4030	Ciprofloxacin	Bharti et al., 2012
36.	*Coriandrum sativum*	Apiaceae	leaves	_	PTCC-1053	Ciprofloxacin, Gentamicin	Hadi et al., 2012
37.	*Carissa opaca*	Apocynaceae	leaves	Methanol	_	Streptomycin	Singh et al., 2012a
38.	*Costus speciosus* (L.) Spreng.	Costaceae	Rhizome	Chloroform, Acetone, Ethanol and Water	MTCC 109	Streptomycin	Kurdekar et al., 2012
39.	*Cotinus coggygria*	Anacardiacaea	leaves	Methanol	_	Streptomycin	Singh et al., 2012a
40.	*Couroupita guianensis*Aubl.	Lecythidaceae	Fruits	Chloroform	MTCC 109; ESBL 3971; ESBL 75799; ESBL 3894; ESBL 3967	Streptomycin	Rauf et al., 2012
41.	*Cupressus sempervirens* L.	Cupressaceae	aerial parts	Methanolic, Ethanolic and Ethyl Acetate	MTCC 618	Pencillin	Chaudhary et al., 2012

42.	*Cynometra travancorica* Bedd.	Fabaceae	Whole plant	Cold water and Ethanolic	–	Ampicilin	John et al., 2012
43.	*Cyperus scariosus*	Cyperaceae	Roots	_	MTCC 4030	Ciprofloxacin	Bharti et al., 2012
44.	*Dactyloctenium indicum*	Poaceae	Whole Plant	Methanol	_	Ciprofloxacin	Doss et al., 2012
45.	*Datura stramonium*	Solanacaea	stem-bark	Ethanolic	KP72011FMC	Gentamycin	Shagal et al., 2012
46.	*Desmodium gangeticum*	Fabaceae	_	Aqueous, Methanolic, Ethanolic	_	Ceftazidime, Carbencillin, Ceftizoxime, Amikacin, Cefotaxime, Ofloxacin, Gentamicin, Amoxicillin, Ciprofloxacin, Cephalexin, Chloramphenicol, Tetracycline	Singh et al., 2012b
47.	*Emblica officinalis*	Euphorbiaceae	fruits	Aqueous, Acetone, Chloroform, Ethyl Acetate and Methanol	–	–	Patil et al., 2012
48.	*Eucalyptus globulus*	Myrtaceae	Leaves	_	MTCC 4030	Ciprofloxacin	Bharti et al., 2012
49.	*Euphorbia hirta*	Euphobiaceae	Leaf, stem, root and fruits	Alkaloids	MTCC 4030	–	Singh and Kumar, 2012
50.	*Ficus benghalensis* Linn.	Moraceae	leaves	Chloroform, Methanol	MTCC B2405	Ciproflaxacin	Koon and Rao, 2012
51.	*Ficus sarmentosa*	Moraceae	Whole plant	n-Hexane, Chloroform, Ethyl Acetate and Methanolic	–	Streptomycin	Rauf et al., 2012
52.	*Garcinia kola*	Clusiaceae	seeds	_	ATCC 11296; KP55; K24; KP63; K2	Ciprofloxacin	Stephen et al., 2012
53.	*Garcinia lucida*	Clusiaceae	seeds	_	ATCC 11296; KP55; K24; KP63; K2	Ciprofloxacin	Stephen et al., 2012
54.	*Gymnema sylvestre* (Retz) R. Br ex. Schultes	Asclepiadaceae	Leaf(L) and stem(S)	Petroleum Ether, Chloroform, Acetone, Methanol, Water	MTCC 109	chloramphenicol and tetracycline	Murugan et al., 2012
55.	*Hallea ledermannii* (Krause) Verdc.	Rubiaceae	leaves	Methanol	_	ciprofloxacin	Adeleke Adesegun et al., 2012
56.	*Isodon rugosus*	Lamiaceae	Whole plant	n-Hexane, Chloroform, Ethyl Acetate and Methanolic	–	Streptomycin	Rauf et al., 2012
57.	*Lagenandra Toxicaria* Dalz.	Araceae	Rhizome	Chloroform, Acetone, Ethanol and Water	MTCC 109	Streptomycin	Kurdekar et al., 2012
58.	*Lobelia nicotianaefolia* Roth ex R. & S	Lobeliaceae	Leaves and roots	Chloroform, Acetone, Ethanol and Water	MTCC 109	Streptomycin	Kurdekar et al., 2012
59.	*Matricaria pubescens* Desf.	Asteraceae	aerial parts	Aqueous, Ethanolic	CIP 106818	Ampicillin	Makhloufi et al., 2012
60.	*Medicago sativa*	Poaceae	Whole Plant	Methanol	_	Ciprofloxacin	Doss et al., 2012
61.	*Melaleuca alternifolia*	Myrtaceae	Leaves	_	MTCC 4030	Ciprofloxacin	Bharti et al., 2012
62.	*Melinis repens*	Poaceae	Whole Plant	Methanol	_	Ciprofloxacin	Doss et al., 2012
63.	*Mimosa himalayana* Gamble	Mimosaceae	leaves	Methanol	_	Doxycycline	Mahmood et al., 2012
64.	*Morinda pubescens* var. pubescens J.E. Smith	Rubiaceae	Leaf (L) and stem bark (SB)	Petroleum Ether, Chloroform, Acetone, Methanol, Water	MTCC 109	chloramphenicol and tetracycline	Murugan et al., 2012
65.	*Murraya paniculata* Linn.	Rutaceae	Whole plant	Petroleum Ether, Ethanol, Methanol, Hydroalcoholic extracts	–	–	Gautam et al., 2012
66.	*Musa paradisiaca*	Musaceae	Flower	Ethanol & EtOH:Water (1:1)	–	Amikacin	Jawla et al., 2012

72.	*Persicaria piripu* (DC.) M.R.Almeida	Polygonaceae	Leaves	Chloroform, Acetone, Ethanol and Water	MTCC 109	Streptomycin	Kurdekar et al., 2012
73.	*Phylanthus niruri*	Euphorbiaceae	Leaves	Methanol	MTCC 3384	Chloramphenicol	Arutselvi et al., 2012
74.	*Picralima nitida*	Apocynaceae	fruits	_	ATCC 11296; KP55; K24; KP63; K2	Ciprofloxacin	Stephen et al., 2012
75.	*Polygala grineris*	Polygalaceae	Leaves	Methanol	MTCC 3384	Chloramphenicol	Arutselvi et al., 2012
76.	*Punica granatum* L.	Punicaceae	peels	_	_	_	Ullah et al., 2012
77.	*Quercus dilatata*	Fagaceae	Fruit	Methanol	_	_	Sarwat et al., 2012
78.	*Remusatia vivipara* (Roxb.) Schott & Endl.	Araceae	Corm	Chloroform, Acetone, Ethanol and Water	MTCC 109	Streptomycin	Kurdekar et al., 2012
79.	*Rhynchosia capitata*	Fabaceae	Whole Plant	Water	_	Ciprofloxacin	Doss et al., 2012
80.	*Ricinus communis*	Euphorbiaceae	leaves	Methanol	_	Streptomycin	Singh et al., 2012a
81.	*Rosmarinus officinalis* L.	Lamiaceae	aerial parts	–	WHO24	Ampicillin	Chobba et al., 2012
82.	*Salvadora oleoides* Decne.	Salvadoraceae	stem	Benzene	MTCC 3384	Streptomycin	Kumar et al., 2012
83.	*Sambucus ebulus* L.	Caprifoliaceae	leaves	Water and Methanol	_	-	Mahboubi et al., 2012
84.	*Sesame Indicum*	Pedaliaceae	White seeds	Aqueous	–	Ceftazidime, Carbencillin, Ceftizoxime, Amikacin, Cefotaxime, Ofloxacin, Gentamicin, Amoxicillin, Ciprofloxacin, Cephalexin, Chloramphenicol, Tetracycline	Singh et al., 2012b
85.	*Sesame Indicum*	Pedaliaceae	Black seeds	Aqueous, Methanolic, Ethanolic	–	Ceftazidime, Carbencillin, Ceftizoxime, Amikacin, Cefotaxime, Ofloxacin, Gentamicin, Amoxicillin, Ciprofloxacin, Cephalexin, Chloramphenicol, Tetracycline	Singh et al., 2012b
86.	*Solanum nigrum*	Solanaceae	Leaves	Methanol	MTCC 3384	Chloramphenicol	Arutselvi et al., 2012
87.	*Stachys pubescen*	Apocynaceae	leaves	_	PTCC-1053	Ciprofloxacin, Gentamicin	Hadi et al.,2012
88.	*Tagetes erecta*	Asteraceae	leaves	Aqueous	_	Gentamicin G30	Dasgupta et al., 2012
89.	*Thymus vulgaris*	Labiatae	Flowering tips and Leaves	_	MTCC 4030	Ciprofloxacin	Bharti et al., 2012
90.	*Trigonella foenum-graecum*	Leguminoseae	Whole Plant	Methanol	_	Ciprofloxacin	Doss et al., 2012
91.	*Withania somnifera*	Solanacae	Ripen fruits	Glacial Acetic Acid, Chloroform, Toluene.	MTCC 4030	Gentamycin	Singariya et al., 2012
92.	*Withania somnifera*	solanacae	leaves	Acetic acid, Ethanol, Acetone, Ethyl acetate, Benzene, Toluene	MTCC 4030	Gentamycin	Singariya et al., 2012
93.	*Withania somnifera*	Solanaceae	Leaf, stem and root	Alkaloids	MTCC 4030	_	Singh and Kumar, 2012
94.	*Woodfordia fruticosa*	Lythraceae	Flower	Methanolic	ATCC 20063	_	Maharjan et al., 2012
95.	*Woordfordia fruticosa*	Lythraceae	Flower	Methanol	_	_	Sarwat et al., 2012
96.	*Zanthoxylum armatum*	Rutaceae	leaves	Methanol	_	Streptomycin	Singh et al., 2012a
97.	*Zanthoxylum rhetsa*	Rutaceae	Leaves	_	MTCC 4030	Ciprofloxacin	Bharti et al., 2012

Table. 2: Essential oil yielding plants showing inhibitory effects towards *K. pnuemoniae*.

S. NO.	PLANT NAME	PLANT PART	STRAIN	REFERENCE
1.	*Allium rotundum*	Flower	PTCC 1290	Dehpour et al., 2012
2.	*Bupleurum falcatum*	Flower	PTCC-1053	Hadi et al.,2012
3.	*Cinnamomum cecidodaphne*	Fruits	MTCC 4030	Bharti et al., 2012
4.	*Cinnamomum zelanicum*	Leaves	PTCC-1053	Hadi et al.,2012
5.	*Coriandrum sativum*	Fruits	_	Suganya et al., 2012
6.	*Coriandrum sativum*	Seeds	MTCC 4030	Bharti et al., 2012
7.	*Coriandrum sativum*	Leaves	PTCC-1053	Hadi et al.,2012
8.	*Cyperus scariosus*	Roots	MTCC 4030	Bharti et al., 2012
9.	*Eucalyptus globulus*	Leaves	MTCC 4030	Bharti et al., 2012
10.	*Matricaria pubescens*	Aerial parts	CIP 106818	Makhloufi et al., 2012
11.	*Melaleuca alternifolia*	Leaves	MTCC 4030	Bharti et al., 2012
12.	*Nardostachys jatamansi*	Roots	MTCC 4030	Bharti et al., 2012
13.	*Rosmarinus officinalis*	Aerial parts	WHO24	Chobba et al., 2012
14.	*Stachys pubescens*	Leaves	PTCC-1053	Hadi et al.,2012
15.	*Thymus vulgaris*	Flowering tips and Leaves	MTCC 4030	Bharti et al., 2012
16.	*Zanthoxylum rhetsa*	Leaves	MTCC 4030	Bharti et al., 2012

Table. 3: Chemical Composition of Essential Oils from plants showing inhibitory effects on the *K. pnuemoniae*.

S. No.	Plant Name	Chemical Composition of Essential Oils
1.	*A. rotundum*	Thiophene, 2,3-dimethyl; Thiophene, 2,4-dimethyl; CIS PROPENYL METHYL DISULFIDE; TRANS PROPENYL METHYL DISULFIDE; Furan, 2-pentyl; Octanal; 1-Hexanol, 2-ethyl; Decane, 3,7-dimethyl; Heptane, 2,3,4-trimethyl; Decane, 3,7-dimethyl; Nonanal; TRANS-PROPENYL PROPYL DISULFIDE; CIS-PROPENYL PROPYL DISULFIDE; 1-Oxa-4,6-diazacyclooctane-5-thion; o-DICHLOROBENZENE; DODEMORPH; DEMETON; Decanal; Benzaldehyde, 4-ethyl; Benzene, 1,3-bis(1,1-dimethylethyl); Tetradecane; PROPAMOCARB; Undecanal; 1,4-Dioxane-2,3-diol; Trisulfide, dipropyl; phthalic thiothionoanhydride; DEMEPHION; 1-Propene, 3,3'-thiobis; Tetradecane; 5,9-Undecadien-2-one, 6,10-dimethyl; 1-Decene; beta.-Ionone; Pentacosane; Phenol, 2,4-bis(1,1-dimethylethyl; TERBUTHYLAZINE; Hexadecane; Cyclododecane; Eicosene; Tetradecane; 2-Pentadecanone, 6,10,14-trimethyl; Dibutyl phthalate; (S)-4,4-Dimethyl-2-(4-methyl-3-cyclohexen-1-yl)-1,5-hexadiene; Phytol; Octadecane; 14-.BETA.-H-PREGNA; 14-.BETA.-H-PREGNA; 1-Hexacosene; 14-.BETA.-H-PREGNA; Eicosane (CAS); 14-.BETA.-H-PREGNA; 14-.BETA.-H-PREGNA; 14-.BETA.-H-PREGNA; HAHNFETT; 14-.BETA.-H-PREGNA
2.	*B. falcatum*	α-Pinene; Pinocarvone; α-Cubebene; Pinocamphone; Heptanal; cis-Verbenol; Myrtenal; Thyopsene; trans-Pinocarveol; Trans-Verbenol; Cuparene; Torilenol; Spathulenol; α-Calacorene; Pentacosane
3.	*C. zeylanicum*	Benzaldehyde; Phenylmethanal; Benzene Acetaldehyde; Acetophenone; Benzaldehyde dimethyl acetal; Benzeneacetic acid; 2-Propenal; Cinannamaldehyde Dimethylc Acetale; 2-Propenoic acid; Ortho Metthoxy Cinnamic Aldehyde
4.	*C. sativum*	α-Pinene; Benzene; γ-Terpinene; Cyclopropane; Linalool L; Geranyl acetate
5.	*E. globulus*	α-Pinene; Camphene; 1,3,8-p-Menthtriene; Nopinen; β –Myrcene; 3-Carene; Eucalyptol; Fenchyl alcohol; Camphor; Linalool; Trimethyl benzylalcohol; Terpineol; D- Vebenone; Camphenol; 4- Carene; Berbenone; α-Bisbolene epoxide; δ-3-Carene; 3-Carene-2-ol; Farnesene
6.	*M.alternifolia*	Trichloromethane, 1,8-Nonadiyne, α-Pinene, 1- Cyclooctyne, β –Myrcene, 2-Propynylcyclopentane, Cymene, α-Limonene, 1,8-Cineole, α-phellandrene, Artemesiatriene, 6-Methyl-3-heptyne, Linalool 13.989 12.77, α-Terpineol, Nitropentane, 3- Heptene
7.	*S. pubescens*	β-Pinene; 1,4-Cyclohexadiene; Myrcene; α- Terpinene; Benzene; Limonene; (E)-β-Ocimene; γ-terpinene; 3-Cyclohexen-1-ol; Linalool; 2,6-Octadien ; Octen-1-ol acetate; 2,6-Octadienal; Linalyl acetate; δ-Elemene; β-Bourbonene; Naphthalene; β-Gurjunene; Bicyclogerm acrene; Caryophyllene oxide; Spathulenol; Germacrene
8.	*T. vulgaris*	β-Ketopropane, Trichloro methane- 1,4- hexadiene , 4-Methyl-3- methylene, 1- Cyclooctyne, β –Pinene, β –Myrcene, β –Cymene, Dimethylsuccinate, α-Terpinene, 2-Nonynoic acid, Durenol, Thymol

CONCLUSION

In recent years, there has been an increase in *Klebsiella* infections, especially in hospitals, mostly due to multiple antibiotic resistant strains. It can evade host defenses in normal and impaired hosts and spreads to the upper or lower respiratory tract, provoking correlate infections or it may invade the bloodstream, causing invasive diseases. Besides, it is constantly being studied for the frequency with which resistance occurs against the most common antibiotics. The assays used in the studies are just preliminary assays that were used to evaluate the inhibitory efficacy of the plants and their essential oils. No biological evaluation was performed. Recommended antibiotic for this bacterium are Carbapenemases. But, the antibiotics used to compare the results of were not Carbapenemases. We suggest addition of *in-vivo* studies using animal models for the biological evaluations and clinical trials before release of such antibiotics would be needed to justify its effect and to further evaluate the potential of these oils as an antibacterial agent in topical or oral applications. The inhibitory effects could be compared to the Carbapenemases or Carbapenemases like antibiotics, to improve the understanding about the action of the antibacterial action of the plant based compoounds.

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