INTRODUCTION

*Streptococcus pneumoniae* is responsible for potential life threatening infections such as pneumonia, otitis media, meningitis, sinusitis and bacteremia. *S. pneumoniae* causes excess morbidity and mortality in young children, the elderly, debilitated patients with compromising medical conditions of the respiratory tract, or decreased immunological function (Bogaert et al., 2004; Reinert et al., 2005). While the burden of pneumococcal disease is globally distributed, it may be most severe in developing countries where it is estimated to be responsible for greater than one million childhood deaths per year (Hausdorff et al., 2001; Kadioglu et al., 2008). Pneumococci are a significant cause of morbidity and mortality in high prevalence of human immunodeficiency virus (HIV) infection (Blossom et al., 2006). *S. pneumoniae* is one of the most important human pathogens, and pneumococcal disease is endemic all over the world. For more than a century *S. pneumoniae* has been known as the most common cause of acute otitis media, sinusitis, and pneumonia and one of the most important causes of bacterial meningitis (Austrian R., 1981). In developing countries pneumonia is a serious disease in children and it is estimated that more than a million children below the age of 5 each year die from pneumococcal pneumonia, (Monto A.S., 1989). In the United States the pneumococcus each year probably accounts for 3000 cases of meningitis, 500,000 cases of pneumonia, and 7,000,000 cases of otitis media. (Austrian R., 1999).

The incidence of pneumococcal pneumonia has probably not decreased significantly during the previous century, but the case fatality rate has decreased dramatically with the advent of antibiotics. There has also been a shift toward the disease becoming severe in mostly the elderly and those with underlying diseases. The total yearly incidence of pneumonia in Western populations is around 1% and *S. pneumoniae* is probably responsible for almost half of the cases of community-acquired pneumonia (CAP). (Heffron R., 1939 : Kalin M., 1983; Burman L.A et al., 1985; Ortqvist, A et al., 1990; Fang G.D et al., 1990; Ruiz-Gonzalez A et al., 1999). Thus almost five in 1000 persons each year contract pneumococcal pneumonia, with the incidence being several times higher in the very young and the elderly. (Burman L.A et al., 1985; Jokinen C et al., 1993; Scott L.A et al., 1996; Marric T.J et al., 1999). The major cause of pneumococcal bacteremia is pneumonia. The total annual incidence of pneumococcal bacteremia in North America and Europe is at least 10 to 20 per
100,000 individuals, but a more correct figure may well be more than 40 per 100,000. The risk of invasive pneumococcal disease has been found to be more than 20-fold greater in small children if they are attending day care centers (Gessner BD et al., 1995; Takala A.K et al., 1995).

*Streptococcus pneumoniae* has a distinct polysaccharide capsule (slime) that confers virulence to the organism (Brooks et al., 2004). *Pneumococci* are classified into 90 different serotypes based on the polysaccharide capsule. Cell wall components of *Pneumococci* produced the intracellular toxin autolysin. This autolysin produced enzyme like Protease, Hydrolase, Amylase, and Phospholipases which involved mainly in the inflammation caused by infection. The inflammation process fully develops only after lysis of bacteria by autolysin. Since inflammation is thought to induce most of the symptoms of pneumococcal disease, this group of virulence factors directly responsible for the morbidity and mortality caused by *Pneumococci*. Pneumococcal enzymes, such as autolysin, neuraminidase, hyaluronidase and IgA1 protease, have also been suggested to play a role in the pathogenesis of pneumococcal disease (Paton et al., 1993; AlonsoDeVelasco et al., 1995; Brooks-Walter et al., 1999). Extracellular phospholipases and protease synthesized by *Pneumococci* facilitate the ability of organisms to injure, invade the tissue of various host cells (Silverman et al., 1992). Among the Pneumococcal hydrolytic enzymes, protease enzyme neuraminidase play a significant role in the virulence of pneumococcal disease. *S. pneumoniae* synthesized slime that confers virulence to the organism. Biofilms are structured populations of microorganisms adhered to a surface and embedded in an extracellular matrix consisting mainly of exopolysaccharides (sometimes bound together by proteins and DNA). Slime production by *S. pneumoniae* enhances the multi-drug resistant strains.

Frighteningly, the number of reported multi-drug resistant strains have emerged and increased markedly over the last 20 years (Mera et al., 2005). The global emergence of antimicrobial resistance in *S. pneumoniae* is a serious concern (Felmingham et al., 2004). Before the antibiotic era, the population of *Pneumococci* isolated from humans was mainly dominated by strains with capsular polysaccharides (Griffith, 1928; Finland & Barnes, 1977). Within the last 25 years, escalating emergence of penicillin and multidrug resistant *S. pneumoniae* have been witnessed which was spread worldwide (McGee et al., 2001). The failure of antibiotics to treat a range of pneumococcal infections due to drug resistance (Hart
and Kariuki, 1998) and 35% of pneumococcal illness is due to drug resistant S. pneumoniae (Jones et al., 2002; Livermore, 2003).

Identification and confirmation of multiple resistant pneumococcal strain is very difficult task for clinical labs during old days. Early diagnosis of S. pneumoniae infection improves clinical outcomes and treatment is also easy (Tunkel et al., 2004). In early times, the only way to detect and identify pneumococcus was to inoculate a small mount of sputum into the peritoneal cavity of white mice. After death, mouse blood was drawn and cultivated in broth and on blood agar plates and the colonies were examined (White 1938). In the 1880s, Gram made his staining experiments to visualize the bacteria from lung tissue specimens and found bacteria that were stained dark with aniline gentian violet while others were not (White, 1938). Pneumococcus was one of the first bacteria demonstrated with the Gram stain (Watson et al., 1993). Pneumococcus is routinely identified by four phenotypic characteristics which were colony morphology on a blood agar plate, bile solubility, optochin sensitivity and the presence of a capsule and then biochemical tests was emerged for identification of Pneumococcus (Lund, 1959; Austrian 1975; MacFaddin 1976; Lund and Henrichsen 1978; Mundy et al., 1998; Ruoff et al., 2003). Recently studies suggested that, PCR tests achieve the accurate etiological diagnosis of pneumonial infection (Pandit et al., 2005). Among the PCR tests, 16s r DNA sequencing is very effective which is designed specifically for S. pneumoniae and it provide both accurate etiological diagnosis and phylogenetic position of S. pneumoniae (Bosshard et al., 2004; Kotilainen et al., 1998; Poppert et al., 2005).

Allium cepa Linn is a member of the Liliaceae, which consists of over 250 genera and 3700 species. The plant A. cepa (Liliaceae) are proved to shown the antidiabetic (Galal E.E et al., 1965), antioxidant (Dhanprakash B.N et al., 2007), antihypertensive (Sakai Y et al., 2003), antithrombotic (Yamada, K et al., 2005), hypoglycemic (Composite K.E et al., 2003), antihyperlipidemic (Lata S et al., 2003). The bulb of A. cepa contains Kampferol, β-sitosterol, ferulic acid, myritic acid, prostaglandins. Bulb extract shown to have ecobic effect in rats (Chatterjee T.K, 1997). Traditionally plant containing these constituents used as abortificiant, the bulb extract of A. cepa showed ecobic effect in mice and rats (Saharaf, A 1965).
*Allium sativum* L. (*Alliaceae*) is used as spice and for treatment of cough and chest pain (Hamel, 1975). Groppo et al. (2007) reported that fresh garlic shows good antimicrobial activity on oral streptococci. *A. sativum* has been used in the history for both culinary and medicinal purposes. They exhibit different properties such as antibacterial, anti-fungal, anti-septic, anti-viral, expectorant, and anti-histamine. It has been used as a food additive and also used in traditional remedies in flavonoids and a principle odour allicin (diallyl thiosulphinate). The extracts have been found to anti-histamine. It has been used as a food additive and also used in traditional remedies in flavonoids and a principle odour allicin (diallyl thiosulphinate). The extracts have been found to have a significant protective action against a fat induced increase in serum cholesterol and plasma fibrinogen, fibrinolytic activity and also possess pharmacogenic properties.

The genus *Ficus* (*Moraceae*) includes some 750 species of woody plants occurring in most tropical and subtropical forests throughout the world (Berg C.C., 1989). Many *Ficus* species are commonly used in traditional medicine to cure various diseases. They have long been used in folk medicine as astringents camminatives, stomachics, vermifuges, hypotensives, antihelmintics and anti-dysentery drugs (Trivedi, P., et al., 1969). Some of the the most important species of *Ficus* are, *F. racemosa*, *F. religiosa* and *F. bengalensis*. The bark, leaves and fruits of this group are used as astringent, haemostatic, anti-septic, anti-inflammatory, antioxidant and anticancer agent and also in the treatment of diarrhoea, dysentery, and in the treatment of skin diseases, ulcers, vaginal disorders, leucorrhoea, menorrhagia, deficient lactation (Khare C.P., 2004).

However, the present study is undertaken to evaluate antibacterial activity from *A. cepa* and *A. sativum, F. bengalensis* against human pathogenic organism *S. pneumoniae*. Hence, the present study has attempted to isolate and identify the bioactive compounds against oral *S. pneumoniae* isolated from chronic illness patients.
On the basis of the above facts and information, the present work has been designed and planned to evolve strategy for the identification of bioactive compounds from the medicinal plants against \textit{S. pneumoniae} causing chronic disease in human beings with the following objectives

- To isolate and identify \textit{S. pneumoniae} from the oral cavity of infected persons,

- To screen the multiple resistant of \textit{S. pneumoniae} using biochemical and virulent (Slime, Phospholipase and Protease) methods,

- To confirm the species identity of \textit{S. pneumoniae} using 16S r DNA sequencing study,

- To analyze the phytochemical compounds of medicinal plants such as \textit{A. cepa}, \textit{A. sativum} and \textit{F. bengalensis} using Gas Chromatography-Mass Spectrometry (GC-MS),

- To identify and elucidate the structures of bioactive compounds from active fraction of plant extracts,

- To study the antibacterial activity of the medicinal plant extracts using different solvents, and

- To identify the best bioactive compound by molecular docking using bioinformatics tools.