INTRODUCTION
Staphylococci have emerged and persisted over the years as important hospital and community acquired pathogens (Pittet and Wenzel, 1995; Steinberg et al., 1996). They produce a range of pathogenic enzymes and a variable number of membrane-damaging exotoxins that are directed toward the destruction of host cells. Virulence cannot be explained in terms of a single factor. Many products have similar biological effects and it is the interaction of the total harmony of the Staphylococcus that makes it highly pathogenic (Aderson, 1976). Both coagulase positive and coagulase negative Staphylococcus aureus are extremely adaptable pathogens (Thornsberry, 1988). They are the predominant causative agents of many pyogenic infections. The most serious infections are bacteremia, endocarditis, osteomyelitus, toxic shock syndrome, food poisoning and the nosocomial infections (Lowy, 1998).

Staphylococcal infections are best treated with a bactericidal antibiotic that is able to penetrate intracellular organisms surrounded by dense tissue. The semisynthetic penicillins, cephalosporins and aminoglycosides fall into this category. Vancomycin (glycoprotein) is the latest drug added. Owing to frequent use of antibiotics, development of antibiotic resistance in Staphylococci has become a very serious problem (Gupta et al., 1999).
Antimicrobial resistance is not new, but the number of resistant organisms, the geographic locations affected by drug resistance, and the breath of resistance in single organisms are unprecedented and mounting (Levy, 2002). Disease and disease agents that were once thought to be controlled by antibiotics are returning in new leages resistant to these therapies (Levy and Marshall, 2004). The organism is increasingly becoming resistant to many of the antibiotics including methicillin (Parker and Hewitt, 1970) and vancomycin (Schwalbe et al., 1987). For last few years, methicillin resistant \textit{S. aureus} (MRSA) and vancomycin resistant \textit{S. aureus} (VRSA) (Hirarnatsy et al., 1997) have been the focus attention because of their increasing involvement in causing infections particularly, in hospitalized patients (Deshpande et al., 2004). Although, the incidence of MRSA and VRSA varies from region to region, it has been steadily increasing worldwide. The emergence of these multidrug resistant strains of \textit{S. aureus} is due to the widespread unbridled dispensing of antibiotics by formularies in our country that has fueled the antimicrobial resistance. Vancomycin resistant \textit{S. aureus} strains are likely to pose a major therapeutic challenge in the future (Longzhu et al., 2003).

The emergence of antimicrobial resistance among a multitude of bacterial pathogens has become a critical problem in the modern medicine. The economic impact of managing infections caused by antibiotic –resistant bacteria is substantially high (Harrison and Lederberg, 1998). As bacterial resistance is a serious worldwide problem, development of novel antibacterial
therapies must become a high priority (Caroline et al., 2003). Therefore, antibiotics are no longer the ultimate weapons in the war against antibiotic resistant bacteria and lead to the possibility of an emerging “Post-antibiotic era” (Tenover and Hughes, 1996). This has spurred biomedical researchers to expand their efforts to identify new technologies and products that employ novel mechanism or action against the “super-bugs” (Rahman et al., 1991 and Chopra et al., 1996).

The discovery of bacteriophage is one of most important milestones in the history of biomedical research, one that has led to many fundamental discoveries and breakthroughs in the life sciences. In the pre-antibiotic era of the early 20th century, the potential of bacteriophages to be a powerful tool in dealing with infections due to multidrug resistant bacteria captured the imagination of scientific communities and inspired several researchers. Lytic phage therapy has been proposed as a natural alternative approach to conventional antibiotics (Alisky et al., 1998 and Carlton, 1999). Non-controlled clinical studies have shown that, phages can be effective in combating infections caused by a variety of pathogen in humans (Sulakvelidze et al., 2001 and Summers, 2001).

The concept of phage therapy to treat bacterial infections was born with the discovery of the bacteriophage almost a century ago. After a chequered history, its current renaissance is fueled by the dangerous appearance of antibiotic-resistant bacteria on a global scale. As a mark of this renewed
interest, the unanswered problems of phage therapy are now being addressed, especially for human use (Jameel, 2003). Recently, interest in phage therapy, the use of phages to control bacterial infections, has been rekindled (Fischetti, 2001; Summers, 2001 and Stone, 2002). This is mainly to overcome the urgent problem of treatment of pyogenic infections due to multidrug resistant strains of *S. aureus*.

In view of the alarming increase in multiple drug resistance and the possible applicability of phage therapy, the present study on **Exploration of bacteriophage as a potential antimicrobial agent against the MDR strains of Staphylococcus aureus** was carried out with the following major objectives.

- Isolation of clinical strains of *Staphylococcus aureus*.
- Assessment of antibiotic susceptibility pattern and multiple drug resistance of *S. aureus*.
- Detection and distribution of bacteriophages in various natural sources.
- Screening and selection of potential bacteriophages specific to antibiotic resistant *S. aureus*.
- Determination of *in vitro* activity of potential bacteriophages and influencing factors.
- Standardization and formulation of pathogen and phage doses.
- Evaluation of *in vivo* efficacy of potential bacteriophage against drug resistant pathogen.
• Characterization and grouping of detected potential bacteriophage.