INTRODUCTION
Bacteriophage therapy was initiated in 1921 by Bruynoghe and Maisin. A little known fact is that the first main use of phage therapy was as an antibiotic (Stewart, 2003). Although, the results were promising, little was accomplished in this field during the following years. The idea of potential applications of bacteriophage therapy was abandoned after the introduction of advanced antibiotics into medical practice (Ackermann and DuBow, 1987).

Today’s escalating antibiotics crisis is the direct result of the large scale and indiscriminant use, which has triggered an increase in the quantity, variety and proliferation of multidrug-resistant virulent bacterial pathogens. These pathogens have developed resistance to virtually all-extant antibiotics (Cohen, 1992 and Kutter, 1997) including, the most advanced drugs. The medical community has thus inadvertently entered the “Post-antibiotic” era, with no conventional remedy insight. The discriminate over-use of antibiotic has succeeded in eradicating only the antibiotic-susceptible infectious strains while empowering highly resistant “Superbug” (Slopek et al. 1983; Alisky et al. 1998). A valid, proven and practical alternative to the chemical antibiotic treatment of bacterial infections has been successfully practiced from as early as the late 1930’s. Phage therapy is a method of antibacterial treatment that harnesses the bacterial–killing properties of otherwise harmless viruses (Summers, 1999).

Bacteriophages are viruses that attack bacteria, multiply within and cause disruption of bacterial cells (lysis). Their lytic action is highly specific...
Phages can have either a lytic or a lysogenic life cycle. The lytic phages are most suitable candidates for phage therapy. Phages are specific to their particular host, which they will infect and disrupt the metabolism. Subsequently they cause the production of metabolites in the favour leading to formation of progeny phages and finally releasing these on cell lysis. The process continues until the majority, or in some cases, the entire bacterial population is destroyed (Sulakvelidze et al., 2001 and Ahmad, 2002).

*Pseudomonas aeruginosa* is the epitome of an opportunistic pathogen of humans. The bacterium almost never infects uncompromised tissues, yet there is hardly any tissue that it cannot infect, if the tissue defenses are compromised in some manner. It is especially associated with infections of individuals immunocompromised as a result of burns and underlying diseases including cancer, diabetes and cystic fibrosis (May, 1991 and Kenneth, 2002).

The virulence of Pseudomonas is multifactorial because of its various structural components and production of variety of toxins and enzymes (Murry et al., 1990). Some of the important infections due to *Pseudomonas aeruginosa* are bactemia, endocarditis, chronic otitis, pulmonary infections, eye infections, wound (burnt) infections and urinary tract infections.

Until the 1960's, Pseudomonas infections were usually treated with polymyxins, agents that exhibit considerable toxicity. With the development of antipseudomonal β-lactam compounds, including piperacillin, ticarcillin, cefatazidime, meropenem and aminoglycosides such as gentamicin and tobramycin, treatment with a combination of an aminoglycosides and a
β-lactum antibiotics was commonly adopted (Cohen, 1992). Antibiotics likely to be most effective are the aminoglycosides, tobramycin and gentamicin in combination with antipseudomonal penicillin such as ticarcillin, azocillin and pipercillin. For the treatment of serious hospital acquired infections due to *P. aeruginosa* (Norrby et al., 1993) quinolones, in particular ciprofloxacin, have provided a major advance as the first highly active and effective antipseudomonal agents. Despite significant improvements in the antipseudomonal activity of these antibiotics, larger than normal doses are necessary in severe infections. A further problem with *P. aeruginosa* is that, many strains do not respond clinically although, apparently sensitive to the antibiotics *in vitro* (Govan and Nelson, 1992).

*P. aeruginosa* has high intrinsic resistance to many antibiotics at levels attainable in body tissues. It is notorious for its resistance to antibiotics and is, therefore, a particularly dangerous and dreaded pathogen (Kenneth, 2002). The bacterium is resistant naturally to many antibiotics because of its inherent attributes to acquire and achieve the resistance. Obvisouly, if a bacterial pathogen is able to develop or acquire resistance to an antibiotic, one must find new or different antibiotics to fill the place of the old one in the treatment regimes. Pseudomonas is known to bear an antibiotic resistance plasmid and also is capable of transferring the related genes by either transduction or conjugation. The futility of treating Pseudomonas infections with antibiotics is most dramatically illustrated in cystic fibrosis patients, virtually all of whom eventually become infected with a strain that is so resistant that it cannot be treated. Phage therapy seems to be a better alternate and effective over
antibiotic therapy (Sulakvelidze et al., 2001). The major merits of phage therapy over antibiotic therapy according to Ahmad (2002) are highly specific to the targeted infection, once applied it can continue working as long as the host (infection) persists, grow and destroy at the sight of infections, hence, available where most needed with no disruption to normal flora.

Therefore, the present study on **Exploration of bacteriophage as a novel antimicrobial agent against the MDR strains of Pseudomonas aeruginosa** was carried out with following major objectives.

- Isolation and characterization of *P. aeruginosa* from the clinical samples.
- Determination of antibiotic susceptibility pattern and multiple drug resistance of *P. aeruginosa*.
- Detection of bacteriophages from various natural sources.
- Screening and selection of phage specific to MDR strain of *P. aeruginosa*.
- Assessment of *in vitro* activity of selected phages.
- Factors influencing the *in vitro* activity of bacteriophages.
- Standardization of phage dosage and *in vivo* efficacy of potential phage.
- Characterization of detected bacteriophage by electron microscopic image and molecular components.