ABSTRACT
Bacterial infections are among the major indices of health hazard threatening public health and welfare. They are the leading cause of starvation and death the world over. Several methodologies were applied to combat the menace among which are the use of chemotherapy, immunotherapy, probiotics, and other preventive measures. Ironically, despite all the advancements in technological know-how and high medical-care, these methodologies have adverse side effects and drug resistant strains of bacteria are increasing at an alarming rate due to over-prescription and misuse of drugs. The consequent effect of which poses a threat to modern medicine that if care is not taken, untreatable bacterial infections might soon reach a point beyond control; which would subsequently lead to the re-emergence of diseases with fatal consequences. One such measure of combating this menace is the use of phage-therapy, which is the nature’s own method of combating bacteria. It involves the use of bacteriophages (small viruses that predate bacteria) to cure bacterial infections. It is quicker, safer and specific in action with no side effects. This study aimed at enhancing the understanding of the potentials of phage-therapy in the prevention and treatment of bacterial infections and other microbial pathogens. This was achieved through comparison with the most common and contemporary methods available in the world today.

Keywords: Antibiotics, Bacteriophages, Chemotherapy, Immunotherapy, Phage-therapy.
The chemotherapeutic agents act by killing rapidly dividing cells as such can affect normal proliferating cells of the liver, bone marrow, digestive tract and hair follicles (Hirsch, 2006). The rapid evolution of quinonone resistance, even during the course of treatment by numerous bacterial strains such as *Staphylococcus aureus*, Enterococci spp., and *Streptococcus pyogenes* is another side effect of using chemotherapy (Norris and Mandell, 1998). Furthermore, some chemotherapeutic agents such as Ciprofloxacin and Levofloxacin, used against life threatening bacteria, increased the risk of cardiotoxicity, arrhythmias, anti-coagulant effects and non-absorbable complexes formation as well as the risk of toxicity (Cabeen and Jacobs-Wagner, 2005). Moreover, frequent use of chemotherapeutic agents leads to rapid evolution of drug resistant bacterial strains such as *Staphylococcus aureus*, Enterococci spp. and *Streptococcus pyogenes* (Norris et al., 2007), besides several side effects such as nausea, diarrhea, constipation and anaemia.

Antibiotics are substances mostly produced by bacteria and few fungi that kill or inhibit microbial growth of infectious organisms (Donnenberg, 2000). They are chemicals, which in low concentrations, can selectively kill or inhibit the growth of most pathogenic microorganisms. They are generally used to control diseases caused by pathogenic bacteria (Yusha’u et al., 2010). The action of individual antibiotics varies with the location of the infection, the ability of the antibiotic to reach the infection site and the ability of the microbe to inactivate or excrete the antibiotic. The anti-bacteriocidal activity of the antibiotics is mostly growth-phase-dependent (Nicholson et al., 2000). They can have a narrow spectrum i.e. targeted particular types of bacteria by having a specific target on either gram-negative or gram-positive bacteria, or can have a wide spectrum i.e. affect a wide range of bacterial strains. The Tigecyclines for instance have a wide spectrum of anti-bacteriocidal action, while Daptomycin and Linezolid have narrow spectrum as they tend to act vigorously on Gram-positive bacterial strains. Some, such as penicillin and cephalosporin, targeted bacterial cellwalls inhibiting the synthesis of peptide link between the cellwall molecules, leading to bursting or lysing of the cellwall. Some affect the cell membranes such as polymyxins or interfere with essential bacterial enzymes such as quinolones, aminoglycosides, macrolides and tetracyclines (Pelczar et al., 1999). However, some antibiotics such as streptomycin, chloramphenicol and tetracycline bind to 70s bacterial ribosomes inhibiting RNA and protein synthesis in the bacterial cell (Walsh and Amyes, 2004). Some antibiotics such as Chloramphenicol, Erythromycin, Sulphonamides and Tetracyclines are biostatics i.e. inhibit the growth and multiplication of susceptible organisms. But growth and multiplication of the organisms resume if the agent is removed. However, some antibiotics such as streptomycin, cephalosporins, penicillins and polymyxins are biocidals i.e. kill the microorganisms (Taylor et al., 2005).

Prolong use and misuse of antibiotics make some of the bacterial strains to be tolerant to their actions, thereby becoming resistant to such drugs. Slight change in the target of the antibiotic makes it ineffective such as resistance to streptomycin due to change in ribosomal structure to which the antibiotic binds. A change in only one amino acid in one of the ribosomal proteins as a result of mutation can be sufficient in inducing antibiotic resistance (Poehlsgaard and Douthwaite, 2005). The over-use and misuse of antibiotics give room for the breeding of super bacteria resistant to entire antibiotics (Nicholson et al., 2000) through the evolution of mutants with slightly different molecules in their cellwalls that the antibiotic cannot alter (Lewis et al., 2002). The emergence of antibiotic-resistant bacteria is therefore closely related to the extent to which antibiotics are used in humans and items of human diet. Resistance may also occur through exclusion of the antibiotic or destruction by enzymes inside the cells being targeted. For instance, a group of enzymes known as penicillinases hydrolyses and destroys penicillins and cephalosporins; meaning that the bacterium has developed resistance to those antibiotics (Taylor et al., 2005). Beside these, antibiotics confer side effects that can be fatal depending on the type of antibiotic used and the microbe targeted. The adverse effects ranges from fever, nausea, allergy, diarrhea (Anonymous, 2010) and the subsequent effect of disrupting the balance of the normal microbial flora leading to over-growth of fungal species such as *Candida albicans* in vulvo-virginal area (Piroha and Garland, 2006).

**Immunotherapeutic Method of Controlling Bacterial Infections**

The immune system is remarkably effective at keeping potentially infectious bacteria, viruses and tumor cells from invading the body systems. This efficacy of the immune system can be amplified (Lewis et al., 2002). Immunotherapy is the use of Biological Response Modifiers through an array of treatment strategies based upon the concept of modulating the immune system to achieve a prophylactic and/or therapeutic goal. These modifiers are agents that modify the hosts’ response to pathogens with resultant beneficial prophylactic or therapeutic effects. Biological Response Modifier-agents include vaccines, interferons and interleukins (Rosenberg et al., 1999). Immunity to infectious organisms can be achieved by active or passive immunization. The goal of passive immunization is a transient protection or alleviation of an existing condition, whereas the goal of active immunization is the elicitation of protective immunity and immunologic memory. Active and passive immunization can be achieved by natural or artificial means (KAPLAN, 2008). When a single B cell for instance recognizes a single foreign antigen, it manufactures a single or monoclonal type of antibody. A large amount of a single antibody type would make a powerful drug because of its great specificity. It could be used to target a particular pathogen or cancer. The monoclonal antibodies (Mab) are therefore pure preparations of a single antibody type that recognize a single antigen. They are useful in diagnosing and treating diseases because of their specificity (Lewis et al., 2002).
The limitations of immunotherapy lie on the fact that they are useful only for people with allergic rhinitis, asthma or more recently people with advanced skin cancerous tumors (Rosenberg et al., 2008). Other risk factors associated with immunotherapy include the generation of IgG or IgM anti-isotype antibodies through the introduction of antibodies from other species leading to Type III hypersensitivity reactions or if IgE antibodies are generated cause systemic anaphylaxis. It can also elicit responses against minor immunoglobulin polymorphisms or allotypes (KAPLAN, 2008).

**Probiotics Method of Controlling Bacterial Infections**

Probiotics administration involves the employment of live culture which may establish itself as symbionts competing, inhibiting or simply interfering with colonization of pathogens. They may produce antibiotics or bacteriocin, especially providing the drug *in-vivo* and *in-situ*, thereby avoiding side effects of systemic administration. Probiotics are live micro-organisms such as lactic acid bacteria (LAB) which when administered in adequate amount confer a health benefit on the host (Anonymous, 2009). Although probiotics are claimed to strengthen the immune system, combating allergies, excessive alcoholic effects, they are useful only for people with allergic rhinitis, asthma or more recently people with advanced skin cancerous tumors (Rosenberg et al., 2008). Other risk factors associated with immunotherapy include the generation of IgG or IgM anti-isotype antibodies through the introduction of antibodies from other species leading to Type III hypersensitivity reactions or if IgE antibodies are generated cause systemic anaphylaxis. It can also elicit responses against minor immunoglobulin polymorphisms or allotypes (KAPLAN, 2008).

**Phage-therapy Method of Controlling Bacterial Infections**

Bacteriophages or ‘phages’ are the most profuse organisms on earth. It was estimated that $10^{25}$ phages commence new infection cycle every second of the day (Pedulla et al., 2003). They exhibit extraordinary diversity found in any environment colonized by bacteria to the extent that there is hardly a single species of bacteria where sufficient investigation has not found a phage. The phage nucleic acids exist either as double- or single- stranded DNA, or as a single-or double- stranded RNA (Schlegel, 2002). They are any of various viruses that are parasites of bacteria. Bacteriophages that lyse a variety of indigenous bacteria including *Pseudomonas* spp., *Agrobacterium* spp., *Photobacterium* spp., and various non-marine contaminants, particularly members of *Enterobacteriaceae* (Schlegel, 2002) were isolated. Due to their remarkable antibacterial activity, phages have been used to treat human and economically valuable animal infections since before the early 40s. During World War II, phage-therapy received momentum among the Soviet forces that used it to treat many soldiers infected by various bacterial diseases such as dysentery and gangrene. The success rate was as good as, if not better than, that of any antibiotic (Sooltill, 2002). Since the 1940s, research with bacteriophages, has resulted in establishing nucleic acids as the genetic material of life and has been central in the new field of molecular biology (Anonymous, 2009). Political reasons associated with cold war (Summers, 2001) and the advent of antibiotics caused a decline of phage-therapy. The presence of phages is recognized by the appearance of plaques or lytic holes in continuous bacterial lawn which in bacterial suspension can easily lead to a complete lysis in a short period of time (Schlegel, 2002).

Phage-therapy is currently a conventional therapeutic method of combating infections caused by bacterial populations (Parfitt, 2005). It was discovered further that a phage could integrate its genes into that of its bacterial host and be transmitted from generation to generation as part of the host's own chromosome (Anonymous, 2009). In the case of some bacterial species such as *Haemophilus influenzae* and *Bacillus subtilis*, native DNA isolated from bacteriophages can infect them through a process of genetic transformation called 'transfection' (Schlegel, 2002). Phages tend to be more successful than antibiotics and other therapeutic methods because of their relative ability to eradicate bacterial infections and chronic polymicrobial bio-films along with other strategies. They were recently been used in systemic and intracellular infections (Piris, 2000). Results from 500 trials in 1994 had demonstrated that, phage-therapy could improve the success of skin grafts by reducing the underlying *Pseudomonas aeruginosa* infection. Its significance in preliminary *in-vitro* experiments for cells in tissue culture against tumor agents had also been established (Bar et al., 2008). Even though phages are non-motile, a suspension of free phage particles when mixed with a suitable bacterial suspension leads to the attachment of the phage particle to a bacterial surface through adsorption, followed by injection of the phage DNA. Eventually, after a period of synthesis and maturation of phages, lysis of the host cells liberates newly formed phage particles into the suspending medium (Schlegel, 2002).

Bacterial infections treated with phage-therapy include, among others: *laryngitis, dermatitis, dysentery, conjunctivitis, periodontitis, sinusitis*, urinary tract infections, *burns, boils* and polymicrobial films on chronic wounds (Summers, 2001). It had also been successfully used against *Campylobacter* in raw foods, *Listeria* in fresh foods (McGrath and Van Sindren, 2007), *Lactococcus* and *Vibrios* in fish aquaculture and against wound infections caused by facultative microbes such as *Staphylococcus* and *Streptococcus* strains. Phage therapy was used by the United States Food and Drug Administration (FDA) to control *Listeria monocytogenes* bacteria in cheese, making it safe for consumption. The study of phages has important implications in medicine and genetics, specifically in the understanding of virus infections, genetic defects, human development and mal-development, the causes of cancer, and resistance of bacteria to antibiotics (Anonymous, 2009).
Although bacteria are able to develop resistance to phages, the resistance might easily be over-come. Phages are more specific in action, targeting only single or few strains of bacteria (Schlegel, 2002). More so, traditionally, antibiotics usually have a wide range of side effects, killing both harmful and useful bacteria such as those facilitating food digestions, but phages attack a specific bacterial strain. Furthermore, phage therapy is free from severe adverse effects as compared to other therapeutic methods and is faster in action once the exact bacteria are identified and phage administered. It is therefore a promising approach in combating antibiotic and other therapeutic resistant pathogens. The cost of isolation and preparation of phage solutions are far less than those for antibiotics. Recent Polish trial on immune response to phages has demonstrated the effects of phages as therapeutically significant. Beside these, bacteriophages can be easily isolated by suspending a host bacterium in a nutrient medium and inoculating with material from a location where the bacterial strain occurs naturally (Schlegel, 2002). Thus, phage-therapy could serve as a complimentary promising method of treating bacterial infections, more particularly those caused by drug resistant bacterial strains.

REFERENCES
