International Journal For Advanced Research In Science & Technology
A peer reviewed international journal
www.ijarst.in
ISSN: 2457-0362

Multidrug-resistant bacteria are no match for silver nanoparticles, a potent nanoweapon.

[1]DHANUNJAYA RAO KODALI, Asst.Prof, M.Sc.,M.Tech

kodalidhana@gmail.com
[2]MOHAMAD JAHANGIR PASHA, Asst.Prof, M.Sc.,
jahangir.475@gmail.com,
[3]MANCHIREDDY CHANDRA SEKHAR REDDY , Asst.Prof,M.Sc,B.Ed,
mcr.manch@gmail.com,
[4]DOOPATI PITCHAIAH,Asst.Prof, M.Sc,
doopati@gmail.com,

Department of H&S,

Nagole Institute Of Technology,

Hyderabad – 500001,
Telangana India.

Abstract

The pharmaceutical and biomedical industries are now confronted with the issues of an ever-increasing number of people who are multidrug resistant (MDR). microorganisms that cause disease Drugs aid in the reemergence of MDR microorganisms. for the bacteria' survival, which is the acquisition of antibiotic resistance, or as well as the ability to reproduce under unfavourable conditions. Bacterial infections that are multidrug resistant mortality, morbidity and the expense of long-term therapies are all significantly increased as a result Consequently, the creation, modification, or search for antimicrobial agents is essential..

The development of chemicals capable of killing MDR bacteria is a top goal. of study. Silver has been used for thousands of years in different compounds and bhasmas. Ayurveda has used it for centuries to treat a variety of bacterial diseases. As Silver nanoparticles may be a novel treatment option for antibiotic-resistant bacteria. The bactericidal activity of silver nanoparticles against MDR bacteria is examined in this review. Multi-actional mechanism Resistance to drugs may be treated and prevented using nanotechnology.microbes.

Keywords

Multiple -drug- resistant methicil lin -resistant Staphylococcus aureus silver nanoparticles as a nanoweapon Staphylococcus aureus that is resistant to vancomycin

Introduction

Resistance in human infections is a major problem in pharmaceutical and biomedical industries. Anxieties regarding the development and reemergence of drug-resistant microorganisms are fueled by data on antibiotic resistance.

organisms that feed on other living things (Tenover 2006). Once a person has been infected, they are at risk. It's almost impossible to treat an infection caused by MDR bacteria. And Because of this, he or she will have to stay in the hospital for longer, and A multi-drug regimen of broad-spectrum antibiotics, which are less effective, toxic and costly, is required (Webb et al. 2005). As a result, the creation or improving the effectiveness of antibacterial chemicals Bacterial activity is an important study focus in this field. in the present day and age (Humberto et al. 2010). Nanotechnology offers a solid foundation for future changes and improvements to the potential diagnostic, biomarker, cell-labeling, contrast agents for biological imaging features of metal nanoparticles, treatment of different illnesses using antimicrobial agents, medication delivery systems, and nanodrugs Duran (2008) and Singh and Singh (2011) Because of this, researchers are looking into the matter. universal nanoparticles, as well as silver

The issue of MDR bacteria emerging may be addressed with the use of nanoparticles (Gemmell et al. 2006). As a result of its high antibacterial properties, silver been in widespread usage since antiquity In spite of this, though, advances in antibiotics and the medicinal uses of silver decreases in use of antimicrobials were seen

as well as Schluesener (2008)). The antimicrobial properties of silver may be used in a variety of ways. Increasing their size at the nanoscale is possible. To combat bacteria, silver nanoparticles have changed their physiochemical characteristics. their large surface area to volume ratio and their small volume unique chemistry and physics (Kim et al.) Silver

International Journal For Advanced Research In Science & Technology
A peer reviewed international journal www.ijarst.in
ISSN: 2457-0362

nanoparticles with a diameter of 10–100 nm were synthesised in both Gram-negative and Gram-positive bacteria Microorganisms that are both Gram positive and Gram negativeet al. It has been shown by several scientists that silver nanoparticles are effective bactericides against pathogenic and MDR bacteria as well as bacteria sensitive to multiple medicines. among the potent tools available to combat MDR bacteria are E. coli, an ampicillin-resistant Pseudomonas strain, and other bacterial pathogens Keywords antibiotics that are resistant to methicillin Multiple drug resistance in the bacteria Staphylococcus aureus; silver nanoparticles, nanoweapons, and other nanoscale technologies staphylococci resistant to vancomycin aureus. Correspondence departmental official Mahendra K. Rai, Humans who are multidrug resistant (MDR) face increasing obstacles. microorganisms that cause disease. Drugs aid in the reemergence of MDR microorganisms. for the bacteria' survival, which is the acquisition of antibiotic resistance, or as well as the ability to reproduce under unfavourable conditions. illnesses caused by MDR bacteria prolonging therapies has been shown to raise mortality, morbidity, and cost significantly. As a result, antimicrobial development, modification, or research Antimicrobial compounds with bactericidal capability against MDR microorganisms is a key topic of research in the field of investigation. A variety of compounds and bhasmas containing silver have been discovered. " Ayurveda has used it for centuries to treat a variety of bacterial diseases. As Silver nanoparticles may be a novel treatment option for antibiotic-resistant bacteria. Silver nanoparticles have been shown to be bactericidal against MDR bacteria in this review. This multiple-action therapy and prevention of drug-resistant disease may be achieved with the use of nanoweapons. microbes. coli, Streptococcus pyogenes, erythromycin-resistant, Staphylococcus aureus, methicillin-resistant, and Staphylococcus aureus, vancomycin-resistant (VRSA).

Silver-based antimicrobials: prehistorical, historical and contemporary status

Silver is a basic, uncommon and naturally occurring element, which is slightly harder than gold, exceedingly ductile and malleable, having the greatest electrical and thermal conductivity with least contact resistance among all metals

(Susan et al. 2009). Silver has been around since the dawn of time. been utilised for creating utensils, jewelry, dental alloy, photography, monetary currencies, explosives, etc. (Chen and Schluesener 2008). Before the beginning of antibiotics Traditionally, silver was employed for its antibacterial property, notably for the treatment for open wounds and burns (Moyer et al. 1965). They were well aware of it in the past. silver's ability to kill bacteria Silver ions bind to proteins and undergo structural changes in the bacterial cell as a result of their highly reactive nature.

distortion of the cell's cytoplasmic and nuclear membranes and death. Bacterial DNA is denatured by binding to silver ions, which inhibits the bacteria's ability to replicate Castellano and coworkers (2007; Landsdown 2002). ions of silver react with thiol group of proteins, followed by DNA condensation leading in the cell death (Feng et al. 2000). (Feng et al. 2000). Ancient antimicrobial silver compounds, such as silver nitrate and silver sulfate, have been used for centuries. sulfadiazine, silver zeolite, silver powder, silver oxide, silver chloride, and silver cadmium powder are all included in this mixture.

Nitrosamine, an element found in silver (AgNO3)

Lapis infernalis (Latin for "Lunar caustic") is the Latin term for silver nitrate, which is known in English as "Lunar caustic" (French). The therapy used silver nitrate for the treatment of sexually transmitted infections, salivary gland fistulas and perianal and bone infections in the 1700s (Landsdown 2002). Treatment with silver nitrate was common in the 19th century. an epithelialization of silver nitrate and crust development on the surface of burns were thought to be facilitated by the chemical. slashes (Castellano et al. 2007). In 1881, silver nitrate eye was invented. drops were employed to treat ophthalmia by Carl S. F. Crede. Later, B. Crede created silver-impregnated neonatorums.

supplies for skin-transplant wound dressing (Lands down 2002). Neisseria gonorrhoeae transmission was prevented in 1884 by using aqueous silver nitrate drops. children born to infected moms (Silvestry Rodriguez et al. 2007). Zero percent silver nitrate in powder form. it was said that the solution was used to cure burns. antibacterial properties of this solution No, it's not Staph. aureus, nor does it include E. coli or Ps. interfere with the growth of the epidermis Conway (1970).

International Journal For Advanced Research In Science & Technology
A peer reviewed international journal www.ijarst.in
ISSN: 2457-0362

Antioxidant: Sulfadiazine of silver (AgSD)

As a water-soluble cream, it's a broad-spectrum bactericidal that contains silver and sulfadiazine. For the most part, it's utilised for the therapy for burn wounds. It causes membrane damage by attaching to cell components, such as the cytoplasmic membrane. Transcription suppression by DNA (Atiyeh et al. 2007) Base pair-binding (Maple and colleagues). It was in 1992 (Mcdonnell and Russell 1999). A compound that contains silver sulfadiazine burns were treated with a special cream. also showed significant antibacterial potential against Bacteria like E.coli, Staph. aureus, Klebsiella sp, and Pseudomonas sp.

Zeolite, silvery in colour.

Silver zeolite is an alkaline earth complex. metal and crystal alumino silicate, with some of the latter replaced by Using the ion exchange phenomena, produce silver ions. When you're in Japan, Silver zeolite coating on ceramics is antibacterial. a variety of ways to keep things safe and secure preservation of food, sterilisation of medica equipment, and materials cleaning (Kawahara and colleagues, 2000) The study by Matsumura et al. In 2003, Matsumura et al. indicated that silver zeoli might have two probable mechanisms of action: When silver zeolite is exposed to bacteria, the silver ions enter the cells and destroy them. (ii)Reactive oxygen species production in the bacterial c ell and inhibition of respiratory enzymes a location where silver ions are present leads to the presence of bacterial cells harmful.

Nanoparticles

Nanoparticles of silver

Smaller-than-100-nanometer-sized silver nanoparticles comprise Approximately 10,000–15,000 silver atoms 2007) and the Warheit et al. The metallic silver is refined into ultrafine particles by a process known as particle engineering.a wide variety of physical techniques, such as spark discharge, electrochemical reduction, and solution irradiation and the synthesis of cryochemicals (Chen and Schluesener 2008). Chemical and biological techniques may also be used. For making silver nanoparticles. Important physicochemical features of the silver nanoparticles such is pH-dependent solid-to-solvent partitioning in terms of particle size and biological activity, as compared to conventional metals 2007). For millennia, silver nanoparticles have been used in many applications. of their distinct chemical and physical properties, they've been discovered to be antibacterial agents. characteristics of matter Kim et al. 2007). Silver nanoparticles provide the following beneficial biological properties:

They have bactericidal efficacy. rapid action against a wide range of microorganisms, particularly those resistant to antibiotics (Percival et al., 2007) inactivator of fungus, such as Aspergillus niger, Saccharomyces and Candida. 5–10 nm-sized silver nanoparticles At a 20 nm radius, the HIV-1 virus can't replicate. (Sun 2005; Humberto and et al. 2010). These are not limited to the expression of proteinases that are crucial in the synthesis of proteins inflammatory and repair mechanisms, but they also work to reduce inflammation. Inflammatory cells are killed off by the cytokines tumour necrosis factor (TNF), interleukin-12 (IL-12), and interleukin 1b (IL1b). 2004). Additionally, silver nanoparticles are implicated. for wound healing, cytokine modulation 2007) and the prevention of the growth of biofilms.

Silver nanoparticles

antimicrobials that cover a wide range Silver nanoparticles have been shown to be effective against a wide variety of microorganisms, including antibiotic-resistant bacteria, by a number of studies (Table 1). New-generation antimicrobials are another name for silver nanoparticles (Rai et al. 2009). In this study, the silver nanoparticles' bactericidal ability was actively shown by the research team. Staph. aureus and E. coli were shown to be susceptible to the silver ion-mediated bactericidal effect, as described by Feng et al. Silver nanoparticles have been shown to be bactericidal against E. coli, a model for Gram-negative bacteria, by Sondi and SalopekSondi (2007). It was shown that silver nanoparticles interact with bacterial cell membrane building blocks, causing cell damage in the SEM analysis and EDAX investigation, which led to the conclusion that silver nanoparticles cause cell damage. It was shown that silver ions have the ability to kill bacteria when applied to E. coli utilising energy-filtering transmission electron microscopy (TEM), two-dimensional electrophoresis (EDX), laser desorption ionisation (LDI), and time-of-flight mass spectrometry (TOF MS) (MALDI-TOF MS). According to the findings of this research, silver ions enter bacterial cells and have an effect on the

International Journal For Advanced Research In Science & Technology
A peer reviewed international journal www.ijarst.in
ISSN: 2457-0362

ribosomal subunit protein and a few key enzymes (Yamanaka et al. 2005).

The antibacterial potential of nanoparticles against E. coli in liquid and solid media was explored by Baker et al. (2005), who synthesised them using inert gas condensation and co-condensation procedures. They found that the nanoparticles were cytotoxic to E. coli. Gram-negative E. coli was subjected to a research by Morones et al. in 2005 to see whether silver nanoparticles with a size range of 1–100 nm had any bactericidal effects. Silver nanoparticles interact with bacteria by growing the bacterial cells to mid-log phase, measuring the OD at 595 nm, and seeing that concentrations more than 75 lg ml)1 were fatal for bacterium growth (Kim et al. 2007). Silver–water dispersion solution and 19 antibiotics were examined by De'Souza for their antibacterial properties (15-nm-diameter silver nanoparticle clusters containing silver ions produced by an electrocolloidal silver process). Amoxicillin and clindamycin were shown to be effective against MDR E. coli, Staph. aureus, Salmonella typhi, Shigella flexneri, and Bacillus subtilis. Staph. aureus 6538 P, Salm. typhi, Sh. flexneri, and B. subtilis all demonstrated an additive impact when amoxicillin or clindamycin was combined with silver–water dispersion, but the combination of silver–water dispersion and amoxicillin showed an antagonistic effect with MRSA (De Souza et al. 2006). It has been shown that silver nanoparticles may be used to kill bacteria by infusing them into textile fibres, and Duran et al. (2007a) used scanning electron microscopy (SEM) and energy-dispersive spectroscopy (EDS) to demonstrate their antibacterial properties. They stated that silver nanoparticle-impregnated cotton textiles had a powerful bactericidal effect. E. coli and Staph. aureus are both effectively and strongly inhibited by polyvinyl alcohol nanofibres loaded with silver nanoparticles. Their application in wound dressings has been advocated and tested (Jun et al. 2007). An investigation on the effects of silver nanoparticles and antibiotics on bacteria was carried out by Shahverdi et al in 2007. The silver nanoparticles were created utilising Klebsiella.

Table 1 Activity of silver nanoparticles against broad spectrum of bacteria

S. No.	Different forms of silver	Target organisms	References
1.	Silver ions	*Staphylococcus aureus* and *Escherichia coli*	Feng et al. (2000)
2.	Silver nitrate	Periodontal pathogens	Spacciapoli et al. (2001)
3.	Silver zeolite	*E. coli*	Matsumura et al. (2003)
4.	Silver nanoparticles	*E. coli*	Sondi and Salopek (2007) Pal et al. (2007)
5.	Silver ions	RNA viruses	Butkus et al. (2004)
6.	Silver nanoparticles	*E. coli*, *Vibrio cholerae*, *Pseudomonas aeruginosa* and *Salmonella typhus*	Morones et al. (2005)
7.	Silver nanoparticles	*E. coli* in liquid and solid medium	Baker et al. (2005)
8.	Silver ions	*E. coli*	Yamanaka et al. (2005)
9.	Silver nanoparticles	*Staph. aureus* and *E. coli*	Shahverdi et al. (2007)
10.	Super paramagnetic silver nanoparticles, bifunctional Fe_3O_4 @Ag nanoparticles	*E. coli*, *Bacillus subtilis* and *Staphylococcus epidermidis*	Gong et al. (2007)
11.	Nanofibres impregnated silver nanoparticles	*E. coli* and *Staph. aureus*	Jun et al. (2007)
12.	Silver nanoparticles on cotton Fabrics	*Staph. aureus*	Duran et al. (2007)
13.	Silver nanoparticles impregnated on the wound dressing	*E. coli* and *Staph. aureus*	Maneerung et al. (2008)
14.	Silver nanoparticles	*E. coli*, *Salmonella typhi*, *Staphylococcus epidermidis Staph. aureus*	Ingle et al. (2008)
15.	Silver nanoparticles	*Phoma glomerata*, *Phoma herbarum*, *Fusarium semitectum*, *Trichoderma* sp. and *Candida albicans*	Gajbhiye et al. (2009)
16.	Silver nanoparticles	*E. coli*, *Staph. aureus* and *Ps. aeruginosa*	Birla et al. (2009)
17.	Silver nanoparticles	*E. coli* and *Staph. aureus*	Gade et al. (2010)
18.	Silver nanoparticles	*E. coli* and *Ps. aeruginosa*	Geethalakshmi and Sarada (2010)
19.	Silver nanoparticles	*E. coli*, *Staph. aureus* and *Ps. aeruginosa*	Bonde et al. (2011)
20.	Silver nanoparticles	*Ps. aeruginosa*, *Staph. aureus*, pathogenic fungi *Aspergillus flavus* and *Aspergillus niger*	Govindaraju et al. (2010)
21.	Silver nanoparticles	*Staph. aureus*, *E. coli*, *Klebsiella pneumoniae*, *B. subtilis*, *Enterococcus faecalis*, *Ps. aeruginosa*	Namasivayam et al. (2011)
22.	Silver nanoparticles coated medical devices	*Staph. aureus* and *Streptococcus mutans*	Ki-Young (2011)
23.	Bacterial cellulose-silver nanoparticles composite	*E. coli* and *Staph. aureus*	Hemane et al. (2011)

penicillin G, amoxicillin, erythromycin, clindamycin, and vancomycin were tested against Staph. aureus and E. coli using the antibiotics alone and in combination. Antibiotics' antibacterial activity was significantly increased in the presence of silver nanoparticles, and nanoparticles and erythromycin had the best synergistic activity against Staph. aureus (Shahverdi et al. 2007). Silver nanoparticles were synthesised by Fusarium acuminatum and tested against four human pathogenic bacteria, including E. coli, Salm. typhi, Staphylococcus epidermidis, and Staph. aureus, to see how effective they were in killing germs. Ingle et al (2008). For each of the aforesaid bacteria, mycogenic silver nanoparticles had bactericidal potential that was 1–2 times more than that of pure silver ions. Staph. aureus had the highest antibacterial activity, followed by Staph. epidermidis and Salm. typhi, while E. coli had the

lowest. Scientists have discovered that silver nanoparticles coated with bacterial cellulose have antibacterial properties against E. coli and Staph aureus (2008). Silver nanoparticles from Phoma glomerata were synthesised extracellularly and tested against E. coli, Staph. aureus, and Pseudomonas aeruginosa by Birla and colleagues (2009). Silver nanoparticles in conjunction with antibiotics were tested against E. coli, Staph. aureus, and Ps. aeruginosa, respectively. As a result of their research, the scientists determined that the biosynthetic process of nanoparticle production is environmentally benign; hence, silver nanoparticles are a viable response to the rising resistance of antibiotics to bacterial antibiotic resistance. Using the Alternaria alternata, Gajbhiye et al. (2009) synthesised silver nanoparticles extracellularly for the first time. A wide range of bacteria may be killed by silver nanoparticles (Table 1). Silver comes in a variety of forms, therefore this isn't an issue. Target organisms References 1. Silver ions Staphylococcus aureus and Escherichia coli Feng et al. (2000) (2000) (2000) 2. Silver nitrate Periodontal pathogens Spacciapoli et al. (2001) (2001) (2001) 3. Silver zeolite E. coli Matsumura et al. (2003) (2003) (2003) 4. Silver nanoparticles E. coli Sondi and Salopek (2007) (2007) (2007) Pal et al. (2007) (2007) (2007) 5. Silver ions RNA viruses Butkus et al. (2004) (2004) (2004) 6.

Silver nanoparticles E. coli, Vibrio cholerae, Pseudomonas aeruginosa and Salmonella typhus Morones et al. (2005) (2005) (2005) 7. Silver nanoparticles E. coli in liquid and solid medium Baker et al. (2005) (2005) (2005) Infection using silver ions in E. coli by Yamanaka and colleagues (2005) (2005) E. coli and Staph aureus infected with silver nanoparticles Shahverdi and colleagues (2007) (2007) Silver nanoparticles, bifunctional Fe3O4, and @Ag nanoparticles E. coli, B. subtilis, and S. epidermidis Gong and colleagues (2007) (2007) E. coli and Staph. aureus were treated with nanofibres containing silver nanoparticles impregnated with nanoparticles. A study by Jun et al (2007) Staph. aureus may thrive on cotton fabrics coated with silver nanoparticles.

A study by Duran et al (2007) E. coli and Staphylococcus aureus wound dressings coated with silver nanoparticles Maneerung and colleagues (2008) Staph. aureus, E. coli, Salmonella typhi, and Staphylococcus epidermidis were all tested using silver nanoparticles by Ingle et al (2008) Gajbhiye et al (2009) found that silver nanoparticles were effective in treating fungi such as Phoma herbarum, Phoma glomerata, Fusarium semitectum, Trichoderma sp and Candida albicans (2009) 16. E. coli, Staph. aureus, and Ps. aeruginosa treated with silver nanoparticles Birla et al. (2009) (2009) E. coli and Staph. aureus nanoparticles coated with silver Gade et al (2010) E. coli and P. aeruginosa silver nanoparticles Geethalakshmi and Sarada (2010) 19-silver nanoparticles E. coli; Staph aureus; and Ps. Aeruginosa; and Bonde et al. (2011) analysed the effects of these silver nanoparticles on the three bacteria (2011) Silver nanoparticles Ps. aeruginosa, Staph. aureus, and harmful fungus Aspergillus flavus and Aspergillus niger Govindaraju et al. (2010) (2010) There are a variety of microorganisms that have been shown to be resistant to silver nanoparticle treatment, including staph and E. coli, as well as bacteria like Klebsiella pneumoniae and B. subtilis (2011) Staphylococcus aureus and Streptococcus mutans medical devices coated with silver nanoparticles (2011) 23. E. coli and Staph. aureus were combined into a bacterial cellulose-silver nanoparticle composite. Hernane and others (2011) Silver nanoparticle anti-MDR

crobiology 112 (841-4852), 841-852 (2012) The 2012 annual conference of the Society for Applied Microbiology In this case, the authors. Nanoparticles alone and in combination with fluconazole were tested for their fungicidal properties. Fluconazole with silver nanoparticles increased the antifungal activity of fluconazole against Candida albicans, Phoma herbarum, Fusarium semitectum, Trichoderma sp. and Candida glomerata, confirming the antifungal capabilities of silver nanoparticles. Opuntia ficus-indica was used to produce silver nanoparticles, which were tested against E. coli and Staph. aureus for their antibacterial properties.

To their surprise, they discovered that silver nanoparticles in conjunction with commercially available medicines showed outstanding antibacterial activity. Silver nanoparticles were synthesised from the leaf extract of Murraya koenigii, an Indian curry leaf tree, and their antibacterial activity against pathogenic bacteria such as E. coli, Staph aureus, and Ps. aeruginosa was studied both singly and in combination with commercially available antibiotics gentamycin, ampicillin, tetracycline, and streptomycin (Bonde et al. 2012). When silver nanoparticles and gentamycin were used together, they found that E. coli was killed by an increase of fourfold. Tetracycline in conjunction with nanoparticles was shown to be most efficient against

International Journal For Advanced Research In Science & Technology
A peer reviewed international journal www.ijarst.in
ISSN: 2457-0362

Staph. aureus (216), however they concluded that regular antibiotics might be used against antibiotic-resistant organisms successfully if they were combined with silver nanoparticles. Silver nanoparticles of 19–23 nm size synthesised electrochemically in polyamide-hydroxyurethane media have recently been studied for their antibacterial properties (Stefan et al. 2011).

E. coli and Staph. aureus were evaluated using the disc diffusion technique for antibacterial activity. At a concentration of 5 lg/ml, silver nanoparticles with a diameter of 23 nm were shown to be highly bactericidal against Staph aureus. A study by Knetsch et al. (2011) found that applying a silver nanoparticle coating to the surface of medical equipment was effective in preventing bacterial adherence and subsequent biofilm development. Nanoparticles may be put on the device's surface, where silver progressively releases off the surface and kills the bacterial population in the vicinity. Staph. aureus, Streptococcus mutans, and Candida albicans were investigated for their antibacterial efficacy by Ki-Young (2011) using silver nanoparticles and tissue conditioner. Staph. aureus and Strep. mutans were discovered to be bactericidal when silver nanoparticles combined with tissue conditioner were used. At concentrations more than 1% silver nanoparticles, no viable cells were found. When tested against C. albicans, a tissue conditioner containing 0 to 5% silver nanoparticles demonstrated fungicidal activity. No CFU more than 20 percent was found. Candida glabrata and Fu

sarium oxysporum were mostly used in the manufacture of silver nanoparticles described by Namasivayam et al. (2011). Staph. aureus, E. coli, Klebsiella pneumoniae, Bacillus subtilis, Enterococcus faecalis, and Pseudomonas aeruginosa were tested, as were silver nanoparticles, for antibiotic resistance. A substantial antibacterial effect was found in the silver nanoparticles manufactured by the researchers (Table 1).

Using silver nanoparticles to combat germs that are resistant to many drugs

Drug-resistant bacteria

Before Sir Alexander Fleming's 1929 discovery and application of penicillin, microorganisms had the inherent potential to acquire resistance to antibiotics. Scientists and researchers have a tremendous difficulty in dealing with the ever-increasing bacterial resistance profile. The widespread and sometimes indiscriminate use of antibiotics, insecticides, and other related substances in agriculture has created a worldwide issue of rising antibiotic resistance. When a microorganism and its offspring can survive and thrive in circumstances that would otherwise kill them or hinder their growth, they are said to be drug resistant, according to the Institute of Food Technology, England. Drug resistance in bacteria was found to be linked to the presence of multiple enzymes, according to Abraham and Chain (1940), who also warned that the overuse of antibiotics could lead to resistance development and the spread of mutant strains that are resistant to antibiotics throughout the natural environment. When bacteria are exposed to an antibiotic but not killed, they may acquire resistance by altering their cell structure or metabolism such that the antibiotic can no longer kill them. As a result, antimicrobial exposure provides bacteria with the chance to develop resistance. Resistant organisms may be created by a variety of means such as genetic mutation, genetic material change, or the acquisition of additional genetic material. It is possible for bacteria to pass on their resistance either vertically (to their progeny) or horizontally (to neighbouring bacteria) after they have acquired it through the processes of transduction (the transfer of DNA between two bacteria via bacteriophage), transformation (the uptake of DNA from the external environment by bacteria), or conjugation (direct cell-to-cell contact to transfer DNA; Slonczewski and Foster, 2009). M.K. Rai and co-authors. Silver nanoparticle activity against MDR bacteria in 2012 The Authors Journal of Applied Microbiology 112, 841–852 a 2012 The Society for Applied Microbiology 845

Antimicrobial activity mechanisms and resistance mechanisms

The ability of an antimicrobial medicine to affect just the parasite and not the host is a crucial aspect of an ideal antimicrobial drug. Rather of attacking the host cell, ideal antimicrobial medicines would focus on the anatomical features and metabolic processes found only in microorganisms. Antimicrobial resistance in bacteria is mediated by a number of mechanisms, the most important of which are changes in the permeability of the bacterial cell wall, the removal of antimicrobial agents via efflux pumps of membrane, the modification of drug action sites, and the inactivation of antimicrobial agents (Cebrian et al. 2003; Biyela et al. 2004). Table 2 lists the main

International Journal For Advanced Research In Science & Technology
A peer reviewed international journal
www.ijarst.in
ISSN: 2457-0362

classes of antimicrobial drugs, their modes of action, and their resistance profiles**.**

Multidrug-resistant bacteria may be killed by silver nanoparticles.

Antimicrobial silver nanoparticles are widely employed. They're effective against MDR bacteria. MRSA and other MDR strains were tested for antibacterial activity by Panacek et al. (2006), who created a one-step procedure for synthesising silver nanoparticles. MRSA and Gram-positive and Gram-negative bacteria are both susceptible to the bactericidal effects of colloidal silver nanoparticles. Percival et al. (2007) claim that silver nanoparticle antibacterial agents, including antibiotic-resistant bacteria, are effective against Gram-positive and Gram-negative bacteria alike. Members of the genera Acinetobacter, Escherichia, Pseudomonas, Salmonella and Vibrio belong to the Gram-negative family of organisms. Bacillus, Clostridium, Enterococcus, Listeria, Staphylococcus, and Streptococcus are examples of Gram-positive bacteria. Inhibiting biofilm formation protects the bacterial colony from antibiotics and the human immune system by preventing the growth of antibiotic-resistant bacteria like methicillin- and vancomycin resistant Staphylococcus aureus (MRSA and VRSA) and Enterococcus faecium. Nanoparticles with a diameter of 100 nm were used in a research to test the antibacterial activity of silver nanoparticles against MRSA and non-MRSA in LB broth (Ayala-Nunez et al. 2009). Silver nanoparticles were shown to have bactericidal effect against MRSA and non-MRSA bacteria at varying concentrations.

At doses over 135 mg ml)1 when the inoculum was 105 CFU ml)1 both MRSA and non-MRSA were suppressed. A study by Espinosa-Cristobal et al. employed silver nanoparticles to treat tooth cavities (2009). For this reason, they tested the antibacterial properties of three different sizes of silver nanoparticles and reported their MIC. When the particle size is reduced, the bactericidal ability of silver nanoparticles is increased against Strep. mutans. Staph. aureus-induced silver nanoparticle production was reported by Nanda and Saravanan (2009). Staph. aureus, methicillin-resistant Staph. epidermidis, Strep. pyogenes, Salmonella typhi, and Klebsiella pneumoniae were tested for their antibacterial properties using these silver nanoparticles. They found that methicillin-resistant Staph. aureus was the most bactericidal, followed by methicillin-resistant Staph.

Table 2 Mechanisms of action and resistance of major categories of antimicrobial agents

Antimicrobial group with examples	Mode of action	Mechanism of resistance	References
1. Beta-lactams monobactams, cephalosporins, carbapenems	Inhibit petidoglycan layer synthesis of cell wall	Production of Beta lactamase to destroy the Beta-lactams	Poole (2004)
2. Aminoglycosides streptomycin, kanamycin, tobramycin, gentamicin	Inhibit bacterial protein synthesis by binding 30S ribosomal subunits	Antibiotic inactivation by plasmid- and transposon encoded modifying enzymes	Kotra et al. (2000)
3. Phenicols chloramphenicol florfenicol	Binds reversibly to the teptidyltransferase component of the 50S ribosomal subunit prevent the transpeptidation of peptide chain elongation	Acquisition of plasmids encoding chloramphenicol acetyltransferases (CAT) and which enzymatically inactivate the drug	Falagas et al. (2008)
4. Sulfonamides and trimethoprim prontosil, gantrisin, erythromycin-sulfisoxazole	Act competitively inhibiting bacterial modification of para-aminobenzoic acid into dihydrofolate thus interfering with folic acid metabolism	Owing to acquisition of plasmid that encode a drug-resistant dihydropteroate	Chopra (2007)
5. Tetracycline chlortetracycline oxytetracycline, demeclocycline, doxycycline	Binds reversibly to the 30S ribosomal subunits, which blocks the access of aminoacyl t-RNA to the RNA-ribosome complex, to prevent bacterial polypeptide synthesis	Chromosomal mutations affecting outer membrane permeability	Chopra (2007) Falagas et al. (2008)
6. Quinolones/fluoroquinolones nalidixic acid	The target is DNA gyrase, essential enzyme for DNA replication	Target gene mutation and removal by efflux pumps	Hooper (2000) Falagas et al. (2008)

Epidermidis and Strep. pyogenes, whereas Salm. typhi and Kl. pneumoniae had only modest action. They also found that silver nanoparticles were efficient antimicrobials against the drug-resistant bacteria MRSA and MRSE, with MRSA showing the most activity, followed by MRSE. Antibacterial activity was assessed by employing luciferase-based bacterial cell viability assays against erythromycin-resistant Strep. pyogene, ampicillin-resistant E-coli, MDR Ps. aeruginosa and drug-susceptible strains such as Streptococcus, E-coli, and P. aeruginosa. Between 30 and 100 mmol/l)1 of silver nanoparticles were shown to be effective (Humberto et al. 2010). Both bactericidal and bacteriostatic effects were shown against Staph. aureus, MSSA, and MRSA when silver nanoparticles in the 5–10 nm size range were used. Sol–gel method was used to synthesise colloidal silver nanoparticles with a size range of 20–45 nm, and the broth microdilution method was used to determine their antibacterial activity with MIC against E. coli, Staph. aureus, Candida albicans, Bacillus subtilis, Salmo typhimurium, Penicillium pneumoniae, and Klebsiella pneumoniae (Lkhagvajav

International Journal For Advanced Research In Science & Technology
A peer reviewed international journal www.ijarst.in
ISSN: 2457-0362

et al. 2011). As shown in Table 3, silver nanoparticles have bactericidal power against MDR microorganisms.

Mechanism of action against bacteria

Bacteria are divided into Gram-positive and Gram-negative groups according to the structure and content of their membranes. The peptidoglycan layer in the cell wall of these bacteria differs from that of other bacteria in that it is located outside the cytoplasmic membrane. On the other hand, Gram–negative bacteria have a 2- to 3-nm thick peptidoglycan layer on their cell walls, which is covered by an outer membrane made up of polyphospholipids and lipopolysaccharides that face the outside world. In spite of the vast research into silver nanoparticles' antibacterial properties, the method by which they kill bacteria is still a mystery.

As a result, the major structural change in the cell membrane occurs and the cell's permeability is increased by using silver nanoparticles, according to certain research. If the cytoplasmic membrane does not regulate the transport, then cells die (Morones et al. 2005; Sondi and Salopek-Sondi 2007). An alternative explanation for the antibacterial properties of silver nanoparticles is that they cause membrane damage by causing the production of free radicals (Kim et al. 2007). Based on silver nanoparticle interactions with DNA and other chemicals, Morones and colleagues (2005b) advanced the notion that the damage might be produced by the interaction of silver nanoparticles with the thiol groups in essential enzymes and phosphorus-containing bases. This interaction may inhibit cell division and DNA replication, which eventually results in cell death. " However, no DNA damage was seen in the experiment (Hwang et al. 2008).

There is evidence that silver nanoparticles alter the phosphotyrosine profile of suspected bacteria-derived peptides, which may influence cell signalling and hence impede bacterial growth (Shrivastava et al. 2008). Silver nanoparticles and silver ions may have a synergistic harmful impact on the stress-specific bioluminescent bacteria, according to Hwang et al. (2008). Reactive oxygen species are produced as a result of ions moving into cells. As a result of nanoparticle-induced membrane damage, cells cannot properly expel the silver ions and so reduce their effectiveness (Hwang et al. 2008). Antibacterial activity against Gram-negative bacteria was studied by Morones and colleagues (2005), who found that silver nanoparticles adhere to the cell membrane, penetrate inside bacteria, and release silver ions; this suggests that silver nanoparticles disrupt cell function. Antibiotic-resistant bacteria like methicillin- and vancomycin-resistant Staphylococcus aureus (MRSA and VRSA) and methicillin-resistant Enterococcus faecalis (MRE) can be killed by silver nanoparticles, which are effective against a wide range of Gram-negative bacteria, including Acinetobacter, Escherichia coli, Pseudomonas aeruginosa, Salmonella, and Vibrio A biofilm is an extracellular polysaccharide matrix that is produced by microorganisms that are linked to the surface of other microorganisms. The bacterial colony is protected by biofilm, which functions as an effective barrier against antimicrobial agents and the host's immune system. Silver nanoparticles have been shown to prevent biofilms from forming (Percival et al. 2007). Silver nanoparticles,

according to Klueh et al. (2000), limit bacterial growth by inactivating proteins in the cells. Sulfhydryl groups (SH) in enzymes are deactivated by silver atoms. By creating a persistent S-Ag bond with the thiol group of the compounds, silver affects the function of chemicals in the cell membrane, which is critical for transmembrane energy production and ion transport. Oxygen molecules in the cell and hydrogen atoms of thiol groups react with silver to generate disulfide bonds (R-S-S-R). Silver aided in the development of disulfide bonds, which alter the structure and function of biological enzymes. Succinyl co A synthetase, maltose transporter (MalK), and fructose bisphosphate adolase were shown to be affected by treatment with 900 ppb Ag+ solution, as was 30S ribosomal subunit. Another theory held that silver ions interfere with protein translation by attaching to and deactivating the 30S ribosomal subunit. Upon treatment with Ag+87, the enzyme succinyl coenzyme A synthase was shown to be downregulated. Because proteins play a key role in many cellular processes, the silver nanoparticles harm the bacteria and cause cell death (Yamanaka et al. 2005). Ag+ ions, which enter cells and intercalate between DNA's purine and pyrimidine bases, may be responsible for silver nanoparticles' antibacterial action, according to Klueh et al. (2000). These base pairs disrupted the hydrogen bonding between the two antiparallel strands, resulting in DNA molecule denaturation (Klueh et al. 2000). In Fig. 1, silver nanoparticles against bacteria demonstrate all of their multi-actional behaviours.

International Journal For Advanced Research In Science & Technology
A peer reviewed international journal www.ijarst.in
ISSN: 2457-0362

Silver nanoparticles' bactericidal properties are influenced by a variety of factors.

Size

The tiny size of nanoparticles in comparison to bulk materials alters their reactivity and characteristics. The greater the surface-area-to-volume ratio, the greater the bactericidal activity of a smaller particle.

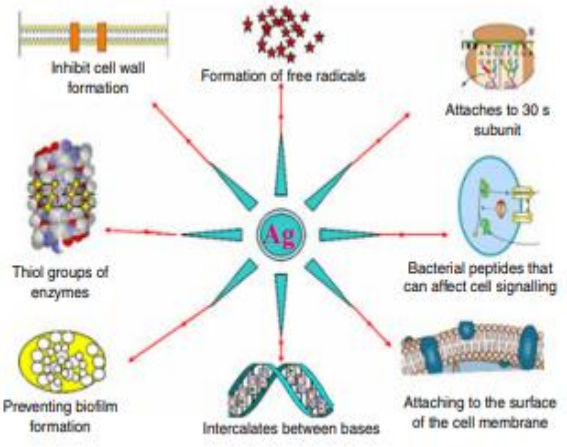

Figure 1 Silver nanoparticles showing multiple bactericidal actions.

The size of the silver nanoparticles has an effect on the silver nanoparticles' ability to conduct electricity. If the nanoparticles are small, they have a greater surface area in touch with the bacterial cells, resulting in more interaction. Due to their tiny size and high proportion of contact with bacteria, nanoparticles smaller than 10 nm have a higher reactivity and hence are more likely to interact with bacteria through an electrical effect. Due to their size, silver nanoparticles have a bactericidal effect (Morones et al. 2005; Raimondi et al. 2005). Panacek et al. (2006) evaluated the size dependence of nanoparticle bactericidal potential and found that nanoparticles with a diameter of 25 nm had the best antibacterial activity.

Shape

Studying the suppression of bacterial growth by variably shaped nanoparticles shows that the bactericidal potential of nanoparticles is also affected by their forms (Morones et al. 2005). In a separate investigation, Pal et al. (2007) found that citrate-reduced citrate nanoparticles spherical, rod, and triangular were effective against E. coli at various doses. When used against E. coli, triangular nanoparticles outperformed spherical nanoparticles, which outperformed rod-shaped nanoparticles again (Pal et al. 2007). The structure of silver nanoparticles also influences their antibacterial properties.

Concentration

In a 2005 research, Morones et al. (2005) found that silver nanoparticles of sizes 1–100 nm had a bactericidal impact on Gramnegative bacteria E. coli. When they grew bacteria to mid-log phase, they measured the OD at 595nm, examined the influence of various doses of silver on the development of bacteria (up to 75 lg/ml)1 and found that there was no substantial growth of bacteria above that concentration (Morones et al. 2005).

Dose

An investigation on the synthesis and dose-dependent effects on Gram-negative and Gram-positive bacteria was conducted. In contrast to Gram-positive bacteria, silver nanoparticles were discovered to exhibit significant bactericidal action against Gram-negative bacteria. This activity was found to be dosage dependant (Shrivastava et al. 2008).

Conclusions

The reemergence of MDR pathogens and parasites is a direct result of human pathogens' increasing resistance to antibiotics. Such infections need the use of broad-spectrum antibiotics as part of a comprehensive treatment plan. However, the effectiveness, toxicity, and cost of these therapies are all much worse. With the aid of silver nanoparticles, nanotechnology offers an excellent platform for overcoming the resistance issue. Silver's antibacterial activity has been documented in Ayurveda and homoeopathy dating back thousands of years. It is possible to boost the bactericidal potential by altering the chemical and physical characteristics at the nanoscale, resulting in a rise in surface area to volume ratio. Gram-positive and Gram-negative bacteria are both sensitive to silver nanoparticles with a size range of 10–100 nm, making them excellent bactericides. It is thus expected that antibacterial silver nanoparticles, such as Ps. aeruginosa and MRSA and VRSA, will be deployed as formidable weapons in the fight against MDR bacteria such as Ps. aeruginosa.

References

International Journal For Advanced Research In Science & Technology
A peer reviewed international journal www.ijarst.in
ISSN: 2457-0362

[1] Abraham, E.P. and Chain, E. (1940) An enzyme from bacteria able to destroy Penicillin. Nature 146, 837. Ahmad, Z., Pandey, R., Sharma, S. and Khuller, G.K. (2005) Alginate nanoparticles as antituberculosis drug carriers: formulation development, pharmacokinetics and therapeutic potential. Indian J Chest Dis Allied Sci 48, 171–176.

[2] Ansari, M.A., Khan, H.M., Khan, A.A., Malik, A., Sultan, A., Shahid, M., Shujatullah, F. and Azam, A. (2011) Evaluation of antibacterial activity of silver nanoparticles against MSSA and MSRA on isolates from skin infections. Biol Med 3, 141–146.

[3] Atiyeh, B.S., Costagliola, M., Hayek, S.N. and Dibo, S.A. (2007) Effect of silver on burn wound infection control and healing: review of the literature. Burn 33, 139–148. Ayala-Nunez, N.V., Villegas, H.H.L., Turrent, L.C.I. and Padilla, C.R. (2009)

[4] Silver nanoparticles toxicity and bactericidal effect against methicillin resistant Staphylococcus aureus: nanoscale does matter. Nanobiotechnology 5, 2–9. Baker, C., Pradhan, A., Pakstis, L., Pochan, D.J. and Shah, S.I. (2005) Synthesis and antibacterial properties of silver nanoparticles.

[5] J Nanosci Nanotechnol 2, 244–249. Bellinger, C.G. and Conway, H. (1970) Effects of silver nitrate and sulfamylon on epithelial regeneration. Plast Reconstr Surg 45, 582–585. Bhol, K.C., Alroy, J. and Schechter, P.J. (2004) Anti-inflammatory effect of topical nanocrystalline silver cream on allergic contact dermatitis in a guinea pig model.

[6] Clin Exp Dermatol 29, 282–287. Birla, S.S., Tiwari, V.V., Gade, A.K., Ingle, A.P., Yadav, A.P. and Rai, M.K. (2009) Fabrication of silver nanoparticles by Phoma glomerata and its combined effect against Escherichia coli, Pseudomonas aeruginosa and Staphylococcus aureus.

[7] Lett Appl Microbiol 48, 173–179. Biyela, P.T., Lin, J. and Bezuidenhout, C.C. (2004) The role of aquatic ecosystems as reservoirs of antibiotic resistant bacteria and antibiotic resistance genes.

[8] Water Sci Technol 50, 45–50. Bonde, S.R., Rathod, D.P., Ingle, A.P., Ade, R.B., Gade, A.K. and Rai, M.K. (2012) Murraya koenigii-mediated synthesis of silver nanoparticles and its activity against three human pathogenic bacteria.

[9] Nanosci Meth 1, 25–36. Butkus, M.A., Labare, M.P., Starke, J.A., Moon, K. and Talbot, M. (2004) Use of aqueous silver to enhance inactivation of coliphage MS-2 by UV disinfection. Appl Environ Microbiol 70, 2848–2853.

[10] Castellano, J.J., Shafii, S.M., Ko, F., Donate, G., Wright, T.E., Mannari, R.J., Payne, W.G., Smith, D.J. et al. (2007) Comparative evaluation of silver-containing antimicrobial dressings and drugs. Int Wound J 4, 14–22. Cebrian, L.E., Sirvent, J.C., Rodriguez, D., Ruiz, M. and Royo, G.

[11] (2003) Characterisation of Salmonella spp. mutants produced by exposure to various fluoroquinolones. Int J Antimicrob Agents, 22, 134–139. Chen, X. and Schluesener, H.J. (2008) Nano-silver: a nanoproduct in medical application.

[12] Toxicol Lett 176, 1–12. Chopra, I. (2007) The increasing use of silver-based products as antimicrobial agents: a useful development or a cause for concern. J Antimicrob Chemother 59, 587–590.

[13] De Souza, A., Mehta, D. and Leavitt, R.W. (2006) Bactericidal activity of combinations of silver–water dispersion with 19 antibiotics against seven microbial strains.

[14] Curr Sci, 91, 926–929. Duran, N., Marcarto, P.D., De Souza, G.I.H., Alves, O.L. and Esposito, E. (2007) Antibacterial effect of silver nanoparticles produced by fungal process on textile fabrics and their effluent treatment.

[15] J Biomed Nanotechnol 3, 203–208. Espinosa-Cristobal, L.F., Martinez-Castanon, G.A., MartinezMartinez, R.E., Loyola-Rodriguez, J.P., Patino-Marin, N., Reyes-Macias, J.F. and Ruiz, F. (2009) Antibacterial effect of silver nanoparticles against Streptococcus mutans.

[16] Mater Lett 63, 2603–2606. Falagas, M.E., Grammatikos, A.P. and Michalopoulos, A. (2008) Potential of old-generation antibiotics to address current need for new antibiotics.

[17] Expert Rev Anti Infect Ther 6, 593–600. Feng, Q.L., Wu, J., Chen, G.Q., Cui, F.Z., Kim, T.N. and Kim, J.O. (2000) Mechanistic study of the antibacterial effect of silver ions on Escherichia coli and Staphylococcus aureus

[18] J Biomed Mater Res 52, 662–668. Gade, A., Gaikwad, S., Tiwari, V., Yadav, A., Ingle, A. and Rai, M. (2010) Biofabrication of silver nanoparticles by Opuntia ficus-indica: in vitro antibacterial activity and study of the mechanism involved in the synthesis. Curr Nanosci 6, 370– 375. Gajbhiye, M., Kesharwani, J., Ingle, A., Gade, A. and Rai, M. (2009) Fungus-mediated synthesis of silver nanoparticles and their activity against pathogenic fungi in combination with fluconazole. Nanomedicine 5, 382–386. Geethalakshmi, R. and Sarada, D.V.L. (2010) Synthesis of plant-mediated silver nanoparticles using Trianthema decandra extract and evaluation of their anti microbial activities.

[19] Int J Eng Sci Technol 2, 970–975. Gemmell, C.G., Edwards, D.I. and Frainse, A.P. (2006) Guidelines for the prophylaxis and treatment of methicillin-resistant Staphylococcus aureus (MRSA) infections in the UK. J Antimicrob Chemother 57, 589–608. Gong, P., Li, H., He, X., Wang, K., Hu, J., Tan, W., Tan, S. and Zhang, X.Y. (2007) Preparation and antibacterial activity of Fe3O4@Ag nanoparticles. Nanotechnology 18, 604–611. Govindaraju, K., Tamilselvan, S., Kiruthiga, V. and Singaravelu, G. (2010) Biogenic silver nanoparticles by Solanum torvum and their promising antimicrobial activity antimicrobial activity of silver nanoparticles. J. Biopest. 3, 394–399. Gu, H., Ho, P.L., Tong, E., Wang, L. and Xu, B. (2003) Presenting vancomycin on nanoparticles to enhance antimicrobial activities. Nano Lett 3, 1261–1263.

[20] Hernane, S.B., Regiani, T., Marques, R.F.C., Lustri, W.R., Messaddeq, Y. and Ribeiro, S.J.L. (2011) Antimicrobial bacterial cellulose-silver nanoparticles composite membranes. J. Nanomate. 721, 631–639. Hooper, D.C. (2000) Mechanisms of action and resistance of older and newer fluoroquinolones. Clin Infect Dis 31, S24– S28. Humberto, H., Lara, V., Ayala-Nunez, N.V., Carmen, L.D., Ixtepan, T. and Cristina, R.P.

[21] (2010) Bactericidal effect of silver nanoparticles against multidrug-resistant bacteria. World J Microbiol Biotechnol 26, 615–621. Hwang, E.T., Lee, J.H., Chae, Y.J., Kim, Y.S., Kim, B.C., Sang, B. and Gu, M.B. (2008) Analysis of the toxic mode of action of silver nanoparticles using stress-specific bioluminescent bacteria.

[22] Small 4, 746–750. Ingle, A., Gade, A., Pierrat, S., Sonnichsen, C. and Rai, M. (2008) Mycosynthesis of silver nanoparticles using the fungus Fusarium acuminatum and its activity against some human pathogenic bacteria. Curr Nanosci 4, 141–144. Jun, J., Yuan-Yuan, D., Shao-hai, W., Shao-feng, Z. and Zhongyi, W. (2007) Preparation and characterization of antibacterial silver-containing nanofibers for wound dressing applications.

[23] J US China Med Sci 4, 52–54. Kawahara, K., Tsuruda, K., Morishita, M. and Uchida, M. (2000) Antibacterial effect of silver zeolite on oral bacteria under anaerobic condition. Dent Mater 16, 452–455. Kim, J.S., Kuk, E., Yu, K.N., Kim, J.H., Park, S.J., Lee, H.J., Jeong, D.H. and Cho, M.H. (2007) Antimicrobial effects