Volume 4, Issue 1-4, 2017, 66 - 80 ISSN 2393-0586
Biomaterials and Tissue Engineering Bulletin
http://btebulletin.com/
Review Article Open Access Journal
Received: 25.03.2017 / Revised: 28.05.207 / Accepted: 18.06.2017 / Published on-line: 11.08.2017

Organic-inorganic antimicrobial nanostructures for health care applications

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ABSTRACT
In recent years, the drug resistant microorganisms are a serious and increasing public health problem. New strategies for controlling bacteria activity are urgently needed and nanomaterials can be a very promising approach, as the small size of the particle gives large surface area and consequently reactivity (and in many cases toxicity) increases substantially. The most tested metallic nanoparticles are silver, copper, gold, aluminum, titanium, iron, zinc, bismuth and others. Some of these metals have been coated onto several other materials. Another strategy is to incorporate these metals into a substrate such as polymethyl methacrylate forming organic-inorganic antimicrobial nanostructures. With respect to bacteria and fungi, the most frequent candidates for microbial experiments are: *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Klebsiella pneumonia*, *Bacillus subtilis among* other species. The antimicrobial potential of these nanostructured particles, their mechanism of action and health care applications are presented and discussed at length in this review.

Keywords: *Organic nanocomposites, Inorganic nanoparticles, Antimicrobials, Health care, Applications, Wound healing, Nanomaterials.*

1. INTRODUCTION

An antibacterial agent plays a very important in medicine, textile industry, food packaging, water disinfection, pharmaceutics and hygiene products (Malmsten, 2014). Significant efforts have focused on the development of new organic/inorganic or (organic-inorganic) nanostructured materials in order to overcome illness and diseases caused by harmful microorganisms. Conventional antimicrobial agents and their applications to various industries have been reported but, of late, the nanocomposite have proved their own significance owing to the fact that organic-inorganic nanostructured materials can acquire excellent antibacterial activity useful for various applications. The high surface to volume ratio and the improved surface reactivity of nanocomposite are important properties for antimicrobial activity. These properties help to inactivate the growth of microorganism than their micro- or macro-scale counterparts. Several materials like metal oxides (zinc oxide, titanium dioxide, aluminum oxide and magnesium oxide), metal ions (silver, gold, copper and platinum) and modified nanoclay have been used extensively to control the growth of the microorganism. Kanmani and Rhim (2014) have utilized organic acids, natural polymers and antimicrobial agents like EDTA, sorbic acids, chitosan, thymol, carvacrol and antibiotics which provided the antimicrobial function.

This review focuses on organic-inorganic nanostructured materials which can inhibit the growth of bacteria, fungi and protozoa. Nanosized antimicrobial polymers have been reported to be better antimicrobial agents than the macromolecular polymers by Gonzalez *et al.*(2015). Nonstructural features of the surface of these materials have been found to alter three-dimensional conformation of proteins, which can also have a potential effect on biofilms (Campoccia, 2013). Moreover, Li *et al.*(2008) have proved that nanomaterials are excellent absorbents and catalysts because of their specific large surface area and resultant high reactivity. The extremely large surface area leads to an improvement of antibacterial properties of the organic materials.

The present review provides an overview of latest innovations in the antimicrobial organic-inorganic nanostructured materials. It is organized into sections that discuss the basic properties of organic nanostructure, inorganic nanostructure, combination of organic-inorganic nanostructured materials used till date and their major health care applications. Additionally, this review surveys important scientific research and developmental works pertaining to antibacterial behavior using nanotechnology as a new means to deliver health care applications. An outlook which envisions the importance of using an organic-inorganic nanocomposite as an antimicrobial agent in various industries is also outlined.

2. INORGANIC NANO-STRUCTURED MATERIAL LOADED INTO ORGANIC CARRIERS

The design, synthesis and selection of an organic nanostructured material are significant steps in the development of various novel organic/inorganic hybrid materials.

The organic/inorganic nanoparticle incorporated in polymers allows novel materials to be obtained with modulated and distinct electrical, optical and catalytic properties.

In recent years, many naturally occurring organic polymers such as proteins, peptides, liposomes, cyclodextrins and dendrimers have been utilized as a carrier for metallic as well as non-metallic nanostructured materials.

2.1. Liposomes.

Liposomes are the spherical vesicles which have at least one lipid bilayer. Liposomes are self-assembled from dispersion of amphiphilic lipids in water. Since they have amphiphilic structures, they can be used to trap and carry both hydrophilic and hydrophobic materials.

A liposome can be used as a carrier for administration of pharmaceutical drugs, nutrients and nanoparticles. These are widely used in drug-delivery systems as agent for transfer, container for storage and for controlled release of agents (Volodkin et al., 2007; Huwyler et al., 1997).

The particle size of liposomes varies in the range of nanometers to macrometers was reported by Montazer *et al.*(2007). Other than pharmaceutical applications, liposomes are also useful in the textile processing (Barani and Montazer, 2008). Fluidity and permeability of the barrier of a lipid can be increased via loading nano-sized silver and gold particles into the structure of liposomes, as shown by Park and co-workers (2005). It appears that loading inorganic nano-structured material into liposomes can produce an active agent that can present controlled release textile modification. Moreover, thermal and mechanical stability of liposomes with the release of nanostructured materials should be determined in practical case. The active group of liposomes is used to attach textile substrate or stabilized on the fabric surface using different types of stabilizers. To carry different types of textiles compounds liposomes have been used extensively in textile industry. Thus, liposomes should be resistant against thermal, mechanical and chemical textile processing necessary during the steps of manufacture. Additionally, alkaline stability of laundering should also be tested for liposomes. Barani *et al.*(in press) have shown that the phospholipid layers act against bacterial growth and thereby reduced the anti-bacterial properties. Nonetheless, this was overcome by incorporating silver nanoparticles into phospholipid bilayer which enhances the anti-bacterial effects. In addition, thermal stability and of matrix and stabilizer in the autoclave condition i.e. 121 ºC for 30 min, especially for medical usages of antimicrobial textiles should be dealt with.

2.2. Chitosan Nanoparticles.

Chitosan is a polysaccharide which is derived from chitin, it is a natural product obtained from the exoskeleton of crustaceans, insects and wall of fungi. Chitosan is used for several biomedical applications because of its unique properties like biocompatibility, gel formation, adsorption capacity, nontoxicity and nonimmunogenicity. Chitosan can be utilized as an additive as spinning antimicrobial fibers, finishing agent and for surface modification mainly of cellulose, cellulose/polyester and wool fibers as an antimicrobial for textile industry (Fouda *et al.*2009). Chitosan is positively charged and soluble in acidic to neutral solutions because the amino groups in chitosan have a pKa of ~6.5. The antimicrobial function arises from its polycationic nature. It is caused by the protonation of amino groups at the C-2 atoms of the glucosamine units. The positively charged amino groups of chitosan can bind to the negatively charged bacterial surface, which resulting in the disruption of cell membrane and an increase in its permeability. It also interacts with the DNA of microorganisms to prevent protein synthesis. The antimicrobial efficiency of chitosan depends upon degree of deacetylation, its average molecular weight and the ratio between protonated and unprotonated amino groups in molecular structure. It is supposed that chitosan of a low molecular weight is having more antimicrobial activity than chitosan oligomers; efficiency also increases with increased deacetylation, which can exceed 90%. Chitosan is having a drawback it act as an weak adhesive to cellulose fibers which ultimately results in gradual leaching from the fiber surface with repetitive washing. Several cross linking agents are used to enable binding of chitosan to cellulose fibers such as polycarboxylic acids (1, 2, 3, 4- butantetracarboxylic and citric acids) and derivates of imidazolidinone. Also, the reactivity of quaternized chitosan has been enhanced by introducing functional acryl amido methyl groups to the primary alcohol groups (C-6), that leads to form covalent bonds with cellulose in alkaline conditions.

A variety of metal oxide NPs can be encapsulated into chitosan, viz. copper, zinc oxide, silver etc. Use of chitosan NPs offer additional advantages such as, ability to control the release of bioactive agents and ability to avoid the utilization of hazardous organic solvents while fabricating NPs as chitosan requires acidic environment. Because of these reasons this nanomaterial is extensively used for drug delivery systems. Moreover, the combination of chitosan with inorganic NPs is an efficient approach to produce antibacterial materials with improved functional as well as enhanced antimicrobial properties. The Ag-zeolite or Ag- hydroxyapatite–chitosan nanocomposite provided the increased mechanical strength and water barrier properties were reported by Rhim *et al.*(2006) and Saravanan *et al.*(2011). Chitosan–Ag–ZnO composite showed enhancement in the antimicrobial activity was found by Li *et al.*(2010 a). The ZnO-chitosan complexes in various applications such as in film formation, membranes and dyes have significantly improved antibacterial properties as compared to chitosan has been proved by Li *et al.*(2010 b) and Salehi *et al.*2010). Shafei and Abou-Okeil (2011) have shown several advantages of combining chitosan with ZnO have also provided alternative to the widely used Ag NPs.

2.3. Dendrimers.

These are regularly branched 3D artificial molecules produced by incorporating repetitive branching sequences to create architecture with high level of size controlled uniformity (Tan *et al.*1999; He *et al.*1999; Balogh *et al.*2000). The concentration of high molecular surface functional group dendrimers can provide antibacterial properties to the interacting molecule. Chen and Cooper *et al.*(2000) have indicated that highly branched dendritic structures are useful due to their antimicrobial efficacy. The antibacterial properties of water soluble dendrimers can be altered to make them useful for clinical applications by addition of water and interaction with bacteriostatic weak water soluble or insoluble antibiotics. The bacterial infections remain main causes of mortality in hospitals. The sulfonamides are extensively used these bacterial infections of urinary tract and respiratory tract.

Dendrimers can serve as nano-reactors with the ability to pre-organize metallic elements (Raveendran *et al.*2006; Balogh *et al.*2001). Metals are placed at different positions of dendritic architectures such as branching centers, terminal units, structural auxiliaries, or as building blocks and connectors (Newkome *et al.*1999). They possess several unique properties that make them efficient NP carriers for the antimicrobial drug delivery. The highly branched 3D structure provides a large surface area to size ratio resulting in greater reactivity with microorganisms in vitro. The availability of functional surface groups, polydispersity and their ability to mimic cell membrane makes them a potential drug carrier. Equally hydrophilic as well as hydrophobic agents can be loaded at the same time either by encapsulating drug within the dendritic structure, or by interacting with the drugs at their terminal groups via electrostatic, or covalent bonds also due to the availability of functional groups. Sajja *et al.*2009 have studied that dendrimers with specific and high binding affinity to a broad variety of viral and bacterial receptors can be synthesized. Dendrimers surfaces can be functionalized with PEG which allows the delivery system to circulate in the body for prolonged time and hence maximizing the opportunity of drug to reach the targeted site.

2.4. Nano-Capsules.

Nano/micro-capsules in addition to peptides, dendrimers and liposomes can be used for carrying, storage and delivery of bioactive agents in different objectives was revealed by Volodkin *et al.*(2004). Mostly, these are core-shell structures composed of a shell made up of natural or synthetic polymers and a core containing compounds of different bio-active agents viz. vitamins, catalysts, hormones, drugs, deodorants and proteins. The Ciba has company presented a novel technology of nano-encapsulation to achieve permanent antimicrobial efficiency on cotton fabrics. Ciba Tinosan CEL is commercial products which are available based on this concept (Mao, 2002). The loaded agent may be dispersed at core of capsule or aggregated in its central part. So far, releasable capsules used for delivering, carrying and controlled release of active agents, should release the loaded active agent using a repeatable controlled release mechanism. The size and size distribution of capsules decrease with the increase of stirring rate i.e. from 3000 to 9000 rpm and content of emulsifier during encapsulation of n-octa-decane has been found by Zhang *et al.*(2004). They have focused on the effect of diameter on crystallization behavior of phase change materials. These are also chosen for textile modification because they are not affected during vigorous stirring and ultra-sonication required in order to achieve nano-sized emulsions (Watnasirichaikul *et al.*2000). Several researchers such as Oku *et al.*(2000) have successfully encapsulated nano-silver via chemical reduction of silver nitrate with the aim of achieving at special electronic properties. Shim *et al.*(2002) have successfully encapsulated ZnO NPs into poly (methyl-methacrylate) (PMMA). However, they did not report the evaluation of anti-bacterial efficiency of encapsulated nano-silver or nano-ZnO.

2.5. Cyclodextrin (CDs).

Cyclodextrins are a family of cyclic oligosaccharides composed of α-1, 4-linked glucopyranose subunits and are useful as molecular complexation agents (Singh *et al.*2002). Cyclodextrins are of three types: α-CD, ß-CD and γ-CD composed of six, seven and eight α-1, 4-linked glycosyl units, respectively. CDs are produced by the enzymatic degradation during destruction process of starch (Martin, 2004). From all the three types ß-CD is the most available and useful one with lower price. The mainly prominent feature of CDs is their capability to form molecular complexation with a wide range of solid, liquid and gaseous compounds. They can be utilized in the control release of perfumed materials and guest molecules as a retarding effect in finishing baths and dyeing and as an absorbent of smell. Additionally, they can also be used in as drug release in the textile industry (Voncina et al., 2007; Vogtle 1991; Szejtli 2004). Martin, (2004) has studied the toxicity of cyclodextrin as fabrics they are in direct contact with human skin and the results in his study has shown that in higher concentrations they may be harmful to human body. ß-CD has been introduced as a food additive in Germany from November 13, 2000, and showed no allergic impact. Szejtli *et al.*has reported the grafting of CDs onto cellulose fibers by using epichlorohydrin as a cross-linking agent.

There is incorporation of CDs into synthetic or natural polymeric material by means of either physical or chemical paths involving cyclodextrin derivatives which is carrying variety of functional groups. The fixing of CDs into cotton and wool fibers using poly carboxylic acids as cross-linking and binding agents has been studied recently by Denter, (1996). Similarly, Martel *et al.*(2002) has concluded that grafting occurred through the formation of a cross-linked copolymer between PCA and CDs was not covalently fixed to fibers, but are entangled or physically adhered into the fibrous network. Similarly, polyester spacers has been modified by ß-CD and stabilized with citric acid. In addition Montazer *et al.*(2010 (b)) have also loaded ß-CD with sodium diclofenac for wound dressing purposes. Besides, cyclodextrins has the potentiality of being loaded with inorganic nanomaterials to carry these NPs to textile materials through different processing and making them stabilized on the fabric surfaces using different cross-linking agents

3. INORGANIC NANO-STRUCTURED MATERIALS AND THEIR NANO-COMPOSITES

The most appropriate inorganic nano-structured materials in this group are: TiO_2 and its metallic and non-metallic nano-composites, silver and nano-structured materials based on silver, ZnO nanoparticles, Cu nanoparticles, gold nanoparticles, anti-bacterial agents based on Gallium, carbon nanotubes (CNTs), nano-clay and modified species of nano-clay including silver–

chitosan/clay, clay–polyvinyl pyridinium and silver-modified montmorillonites. In addition, these inorganic NPs have wide range of applications especially in the field of antimicrobials (Otari *et al.*2013), nanobiosensors (Satvekar *et al.*2014, Satvekar *et al.*2015 (a), Satvekar *et al.*2015 (b)) and pathogen detection (Tiwari *et al.*2015 (a), Tiwari *et al.*2015 (b), Tiwari *et al.*2015 (c)).

3.1. Titanium dioxide Nanoparticles (TiO_2NPs).

$TiO_2$is commonly used as semiconducting metal oxide, photocatalyst which shows photo-catalytic antimicrobial activity (Allahverdiyev et al., 2011). These NPs are versatile with an ability to kill both gram positive and gram negative bacteria was shown by Wei *et al.*(1994) (Elliott, 2010). In addition, TiO_2 shows their efficiency against several viruses and parasite species (Brady-Estevez, 2008; Zan *et al.*2007; Allahverdiyev *et al.*2013). TiO_2NPs generates free radical oxides and peroxides, which show strong antimicrobial activity with broad reactivity against many infectious microbes. Blecher *et al.*(2011) the ROS which has been generated causes damage in the membrane, DNA, RNA and proteins any other biomacromolecules and functions of the bacterial cell. Kuhn *et al.*(2003) had reported the antimicrobial activity ofTiO_2 NPs and their results revealed that it has shown the highest antimicrobial activity for E. coli, followed by P. aeruginosa, S. aureus, E. faecium and C. albicans. It is also effective against many bacteria including spores of Bacillus (Hamal *et al.*2010), which is the most resistant organism known. Muranyi *et al.*(2010) has reported that TiO_2 doped with different metals enhances the antibacterial activity of TiO_2 by improved light absorption and photo catalytic inactivation. Particularly, the visible light driven photo catalytic inactivation process have been reported for TiO_2 modified with metals for ex. iron, copper, vanadium and tin or non-metals for ex. nitrogen, sulfur and boron. The most efficient approach to extend the photo response of titania into visible range is doping or surface modification with transition metals. The modified TiO_2 NPs have several advantages like it is non-hazardous, easily recyclable and inactivate most of the pathogenic microorganisms. The current literature also reveals that there is an enhancement in its bactericidal activity. Antibacterial activity of Cu/TiO_2 nano-composites in the dark and in the visible light is well accepted at higher composition of Cu. A strong incentive and driving research in this area reveals the urge to develop visible light driven copper-doped (Yadav et al., 2014). Recently, a variety of methods such as templates, polymers, structural directing reagents, hydrothermal/solvo thermal and sol-gel methods have been developed to synthesize un-doped/doped TiO_2 nanostructures. Out of these methods use of templates and structural directing reagents generally complicates the preparation process and also increases the production cost. The conventional hydrothermal/solvo-thermal processes are often time and energy consuming. Amongst these the sol-gel method is having overriding advantages and commonly used method for the synthesis of TiO_2 NPs. Sugimoto *et al.*(2003) has prepared TiO_2nanoparticles with different sizes and shapes by changing the reaction conditions using sol–gel method. Similarly, Znaidi *et al.*(2001) has successfully synthesized well dispersed, highly crystalline TiO_2 NPs using the modified sol-gel methods. There are reports on bactericidal activity of nitrogen-doped metal oxide nanocatalysts on E. coli biofilms and on the photocatalytic oxidation of biofilm components onTiO_2coated surfaces. In brief, TiO_2 photocatalysts is used as alternative for self-disinfecting contaminated surfaces. By the further development it may provide potent disinfecting solutions for prevention of bio-films formation. TiO_2 photocatalysts can be utilized as effective bio-films disinfectant in food processing industries. Kuhn *et al.*(2003) reported that antimicrobial efficiency of TiO_2 NPs was determined by cell wall complexity.

3.2. Antibacterial Mechanism of Action of TiO_2.

TiO_2irradiation by light with more energy compared to its band gaps leads to generation electron-hole pairs that induces redox reactions at the surface of the TiO_2. Thus, electrons in TiO_2jump from the valence band to the conduction band, the electron (e^-) and electric hole pairs (h^+) are formed on the surface of photocatalyst. The negative electron and oxygen atom combine to form O_2^- and the positive electric holes in combination with water will produce OH^- ions. Eventually, various highly active oxygen species can oxidize organic compounds of cell to CO_2 and H_2O. Hence, TiO_2 can decompose common organic matters in the air such as odor molecules, viruses and bacteria.

3.3. Silver Nanoparticles (Ag NPs).

The silver ions or silver based nanomaterials are popularly known for their wide spectrum antimicrobial agent against bacteria, fungi and viruses has been reported by Rai *et al.*(2009). There are several forms of silver such as metals, sulfadiazine and nitrates which been used for the water purification and disinfection of medical devices. Ag-based nanomaterials are commonly used in the field of medicine to treat wound, burns and infectious diseases (Avalos *et al.*2014; Elliott, 2010; Aditya et al., 2013). The antimicrobial potential of silver and silver based nanomaterials has been well reported by Rai *et al.*(2009) the effect of size, shape and mechanism of action is explored well by them in detail. Panacek *et al.*(2006) have shown that small diameter of Ag NPs has more antimicrobial effect than large sized particles. Furthermore, bacteria are less prone to develop resistance against silver than against conventional antibiotics was proved by Leid *et al.*(2012) and Chernousova and Epple (2013). The concurring antimicrobial effect of silver nanoparticles with antibiotics on Gram positive and negative bacteria was explored in detail by Khurana *et al.*(2014) and Shahverdi *et al.*(2007). Nevertheless, despite the ongoing debates, silver based nanomaterials are perhaps the most promising antibacterial metal nanoparticles.

Silver nanoparticles likely have multiple mechanisms of antibacterial activity. It has been used historically as a natural metal against microbes. Ag NPs were shown to inhibit growth of Gram-negative species of bacteria like Vibrio cholerae, E. coli, P. aeruginosa and Salmonella typhi by agar diffusion method. There are number of mechanism by which Ag NPs show the bactericidal effect. Firstly, membrane permeability was thought to be effected by the presence of large number of NPs inside the bacteria. Due to the interaction of Ag NPs with the bacterial membrane and intracellular proteins mostly sulfur-containing membrane proteins and phosphorus-containing DNA obstruct with process of cell division and leads to cell death. After exposing to the same concentration of silver ions to both gram positive and gram negative bacteria in a comparison study both species exhibited condensation of DNA, cell membrane separation from the cell wall, and cell wall damage (Feng et al., 2000). These characteristics are indicative of distressed bacteria that are being damaged; silver ions were also detected within the cytoplasm of each bacteria type. From these observations the role of silver ion in antibacterial mechanism is clear. Pal et al., (2007) has compared the antimicrobial properties of different shapes nanostructures of silver and concluded that truncated triangular silver nanoplates and nanospheres were more effective at reducing E. coli viability than silver nanorods or ionic silver. Silver is a safer in comparison with several organic antimicrobial agents that have been avoided owing to the risk of their harmful effects on the human body. Silver has been described as an 'oligodynamic' because of its bactericidal property and owing to its presence in variety of commercial products. Its curative property has been proven against a broad range of microorganisms. Over 650 disease causing organisms inside body even at low concentrations of silver showed best effect. Silver is also known to inhibit a number of oxidative enzymes such as yeast alcohol dehydrogenase, the uptake of succinate by membrane vesicles and respiratory chain of Escherichia coli, causing metabolite efflux and interfering with DNA replication. Ag can combine with the cell wall, cytoplasm and the cell envelope. The attachment of silver ions or NPs to bacteria is due to the electrostatic interactions with negative charge of bacterial cell wall and it is one of the mechanism by which silver ions ruptures the bacterial cell membrane and causes cell death. Usually, low concentrations of Ag^+ induce a huge proton leakage through the bacterial membrane and causes cell death. Likewise, nanomolar concentration of Ag NPs can be efficient while Ag ions are required at the micromolecular level. Kim *et al.*(2007) proposed that the antimicrobial mechanism of Ag NPs is related to the formation of free radicals and successive free radical-induced membrane damage. They confirmed that antimicrobial activity of Ag NPs and silver nitrate was influenced by N-acetylcysteine (NAC).

They have also studied that free radicals might have been derived from the surface of Ag NPs were responsible for the antimicrobial activity through ESR (electron spin resonance).

3.4. Antibacterial Mechanism of Action of Ag NPs.

The short explanation of antimicrobial mechanism can be explained as follows: In general, metal ions demolish or pass through the cell membrane and bond to the sulfdryl (–SH) group of cellular enzymes. The resulting critical decrease of enzymatic activity causes metabolisms change in microorganism and inhibits their growth, equal to the cell's death. The metal ions also catalyze the production of oxygen radicals that oxidize molecular structure of bacteria. The following reaction shows formation of reactive oxygen species:

$$H_2O + 1/2\ O_2 \xrightarrow{\text{Metal ion}} H_2O_2 \rightarrow H_2O + O$$

The produced reactive active oxygen diffuses from fiber to the surrounding environment and does not require any direct contact with bacteria. Thus, metal ions inhibit the multiplication of micro-organisms. Silver ions can lead to denaturing of protein and cell death because of their reaction with nucleophilic amino acid residues in proteins, attach to amino, sulfhydryl, imidazole, carboxyl and phosphate groups of membrane or enzyme proteins. By forming R–S–S–R bonds respiration blocking and cell death may also be caused. Kumar *et al.*(2004) have proposed these bonds may be formed via reaction between silver in oxidic form and sulfhydryl (–S–H) groups.

3.5. Aluminum Nanoparticles (Al NPs).

Aluminum nanoparticles have a wide range of applications in industrial as well as in the personal care products. Ansari *et al.*(2014) had studied the detail mechanism action of aluminum nanomaterial for E. coli which is ultimately leading to cell death. It is not clear if Al2O3 NPs are appropriate for antibacterial treatment. Firstly, their bactericidal effect is relatively mild and high concentrations are required to show the effect. Or, combination of other nanostructured materials such as Ag, Cu or ZnO is to be needed. Secondly, there is an ability to promote horizontal transfer of multi resistance genes mediated by plasmids across genera. Sadiq *et al.*(2009) have studied the growth-inhibitory effect of Al2O3 NPs over a wide concentration range 10–1000 μ g/m on Escherichia coli. Differences are observed between the treated and untreated cells structures when explored by using Fourier transform–infrared spectroscopy. Alumina NPs have exhibited a mild growth-inhibitory effect, only at very high concentrations and it is attributed to surface charge interactions between the particles and cells. It is possible that the free-radical scavenging properties of the particles might have prevented cell wall disruption and drastic antimicrobial action. Alumina is having a corundum-like structure, and it is thermally stable over a wide range of temperature. They carry a neutral charge on its surface on its surface at near-neutral pH. Due to the electrostatic interaction between the E. coli (negatively charged) and the particles (positively charged) results in the adhesion of the NPs on the bacterial surfaces (Li and Logan 2004). The rate of adhesion of NPs is directly propositional to the concentration of NPs which ultimately results in decrease in growth. Along with electrostatic interaction, hydrophobic interactions and polymer bridging may be responsible for the phenomenon of bacterial adhesion onto the particles. The antimicrobial property of these metal oxides is attributed to the generation of reactive oxygen species (ROS) which causes the disruption of cell wall and consequently leading to cell death (Rupareli *et al*., 2008). However, alumina NPs may act as free radical scavengers and are able to rescue cells from oxidative stress-induced cell death. This phenomenon is appears to be dependent upon structure of the particle but independent of its size within the range of 6–1000 nm.

Like TiO_2 NPs, Al_2O_3 in combination with silver shows enhanced inhibitory effects on the microbes. Bala *et al.*(2011) synthesized the titania– silver (TiO_2–Ag) and alumina–silver (Al_2O_3–Ag) composite NPs by wet chemical method and their surfaces were modified by oleic acid to attach the silver NPs. The antibacterial evaluation was performed by disc diffusion assays against E .coli and S. epidermidis showed that Al_2O_3–Ag and TiO_2–Ag nano-composites had enhanced antimicrobial activity.

3.6. Zinc oxide Nanoparticles (ZnO NPs).

ZnO NPs are having antimicrobial activity against wide range of microorganisms. The antimicrobial activity of these NPs is dependent on the concentration as well particle size of the synthesized NPs was proposed by Palanikumar *et al.*(2014). Vigneshwaran *et al.*(2006) and Becheri *et al.*(2007) have shown that ZnO NPs are of relatively low cost and effective in size dependency, white appearance and UV-blocking property. ZnO is also used to strengthen polymeric nano-composites. ZnO NPs also exhibit enhanced wear resistant phase and anti-sliding phase in nano-composites as a result of their high elastic modulus and strength. These NPs produce the largest amount of hydrogen peroxide which is attributed for antibacterial effect. So far, the mechanism of antibacterial activity of ZnO NPs not fully understood. Zinc ions are known to inhibit the multiple processes in bacterial cell, for example trans-membrane proton translocation, glycolysis and acid tolerance Phan *et al.*(2004).

The zone of inhibition in well diffusion assay clearly indicates the presence bactericidal effect of ZnO NPs by disrupting the cellular membrane of bacteria. It was noted by Zhang *et al.*(2007) that, rupture in cell membrane of bacteria is may be due to surface activity of contact of ZnO NPs on the cell membrane. The contact between bacterial cell wall and NPs is initiated due to presence of surface charges on the metal oxide NPs (Stoimenov *et al.*2002) and the electrostatic interactions which is present between both of them (Neal *et al.*2008). These interactions were further confirmed by Zhang *et al.*(2010) by the use of electrochemical measurements. After contact of bacterial cell membrane with ZnO NPs there is a generation of high rate of surface oxygen species from the NPs which ultimately leads to the death of bacteria by chemical interactions between hydrogen peroxide and membrane proteins Zhang *et al.*(2010). This damage to the cell membrane directly leads to the leakage of cytoplasmic contents Sharma *et al.*(2010), proteins, minerals and genetic material viz. DNA and RNA, causing the cell death. It was observed that there is difference in bactericidal effect in the concentration which may be due to the difference in generation of H_2O_2 in metal oxide and this generation was linearly proportional to their metal oxide NPs concentration. Yamamoto *et al.*(2000) have studied the variation in concentration of H_2O_2 under different concentration of ZnO NPs. The size of metal oxide is found to play a very essential role in determining the antibacterial activity. Ramamoorthy *et al.*(2013) have shown that smaller size of NPs have higher bactericidal activity. Higher bactericidal activity of smaller sized NPs may be due to large surface area to volume ratio and surface activity of metal oxide. Yamamoto *et al.*have proved that, the generation of H_2O_2 depends strongly on the surface area of ZnO NPs which results in more oxygen species on the surface and have higher antibacterial activity of the smaller NPs Yamamoto *et al.*(2000). The ZnO NPs have been widely studied by Brayner *et al.*(2006) and Jones *et al.*(2008) for antibacterial activity with different pathogenic and nonpathogenic bacteria. The ZnO NPs have been widely used in the field of cosmetics, drug carriers and filling materials because it is nontoxic, biocompatible and biosafe (Rosi and Mirkin, 2005). There are several topical antimicrobial agents which have been utilized in the area of wound care in order to prevent the wound from the microbial infections.

Behnajady *et al.*(2006) proved the potentiality of ZnO for removing dye from textile effluent under UVC light. The TiO_2 and ZnO is an n-type of semiconductor, only these two metal oxides have sufficient stability on photo-excitation state. The band gap energy of ZnO is 3.37 eV and their stability can be justified with decreasing the possibility of electron–hole re-combination. ZnO powders can also absorb infra-red light and infra-red electromagnetic wave with 5–16.68 dB in the range of 2.45–18GHz. ZnO is also utilized to strengthen polymeric nano-composites and as a consequence of their high elastic modulus and strength they used for enhancement wear resistant phase and anti-sliding phase in composites as a consequence of their high elastic modulus and strength.

Li and colleagues (2007) have reported the durability of antibacterial activity of ZnO NPs functionalized cotton fabric to sweat. The cotton fabrics at a concentration of 11 g/L ZnO has been treated and padded them to 100% wet pick-up. Finally, durability of antibacterial activity of the finished fabric in acidic, alkaline and inorganic salt artificial sweat solution has been evaluated. For producing acrylic composite resin tetrapod-like NPs of ZnO was also been utilized by Xu. *et al.*2003. Pan *et al.*(2001) have produced ZnO nanowires, nano-belts, nanotubes and nanocages. ZnO nano-rod on cotton fabric samples has been grown through the dip-pad-cure process by Xu and Cai (2008).

ZnO NPs have applications not only for medicinal purpose but it is also used in food packaging systems by inhibiting certain food borne pathogens. ZnO have a good potential to be coated on plastic films to male antimicrobial packaging against bacteria such as E. coli and Staphylococcus. Furthermore, they are stable under harsh conditions and comparatively low toxicity combined with the potent antimicrobial properties favors their application for being an antimicrobial. ZnO NPs have minimal effect on human cells, which recommend them to be used in agricultural and in food industries. The antimicrobial activity of ZnO NPs have been reported by Jiang *et al.*(2009) against the food related bacteria like Escherichia coli, Bacillus subtilis and Pseudomonas fluorescens. The strong antimicrobial activity of ZnO NPs in which NPs could completely lyse the food borne pathogenic bacteria like Staphylococcus aureus and Salmonella typhimurium is studied by Liu *et al.*(2009). Jin *et al*., (2009) has reported that ZnO NPs of 12 nm diameter inhibits the growth of E. coli by process of disintegrating the cell membrane and by increasing membrane permeability. It is supposed that with decreasing particle size, number of ZnO powder particles per unit volume of powder slurry increases resulting in increased surface area as well as generation of H_2O_2.

3.7. Copper Nanoparticles (Cu NPs).

Cu NPs have high potency for bacterial cell filamentation and cell killing. Although CuO NPs have shown antimicrobial effect as reported by Ren *et al.*(2009) the efficacy of these NPs were obtained to be less to that of other metal oxide NPs. Pape *et al.*(2002) have reported that CuO NPs also show less antibacterial activity is than that of silver NPs. Enhancement in the electrical conductivity has been reported by Wel *et al.*(2008) after coating of Cu on fabrics. CuO is monoclinic structure with a semiconducting property. It exhibits a variety of potentially of physical properties such as superconductivity, high temperature, spin dynamics and electron correlation effects. CuO is simplest member of the copper family and therefore it finds wide range applications. CuO crystal also has photovoltaic or photocatalytic properties and photoconductive functionalities. Despite of all these functionalities less information is available on the antibacterial activity of CuO NPs.

CuO is cheaper than Ag and Au and it easily mixes with other polymers to form nanocomposite along with advantages of being chemically and physically stable it has been widely used in variety of applications (Xu *et al.*1999). CuO NPs can be prepared with extremely high surface areas and unusual crystal morphologies that can be further show its useful potential as an efficient antimicrobial agent. These NPs are also effective in killing bacterial pathogen and can be utilized against hospital-acquired infections. However, high concentration of CuO NPs is required to achieve the bactericidal effect. Moreover, time-kill experiment results suggest that Gram-negative strains showed a greater susceptibility to CuO NPs combined with Ag NPs. However, in comparison to contact killing ability the release killing ability has shown more effect against MRSA strains. Thus, we can conclude that by the release of ions to local environment is mandatory for optimal antimicrobial activity. Cu NPs have a high antimicrobial activity against B. subtilis, may be due to greater abundance of carboxyl and amines groups on cell surface of B. subtilis and greater affinity of copper towards these groups. The released Cu ions may also interact with DNA molecules and intercalate with nucleic acid strands. Cu ions inside bacterial cells also disrupt biochemical metabolic processes. The exact mechanism behind bactericidal effect of Cu NPs is not clear. The schematic representation of various organic-inorganic nanostructure materials is shown in Figure 1.

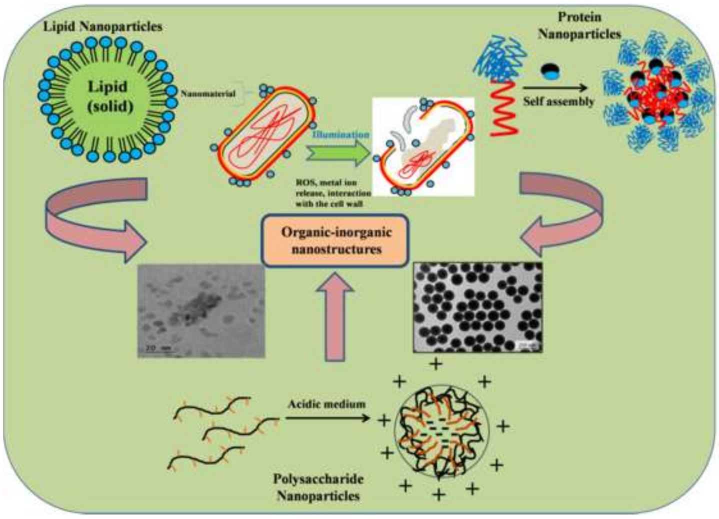

Figure 1. The schematic representation of organic-inorganic nanostructure materials.

3.8. Magnesium oxide Nanoparticles (MgO NPs).

MgO NPs are advantageous antibacterial metal oxide that has bactericidal activity. They were reported to exhibit efficient antimicrobial activity against bacteria both Gram-positive and Gram-negative, viruses and spores. The benefit of MgO NPs in comparison to other metal oxide NPs is that it can be prepared from available and economical precursors and solvents. Mg can be used in various nanomaterial in the form of MgO or MgX2 for ex. MgF_2 (Pelgrift and Friedman, 2013). Additionally, to inducing ROS Mg-containing nanomaterial may directly inhibit vital enzymes of the bacteria.MgF_2 nanomaterial were found to prevent biofilm formation of E. coli and S. aureus. MgF_2 NPs attach to penetrate into the cells. They cause disruption in the membrane potential, induces membrane lipid peroxidation and after internalization it interacts with chromosomal DNA. Because of all these beneficial properties MgF2 NPs can be coated to avoid biofilm formation. MgO prepared by an aerogel procedure (AP-MgO) yields polyhedral and square shaped NPs having around 4 nm diameters and arranged in porous structure and pore volume. A fascinating property of AP-MgO NPs is their capacity to adsorb, to retain for a long time significant amounts of elemental bromine and chlorine.

AP-MgO nanoparticles are found to possess many properties that are desirable for a potent disinfectant. As, they have enhanced surface reactivity and high surface area, the nanocrystals adsorb and carry a high load of active halogens. The small size allows them to cover the bacteria cells to a high extent and bring halogen in an active form in high concentration in proximity to the cell. Standard bacteriological tests have shown that MgO NPs have excellent activity against E.coli and Bacillus megaterium and a good activity against spores of Bacillus subtilis. The bioactivity of AP-MgO/X2 NPs is due to the positive charge they have in water suspension, opposite to those of the bacteria and spore cells, which enhances the total bactericidal effect. Studies by microscopic techniques (Atomic force and electron microscopy) revealed that halogenated MgO has a very strong influence on microorganisms and their membranes. In general, chlorine and bromine treated MgO NPs have a stronger and faster effect on the killing action of both bacteria and spores.

3.9. Gold Nanoparticles (Au NPs),

Gold NPs are known as a novel therapeutic for biomedical application. Because of their potent antibacterial effectiveness against acne or scurf they are extensively used in soaps and cosmetic products. They can remove waste materials from the skin and control sebum. Zhang *et al.*(2008) have proposed the inhibit growth and multiplications of different microbes with Au NPs efficiently against both Gram positive as well as Gram negative and fungi. Au NPs have also been used as a carrier core coated antibiotics like gentamycin, streptomycin and neomycin. Au NPs was produced by Yonezawa and Kunitake (1999) stabilized with sodium (3-mercaptopropionate) (MPA) via reduction of HAuCl4. The result that Au nano-composites have an strong antibacterial efficiency against both gram negative and gram positive bacteria, viz. Pseudomonas aeruginosa, E. coli, Micrococcus luteus and Staphylococcus aureus. Metallic NPs may change the metabolite pathway and the release mechanism of bacterial cells. Au/drug nano-composites showed a better antibacterial efficiency. Au NPs have also been loaded inside the liposome which lead to an increase in the fluidity and permeability of barrier of the lipid and provide a kind of thermally sensitive liposome. So, these systems have potentially been suggested for controlled release delivery system at particular temperatures.

Since 2500 B.C. in the Chinese medical history gold has been used therapeutically. In the Indian Ayurvedic medicine red colloidal gold is used for rejuvenation and revitalization and named as ‘Swarna Bhasma’. In the 16th century gold was suggested for the treatment of epilepsy, 19th century gold was used in the treatment of syphilis. The gold based therapy for tuberculosis was introduced in 1920s by Robert Koch. The main clinical uses of gold compounds are in the treatment of rheumatic diseases including juvenile arthritis, psoriasis, discoid lupus erythematosus planindromic and rheutamitism. Au NPs are exploited in organisms because of their biocompatibility with body. They are considered to be biologically inert however can be engineered to acquire photothermal or chemical functionality. Au NPs can be combined with photosensitizers for photodynamic antimicrobial chemotherapy. On near infrared (NIR) irradiation the gold based nanomaterials, Au nanocages, Au nanospheres and

Au nanorods with characteristic NIR absorption can destroy cancer cells and bacteria via photo thermal heating. Light absorbing Au NPs conjugated with specific antibodies have also been exploited to photothermally kill the bacteria Staphylococcus aureus by using laser. Norman (2008) has reported the functionalization of the Au NPs as photothermal agents for hyperthermically killing pathogens. The further efficacy of the antibacterial activity of Au NPs can be increased by adding antibiotics. Similarly, the antimicrobial activity of antibiotic vancomycin was enhanced on coating with Au NPs against vancomycin resistant enterococci. Au NPs binds to the DNA of bacteria and inhibit the uncoiling and transcription of DNA. The Au NPs can be used for coating onto a variety of surfaces for example fabrics for handling of wounds, implants and glass surfaces to maintain hygienic conditions in hospitals, home and other places.

3.10. Iron oxide Nanoparticles (Fe_3O_4 NPs).

Fe_3O_4 NPs represent an additional class of antimicrobial materials that are being utilized for their use in health care applications. These materials can be tailored to introduce antimicrobial properties when synthesized as nanosize particles. Fe_3O_4 NPs demonstrate anti adherent properties and significantly reduces the growth of both Gram-negative as well as Gram-positive bacterial colonization. Au NPs and nanorods have been reported to be bactericidal when photothermally functionalized. Fe_2O_3 were shown to reduce the growth of S. aureus viability. It is having a chain-like structure with a length of 100–200 nm.

The antibacterial mechanism of Fe_2O_3 NPs was thought to be related to the ability of NPs to penetrate inside cell and to generate reactive oxygen species. It was observed that high concentration of NPs viz. 100 µg/mL, 1 mg/mL and 2 mg/mL leads to the increase in number of dead cells which has been estimated by live/dead assay. Antibacterial activity was again ascribed to increasing oxidative stress and bacteria membrane interference. The negative zeta potential of NPs, and minimal electrostatic interactions with negative bacteria surface charges, explains why there is need of relatively high concentrations of NPs for an antibacterial effect. Fe_2O_3 NPs are of particular interest not only because of their natural antibacterial properties, but also due to their super ¬paramagnetic properties. This allows particles to be directed inside the body with a magnetic field, possibly after coating with some type of antimicrobial agent.

3.11. Nitric oxide Nanoparticles (NO NPs).

Nitric oxide nanomaterial represents a promising antibacterial compound owing to the low risk of possible resistance. NO is involved in multiple mechanisms of antimicrobial activity. The antibacterial property of nanomaterial is size and shape dependent. Smaller the size of the particles with a higher will be its efficiency to kill bacteria. NO is an endogenously produced molecule and it is involved in various physiological functions. Despite of all its advantages, its clinical value is limited mainly because it is extremely reactive. The NO nanomaterial differs from other metal oxides because it is specifically affecting reactive nitrogen species (RNS), rather than ROS. NO is effective in killing methicillin resistant S. aureus which causes skin infections and it aid in enhancement in wound healing process of normal and diabetic mice. NO nanomaterial is also effective in biofilm elimination of multiple bacterial species.

The effectiveness of NO as a wide spectrum, versatile antimicrobial has stimulated an intense race to translate our vast understanding to the bedside. Numerous NO coated biomaterials are under progress which has confirmed the decrease of biomaterial-associated infections. NO-releasing carbon-based coatings when added to polypropylene meshes, reduces risk of infectious diseases or complications after abdominal wall surgeries and had significant bactericidal effect on in-vitro biofilms of S. aureus, viruses and pathogens. Likewise, coating medical grade silicone elastomer implants with a sol-gel-derived film is capable of storing and releasing NO in a murine model. It has been also resulted that there is 82% reduction in the number of infected subcutaneous implants inoculated with S. aureus prior to wound closure. Additionally, NO releasing nanoparticles holds remarkable potential as a suitable drug for topical treatment in cutaneous and subcutaneous wounds (Nablo *et al*., 2005). NO have an ability to reduce bacterial load and accelerate wound healing process inspired the widespread development of NO in a range of vehicle formulations.

3.12. Graphene.

Graphene is widely used in the field of nanomedicine specifically for biosensors and diagnostics. An increasing number of studies have been reported on the potential use of graphene for drug delivery applications. These graphene related materials exhibit unique electronic, thermal and mechanical properties and hold great promises in potential applications, such as supercapacitors, conductive thin films, nanoelectronics, nanosensors and nanomedine. Graphene oxide (GO) is usually used as drug carrier, frequently after additional surface modification. The antibacterial activity of graphite (Gt), graphene oxide (GO), graphite oxide (GtO) and reduced graphene oxide (rGO) toward E. coli was compared by Liu *et al.*(2011). The antimicrobial potency of these materials decreased in order GO > rGO > Gt > GtO under similar concentration and incubation conditions. Graphene nanosheets were furthermore demonstrated to disrupt cell membranes, as no production of reactive oxygen species was detected. Depend on this, a three-step antimicrobial mechanism was proposed, including initial cell deposition, causing membrane stress by direct contact with sharp nanosheets, in turn initiating superoxide anion in dependent oxidation. Liu *et al.*(2012) have studied the antibacterial activity of GO sheets.

These sheets are differing in lateral size by more than 100 times and found that larger GO sheets to display stronger antibacterial activity than smaller ones against E. coli. Sawangphruk *et al.*(2012) has reported that graphene oxide possesses antifungal properties and inhibiting mycelial growth for F. oxysporum, A. niger and A. oryzae. On the other hand, graphene can be utilized as carrier for other antimicrobial agents. Nguyen *et al.*(2012) have investigated graphene decorated with Ag nanoparticles. It was noticed that highly dispersed NPs of varying shape and size were adhered to graphene sheets. These composites showed higher antibacterial activities against the bacterial species like E. coli, L. anguillarum, S. aureus and B. cereus. Likewise, Ag NPs were deposited on GO and inhibition of growth kinetics was noted particularly for P. aeruginosa by Das *et al.*(2011). Carpio *et al.*(2012) have synthesized PVK-graphene oxide (GO) nanocomposite studied the antimicrobial effects on both planktonic microbes and biofilms.

4. APPLICATIONS OF ANTIMICROBIAL NANOSTRUCTURES FOR HEALTH CARE

4.1. Medical Applications of Antimicrobial Nanostructures.

Nanostructure materials have wide range of applications such as wound dressing, tissue engineering, artificial organs, stem cell scaffolds, dentistry and photo catalytic antimicrobial therapy and so on. Various medical devices have been coated with the nanostructured antimicrobial material to diminish microbe adhesion and biofilm formation and to further reduce the risk of microbial infections. Nanostructure antimicrobial material offers vast opportunities and applications in health care as well in biomedical implants coating, including medical devices catheter, stents and contact lenses. The use of Ag NPs provides antimicrobial activity to orthopedic, bone and dental implant without affecting the cytotoxic and mechanical characteristics. The drug delivery based on an antimicrobial nanostructure improves the therapeutic efficacy and safety of the drug and bioactive compounds, since they are delivered at the targeted site with a controlled release rate. These nano-delivery systems can be tailored for its shape, size, controlled composition and morphology.

4.2. Advantages of Nanomaterials in Wound Care.

The new emerging trend of nanotherapies represents a new class of treatment which is currently available to enhance the medical treatments, improve the standard care and prognosis for diseases like wound healing. An increasing number of products emerging from the application of nanotechnology to the science of wound healing are currently under clinical investigations. The current nanoscale strategies, both the carrier, drug related and scaffold can target the different phases of wound repair mechanism. In recent years, nanomedicine has experienced a progressive expansion i.e. its great potential has attracted considerable interest. Likewise, the researchers have also gained knowledge at the molecular and cellular level which helps them to develop new therapeutic strategies which can act directly on cellular and sub-cellular events during the healing process. By the use of nano-therapies it has been possible to overcome the dimensional barrier of currently used remedies for wounds, to reach the target site by exerting the therapeutic action of nanomaterial at the site of chronic condition. Nano-carriers possess a huge potential, as nanoparticles-based delivery systems can be highly advantageous to augment the therapeutic power of biological and synthetic molecules. Nonetheless, the therapeutic properties of these NPs need to be carefully assessed before introducing them into clinical trials or practice. Particularly, the release of active peptides may possibly cause interferences with some biological functions and cellular processes. In order to reach at targeted site NPs are incorporated with the site specific ligands. Additionally, a wide variety of biomaterials have been prompted to meet the specific biological requirements G. Wang and H. Uludag *et al.*(2008). This could be particularly critical for tissue regeneration, where the biomaterial properties could supplement the reparative process, or delay it due to undesirable attributes of the material. The innovative potential offered by nano-therapeutics applied to wound healing involves the need to develop the international standards on their biocompatibility and toxicity. To prove beneficial a safe and targeted use is required in order to treat the wounds.

4.3. Nanobiomaterials for Ulcer Management.

The significant features which support the application of nano-biomaterials in wound healing are; (i) their low dimensionality (1-100 nm) because of which they possess a high surface to volume ratio; and (ii) the variety of shapes in which these materials can be prepared viz. NPs, nanocrystals, nanotubes, nanowires, nanofibers and quantum dots, etc. which gives freedom to choose application specific nanomaterial. Moreover, nanomaterials can be used as filling materials providing mechanical strength and therapeutics advantages, supported with antimicrobial and antioxidant properties simultaneously. In the tissue repair process the advantages of these nanomaterials are their suitability to make them into thin films. Besides, their diameter and pore size are of nearly identical with those of natural tissue fibers, and their mechanical strength and light weight prevents compression of wounded tissue in situ. These properties offer an exclusive advantage in the healing process, particularly when there is a need to cover a large surface area to protect the skin and stimulates a rapid healing, for example in chronic wounds and burn cases. A broad variety of nanoscale materials reported in literature have found application in wound care. Nano-biomaterials also aids in loading of drug molecule simply by controlling porosity of nanofiber or nanoparticles structure (Rohiwal *et al.*2015 (a); Rohiwal *et al.*2015 (b); S. S. Rohiwal and S. H. Pawar, 2014) which will release the drug or topical agents at the wounded site. Additionally, nanofibers are designed specifically to offer mechanical support coupled with curative payoff as wounded tissue frequently lose epidermal layer that constitute a mechanical barrier. The high surface-to-volume ratio and wide range of availability of pore size distribution gives a framework for growth and proliferation of cells in in vitro on artificially designed tissue scaffolds.

Biodendrimers, hydrogels, electrospun nanofibers and different polymer therapeutic conjugates have been used extensively for drug delivery. Additionally, the other supplements such as vitamins, antioxidants and nutrients also aid in wound healing processes was reported by Singh *et al.*(2010). The schematic representation of applications of an organic-inorganic nanostructure material is shown in Figure 2.

Figure 2. The schematic representation of applications of organic-inorganic nanostructure materials.

4.4. Nanomaterials for Textile Modification.

Nano-structured organic-inorganic material contributes very important role in textile industry particularly for producing high performance textiles. This paper reviews the application of nano-structured organic-inorganic materials for anti-bacterial modification of polymeric materials and textile. Due to their unique properties of metallic and inorganic nano-structured materials are developed for surface modification of textiles fabrics. In the textile industry there are two challenging tasks i.e. fiber and film processing of molding polymeric materials. Additionally, the bulk modification of constant multi-filament yarns is a very sensitive process. Several researchers have focused on the bulk modification of filament yarns by varying the concentrations of nanocomposite fillers using the procedure of melt mixing of different silver based fillers like silver/zinc and Ag/TiO_2 and polymer powder of three different mixing compositions have proved its remarkable potential for mass production when performed on a pilot plant scale (Dastjerdi et al., 2008; Dastjerdi et al., 2009; Dastjerdi et al., 2010; Genzer and Efimenko 2006). This method is an environmental-friendly, high-quality and easily adaptable industrial modification method. Nonetheless, there are some limitations it is restricted to synthetic fiber and particles located in the central part of the filaments not incorporated in the antibacterial performance. Additionally, similar kind of problem is observed when there is reduction of metallic salts to nanoparticles impregnated into the bulk polymeric matrix. Meilert *et al.*(2005) have used poly carboxylic acids as spacers for attaching TiO_2 NPs to the fabrics.

Wang *et al.*(2007) have utilized the argon plasma grafting NPs on wool surface. Similarly, Yuranova *et al.*(2003) have successfully deposited NPs from their metallic salt solution on the surface pretreated with RF-plasma and vacuum-UV. There are so many methods which are utilized for the modification of the polymeric substrate such as sol–gel processing (Mahltig *et al.*2005; Daoud *et al.*2004; Zhang *et al.*2009), sputtering of NPs during plasma polymerization (Hegemann *et al.*2007), loading of NPs into liposomes (Park *et al.*2005, Park *et al.*2006), use of nanoporous structure of cellulose fiber as a nano-reactor for in situ synthesis of metallic NPs (He et al., 2003) etc.

Potiyaraj *et al.*(2007) have proposed a process to grow Ag NPs via successive treatment of $AgNO_3$ and AgCl. Similarly, Yuranova *et al.*(2006) have utilized SiO_2 as a binder for TiO_2 cotton surfaces modification, whereas, Jiang *et al.*(2005, 2007) have utilized the chemical pleating for functionalization of fabrics with NPs. Fabrics have been coated with functionalized and dispersed CNTs in hydrophilic polyurethane (HPU) solution by Mondal and Hu (2007). Montazer *et al.*(2010) have prepared the photo-stabilized wool fabric with nano-TiO_2. Several preparatory steps are needed like neutralization, functionalization, curing, washing, drying, final treatment and other processing for the stabilization of inorganic nano-structured materials on the textile surfaces. These processing are expensive and very lengthy for large scale manufacturing and/or are hazardous for the environment because of the use of many organic solvents or chemicals.

The majority of them cause a reduction in softness, tensile properties, appearance, and abrasion resistance, may affect other properties of textiles even it may lead to color changing. Other than economical disadvantages like being costly and time-consuming, the remains of free radical during usage on clothing can lead to health risks for people. The usage of acrylic binder for fixation of zinc oxide/soluble starch nano-composite particles on cotton fabrics lowers down the comfort of cloth and decreases the abrasion resistance (Vigneshwaran et al., 2006).

Similarly, researchers have also used polysiloxane which is having many unique properties like good resistance against oxygen radicals, environmental friendliness, blood and biocompatibility, softness, good releaseability, comfort, dimension stability, flexibility, good durability, water repellency and anti-pilling (Rolland *et al.*2004; Shah et al., 2004; Kim et al., 2001; Oh et al., 2002; Kweon, 1998, Chung et al., 2009; Kim et al., 2006). By applying the optimum mixture of nano-structured material these functional coatings are prone to key promotion in durability and performance for multi-functional and technical textiles.

4.5. Antimicrobial Nanostructures Materials for Food Packaging.

Antimicrobial function of some nanostructured materials has long been renowned and utilized in various industries, including the packaging and food sector. The advantageous properties (particle size, surface area and reactivity) of these nanostructured antimicrobial materials are particularly effective to inactivate microorganisms. Generally used or tested nanocomposite antimicrobial materials include metal oxide like titanium dioxide, magnesium oxide, zinc oxide, metal ions (silver, gold, platinum and copper). Natural biopolymers such as chitosan and natural antimicrobial agents viz. carvacrol, thymol, isothiocyanate, nisin, antibiotics, enzymes like lysozyme, peroxidase and synthetic antimicrobial agents and organic acids like EDTA, quaternary ammonium salts, benzoic, propionic and sorbic acids are also used to offer antimicrobial function. The novel organic-inorganic nanostructures packaging materials with antimicrobial functions have a great potential for an active food packaging.

There are chances of contamination in many food products by microorganisms which causes infections, and serious illness, they also reduces the shelf life of food. Conventionally, various chemical and physical food preservation methods have been utilized in the food industry in order to reduce risk of food spoilages, extend shelf-life and to maintain food quality. But due to increase in food demand by the customers the minimally processed and ready-to-eat fresh foods have been increased in the recent years. Therefore, to secure human health and to avoid contaminations researchers investigated an alternative technology for food providing safety and healthy food and new food packaging technologies are constantly being developed to meet up this goal. The packaging with the help of antimicrobial is a promising active food packaging technology which is formed by incorporation or immobilization of antimicrobial agents into the food packaging system.

There are various natural as well as synthetic polymeric materials were used as matrix system. Nanostructured inorganic materials, like metallic oxides, nanoclays (NCs), or nanosized metals, are more stable and possess high area surface-to-volume ratio and increased surface reactivity with potent antimicrobial effect. Thus, a variety of nanosized antimicrobial materials have gained special attention in the food packaging division to expand effective antimicrobial nanocomposite packaging systems.

Antimicrobial nanostructured packaging materials appear to have a very clear future for a broad range of applications in the food and biomedical industries, particularly for the innovative active packaging system. Nanomaterials are also being utilized in food packaging systems as antimicrobial agents, oxygen scavengers, fillers and nanosensors. Likewise, incorporation of nanomaterials into the packaging system can improve the film flexibility, degradability, gas barrier properties, mechanical property, and heat stability.

The major functional properties of packaging system can be implemented and extended by nanomaterials. The polymer-based nanocomposite has potential properties to be used in variety of food packaging applications viz. cheese, processed meats, cereals, confectionery, boil-in-bag foods, in addition to, in extrusion coating applications for fruit juices and dairy products (Smolander, 2003). Additionally, polymeric nanocomposites with antimicrobial property have a huge potential in food packaging industry for controlling undesirable microorganisms. By means of the incorporation of active molecules, such as antimicrobial compounds either in or coated onto the packaging materials microorganism growth can be controlled (Appendini, P. and Hotchkiss, J. H., 2002, Suppakul et al., 2003, Nigmatullin et al., 2008).

Nanostructured antimicrobial materials are mostly effective, because of the enhanced surface reactivity and high surface-to-volume ratio of the nanosized antimicrobial agents which are making them able to control growth of microorganisms. A variety of nanostructure or nanocomposite materials with antimicrobial functions are beneath development, for example organically modified nanocomposite with quaternary ammonium salts, nano-sized metal and metallic oxides.

The most important food applications for antimicrobial nanostructure films include fish, meat, bread, poultry, fruits, cheese and vegetables (Kerry *et al.*2006; de Oliveira et al., 2007; Moreira et al., 2011). Also, smart nanocoatings as well as self-cleaning materials that isolate pathogens, destroy bacteria, or which fluoresce under certain conditions are under improvement for the packaging applications (Carneiro et al., 2011).

5. SUMMARY AND PERSPECTIVES

Organic - inorganic antimicrobial nanostructured materials have created new interesting applications in several fields due to their undeniably unique properties. On one hand, these demonstrated applications have already led to the production of novel materials for practical use; these successes have given an impetus, on the other hand, to develop several yet unexplored antimicrobial materials in the nanoscale range, for health care, in the coming years. Of course, care has to be taken that the antimicrobial nanostructure materials to be developed in future do not result in development of resistance. Rather, the future research must strive to develop novel nanocomposite materials which can aid to control the production of microbes.

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6. CONFLICTS OF INTEREST

The authors declare no conflict of interest.