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Toxicity of Graphene Based Nanomaterials Towards Different Bacterial Strains: A Comprehensive Review

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Abstract: Nanomaterials including graphene and its derivatives have attained immense popularity among scientific community due to their unique properties. Graphene (G), graphene oxide (GO), reduced graphene oxide (rGO) and their nano-composites have shown to possess enormous potential in the field of nanomedicines. Graphene family nanomaterials (GFNs) have extensively being used in different fields including antibacterial formulations. Mechanisms underlying the toxicity of GFNs involve the interaction of sharp edges of graphene derivatives with the bacterial cell wall, charge transfer and formation of huge number of reactive oxygen species. The use of graphene derivatives including GO-Ag nanocomposites, polydopamine-graphene nanosheets, rGO-Iron oxide NPs, Pluronic-GO, G-Carbon Nanotubes-iron oxides, Ag-rGO-Fe_3O_4-polyethylenimine composites, ZnO-GO and Cystamine-GO has revealed a strong antibacterial action against a variety of bacteria. In this paper, an attempt has been made to comprise the latest approaches being put forward in various researches based on the antibacterial action of graphene based nanomaterials and their composites.

Keywords: Graphene Family Materials, Nanomedicines, Graphene Oxide, Silver Nanoparticles, Graphene Quantum Dots, Antibacterial Action

1. Introduction

The well-publicized and now famous, Graphene, is world's first 2D material. Since its isolation in 2004, it has captured the attention of scientists, researchers and industry worldwide as the vast amount of products, processes and industries which graphene can create, all stem from its amazing properties. Different recent studies have been conducted using this wonderful material in varied fields including nanomedicines [1-7]. Graphene is a monolayer thick, two dimensional form of carbon atoms linked together in a hexagonal lattice. The sp^2 hybridization of all bonds across the sheet gives rise to its interesting and unique properties. Graphene is believed to be composed of benzene rings stripped of their hydrogen atoms [8] and thus graphene can be considered to be a 2 dimensional form of its analogue graphite [9]. Graphene is regarded as the thinnest material in the world as it is only one carbon atom thick [10], although its surface area may be up to 1 cm^2 [11, 12]. Related materials include few-layer graphene (FLG), graphene nanosheets, graphene oxide (GO), reduced graphene oxide (rGO) which are included in graphene family materials (GFMs) [13].

There are many ways to synthesize graphene, such as exfoliation and cleavage, chemical vapor deposition (CVD), thermal decomposition, and electrochemical reduction [14]. Different studies [15-19] also report methods to synthesize this material. Graphene has unique physico-chemical properties including a high surface area, extraordinary electrical and thermal conductivity, strong mechanical strength being 200 times stronger than steel and incredible flexibility [20, 21]. The excellent electronic transport properties and high surface-to-volume ratios give it unique mechanical and rheological properties, and resistance to degradation [22]. It is ultra-light, tough, a superb conductor and it can act as a perfect barrier preventing even helium to pass through it. Graphene, being the thinnest known material

can be used in biosensors [23], transparent electrodes [24] and high energy supercapacitors [25]. Graphene surface and edges facilitate its attachment to biological molecules and adhesion to cells [26, 27]. Formation of reactive oxygen species (ROS) was also reported to be a key mechanism for the antibacterial action of graphene and its derivatives. As many antibiotic-resistant bacterial strains have developed, there is an increasing need to evaluate and develop alternative methods for antibacterial treatment [28-32]. It has been reported that many carbon allotropes including nanotubes, fullerenes, diamond nanoparticles and graphene as well, possess antimicrobial properties [33-35]. Its activity has also been reported to be more effective than some currently used therapeutic antibiotics [12, 32]. Thus, in this paper, an attempt has been made to evaluate the latest approaches and researches in the field of antibacterial activity of graphene and its nano-composites to different bacterial strains showing their enormous potential for their future use in the field of nanomedicines.

2. Toxicity of Graphene Based Nanomaterials

2.1. Graphene Oxide

As graphene is quite expensive and relatively hard to produce, great efforts are being made to find an effective yet inexpensive way to make and use graphene derivatives or related materials. GO is one of those materials. It is a single-atomic layered material, made by the powerful oxidation of graphite. Being cheap and abundant, it possesses many interesting properties and has numerous exciting applications. When GO sheets are fixed onto cotton fabrics, strong antibacterial property and great laundering durability were reported [36]. These flexible, foldable and re-usable GO-based antibacterial cotton fabrics were prepared by direct adsorption, radiation-induced crosslinking and chemical crosslinking. Antibacterial tests of all these GO-containing fabrics revealed strong antibacterial property and inactivation of 98% bacteria. These fabrics were found to kill more than 90% of bacteria even after being washed for 100 times and caused no irritation to skin in experiments on rabbit [36]. The fact that GO can be mass-produced and easily processed, has given way to make flexible paper with antibacterial property and low cost, which may find important clinical applications. It was observed that this graphene-based nanomaterial can effectively inhibit the growth of *Escherichia coli* while showing minimal cytotoxicity [37].

Photothermal treatment of GO using near infrared laser reported surface activation of GO nanoflakes resulting in killing of *Pseudomonas aeruginosa and Staphylococcus aureus* [38]. Transmission electron microscopy (TEM) images also revealed that the cell wall and membrane of *Streptococcus mutans, Porphyromonas gingivalis and Fusobacterium nucleatum* [39] which have a close relationship with periodontal diseases lost their integrity and the intracellular contents leaked out when treated with GO. This highlights its promising application in dental care and therapies against dental caries. The edges of GO nanowalls play an integral part in its antimicrobial mechanism [26]. However by using the Langmuir-Blodgett technique to immobilize flat graphene oxide sheets on a PET substrate, to observe its antibacterial activity concluded that contact with the edges is not a fundamental part of the mechanism [40]. Antibacterial activity of GO might also be because of production of superoxide radical anion which leads to cell death as seen in *P. aeruginosa*, which was further confirmed through nuclear fragmentation [41]. Many other factors may also influence graphene family nanomaterial's biological interactions with cells, and it was also seen that the antibacterial activity of GO sheets toward *E. coli* cells is lateral size dependent [42]. Larger GO sheets show stronger antibacterial activity than smaller ones, as they more easily cover cells, and cells cannot proliferate once fully covered, resulting in the cell viability loss as observed in the colony counting test. In contrast, small GO sheets adhere to the bacterial surfaces. They cannot effectively isolate cells from environment and also show different time and concentration dependent antibacterial activities. Hence, it is important to tailor the lateral dimension of GO sheets to optimize the application potential with minimal risks for environmental health and safety [42].

On a controversial note it was seen that, in saline, bare GO sheets were intrinsically bactericidal, yielding a bacterial survival percentage of <1% at 200 μg/mL [43] whereas when saline was supplemented with Luria-Bertani (LB) broth, it progressively deactivated its bactericidal activity. 10% LB made GO to be completely inactive, instead showing approximately 100-fold bacterial growth [43] concluding that non-covalent adsorption of LB components on GO basal planes may be a global deactivation mechanism for GO's cytotoxicity. A sudden decrease in environmental salinity and a Biocompatible Block Copolymer (Pluronic F-127) was found to increase antibacterial activity of GO. Hypo-osmotic stress induced by water shock makes gram-negative pathogens more susceptible to Pluronic-GO that can populate around bacterial envelopes favoring the interactions between GO and bacteria. Pluronic also significantly suppresses the toxicity of GO toward human fibroblast cells making this hypotonic Pluronic-GO mixture both safe and effective in bacterial disinfection applications [44]. Cystamine-conjugated GO with low cytotoxicity, but strong reactive oxygen species effects and high antibacterial activity was prepared showing minimum inhibitory concentrations values of 1 μg/mL against *E. coli* and *Salmonella typhimurium*, 6 μg/mL against *Enterococcus faecalis* and 4 μg/mL against *B. subtilis* [45].

2.2. Reduced Graphene Oxide

The reduced graphene oxide (rGO) is usually considered as one kind of chemically derived graphene which is prepared from reduction of GO by thermal, chemical or electrical treatments. Hence, some other names have also been given to rGO, such as functionalized graphene,

chemically modified graphene, chemically converted graphene, or reduced graphene [46]. Different reduction processes result in varied properties that in turn affect the final performance of materials or devices composed of rGO. The physico-chemical properties of these graphene derivatives, such as density of functional groups, size, and conductivity, can be precisely tailored to either reduce their health and environmental risks or to increase their application potential [47]. Antibacterial property of rGO results from the production of superoxide radical anion which induced oxidative stress, loss of cell viability and DNA fragmentation in *P. aeruginosa* [41]. Some studies also suggest that antimicrobial actions of rGO are contributed both by oxidation stress and membrane contact. Using *E. coli*, a three-step antimicrobial mechanism was proposed, which included initial cell deposition on graphene-based materials, membrane stress caused by direct contact with sharp nanosheets and the ensuing superoxide anion-independent oxidation. This new carbon nanomaterial may also find important environmental and clinical applications as it can be used to produce macroscopic freestanding rGO paper that can be conveniently fabricated from their suspension via simple vacuum filtration which effectively inhibits the growth of *E. coli* [37].

Table 1. *Comparative analysis of antibacterial action of graphene based composites on different bacterial types.*

S. No.	Study	Graphene or composites used	Bacteria used in the study	Result
1.	Pan et al. 2015 [60]	rGO-IONP	Methicillin-resistant *Staphylococcus aureus* (MRSA)	Upon exposure to a near-infrared laser, rGO-IONP synergistically generated localized heat and large amounts of hydroxyl radicals, which inactivated MRSA.
2.	Karahan et al. 2015 [44]	Pluronic-GO	Daily-life bacteria	The antibacterial activity of GO at a low concentration (50 µg/mL) increases from <30% to virtually complete killing (>99%) when complemented with water shock and Pluronic (5 mg/mL) at approximately 2-2.5 h of exposure.
3.	Hui et al. 2016 [64]	C60-GQD	*Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli* and *Pseudomonas aeruginosa*	C60-GQDs effectively kill *S. aureus* but not *B. subtilis*, *E. coli* and *P. aeruginosa.* Surface-Gaussian-curvature match between a GQD and a target bacterium may play important role
4.	Sharma et al. 2015 [61]	G-CNT-iron oxides	*Escherichia coli* and *Staphylococcus aureus*	Composites can remove pollutants and inactivate bacteria efficiently in water. Composites also help in removal of metals including Cu, Pb, Cr(VI) and As
5.	Zhong and Yun 2015 [66]	ZnO-GO	*Escherichia coli* and *Salmonella typhimurium*	MIC was found to be 6.25 µg/mL for *E. coli* and *S. typhimurium*, 12.5 µg/mL for *B. subtilis* and 25 µg/mL for *E. faecalis*. A vast number of ROS formed on the surface of composites improved antibacterial property
6.	Wang et al. 2015 [62]	Ag-rGO-Fe_3O_4-PEI composites	*Escherichia coli* O157:H7	Killing rate of 99.9% is achieved for the *E. coli* O157:H7 by using a composite dosage of 0.1 µg/mL under a 0.5 min. near infrared laser irradiation
7.	Shao et al. 2015 [49]	GO-Ag	*Escherichia coli* ATCC 25922 and *Staphylococcus aureus* ATCC 6538	Excellent antibacterial activity was found against both the strains
8.	He et al. 2015 [39]	GO nanosheets	*Streptococcus mutans*, *Porphyromonas gingivalis* and *Fusobacterium nucleatum*	Good antimicrobial property was found; may have an application against dental pathogens
9.	Shahnawaz et al. 2015 [38]	GO	*Pseudomonas aeruginosa* and *Staphylococcus aureus*	Laser mediated the surface activation of GO which offered high antibacterial property
10.	Nanda et al. 2015 [45]	Cystamine-GO	*Escherichia coli*, *Salmonella typhimurium*, *Enterococcus faecalis* and *Bacillus subtilis*	Cystamine-conjugated GO showed low cytotoxicity, but high antibacterial activity. MIC values were found to be 1 µg/mL against *E. coli* and *S. typhimurium*, 6 µg/mL against *E. faecalis*, and 4 µg/mL against *B. subtilis*
11.	Tian et al. 2014 [57]	GO-IONP-Ag nanocomposites	*Escherichia coli* and *Staphylococcus aureus*	Remarkable synergistic antibacterial effect to inhibit *S. aureus* was found
12.	Yu et al. 2014 [58]	Ag/HNTs/rGO	*Escherichia coli* and *Staphylococcus aureus*	Ag/HNTs/rGO possess enhanced antibacterial ability against *E. coli* and *S. aureus* compared with individual silver nanoparticles, rGO nanosheets or their nanocomposites
13.	Li et al. 2014 [70]	Large area monolayer	*Escherichia coli* and	Graphene films on Cu and Ge showed high inhibition to the growth of

S. No.	Study	Graphene or composites used	Bacteria used in the study	Result
		graphene film on Cu, Ge and SiO_2	*Staphylococcus aureus*	both bacteria, especially *S. aureus.* Graphene film on SiO_2 failed to significantly restrict the proliferation
14.	Ristic et al. 2014 [63]	GQDs	Methicillin-resistant *Staphylococcus aureus* (MRSA) and *Escherichia coli*	The induction of oxidative stress in bacteria exposed to photo-excited GQD was confirmed by staining with a redox-sensitive fluorochrome dihydrorhodamine 123. Neither GQD nor light exposure alone were able to cause oxidative stress and reduce the viability of bacteria
15.	Wang et al. 2014 [65]	ZnO-GO composites	*Escherichia coli*	GO helped the dispersion of ZnO-NPs which lead to the intimate contact of *E. coli* with ZnO-NPs resulting in bacterial cell death
16.	Zhu et al. 2013 [51]	GO-AgNP composites	*Escherichia coli* and *Bacillus subtilis*	The antibacterial activity of GO-AgNPs was found to dependent on the size of AgNPs. The positive charged surface of hybrids increased the electrostatic interaction of bacterial cell membrane with nanohybrids resulting in enhanced antibacterial activity
17.	Hong et al. 2013 [69]	PVdF nanofiber membranes incorporated nanosilver or GO	*Staphylococcus aureus*, *Klebsiella pneumonia* and *Escherichia coli*	200 ppm of AgNPs in the PVdF nanofiber had 99.9% of growth inhibition of *S. aureus* and *K. pneumonia.* 0.2 wt% of GO in the PVdF electrospinning solution was found to have 99.6% of disinfection property to *E. coli*
18.	de Faria et al. 2014 [54]	GO-Ag nanocomposites	*Pseudomonas aeruginosa*	High biocidal activity with MIC was found to be ranging from 2.5 to 5.0 µg/mL; 100% inhibition rate to *P. aeruginosa* adhered on stainless steel after exposure to the GO-Ag nanocomposite for 1h
19.	Ocsoy et al. 2013 [55]	Ag-dsDNA-GO composites	*Xanthomonas perforans*	Ag-dsDNA-GO at 100 ppm on tomato transplants in a greenhouse significantly reduced the severity of bacterial spot disease compared to untreated plants
20.	Wang et al. 2013 [59]	Ag-coated GO-Au nanosheets	*Escherichia coli*	GO-Au-Ag exhibited an enhanced antibacterial activity against *E. coli*, higher to unassembled Au-Ag NPs and ionic Ag
21.	Tang et al. 2013 [50]	GO-Ag nanocomposites	*Staphylococcus aureus* and *Escherichia coli*	Strong antibacterial activities were found at 2.5 µg/mL. The toxicity was found to be more against *E. coli* as compared to *S. aureus*
22.	Zhao et al. 2013 [36]	GO-based antibacterial cotton fabrics	Daily life bacteria	These fabrics can kill >90% bacteria even after being washed for 100 times; no irritation to rabbit skin was revealed
23.	Ouyang et al. 2013 [68]	PLL-rGO-CuNPs	*Staphylococcus aureus* and *Escherichia coli*	CuNPs on PLL-rGO were more stable than those on polyvinyl pyrrolidone, resulting in long-term additively antibacterial effect
24.	Das et al. 2013 [53]	GO-AgNPs	*Staphylococcus aureus* and *Bacillus subtilis*	100% killing of bacterial colonies was obtained using GO-Ag NPs suspension whereas percentage of the killing bacterial colonies by AgNPs (without GO) was 96-97%
25.	Gurunathan et al. 2012 [41]	GO and rGO	*Pseudomonas aeruginosa*	GO and rGO showed dose-dependent antibacterial activity against P. aeruginosa cells through the generation of reactive oxygen species, leading to cell death, which was further confirmed through resulting nuclear fragmentation
26.	Liu et al. 2012 [42]	GO	*Escherichia coli*	Larger GO sheets showed stronger antibacterial activity than smaller ones in colony counting test with different time- and concentration-dependent antibacterial activities
27.	Liu et al. 2011[47]	Gt, GtO, GO and rGO	*Escherichia coli*	GO dispersion showed the highest antibacterial activity under similar concentration and incubation conditions, followed by rGO, Gt, and GtO
28.	Cai et al. 2011 [48]	BB-rGO-TTP	Gram-positive and Gram-negative bacteria	Excellent synergistic antibacterial activity, specific targeting capability, water solubility and mild cytotoxicity
29.	Hu et al. 2010 [37]	GO and rGO	*Escherichia coli*	Inhibited the growth of *E. coli* while showing minimal cytotoxicity

GO, Graphene oxide; rGO, Reduced graphene oxide; IONP, Iron oxide nanoparticles; GQD, Graphene quantum dot; CNT, Carbon nanotubes; ROS, Reactive oxygen species; PEI, polyethylenimine; MIC, Minimum inhibitory concentration; HNTs, Halloysite nanotubes; PLL, poly-L-lysine; MBC, Minimum bactericidal concentration; NPs, Nanoparticles; PVdF, Polyvinylidene fluoride; Gt, Graphite; GtO, Graphite oxide; BB, Brilliant blue; TTP, Tetradecyltriphenylphosphonium bromide

2.3. Graphene - Ag Composites

Though silver nanoparticles are being increasingly used in daily life for their antibacterial properties, but their low stability and high cytotoxicity hamper their practical applications [48]. As a result many hybrid materials of silver are being made by different methods which exhibit strong antibacterial properties against many gram positive and gram negative bacterial strains. Graphene and silver nanoparticles (AgNPs) are considered important building blocks for the synthesis of functional nanomaterials for bio-related

applications [49]. Antibacterial agents where silver nanoparticles are anchored in GO have shown promising potential. However, factors affecting their antibacterial activity as well as the underlying mechanism remain unclear [50]. The antibacterial activity of GO-AgNPs might be dependent on the size of AgNPs, as it was seen that small AgNPs modified GO sheets show more effective antibacterial capability than that of large AgNPs modified GO sheets. Comparing with AgNPs alone, the enhanced antibacterial activity of GO-AgNPs against gram negative bacterial strain of *E. coli* and gram positive bacterial strain of *B. subtilis* might not only be due to high stability of AgNPs anchored on GO sheets, but also the positive charged surface of hybrids which increases the electrostatic interaction of bacterial cell membrane with nanohybrids [51]. Many facile strategies to decorate AgNPs onto rGO are being used. Fabricated rGO-AgNP films that exhibit excellent antibacterial activity and high biocompatibility have been prepared by the simultaneous reduction of silver ions and GO nanosheets. They can be further fabricated into a dimension adjustable rGO-AgNP multi-layered film by thermal-driven self-assembly process [52]. Conjugation of AgNPs with desired morphologies (densities, sizes and shapes) onto GO using a method based on electrostatic interactions using polydiallyldimethylammonium chloride (PDDA) as an adhesive agent [51] resulted in enhanced colloidal and photo-stability as compared with AgNPs alone. GO-AgNPs suspension can also be prepared by chemical reduction of silver metal ions by sodium borohydride ($NaBH_4$) in the presence of tri-sodium citrate, which acts as a stabilizing agent to prevent agglomeration of the nanoparticles. Leakage of sugars and proteins from the cell wall of both *S. aureus* and *Bacillus subtilis* on interaction with this GO-AgNPs suspension resulted in 100% killing of bacterial colonies [53]. A GO-Ag nanocomposite prepared in the presence of silver nitrate and sodium citrate resulted in its anti-biofilm activity toward *P. aeruginosa* adhered on stainless steel surfaces. This nanocomposite may be applied as antibacterial coating material to prevent the development of biofilms in food packaging and medical devices [54]. DNA-directed AgNPs can also be grown on GO. These Ag-dsDNA-GO composites were found to effectively decrease *Xanthomonas perforans* cell viability in culture and on plants. Application of Ag-dsDNA-GO at 100 ppm on tomato transplants in a greenhouse experiment significantly reduced the severity of bacterial spot disease [55].

The ratio of AgNPs to GO plays a crucial role in deciding the magnitude of the antibacterial action of the composites. GO-Ag nanocomposite is much more effective with an optimal ratio of AgNPs to GO and shows synergistically enhanced and strong antibacterial activities even at a low dose of 2.5μg/mL. In a study, the findings show that the mechanism of the antibacterial effect of these nanocomposites is species-specific being more toxic to *E. coli* as compared to *S. aureus*. Antibacterial action functions through disrupting bacterial cell wall integrity in the case of *E. coli* whereas it exhibits bacteriostatic effect on *S. aureus* by inhibiting cell division [50]. Inspired by mussels, a mild and environment friendly method was used to synthesize silver nanoparticles on functionalized polydopamine - graphene nanosheets (PDA-GNS) with uniform and high dispersion resulting in Ag-PDA-GNS hybrid material which exhibited strong antibacterial properties towards both Gram-negative and Gram-positive bacteria due to the synergistic effect of GNS and AgNPs [56]. AgNP-sodium 1-naphthalenesulfonate (NA)-rGO hybrid showed excellent water solubility and low cytotoxicity indicating a great potential application in formulating sprayable antibacterial solutions [48].

By growing both iron oxide nanoparticles (IONPs) and silver nanoparticles on the surface of GO, a synergistic GO-IONP-Ag nanocomposite was obtained which proved as a novel multifunctional antibacterial material as it shows much higher antibacterial efficiency toward both *E. coli* and *S. aureus* compared with AgNPs alone. With magnetic IONPs existing in the composite, it can be easily recycled by magnetic separation, allowing its repeated use along with easy preparation and cheap cost. GO-IONP-Ag developed in this way, may find potential applications as a useful antibacterial agent in the areas of healthcare and environmental engineering [57]. Another sandwich-like antibacterial reagent, silver nanoparticles/halloysite nanotubes/graphene nanocomposite (Ag-HNTs-rGO) was constructed by direct growth of silver nanoparticles on the surface graphene-based HNTs nanosheets combined by adhesion effect of L-3, 4-dihydroxyphenylalanine (DOPA). After self-polymerization this nanocomposite also showed enhanced antibacterial ability against *E. coli* and *S. aureus* [58]. Water-dispersible two-dimensional assemblies of Au-Ag core-shell nanoparticles were obtained through a highly selective electroless silver deposition on pre-assembled gold nanoparticles on bovine serum albumin (BSA)-coated graphene oxide (BSA-GO). These composites exhibited an enhanced antibacterial activity against *E. coli* as compared to unassembled Au-Ag nanoparticles and even ionic Ag. This enhanced activity might have resulted from increased local concentration of silver nanoparticles around the bacterium and a polyvalent interaction with the bacterial surface. High colloidal stability of this novel nanocomposite against the formation of random nanoparticle aggregates assures a minimized activity loss [59].

2.4. rGO-Iron Composites

rGO-IONP composites have shown to inactivate methicillin-resistant *Staphylococcus aureus* (MRSA). An rGO-IONP nanocomposite system was synthesized by the chemical deposition of Fe^{2+}/Fe^{3+} ions on nanosheets of rGO in aqueous ammonia. Its antibacterial efficacy was evaluated using a mouse model infected with MRSA. Results revealed that the composite synergistically induced physical and chemical damage to MRSA by producing large amounts of hydroxyl radicals, upon exposure to a near-infrared laser. The in-vivo results revealed that combined treatment of localized heat and oxidative stress accelerated the healing of wounds

associated with MRSA-infected abscesses [60]. Hence, this composite can be used to inactivate multiple-drug-resistant bacteria in subcutaneous infections. Advances have also been made to provide clean and affordable water by protecting source and purifying polluted waters with the help of graphene-carbon nanotubes-iron oxide nanocomposites. They can remove pollutants and inactivate bacteria efficiently in water, as they exhibit large surface area and sorption sites that provide higher adsorption capacity to remove pollutants than other conventional adsorbents having three-dimensional structure. These magnetic graphene-based nanomaterials were used for inactivation *E. coli* and *S. aureus* and these can easily be separated out from the treated water using an external magnet [61]. Another Ag-rGO-Fe_3O_4-PEI composite prepared by in-situ growth of silver nanoparticles onto the polyethylenimine (PEI) mediated magnetic reduced graphene oxide (rGO) proves to be a novel bactericidal material. This composite exhibited excellent antibacterial performance against *E. coli* O157:H7. Its bacterial inhibition capability was found to depend on the dosage and mass ratio within a certain range, showing a killing rate of 99.9% for *E. coli* by using a dosage of 0.1μg/mL [62].

2.5. Graphene Quantum Dots

Graphene quantum dots (GQDs), a new class of carbon nanoparticles, generates ROS when photo-excited (470 nm, 1 W) inducing oxidative stress. Methicillin-resistant *Staphylococcus aureus* (MRSA) and *E. coli* were found to be inhibited by cell membrane damage. In the same study, mouse spleen cells were found to be less sensitive indicating a selective antibacterial photodynamic action of GQDs [63]. In an another study, *S. aureus*, including its antibiotic-tolerant persisters were found to be killed by C60-GQDs. The Surface-Gaussian-curvature match between GQD and the target bacterium plays a critical role in the association of the GQD with bacterial cell surface considered to be the initial step for cell envelope disruption [64].

2.6. ZnO-GO Composites

Synergism of GO and zinc oxide nanoparticles (ZnO-NPs) led to the superior antibacterial activity of the ZnO-GO composites, inhibiting bacterial growth and propagation. GO helped the dispersion of ZnO-NPs, slowed the dissolution of ZnO, acted as the storage site for the dissolved zinc ions, and enabled the intimate contact of *E. coli* with ZnO-NPs and zinc ions inducing bacterial death [65]. Excellent antibacterial activity of these composites was observed at minimum inhibitory concentrations of 6.25 μg/mL for *E. coli* and *Salmonella typhimurium*; 12.5 μg/mL for *B. subtilis* and 25 μg/mL for *Enterococcus faecalis* due to vast number of reactive oxygen species formed on the surface of composites [66]. A water-soluble brilliant blue/reduced graphene oxide/tetradecyltriphenylphosphonium bromide composite (BB-rGO-TTP), displayed excellent synergistic antibacterial activity, specific targeting capability and mild cytotoxicity [67]. Antibacterial activity of copper nanoparticles (CuNPs) was found to be improved by using a poly-L-lysine-modified reduced graphene oxide (PLL-rGO) as the carrier of CuNPs. PLL-rGO-CuNPs hybrid showed a long-term antibacterial effect both on *E. coli* and *S. aureus* along with excellent water-solubility, suggesting its great potential application in microbial control [68]. More than 200 ppm of silver nanoparticles in the polyvinylidene fluoride (PVdF) nanofiber had 99.9% of growth inhibition of *S. aureus* and *Klebsiella pneumonia*. It was also found that 0.2 wt% of graphene oxide in the PVdF electro-spinning solution had 99.6% of disinfection property to *E. coli* [69]. Graphene films on copper (Cu) and germanium (Ge) can also surprisingly inhibit the growth of both *S. aureus* and *E. coli*, especially the former by causing membrane damage and destroying membrane integrity [70]. However, the proliferation of both bacteria cannot be significantly restricted by the graphene film on SiO_2 and no evident membrane destruction is induced by graphene on SiO_2. This study may provide new insights for the better understanding of antibacterial actions of graphene film and for the better designing of graphene-based antibiotics and other biomedical applications [70].

3. Conclusion

Graphene has emerged as a dynamic nanocarbon with unique properties. Graphene and its derivatives including GO and rGO, along with their nanocomposites possess excellent antibacterial properties. Almost 100% bacterial killing rates can be achieved using very low concentrations with minimal cytotoxicity. After going through the latest researches based on the antibacterial action of graphene based nanomaterials, it can be summarized that these moieties can effectively be used in the field of antibiotics for making antimicrobial formulations including antibacterial papers and lotions. Further, the authors are of the view that graphene based research in future will surely open up new gateways in the field of nanomedicines with the development of new and innovative antibacterial formulations.

Abbreviations

AgNPs: Silver nanoparticles
BB: Brilliant blue-reduced graphene oxide
BSA: Bovine serum albumin
CNT: Carbon nanotubes
CuNPs: Copper nanoparticles
CVD: Chemical vapor deposition
DOPA: L-3, 4-dihydroxyphenylalanine
FLG: Few-layer graphene
GFMs: Graphene family materials
GO: Graphene oxide
GQDs: Graphene quantum dots
Gt: Graphite
GtO: Graphite oxide
HNTs: Halloysite nanotubes
IONPs: Iron oxide nanoparticles
LB: Luria-Bertani

MBC: Minimum bactericidal concentration
MIC: Minimum inhibitory concentration
MRSA: Methicillin-resistant *Staphylococcus aureus*
NA: Sodium 1-naphthalenesulfonate
NPs: Nanoparticles
PDA-GNS: Polydopamine - graphene nanosheets
PDDA: Polydiallyldimethylammonium chloride
PEI: polyethylenimine
PLL: poly-L-lysine
PVdF: Polyvinylidene fluoride
rGO: Reduced graphene oxide
ROS: Reactive oxygen species
TEM: Transmission electron microscopy
TTP: Tetradecyltriphenylphosphonium bromide

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