Review

Light-Activated Heterostructured Nanomaterials for Antibacterial Applications

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Abstract: An outbreak of a bacterial contagion is a critical threat for human health worldwide. Recently, light-activated heterostructured nanomaterials (LAHNs) have shown potential as antibacterial agents, owing to their unique structural and optical properties. Many investigations have revealed that heterostructured nanomaterials are potential antibacterial agents under light irradiation. In this review, we summarize recent developments of light-activated antibacterial agents using heterostructured nanomaterials and specifically categorized those agents based on their various light harvesters. The detailed antibacterial mechanisms are also addressed. With the achievements of LAHNs as antibacterial agents, we further discuss the challenges and opportunities for their future clinical applications.

Keywords: heterostructured nanomaterial; antibacterial agent; antibacterial mechanism; reactive oxygen species; light-activated; synergistic effect

1. Introduction

Antibacterial studies have become more significant because of the increased of multidrug-resistant (MDR) bacteria in this era [1–10]. Various mechanisms can stimulate antibacterial resistance, including overuse of antibiotics and the delivery of bacteria by different routes [11–13]. A recent report indicates that by 2050, antibacterial resistance will be a tremendous public health threat with the potential to cause the death of ten million people each year [14]. Therefore, development of new types of antibacterial agents against MDR bacteria is an urgent task. The development of new antibacterial agents inspired the researchers for the investigation of nanomaterials which can eliminate MDR bacteria without the help of antibiotics [15–19].

Nanomaterials—including metals, metal oxide, semiconductors and polymers—have been extensively studied for applications in nanoscience and nanotechnology, due to their superior chemical and physical properties [20–35]. Among nanomaterials, the heterostructured nanomaterials have shown unique optical properties, including the increase of light absorption and the extension of absorption region [36–41]. Recently, great advancements have been reported in the application of LAHNs as antibacterial agents. With the rise of light absorption and the extension of absorption...
region, heterostructured nanomaterials have shown superior antibacterial activity, based on reactive oxygen species (ROS) generation under light illumination [42–48]. The emphasis of this review is on the mechanism study of light-induced ROS generation from heterostructured nanomaterials by synergistic effect. Recent achievements with the uses of LAHNs as antibacterial agents are classified by their various light harvesters. Finally, challenges and perspectives for LAHNs as antibacterial agents are also provided.

2. Antibacterial Nanomaterials Based on Light-induced ROS Generation

Titanium dioxide (TiO$_2$) materials have been found to possess remarkable biocompatibility and low cell toxicity with significant antibacterial activity [49–58]. Recently, TiO$_2$-based nanomaterials were popular materials with substantial amount of antibacterial activities, and their antibacterial activities could be further enhanced by light irradiations with various wavelengths, including ultraviolet (UV) light, visible light and near-infrared (NIR) light due to the increase of ROS generation [59–67]. For example, with UV light irradiation, heterostructured Ag-TiO$_2$ nanoparticles have displayed higher bactericidal activity compared to that of only UV irradiation, Ag nanoparticles under UV irradiation or TiO$_2$ nanoparticles under UV irradiation (Figure 1) [68]. With UV light illumination, the augmentation of bactericidal activity of hybrid Ag-TiO$_2$ nanoparticles indicated that Ag nanoparticles loaded onto TiO$_2$ nanoparticles served as electron traps to prevent recombination of electron and hole in hybrid Ag-TiO$_2$ nanoparticles. The photo-exited electrons were generated and then transferred to Ag nanoparticles to extend the life of electron-hole pairs. In the system of hybrid Ag-TiO$_2$ nanoparticles, the increases of electron-hole pairs enhanced ROS generation for the destruction of bacterial membrane or DNA [69–74]. In the work, hybrid Ag-TiO$_2$ nanoparticles provided more effective bactericides with light irradiations; however, the uses of hybrid Ag-TiO$_2$ nanoparticles as an antibacterial agent were challenging in practical application due to their high cytotoxicity and facile accumulation in tissues and organs.

![Figure 1. IC50 values of different hybrid Ag-TiO$_2$ nanoparticles with and without UV light irradiations. TiO$_2$ P25 (Degussa P25) and TiO$_2$ R-902 (DuPont Ti-Pure R-902) were two commercial TiO$_2$ nanoparticles. Two different molar ratios of AgNO$_3$ and TiO$_2$ including 1:10 and 1:50 were respectively employed to prepare Ag nanoparticles deposited onto the TiO$_2$ nanoparticles by NaBH$_4$ reduction and UV photoreduction to form the samples of Ag-P25 1:10 NaBH$_4$, Ag-P25 1:50 NaBH$_4$, Ag-P25 1:50 UV, Ag-R902 1:10 NaBH$_4$, Ag-R902 1:50 NaBH$_4$ and Ag-R902 1:50 UV. Ag nanoparticles and AgNO$_3$ were purchased from QuantumSphere, Inc. Reproduced with permission from ref. [68]. Copyright © 2011, American Chemical Society.](image-url)
Nanocomposites of AgVO₃ quantum dots (QDs) deposited onto TiO₂ nanospheres (TiO₂/AgVO₃) have shown high-performance photocatalytic capability with visible light irradiation [75–77]. TiO₂/AgVO₃ nanocomposites incubated with E. coli have been investigated to study their light-induced bacterial inactivation with illumination of visible light. In the control experiment, after visible light irradiation over 120 min, TiO₂ nanospheres were inactivated only 0.13 log of E. coli. With the use of TiO₂/AgVO₃ nanocomposites as photocatalysts, all of E. coli were killed under visible light irradiation over 120 min. After TiO₂/AgVO₃ nanocomposites incubated with E. coli, with visible light irradiation; the shape of E. coli was destroyed. Moreover, there were no obvious changes of bacterial inactivity of TiO₂/AgVO₃ nanocomposites after three cycling antibacterial tests under visible light irradiation indicating that TiO₂/AgVO₃ nanocomposites were good photocatalysts with superior stability. For the photocatalytic disinfection mechanism, AgVO₃ QDs were excited to offer light-induced pairs of electrons and holes with visible light illumination and then the light-induced electrons located in the conduction band of AgVO₃ QDs were easily delivered to the conduction band of TiO₂ (Figure 2). The light-induced electrons in the conduction band of TiO₂ could react with oxygen in medium to form -O₂⁻. Moreover, the holes located in the valence band of AgVO₃ QDs could be delivered to their surface to inhibit the growth of E. coli. To sum up, the light-induced electron-hole pairs in TiO₂/AgVO₃ nanocomposites were efficiently separated to improve the light-induce antibacterial activity of E. coli.

![Figure 2](Nanomaterials.pdf)  
**Figure 2.** Antibacterial mechanism of TiO₂/AgVO₃ nanocomposites with visible light illumination. Reproduced with permission from ref. [75]. Copyright © 2019, Elsevier.

Natural polymers of cellulose are intensively used in daily life [78–80]. However, the application of cellulose has been limited, due to its susceptibility to microorganism growth. In recent advancements, a simple sol-gel approach has been used to conjugate the cellulose scaffold with Ag/TiO₂ nanoparticles (Ag/TiO₂/cellulose) against bacteria (Figure 3) [81]. The antibacterial activities of nanocomposite film of Ag/TiO₂/cellulose, film of pristine cellulose and nanocomposite film of TiO₂/cellulose have been investigated with E. coli with and without UV light irradiation. The bactericidal performance of the nanocomposite film of Ag/TiO₂/cellulose with Ag content of 0.030 wt% has shown the best 99.9% inactivation of E. coli with UV light illumination. The results suggest that the nanocomposite film of Ag/TiO₂/cellulose exhibit superior bactericidal performance against E. coli because of the synergistic effect of Ag nanoparticles and anatase TiO₂ nanoparticles. Under UV light irradiation, TiO₂ nanoparticles may generate ROS—including -OH, -O₂⁻ and H₂O₂—prompting bacterial death. Moreover, Ag nanoparticles may capture electrons, restraining the recombination of photon-induced
electron/hole pairs for the increase of ROS formation. Overall, the bactericidal performance of the nanocomposite film of Ag/TiO$_2$/cellulose was significantly enhanced under UV light irradiation.

Au-TiO$_2$ nanocomposites embedded into a degradable and antibacterial sodium alginate films have been developed by food packaging industries against bacteria [82]. Sodium alginate/Au-TiO$_2$ nanocomposite (SAT) films were respectively improved ~60% and ~50% for S. aureus and E. coli in dark. With the use of SAT films, 90% of S. aureus and 97.1% E. coli were killed without light illumination, respectively. However, after light illumination for 20 min, the antibacterial abilities of SAT films were respectively improved ~60% and ~50% for S. aureus and E. coli. The improvement of antibacterial abilities of SAT films may be attributed to that the nanocomposites of Au-TiO$_2$ increased light absorption and transfer capability due to their plasmonic effect. The plasmonic Au nanoparticles in SAT films may harvest light to produce light-induced photons for the increase of ROS to kill bacteria.

**Figure 3.** Schematic illustration of preparation of the nanocomposite film of Ag/TiO$_2$/cellulose and its antibacterial mechanism. Reproduced with permission from ref. [81]. Copyright © 2018, MDPI.

**Figure 4.** Antibacterial activities of saline solution, sodium alginate/TiO$_2$ nanocomposite (ST) film and sodium alginate/Au-TiO$_2$ nanocomposite (SAT) film for S. aureus and E. coli with and without visible light illumination, respectively. Reproduced with permission from ref. [82]. Copyright © 2018, MDPI.
The nanocomposites of lithium-titanate (Li-TiO$_2$) in the low-density polyethylene (LDPE) matrix have shown a significant increase in killing efficiency for *S. aureus* with visible light illumination [83]. In the heterostructured nanocomposites of Li-TiO$_2$/LDPE, the oxygen vacancies of Ti$^{3+}$ and interaction of Li-O-Ti bond reduced the band gap of TiO$_2$ nanoparticles, resulting in their response to visible light (Figure 5). LDPE alone did not show any antibacterial activity for *S. aureus*. With the dopant of Li-TiO$_2$ of 1 wt%, the heterostructured nanocomposites of Li-TiO$_2$/LDPE inhibited the growth of *S. aureus* by 94% after visible light irradiation for 6 h, then raised the inhibition rate to 99% within 12 h under visible light irradiation. From the results of the scavenger test, the intensified bactericidal effect of the heterostructured nanocomposites of Li-TiO$_2$/LDPE were ascribed to the productions of powerful oxidants including -OH and -O$_2^-$ under visible light irradiation. These powerful oxidants may particularly react with the polyunsaturated phospholipid composition of the bacterial membrane to form water and carbon dioxide.

**Figure 5.** The antimicrobial mechanism of the heterostructured nanocomposites of Li-TiO$_2$/LDPE against *S. aureus*. Abbreviation: valence band: VB; conduction band: CB. Reproduced with permission from ref. [83]. Copyright © 2019, Elsevier.

The heterostructured nanomaterials of copper-doped TiO$_2$ (Cu-TiO$_2$) have been applied as an antibacterial agent against *E. coli* and *S. aureus* with visible light illumination [84]. By utilizing dopant of oxidizing copper, Cu-TiO$_2$ nanomaterials revealed the increase of absorption in visible region and the band gap of Cu-TiO$_2$ nanomaterials was reduced to 2.8 eV. The photo-induced bactericidal activity of Cu-TiO$_2$ heterostructured nanomaterial have been respectively executed with and without visible light illumination (Figure 6). Without photocatalysts, the *E. coli* and *S. aureus* bacteria continued growing under light and dark conditions. Moreover, in the dark, the Cu-TiO$_2$ nanomaterials, anatase TiO$_2$ nanoparticles and rutile TiO$_2$ nanoparticles had no significant bacterial growth after culture for 90 min. After visible light irradiation for 30 min, the Cu-TiO$_2$ nanomaterials had achieved 99.9999% bacterial reduction. However, to obtain 99.9999% bacterial reduction, both anatase and rutile TiO$_2$ nanoparticles required light irradiation for 60 and 90 min, respectively. In comparison with anatase and rutile TiO$_2$ nanoparticles, Cu-TiO$_2$ nanomaterials showed better antibacterial activity. The results indicate that the dopant of Cu in Cu-TiO$_2$ nanomaterials may improve the visible absorption efficiency to enhance bacterial inactivation. After the absorption of light, the charge carriers formed on p-n junction of Cu$_2$O-TiO$_2$ nanomaterials and then reacted with the oxygen and water incorporated on the surface of Cu$_2$O-TiO$_2$ nanomaterials to become radicals to disrupt bacterial membrane and cause bacterial gene alteration to kill bacteria.
As shown in Figure 7, TiO\(_2\) nanomaterials (DNA, RNA) to cause death of bacteria. According to the reaction of holes located in the valence band of TiO\(_2\), combined with TiO\(_2\) could increase the production of \(\cdot\)O\(_2\)\(^\cdot\) to react with \(\text{H}_2\text{O}_2\) for the generation of OH radicals resulted from the reactions of Fenton and photo-Fenton. Furthermore, water or hydroxyl groups adsorbed onto anatase nanolayer coated with TiO\(_2\) nanograin chains may be driven into the valance band of \(\text{Fe}_3\text{O}_3\) thin film could be applied to enhance the photocatalytic capability of the coated Fe\(_3\)O\(_3\) nanograins. The anatase TiO\(_2\) nanolayer could increase the production of \(\text{Fe}^{2+}\) to react with \(\text{H}_2\text{O}_2\) for the generation of OH radicals resulted from the reactions of Fenton and photo-Fenton. Furthermore, water or hydroxyl groups adsorbed onto anatase TiO\(_2\) nanolayer may be used to trap the holes to produce ROS of hydroxyl radicals for the bactericidal activity enhancement to bacteria.

The thin film of photocatalyst of \(\alpha\)-Fe\(_2\)O\(_3\) nanograins incorporated with anatase TiO\(_2\) nanolayer (TiO\(_2/\text{Fe}_2\text{O}_3\)) exhibited bactericidal activity against \(E.\ coli\) with visible light illumination [85]. The bacterial inactivation of the anatase TiO\(_2\), \(\alpha\)-Fe\(_2\)O\(_3\) and TiO\(_2/\alpha\)-Fe\(_2\)O\(_3\) thin films has been studied in the bacterial model of \(E.\ coli\) under visible light illumination, with and without \(\text{H}_2\text{O}_2\) (Figure 7). As shown in Figure 7, TiO\(_2/\alpha\)-Fe\(_2\)O\(_3\) thin film reveals the reduction rate of \(2.6 \times 10^{-2}\) and \(6.5 \times 10^{-2}\) min\(^{-1}\) without and with \(\text{H}_2\text{O}_2\) for \(E.\ coli\), reflecting a better antibacterial activity than anatase TiO\(_2\) and bare \(\alpha\)-Fe\(_2\)O\(_3\) thin film. The better bacterial inactivity of TiO\(_2/\alpha\)-Fe\(_2\)O\(_3\) thin film may be ascribed to the heterostructure of TiO\(_2/\text{Fe}_2\text{O}_3\). Through visible light irradiation onto TiO\(_2/\text{Fe}_2\text{O}_3\) heterojunction, electrons located in the valence band of Fe\(_2\)O\(_3\) may be excited to the conduction band—and then, electrons located in the valence band of TiO\(_2\) may be driven into the valance band of Fe\(_2\)O\(_3\). Therefore, the anatase TiO\(_2\) nanolayer coated with TiO\(_2/\alpha\)-Fe\(_2\)O\(_3\) thin film could be applied to enhance of the photocatalytic capability of the coated Fe\(_3\)O\(_3\) nanograins. The anatase TiO\(_2\) nanolayer could increase the production of \(\text{Fe}^{2+}\) to react with \(\text{H}_2\text{O}_2\) for the generation of OH radicals resulted from the reactions of Fenton and photo-Fenton. Furthermore, water or hydroxyl groups adsorbed onto anatase TiO\(_2\) nanolayer may be used to trap the holes to produce ROS of hydroxyl radicals for the bactericidal activity enhancement to bacteria.

Recent developments of implants have focused on the design of their surface in terms of bacterial inactivation and reusable feasibility. The dopants nitrogen (N) and bismuth (Bi) in TiO\(_2\)—incorporated with the plasma electrolytic oxidation (PEO)—revealed light-induced antibacterial activity and re-activation potential [86]. With the dopant Bi, the band gap energy of TiO\(_2\) was shifted to the visible light region. To confirm the in vitro antibacterial effect, the photocatalysts of TiO\(_2\) coated with urea (Urea-TiO\(_2\) group), TiO\(_2\) doped with Bi (Bi-TiO\(_2\) group) and TiO\(_2\) co-doped with urea and Bi (Urea, Bi-TiO\(_2\) group) were applied as antibacterial agents for two biofilms, including \(\text{Streptococcus sanguinis}\) and \(\text{Actinomyces naeslundii}\). The results of the in vitro antibacterial tests indicated that the urea, Bi-TiO\(_2\) group presented the best performance in bactericidal activity with visible light illumination. With a synergistic effect of N and Bi under visible light illumination, the narrowed band gap of Bi\(_2\)O\(_3\) combined with TiO\(_2\) could facilitate electrons migration from the valence band to the conduction band located in TiO\(_2\) and Ti\(^{3+}\) sites to react with \(\text{O}_2\) to form \(\cdot\text{O}_2\)\(^\cdot\) and also \(\cdot\text{OH}\) radical could be produced according to the reaction of holes located in the valence band of TiO\(_2\) with \(\text{H}_2\text{O}\) (Figure 8). The ROS of \(\cdot\text{O}_2\)\(^\cdot\) and \(\cdot\text{OH}\) may induce damage of bacterial wall, membrane, organelles, proteins and genetic materials (DNA, RNA) to cause death of bacteria.

**Figure 6.** Mechanisms of photocatalytic antibacterial activity (a) p-n junction by heterostructured Cu\(_2\)O and TiO\(_2\) (b) Type-2 heterostructures of anatase and rutile TiO\(_2\) nanomaterials. Images of \(S.\ aureus\) colonies in the agar plates with (right) and without (left) Cu-TiO\(_2\) nanomaterials after 30 min illumination. Reproduced with permission from ref. [84]. Copyright © 2018, MDPI.
In recent times, nanocomposites of chitosan films containing melon/TiO₂ (CTS/MTiO₂) have been applied for self-cleaning of malachite green and light-induced antibacterial surfaces of *S. aureus* under light irradiation [87]. As the most common graphitic carbon nitride material (g-C₃N₄), melon is a visible-light harvesting molecule. The bacterial inactivation of CTS/MTiO₂ nanocomposites was assessed against *S. aureus* with light illumination (Figure 9). After incubated with *S. aureus* for 3 h, CTS/P25, CTS/MTiO₂ and CTS have revealed different antibacterial activities with and without actinic light irradiations as shown in Figure 9a. Furthermore, in Figure 9b, antibacterial mechanism of CTS/MTiO₂ films has been explained under actinic light irradiation. For the control experiments, chitosan and CTS/P25 films showed no significant bacterial inactivation with and without actinic light.
irradiation for 3 h. On the other hand, CTS/MTiO$_2$ films exhibited an antibacterial rate 99% of S. aureus after 3 h of actinic light irradiation. Previous studies indicated that chitosan films combined neat TiO$_2$ nanoparticles exhibited a bactericidal efficiency of 99.9% for E. coli under light irradiation for 4 h. However, under actinic light irradiation for 4 h, chitosan films combined neat TiO$_2$ nanoparticles had no antibacterial activity for S. aureus. In this aspect, CTS/MTiO$_2$ films had superior antibacterial activity for S. aureus. For the antibacterial mechanism, CTS/MTiO$_2$ films were induced for the formation of ROS such as ·OH, $^1$O$_2$, $^1$O$_2^-$ and H$_2$O$_2$ to damage bacterial cell membrane with actinic light irradiation.

![Figure 9](image)

**Figure 9.** (a) Bacterial culturability of S. aureus with and without actinic light irradiation. (b) Antibacterial mechanism of CTS/MTiO$_2$ films under actinic light irradiation. Reproduced with permission from ref. [87]. Copyright © 2019, Elsevier.

Nanocomposites of uniform TiO$_2$ nanoparticles and graphene sheets (TiO$_2$/GSs) have been fabricated via a facile redox reaction for antibacterial applications [88–93]. TiO$_2$ nanoparticles were anchored on the surfaces of GSs by chemical bonds. Moreover, nanocomposites of TiO$_2$/GSs exhibited broad absorption region from UV light to visible light. The photocatalysts of TiO$_2$/GSs were used to kill E. coli under visible light illumination. Uniform TiO$_2$ nanoparticles showed lower antibacterial capability in comparison with TiO$_2$/GSs nanocomposites due to their large band gap, resulting in very low light absorption in the visible region (Figure 10). UV-Vis absorption spectra of pure TiO$_2$ nanoparticles, TiO$_2$/GSs with TiO$_2$/1.4 wt%, TiO$_2$/GSs with TiO$_2$/4.2 wt% and TiO$_2$/GSs with TiO$_2$/7 wt% have shown in Figure 10a. Under visible light illumination for 12 h, viabilities of E. coli incubated with various TiO$_2$-based nanocomposites have been respectively calculated as shown in Figure 10b. Under visible light illumination, the nanocomposites of TiO$_2$/GSs with TiO$_2$/4.2 wt% revealed the best
antibacterial activity in comparison with TiO$_2$/GSs with various weight ratios, including TiO$_2$/1.4 wt% and TiO$_2$/7 wt%. The superior antibacterial activity of TiO$_2$/GSs nanocomposites may be explained by the increase of light absorption in visible region and effective separation of photo-generated electron-hole pairs because graphene could be applied as an electron acceptor and transporter. With the effective separation of light-generated pairs of electrons and holes, TiO$_2$/GSs nanocomposites may produce more ROS, including ·OH and ·O$_2^-$ for disinfection activity of E. coli. For the nanocomposites of TiO$_2$/GSs with TiO$_2$/7 wt%, the decrease of antibacterial activity may be ascribed to that the active TiO$_2$ nanoparticles were covered by a large number of GSs, forming a shield of active sites on TiO$_2$ nanoparticles.

![Image](image.png)

**Figure 10.** (a) UV-Vis absorption spectra of pure TiO$_2$ nanoparticles, TiO$_2$/GSs with TiO$_2$/1.4 wt%, TiO$_2$/GSs with TiO$_2$/4.2 wt% and TiO$_2$/GSs with TiO$_2$/7 wt%. (b) Viabilities of E. coli incubated with various TiO$_2$-based nanocomposites under visible light illumination for 12 h. The insets are the corresponding photographs of agar plates. Reproduced with permission from ref. [88]. Copyright © 2013, Elsevier.

Heterostructured nanocomposites of reduced graphene oxide and cuprous oxide (rGO-Cu$_2$O) have been prepared by the reduction of copper sulfate on graphene oxide for long-term antibacterial activities [94]. The P-type semiconductor of Cu$_2$O may easily separate its electron-hole pairs under light condition. In this study, the fresh rGO-Cu$_2$O nanocomposites generated more ROS compared to that of fresh rGO and Cu$_2$O (Figure 11). The results indicated that the separation performance of photo-excited charges of Cu$_2$O may be distinctly increased by the combination of Cu$_2$O and rGO due to the improvement of interfacial charge transfer between Cu$_2$O and rGO. The ROS antibacterial mechanism of rGO-Cu$_2$O nanocomposites may be attributed to that the light-induced electrons were delivered from Cu$_2$O to rGO to eliminate the recombination of the pairs of electrons and holes [95]. The photo-excited electrons and holes from Cu$_2$O may be used for disinfection of bacteria [96]. Furthermore, rGO have played an important role for the acceptance of light-induced electrons from Cu$_2$O to provide efficient charge transfer between the heterostructured nanocomposites of rGO-Cu$_2$O and bacteria. The photo-excited electrons and holes may create intracellular ROS such as H$_2$O$_2$, ·OH and ·O$_2^-$. Eventually, the active substances of ROS could cause damage of nucleic acids, inactivation of intracellular protein, disability of the mitochondria and destruction of bacterial membrane.
Figure 11. Reactive oxygen species (ROS) production caused by the heterostructured nanocomposites rGO-Cu$_2$O under light illumination. Reproduced with permission from ref. [94]. Copyright © 2019, Elsevier.

Zinc oxide-selenium (ZnO-Se) heterojunction nanocomposites have been fabricated as antibacterial agents for *S. aureus* [97]. For the control, ZnO nanoparticles showed the zone of inhibition as 3.0 cm for *S. aureus* with visible light illumination. In the contrast, ZnO-Se nanocomposites revealed outstanding antibacterial activity with a zone of inhibition as 5 cm for *S. aureus* with visible light illumination. Furthermore, the bactericidal property of ZnO-Se nanocomposites remained for few days to inhibit the growth of *S. aureus*. The enhancement of antibacterial activity of ZnO-Se nanocomposites could be attributed to the increase of light-harvesting capability for sustainable production of ROS to kill *S. aureus* (Figure 12). To investigate the role of ROS in the antibacterial mechanism, electron spin resonance (ESR) was utilized to assess the types of ROS production from ZnO-Se nanocomposites. The results of ESR experiments demonstrated that ZnO-Se nanocomposite may produce ROS, including singlet oxygen and reactive OH species. Overall, the ZnO-Se heterojunction nanocomposites had long term enhancement of their antibacterial activity with visible light illumination and therefore, may be a potential antibacterial agent.

Figure 12. Antibacterial mechanisms of ZnO-Se nanocomposites with visible light illumination. Reproduced with permission from ref. [97]. Copyright © 2020, Elsevier.
3. Challenges and Opportunities

In this review, we have compiled recent investigations of heterostructured nanomaterials as light-activated antibacterial agents in applications such as medicine, food safety, water sterilization and the textile industry (Table 1). These investigations have demonstrated that heterostructured nanomaterials may be high-performance antibacterial agents due to their synergistic effects under light irradiation. With synergistic effects, heterostructured nanomaterials exhibited excellent antibacterial activities based on the increase of ROS generation under light irradiation. Furthermore, the heterostructures of nanomaterials also inhibited the recombination of photon-induced electron/hole pairs for the increase of ROS formation to kill bacteria. Although various heterostructured nanomaterials have been shown to be light-activated antimicrobial agents, their antibacterial activities still need to be improved. For real clinical applications, the antibacterial efficiency of LAHNs should fit the requirement with a 4-log (99.99%) reduction in bacterial viability, which is one of the leading causes of nosocomial infections in the world. The first challenge to enhance the antimicrobial activity of LAHNs is to increase their synergistic effects. The development of LAHNs with novel compositions would be recommended. The second challenge to improve antibacterial activity for light-activated antimicrobial agents is to combine with other optical properties. For example, the photothermal effect is also used to kill bacteria with light irradiation. Therefore, with ROS generation and photothermal effects, LAHNs may provide better antimicrobial activities. The third challenge for light-activated antimicrobial agents is to increase their biocompatibility for the clinic application. To date, the cytotoxicity of LAHNs is still too high for clinic tests. However, in vitro and in vivo studies of light-activated antimicrobial agents of heterostructured nanomaterials are a critical step for future clinic application. Overall, to realize the antibacterial agents of LAHNs, great efforts are still needed for the improvement of their antibacterial activities. With intensive studies, we believe that antibacterial agents of LAHNs can be utilized as the important antibacterial agents in the near future.

Table 1. Light-activated nanomaterials for antibacterial application in this review.

| Nanomaterials | Light harvester | Light Source | Bacteria | References |
|---------------|----------------|--------------|----------|------------|
| Ag-TiO₂       | Ag             | UV light     | B. subtilis and P. putida | [68] |
| TiO₂/AgVO₃    | AgVO₃         | visible light | E. coli | [75] |
| Ag/TiO₂/cellulose | Ag      | UV light     | E. coli | [81] |
| Alginate/Au-TiO₂ | Au         | visible light | S. aureus and E. coli | [82] |
| Li-TiO₂/LDPE  | Li             | visible light | S. aureus | [83] |
| Cu-TiO₂       | Cu             | visible light | E. coli | [84] |
| TiO₂/α-Fe₂O₃  | α-Fe₂O₃       | visible light | E. coli | [85] |
| U₂Bi-TiO₂      | N and Bi      | visible light | S. sanguinis and A. naeslundii | [86] |
| CTS/MTiO₂     | melon         | visible light | S. aureus | [87] |
| TiO₂/GSs      | TiO₂          | visible light | E. coli | [88] |
| rGO-Cu₂O      | Cu₂O         | sunlight     | S. aureus and E. coli | [94] |
| ZnO-Se        | Se            | visible light | S. aureus | [97] |

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