New generation antimicrobial agents- A Review

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Abstract

Resistant to microbes is a growing menace to the health of human beings. The microbes can easily spread in the environment and may develop resistance against the conventional drugs. The diseases caused by these microbes may lead to roughly about 10 million deaths and the global economic burden of 100 trillion USD by the year 2050. So, synthesis of new and potential antimicrobial agents is an upcoming area of research. The advent of novel nonmaterial is a boon in this area, as they efficiently eradicate disease causing pathogens without any side effects due to their unique physico-chemical properties. Other weapons used in this war against superbugs are also highlighted and various parameters to be taken care of at hospital level, industrial level and individual level are discussed. Collaborative, innovative, inter-disciplinary clinical research is recommended in order to reduce its threat in coming years.

Keywords: *Antimicrobial resistance, selenium nanoparticles, gold nanoparticles,carbon nanoparticles*

Introduction

A microorganism or microbe is a minute living thing that cannot be seen through naked eye. These organisms are found everywhere on the earth's surface which includes air, water, soil , rock, plants, animals even the human body. Microbes may be good or bad. Some of the microbes are beneficial for us and keeps us healthy whereas others are harmful. Disease causing microbes results in infection and disease in human beings, plants or animals. A large amount of the microbes belong to four major groups: bacteria, viruses, protozoa or fungi. Disease-causing microbes are called pathogens, germs or bugs.

Diseases caused by microbes are the major cause of deaths worldwide. Scientist around the world are trying to find a way out to control these germs but it is not an easy mission. Microorganisms easily adjust themselves to the new environment so it is difficult to get rid of them Microbes build up new features and become resistant to those drugs that were once able to destroy

them. This development of new feature is nothing but antimicrobial resistance and the microbes now emerged are referred to as “superbugs”.

Antimicrobial resistance (AMR) develops with time as a result of genetic changes. The process of resistance is accelerated in microbes by the abuse and the excess uses of drugs. These resistant microbes are found everywhere in the environment which includes people, animals, food etc. They can spread between living organisms. The medicines become ineffective and infections continue in the body [1].

It was also seen that excess use of medicines for viral infections and self medication by the humans increase the development of antibiotic resistance [2]. Therefore, it is terribly required to restrict the spread of these resistant microorganisms by providing innovative remedial options such as biotechnological interventions. The causes of development drug resistant microbes are related with human conduct societal level. Another factor resulting in emergence of resistant strains is genetic mutations. [3].

To overcome the problems generated by resistant microbes WHO developed a “Global Action Plan on AMR” in 2015 which initiated the need of a harmonised approach across different sectors [4]. The rapid increase of injurious pathogens and their resistant to drugs encourages the development of advanced healthcare products. Various new drugs have been developed in the past few years such as polymers, peptides, photo thermal agents for treatment of resistant microbes. But these drugs still had some shortcomings which posed a challenge in medical research to develop safe and effective non-antibiotic agents. Later with the invention of nano particles , scientists were encouraged to develop nanoparticle based anti microbial agents. This review summarizes recent advances in nano particle based antimicrobial agents which included selenium nanoparticles, carbon nano tubes etc.

As numbers of national and international initiatives are underway to fight this global public threat, the Indian Academy of Pediatrics has decided to take its wars against the menace of antimicrobial resistance to a new front. Various programs were held by the Academy through its branches, for public awareness as well as increased awareness among health professionals about the gravity of the drug resistance and the importance of judicious use of antibiotics.

Selenium nanoparticles against superbugs

Resistance developed by bacteria against antibiotic therapy is a major concern worldwide for researchers in the medical field. Bacteria reproduce and mutate rapidly and develop resistance against traditional medicines. So, creation of novel and effective antibacterial agents is important and is useful for

a broad range of applications. Synergistic nanocomposite was synthesized on the surface of Selenium nano particles by the conjugation of Quercetin and Acetylcholine. Quercetin has antibacterial activities and acetylcholine is a neurotransmitter. Quercitin and Acetylcholine together increases the activity against superbugs as compared to the activity shown by them individually. The syner gistic nanocomposite is effective at a very low dose. It attaches to the cell wall of bacteria , damaging the membrane showing a amazing anti bacterial effect to inhibit Methicillin-resistant S. aureus, [5]The super bugs includes Mycobacterium tuberculosis, *Enterococcus faecium, Enterobacter cloacae, Klebsiella pneumoniae, Staphylococcus aureus, Acinetobacter baumannii* and *Pseudomonas aeruginosa*[5].

In the previous years some other non antibiotic drugs were also produced. These are the drugs using cationic polymers [6], from peptides [7], using phtothermal agents [8]. All these drugs exhibit antimicrobial activities but some drawbacks were also coupled with them. For example drugs made from peptides degraded easily, cationic polymer antimicrobials could not be used for infection as they showed in vivo hemolysis by formation of nano sized pore resulting in osmotic lysis [9]. Due to the above mentioned problems research was more concentrated in developing nanoparticle based antibacterial agents. Drugs formed using nanoparticles show better efficiency and is less toxic to the human beings.

Selenium has been used in various applications. In one of the study the growth of *S. aureus* was studied in presence of selenium nanoparticles. It was seen that the growth of bacteria was not permitted and skin infections caused by *S. aureus* could be treated [10]. Yip and co-workers padded selenium nanoparticles on fabric to produce antifungal and anti bacterial fabric. Polysaccharides of mushrooms were used alongwith selenium on the fabric.[11]

Quercitin is a flavanoid extracted from vegetables and fruits has the antibacterial properties effective against *Staphylococcus* bacteria species. [12]. Cationic polymers and peptides were used along with nanoparticles to synthesize biodegradable nanoparticles at a very low cost. These biodegradable nanoparticles are used as anti microbial drugs [13].

Activated carbon nanoparticles as antimicrobial agents

In recent years carbon nanoparticles have created interest because of their unique physical and chemical properties. Carbon nanostructures have a large potential to show antibacterial activities. All forms of carbon nanostructures like fullerenes, graphenes, carbon nanotubes or diamond like structures have been used as antimicrobial agents [14]. These carbon nano particles can be generated from bio-waste. The bio-waste which can be used for synthesis of activated carbon nano particles are rapseed oil-

cake, ccunut husk, rice husk,sugarcane waste, kitchen waste, fishtail palm ,sandalwood bark, Caryotaurens seeds etc. These nanoparticles act as antimicrobial agents [15].

Yallapa et al devolped a method for green synthesis of Nano carbon from ground nut shell. Synthesized nano carbons can be used as bacterial inhibitors. So they were checked for antibacterial activity on *Escherichia coli*, *Chromobacterium violaceum* and *Bacillus cereus[*16]. A lot of study has been carried out on the use of activated carbon as antimicrobial agents. These studies depicts that carbon nano particles have good and potential efficiency to inhibit microbes. As the carbon nanoparticles are synthesized at low cost they help in reducing economic burden.

Gold nanoparticles against multi-drug resistant bacteria

Damaged skin can be easily infected by bacteria and pathogens and damage the underlying tissues[17]. The antibiotics were used for the treatment of infections caused on wounds but due to the development of super bugs antibiotics become ineffective[18,19]. But gold nano particles were found effective against these superbugs[20,21]. Gold nanoparticles can be synthesized by reduction of gold salt or using plant extracts. Some studies have proved that gold nanoparticles can be used as antibacterial agents but there were lot of controversy. But later it was found that gold nanoparticles are active at high concentrations.

In one of the study gold nanoparticles were coated with chicken egg white or bovine serum albumin . which is a reducing and stabilizing agent and 2-mercapto-1-methylimidazole(MMT) a novel antibacterial agent can be produced [22,23]. The resulting drug was found to be highly competent antibacterial agent. For the synthesizing ction of gold nanoparticles green and cost effective strategy was used. Gold nanoparticles were functionalized by 2-mercapto-1-methylimidazole molecules consequently e forming antibiotics for both gram-negative and gram-positive bacteria. These AuNPs worked by lyses of bacterial membrane and also accelerates wound healing. Further they can maintain a equilibrium between antibacterial activities and biocompatibility.

Lipopeptide Antibiotics against multidrug-resistant superbugs

Velkov et al.(2018) present octapeptin lipopeptide antibiotics as an alternative against superbugs i.e. gram negative bacteria, that may help to fight polymyxins [24]. Polymyxin E (colistin), an antimicrobial peptide which was avoided in past due to its nephrotoxic and neurotoxic effects is reused against gram negative bacterium. Octapeptins are broad-spectrum lipooctapeptide antibiotics produced by *Bacillus circulans* [25].Polymyxins and octapeptins have the same structure. Since f octapeptins was discovered almost four decades ago, only a restricted data is available for this group of compounds.

Various studies were carried out which proved that octapeptins has in vivo efficiency in rodent models. Although a lot of hurdles came during pre-clinical and clinical studies and which were overcome, the report by Velkov et al raised the expectation that octapeptins and their derivatives may become useful as a new generation of lipopeptide antibiotics for the treatment of life-threatening MDR infections.

Conclusion

Among all the strategies discussed in this paper to make effective antimicrobials selenium nanoparticles have great efficacy as they have lesser side effects to human health. Many other antibiotics are made which have lesser side effect and made by green synthesis but needs time for their better evaluation.

Antimicrobial resistance is a major concern these days. So various researches have been done to overcome this problem like development of nanotechnology, carbon nanoparticles from biowaste and also various modifications have been done in preexisting antibiotics to make them effective against resistant microbes. Excess use of antibiotics leads to antibiotic resistance, so there is need to educate people about this fact. People need to work on fact that " PREVENTION IS BETTER THAN CURE".

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