**Review Article**

**Contribution of molecular methods to reduce the burden of antimicrobial resistance**

**Abstract**

This review seeks to address the various approaches adopted to combat this phenomenon. With scientific facts, latter era has been proven that antibiotics have drastically transformed the way we treat infections nowadays due to several factors that strongly need to be carefully look into for preventive purposes. There are several vital tools for up-to-date medication; nonetheless, inappropriately, their misappropriation has led to the development of bacteria that are resistant to antibiotics. Essentially, excessive prescription has broad-spectrum antibiotics, rather than a more precisely targeted antibiotic based on accurate diagnosis, coupled with patient non-adherence to prescribed dosage and duration, contributes to bacterial survival and subsequent resistance. Several research materials have indicated that bacteria in meat have revealed antibiotic-resistant presence including other food products. Conventional approaches such as prudent use of available antibiotics, one of the ways is avoidance complete suitable immunization, disinfected precautions awareness will greatly aid in the control of cross-transmission of resistant straining among persons; including appropriate screening for resistant strains and separation of carrier patients in order to avoid the spread of the infection. Additionally, updated scientific research and development of antibiotics exercises with accurate innovative mechanism of action were analysed. Furthermore, genomic techniques that have been used to address antimicrobial resistance (AMR) by tracking and analysing the genetic makeup of bacteria are also reviewed. These techniques have been used to identify the genetic mutations that cause AMR, track the spread of resistant strains, and develop new treatments.

**Keywords**: Broad-spectrum antibiotics, Antibiotic resistance, Cross-transmission, Nanotechnology.

1. **Introduction**

There was widespread prevalence of infectious diseases towards the end of the 19th Century, leading to a high mortality rate. The 20th century heralded the evolution and development of antibiotics which was a great response to the yearnings of mankind for a solution to the menace and resulted in a drastic reduction in the death cases recorded (Hutchings *et al.,* 2019; Sharma *et al.,* 2022). In 1910, Salvarsan was produced as the first antibiotic, before the evolution of penicillin, eighteen years after (Hutchings *et al.,* 2019; Waktole and Chala 2023). After some time, resistance was gradually developed and built up by the microorganisms against the antibiotics. Antimicrobial Resistance (AMR) resulted in close to 1 million death cases annually across the globe (Abushaheen *et al.,* 2020; Lahiri *et al.,* 2022; Pasha *et al.,* 2022; Zhang *et al.,* 2022). The phenomenon was linked to uncontrolled, excessive misuse and antibiotic abuse (Chen *et al.,* 2020; Wu *et al.,* 2023; Naeem *et al.,* 2023). The development of antibiotic resistance was considered to be via various mechanisms such as the inactivation of drugs and the formation of biofilm. (Pang *et al.,* 2019; Abushaheen *et al.,* 2020).

The menace was worsened by the slow deployment of novel strategies to tackle AMR, as well as a sluggish response to developing new antibiotics to substitute for those antibiotics that were already rendered impotent by the microbes (Valérie Carole et al., 2018; Gupta & Patil, 2021). World Health Organisation (WHO) called on scientists and researchers globally to come up with substitutes for antibiotics (Årdal *et al.,* 2020; Giráldez-Pérez *et al.,* 2022). Right from the beginning of the 21st century, antimicrobial resistance has a been global issue for humans owing to the abusive use of antibiotics (Machowska and Stålsby, 2019). Poor and unprofessional infection control practices also contributed to the menace of AMR by enhancing the rapid, widespread microbes that were resistant to the environment and the globe at large (Machowska and Stålsby, 2019). In line with a recent study, resistant development has been on the rise as over 70% of microbes have become resistant to drugs used to eliminate them in previous times (Naeem *et al.,* 2023).

Antimicrobial resistance is a high-priority issue or phenomenon where microbes bypass lethal selection pressure via evolution or genetic mutation which enables them to escape being eliminated by antibiotics. It has been widely established that microbes will continue to develop resistance against anti-biotic drugs for as long as possible (Schrader *et al.,* 2020; Uddin *et al.,* 2021; Saxena *et al.,* 2022). The widespread increase in AMR calls for unveiling potent alternatives to address the menace (Gupta *et al.,* 2019; Ajose *et al.,* 2022). Innovative approaches such as genomic techniques and nanotechnology are being explored to combat this phenomenon. Genomic techniques have been used to address antimicrobial resistance (AMR) by tracking and analysing the genetic makeup of bacteria, identify the genetic mutations that cause AMR, track the spread of resistant strains, and develop new treatment (Sekyere and Asante, 2018). The adoption of genomic technologies currently also allowed source-tracing of Antimicrobial resistant (AMR) pathogens including demonstrating of AMR advancement and conduction (Djordjevic *et al*., 2024). Nanotechnology offers immense potential to tackle antimicrobial resistance via several through several pathways and mechanisms such as inhibition of biofilm formation, increased build-up of intracellular drugs, and formation of reactive oxygen species (Naeem *et al.,* 2023). This review elucidates the AMR emergence, how it opposes antibiotics’ roles, its impacts as well as the mechanism of action of several innovative approaches to combat its emergence (Naeem *et al.,* 2023).

**2.0 Rise of Antimicrobial Resistance (AMR) in the 21st Century**

In this 21st Century, the development of antibiotic and its resistance could either be through acquired or natural means (Uddin *et al.,* 2021). Antibiotic resistance mechanisms are exhibited in two major forms which are the normal or innate resistance which entails the expression of genes in the organism and the mediated resistance when they are exposed to antibiotics (He *et al.,* 2020). Microbes can also gain acquired resistance via transposition, mutation of existing DNA within the microbe, genetic conjugation, or acquired DNA translation (Lerminiaux and Cameron, 2019; Mancuso *et al.,* 2021).

There are four major pathways through which the development of bacteria resistance could occur. First, the presence of a lipopolysaccharide layer restricts drug uptake in Gram-negative bacteria, thereby becoming less penetrable against antibiotics such as Vancomycin (Pasala *et al.,* 2021). Secondly, Gram-negative bacteria exhibit resistance against antibiotics as a result of drug efflux via active movement out of cells. Based on their energy supply and structure, numerous drugs and that of toxic compound extrusion, the ATP-binding videotape, resistance-nodulation-cell division, major implementer superfamily, and small multidrug resistance are the 5 main families of efflux pumps (Naeem *et al.,* 2023). Microbes such as bacteria exhibit resistance by altering penicillin-binding protein arrangement and number, and by implication the target of the drugs (Douafer *et al.,* 2019). They also generate diverse enzymes responsible for facilitating adenyl, acetyl, and phosphoryl group transfer to the drug compound, which leads to drug inactivation and resultant resistance against specific drug groups such as fluoroquinolones, aminoglycosides, and chloramphenicol (Naeem *et al.,* 2023). Bacteria cause drug inactivation by modifying the drug’s chemical structure or outrightly destroying it (Abushaheen *et al.,* 2020). Beta-lactam medicines’ chemical structure is made up of a beta-lactam loop on four sides which is truncated by the beta-lactamase released by microbial cells (Naeem *et al.,* 2023).

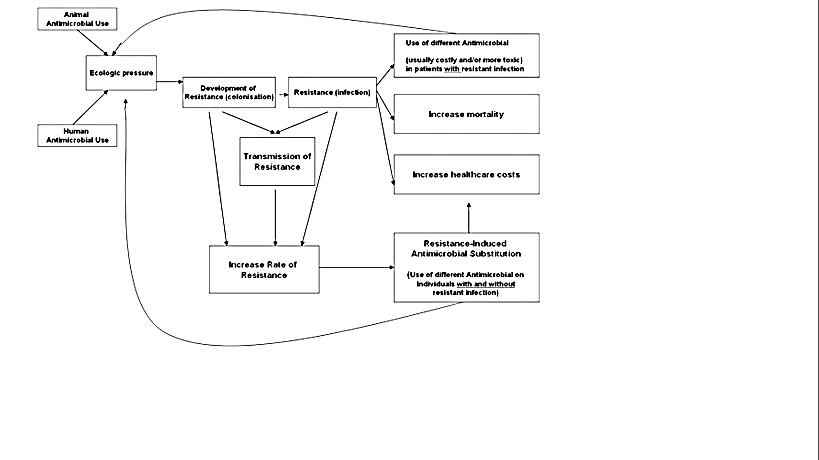
Antibiotic resistance also occurs via the formation of biofilm (Pang *et al.,* 2019). Most microbes especially bacteria release biofilm which facilitates their survival and confers antibiotic and phagocytic resistance (Naeem *et al.,* 2023). Biofilm serves as a solid bacteria shield against antibiotics by entrenching itself in a group of self-generated polymer matrice structures which comprise proteins, polysaccharides, and extracellular DNA. Most fungi and bacteria species undergo biofilm formation as a way to defend themselves and build immunity against infection. They are also considered as a biosensing/communication means among bacteria. By all means, bacteria have developed several strategies and mechanisms to overcome antibiotic impacts (Naeem *et al.,* 2023).

**3.0 The Burden of AMR**

**3.1 Effect of AMR on Public Health and Health Care Systems**

Today, antimicrobial resistance (AMR) poses a worldwide risk (Huttner *et al*., 2013). AMR is already a difficult problem that needs to be tackled in the context of evolving healthcare (Knight *et al.*, 2021). According to (Acar & Röstel, 2001) public health is increasingly being viewed as being threatened by increased antibiotic resistance in bacteria that are significant human pathogens as well as the transmission of antibiotic resistance from hospital-confined environments into open communities. Antimicrobial resistance (AMR) is currently one of the biggest and most urgent threats to public health in the contemporary era. Moreover, it generates key difficulties to the successful prevention and behaviour of chronic diseases. Furthermore, notwithstanding, the several steps that have been taken in the previous few decades to solve this challenge, there are no indications that the worldwide AMR trends will slow down (Dadgostar, 2019). The AMR crisis is becoming terrible and needs urgent attention (Michael *et al*., 2014). According to (Ferri *et al.*, 2017) The unearthing activities of the first antibiotics are consistently improving human health marked the genesis of the antibiotic age. On the other hand, the misuse and abuse of antimicrobials together with human and veterinary medicine have fast-tracked the global spread of antimicrobial resistance in the World (Bloom *et al*., 2018 indicated that the development of antimicrobial resistance (AMR) carries grave consequences, such as a rise in the transmission of infectious diseases, a higher risk of mortality from illnesses that are now regarded as commonplace, and the incapacity to carry out certain medical procedures, like elective surgery, because of untreatable hospital-acquired infections. As mentioned by (Martins and Rabinowitz, 2020) The discovery that the first antibiotics continuously to enhance human health signified the beginning of the antibiotic era. On the other side, the misuse and manipulation of antimicrobials coupled with human and veterinary behaviour have fast-tracked the global expansion of antimicrobial resistance in the World (Michael *et al*., 2014).

It is scientifically proven that AMR is estimated to be responsible for 700 000 deaths annually worldwide; at the same time, by 2050, that number is expected to rise to 10 million fatalities if and only if nothing is done to eliminate the spread. (Ba *et al.*, 2023). In 2013, the United States of America incurred $55 billion in healthcare costs associated to antimicrobial resistance (AMR) only. Over 2 million Americans suffer from resistant illnesses each year, accounting for over 23,000 fatalities. (Dhingra *et al.*, 2020). One of the main contributing factors to the onset and spread of AMR has been the unrestricted use of antibiotics in animal feed. Antimicrobial-resistant bacteria are becoming more commonplace globally, posing a latent pandemic danger to public health and demanding immediate action. (Tufa *et al.*, 2023). It is clear that the penalties of antimicrobial resistance are imperative irrespective of how a nation’s healthcare efforts are controlled (DiazGranados *et al*., 2008). Antimicrobial resistance (AMR) is a global issue caused by a complex web of causes. Finding out how different elements interact is crucial to issue resolution. (Lambraki *et a*l., 2022) See figure 1 below:

**Figure 1:** factor influence antimicrobial resistance and consequences Adopted from (DiazGranados *et al*., 2008).

As indicated by (Paphitou, 2013) since rising AMR poses a hazard to the global public health. In addition, it is recognised well known current efforts are insufficient, several national and international activities, proposals, and initiatives have been established. Amidst these institutions are the European Commission's action plans, World Health Organization's (WHO), and the Infectious Diseases Society of America (IDSA) on the 10 × '20 project implemented, which aims to discover 10 new, effective antibiotics. The main cause of resistance is the usage of antibiotics. According to the CDC, 50% of hospitalised patients' usage of the antibiotics which are drugs related recycled to treat bacterial contaminations is either unsuitable or unnecessary *(Burnham et al*., 2017). More attention is creeping on Antimicrobial resistance (AMR) as it emerged as the World’s chronic public health challenges on a global circle by 2050 if the leasers does not give it an emergency action (Tang *et al*., 2023). From Van *et al*., (2019) studies indicated that antimicrobial contribution in agriculture and food structures might have a substantial impact on the driving of antimicrobial resistance. Research estimates that in the US, about 70% of antibiotics usages to treat humans are available for use in treating animals as veterinary medicine (McKernan *et al*., 2013). Contributions from world scientists on AMR may be problematic to implement; predominantly in developing countries, the burdens for food animals will continue to rise annually (Pokharel *et al*., 2020). Control methods to curb the spread of AMR are desperately needed, but they are complicated by our poor knowledge of the interactions that occur at the microbiological level between infections, AMR-encoding genes, and mobile genetic elements (Waddington *et al.*, 2022).

**3.2 The effects of antibiotic resistance on the economy (AMR).**

It is realized that by 2050, developing nations would have lost roughly 1% of their GDP (Utt & Wells, 2016). Taylor *et al*. have created a hypothetical model to forecast the future economic impacts of AMR on the labor force. The results show that if the present AMR pattern persists, the working-age population of the world will decrease greatly due to the negative impact. Across the board, this shift will be more noticeable in Asia than it will be elsewhere (Taylor *et al*., 2014). In addition, the world will lose roughly $28 billion in Gross Domestic Product (GDP) per year if AMR trends continue in their current direction in the next ten years. According to this estimate, the European Union and the Organization for Economic Cooperation and Development (OECD) view to lose more than the rest of the world, with a projected $20 billion GDP decline (Taylor *et al.,* 2014). It is realized that if at all, the current trends in antimicrobial resistance (AMR) continues in this path, AMR will also have a substantial effect on international trade and will contribute to the reduction of the economy (Lekagul *et al*., 2019). According to CDC estimates, antimicrobial resistance costs the US $55 billion annually, $20 billion for healthcare, and roughly $35 billion for lost productivity (Lekagul *et al*., 2019). Recent World Bank research, by Anderson el al. (2020) indicated that antimicrobial resistance affects decline in revenue in developing nations as compare to other part of the world and upturns the frequency of scarcity. Estimates suggest that by the year 2050, there will be an 11% deterioration in livestock production if ongoing trends in antimicrobial resistance (AMR) continue (Dadgostar, 2019).

After microbes, diseases, moulds, and organisms remain capable towards adaptation, the grow that occurs in the presence of medications which on one occasion exaggerated the free movement, is considered as AMR (Founou *et al*., 2017). Estimates suggest that by 2050, there will be an 11% decline in livestock production if the ongoing trends in antimicrobial resistance (AMR) continue (Dadgostar, 2019). Nowadays, everywhere is indicating that AMR is a grave hazard to the community on public health structures, affecting not only the developing countries (Prestinaci *et al.,* 2015). At the same time, it is also evident that the fact that antibiotics are no longer effective in treating infectious diseases portends a dire future for medical research because of overuse and improper application on the part of consumers (Chokshi *et al.,* 2019). As a matter of fact, if thoughtful consideration is not given to AMR toxicities, they can upshot in protracted sickbay stays, higher healthcare costs, complex expenses for second-line drugs, and cure catastrophes (Founou *et al*., 2017). For example, antimicrobial resistance has been linked to over nine billion euros annually in Europe alone, according to estimates (Llor and Bjerrum, 2014). The cornerstones of contemporary medicine, antibiotics have made significant advancements in healthcare over the past 50 years (Maddocks, 2016). Furthermore, it provides hope and indicates measure negative effects on antibiotic confrontation lessened might have a permanent negative impact on society as a whole.  (Renwick *et al.,* 2016).

**3.2.1 Patient Perspective**

Every year, AMR affects 2 million people in the US, and as a result, about 23,000 people die (Davis et al., 2017). It is also shown that, the estimate of 25000 rates, which is the mortality, indicated by the European Union (EU), is comparable to the annual mortality (World Health Organization, 2018). Decades-long world-wide pains to fight a variety of infectious diseases, such as HIV, TB, and malaria , are also hampered by against biotic struggle (Santos et al., 2015). Treatment-resistant HIV diagnoses are on the rise; in Sub-Saharan Africa (SSA), for instance, 60% of instances of patients with HIV have developed resistance to HIV drugs due to knowledge limitation by users (Llibre, 2017). It is hardly surprising that patients that many people are more likely to die from the infection if they are resistant to HIV drugs (Pinoges et al., 2015). Malaria control efforts to diminish 445,000 as average deaths rate each year from this poisonous sickness are hampered by the intensification in drug confrontation to the disease.

**3.2.2 Healthcare Perspective**

Emerge effects of AMR on healthcare costs are catastrophic (Shrestha et al., 2018). According to the Center for Disease Control (CDC) projections, resistance to antibiotics could potentially result in higher hospital costs when treating patients for any type of bacterial illness by approximately 1,400 dollars alone in the US only (Thorpe et al., 2018). There is a chance that this extra expense will raise to more than $2 billion a year if it remains on the current trends.  (CDC, 2019). According to a number of studies, the annual worldwide cost of AMR might reach over $1 trillion by 2050 (Dadgostar, 2019). AMR's secondary impacts, in addition to its direct cost effects, further tax the healthcare system. In addition, these adverse consequences arise from the inability to appropriately carry out antibiotic-related procedures, which are essential to lower the risk of infection after surgery due to the widespread occurrence of antimicrobial resistance. (Naylor et al., 2000). Additionally, patients receiving organ donations are susceptible to a variety of illnesses; therefore, AMR will make  their implementation extra problematic (Li and Webster, 2018). Treatments for cancer will be impacted by antimicrobial resistance in another unintended way. In addition, knowledge of the potential costs of various AMR secondary effects is incomplete due to a lack of data on their precise costs. (O’neill, 2014).

**4.0 AMR Surveillance, Monitoring, and Control**

According to Baker (2015), in the world today, the treatment shared contaminations like pneumonia, urinary tract infections, and tuberculosis because the care of patients in need of organ transplantation, complex surgery, cancer chemotherapy, and intensive care are all at risk due to the speedy growing and universal blowout of antimicrobial resistance (AMR). Moreover, the absence of knowledge exchange about public health information and surveillance is a fundamental component of public health activities aimed at reducing the prevalence of antimicrobial resistance (AMR) worldwide. Additionally, phenotypic AST has historically been used for AMR surveillance; as it becomes threat to the world there should be adequate awareness and collaboration to decline AMR; however, uniformity is limited by various testing techniques, interpretations, clinical validation of thresholds, and modifications to interpretive guidelines and robust collaborative efforts by all stakeholders (GLASS report, 2021; Baker *et al*., 2018). Many of these restrictions are circumvented by WGS data for many nations, which offers comprehensive insights that can significantly increase the value of AMR surveillance for reduction and limitations (NIHR Global Health Research Unit on Genomic Surveillance of AMR, 2020). The knowledge of AMR's evolution and spread, the development of control methods, the ease with which new and emerging risks can be identified, and the support of novel diagnostic and therapeutic techniques can all be facilitated by such data. If the world collaboratively work hands in hands, the combating of AMR will be done with ease (Perez and Villegas, 2015; O’Brien and Stelling, 2011; Mendelson and Matsoso, 2015).

**4.1 Natural agents used to fight antimicrobial resistance**

Global human health is being threatened by super bacteria’s unstoppable growth and antimicrobial resistance (AMR); antibiotics that we have been using to treat bacterial infections may eventually become ineffective tools, returning us to the dangerous pre-antibiotic age if the issue of antimicrobial resistance is not address (Álvarez-Martínez *et al.,* 2020). However, scientists and organisations from all around the world are aware of this issue, and they are working together to develop methods to deal with the problem of antibiotic-resistant microorganisms. According to Álvarez-Martínez *et al.,* (2020), the 2012 Chennai Declaration of India served as evidence of this, as medical professionals from around the world convened to devise action plans in response to the superbugs’ unstoppable progress. A research by Sultan *et al*, (2018), revealed that acquiring new genetic material, changing the way their genome is expressed, and undergoing mutations, bacteria exploit their genetic flexibility to fend against antibiotic attack. Thus, bacteria that withstand an antibiotic’s onslaught serve as the ancestors of subsequent bacterial generations, exacerbating the resistance issue. Once acquired, antibiotic resistance genes can be horizontally transferred or transferred by division processes from one bacterium to another (Daubin and Szollosi, 2018).

A study by Katz and Baltz, (2016), revealed that natural products (NPs) including other key products are a wide variety of chemicals having a wide range of uses in the agricultural, industrial, veterinary, and other fields. NPs are molecules that are derived from the secondary metabolism of bacteria, fungi, vegetables, and mammals. With a wide variety of chemicals having a wide range of uses in the agricultural, industrial, veterinary, and other fields. (Katz and Baltz, 2016). Since the discovery of novel natural products (NPs), 23,000 have been described. penicillin, and many of them have been shown to be useful resources for pharmacology, insecticides, herbicides, and other fields (Berdy *et al.,* 2012).

Plantsare primary sources of antibacterial natural products (NPs.) The mainstream of biosphere on Globe is completed up of plant creatures, whose Over 80% is made up of biomass of all biomass (Bar-On *et al.,* 2018). Plants require endured, developed, besides adapted to a wide range of environments and challenging circumstances since they first appeared. Because of this adaptive process, they have evolved sophisticated and potent defence mechanisms against abiotic stressors, diseases, and predators, among other external threats (Álvarez-Martínez *et al.,* 2020). Another major source of antimicrobial NPs that gained significant prominence in the 20th century is bacteria, the Waksman platform helped scientists discover most of the antibiotics used in clinics today in the 1940s (Álvarez-Martínez *et al.,* 2020). Particularly from the genus Actinomycetes, bacteria have been the source of numerous of the NPs with antibiotic activity that have been identified is helping. Natural products were the main attraction during the era known as the “Golden Age” of antibiotic discovery, which started in the 1940s (Álvarez-Martínez *et al.,* 2020). Nowadays, of the main origins of AMPs, or antimicrobial proteins or peptides is animals, particularly insects. More than 150 novel AMPs have been isolated or discovered since the discovery of AMPs in 1974; these are primarily cationic peptides with lengths ranging from 20 to 50 residues. The primary mechanism via which these compounds exhibit antimicrobial activity is bacterial plasma membrane disruption, most likely by the formation of holes or ion channels (Barrajon-Catalan *et al.,* 2010). Additionally, several AMPs have demonstrated antiviral, antifungal, and antiparasitic qualities (Falco *et al*., 2013). Pathogenic microorganisms that are gram-negative Aspergillomarasmine A, a polyaminoacid that is naturally produced by Aspergillus versicolor, has the ability to block the enzymes that cause antibiotic resistance in bacteria such as Klebsiella pneumoniae, Acinetobacter species, Pseudomonas species, and Enterobacteriaceae. This medication has been effectively used to overcome resistance in mice infected with meropenem-resistant K. pneumoniae due to the NDM-I protein, making the bacteria susceptible to the antibiotic and putting an end to the infection (King *et al.,* 2014).

Mirandamycin is a quinol with fungal origins that can stop the growth is more effective against Gram-negative bacteria than Gram-positive ones, while both types of bacteria can be that are resistant to antibiotics like MRSA and K. pneumoniae that produces carbapenemase. It works by preventing bacteria from metabolising carbohydrates, which prevents them from fermenting and being transported (Ymele-Leki *et al.,* 2012). There is proof that certain fungus species have antibacterial properties against Gram-positive bacteria. Using Kirby-Bauer assays, extracts from Antimicrobial activity against Gram-positive bacteria such *as S. auerus* and *B. luteus* was demonstrated by *Ganoderma lucidum*, *Ganoderma applanatum*, *Meripilus giganteus*, *Laetiporus sulphureus*, *Flammulina velutipes*, *Coriolus versicolor*, *Pleurotus ostreatus*, and *Panus tigrinus* (Karaman et al., 2010). Antimicrobial drugs serve a critical role in reducing the global burden of infectious diseases; however, the effectiveness of the antibiotics declines when resistant organisms multiply and grow. This type of bacterial resistance to antimicrobial medications poses a serious threat to public health, and resistance rates are increasing globally for all antibiotics, including the primary last-resort drugs (Levy and Marshall, 2004; Mandal *et al.,* 2009). Thus, the pressing need for novel antimicrobial methods has led to a reassessment of the therapeutic use of traditional remedies like plants and plant-based foods like honey (Mandal *et al.,* 2010; Mandal *et al*., 2010). Numerous studies have examined the antibacterial properties of honey in the present day and have found that natural, unheated honey has some broad-spectrum antibacterial action when tested against food spoilage bacteria, mouth bacteria, and pathogenic bacteria (Mandal and Mandal, 2011). One of the first known antibiotics is honey, which dates back thousands of years. Honey was a common natural antibacterial and skin protector utilised by the Egyptians. Hydrogen peroxide (H2O2) is present in honey, which could explain part of its antimicrobial qualities. Moreover, its high sugar content can inhibit the growth of some germs Mandal and Mandal, 2011).

Honey has long been used as a traditional treatment for microbiological infections (Molan, 1992). Manuka (L. scoparium) honey has been studied (Molan, 1992) and it has been shown to be effective against a number of human diseases, such as Salmonella typhimurium, S. aureus, Escherichia coli (E. coli), and Enterobacter aerogenes (Lusby *et al*., 2005; Visavadia *et al*., 2006).

**4.2 Innovative approaches Adopted to combat AMR**

**4.2.1 Genomic technologies**

Argimón *et al*. , (2020) noted that antimicrobial susceptibility testing (AST) based on culture has historically been the primary method for identifying antimicrobial resistance (AMR) and is still the cornerstone of clinical microbiology and patient care. Although phenotyping offers direct visual proof of how a bacteria will react to an antibiotic, it usually yields little to no information about the resistance mechanisms because different genetic clones frequently exhibit the same resistance profiles. According to Sekyere and Asante (2018), the potential of genomic diagnostic procedures for tracking, detecting, isolating, and characterization of antibiotic-resistant bacteria cannot be overemphasised. Furthermore, genomic techniques have been used to address antimicrobial resistance (AMR) by tracking and analyzing the genetic makeup of bacteria. These techniques have been used to identify the genetic mutations that cause AMR, track the spread of resistant strains, and develop new treatments. According to Djordjevic *et al*. (2024), the mobilization, persistence, and abundance of AMR genes and mutations within and between microbial communities may now be tracked thanks to genomic technologies. The modelling of AMR evolution and transmission as well as source-tracing of AMR infections have been made possible by its adoption.

**4.2.1.1 Whole Genome Sequencing (WGS)**

Utilizing a number of genetic analysis techniques that concentrate on specific regions of the bacterial genome, genomic analysis got its start early on (van Belkum *et al*., 2007). The idea of putting more efforts in AMR is something to be handled very seriously.

According to the NIHR Global Health Research Unit on Genomic Surveillance of AMR (2020), multi-locus sequence typing (MLST) is one genetic typing method that offers a higher level of pathogen resolution than AST, but it is also very restrictive because it only describes a small portion of genome surveillance. At the same time, amplification- and non-amplification-based genomic techniques are only employed to study tiny portions of the bacterial genome (Quainoo *et al*., 2017), with restriction on these methods to species-dependent protocols will greatly aid in the process. WGS-based typing of bacterial pathogens includes mobile genetic elements and could provide unprecedented resolution in discriminating even highly related lineages, thereby obviating species-dependent protocols. Whole-genome sequencing (WGS), in contrast, provides genome-wide information at the single nucleotide level that can be used to identify the presence and mechanisms of AMR, as well as pathogen identity, virulence, and ancestry (Didelot *et al*., 2014; Price *et al*., 2013). Considering the advent of next-generation sequencing (NGS), which has contributed to pathogen genomes comparatively at low cost and is determined rapidly from the parallel sequencing, including the DNA fragmentation involvement. (Didelot *et al*., 2014; Ashton *et al*., 2016). WGS technology is being used more and more to address the AMR public health concern, assisting with surveillance and epidemic investigations as well as improving diagnosis and treatments (NIHR Global Health Research Unit on Genomic Surveillance of AMR, 2020; Besser *et al*., 2018). Access to putative virulence factors, disruptive targets, prospective pharmacological molecules, mechanisms of pathogenicity, drug resistance, and transmission, as well as their evolution in infections, has been made possible by whole genome sequencing (WGS) technology (Green et al., 2010; Feng *et al*., 2009). Furthermore, WGS analysis revealed details regarding bacterial strains that were recovered from clinical specimens but were uncultured or difficult to cultivate. Furthermore, conclusions about the nature of AMR evolution and dissemination can be drawn thanks to the fine resolution that WGS offers. These conclusions can aid in the containment of AMR and safeguard public health (Beres *et al*., 2010).

**4.2.1.2 Nanotechnology Approaches**

Nanotechnology captures the study of tiny particles at the nano level and it offers immense potential to tackle antibiotic resistance. Particles within the 1 to 100nm size range are considered to be nanoparticles (Mohajerani *et al.,* 2019). Nanoparticles have aroused the interest of several scientists and researchers, especially in recent decades (Astruc, 2020; Dubadi *et al.,* 2023). They are projected to be crucial in tackling antimicrobial resistance via several through several pathways and mechanisms such as inhibition of biofilm formation, increased build-up of intracellular drugs, and formation of reactive oxygen species(ROS) (Naeem *et al.,* 2023).

Saxena *et al*. (2022) noted that Conventional methods such as phenotypic approaches, biochemical assays, and molecular techniques are laborious, resource-intensive, and require a lengthy turnaround time in order to produce confirming data for AMR diagnosis. On the other hand, the more recent development of methods aided by nanotechnology helps to overcome the shortcomings of classical methodologies and provides more straightforward, sensitive, quick, and economical options for AMR findings. It also presents a promising avenue for tackling antimicrobial resistance (AMR) in food by providing targeted, efficient solutions that minimize the use of antibiotics. According to Chakraborty *et al*. (2022), Recent research has demonstrated the potential of nanoparticle-based solutions to overcome antibiotic resistance in both planktonic and biofilm phenotypes. This is the outcome of combining cutting-edge nanomaterial research with established antibacterial treatments, which have the potential to produce an entirely new class of highly effective active nanocarrier systems (Weldick *et al*., 2022). Through the use of nanomaterials, antibacterial modalities that are new to bacteria and outside of their natural defense repertoire can be accessed. The confinement of materials with multivalent interactions and a high surface-to-volume ratio at the nanoscale is a major factor in the therapeutic effect of nanomaterials. Furthermore, for the safe management of infectious diseases and superfcial infections, metals at nanoscale, metal oxides, organic nanoparticles (NPs), and nanocomposites with strong antibacterial properties are helpful from a strategic standpoint. These antibacterial nanomaterials, also known as nanobiotics, have a variety of chemical compositions and inherent qualities that allow for many modes of exploit touching the bull microorganisms ( [Chakraborty *et al.,*](https://doi.org/10.1186/s12951-022-01573-9) , 2022). Nanomaterial platforms, nanoparticle-based rapid point-of-care (POC) platforms, nano-biosensors, microfluidic-assisted devices, and importantly, nanotheranostic devices for diagnostics and treatment of antimicrobial-resistant infections are examples of rapidly growing nanotechnology approaches used for AMR administration (Saxena *et al*., 2022). When compared to the usage of antibiotics in bulk, antibiotic nanocarriers" based on liposomal, solid/lipid, terpenoid, polymeric, dendrimeric, and inorganic materials have demonstrated good results in improving the overall performance of antibiotics. (Makabenta *et al*., 2021). The instruments of accomplishment of nanoparticles have not been fully investigated in sufficient scope although several researchers have come up with many hypotheses such as bacterial cell homeostasis disturbance and disruption of cell membrane. (Nisar *et al.,* 2019; Kavitha *et al.,* 2023). Diverse mechanisms of action are responsible for how various nanoparticle types combat microbes, this is highly reflected in silver and gold nanoparticles, whereby there is accumulation of silver nanoparticles on the cell wall resulting in disruption, and damage in the cell structure and eventual death (Naeem *et al.,* 2023). The nanoparticles are chemically grouped into inorganic and organic substances. The **Table 1** provides a summary of the mode of action of nanomaterials utilized for AMR monitoring and control.

**Table 1:** Nanomaterials and their mode of action against antimicrobial resistant bacteria

|  |  |  |
| --- | --- | --- |
| **Nanomaterial** | **Mode of action on AMR bacteria** | **Reference (s)** |
| **Nano metal oxides** | | |
| NPs of iron oxide (FeONPs) | Combined with the DNA hybridization method to increase the bacterial 16S ribosomal RNA gene capture. | Chung *et al*. (2013) |
| AgNPs, or silver nanoparticles | Cling to the cell membrane, engage in interactions with membrane proteins, expand the membrane's porosity, and enter and intensify the production of reactive oxygen species (ROS), which obstruct respiration and cause inflammatory responses in addition to bacterial cell lysis.  Possess the ability to cause chromosomal abnormalities, disrupt bacterial DNA transcription and unwinding, and violate DNA chains. This process is going to an end.  The Cause of the bacterial membrane to anchor, which will dissipate the proton motive force and cause jamming of oxidative phosphorylation. | Tripathi and Goshisht (2022); Cheng *et al*. (2022); Johnston *et al*. (2010); Lee *et al*. (2019). |
| Fe3O4 and TiO2 core shell magnetic NPs | The production of ROS that promotes intracellular component ejection and improves cell porosity | Chen *et al*. (2008) |
| Gold NPs (AuNPs) | Accumulate on the cell surface and exert bactericidal effects, which are attributed to the strong electrostatic forces, cytoplasmic leakage, and cell death.  Exhibit facet-dependent antibacterial actions, including the destruction of bacterial membranes, the suppression of cellular enzyme activity, and the consumption of energy. | Okkeh *et al*. (2021); Zheng *et al*. (2020) |
| Quantum dots (QDs) eg Graphene | Destroy the membranes or cell walls of bacteria, release free radicals, bind to genetic material, and stop the bacterial synthesis of energy. Stop the growth.  Increase the formation of ROS in light-activable GQDs by converting light energy into heat, which effectively kills bacteria. | Rajendiran *et al*. (2019);  Courtney *et al*. (2016);  Yu *et al*. (2020) |
| CaF2 NPs | Possess deadly qualities against bacteria due to their adhesion to tooth surfaces and continuous fluoride ion release, which promotes remineralization and reduces virulence. | Kulshrestha *et al*. (2016) |
| ZnO NPs | Causes the loss of membrane integrity by changing Campylobacter jejuni's helical shape to a spherical one. | Xie *et al*. (2011) |
| CuO NPs | Demonstrate excellent antibacterial qualities by rupturing the bacterial cell membrane. | Usman *et al*. (2013) |
| **Organic NPs** | | |
| Liposomes and lipid NPs | Merge with the microbial matrix or the cell membrane to release the prescribed medication into the bacterium, especially against biofilm-mediated recurrent infections. | Wang *et al*. (2021) |
| Nanospheres/Nanocapsules, | The ability to attach to the elements of biofilm and shields antibiotics from deterioration. | Cano *et al*. (2020); Forier *et al*. (2014) |
| **Nanozymes** | | |
| FeO-based artificial peroxidase NPs | Possess highly uneven edges that serve as active sites, rough surfaces that promote bacterial adherence, the capacity to control the formation of reactive oxygen species (ROS), and a talent for photocatalytic activation.  When surface-bound, nanozymes eradicate pathogens and postpone the emergence of resistance; when coated, they have the ability to stop the formation of biofilms. | Meng *et al.* (2020); Gao *et al*. (2021) |
| **Antibacterial surfaces** | | |
| Immobilization of surfaces by TiO2 and AgNPs | Photocatalytic activity, ensuing Reactive oxygen species (ROS) generation. | Santander *et al*. (2018);  Agnihotri *et al*. (2013) |
| **Graphene-Based** | | |
| “Nano-knives” or MoS2, MnO2 | Microsharp edges have the ability to literally break down bacterial cell walls. | Lu *et al*. (2017) |
| The Fullerenes | Physically rupturing the integrity of the bacteria's cell wall will kill them. | Lyon *et al*. (2005) |
| **Nanotubes** | | |
| Carbon nanotubes (CNT) | One of their main mechanisms for having bactericidal effects is to induce oxidative stress. | Hamal *et al*. (2010) |
| Magnetic nanoprobe comprising of Fe3O4@TiO2 core-shell nanostructures | Photo killing of multidrug-resistant organisms under UV irradiation | Chen *et al*. (2008) |
| Au-superparamagnetic iron oxide NPs | Possess a great affinity for the disulphide bond found in bacterial proteins, which influences cell redox balance and metabolism. | Niemirowicz *et al*. (2014) |

**4.3 Future Directions and Outlook**

Globally, antimicrobial resistance continues to pose severe threats and challenges to public health and food safety endeavours. Traditional strategies such as vaccination and antibiotics have proven insufficient in addressing this menace. At the forefront of this combat are genomic approaches such as Short Read Sequence Typing (SRST2), Antibiotic Resistance Gene-Annotation (ARG-ANNOT), and the Comprehensive Antibiotic Resistance Database (CARD) which enable scientists to detect genetic mutations responsible for resistance, monitor the spread of resistant strains, develop targeted treatments and track antimicrobial resistance. Research can leverage these techniques in order to gain deeper insights into the mechanisms responsible for resistance and also foster the development of more efficient counterapproaches.

Undoubtedly, a promising strategy for combating AMR is nanotechnology. Its application in food safety and preservation can translate to a drastic reduction in the predominance of antibiotic-resistant bacteria in foodstuffs, which will in turn impact the protection of public health significantly. Engineered nanoparticles can serve to effectively target and neutralize resistant bacteria via interference with bacterial communication systems and disruption of bacterial cell walls, thereby reducing the need for conventional antibiotics. The exploration of substitute therapies and tools such as probiotics, antimicrobial peptides, and phage therapy can complement efforts in combating AMR. Naturally occurring proteins, antimicrobial peptides capable of killing bacteria present another promising approach. Phage therapy utilize bacteriophages in targeting specific bacterial strains without interfering with the beneficial microbes. Antimicrobial peptides consist of naturally occurring proteins capable of eliminatingl bacteria, thereby offers another promising alternative. On the other hand, probiotics can facilitate the maintenance of a healthy microbiome and inhibit colonization by resistant bacteria.

The implementation of holistic educational programmes on dangers of resistance and responsible antibiotics usage and policies is pivotal to the mitigation of AMR and promotion of sustainable practices. Tackling AMR demands a multidisciplinary approach which entails the involvement of several disciplines, including food science, pharmacology, microbiology and public health, in order to effectively develop and implement innovative solutions. Public awareness campaigns and regulations can minimize resistance incidence significantly. Innovative approaches to combating AMR are vital in protecting public health and ensuring food safety. By incorporating collaborative research into nanotechnology, alternative therapies, genomic techniques, and robust policies, comprehensive strategies can be developed to combat the threats and risks pose by antibiotic resistance in order to safeguard both current and future generations and also sustain the efficacy of antibiotics in the future.

**5.0 Conclusions**

Antimicrobial resistance poses a significant threat to human existence and life globally. Traditional approaches are losing the game very fast against dynamic drug-resistant pathogens. Nanotechnology, though still an infant, presents itself as a viable alternative strategy for the production of future nano-antibiotics and demands immense investment, and commitment. Beyond tackling AMR headlong, nanotechnology will no doubt open us up to various paths in the future. Nanoparticles have superior advantages such as absorption, delivery, longevity, distribution, and controlled release. However, a detailed investigation of nanomaterials is needed to assess their effects on farm animals, the environment prior to implementation on a large scale.

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