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Nanoencapsulation of natural products and their role in the preservation and control of contaminations in the food industry

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Abstract

Microbial resistance is a problem of high notoriety and importance, being investigated in several scientific areas. Directly correlated to the abuse of macrolides in the pandemic context, the difficulty in eliminating resistant microorganisms and the control of bacterial contamination in an industrial food environment have been increasingly worrying nowadays. The present study demonstrates hypotheses of microbial control using the encapsulation of essential oils and products of natural origin through the technology used in nanocomposites. The aid in the prevention and control of microorganisms with high antimicrobial resistance factors in food industry environments can be seen. Furthermore, new approaches and themes applied in the denaturation of pathogenic biofilms and nanoencapsulation and the use of common metals and transition metals are highlighted.

Keywords: antimicrobial resistance; natural products; nanoemulsions; essential oils; food industry.

Practical Application: In this paper, we discuss new approaches and strategies to contain microbial spread and resistance in an industrial food context.

1 INTRODUCTION

In 1941, an enzymatic inhibitor known as penicillin was discovered and titrated as the first antibiotic distributed in a commercial context. Later, discussions about the use of antimicrobials permeated the scientific society through the decades. Currently, the terms correlated with antimicrobial resistance (AMR) are widely addressed and gain prominence for their primary importance in clinical and industrial environments, especially in food processing industries (Zimerman, 2010).

The ability of microorganisms in adapting to drugs and cleaning agents that do not exhibit the pre-established effect is becoming notorious and worrying, and it is possible to observe the expansion of the resistance spectrum over time. In certain bacterial species, such as Gram-positive and Gram-negative cocci and bacilli, and also bacteria of various heterogeneous groups, there are already observable high levels of tolerance, resistance, and adaptation to the unstable environment (Abrantes & Nogueira, 2021).

In several sectors of the food production chain, the presence of resistant bacteria is observable, as well as in the production plants and agropastoral environments, which can exhibit contaminants and biofilm formation in the manufacture and processing of food, and can be problematic due to the pathogenic nature of the strains to humans. For example, *Listeria monocytogenes* and *Staphylococcus aureus* (Gram-positive bacilli and cocci) are bacteria that can contaminate various foods, even in refrigerated and freezing conditions, and are increasingly resistant and harmful due to their biofilm formation capacity (Bland et al., 2022).

The use of nanocompounds in the encapsulation of natural products can assist food industrial environments in combating food contamination, thereby leading to food preservation in the industry, as well as tackling biofilms and resistance factors. Thus, the study aimed to report and discuss information from the literature on the subject.

2 MATERIALS AND METHODS

This research has a descriptive-discursive character, emphasizing as a priority the concept of AMR applied from the perspective of the preservation of environments in the food industry, as well as in the fight against resistant microorganisms through the encapsulation of natural compounds.

Thus, objective searches were performed using databases such as PubMed, SciELO, Google Scholar, and Web of Science.

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During the article search for this bibliographical research, the terms “antimicrobial resistance,” “nanocomposite encapsulation,” “biofilm,” and “food industry” were used, without exclusion criteria, but greater attention was paid to the most recent articles and those with particular applicability in the scope of the review.

3 RESULTS AND DISCUSSION

3.1 Antimicrobial resistance in the global context

At population and global levels, AMR can be widely mediated by indirect effects. There are direct possibilities of competition between resistant microorganisms to infect or colonize hosts; in addition, the indiscriminate use of macrolides has a greater impact on the transmission of susceptible bacteria than others exhibiting resistance factors; that is, the increase in the abusive use of antibiotics will culminate in a higher frequency of microorganisms resistant to this specific type of drug. In addition, the patient-to-patient transmission and the use of antibiotics, which are not independent ways to promote a greater possibility of resistance, are intrinsically correlated (Lipsitch & Samore, 2002).

In this context, it is notorious that AMR can bring silent damage to humanity in a period that is still debatable but not far from the current perspectives, being of a public nature concerned with the factors of resistance and tolerance. Thus, if there is no containment plan organized by managers specialized in the subject, it can be considered a major threat to public health (McEwen & Collignon, 2018).

From a historical perspective, the discovery of microbes directly impacted medical practices and the treatment of infections, revolutionizing medicine’s perspective on microorganisms. Currently, antimicrobials are indispensable in surgeries, cancer treatment, immunological hypersensitivity reactions, and the treatment of critically ill patients, among other possibilities. However, the large increase in AMR has hampered the success of clinical practices and their various scenarios (Khan et al., 2018).

Along with the discovery of antibiotics, resistance factors were discovered at similar times, such as sulfonamides, discovered in 1937, and after a decade, it was already reported that microbial resistance was present. In addition, the discovery of penicillin itself occurred in 1928, and the identification of bacterial penicillinase came a few years later. Penicillin resistance provoked new actions in the scientific community and new searches for compounds such as beta-lactams. However, resistance factors still permeated even the discoveries of science. The adaptability of a microorganism is high, and as well as its survival in extreme conditions, it is also possible to point out the various genetic and gene mutations. In short, the increase in AMR has resulted in scarcity and a reduction in the range of treatments that patients can receive, leading to a rise in morbidity and mortality rates from infections by resistant microorganisms (Jubeh et al., 2020).

The World Health Organization (WHO) highlighted in a new list several names of species of microorganisms resistant to macrolides and antibiotics, highlighting the need for new therapies. Gram-negative organisms are the focus of reporting, particularly those that are resistant to carbapenems, such as *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and Enterobacteriaceae family members that also contain broad-spectrum beta-lactamases (Venter et al., 2019). Resistance factors in microorganisms demonstrate a significant public health challenge worldwide; according to estimates, they caused 700,000 deaths in 2014. Besides, it is estimated that the number of fatalities from microorganisms could reach 10 million by 250 if the necessary social measures are not properly taken (Sekyere & Asante, 2018).

The WHO, together with other institutions that are based on the constant improvement of factors that involve human health, agreed that the dissemination of knowledge related to the abuse of macrolides and resistant microorganisms is an urgent matter and requires a global action plan (Centers for Disease Control and Prevention, 2019; Chiang et al., 2017; Prestinaci et al., 2015). Information on the current magnitude of resistance factors and their possible worrying patterns across various locations worldwide and the main pathogen-drug combination that contributes to the impact of AMR is essential and should be constantly reported (Murray et al., 2022).

Resistant pathogens and antibiotics were observed in human, animal, and environmental organisms across every continent, in the Arctic, and in space facilities. Nonetheless, the occurrence of resistant pathogens can vary according to geographic regions and the concentrations of disseminated macrolides. Global mobility and socioeconomic factors may play a crucial, previously unrecognized role when describing geographic patterns in AMR in comparison to levels considered normal for resistance factors. In addition, nomadic travelers and others from endemic regions are at risk of encountering resistant microorganisms and of spreading and colonizing new areas with these pathogens (Frost et al., 2019).

A study done by Antimicrobial Resistance Collaborators (Murray et al., 2022) has calculated that 1.27 million deaths in 2019 were directly related to resistance in the 88 pathogen-drug combinations that were examined. Also, it has been estimated that in 2019, Australasia possessed the least amount of bacterial AMR burden, with AMR being responsible for 6.5 out of every 100,000 deaths and associated with 28.0 per 100,000 deaths. Western sub-Saharan Africa had the highest burden, with AMR being responsible for 27.3 out of every 100,000 deaths and associated with 114.8 per 100,000 deaths. Methicillin-resistant *S. aureus* was the pathogen that caused over 100,000 deaths and 3.5 million daily deaths due to resistance. With the exception of XDR tuberculosis, there were six additional pathogen-related deaths in 2019. These were third-generation cephalosporin-resistant *E. coli*, carbapenem-resistant *A. baumannii*, fluoroquinolone-resistant *E. coli*, carbapenem-resistant *Klebseilla pneumoniae*, and third-generation cephalosporin-resistant *K. pneumoniae*.

The indiscriminate use of macrolides in medical issues concerning the well-being of humans and animals has intensified the dissemination and acquisition of antibiotic resistance within bacteria. Additionally, the persistent presence of antibiotic residues in aquatic environments and in animals present in seas and rivers highlights the emergence of resistant microorganisms within the aquatic ecosystem, which directly affects food of marine origin and the ecological balance itself (Campista-León et al., 2021).

Recently, the pandemic times caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus have overloaded the systems of different areas across the world. Recent evidence suggests that after the collapse of health systems during the pandemic, the indiscriminate prescription of antibiotics is directly correlated with the number of hospitalized patients with kidney and liver inflammation due to substance abuse. Also correlated with self-medication, patients who abused the use of macrolides to try to prevent a viral agent were a major failure of information proliferated amidst the pandemic chaos (Rawson et al., 2021).

Patients with co-infections with bacteria had a comparatively high rate of adverse drug reactions (ADRs), as confirmed by microbiology, during the first 18 months of the coronavirus disease (COVID-19) pandemic. *P. aeruginosa*, MRSA, CRAB, and *K. pneumoniae* were documented as the most frequent resistance cases, while some isolates of *C. auris* have also been found (Kariyawasam et al., 2022).

Not only bacteria can stop resistance factors, but the fact that there are only three classes of antifungal medications available to treat systemic fungal infections highlights the impact of fungi on human health. These include echinocandins, which prevent the biosynthesis of fungal cell walls; azoles, which target the biosynthesis of ergosterol; and polyenes, which trigger cell lysis by binding ergosterol on the fungal cell membrane. The emergence of multidrug-resistant ones poses a further threat to our meager supply of antifungals (Revie et al., 2018). One of the factors that may contribute to fungal resistance is the difficulty in manufacturing new compounds and drugs that do not boost resistance and maintain the fungal structure without mutations (Chang et al., 2019).

3.2 The dichotomy between the terms tolerance, sensitivity, and resistance

To separate the modalities of survival of microorganisms, "tolerance" and "persistence" were developed (Bigger, 1944; Horne & Tomasz, 1977). But their meanings and ways of being distinguished from one another have remained unclear. In contrast to tolerance, which is more commonly used to describe the capacity of microorganisms to endure a brief exposure to elevated antibiotic concentrations without a modification in the minimum inhibitory concentration (MIC), resistance is quantified by this technique regarding the specific antibiotic and refers to the inherited ability of microorganisms to grow at high antibiotic concentrations independent of the length of treatment.

The definition of tolerance provided by Kester and Fortune (2014) states that tolerance allows bacteria to withstand brief exposure to antibiotics in fatal doses and may be acquired by a genetic mutation or provided by environmental circumstances. Thus, the distinction between the different methods utilized by bacterial cells for survival upon exposure to antibiotics is crucial for numerous reasons (Balaban et al., 2013). First, various survival strategies differ in their essential method of action, which means that therapy will frequently be useless if it is provided independently of the survival strategy, even considering apparent similarities among the molecules (Tuomanen et al., 1986). Also, the mechanisms involving the survival strategy considering different antibiotics may be affected differently by drug reactions. For instance, numerous types of antibiotics will frequently benefit from tolerance by many factors (i.e., growth rate), even though most resistance mechanisms are exclusive to one class of antibiotics (Handwerger & Tomasz, 1985). Different metrics and experimental techniques are needed for each survival tactic when quantitatively measuring resistance, tolerance, or persistence (Brauner et al., 2016).

3.3 Antimicrobial resistance: intrinsic, acquired, and adaptive

Microbes, encompassing bacteria, viruses, fungi, and parasites, exhibit AMR (Morrison & Zembower, 2020) that can be intrinsic, acquired, or adaptive (Christaki et al., 2020). Before the discovery of antibiotics, AMR was already present; however, it was reported in the scientific literature only after their notification. This type of resistance is called intrinsic resistance. The presence of intrinsic resistance is a trait shared by all microorganism species; it is not caused by horizontal gene transfer and is unaffected by selective pressure from antibiotics (Cox & Wright, 2013). As demonstrated by Dancer et al. (1997), it is observed that ampicillin resistance is present in isolated coliform bacteria (older than 2000 years) from glacial waters. In another study, bacteria that were extracted from permafrost that was older than 30,000 years showed vancomycin resistance (D'Costa et al., 2011).

In bacteria, this resistance is highly caused by the outer membrane's impermeability found in the cell envelope of Gram-negative bacteria (Christaki et al., 2020). This outer membrane is important to reduce the rate of small molecule penetration but is unable to entirely block influx, and this fact is not a major factor in drug resistance at a substantial level. Nonetheless, the existence of a secondary factor, like the *P. aeruginosa* periplasmic beta-lactamase or active efflux, can have strong synergistic effects on levels of intrinsic resistance, indicating an interaction between the outer membrane and other resistance mechanisms (Cox & Wright, 2013). Intrinsic genetic alteration, such as mutations or differential genes, also contributes to resistance; any microorganism can have resistance genes that are minimally, stably, or optimally expressed when induced (McCarlie et al., 2020).

Numerous fungal species possess intrinsic resistance to specific antifungal classes, and the underlying mechanisms of this resistance remain incompletely understood (Chang et al., 2019). About the mechanisms known, two distinct drug efflux mechanisms regulate resistance in fungus: the adenosine triphosphate (ATP)-binding cassette (ABC) superfamily and the major facilitator superfamily (MFS). Specific ABC transports are also linked to fungus pathogens' azole resistance, including *C. glabrata*, *C. neoformans*, and *Aspergillus fumigatus*. The electrochemical proton-motive force is used by the MFS to power drug flux; however, this mechanism affects the sensibility of *C. albicans* and *C. dubliniensis* (Cowen et al., 2015).

When microorganisms learn to avoid the mechanisms that pharmaceuticals employ to combat them, it is known as AMR. This resistance can be acquired when a previously sensitive microorganism develops a mechanism of resistance through changes in genetic material through mutation or acquisition from outside sources, or it can be adaptive when induced by specific environmental signals. Adaptive resistance is transient in comparison to intrinsic and acquired resistance (Christaki et al., 2020). Microorganisms have high genetic plasticity, which allows them to continuously change and adjust to antimicrobial stress. This can occur through mutations in genes that decrease drug susceptibility or by horizontal gene transfer, obtaining foreign DNA that encodes resistance determinants (Khan et al., 2018). When an antifungal medication is administered to a patient and they do not respond to it at the recommended dose, this is referred to as clinical resistance and represents therapeutic failure.

A variety of host and microbial factors are involved in the complex process of antifungal resistance development. The host's immune system is essential because fungistatic medications must cooperate in order to control and eradicate the infection. Individuals with severe immune dysfunction are inclined to experience treatment failure because the antifungal medication has to combat the infection without the help of the immune system (McCarlie et al., 2020). The development of drug resistance in bacteria can result from mutations in intrinsic chromosomal genes or from acquiring foreign DNA, like plasmids, which express multiple resistance mechanisms simultaneously. Clonal and polyclonal growth of resistant bacteria and horizontal transmission of resistant plasmids have reduced the efficacy of antibacterial agents (Figure 1).

Resistance in Gram-positive bacteria can arise from two main processes: producing the beta-lactamase enzyme to degrade antibiotics or decreasing their target site's affinity and susceptibility to penicillin-binding protein (PBP), either through the acquisition of exogenous DNA or through modifications to native PBP genes (Jubeh et al., 2020). Despite their simple structure consisting of a protein coat, nucleic acid, viral enzymes, and occasionally a lipid envelope, viruses can also exhibit acquired drug resistance (Kausar et al., 2021). Mutations leading to drug resistance occur in human immunodeficiency virus-1 (HIV-1) due to pressure exerted by antiretroviral therapy, resulting in treatment failure and viral rebound. Treatment-naive people can contract drug-resistant HIV variants, which over time can spread throughout the population, restricting available treatments and posing global clinical and public health implications (Blassel et al., 2021). The potential for vast genetic variability is also seen in influenza viruses. The highly error-prone RNA-dependent RNA polymerase in influenza viruses raises concerns about the potential rise in strains resistant to treatment, raising more inquiries about their transmissibility and viral fitness, along with what tactics should be employed for rapid identification and the effective treatment of these resistant strains (Lampejo, 2020).

Adamantanes, a drug utilized against the influenza virus in 1980, has efficacy rates of up to 90% (Hay et al., 1985).

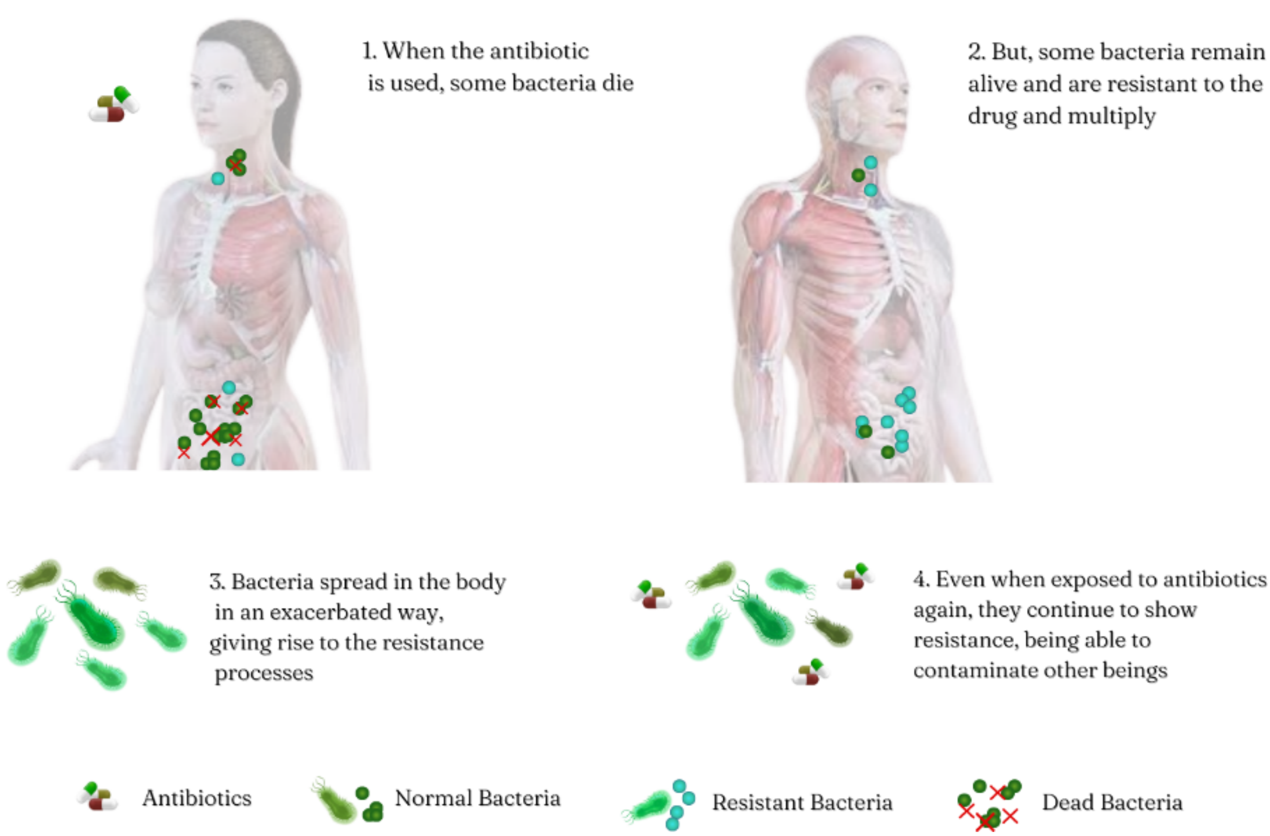

Figure 1. Sequence of antimicrobial resistance in the human body.

Around 45% of all influenza A subtypes in circulation worldwide by 2013, along with over 69% of H1 subtypes and 43% of H3 subtypes, were resistant to adamantanes (Hussain et al., 2017) (Figure 1).

3.4 Resistant organisms in the food industry

In the industrial environment, microbiological contamination is a persistent problem, and its control can cost millions of dollars annually. Food poisoning caused by resistant microorganisms results in serious damage to the health of the worker, the business contributor, and the population, which can be contaminated in the endemic scope. Monitoring and identification pipelines are paramount in detecting resistant organisms, which in turn can develop resistance to commonly used concentrated cleaning products, making it even more difficult to sanitize (Brooks & Flint, 2008).

Some pathogenic-resistant bacterial species have been highlighted in the industrial food environment; among them is *Bacillus cereus*, which is present in raw milk and its derivatives. The beta-hemolytic Gram-positive bacteria can remain in heat exchange equipment, and the standard sanitization is not fully efficient (Faille et al., 2007). In addition, *S. aureus* is also present in the industrial context, with a high tolerance and resistance factor. Such Gram-positive coconuts release phages spontaneously in their surroundings, a common and frequent action in biofilms; however, it is possible to affirm that the release of biofilm phages in food processing equipment is not an uncommon occurrence (Resch et al., 2005).

3.4.1 Biofilms in the food industry

The structure of a biofilm can be defined as an agglomeration of microbial cell structures adhered to the membranous surface, involved in a matrix composed of extracellular polymeric substances consisting of exopolysaccharides, nucleic acids, proteins, lipids, and other biomolecules. The biochemical composition of the biofilm is variable, depending on the microorganism, the number of nutrients available, the substrate, the environment, and metabolomics in general (Karygianni et al., 2020; Rather et al., 2022).

Adhesion surfaces are also determining factors, and they are formed especially on abiotic surfaces, that is, infections associated with the host's original microbiota. Bloodstream and urinary tract infections may be brought on by the biofilm that first developed on medical devices like joint prostheses, catheters, heart valves, and contact lenses. The biofilm is a great protector of microorganisms, preventing the pH from changing, mechanical forces damaging the structure, and blocking defense cells of the human and animal immune systems (Sharma et al., 2019).

The biofilm cycle can be summarized in five steps: Primarily, unmined attachment, in which microorganisms are reversibly adsorbed to a surface via weak interaction (like Van der Waals forces) with an abiotic or a biotic surface. In the background, colonization is performed, where microorganisms possess stronger hydrophilic and hydrophobic interactions that bind them permanently to the surface. The third stage is development, where the proliferation of multi-layered cells accumulates and extracellular polymeric substances are made and released. The fourth stage is the maturation of this biofilm, generating a three-dimensional community with stable conformation and channels to efficiently distribute nutrients and signaling molecules inside the biofilm. Finally, there is active dispersal, in which microorganisms split or detach in groups as a result of interactions with extrinsic or intrinsic factors and then spread to other locations to colonize (Yin et al., 2019) (Figure 2).

Biofilms are prevalent in a wide variety of organisms, including bacteria, archaea, and eukaryotic microbes like fungi. They made their earliest appearance in the fossil record approximately 3.25 billion years ago. These rudimentary biofilms seem to have arisen at the same time as the first indications of an evolutionary shift from a unicellular to a multicellular organization (de la Fuente-Núñez et al., 2013).

Bacterial biofilms are responsible for around 80% of recurrent and chronic microbial infections within the human body. They pose a significant worldwide health risk because of their ability to withstand antibiotics, host defense mechanisms, and external stress factors, leading to persistent chronic infections. Biofilm matrices provide bacteria with additional resistance, making them tolerant to harsh conditions and antibiotics, resulting in the emergence of XDR, multidrug-resistant, and drug-resistant bacteria (Sharma et al., 2019).

Mycobacterium biofilm formation is similar to that of other biofilm communities, but certain mycobacteria have the ability to form biofilms at the air–media interface and on surfaces. Fungal biofilms also make treatment difficult and contribute to high morbidity and mortality rates, making them a significant virulence factor in candidiasis (Pereira et al., 2021).

Unlike classical resistance mechanisms, which include altered sites, reduced permeability of cells, drug-modifying enzymes, efflux pumps, and drug-neutralizing proteins, biofilm communities exhibit antimicrobial resistance through various strategies. These consist of a subpopulation of microorganisms within a biofilm, a modified chemical microenvironment within the biofilm, and slow or insufficient antimicrobial penetration (Sharma et al., 2019). Antibiotic penetration may also be restricted by the way that antibiotics are adsorbed by biofilm constituents or their degradation by hydrolases, like beta-lactamase (de la Fuente-Núñez et al., 2013). Studies have shown that the biofilms of *S. aureus* and *S. epidermidis* considerably decrease the penetration of antibiotics such as oxacillin, cefotaxime, and vancomycin (Singh et al., 2010).

3.4.2 Biofilm dispersion methods

Generally, a highly organized bacterial colony can produce a viscous membrane fixation around itself, which allows communication between bacteria and presents resistance against the human immune system (Cejudo-Bastante et al., 2020). A biofilm complex demonstrates the pathogenic potential, and it can be affirmed that biofilm infections are challenging to treat because of their more effective defense against antibiotics and macrophages in contrast to free-living cells (Deshmukh & Gaikwad, 2022).

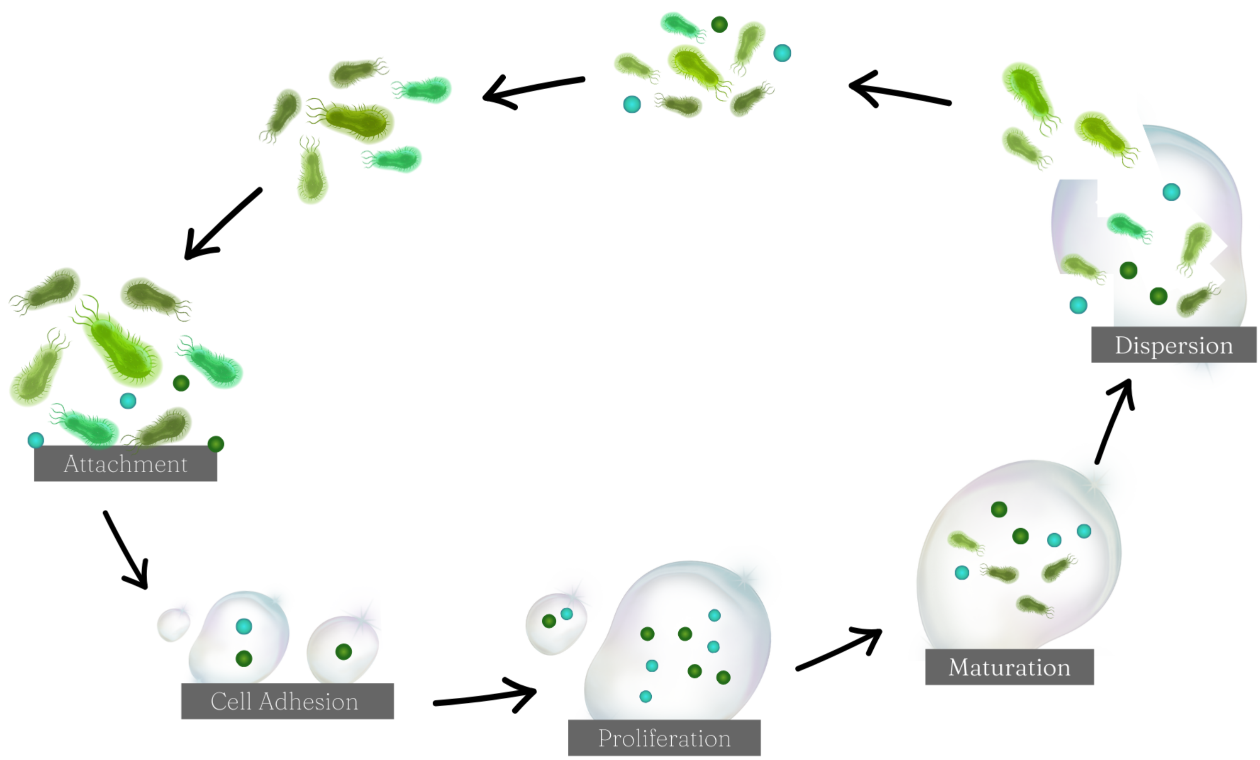

Figure 2. Sequence of the biofilm cycle.

Due to its high strength, new mechanisms can be applied to minimize the mass of the biofilm or can be used for its prevention. Photodynamic therapy can be used in prevention and combat, and biofilm molecules can be an alternative that interferes with bacterial signaling pathways in Gram-positive and Gram-negative species (Fujita et al., 2017). In addition, nanoparticle (NP) encapsulation has a promising effect on the action of biofilm membrane degradation (Jin et al., 2009).

3.5 New trends in combating antimicrobial resistance

AMR is a worldwide theme that popularly solidifies as a problem without a brief positioning of a solution. However, new studies and perspectives on combat are in force in the current contemporary context and have full potential for action in AMR in general (Bumbudsanpharoke et al., 2015). Recent treatments with new approaches to antibiotics demonstrate success, but they are still not 100% passive for AMR (Mühlberg et al., 2020). Antibacterial drug resistance has been steadily rising, posing a serious threat to public health. Their indiscriminate use in agriculture, aquaculture, and the treatment of animal and human health has resulted in serious side effects that have aided in the emergence and dissemination of multidrug resistance (MDR) (Campista-León et al., 2021).

MDR was first linked to serious hospital infections in individuals with compromised immune systems. However, it has now spread to other parts of the community, leading to serious infections with rising death tolls and financial strains from increased medical expenses and disability rates. Usual problematic MDR bacteria encompass methicillin-resistant *S. aureus* (MRSA), vancomycin-resistant MRSA, MDR *P. aeruginosa*, carbapenem-resistant *A. baumannii*, *E. coli*, and *K. pneumoniae*, vancomycin-resistant *Enterococcus* (VRE), and XDR *M. tuberculosis*. Serious infections like bloodstream infections, ventilator-associated pneumonia, surgical site infections, and implant-associated urinary tract infections are caused by these pathogens (Mwangi et al., 2019).

The rise in MDR Gram-negative bacteria has raised concerns worldwide, and these pathogens have been defined as problematic by the WHO and the United States Center for Disease Control and Prevention (CDC). Innovative approaches, including rational drug design and the identification of new mechanisms of action, are critically required in the fight against MDR Gram-negative bacteria (Otsuka et al., 2020).

MDR fungi, such as *C. auris*, have also spread to several countries on four continents. Also, the most frequently reported MDR *Candida* spp. is *C. glabrata*; however, resistance rates are constant, and only a small number of US centers possess over 10% of MDR isolates. In addition, *C. haemulonii*, which is strongly associated with *C. auris* and also displays reduced susceptibility to polyenes and azoles, has mostly been related to superficial infections and exhibits lower virulence as a pathogen (Colombo et al., 2017).

Comprehending the reasons for the overrepresentation of MDR is essential to limit the consequences of resistance. Although numerous explanations have been proposed, it is still unclear how much of the trend is caused by these processes.

The suggested mechanisms are frequently particular to some species and/or subsets of antibiotics. However, the over-representation of MDR is a pervasive pattern, with observed correlations between antibiotic resistance that acts via various mechanisms and between chromosomal and mobile genetic element-associated resistance determinants (Lehtinen et al., 2019). Due to the public health problem, research has proposed ways to combat MDR, among which are biofilm dispersion, NPs, and essential oils (EOs) (see Table 1).

3.5.1 The use of natural compounds as antimicrobial nanomaterials

There are abundant active constituents in nature that are useful in the food industry and can be employed as functional biopreservative ingredients in the packaging of foods. These components possess antioxidant and antimicrobial activities. They are termed natural additives and preferred above chemical agents because of the adverse effects the chemicals cause in food systems (Attaran et al., 2017; Deshmukh & Gaikwad, 2022; Mir et al., 2018).

The utilization of nanomaterials in food packaging in the processing environment has received immense attention in recent times because of their perceived safety, thermostability, and ability to preserve and incorporate essential nutrients. These nanomaterials are utilized in the packaging of food in combination with biopolymers, which possess antioxidant and antimicrobial activities (Bumbudsanpharoke et al., 2015). Nano-food packaging ensures the preservation of food products with enhanced mechanical intensity and antimicrobial activities, revealing the safety status in comparison to traditional packaging systems (Mihindukulasuriya & Lim, 2014; Suvarna et al., 2022).

Food packaging is a vital component of the food processing industry, which is dominated by chemical packaging systems such as synthetic petroleum-derived non-biodegradable polymers. Since this sector is one of the fastest-growing areas in the food processing environment, there is a call for the utilization of natural additives as nanomaterials in food packaging (Attaran et al., 2017; Mir et al., 2018).

Biopolymers, for example, proteins, polysaccharides, and lipids, are usually employed in the food industry to produce biodegradable packaging films that are environmentally friendly. The combination of these biodegradable polymers with natural additives and extracts is one of the most effective avenues to generate innovative nanomaterial products with desired characteristics (Li et al., 2014; Siripatrawan & Harte, 2010). In recent times, biodegradable packaging systems have fostered the use of antioxidants and antimicrobial agents, which has reduced the reliance on chemical additives for food and consumer safety (Deshmukh & Gaikwad, 2022).

Extracts sourced naturally have been employed in the packaging of food for consumer acceptance. These extracts are obtained from plants, spices, herbs, animal origins, and microorganisms, which contain functional components and act as natural defense mechanisms (Banwo et al., 2020; Tiwari et al., 2009). Natural extracts are known as phenolic compounds that possess antioxidant activities. Phenolics of plant origin have been of interest in these contemporary years because of their sources and how compatible they are with biopolymers (Banwo et al., 2021; Deshmukh & Gaikwad, 2022; Oroian & Escriche, 2015).

Natural antioxidants aid in the creation of edible functional nanomaterials for food, which is a crucial component of food packaging because it helps in the preservation of safety and

Table 1. Summary of several recent trends in antimicrobial resistance.

Main results	Objects of study	Topics of interest	References
Computational approaches helped elucidate the AMR mechanisms	ESKAPE pathogens	Genomics, systems biology, and structural biology	Priyamvada et al. (2022)
Conceptual, temporal, and geographical trends using structural topic modeling (STM)	Water and environment microorganisms and multidrug-resistant tuberculosis	Comprehensive overview of the AMR research	Luz et al. (2022)
Highly resistant isolates from pediatric diarrheal patients	Multidrug-resistant *Shigella flexneri* in Pakistan	Increased trend of third-generation cephalosporin resistance	Nisa et al. (2022)
A complete picture of variation in pathogen frequency and antibiotic resistance trends isolated from blood specimens	ESBL-Gram-negative bacilli causing bloodstream infections	China Antimicrobial Resistance Surveillance Trial (CARST) Program, 2011–2020	Yan et al. (2022)
LLE techniques are preferable toward conventional methods for the determination of antibiotics in food	Different extraction techniques in several food matrices	Overview of antibiotic residues in foods of animal origin using liquid-liquid extraction	Khatibi et al. (2022)
Polyindole-based nanocomposites as biomaterial against MDR microbes	Several polyindole-based nanocomposites	Antimicrobial properties of polyindoles in biomedical applications and further research	Pradeep et al. (2022)
Antimicrobial stewardship and restricted antibiotic usage may help contain the further expansion of AMR	*Campylobacter jejuni* and *C. coligenes* identification using MLST	Genomic screening of antimicrobial resistance markers of *Campylobacter* in the United Kingdom and the United States	Van Vliet et al. (2022)
A combination of molecular detection and the influence of patient demographics on the frequency of infections has proven to be robust in infection control	*Staphylococcus* and *Enterococcus*	Nosocomial and community acquired pathogens isolated from clinical specimens at major hospitals in Saudi Arabia	Said et al. (2022)

quality for an extended period. In addition, antioxidants are added to protect food products from rancidity and to decolonize and extend their shelf life. Illustrations of the antioxidant-rich extracts employed as functional edible packaging films are as follows: Pineapple peel and coconut shell extracts obtained from the waste generated from the fruits can be combined with polyvinyl alcohol and corn starch. This enhances the antioxidant activities of the packaging film, while the coconut shell waste possesses a delayed oxidation reaction to packaged sachet soybean oil (Kumar et al., 2021; Tanwar et al., 2021). Red beets are rich in betalains and possess improved antioxidant activities, which can be incorporated in ethylene-vinyl alcohol as packaging film in the food processing environment (Banwo et al., 2020; 2022; Cejudo-Bastante et al., 2020). Camucamu extracts obtained from the antioxidant-rich plant are compatible with Teff starch, which reduces the tensile strength with an increase in the elongation break of the food packaging film (Deshmukh & Gaikwad, 2022; Ju & Song, 2019).

Food safety issues and consumer preferences have implicated the quality parameters of products, which have indicated alternative approaches to food preservation. Consumers are clamoring for foods utilizing natural components as antimicrobials rather than chemicals. These natural antimicrobials keep foods fresh and safe, and their nutritional components intact. Herbs and spices are the reservoirs for antimicrobials that are active against Gram-positive foodborne pathogens. The antimicrobials present in these plant origins may elicit safety and antioxidant activities in the foods and enable them to have a longer shelf life (Tajkarimi et al., 2010).

The antimicrobial properties of nanomaterials are quite interesting due to their ability to prevent the proliferation of spoilage microorganisms and their mechanical intensity, which indicates their use for inhibition of the growth of microbes and transporters of antibiotics in packaging films (Suvarna et al., 2022). Despite these properties, the practical applications in the packaging of food have raised several informative inquiries because of the interactions with food ingredients and the possible safety concerns about the quality of the food. This can be cautioned by the concentration and release of the nanomaterials employed in the food packaging, which ultimately will not affect the food quality (Anvar et al., 2021).

Several natural antimicrobial agents can be incorporated into food packaging films as nanomaterials. Some examples are as follows: Pediocin obtained from *Pediococcus* species of the lactic acid bacteria is combined with polylactic acid biopolymers, which possess activities against *L. monocytogenes* when used in raw ham (Woraprayote et al., 2013). Nisin is a "generally regarded as safe" antimicrobial agent incorporated into several food products. Nisin is combined with pectin and polylactic acid and is usually incorporated into the composite packaging film, where it reduces the proliferation of *L. monocytogenes* and *Alicyclobacillus acidoterrestris* in food products (Wu et al., 2018).

There is a need to ensure the use of microencapsulation, which is aimed at sustaining the stability of food. This will help increase bioavailability and ensure oxidation and hydrolysis under processing conditions. It must be noted that the active food packaging process assists as a hindrance to microbial growth and keeps the sensitive ingredients away from the external environment and adverse conditions such as oxygen, moisture, and temperature. The utilization of naturally sourced food additives with antimicrobial and antioxidant activities as nanomaterials is expected to undergo rigorous screening and must not adversely affect taste, nutritional composition, or health benefits (Banwo et al., 2020).

3.5.2 Essential oils

Recent studies currently report the effectiveness of EOs in directly combating AMR. Such natural compounds produce antibiotic effects that act directly by breaking the bacterial membrane. The membranous wall is crucial in regulating the osmotic pressure in cells and the biomolecule influx. Therefore, a damaged membrane will break the osmotic pressure, which will cause intracellular extravasation and ultimately the destruction of the cell (Li et al., 2014).

Several types of oils extracted from the most diverse plants have antibiotic potential, usually at different scales of potential and performance, which change based on the extracted compound's chemical composition and concentration. Natural compounds such as lavender oil can induce oxidative stress that modifies the permeability of the bacterial membrane, causing its eventual rupture (Mihindukulasuriya & Lim, 2014). In addition, oil extracted from the cinnamon bark also has antibacterial properties, as well as other compounds that present antiviral and antifungal activity, respectively: peppermint and eucalyptus EOs (Mir et al., 2018).

3.5.3 Applicability of nanoencapsulation of essential oils to combat biofilms in the food industry

The diversity of microorganisms present in the food industry can cause large resistant colonies, possibly originating biofilms. New strategies to prevent biofilm formation are in full study and development to prevent bacteria from creating resistance in food processing environments (Galie et al., 2018).

EOs have antibiofilm properties and can be applied in the food industry with minimal restrictions. The encapsulation of EOs by nanocomposites can act directly on the dilution of the membrane present in the biofilm, a new trend in industrial protection measures with full capacity for action (Basavegowda et al., 2020).

Bionanocomposite-based encapsulation containing plant-derived EOs can reduce the contamination and proliferation of fungi and bacteria in processed foods. EOs are used more effectively in food when they are encapsulated in appropriate systems to further increase the biological stability of active compounds. Using the correct systematic order, nanocomposite can ensure antimicrobial activity (Figure 3) (Hossain et al., 2019; Pagnossa et al., 2021).

3.5.4 Nanoparticles

NPs are of nanometric order, commonly used as bacterial growth inhibitors, and are applied as coatings for encapsulation and administration of antibiotics, in which some antibacterial agents are highly favorable for antimicrobial action and have a high evaporation resistance capacity (Hemeg, 2017).

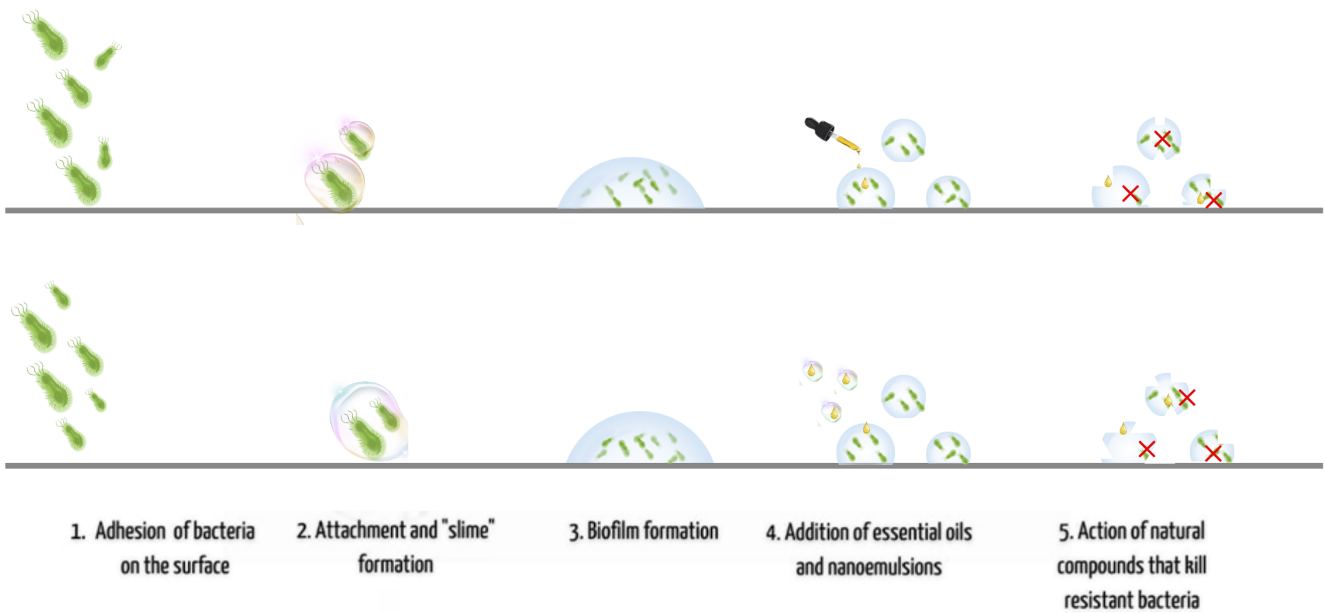

Figure 3. Sequence of bacterial biofilm formation and action of essential oils (upper) and nanoemulsions (lower).

The mechanism of activity among the NPs can happen through different processes. Oxidative stress can disintegrate the membrane or cause severe damage since the release of metal ions by NPs causes the interaction between intra- and extracellular components. In addition, the nonoxidative mechanisms that result in the production via photocatalysis of oxygen-reactive species damage bacterial structures (Herman & Herman, 2014) and may affect the formation of biofilms by the degradation of their membranes (Hu et al., 2019; Pagnossa et al., 2022).

3.5.5 Nanoparticles as quorum sensing inhibitors

In microbial systems, cell-to-cell communication helps the organism adapt to and monitor its surroundings through chemical signaling, cell-to-cell chemical exchanges, and electric signaling. An example of that kind of system is quorum sensing (QS), where bacteria monitor the number of autoinducers, and small chemical signals in their local population. A group of scientists has reported the use of nanomaterials as agents with antimicrobial properties. Compared to their bulk material counterparts, NPs possess unique chemical and physical properties, which allow them to engage with biological systems differently and therefore assist in the activity of antimicrobial agents (Qais et al., 2018).

It has been found that there are many different groups of compounds that can inhibit QS, including phytocompounds and synthetic compounds, which researchers have tested in the search for novel inhibitors (Asfour, 2018). Over the past couple of years, several NPs have been evaluated as antimicrobial substances against a variety of harmful microorganisms (Zaidi et al., 2017). Recently, several studies have demonstrated the possibility of developing NPs with novel properties, including anti-QS characteristics, QS-mediated virulence, and biofilm formation inhibition (e.g., Chaudhari et al., 2015). As a result, most research in this particular area has focused on metallic NPs such as silver NPs. The anti-QS activity of various NPs against several pathogens has been reported.

1. Silver NPs (AgNPs): several studies reported AgNPs showing anti-QS activity against various bacteria, namely *C. violaceum* and *P. aeruginosa* (Ali et al., 2017; Prateeksha et al., 2017; Singh et al., 2015); *S. aureus* (Chaudhari et al., 2015; Masurkar et al., 2012); *L. monocytogenes*, *P. aeruginosa*, *E. coli* (Al-Shabib et al., 2016); *Vibrio fischeri* (Miller et al., 2015), etc.;
2. Selenium NPs (SeNPs): anti-QS activity of SeNPs against *P. aeruginosa* has been described (Prateeksha et al., 2017);
3. Zinc oxide NPs (ZnO-NPs): researchers reported the anti-QS activity of ZnO-NPs against *C. violaceum* (Al-Shabib et al., 2016);
4. Beta-cyclodextrin functionalized silicon dioxide NPs: researchers observed anti-QS activity of beta-cyclodextrin functionalized silicon dioxide NPs over *V. fischeri* (Miller et al., 2015);
5. Silver-titanium nanocomposite (AgCl-TiO_2NPs): it has been reported that AgCl-TiO_2NPs act as anti-QS against *C. violaceum* (Naik & Kowshik, 2014).

The global AMR crisis can be resolved with the use of QS inhibitions, which disrupt the mechanisms by which bacteria communicate with one another (QS) to control the production of virulence factors by bacterial cells (Saleh et al., 2019).

Researchers have recently been interested in using nanotechnology to develop advanced nanomaterials designed to target QS-regulated virulence factors. As a result, alternative antibacterial therapies can be developed, and these are the starting points for their development (Singh et al., 2015).

3.5.6 Nanoparticles in food packaging

The distinct chemical and physical characteristics of nanomaterials make them an excellent option for use as an appropriate addition to polymers to enhance the efficiency of these polymers due to their distinct physical and chemical properties. Several nanofillers have been developed in recent years, such as silicate and clay nanoplatelets, silica NPs, graphene, and carbon nanotubes (CNTs). These nanofillers are important because they can maintain color, flavor, and texture, decrease spoilage, and increase stability during storage (Sorrentino et al., 2007). Nanomaterials have demonstrated antimicrobial properties, resulting in their widespread use in food packaging due to their antimicrobial properties (Huang et al., 2015). There are several possible applications of metal nanomaterials, including protection from microorganisms in infant bottles, but this is dependent on how accurately their synthesis is controlled as well as on their composition (Alfadul & Elneshwy, 2010; Emamhadi et al., 2020).

3.5.7 Nanoclay

As a result of the high benignity and stability of nanoclay for food packaging, it is being used to formulate polymers into nanocomposites for food packaging (Silvestre et al., 2011) due to its ease of processing, significant enhancement, low cost, and availability (Radfar et al., 2020). Also, clay nanomaterials, called montmorillonite (MMT), are found in nanocomposites (Horue et al., 2020), which are formed from volcanic ash (Bai et al., 2020).

Clusters of platelets are found in nanoclays with low surface exposure. Due to the elevated surface area received (over 750 m^2/g), they can uniformly intercalate into the polymer. A considerable amount of resistance to gas infiltration is associated with nanoclay when it spreads into polymers. Nanocomposite resistance performance is highly influenced by the clay filler ratio and volume fraction, in addition to the degree of orientation and dispersion of the clay filler (de Abreu et al., 2010). There is a correlation between the higher barrier effectiveness of packaging materials containing exfoliated nanomaterials when compared to packaging materials without exfoliated nanomaterials (Silvestre et al., 2011). Several studies suggest that nanocomposites, such as nanoclays, can increase the antibacterial activity of food packaging and extend the retention period due to their tortuosity effect (Girdthep et al., 2014; Tajeddin et al., 2019).

3.5.8 Zinc oxide

Chemical or physical vapor reactions have been used to synthesize ZnO NPs, which are inorganic metal oxides (Casey, 2006). The production of ZnO NPs may also be achieved by utilizing chemical reactions using a variety of precursors and synthesis techniques such as precipitation, thermal decomposition, and hydrothermal methods (Espitia et al., 2012). Since ZnO NPs are antimicrobial and ultraviolet (UV) blocking, the use of ZnO NPs as food packaging has become more popular, as a result of the NPs being cheaper than Ag NPs and having antimicrobial properties (Emamifar et al., 2010). As a result of the incorporation of zinc oxide NPs within polymer films, the characteristics of packaging, like durability, mechanical strength, and blockage properties, can all be greatly improved (Espitia et al., 2012).

3.5.9 Silver

There is a growing interest in AgNPs as a potential material that can be used in a variety of functions, like food packaging, for example. By using ex situ and in situ techniques, it is possible to synthesize a nanoscale particle of silver. By ex situ processes, AgNPs are reduced by borohydride and then dispersed within a polymerization formulation to remove the borohydride ions from the AgNPs. Because of its broad spectrum of inhibitory properties against microorganisms, nanosilver is widely used in dry-cleaning solutions and detergents. Furthermore, it has been shown that it has excellent antimicrobial performance against many different kinds of bacteria strains, including drug-resistant ones (Birla et al., 2009; Li et al., 2011).

In the polymeric film, the AgNPs are immobilized and incorporated into the polymeric material, resulting in uniformly dispersed particles and a smooth surface. It has been suggested that harm to the bacteria's membranes and cell walls is among the most basic systems that AgNPs use to achieve their antimicrobial properties. AgNPs are antibacterial because they are formed as a result of the reaction of dissolved oxygen and hydrogen ions with metallic AgNPs. According to Lok et al. (2007), the oxidized surface of silver atoms is responsible for the antibacterial characteristics of AgNPs.

Several factors give AgNPs their antibacterial activity, but the most important include their dispersion and size, which range from 1 to 10 nm, and their surface area, which allows them to discharge ionic silver. There may also be other factors contributing to the antimicrobial performance of AgNPs, such as their surface charge, solubility, and agglomeration level (Duncan et al., 2011). It should be noted that AgNPs are not just antimicrobial but can also function as ethylene blockers by taking in and breaking down the ethylene that fruit metabolism releases in addition to their antimicrobial properties.

3.5.10 Titanium dioxide

Titanium dioxide (TiO_2) NPs can be produced in numerous ways, and sol-gel processing represents the method most frequently employed. In addition to its UV-blocking properties, TiO_2 has strong photostability and is a commonly studied semiconductor due to its excellent UV-blocking properties. As a result of adding TiO_2 nanoparticles to polymeric films for food packaging, the high transparency is preserved, but the detrimental effects of UV light on food components are also mitigated (Duncan et al., 2011). It has been demonstrated that TiO_2 nanoparticles have both self-cleaning capabilities and antibacterial properties because of their photocatalytic activity when exposed to UVA, blacklight, or a combination of these irradiations. Using TiO_2 as a starting material for integrating into ethylene/vinyl alcohol and chitosan for the synthesis of nanocomposite materials (Cerrada et al., 2008; Díaz-Visurraga et al., 2010) has been researched for potential biocidal application in food packaging for a long time. On Gram-positive bacteria, TiO_2 nanoparticles exhibit a significantly greater antimicrobial effect than nanoparticles of other minerals (Xing et al., 2012).

3.5.11 Carbon nanotube

A CNT is a hollow tube formed by carbon atoms whose diameter is within the nanometer range, which can be a CNT with one wall or multiple walls (Liao et al., 2019). Lau and Hui (2002) have demonstrated that CNTs have a very high ratio of length-to-diameter and theoretical Young's modulus. It has been shown that CNTs are not only used as mechanical tools to improve polymer components in food packaging but also as potent antimicrobial agents (Lau & Hui, 2002). Because CNTs have the ability to puncture microbial cell membranes and cause permanent harm, they have been used to enhance the mechanical properties of polymer components in food packaging (Kang et al., 2007).

3.5.12 Copper and copper oxide

Copper NPs have been synthesized from copper (II) hydrazine carboxylate in an aqueous solution through two thermal and sonochemical reductions (Llorens et al., 2012). There is a relatively low reduction potential of CuO/Cu^{2+} for copper NPs, which results in their rapid oxidation. Copper's properties can be enhanced by combining them with NPs that disperse well in aqueous solutions, improving its disinfecting effect. Thus, given the higher mobility of copper ions released by this process, they could contact and react with the cell membranes more easily (Conte et al., 2013). A common method of preparing CuO is by reducing it with $NaBH_4$, which causes the solution to rapidly oxidize to produce an antimicrobial effect when it is dissolved in an ammonium solution (Kotelnikova et al., 2007).

4 CONCLUSION

In a way, the food industry is subject to contamination by pathogenic microorganisms. However, it is fully possible to control the advance of resistant bacteria through the encapsulation of EOs by bionanocomposites, directly assisting in the degradation of the biofilm membrane and, consequently, preventing the appearance of resistant bacteria in the local scope of the food industries. In addition, encapsulation may be viable for preventing diseases harmful to human health.

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