



Review Article

Plant-derived bioactives and green-synthesized nanoparticles in food packaging: A bibliometric-aided appraisal of efficacy, migration, and regulatory constraintsYunus Başar^{1*}, Nurten Toy^{2,3}, Muhittin Kulak⁴

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Abstract

Microbial proliferation and lipid oxidation are major causes of food loss and foodborne risks. Regulatory reassessments and consumer concerns have increasingly restricted the use of various synthetic preservatives and antioxidants. Consequently, plant-derived bioactive agents, including essential oils (EOs) and phenolic compounds, and green synthesized metal and metal oxide nanoparticles (NPs) have emerged as complementary candidates for food preservation and active packaging. This review integrates antimicrobial and antioxidant mechanisms with a bibliometric-supported mapping of the food packaging literature (SCOPUS, engineering domain; 284 keywords, 10 clusters; VOSviewer). Network analysis identified biodegradable matrices (chitosan, gelatin, starch, pectin, and alginate), antimicrobial and antioxidant activity, essential oils, plant-derived compounds such as curcumin and carvacrol, and "active packaging," strongly associated with electrospinning as a prominent manufacturing approach, as the central theme. Separate clusters highlighted sustainability and barrier performance. The review also examines translational limitations, particularly migration, toxicology, and regulatory uncertainty. Bulk transfer from packaging to food depends on polymer embedding, food acidity, and thermal history; however, current evidence often fails to distinguish the release of particulate nanoparticles from oxidative dissolution to ionic species, despite their differing toxicological and regulatory effects. Silver toxicology continues to focus predominantly on ionic behaviour, contributing to ongoing uncertainty in European safety assessments. This study reveals that the main limitations stem from reproducibility and regulatory fit rather than efficacy; the primary problems are variability in plant extracts, unstandardized NP characterization, discrepancies between *in vitro* and real food performance, and the lack of nano-specific regulatory processes.

Keywords: Active packaging, Bibliometric analysis, Food preservation, Green-synthesised nanoparticles, Nanotoxicology.

Introduction

The issue of food safety is a critical global public health problem that has yet to be adequately

addressed. The World Health Organization's Foodborne Disease Burden Epidemiology Reference Group has attributed approximately 600 million

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<https://doi.org/10.30466/fsp.2026.57582.1041>

Received: 03 September 2026

Accepted: 17 October 2026

Available online: 15 November 2026

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illnesses, 420,000 deaths, and 33 million disability-adjusted life years per year to 31 foodborne hazards, with children under five years of age bearing about 40% of that burden (Havelaar et al., 2015). The authors of these estimates acknowledge that they are conservative in nature, as they exclude several chemical hazards and are based on surveillance systems that vary significantly in their sensitivity across different regions. This results in a bias towards underestimation, particularly in low- and middle-income settings. In such contexts, ready-to-eat foods have been identified as recurrent points of failure (Makinde et al., 2020). A quantitative loss problem is also evident in parallel: approximately 13% of global food production is lost between post-harvest and retail, and a further 19% of the food available to consumers is wasted at retail, food-service, and household levels (UNEP, 2024). It has been established that a significant proportion of the observed burdens is attributable to two distinct deterioration pathways: microbial proliferation and lipid oxidation. These pathways converge at the interface of the food packaging, which has been identified as a viable point of intervention.

Since then, a partial update of these estimates has become available, covering 22 of the original 31 hazards. For the 14 principal diarrheal hazards, it was estimated that foodborne transmission caused 666 million cases of illness, 265,000 deaths, and 15.2 million DALYs lost worldwide in 2021 (Majowicz et al., 2026). These figures are broadly consistent with the 2010 estimates, although they are not directly comparable because of the different sets of hazards and reference years.

The conventional response has been chemical, in the form of synthetic antimicrobials and antioxidants added to the product or, less frequently, to the packaging. However, three distinct pressures now constrain this approach, and they should be distinguished because the supporting evidence varies in strength (Sarkhel et al., 2026). The first is toxicological and regulatory. Long-authorized synthetic antioxidants, butylated hydroxyanisole, butylated hydroxytoluene, and tert-butylhydroquinone, have undergone repeated re-evaluation of their metabolic fate and potential adverse effects (Mika et al., 2023), and the principle that a long history of use does not guarantee

permanent authorization was made explicit when the European Food Safety Authority (EFSA) concluded that titanium dioxide (E 171) could no longer be considered safe as a food additive due to concerns regarding genotoxicity (EFSA, 2021a).

The second is commercial, as consumer demand for 'clean-label' formulations has evolved from a niche preference to a key driver of reformulation. However, natural substitutes rarely offer a one-to-one functional replacement for synthetic preservatives and typically incur higher costs, have narrower pH and temperature operating windows, and result in a shorter effective shelf life (Chauhan & Rao, 2024). The third issue is microbiological: reliance on a small number of preservative chemistries exerts continuous selective pressure on spoilage and pathogenic flora (Asadi et al., 2026). It is important to state clearly that regulatory and commercial trends are well documented, whereas the causal link between authorized preservative use at permitted levels and consumer health outcomes remains contested and should not be presented as proven.

In this regard, two research lines have emerged as potential solutions. The first exploits plant secondary metabolites directly, with essential oils and phenolic compounds acting as antimicrobial and antioxidant agents through membrane destabilization, interference with energy metabolism, radical scavenging, and metal chelation (Başar et al., 2026a; Başar et al., 2026b; Başar et al., 2024). The second approach uses the same metabolites indirectly as reducing and capping agents in the aqueous synthesis of metal and metal oxide nanoparticles (Umaru et al., 2026). This yields materials whose antimicrobial activity derives from ion release, reactive oxygen species generation, and interaction with cellular targets (Arağan et al., 2026; Godoy-Gallardo et al., 2021). These two approaches are increasingly being combined within a single biopolymer matrix, and the resulting composite films, coatings, and nanofibers represent the current frontier of active and intelligent packaging (Bisht et al., 2025; Dube, 2025). However, the literature is strongly asymmetric: reports of efficacy vastly outnumber studies addressing migration, oral toxicology, sensory acceptability, and regulatory feasibility. This review therefore:

(i) summarizes the mechanistic basis of plant-derived bioactives and green-synthesized nanoparticles in food systems;

(ii) maps the thematic structure of the food packaging literature using keyword co-occurrence analysis; and

(iii) critically evaluates the safety, toxicological, and regulatory constraints that currently prevent laboratory performance from being realized in a commercial context. The scope is deliberately restricted to food-contact and preservation applications; biomedical uses of the same materials are not included.

Plant-derived natural products

Phenolics and essential oils

There are more than 3,000 species of aromatic plants worldwide (Bakkali et al., 2008). These plants are widely used in traditional medicine and the food industry because of their secondary metabolites, including phenolic compounds, flavonoids, terpenes, and alkaloids (Boukraâ et al., 2026a; Tekeli et al., 2026). Essential oils (EOs) are mixtures of various volatile compounds with a characteristic aroma, obtained from plant parts such as flowers, fruits, seeds, stems, and leaves (Boukraâ et al., 2026b; Ríos, 2016). Phenolic compounds are phytochemicals commonly found in plant tissue that possess numerous bioactive properties. Although they are not nutrients themselves, consuming them provides health-protective effects (De la Rosa et al., 2019).

Owing to the rapid growth of the global population, consumers are demanding safe, pathogen-free food with a long shelf life. To avoid posing any health risks to consumers, it is crucial that foods are free from pathogenic bacteria, fungi, and unpleasant odours or tastes (Makinde et al., 2020). For this reason, the food industry is shifting its focus from synthetic to natural preservatives (Faheem et al., 2022). Owing to their bioactive compounds, such as terpenoids and phenols, EOs can delay oxidative reactions, prevent the formation of free radicals, and inhibit the growth of foodborne pathogenic bacteria (Khan et al., 2023). EOs, also known as aromatic hydrocarbons, terpenes, terpenoids, phenylpropene, esters, and aldehydes, are reported to possess

numerous biological activities, including antiviral, antifungal, antibacterial, insecticidal, and antioxidant effects (Angane et al., 2022; Chi et al., 2025). Owing to their antioxidant and antibacterial properties, EOs are used as green additives in foods as an alternative to traditional synthetic chemicals, with the promise of improving food safety and shelf life (Di Matteo et al., 2024). EOs are considered safe preservatives in meat and meat products during food processing and preservation because they act as natural antibacterial and antioxidant agents in meat and meat products (Yaş et al., 2026; Zhang & Piao, 2023). Phenolic compounds are closely related to the sensory and nutritional quality of fresh and processed plant foods (Ho, 1992). They prevent the formation of undesirable colours and flavours in fruits and vegetables, act as substrates for enzymatic browning, and also play a role in flavour characteristics (Cheynier, 2012; Tilley et al., 2023). Therefore, phenolic compounds are known as natural antioxidants. The most commonly used plants in the food industry include thyme, rosemary, basil, cinnamon, mint, cloves, garlic, ginger, and sage. These plants are rich in phenolic compounds and volatile oils (smell pleasant).

Essential oils are most commonly recovered by steam or hydrodistillation, with cold pressing used for citrus peel oils and solvent extraction, supercritical CO₂ extraction, and microwave-assisted techniques offering higher selectivity or lower thermal degradation of labile constituents at correspondingly higher cost and complexity (Asbahani et al., 2015). Beyond distilled oils, crude and purified plant extracts (aqueous, hydro-alcoholic, or supercritical) are directly incorporated into packaging films and coatings as antimicrobial and antioxidant agents, either dispersed in the polymer matrix or immobilized via encapsulation, with the choice of extraction method and solvent polarity strongly influencing which phenolic or terpenoid fraction is available for release (Bisht et al., 2025). The food matrix into which these compounds are released is not interchangeable: reported efficacy and required dosage differ substantially between high-fat matrices such as meat and dairy, where lipophilic constituents partition into the fat phase and lose activity against the aqueous bacterial environment, and high-moisture, low-fat matrices such as fresh produce, seafood, and

bakery products, where volatilization and protein binding instead dominate losses (Hyldgaard et al., 2012).

Antimicrobial and antioxidant mechanisms

Today, many diseases are related to oxidative stress, which stems from an imbalance between the production and neutralization of pro-oxidants (Abeyrathne et al., 2022). Antioxidants are natural or synthetic compounds that inhibit or delay oxidation. Secondary metabolites found in plant structures are known to be effective antioxidants (Erenler et al., 2024). They can interact with free radicals and prevent oxidation without harming host cells (Chandimali et al., 2025). They can act through various mechanisms, such as scavenging free radicals that initiate and propagate peroxidation, chelating metal ions that accelerate oxidation, quenching superoxide ions to prevent hydroxyl radical formation, breaking the auto-oxidation chain reaction, and reducing localized oxygen concentration in the product (Munekata et al., 2020; Oroian & Escriche, 2015). Recently, there has been a shift in the food industry towards natural antioxidants due to the health risks associated with artificial antioxidants. Phenolic flavonoids found in plants can act as reducing agents, hydrogen donors, singlet oxygen and superoxide radical scavengers, and metal chelators (Carocho & Ferreira, 2013). Therefore, the addition of natural antioxidants to food products at an industrial level is considered safe (Lourenço et al., 2019).

As an alternative to synthetic preservatives, EOs are natural food preservatives. EOs are known natural antimicrobial agents (Asbahani et al., 2015; Temel et al., 2026). EOs are generally considered safe (GRAS) because they extend the shelf life of perishable food products by preventing the spread of foodborne pathogens (Angane et al., 2022). While some EOs are more effective against Gram-positive bacteria, others are reported to be more effective against Gram-negative bacteria (Angane et al., 2022). The specific molecules contained within the EOs determine this difference. However, mechanisms by which EOs inhibit bacterial growth may include disruption of the bacterial outer membrane or phospholipid bilayer, increased membrane fluidity leading to leakage of potassium ions and protons, interference

with glucose uptake, and inhibition of enzyme activity (Cho et al., 2020; El-Sakhawy et al., 2026). Therefore, given the growing interest in the food industry and consumers' increasing preference for 'natural' and 'safe' products, the use of phenolic compounds and EOs is on the rise.

Green-synthesized nanoparticles

Nanocompounds are widely used as antimicrobial agents, anticancer agents, drug delivery vehicles, formulations for functional foods, pathogen identification, and in the food and pharmaceutical packaging industries (Mayegowda et al., 2023). At the intersection of nanotechnology and sustainable applications, green nanotechnology offers solutions to environmental and health problems associated with traditional nanomaterial synthesis and applications (Kazemi et al., 2023; Yenigün et al., 2026). The demand for sustainable and eco-friendly approaches is increasing. Green nanotechnology encompasses a wide range of strategies that minimize the use of hazardous chemicals, reduce energy consumption, and promote the use of renewable and biological resources (Basar et al., 2026c; Yiğit et al., 2025). This synthesis route is generally lower-energy, solvent-sparing, and more readily scalable than conventional chemical reduction, and the resulting particles are often reported to be colloiddally stable (Osman et al., 2024). However, process sustainability should not be equated with product safety: nanoparticles synthesized using plant or microbial extracts still require independent physicochemical characterization and toxicological assessment, since a biogenic capping layer does not by itself confer biological inertness (Hamed et al., 2023). Nanoparticles (NPs) synthesized using plant or microbial extracts remain an eco-friendly and cost-effective synthesis approach (Aslan et al., 2025; Başar et al., 2026d). The key point here is that nanoparticles conjugated with secondary metabolites contained in the plant have become reducing and stabilizing agents with antioxidant activity due to their smaller size and higher permeability (Başar et al., 2026d; Erenler et al., 2023). Studies have reported high bioavailability and minimal side effects (Vijayaram et al., 2024).

The mechanism of NPs formation via green synthesis is based on the reduction of bioactive compounds found in plant extracts by metal ions present in solution (Başar, 2026; Kazemi et al., 2023). This process can vary depending on the plant extract and the type of NPs metal synthesized. While bioactive compounds in plants can function as both reducing and stabilizing agents during nanoparticle synthesis (Mittal et al., 2014), biomolecules can function as coating and stabilization agents (Somasundaram & Edamana, 2015). In the synthesis of metal nanoparticles using plant extracts, the plant extract is first boiled in a specific solvent (water, ethanol, or methanol); then, filtration is performed, and a metal salt solution is added to the resulting extract, and the mixture is left to stand (Kalaiyarasi et al., 2025). Changes in the colour of the solution are observed, which indicates that the synthesized nanoparticles have been produced (Kazemi et al., 2023).

Nanotechnology is used in the food industry for additives, packaging, and food storage. Inorganic nanomaterials consist of elements such as Ag, Fe, Ca, Mg, Se, and silicates. Metal (oxide) nanomaterials are increasingly used in various consumer products, including surfaces and packaging materials that come into contact with water and food (Sekhon, 2010).

In the food industry, silver and zinc are the most commonly used particles. Zinc is an essential trace element that is generally considered safe by the FDA; therefore, its use as a food additive is permitted. ZnO nanoparticles have been incorporated into polymeric matrices to enhance the antimicrobial properties of packaging materials used in food preservation and to improve some packaging characteristics (Espitia et al., 2025). Silver nanoparticles (AgNPs) have been reported to exhibit antibacterial, antiviral, and antifungal properties (Nicolae-Maranciuc & Chicea, 2025). These properties may be revealed through mechanisms such as disrupting microbial membranes, forming reactive oxygen species (ROS), and interacting with essential cellular proteins (Pangli et al., 2021). However, the direct use of AgNPs is limited by factors such as poor stability and potential toxicity to human cells (Dube & Okuthe, 2025). In addition to silver and zinc oxide, green-synthesized nanoparticles of copper, iron, magnesium, selenium,

and gold have been reported for use in food-related antimicrobial and antioxidant applications. These nanoparticles have distinct dissolution rates, ion-release profiles, and toxicological signatures. Consequently, the migration and safety data compiled for AgNPs should not be extrapolated to these other nanoparticle chemistries without chemistry-specific data (Arağan et al., 2026; Başar et al., 2026e; Mayegowda et al., 2023).

Current studies reveal that nanoparticles synthesized using plant extracts possess high biological activity and offer versatile application potential in food systems, such as natural food preservatives, active packaging systems, edible coatings, functional foods, and smart packaging technologies (Bisht et al., 2025; Dube, 2025; Sarkhel et al., 2026).

Applications in food safety and packaging: a bibliometric-aided analysis

Packaging is a crucial factor in the food chain, further meeting the needs of food quality and safety from production to the final stage of consumption. The surge of interest in packaging is a consequence of the ever-increasing population and increased food demand and consumer trends (Vilela et al., 2018). Packaging prevents any potential undesired chemical and biological modifications by acting as a barrier to protect the food from environmental factors, including oxygen, moisture, light, pests, volatiles, and both chemical and biological contamination (Yildirim et al., 2018). In their review, Yildirim et al. (2018) discussed how active packaging systems are designed to deliberately incorporate components that release or absorb substances to extend shelf life or improve the condition of packaged food, according to European regulation (EC) No 450/2009. Such packaging systems enhance food safety by exhibiting active functions, such as antimicrobial and antioxidant activity, oxygen and ethylene scavenging, and carbon dioxide emission. In packaging systems, a significant shift has been observed from synthetic to natural antioxidants, with lower toxicity and higher safety. This shift was due to the reported side effects of synthetic antioxidants, namely butylated hydroxytoluene, butylated hydroxyanisole, and tert-butylhydroquinone (Nieva-Echevarría et al., 2015).

Considering the thematic content and evolution of the studies dealing with food packaging, we performed an exploratory search using the string TITLE-ABS-KEY (packaging AND food), restricted to the Scopus “Engineering” subject area (all document types, no date restriction; search exported from Scopus to VOSviewer for keyword co-occurrence analysis, full-counting method). The query was *TITLE-ABS-KEY [(packaging AND food) AND (“green synthesis” OR “green synthesized” OR biosynthesis OR nanoparticle* OR “plant extract*” OR “essential oil*”)]*. Regarding the thematic content, we obtained 11 clusters corresponding to 319 items (**Fig. 1**). According to the network, “active packaging” was found to be the most central and highly connected theme, as expected. This hub was strongly associated with biopolymer-based materials, such as chitosan, gelatin, starch, pectin, and alginate. Such a critical thematic hub clearly indicates a dominant focus on biodegradable matrices for active packaging applications. This impressive interest has been discussed in a quite number of comprehensive reviews (Flórez et al., 2022; García-Guzmán et al., 2022; Luo et al., 2022; Metha et al., 2024; Roy et al., 2023; Wang et al., 2018). Critically, we further observed a major research direction centered on bioactive functionality, which is highlighted by frequent links to antimicrobial, antibacterial, and antioxidant activities. These terms commonly co-occur with essential oils (**Fig. 2**) and plant-derived extracts (i.e., curcumin and carvacrol) (**Fig. 3**).

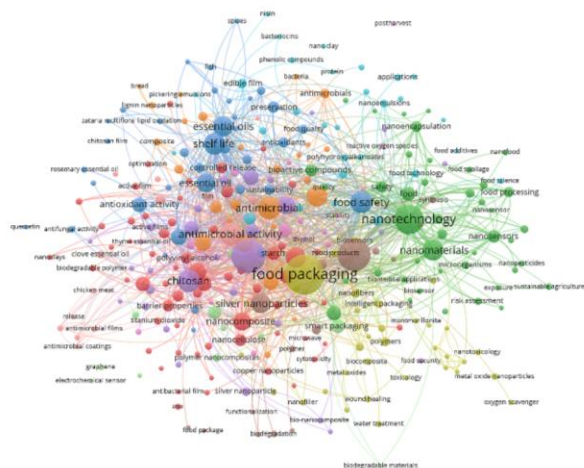


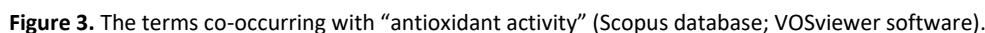
Figure 1. Co-occurrence network of keywords. The figure was constructed using VOSviewer software, being based on the keywords given in the studies retrieved from SCOPUS database.

Given its special focus on curcumin, it exhibits notable effectiveness in reducing microbial contamination, preventing oxidative degradation, and serving as real-time indicators of food freshness. However, it also has some limitations concerning its use in packaging applications owing to its poor stability and low solubility (Devi et al., 2025). In addition to the report of Devi et al. (2025), the authors have discussed and addressed smart packaging systems to make curcumin suitable and overcome its poor water solubility and instability (Dube, 2025; Qu et al., 2023; Ranade et al., 2025; Roy et al., 2022). In the case of carvacrol use, Nostro and Papalia (2012) have detailed how carvacrol, either alone or combined with synergistic products, can be incorporated into different formulations for food packaging applications, further discussing and describing carvacrol as a food preservative or antimicrobial agent in food packaging materials (Nostro & Papalia, 2012). Our bibliometric analysis (**Fig. 1-3**) emphasizes the use of natural additives to improve food preservation and safety.

In addition, we observed strong connections between electrospinning, biopolymers, and bioactive functionality in food packaging research (**Fig. 4**). Electrospinning, as a central methodological node, is closely linked to chitosan, gelatin, and zein, emphasizing its importance in producing nanofibrous materials with enhanced performance. As reported in the literature, there are strong associations between chitosan and antibacterial and antioxidant activities, indicating its central role in antimicrobial packaging. Our bibliometric analysis confirms that the presence of electrospinning and nanofibers reflects growing interest in advanced fabrication strategies to enhance functional efficiency.

Another prominent cluster addresses sustainability, integrating biodegradable packaging, sustainable packaging, life cycle assessment, and circular economy. The relevant cluster demonstrates increased attention to environmental impacts. In parallel, modified atmosphere packaging (MAP) and shelf-life extension are closely linked to food safety, oxygen permeability, and lipid oxidation, underscoring the importance of gas control and barrier properties. Finally, a technology-oriented cluster focuses on material performance, including

and safety, a multidisciplinary field integrating material science, food preservation, and sustainability is required (**Fig. 5**).



Safety, toxicity, and regulatory considerations

Migration

Any concept of active packaging is inherently a controlled-release mechanism, making its safety evaluation essentially a matter of mass transfer; what percentage of the incorporated bioactive substance reaches the food, in which chemical format, and under what circumstances? According to European regulations, materials intended for contact with food must not release components in amounts that could threaten human health or significantly change the composition or sensory qualities of the food (Regulation (EC) No 1935/2004). For plastics,

this general requirement is implemented through an overall migration limit as well as specific migration limits for certain substances, which are assessed using standardized food simulants under time-temperature conditions chosen to reflect the most likely worst-case scenarios (Regulation (EU) No 10/2011). Active and intelligent materials have the added requirement that the substance being deliberately released must also adhere to food-additive regulations (Regulation (EC) No 450/2009), a requirement that is often overlooked in the packaging literature, where the inclusion of essential oils is highlighted as a material innovation without mentioning the need for additive authorization under Regulation (EC) No 450/2009.

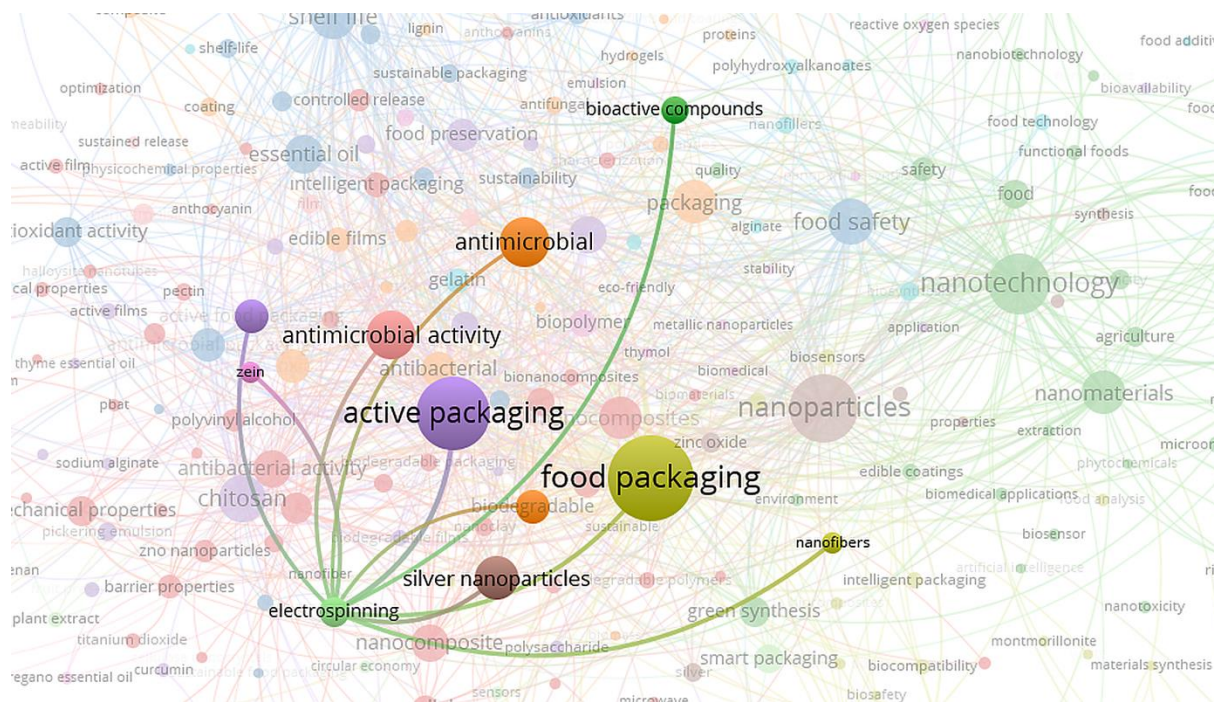


Figure 4. The terms co-occurring with the “electrospinning” (Scopus database; VOSviewer software).

In the case of nanoparticle systems, Echegoyen and Nerín (2013) demonstrated the migration of silver from commercial nanosilver containers, reporting that the silver migration was lower than those values proposed by the European legislation (Echegoyen & Nerín, 2013). However, the authors noted that the migration values were higher in the case of heating in a microwave oven compared to a conventional oven. Furthermore, Cushen et al. (2014) evaluated and simulated the migration of silver and copper nanoparticles from polyethylene nanocomposites

(Cushen et al., 2014). They reported that the mass fraction of the nanofiller was the dominant factor determining migration, in accordance with particle size, temperature, and contact time. Nevertheless, a critical synthesis of some twenty migration studies concluded that nanoparticles fully embedded in a polymer were effectively immobilized, and that much of the reported 'nanoparticle migration' can be more parsimoniously explained by the oxidative dissolution of silver (Ag) ions during sample

handling under mildly reducing conditions, followed by the reformation of particles (Störmer et al., 2017).

The rate and extent of this release are governed by polymer-bioactive interactions, which are rarely characterized systematically. Hydrophilic biopolymers, such as chitosan, starch, and gelatin, retain phenolic compounds primarily through hydrogen bonding. These biopolymers can exhibit burst release in aqueous or high-humidity food environments. In contrast, more hydrophobic matrices retard release through slower diffusion.

However, they can also sequester lipophilic essential oil constituents so effectively that the concentrations of these compounds in the package never reach the food surface (Flórez et al., 2022; Luo et al., 2022). The choice of compatibilizer, crosslinking density, and the plasticizing effect of the bioactive itself on the polymer network can further alter both diffusion coefficients and mechanical performance. Consequently, migration and efficacy data obtained for one polymer-bioactive pairing cannot be assumed to be applicable to another without matrix-specific testing (Sarkhel et al., 2026).

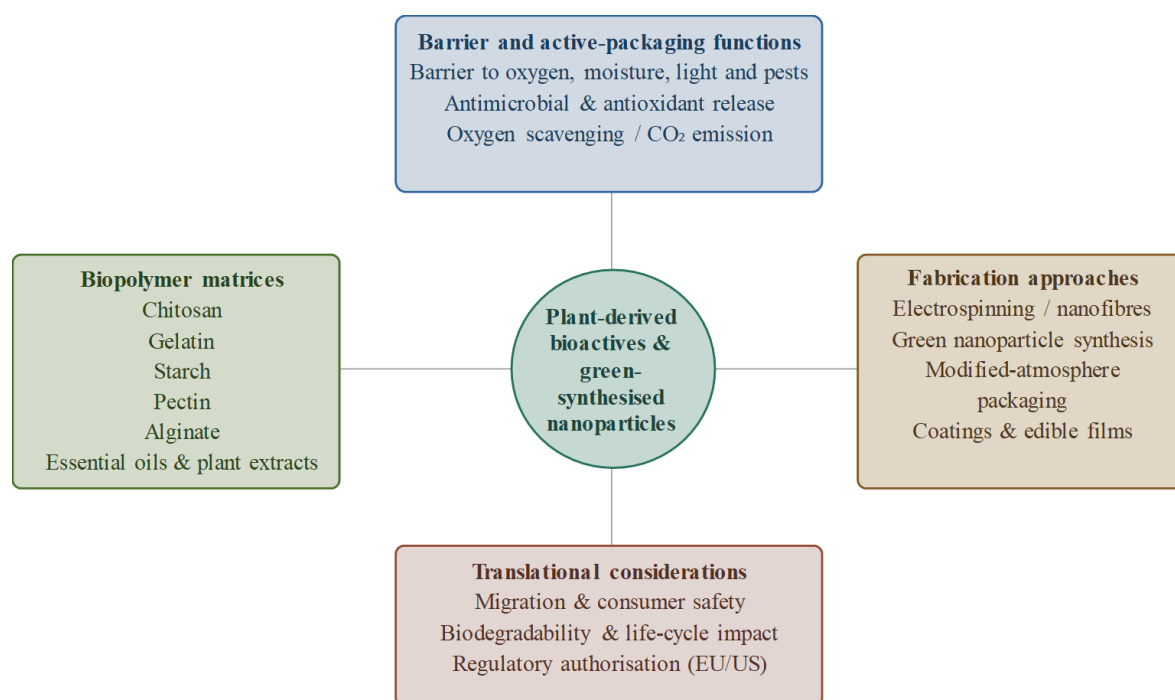


Figure 5. Emerging trends and innovations in food packaging, a multidisciplinary perspective on safety, sustainability, and preservation.

Consumer safety

Consumer risk is the product of exposure and hazard, and the oral hazard database for silver is instructive precisely because it complicates the simple narrative. In a 28-day repeated oral-dose study in rats, organ silver concentrations correlated with the Ag⁺ content of the administered suspension rather than with particle number, indicating that ionic rather than particulate silver dominates intestinal passage; silver was cleared from most

tissues within eight weeks but was retained in brain and testis, and- mechanistically important- particles were detected in animals dosed with AgNO₃, demonstrating *in vivo* particle formation from ions (Van der Zande et al., 2012). The study by Qi et al. (2023) has mechanistically characterized the gastrointestinal transformation, absorption, and toxicological mechanisms of AgNPs after oral exposure (Qi et al., 2023). Further, less frequently discussed dimension of consumer safety concerns microbiology rather than toxicology. Exposure to

sub-inhibitory levels of silver can select for silver-resistant phenotypes and, through co-selection, for antibiotic-resistance determinants (McNeilly et al., 2021).

Therefore, deploying a broad-spectrum metal biocide across a high-volume consumer product category is not risk-neutral, even where consumer migration is negligible. This consideration is largely absent from the literature on applications. The hazard profile of essential oils is generally more favourable because many of their constituents hold GRAS status; however, the binding constraint then shifts to organoleptic acceptability. Essential oil constituents partition into lipid and protein phases and bind food macromolecules. Consequently, concentrations that are effective in real matrices are consistently higher than *in vitro* minimum inhibitory concentrations. The necessary increase often exceeds the sensory detection threshold (Gcabashe et al., 2026; Hyldgaard et al., 2012). Although encapsulation, nanoemulsion, and vapor-phase delivery mitigate this trade-off, they do not abolish it (Qu et al., 2023; Ranade et al., 2025; Roy et al., 2022).

Current gaps

We have identified three gaps that appear to be decisive. The first concerns speciation and dosage. The regulatory record for silver is unusually explicit on this point. In 2016, EFSA re-evaluated silver (E 174) and found that the available information was insufficient to assess its safety. This was principally because the nanoparticle content and ionic release of the additive were uncharacterised, and the test materials used in the available toxicological studies could not be related to it (EFSA, 2016). Following a further call for data, the Panel again concluded in 2025 that it could not make a safety assessment, citing inadequate physicochemical characterization and inadequate genotoxicity and subchronic toxicity data (EFSA, 2025). Therefore, nearly a decade of sustained regulatory attention has failed to close the data gap for a material that is routinely described as safe in packaging literature.

The second gap concerns exposure realism. Migration testing uses simulants under abusive conditions rather than realistic distribution and storage profiles, and toxicological testing uses doses

far above realistic levels. Neither method reflects the exposure actually experienced by consumers. Probabilistic exposure modelling that takes into account both measured migration and food consumption data would provide a much clearer picture than either method on its own, and would also make the associated uncertainty explicit.

The third issue concerns the green synthesis premise itself, which should be stated directly. The fact that a nanoparticle is produced by a low-energy, solvent-sparing, plant-mediated route says nothing about the resulting particle's toxicology: the hazard lies in the particle's surface chemistry and corona, not the synthetic route. The phytochemical capping layer alters the surface charge, dissolution kinetics, and protein corona formation relative to chemically synthesized counterparts. Therefore, it requires assessment in its own right, rather than a read-across in either direction. The EFSA guidance on the risk assessment of nanomaterials in the food and feed chain sets out the required characterization and testing strategy and applies irrespective of the synthesis route (EFSA, 2021a). Framing green synthesis as intrinsically safe confuses process sustainability with product safety. These are logically independent claims that require separate evidence.

Challenges and future perspectives

Among the challenges observed, translation of the green-synthesized nanoparticles and EO-functionalized films from the laboratory to production process control rather than laboratory efficacy is a critical rate-limiting step. For instance, the phytochemistry of the extracts clearly exhibits significant variations according to the species, chemotype, origin, and extraction conditions, which further affects the particle size, morphology, and colloidal stability (Singh et al., 2023). Therefore, standard process control cannot be applied to the extract itself until the uncharacterised mixture is standardized, since the reducing and capping functions reside in the mixture rather than a defined reagent. In this regard, the following practical approaches have been identified as effective routes to this objective: the utilization of fractionated extracts, the implementation of spectroscopically fingerprinted feedstocks with established

acceptance criteria, and the employment of continuous-flow reactors. However, techno-economic and life-cycle assessments against relevant competitors are habitually deferred because the 'green' label only covers the synthesis step and not the full cradle-to-grave profile once cultivation, solvent recovery, and end-of-life are included. In the context of EOs delivery, spray drying is a scalable method. However, it should be noted that this process can result in the degradation of thermolabile constituents. Coacervation, liposomal, and electrospun systems offer enhanced protection; however, they are more costly and less readily available for utilization (Gcabashe et al., 2026).

Considering the aforementioned factors, it is imperative to implement a standardization process at three distinct levels. First, it is imperative to characterize the materials in accordance with the EFSA template (EFSA, 2021b), as cross-laboratory comparison is impossible without it. This includes the measurement of particle size, hydrodynamic diameter, PDI, zeta potential in the relevant medium, crystallinity, and dissolution kinetics. Bioactivity testing is predominantly reliant on inhibition-zone diameters, which is a semi-quantitative screen that is unsuitable for comparative claims. Therefore, the minimum requirement is the determination of minimum inhibitory and minimum bactericidal concentration values with standardized inoculate, dose-response characterization, and dissolution controls separating ionic from particulate effects. The validation in food is the weakest link, as in vitro screening significantly outweighs matrix-realistic shelf-life studies that combine microbial enumeration, oxidation indices, and sensory/consumer data (Gcabashe et al., 2026). It has been demonstrated that the inhibition of *E. coli* on agar is a material result, not a preservation result.

The absence and lack of harmonization of regulatory frameworks represent a significant impediment to the commercialization of nanomaterials. For instance, the EU requires explicit authorization for nanoforms under Annex I of Regulation (EU) No 10/2011 (EFSA 2021b), the US evaluates nanoscale particle-size reduction on a case-by-case basis without a positive list (FDA, 2014), and other jurisdictions fall between or lack nano-specific provisions entirely, resulting in an identical film

being lawful in one market and unassessed in another. While full convergence is improbable, four objectives appear to be within reach: the establishment of an operational definition of "nanoform" for food contact that is mutually agreed upon, the validation of methods that can differentiate particulate from ionic migration, the mutual acceptance of characterization dossiers, and the explicit treatment of materials synthesized using green methods. The Codex Alimentarius Commission is the most suitable venue for the first and fourth objectives, while standardization bodies are well-positioned to address the second objective.

Conclusion

Evidence suggests that plant-derived bioactives and green-synthesised nanoparticles are technically credible contributors to food preservation and active packaging. The mechanistic basis of these phenomena is reasonably well established. Membrane destabilization, interference with energy metabolism, radical scavenging, and metal chelation are the mechanisms responsible for the former, while the latter involves ion release, reactive-oxygen-species generation, and interaction with cellular targets. The bibliometric structure of the field described above shows a mature, multidisciplinary research programme organized around biodegradable matrices, bioactive functionality, and, increasingly, sustainability and controlled release.

Notwithstanding, the conclusion of this review is a qualified one. The evidence supporting efficacy is considerably stronger than the evidence supporting safe, reproducible, and lawful deployment, and the asymmetry is systematic rather than incidental. The present study proposes three hypotheses designed to summarize the current position, each formulated in such a way as to be amenable to empirical testing. Firstly, it is evident that the measurable migration from fully embedded nanocomposite systems is predominantly ionic in nature rather than particulate. This assertion can be substantiated through the systematic application of single-particle ICP-MS across a range of material types, simulants, and thermal histories. Furthermore, this hypothesis would be invalidated by the reproducible detection of intact primary particles under realistic contact

conditions. Secondly, it is posited that the discrepancy between the *in vitro* and *in-food* efficacy of EOs is predominantly attributable to partitioning and macromolecular binding, as opposed to loss of intrinsic activity. This hypothesis can be evaluated through the quantification of free versus bound active concentration *in situ*, and the subsequent correlation with observed inhibition. Thirdly, batch-to-batch variability of the reducing extract is identified as the principal source of irreproducibility in green synthesis. This hypothesis can be tested by co-varying spectroscopically fingerprinted extracts against particle attributes and bioactivity in a designed experiment. Until such questions are addressed through matrix-realistic, adequately powered, and methodologically standardized studies, the appropriate scientific posture is neither the uncritical optimism that characterizes much of the applications literature nor dismissal of a promising technology, but recognition that the decisive constraints have shifted. These issues are no longer primarily concerned with chemistry; rather, they are questions of metrology, exposure assessment, and regulatory design.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Disclaimer

Generative AI tools were used solely to assist with the preparation of some figures and for language and grammatical editing of selected parts of the manuscript. AI tools were not used to generate research data, perform data analysis, draw scientific conclusions, or make decisions regarding the interpretation of the results. All AI-assisted content was carefully reviewed and verified by the authors, who take full responsibility for the accuracy, integrity, and final content of the manuscript.

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