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Review

Biodegradable Active Packaging with Controlled Release: Principles, Progress, and Prospects

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ABSTRACT: Climate change is accelerated by increasing food waste; more importantly, this pressing challenge is compounded by the environmentally damaging effects of conventional plastics used in food packaging. We have critically reviewed active release packaging as an innovative solution to address these concerning effects. Particular attention is paid to controlled release, encapsulation methods, and natural active agents. Other aspects of active packaging development such as stringent safety legislations are also discussed, alongside highlighting developmental hurdles. Certain technologies are underscored as revolutionary for the field of active packaging: in particular, stimuli-responsive materials, reliable controlled-release mechanisms, and the synergy of active packaging and intelligent packaging. Encapsulation is described as an important method of achieving controlled release. The potential of electrospun biopolymeric fibers to encapsulate natural antimicrobial or antioxidant molecules is also noted. Importantly, the review discusses the incorporation of nanomaterials and subsequent increased commercialization success due to the modulation of Bioplastic properties. In order to outcompete inexpensive petroleum-based plastics, these novel packaging materials must have good mechanical properties, good barrier properties, well-defined controlled release studies, and good biodegradation rates. Overall, it is evident that biopolymeric active-release packaging incorporating natural active compounds will serve as a high-potential, sustainable replacement for ubiquitous petroleum-based plastics.

KEYWORDS: *active packaging, plastics, controlled release, food, biodegradable, natural, encapsulation*

1. INTRODUCTION

1.1. Conventional Plastics Contributions to Municipal Waste. Currently, there is a clear movement toward reusable, recyclable, or compostable packaging. In fact, many countries have already banned certain single-use plastics. In the US, the Break Free From Plastic Pollution Act of 2020 aims to phase out single-use products such as plastic utensils.[1] The bill also sets out minimum required percentages of reusable, recyclable, and compostable products and materials used to make products.[1] The 2021 EU single-use plastic plan pledged to use only recyclable or reusable plastics for commonly used items by 2030.[2] Similarly, the UK has pledged to eliminate single use plastic and associated waste by 2042.[2] Zhao et al.[3] reported that over 99% of plastics used currently are petroleum-based and not biodegradable. Worldwide, food packaging is the third largest industry and the single-largest contributor to solid waste.[3,4] This detrimental effect has been highlighted by the COVID-19 pandemic due to increasing packaging waste from delivery services and a fear of contamination increasing disposal over the reuse of materials.[5] Therefore, the packaging industry requires a shift in focus toward a more sustainable future. The research into, and commercialization of, biodegradable packaging will be pivotal to this revolution.

Despite environmental concerns, plastic packaging is necessary to avoid food contamination and prolong the shelf life of food. Removing packaging would incur a greater reliance on refrigeration and so increase energy consumption and related greenhouse gas (GHG) emissions.[2] Furthermore, packaging greatly reduces food waste and prevents hygiene risks in supermarkets.[2] Strikingly, food waste is one of the largest contributors to climate change, due to the associated GHG emissions from landfill, emitting in excess of 3.3 Gt of CO_2 per year.[6] Food packaging should protect from oxygen, water vapor, UV light, and chemical or microbial contamination.[7] Unfortunately, the properties of petroleum-based plastics are ideal for this application. Furthermore, fossil fuel-derived plastics are lightweight and have relatively low production and transportation costs.

1.2. Recycling. Petroleum-based plastics such as polyethylene (PE) and polypropylene (PP) have become increasingly criticized due to their damaging impact on the environment. Used primarily in the packaging industry, these common plastics may form microplastic debris when disposed of. Microplastics pollute marine environments, and there are concerns of this plastic debris entering the food chain through

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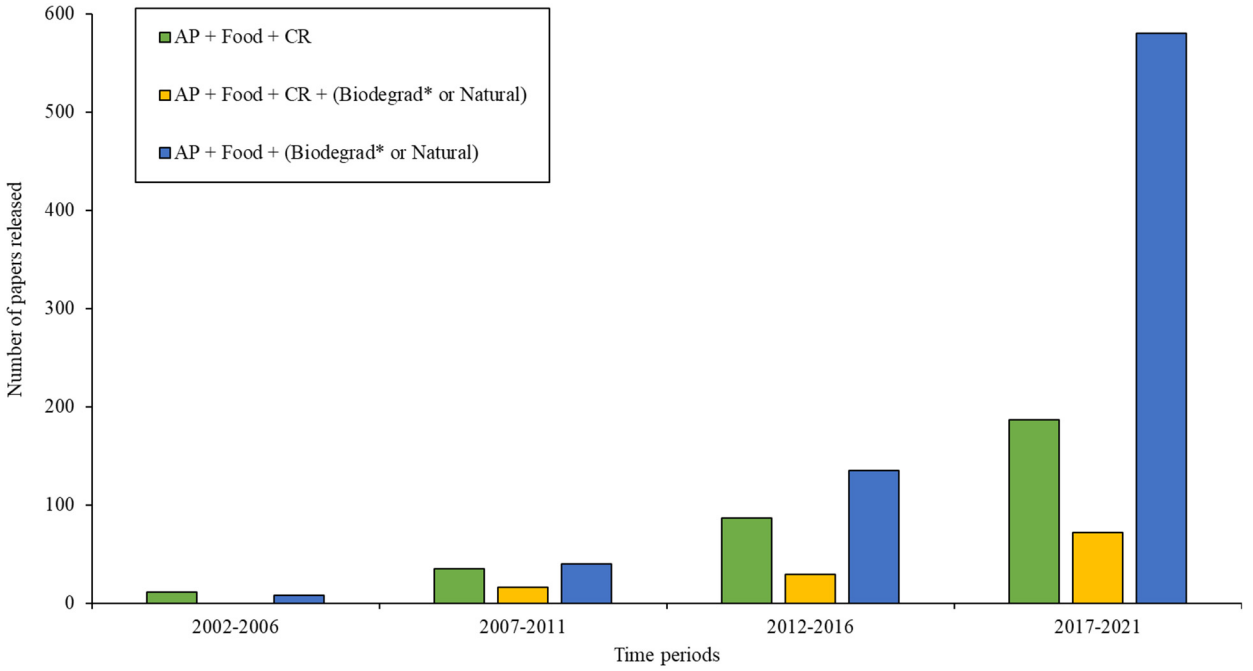

Figure 1. Representation of the number of papers released containing specific keywords relating to active packaging (AP), controlled release (CR), and biodegradability. Biodegrad* represents the truncation of at the root of the word to include biodegradation, biodegradable, and biodegradability. The trend shows a clear increase in related publications and research focusing on active packaging and improving the sustainability of this invention, over the last 20 years. It highlights the importance of biodegradability and the use of natural compounds. Figure 1 also suggests that the controlled release is currently poorly developed in active packaging. The data was obtained from a Scopus search of keywords and was reprocessed into a chart for visualization purposes.

assimilation.[8] Bouwmeester et al.[9] reviewed this topic, assessing the occurrence of microplastics in food and associated health impacts. The majority of plastic usage is for the packaging industry.[3] Of the plastic consumed, around 80% is sent to landfill, 17% is recycled or incinerated, and 3% ends up in waterways.[3] Strikingly, in 2017, the UK parliament reported that less than 50% of UK plastic was collected for recycling and only 34% of this material was recycled in the UK.[2] The remaining was exported to countries, often with a poorer waste infrastructure, and likely ended up in landfill or the natural environment.[2]

Options available for reducing plastic waste currently include reusing, replacing, recycling, or removing plastics. Other initiatives have included monetary incentives and returnable schemes for reusable containers. Conventional methods of plastic waste reduction, particularly recycling, are limited by consumer participation and have issues with plastic contamination, color, and size. During recycling, the chain lengths of plastics are reduced, meaning the lifetime of the material is also greatly reduced.[2] UK policies often focus on recycling schemes, but misinformation or confusion about recyclability, along with contamination means that many recyclable plastics end up in landfill to avoid laborious sorting processes.[2]

1.3. Food Waste and Climate Change. Commercially, there is a high consumer demand for both fresh food with an extended shelf life and a reduced environmental footprint of food packaging. Consequently, there is a demand for biodegradable polymers. The unsustainable use of crude oil as a feedstock to make traditional plastic provides a market for biopolymers to emerge into. In fact, the bioplastics market is forecast to grow to over 6 billion USD by 2023, doubling the market value from 2018.[10] Interest from food packaging and distribution industries has also been documented concerning the replacement of synthetic polymers.[11]

The primary mechanism of food degradation is lipid oxidation, often driven by thermal processes.[10] Alongside foodborne diseases due to microbial outbreaks, food degradation also leads to disposal by consumers or retailers. The 2021 UNEP food waste index report estimated that 931 million tonnes of food waste was generated in 2019, amounting to around 17% of total global food production.[12] As a result of this, there is a drive toward packaging that can inhibit microbial growth in food, while maintaining food-quality and safety.

1.4. Active Packaging As a Tool to Tackle Food Waste and the Plastic Crisis. Active packaging (AP) functions by either releasing active antioxidant or antimicrobial compounds or sequestering certain gases, with an aim to delay food degradation. The concept of AP was introduced as a response to market trends and changes in consumer demands. The European FAIR-project CT 98-4170 defined active packaging as "a type of packaging that changes the condition of the packaging to extend shelf-life or improve safety or sensory properties while maintaining the quality of the food".[13] This may include intrinsic properties of the polymer material or the deliberate inclusion of active substances to the polymeric matrix. Theoretically, the active ingredients of the packaging material may prevent the degradation of food by preventing contamination in order to extend shelf life and reduce food waste. The first patents for active packaging materials date back to the early twentieth century; however, markets are only recently picking up this technology and so it is still considered innovative in the food packaging sector.[14] Currently, innovation is focused on the translation of this technology to biodegradable materials to tackle plastic waste. Indeed, the

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trend in published research concerning active packaging over the past 20 years as seen in Figure 1 confirms this. To this end, active packaging may serve as a solution to the problems of food waste and plastic waste.

Types of active packaging include migratory AP, non-migratory AP, release AP, and scavenger AP. Examples of scavenger methods include oxygen, ethylene, moisture, and CO_2 absorbers. On the contrary, release strategies for active release packaging may include antimicrobial, antioxidant, or CO_2 release. Controlled release represents a further development in which the active agent concentration is maintained over a prolonged period. LaCoste et al.[15] initially described the idea of controlled release packaging (CRP). Controlled release has been widely utilized for drug delivery in the healthcare field. However, currently, CRP has limited applications in commercial food packaging, despite a vast increase in research over recent years (Figure 1). Furthermore, when designing active packaging, it is vital that the release rate of the active agent is balanced with food oxidation kinetics, related to degradation rate.[10] Most studies on AP in the literature focus on the inhibition of microbial growth in order to maintain food freshness.[16]

1.5. Overview of Important Developments in Active Packaging. The incorporation of nanotechnology has become increasingly popular over recent years, and stimuli-responsive materials are beginning to gain attention in the literature.[16] Important developments in research concerning active packaging are emerging, particularly the use of nanocomposites in polymeric matrixes to enhance mechanical properties, encapsulation technologies for controlled release, stimuli-responsive release packaging, and the development of edible packaging.[2,10,16] In-depth reviews on the general aspects of active packaging have been reported recently.[4,17] Reviews focusing on the active agent, with several reports exclusively discussing natural active agents, have been produced.[7,11,18−22] Controlled release has also been reviewed in the context of antioxidant release.[10,23] Furthermore, the safety aspects of active packaging have been reviewed.[24,25] Lastly, Zanetti et al.[26] and Becerril et al.[27] reviewed encapsulation methods for active packaging. Hence, while there have been multiple reviews concerning active packaging and related subtopics, we review a combination of different aspects—and so provide a distinct overview of the subject—with a discussion of novel research. Figure 2 shows a pictorial outline of this review article, indicating the key topics covered.

The objectives of this literature review are to discuss, in terms of active packaging, (1) the active agent, (2) the importance of controlled release, and (3) natural active agent encapsulation. Recent research in the field will be underscored, hurdles to commercial development will be discussed, and the future scope will be evaluated.

2. LESS PLASTIC, MORE TEA: THE ACTIVE AGENT FOR ACTIVE PACKAGING

2.1. State-of-the-Art and Recent Advances in Active Packaging. Active packaging is a promising research area due to the diversity of materials possible and the variety of foods that may be protected. Overall, the critical factors to consider in the development of active packaging include the method of incorporation of the active agent, the biopolymer choice, the active agent release mechanism, and the effect of the active agent on food and safety concerns.[16] Related to this, the packaging must be correctly labeled with the added active

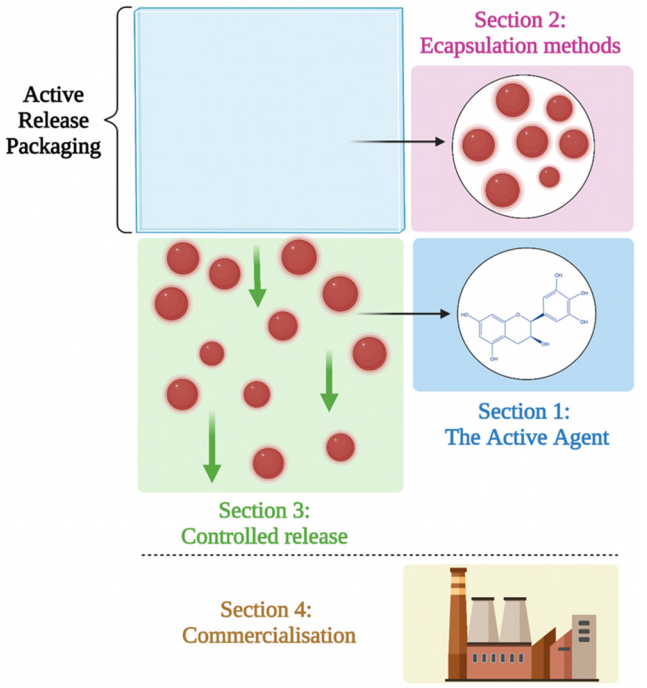

Figure 2. Schematic overview of the sections covered in this review. Green tea extract (epigallocatechin gallate) is used as an example of a natural antioxidant, created with biorender.com. The different bioplastics utilized to form the substrate of active packaging are beyond the scope of discussion in this particular review.

compounds declared.[28] The field of research concerning active packaging is moving toward the exclusive use of biodegradable and biocompatible materials. The research field is also shifting toward the exclusive use of natural compounds to enhance sustainability and, in some cases, sensory properties.[29] As a result of this, only biobased and biodegradable additives and polymers will be discussed in detail in this review.

2.1.1. Traditional Food-Preservation Techniques. Conventional plastic packaging is considered inert as it does not allow for molecular transfer between the packaging material and the headspace or food. However, methods to prolong food shelf life have been utilized in combination with conventional plastic packaging materials. Modified atmosphere packing (MAP) and vacuum packing have traditionally been used to preserve food commercially. Other preservation methods include freezing, drying, heat or irradiation treatment, and the addition of salts or antioxidants to food.[7,10,28] However, MAP and vacuum packing, often based on petroleum-based PET, do not completely remove oxygen or moisture or protect from light.[4,13] These environmental factors enhance food-degradation.[4] To overcome this shortcoming, MAP has been combined with oxygen-scavengers commercially to remove residual oxygen.[4,13]

2.1.2. Prevention of Microbial Accumulation in Packaging to Combat Food Spoilage. The need to more effectively prevent the accumulation of microorganisms that cause food spoilage inspired the invention of active packaging (AP). In this technology, the active agent within the packaging interacts with, and plays an important and dynamic role in, the preservation of food.[30] The mechanism of action depends on the volatility of the active compound, whereby volatile compounds diffuse through the headspace (indirect contact) and nonvolatile substances diffuse through the packaging

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directly to the food surface (direct contact).[16] In addition to elongating food shelf life, sustainable AP technology should enhance material properties such as gas-barrier properties, mechanical properties, moisture absorption, and UV-protection, while retaining good biodegradability.[4]

2.1.3. Active Release Packaging Technology. Technological advances have been made such that the active agent may be directly incorporated into the polymer structure rather than formulated into sachets.[10,28] However, sachets are still commercially used, along with absorbent pads used in meat trays.[28] Direct incorporation into the polymer addresses safety concerns regarding possible leakage of the sachet-contents onto packaged food and related fears of ingestion.[10,28] Types of AP based on this direct incorporation may be divided into groups described by the terms "scavengers" and "emitters". The former includes O_2 and CO_2 scavengers. High levels of O_2 can facilitate microbial growth; thus, the scavengers function to reduce these levels in order to prolong food freshness. Oxygen scavengers are often based on iron oxidation, though glucose oxidase has also been used.[11,13] The latter include CO_2, SO_2, ethanol, antioxidant, and antimicrobial emitters, which may act by either direct or indirect contact with the food. This review will focus on "active release packaging" and emission technology, particularly of antioxidant and antimicrobial compounds.

2.1.4. Antioxidant and Antimicrobial Compounds for Active Release Packaging. Antioxidants (AOs) limit oxidation of fatty-acid components by preventing radical-formation and may include plant extracts, essential oils (EOs), spices, or herbs. Specific examples include L-ascorbic acid, L-tyrosine, green tea extract (GTE), polyphenols, thymol, and tocopherol. Antimicrobial (AM) agents prevent microbial growth by various mechanisms such as bacterial membrane damage.[4] AM agents may include organic acids, metal oxides, metal nanoparticles, ethanol, EOs, or bacteriocins.[4,31] Additionally, Chen et al.[32] showed the inherent antimicrobial effect of the biopolymer chitosan and derivatives, by measuring the minimum inhibitory concentrations against common food bacteria and applying this to oysters to extend their shelf life. Interestingly, this research mimics nature since chitosan is derived from the skeleton of shellfish. Additionally, the use of inherently antimicrobial biopolymers reduces the need for additives and, therefore, the complexity of the packaging. Furthermore, silver nanoparticles (NPs), among other metals, have traditionally been used as antimicrobial agents. Silver NPs adhere to bacterial membranes and/or penetrate into bacterial cells to achieve their antimicrobial action.[4] However, these nanoparticles pose a cytotoxicity risk to humans.[13] *In vitro* tests carried out by Carrola et al.[33] recorded the toxicity of Ag NPs to human cells using NMR metabolomics, which they report to be a promising method to screen the toxicity of nanomaterials. It may be possible to control the release of Ag^+ ions and hence suppress toxicity through immobilization of the nanoparticles.[4] However, this would require stringent migration studies. Similarly, concerns have arisen regarding the use of the synthetic AOs butylated hydroxytoluene (BHT), which may accumulate in adipose tissue, and butylated hydroxyanisole (BHA), which may be considered carcinogenic.[18,34]

2.1.5. Emerging Shift toward the Exclusive Use of Natural Additives. Many natural substances are generally recognized as safe (GRAS).[28] The incorporation of natural active agents into packaging is becoming more common as these compounds are more likely to be accepted by the consumer. This may be due to a common perception that natural agents may be less likely to cause harmful effects on food than synthetic agents. Table 1 shows the findings of several recent experimental papers published on the topic of active packaging, specifically incorporating natural active agents. The table describes the use of both encapsulated and nonencapsulated active agents for biopolymer-based AP, an overview of key results, and the application of the material from each study. There has been a recent review on this topic by Santhosh et al.[35] discussing the benefits of using natural additives, specifically polyphenols extracted from plant byproducts. Relating to this, the use of biopolymers is increasingly more common and the compatibility of the active agent with the packaging material is important. This, along with the film-formation method among other factors, often determines the mechanical and physical properties of the material. Consumers at present prefer the use of biodegradable and "nontoxic" or "natural" ingredients over synthetic compounds. Therefore, with the use of natural additives, there should be fewer developmental hurdles such as toxicity-related safety regulations and consumer nonacceptance.[21] There is a vast amount of research based on the use of petroleum-based plastics such as LDPE, with active agents incorporated.[36] However, this review will focus on the use of bioplastics incorporating natural active compounds.

2.1.6. Evaluating the Antimicrobial Activity of the Active Component. The release of an active compound from packaging must be tightly controlled by mechanisms within the material in order to minimize risk to consumers, emphasizing the benefits of using natural additives. The diffusion of antimicrobials from packaging has been prominent in the literature for over 20 years, with Han and Floros (1998) among the authors reporting a number of papers on the subject.[37] To understand the mechanism of release, the antioxidant or antimicrobial activity of both the food and the packaging itself should be measured; the activity within the headspace may also be measured.[28] Common microbes related to food spoilage include *E. coli*, *L. monocytogenes*, *B. subtilis*, *S. aureus*, and *A. niger*.[4] Literature studies often test *E. coli* and *S. aureus* as examples of Gram-positive and Gram-negative bacteria, respectively. The minimum inhibitory concentration (MIC) is the lowest concentration of antimicrobial in the polymer, which results in complete inhibition of microorganism growth.[19] Experimentally, antimicrobial activity may be determined by measuring zones of inhibition in agar diffusion assays with a circular piece of active film on a plate inoculated with food-spoiling bacteria; this may be termed the "disc diffusion method".[38] Alternatively, cell-viability assays may be used. Laboratory tests used to determine the MIC may be misleading in buffer solutions as the tested microorganisms may be able to recover from the antimicrobial attack in the presence of nutrients.[19]

2.2. Evaluating the Antioxidant Activity of the Active Component. The antioxidant behavior of the active compound may be measured on the basis of its electron transfer capability by radical scavenging using the "DPPH" or "ABTS" methods.[28] Food, or a liquid food simulant, is exposed to the active film to allow for the release of the agent; then, the inhibition of the 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical is measured.[28] Alternatively, 2,2′-azinobis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) may be used as a radical cation. The antioxidant activity is elucidated by absorbance measurements using a spectrophotometer.[38] Another common method is to determine the total phenolic content (TPC), since

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Table 1. Recently Published (2019–present) Research Concerning Biopolymers and the Controlled Release of Natural Active Agents for Active Packaging

encapsulation	biopolymer	natural active agent and encapsulation method		results obtained	application	reference
encapsulated	corn-starch (CS)	tea polyphenol (TP)	porous starch (PS)	Improved mechanical properties of the film with encapsulation. Release kinetics studies showed slower TP release with encapsulation. TP increased the radical scavenging activity from 1.5% to 79% (CS-TP-PS).	ethanol 50% (v/v)	71
	carboxymethyl-cellulose (CMC)	vitamin E	polycaprolactone (PCL) nanocapsule	Films with 30%–70% nanocapsule content were studied. Increasing vitamin E content linearly increased antioxidant potential of the film.	ethanol 95%	94
	zein or PLA	carvacrol	electrospun fibers	Encapsulation enhanced the sustained release of carvacrol. Tested on mold and yeast, 99.6% of mold growth was inhibited by 20% carvacrol content.	bread preservation	49
	PLA fibers coated with PVA/PEG	thyme essential oil (EO)	porous PLA electrospun fibers	Humidity-controlled release was achieved by adjusting the relative humidity (RH) from 20% to 80%. Coating with PVA/PEG improved hydrophilicity. Successful inhibition of *E. coli* and *S. aureus*.	strawberry preservation	95
	collagen/zein	gallic acid (GA)	electrospun fibers	Films containing 8% (w/w) GA significantly halted tilapia muscle deterioration.	tilapia fillet preservation	43
	pullan/gelatin films	clove essential oil	nanoemulsion (NE) and Pickering emulsion (PE)	The PE had a better slow-release profile than the NE. The active film had excellent mechanical properties and good antioxidant capacity.	ethanol 95%	96
	pectin	marjoram EO	nanoemulsion and Pickering emulation	Marjoram EO loaded films had strong antimicrobial and antioxidant activity. The PE films had good mechanical properties and provided slower release of the active agent.	ethanol 95%	97
	N/A	cinnamaldehyde	halloysite nanotubes (clay)	Oppositely charged polyelectrolytes were used to cap the ends of the nanotubes to successfully control the release with pH-controlled "gates".	fresh wheat noodle preservation	98
	cellulose, zein, and starch	cocktail of thyme oil, citric acid, and nisin. With cyclodextrin inclusion complexes of thyme oil, sorbic acid, and nisin	cyclodextrin inclusion complexes and electrospun fibers of cellulose nanocrystals, zein and starch	The release was enzyme-responsive due to the degradation of zein by protease. The release was RH-responsive due to the nature of cyclodextrin inclusion complexes at high RH. Multistimuli-responsive fibers were achieved. Successful inhibition of *L. innocua*, *E. coli*, and *A. fumigatus*.	water	62
	PHBV (electrospun)	eugenol	mesoporous silica nanoparticles (NPs)	NPs containing eugenol were loaded into the film by electrospinning. The antimicrobial activity was tested over 15 days in both open and closed conditions to simulate real packaging. The activity was higher in the closed system as eugenol was able to accumulate in the headspace.	N/A	99
	zein	pomegranate peel extract	chitosan NPs	Cold nitrogen plasma treatment was used to maintain the sustained release of polyphenols. The active film had improved thermal properties over the bare film. The active film had strong antimicrobial activity against *L. monocytogenes*.	pork preservation	100

encapsulation	biopolymer	natural active agent	results obtained	application	reference
nonencapsulated	chitosan	onion-skin ethanolic extract (OSEE)	OSEE decreased the mechanical properties of the film, but improved water resistance. Increasing opacity with increasing OSEE content was reported. Successful inhibition of *S. aureus* and *E. coli* with good antioxidant activity.	lard preservation	101
	PVA	clove essential oil	PVA film with 1% CEO reduced fungal growth over 21 days of storage (13 °C, 75% RH). Interestingly, a pleasant odor intensity was recorded.	table grape preservation	102
	cassava starch and whey protein	rambutan peel extract and cinnamon oil	Native starch (NS) and acetylated starch (AS) were used. AS enhanced the polyphenol release and radical scavenging capability. The antibacterial capacity in real food was determined, and dependent on the food components.	salami preservation	103
	PLA	curcumin	Curcumin addition increased surface hydrophobicity. The film was yellow in color, but transparent. Potent antioxidant activity was achieved.	water	104
	CMC-carrageenan	Berberine-baicalin (BB) NPs	The film was composed of self-assembled BB NPs in sodium CMC-carrageenan. The research reported that sunlight creates reactive oxygen species (ROS), creating photodynamic antibacterial activity. Successful inhibition of *E. coli* and *S. aureus* was achieved.	chicken preservation	105
	chitosan	banana peel extract (BPE)	Valorization of banana food waste. The films tested contained 4%, 8%, and 12% BPE and excellent antioxidant activity was achieved. The antioxidant activity was shown on improving the quality of apple during storage.	apple preservation	39
	gellan gum	anthocyanins (*Clitoria ternatea* (CT) extract)	Heat-treated soy protein isolate (HSPI) was able to interact with the gellan gum and CT. HPSI modified film properties such as the water vapor pressure. Controlled release of the active agent was achieved at pH > 6. The films were intelligent and changed color with the increase of total volatile basic nitrogen (TVBN).	shrimp preservation	45
	gelatin	*Malpighia emarginata* waste extract	The oxidation of beef patties during frozen storage was delayed using a film containing 4% of the active agent. The control of color changes and oxidation reactions in lipids and proteins was achieved.	beef patty preservation	106
	pectin	mango peel extract	Valorization of mango waste. The phenolic extract had good thermal stability. Highlighted the possibility of coating application of the film. Higher antioxidant activity (DPPH) with mango peel extract incorporated in film.	N/A	107

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Table 1. continued

encapsulation	biopolymer	natural active agent	results obtained	application	reference
	alginate	aloe vera and garlic oil	Active agents improved UV-barrier properties and mechanical properties. The transparency of the film was retained. The active agents improved the antimicrobial properties of this edible film.	tomato preservation	108

phenolic substances contribute largely to the AO activity.[39] Evaluation of the release properties will be covered in Section 3.5 of this review.

Alternatively, experiments measuring the direct effect of the active agent on food may report color changes using a colorimeter or weight loss of the food over time.[38] To elucidate antioxidant or antimicrobial activity, these reports may compare the physical film properties from these tests between biopolymeric films with and without the active agent.[38] Active packaging has a wide impact due to high levels of variability; it has applications for the preservation of meat, fish, bread, cheese, fruit, and vegetables among other foodstuffs.[7,13]

2.2.1. Barriers for Commercialization of Active Release Packaging. Active agents may alter the mechanical, barrier, organoleptic, and optical properties of packaging systems.[18,19] Aromatic active agents such as EOs may have specific odors that may affect the organoleptic properties of food, especially considering the high concentrations of EO often required for good antioxidant capacity.[18] Higueras et al.[40] reported unacceptable sensory deterioration of chicken fillets due to large amounts of the antimicrobial carvacrol retained by the chicken proteins after release from a chitosan-cyclodextrin film. On the contrary, Rehman et al.[41] indicated that a composite film containing rosemary essential oil improved the organoleptic properties of lamb rather than imposing a negative effect. Therefore, it is possible for the alteration of properties to be beneficial if optimized, and so the properties should be measured on the bare film in parallel to the active film for comparison. Concerning other packaging properties, Wu et al.[42] recorded that adding green-tea extract (GTE) (0.3 to 0.7% w/v) to an edible gelatin-based film decreased the moisture content and the water vapor permeability of the film. Interestingly, the group found an increase in thermal stability due to protein-polyphenol interactions indicated by FTIR measurements.[42] Interactions of this nature may be tuned in future studies to optimize packaging properties through experimental design. Furthermore, the group reported that the antioxidant activity, measured by the TPC and DPPH methods, decreased during storage for 180 days.[42] This highlights an important area not often covered in the literature; the active agent must be capable of maintaining its properties during storage and transport.

2.2.2. Stability of the Active Compound and Limitations of Food Simulants. Another issue concerns the low thermal stability and high volatility of many antioxidant compounds, which may lead to issues with film fabrication and processing.[18] If a volatile active compound is used, the film should have high barrier properties in order to prevent loss of the compound *via* permeation.[34] The preservation effect of films is commonly tested on liquid food simulants; however, it is beneficial for development to test the effect on actual food systems as a more accurate representation of *in situ* activity. In fact, the lack of food preservation testing on real food was highlighted in 1999 and remains a developmental issue.[13] Examples of literature reports utilizing food as the experimental substrate include Zhang et al.[39] who reported a chitosan-based film coating treatment with banana peel extract (4%−12% content) and the application of this to apples. They reported a significant increase on quality of the fruit upon storage with the active agent compared to the chitosan film alone.[39] This study incorporates the valorization of waste materials, in this case banana peels, with the use of the biodegradable and biobased

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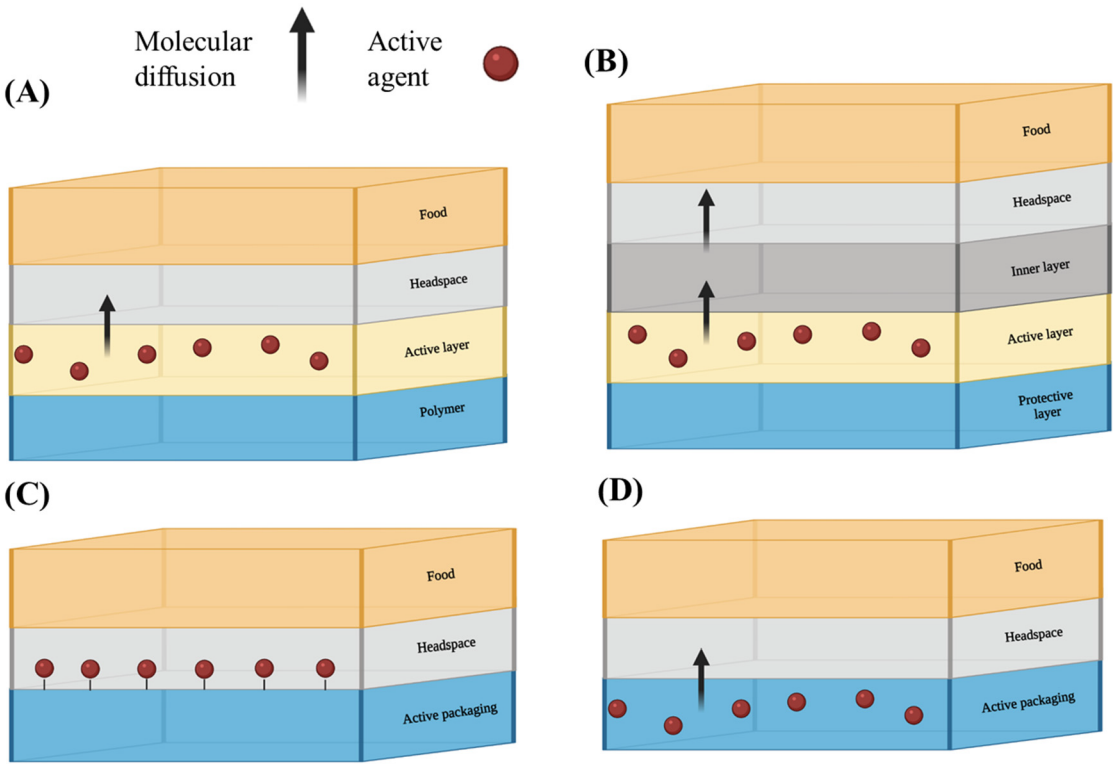

Figure 3. Schematic diagrams showing controlled release or encapsulation mechanisms, focusing on release systems: (A) active layer (lamination), (B) multilayer film, (C) covalent attachment to polymer surface, and (D) direct incorporation into polymer matrix, which may include encapsulation,[10,28] created with biorender.com.

polymer chitosan. Therefore, this study represents a highly sustainable choice of raw materials. Additionally, Song et al.[43] reported that collagen and zein electrospun films loaded with gallic acid (8% w/w) increased the shelf life of fish muscle by at least 2 days. Similarly, this study utilizes a natural, phenolic, active agent with biobased and biodegradable polymers. Interestingly, the use of electrospinning rather than film-casting may be beneficial, since film-casting can often be highly variable and less suitable for scale-up opportunities.[10] Nanoparticles are often used in active packaging. However, knowledge on the effects of nanomaterials on food when incorporated in packaging is limited, possibly due to the complexity of food.[44] Therefore, further research is necessary to detect, characterize, and quantify the nanoparticles due to strict safety regulations.[44] Further detail of these safety regulations will be covered in Section 5.3.

3. CONTROLLED RELEASE: A BALANCING ACT?

3.1. Outcompeting Traditional Methods of Food Preservation. Traditionally, absorbing sachets, pads, and self-adhesive labels have been used within packaging.[10,28] Generally, the active component may be incorporated by coating by adsorption onto the polymer surface, covalent immobilization onto the polymer surface or direct incorporation into the polymer structure. However, the use of inherently antimicrobial or antioxidant polymers such as chitosan is also common, and may simplify the manufacturing process.[39] Controlled release active packaging provides many benefits over traditional methods of extending food shelf life. Through achieving controlled release, it is possible to tune the antioxidant activity to the storage of the food within the packaging to maximize the freshness. The use of sachets has previously raised concern due to potential splitting to release the components onto food and fears of subsequent ingestion.[10,28] Public acceptance is generally considerably higher when the active component is derived from a natural, rather than synthetic, source. Many active agents and bioplastic materials may be derived from plants as a renewable resource. While traditional materials such as absorbing pads are still commonly used, the end of life scenario of these materials remains a concern.

3.2. From Drug-Delivery Concepts to Next-Generation Food Packaging. The principles of slow release and triggered drug delivery serve as foundations that may be exploited to make next-generation plastics for food packaging. The concept of controlled release in the medical industry is based on the gradual release of a payload of drug, often to a specific area. This may be exploited to incorporate natural active agents into biopolymeric materials for active packaging. Due to safety legislation and efficacy requirements for the commercial viability of active packaging, the release of the active agent must be tightly controlled by mechanisms inside the material. A specific amount of the active agent may then be released by this mechanism at a sustained rate, over an extended period. The initial release may be induced by external stimuli such as temperature or pH changes; further release of the substance may then continue at a reduced and controlled rate.[10] During the release of the active substance, it will migrate *via* an indirect or direct mechanism. If the compound is encapsulated, it will first need to diffuse from the carrier into the polymeric matrix.[10]

Additionally, intelligent or "smart" packaging has been a vital development in the research field. Intelligent packaging monitors the condition of food during transportation and

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storage using sensors, often attached to the surface of the packaging material.[18] These sensors act as ripeness indicators by monitoring external environmental conditions to extrapolate the degree of microbial spoilage.[18,30] Intelligent packaging films may monitor pH variations, which are often proportional to food deterioration.[45] Other examples include humidity sensors, gas sensors, and time−temperature indicators (TTIs). The triggered release by pH changes is particularly interesting for the purposes of controlled release. Wu et al.[45] reported the controlled release of anthocyanins from a gellan gum film at pH values above 6. This environmentally responsive packaging may be considered both "active" and "intelligent". The group reported that the triggered release was due to a difference in binding affinities between the active agent and the film at different pH values.[45] Release mechanisms similar to this may be important in achieving controlled release. Since the degradation for food causes pH variations, and bacteria grow best at neutral pH, a system with controlled release at a similar pH should incur an improved antibacterial activity.[46]

3.3. Technologies Used for Facilitating Controlled Release. Common technologies for facilitating controlled release from biopolymers include encapsulation, surface coating (adhesion), noncovalent immobilization, covalent immobilization, polymer blending, matrix cross-linking, chemical modification of polymers, and fatty-acid incorporation.[10,18,47] Covalent immobilization on the material surface may be achieved by chemical, UV, or ionized gas treatment.[10] The literature also reports the use of multilayer films whereby layer-by-layer self-assembly is used to form a film composed of an inner layer, a protective later, an active layer, and an outer layer.[10] The role of the inner layer is to control active agent release from the active matrix layer, and the role of the barrier layer is to prevent loss of the active agent to the environment.[19] Figure 3 depicts four different methods of achieving controlled release of an active agent from packaging materials including lamination, multilayer packaging, covalent attachment, and direct incorporation into the polymer. If the technology used for controlled release is entrapment within the polymeric matrix, film thickness will play an important role in the diffusion characteristics of the active compound.[19] The release rate is predicted to decrease with increasing film thickness.[48] However, if the active agent is covalently bonded to the polymer surface for slow release, the activity may be independent of film thickness.[19] This method may be beneficial if the environmental conditions do not promote hydrolysis, since the safety regulations are less stringent if the component does not come into direct contact with food.[19]

3.3.1. Manipulating the Rate of Migration of the Active Compound. Crucially, for the efficiency of active packaging, the rate of release of the active compound should be comparable to the food degradation rate.[10] A key challenge in AP development is to obtain and maintain an optimal concentration of the active agent released into the packaging headspace or onto the food over a suitable period. Therefore, research on controlled release of an active agent should determine the rate of release and elucidate kinetic parameters, where possible. Put simply, if the release is too slow, it will lead to insufficient inhibition of food degradation and if the release is too fast, the excess of active compound may interact unfavorably with food. The release rate is generally related to the concentration of the active agent in the film and the film thickness; therefore, these parameters must be recorded to enable a comparison of results. The percentage content of the active agent will affect the film morphology and the release rate and should always be clearly reported with corresponding data.[49] Environmental parameters that affect the release of the active agent include UV radiation, ionic concentration, and enzymatic degradation.[10]

3.3.2. Important Factors Affecting the Migration Rate of the Active Compound. Diffusion studies on the active agent release from the polymer are important for developing controlled release packaging. Theoretically, an initial release is expected at a heightened rate, followed by a plateau at a reduced rate.[47,50] The substrate used for testing is not standard in the literature and varies between food simulants, which are more commonly used, and actual food. Food simulants include 95% ethanol (v/v) for high fat content foods, pure water for aqueous media, 50% ethanol (v/v) for oil in water emulsions or high alcohol content foods, and 3% acetic acid (v/v) for low pH aqueous foods.[39] The release depends on the active agent and the simulant used. This was highlighted by Lopez-Cordoba et al.,[51] describing the change in release profile of polyphenols in different simulants depending on their polarity. Importantly, the solubility of the biopolymer should be taken into account, for example, studies using HPMC in ethanol−water simulants would not accurately test the release from the film due to high solubility in many cases.

Particle size and distribution of the active compound have the most significant effect on the retention inside the polymer matrix and hence the release rate.[10] In fact, the diffusion coefficient increases exponentially with an increase in particle size, and an even distribution of particles is important for controlled release.[10] Relating to this, the degree of crystallinity affects the release rate due to a reduction in the length of the migration path.[10] Boonnattakorn et al.[52] reported an increase in release rate of mangiferin with decreased crystallization of their active film based on ethylene vinyl acetate, achieving a controlled release of the active agent. Similarly, the inclusion of nanofillers reduces the polymer torsion and film flexibility, reducing the release rate due to an increase in diffusion path length.[10,16]

The molecular weight of the active agent and its affinity to the polymer are important parameters for effective controlled release. Plasticizers, such as ethylene glycol and glycerol, increase the release and diffusion rates due to an increase in free volume inside the polymer matrix.[10,16] However, the addition of plasticizers may increase oxygen permeability or alter food aromas; thus, caution should be taken.[4] Polarity effects of the film and the active compound may affect the release rate depending on the interaction strength between the two components, reiterating the importance of active agent-biopolymer compatibility.[10] For example, strong noncovalent interactions between hydrophobic cellulose acetate films and low polarity active compounds would incur slow release rates.[10] As mentioned, the external environment also influences release rate. Kurek et al.[53] reported an increase in carvacrol release rate from a chitosan-based film with increasing temperature or humidity and deduced that chitosan films were plasticized by water molecules. This relates to environmentally controlled release of active agents from packaging materials, which poses a promising research direction due to the ability to trigger release of antioxidants or antibacterial compounds to coincide with common environmental conditions that enhance food degradation. Interestingly, food

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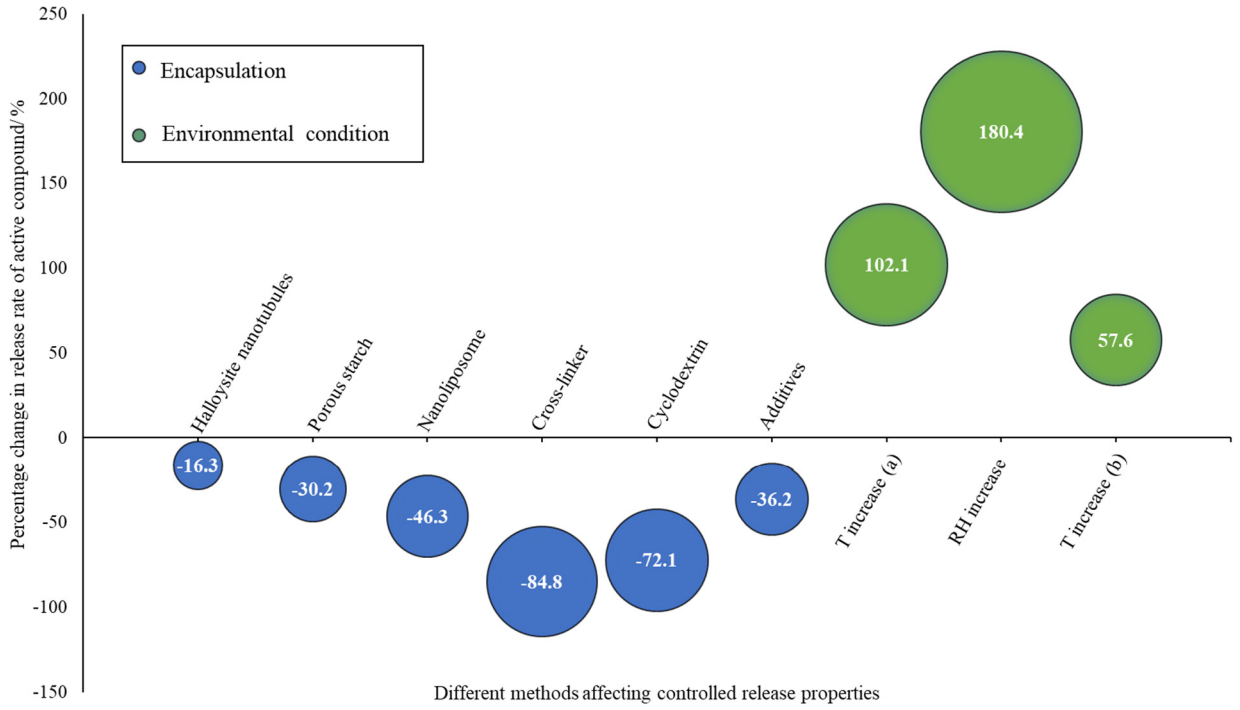

Figure 4. Schematic depiction of the effect of certain encapsulation methods and environmental conditions on the rate of controlled release of an active agent. This is depicted using the percentage change in rate, where a negative value indicates a reduction in rate with the utilization of the method specified. The data was extracted from references noted in Table 2; for consistency, the values were taken from between 20 and 25 h of experimental time. The figure shows the potential of encapsulation to control the release in active packaging and the potential of stimuli-responsive packaging to trigger the release of the active compound. Table 2 describes the specific conditions of these experiments. Variables such as film thickness, simulant type, and biopolymer type are not consistent in this plot; therefore, it may act only a visual example.

characteristics including fat content, pH, and water activity affect the release rate.[28]

3.4. Quantification of the Release Properties of Active Films. Literature reports utilize varying values and parameters to describe the controlled release properties of active packaging films. These parameters include rate constants, diffusion coefficients, and the cumulative release (%). However, kinetic data is scarce in the literature and suppression or release experiments often report only the values obtained rather than modeling this mathematically to obtain rate data. The suppression rate, in relation to the activity of the antimicrobial or antioxidant agent, may also be reported. Additionally, the change in related parameters over time may be utilized. These may include the size of a zone of inhibition, the DPPH or ABTS results, the reducing power, the TPC, the MIC, or the number of viable bacterial cells (CFU mL^{-1}).

Different mathematical models have been used to describe the mass transfer kinetics and controlled release mechanisms. These methods include zero or first order kinetics, Fick's law, and Peppas, Hixson-Crowell, Kopcha, and Higuchi methods.[54] For determining diffusion coefficients, Fick's law is one of the most used models in the literature. The Peppas equation has a release component (n); the value between 0 and 1 of this component determines the transport mechanism, for example, Fickian diffusion.[54] Estevinho et al.[54] reported an interpretation of the value of "n" related to a film, cylinder, or sphere and their respective release mechanisms. The difficulty formulating literature comparisons arises due to the difference in release mechanisms due to the variability of the films reported. Variables include the incorporation of different active agents, the biopolymer choice, the method of encapsulation, and the film-formation technique. Consequently, it can be very difficult to compare different studies and draw conclusions of relative efficiency even when these values are reported.

Analytical devices for the quantification of the sustained release rate and data-extraction thereof include UV-spectrophotometry, cyclic voltammetry, gas chromatography, and high performance liquid chromatography.[55] The chromatographic instruments are often coupled to a mass spectrometer or a flame ionization detector (FID).[55] Volatile active compound desorption may be monitored by thermogravimetric analysis (TGA).[56] Absorbance monitoring and UV−visible spectroscopy are other common methods used for quantification.[28,57] Overall, the volatility of the active agent determines the choice of analytical equipment.[24] Experimentally, quantification is usually achieved by aliquot removal and successive tests.

3.5. Examples of Controlled Release Studies. The mechanism of controlled release from biopolymers is often overlooked from discussions in publications, and studies that determine rates from controlled release mechanisms often investigate only short time scales.[10] Most studies tend to use liquid food simulants. To provide data that more closely relates to the ultimate application of the film, studies on real food may be more reliable.[24] However, due to the complex nature of food, studies either (i) use food simulants only or (ii) use food to obtain qualitative measurements such as appearance over time. The development of analytical methods more suited to complex foods may aid the determination of controlled release mechanisms.[24] Quantification methods often include UV−visible spectroscopy to determine the amount of active compound released.[57] For example, Granda-Restrepo et al.[58] monitored the release kinetics of tocopherol from a film into milk powder using HPLC and modeled this to Fick's diffusion to calculate diffusion coefficients (D). The group achieved

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Table 2. Conditions Used in the Examples Selected for Figure 4

method	specific conditions used	reference
T increase (b)	Release of nisin from HMPC film into water−ethanol simulant 5:95 (v/v) compared at 4 and 40 °C. Fractional nisin migration (mass released) over time was measured.	109
RH increase	Release of thyme essential oil from PLA nanofibers coated with PVA/PEG was compared at 20% and 50% RH. Measured as cumulative release (%).	95
T increase (a)	Release of nisin from PLA film into water−ethanol simulant 5:95 (v/v) compared at 4 and 40 °C. Fractional nisin migration (mass released) over time was measured.	109
additives	Release of *Clitoria ternatea* anthocyanins (CT) extract from gellan gum (G) film was measured by cumulative release (%). Additives included heat-treated soy-protein isolate, which interacted with gallic acid and CT to achieve controlled release. Comparison between no additives, and additives.	45
cyclodextrin	The release of *a*-tocopherol from cyclodextrin inclusion complex within LDPE versus no cyclodextrin. Migration of tocopherol was measured.	74
cross-linker	Monolayer cross-linked PVOH film using glyoxal. Comparison of 0.077% and 7.7% w/w glyoxal. Lysozyme release is measured.	47
nanoliposome	Thyme extract release from whey protein isolate films, effect of nanoliposome encapsulation. Released extract (ppm) in 95% ethanol measured.	110
porous starch	Release of tea polyphenols from corn starch film, the effect of encapsulating in porous starch. The cumulative release rate is measured.	71
halloysite nanotubule	PHBV film with oregano essential oil (EO). The effect of combining with clay (halloysite). The percentage release of oregano EO was measured.	57

good release properties between 20 and 40 °C, a temperature range that is suitable for shelf-storage; however, the work implies that the desired effect is greater at temperatures above 30 °C. More recently, Ramos et al.[59] studied and quantified the controlled release of thymol and silver NPs from PLA-based films over 15 days using HPLC-UV and inductively coupled plasma (ICP)-MS, respectively. The group described non-Fickian release behavior of the active thymol and nonmigratory silver NPs. The latter point addresses a concern with the migration of metal nanoparticles in relation to safety regulations on food-contact materials. A representation of different studies on controlled release rates is shown in Figure 4, with the experimental conditions provided in Table 2. Figure 4 shows that, on average, encapsulation methods decrease the rate of release whereas environmental conditions can be utilized to trigger release mechanisms at an increased rate.

3.6. Environmentally Responsive and Responsible Packaging. Future development of controlled release systems with well-defined release properties and rates are likely to rely on encapsulation methods and the utilization of nanotechnology. One interesting area of research is the triggered release of active agents. The stimulus may be an increase in temperature or humidity as microorganisms are more likely to accumulate in warm, humid environments. Recent research has described the stimulated and controlled release of epigallocatechin-3-gallate (EGCG) from a hydroxypropyl methylcellulose (HMPC) film by tuning either temperature or pH.[60] The group reported that pH increased in response to bacterial growth, inducing a transformation from phenol type to quinone, and that the films changed color due to this transformation.[60] The benefit of this system is that it may act as a freshness indicator as well as extending the shelf life. Furthermore, Min et al.[61] reported the humidity-controlled release of thyme essential oil from within PLA nanofibers coated with PVA/PEG film. Unlike the previous study, this material does not provide a visual readout to indicate food quality. Similarly, Aytac et al.[62] formed multistimuli-responsive films based on cellulose nanocrystals, zein, and starch electrospun fibers designed to release natural antimicrobials in response to humidity and enzyme triggers. The enzymatic degradation of zein was reported to enhance the release of active ingredient from the fibers.[62] An advantage in comparison to the previous study is the use of biobased, biodegradable components in this packaging system.

The predictability and reproducibility of release tests are vital for the safety compliance of active packaging. In order to prolong the shelf life of food, the packaging must also release an amount of the active agent, greater than the MIC, for an extended duration. Furthermore, it is vital that the materials can retain their release properties during manufacture and storage. However, Carrizo et al.[63] reported that radical scavengers such as antioxidants may not require migration to the headspace or food to elicit their effect. This represents an interesting area of development that has the potential to boost commercialization success if the antioxidant does not need to come into direct contact with food.[63]

The most important factors determining the future scope of controlled release for active packaging are the need to overcome implementation costs and the requirement to adhere to safety regulations. In short, controlled release studies should (a) identify potential food contaminants, (b) quantify the amount of each of these substances that may come into contact with food, and (c) determine their respective toxicities.[24] When determining (a), one should also take into account possible biotransformation products that may arise from interaction with food-borne microorganisms.[24]

3.7. Reducing the Carbon Footprint of Active Packaging. Active packaging materials may be made using conventional fossil-fuel-based polymers; however, this does not tackle the environmental issues associated with the end-of-life scenarios for plastic waste. These associated environmental issues include the release of greenhouse gases from landfill and microplastic pollution in waterways. The development of biodegradable active packaging aims to reduce the carbon footprint associated with food packaging materials and therefore contribute to a more circular economy. The "active" nature of the packaging aims to prolong food shelf life and reduce carbon emissions related to food wastage. Moreover, the importance of utilizing biodegradable or biobased plastics for active packaging may be highlighted using lifecycle analysis (LCA). Often the most sustainable materials are derived from valorizing waste materials to reduce the overall environmental footprint of a manufacturing process. The circularity of active packaging as a material relies on renewable or recycled raw materials, the use of renewable energy, and compostability or biodegradability.

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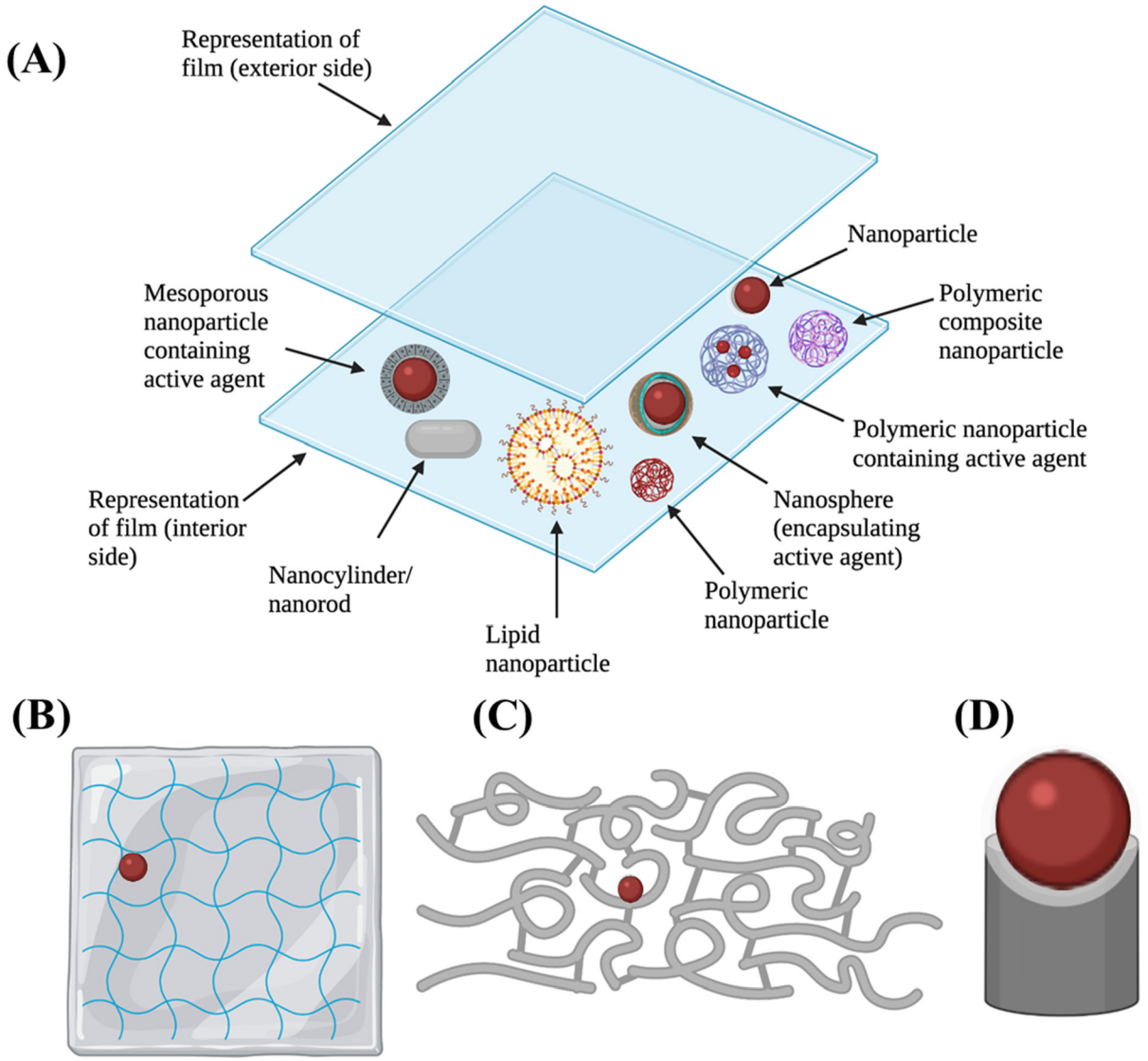

Figure 5. Illustration of some possible methods of encapsulation of the active agent (A) within a polymeric film (not to scale), (B) within a hydrogel matrix, (C) within fibers formed by electrospinning or cross-linking, and (D) within an inclusion complex formed using a cyclodextrin, created with biorender.com.

4. ENCAPSULATION METHODS: THE NANOTECHNOLOGY REVOLUTION

4.1. Encapsulation of the Active Agent to Facilitate Controlled Release. Active packaging undoubtably faces challenges to development. The low molecular weight of active compounds may lead to premature release from the polymer matrix and the protection of the active agent during manufacture and storage.[18] In theory, encapsulating the active agents should reduce the rate of release and, if optimized, enable controlled release. Encapsulation is a common method employed to protect the active agent, and it involves trapping a compound inside the core of a protective, often polymeric, matrix. The encapsulation efficiency (EE) (%) is an important concept to consider and should be included in release studies where applicable. This may be calculated as the ratio between the final amount of active agent encapsulated within the film (actual content) and the initial amount in solution (theoretical content).[64] Experimentally, this may be carried out using a UV−visible spectrometer or other quantitative analytical techniques.[65] Similarly, the entrapment efficiency of the active agent depends on the noncovalent interactions that may develop inside structures with cavities such as cyclodextrins.[65] To this end, the entrapment depends on the specific structure of the active agent utilized. Lee et al.[65] reported inclusion complexes with 59% EE of methyl salicylate, following first-order release kinetics. However, similar studies have reported higher entrapment efficiencies up to 85%.[66]

4.2. Nanoparticles and Nanofillers as Reinforcements for Biopolymers. The nanotechnology field has recently emerged and nanocomposites have been at the forefront of active packaging development since their invention.[30] These structures provide great potential to overcome existing challenges relating to AP. Nanotechnology has facilitated the reduction in film-thickness of packaging polymers, reducing the weight and therefore the transportation costs.[11] Nanofillers and nanoparticles are capable of acting as reinforcements to improve biopolymer mechanical properties, reducing the demand for raw materials and property-modulating additives.[17] The incorporation of nanofillers may increase the tensile strength of the resulting composite films and may also contribute to antimicrobial activity.[4,11]

4.2.1. Polymeric and Lipid-Based Nanocarriers for Encapsulation. Nanocomposites are multiphase materials containing at least one dimension below 100 nm. Nanofiller technology alters, and may improve, film properties such as flexibility, barrier properties, polymer crystallinity, and, thus, biodegradation rate.[17] Nanocarriers provide a useful encapsulation technology to facilitate controlled release.[10] Encapsulation may be achieved using a polymeric nanocarriers

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including nanoparticles, nanocapsules, nanospheres, dendrimers, and hydrogels.[67] Polymeric materials used for encapsulation commonly include alginate, chitosan, cellulose, gelatin, or k-carrageenan.[54] For example, Hosseni et al.[50] reported oregano EO loaded chitosan nanoparticles with 47% EE. The study reports an initial quick release of the EO, followed by controlled release, with chitosan nanoparticles in the size range 40−80 nm. Lipid nanocarriers may also be used, and these include liposomes, micelles, lipid nanoparticles, and nanoemulations.[67] Importantly, nanoliposomes may provide protection for natural compounds during processing and storage.[68] However, it has been noted that lipid nanoparticles may have instability problems relating to initial burst-release effects.[69] Alternative nanocarriers may include quantum dots, metal nanoparticles, silicates, carbon nanotubes, starch nanocrystals, cellulose nanoreinforcements, and clays.[17,67]

Nanoparticles may be loaded with an active agent and incorporated into a biopolymer to form a composite film. Wrona et al.[70] designed a delivery system based on PLA nanoparticles loaded with green tea extract. Importantly, they discovered that incorporating different sizes of nanoparticles enhanced controlled release and the antioxidant effect.[70] Other examples include a recent study by Miao et al.,[71] reporting the encapsulation and slow release of tea polyphenols. Porous starch was fabricated by enzymatic hydrolysis and was used as the encapsulating polymer.[71] The study described that porous starch had affinity to the tea polyphenols and enabled a slow and sustained release to achieve the desired effect. Additionally, solid lipid nanoparticles were utilized for active-component encapsulation and controlled release by Tonyali et al.;[69] they reported that crystallization increased the release or expulsion of natural active compounds. In this study, palm oil was utilized as a component of the lipid emulsion, reducing the sustainability of the system. Figure 5 shows, pictorially, a number of different encapsulation methods employed in active packaging including the use of hydrogels and cyclodextrins, nanoscale encapsulation, and encapsulation within fibers.

4.2.2. Encapsulation within Cyclodextrins, Zeolites, and MOFs. Other methods of encapsulation include cross-linking, zeolites, silicas, and cyclodextrins. Cyclodextrins have a hydrophobic cavity and have been reported to retain essential oils such as *S. montana* and *P. racemosa*.[72] The formation of inclusion complexes using cyclodextrins has been utilized widely in the literature. Velazquez-Contreras et al.[73] reported the formation of a composite film of PLA containing carvacrol monoterpene complexed in β-cyclodextrins, resulting in a significantly improved shelf life of berries in comparison to commercial clamshell packaging. Furthermore, Siró et al.[74] reported a long-term (167 days) experiment and concluded that cyclodextrin-mediated complexation may be the key to long lasting antioxidant effects. Similarly, zeolites such as halloysite nanotubes may form nanocomposites. Zeolites have been described as safe and easy to integrate into polymers, with good encapsulation capabilities.[18] In addition, metal−organic frameworks (MOFs) represent a major progression in the field of AP. Sharanyakanth and Radhakrishnan[75] recently reported a review of MOFs in the food packaging industry, describing the microencapsulation of active compounds using MOFs and the related enhancement of stability and controlled release properties. Active agents have also been filled inside mesoporous silica for controlled release purposes.[4] This system was initially investigated for stimuli-responsive drug delivery but is of interest also for packaging applications.[4] For example, Wu et al.[76] reported curcumin loaded mesoporous silica nanocarriers in a chitosan-based film with a pH-controlled release function. The mesoporous silica was reported to enhance the sustained release of the active agent from the packaging material.[76]

4.2.3. Hydrogels and Electrospun Fibers for Encapsulation. Controlled release on the basis of hydrogels is common in transdermal drug delivery scenarios; however, it is gaining traction in the active packaging field. Hydrogel systems may also be used for encapsulation and controlled release purposes. Konwar et al.[77] designed a nanocomposite hydrogel based on chitosan and iron oxide coated graphene oxide and reported that this hydrogel was active against both Gram-positive and Gram-negative bacteria. Batista et al.[78] reviewed the use of hydrogels for active packaging and highlighted chitosan as a biopolymer used to develop hydrogel matrixes for active agent release. Nanoparticles may also be incorporated into this hydrogel to produce antimicrobial activity; this area of research is now emerging and has promising potential due to the inherent swelling properties of hydrogels relating to the release of active compounds.[78] Similarly, Fu et al.[79] reported smart cellulose-based hydrogels; these hydrogels released active compounds specifically for biomedical drug delivery applications in response to external stimuli. This particular environmentally responsive technology has future application potential in the field of active packaging. Furthermore, electrospun nanofibers have been highlighted as a revolutionary technology.[49,61] Electrospun nanofibers have also recently been reported as nanoencapsulation materials for active agents. Wang et al.[55] reported the encapsulation of curcumin in electrospun zein-based nanofibril films. The group determined the antibacterial effects of the packaging material; however, packaging systems should also be applied to a food system to determine if this effect translates to the eventual application of the material. For example, antioxidant gallic acid was loaded into HPMC-based electrospun nanofibers, and the packaging material was reported to reduce the oxidation of walnuts during 21 days of storage.[80]

4.3. Experimental Methods of Microparticle, Nanoparticle, and Fiber-Formation for Encapsulation. Experimentally, spray drying is a highly reproducible technique for the microencapsulation of active agents.[54] Spray-drying is fast and inexpensive. This technique has been used to prepare microcapsules of cyclodextrin inclusion complexes.[54,73] Other common techniques include nanoemulsion, nanodispersion, emulsification-solvent evaporation, and coacervation.[26] Emulsification-solvent evaporation is a common method of nanoparticle formation that has been used to fabricate PLA nanoparticles.[70] However, this technique has high variability and so optimization experiments may be required.[70] For nanocomposite fabrication, there are three primary methods. First, the nanocomposite may be swollen in solvent and added to the polymer solution, followed by solvent evaporation.[30] The nanofiller may also be swollen by absorption of the monomer, followed by initiation of polymerization.[30] Lastly, and most commonly utilized, the nanocomposite filler may be added directly to a molten polymer.[30] Furthermore, electrospun fibers have been used to encapsulate active agents efficiently. This method of encapsulation is promising and may soon move to the forefront of encapsulation technology in the AP industry.[49,67] Similarly, electrospraying has been used to form micro and nanocapsules.[81] Other possible techniques include spray-cooling, utilizing a spinning disk or fluidized bed, and liposome entrapment.[54]

4.4. Beyond Technology: Public Acceptance, Safety Concerns, and Stability during Storage. Safety considerations for this technology include potential differences in the action of the active agent after encapsulation and the potential cytotoxicity of the active agent or the encapsulating matrix. Moreover, it is important to determine the composition of the compound released, as it may not be the same as the encapsulated mixture. Currently, there is a lack of knowledge about the ecotoxicity of certain nanoparticles and nanocomposites.[17] Due to the high surface area to volume ratio of nanoparticles, their properties are often unique and lead to safety concerns.[4] In order to adhere to strict safety legislation, further research and migratory tests are required to improve the safety profile of nanofillers containing active agents.[17] Specifically, regarding the use of biopolymers, the effect of nanoparticles on biodegradability is an important factor. This effect is disputed in the literature and will likely depend on the biopolymer and nanomaterial used. On one hand, nanomaterials may modify crystallinity of bioplastics, increasing crystallinity.[17] On the other hand, nanofillers may reduce access to polymeric chemical bonds, reducing biodegradation by microorganisms.[82]

Public acceptance relies on the safety of the packaging material and, increasingly, its environmental footprint.[18] Therefore, the combination of natural active agents and biopolymers is the most likely to be successful in terms of consumer acceptance. For encapsulation technology to be implemented successfully, it must enable the

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efficient and durable controlled release of the encapsulated agent. Nanofillers and other encapsulation methods need to be both efficient in preserving food and stable during storage.[4] In fact, the long-term stability of encapsulated active compounds is likely to be required by food industries.

5. STRINGENT SAFETY REGULATIONS AND TOXICOLOGICAL EVALUATION METHODS

5.1. US, UK, and EU Regulations on Active Packaging. One vital challenge to AP development is the need to satisfy complex safety regulations. The FDA regulations outline the concentration levels of active components that require (i) regulation, (ii) food contact notification, and (iii) food additive petition.[83] These values are <0.5 ppb, <1 ppm, and >1 ppm, respectively.[83] EU regulations require that any active materials to be identified and labeled to inform the consumer of nonedible parts, for example, labeling with "DO NOT EAT".[84] The label should describe that the packaging is nonedible if this is the case; it should also list both packaging and food ingredients. There are concerns about insufficiently labeled product descriptors not clearly identifying components of packaging materials. However, all packaging materials and additives that come into direct contact with food such as antimicrobial agents must meet food additive standards in order to be used commercially.[19] Where the active agent does not detach from the packaging surface, this regulatory hurdle is less relevant, since there is no direct contact with the food.[19] Nonetheless, controlled release mechanisms show high promise in terms of inhibiting microbial growth on food using active packaging.

Moreover, the specific concerns are the dosage or exposure level of the packaging components to ensure both the safety of the food contact material and prevent the modulation of the organoleptic properties of food.[84] EFSA defines the maximum migration of active components as 0.01 mg/kg of food for compliance.[84] Careful assessment of the regulations by specific governing bodies may reduce the challenges faced by active packaging. For example, the active agent should be part of the list of authorized substances and GRAS in order to achieve the desired compliance.[85] To this end, naturally sourced or typically food-related active agents such as tea extracts, essential oils, and fruit extracts may be considered a good starting point for development. Other methods possible to overcome these challenges include the use of a "functional barrier" to reduce migration of active compounds to food.[83] Nonmigratory active packaging may also be possible; however, this may not be classified as 'controlled release active packaging'.[83] Overall, active packaging is undoubtably a promising technology, and while the strict legislations will always remain for food-contact materials, there are certainly strategies available to comply with these and thus allow for commercialization.

5.2. Safety Legislation for Substances Added to Food Packaging. The investigation of the migration of substances intentionally added to food packaging is critical as these substances may be possible food contaminants. The limits of certain substances and materials intended to come into contact with food are outlined in the Commission Regulation No 10/2011, which states that migration of an active agent should not exceed 0.01 mg/kg of food.[24] This value of concentration is highly important for commercialization through adhering to safety regulations. However, the toxicity of the added compound should also be investigated, for example, by using the threshold of toxicological concern (TTC) method.[24] Sadeghi and Seo (2021) recently published a paper describing "Photografting coating", which employed a strong covalent linkage between the active compound and the packaging in order to prevent migration altogether and overcome safety concerns.[86] They described that polymerization-based grafting to or from the film is also likely to prevent sensory changes to food.[86] Using this method, vanillin was grafted to a PET film and was found to be active against Gram-positive bacteria.[87]

5.3. Toxicological Studies for Active Packaging Safety Evaluation. One area that requires further research for commercial incorporation is the cytotoxicity of nanoparticles used in biopolymeric composites. Similarly, ecotoxicity studies of bionanocomposites for food packaging applications are not well-documented.[17] These studies are required for a full environmental impact assessment to enable the commercial use of the material.[17] Due to the increase in research into nanoparticles for the encapsulation of active components, an understanding of their toxicity and quantification of this is required for success in active packaging development.[83] Buchman et al.[88] reported an overview of the mechanisms of nanoparticle toxicity and moreover described design routes to reduce the environmental impact of nanoparticles. As well as environmental impact, the analysis of mutagenicity and genotoxicity of each component of packaging is vital.[85] Because these components may be considered as food contact materials, the effect on human health must be determined. Commonly used methods for toxicological evaluation are oxidative stress assays, cell viability assays, and cell proliferation assays.[89] The lethal dose (LD_{50}) describes the amount of sample that kills 50% of a test sample. This value should also be determined and related to the dose used in, and released from, the packaging.[89]

Additionally, a distinct lack of conclusive migration assays limits the further development of AP technology due to stringent regulations surrounding the use of materials that come into direct contact with food.[17] Furthermore, many studies are conducted in buffer, whereas utilizing real food nutrients may alter the results obtained. Essential oils have been thoroughly studied for applications in controlled release AP technology. However, many experimental studies utilize high concentrations of EO, which may lead to regulatory concerns and affect properties of food during commercial application.[19]

5.4. Successful Examples of Commercialized Active Packaging. Currently, the large amount of research on this topic is not reflected in the small number of commercialized systems. The project "YPACK" recently completed a three-year funding scheme from the EU Horizon 2020 Research and Innovation Programme.[90] Under this project, many biodegradable active packaging materials were reported.[91,92] The outcome of the scheme was the development of a biodegradable PHBV film. However, EU regulatory concerns prevented the development of the active film to commercialization in 2020.[90]

Some other examples of commercialized active packaging system include the antimicrobial films Zeomic (Japan), WasaOuro (Japan), and Microgarde (USA) (Firouz et al. 2021). The seemingly controversial aspect of active packaging commercialization is the requirement to be able to demonstrate benefits over synthetic plastics, including proven biodegradability. The bioplastic composites need to have good physical and mechanical properties for packaging applications. The packaging materials must also adhere to stringent safety regulations, particularly concerning the active ingredient and its possible migration. Perhaps, therefore, the future of active packaging relies on the use of natural active agents, biopolymers with proven biodegradability, experiments utilizing real food, and stringent migratory experiments.

6. CONCLUDING REMARKS ON THE POTENTIAL OF ACTIVE PACKAGING TECHNOLOGIES

6.1. Outlook on Active Packaging: Properties, Costs, and Safety Concerns. With a global focus on the reduction of carbon emissions to "Net-Zero", it is clear that the replacement of fossil-fuel-based plastics with biobased, biodegradable plastics provides a more promising future for the packaging industry. The LCA of a material assesses the environmental impact it has during its lifetime. Conventional plastics face an end-of-life scenario in landfill. Therefore, in order to provide environmental benefits, the source of bioplastics should be a renewable raw material and the material should be biodegradable within a suitable time frame.

Unfortunately, biopolymers often have inferior material properties in comparison to conventional plastics. In order for biobased active packaging to become viable, properties such as mechanical strength, thermal stability, and barrier properties

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must be improved.[11] Related to this, the cost of processing and the marketability are key challenges that must be overcome in order to outcompete petroleum-based plastics. Furthermore, consumer acceptance issues often arise and hinder development. Consumers may have safety concerns, environmental concerns, and concerns on the possible changes to the organoleptic quality of food.[18] Lastly, achieving controlled release of the active agent is vital to achieve efficacy and adhere to safety legislations.

Food safety agencies including the US Food and Drug Administration (FDA) and the European Commission (EC) have regulated and legislated food packages. For instance, the EC Regulation No 450/2009 describes a list of authorized substances that interact in a direct manner with food or its environment.[93] The overall aims of active packaging are to reduce environmental impacts of plastic waste and to reduce food waste. In order to achieve this, biobased materials are required to have the appropriate properties for applications in food preservation, and their implementation must not raise safety concerns.[16]

6.2. Persisting Challenges to Active Packaging Development. Biodegradable active packaging undoubtably has a reduced environmental footprint in comparison to traditional petroleum-based plastics. This technology prolongs food shelf life and reduces food spoilage, hence reducing food wastage. Unfortunately, traditional plastics are familiar and inexpensive consumer materials. From an economic point of view, this means that active packaging must compete with these materials in properties and cost criteria. Currently, the mechanical and barrier properties of bioplastic composites require optimization to achieve this. For AP to be beneficial, it must have improved sustainability, measured by good biodegradation, and the use of safe materials throughout its lifecycle. There must also be a sustainable supply of the raw material to make the biopolymer. Importantly, the AP material must be highly efficient at preserving food, whist being capable of maintaining properties and stability during storage and transport. Moreover, future management of controlled release may rely on stimuli-responsive materials. Furthermore, improvement to the commercial viability of these materials will rely on improved information about the efficacy and benefits of bioplastic-based active packaging.

6.3. Overcoming Developmental Hurdles to Commercialization. As previously noted, few AP materials have been successfully commercialized to date. It is likely that this is due to various hurdles to AP development for the material to be considered effective and safe. These hurdles may include the potential adverse effects on food quality and organoleptic properties, strict legislative safety regulations, and possible consumer resistance. Economic factors may also prove problematic as bioplastic formation is expensive. Furthermore, the ideal end-of-life scenario for biodegradable bioplastics is composting; therefore, the material is unlikely to be reused. This means that, for a relatively high cost, the lifetime of the material is short in many instances. Currently, there is a lack of suitable scale-up technology applicable to certain bioplastics. This means that manufacturing costs are high, and therefore, the widespread implementation of AP technology would be costly. As a result of this, investments are required in order to drive further research and fund scale-up procedures.

There is a lack of research into the antimicrobial effectiveness on an industrial scale. While there is potential to model this computationally, the correlation would not be exact. Laboratory tests are not able to replicate the conditions experienced by packaging during storage, transport, and distribution. Similarly, research studies often focus on packaging properties in isolation rather than the behavior of the packaging with food materials, which may risk commercialization failure. Future studies should endeavor to test the effect of packaging materials on real food in addition to food simulants and diffusion-based mathematical modeling.

6.4. Technology Transferrable in Wider Environmental and Medical Applications. The synergy of active packaging and intelligent packaging is an interesting concept mentioned in this review. Theoretically, IP may monitor the activity or performance of AP and indicate to the consumer information about food-freshness. This combination has the potential to revolutionize the food packaging industry. Research on these technologies individually is thorough, however the combination of these technologies is not often reported.

The technology described in this review is transferrable to the water sector for desalination and wastewater treatment. It is also transferrable to the healthcare sector for the production of wound-healing bandages or patches. The application of active films to water filtration membranes would prevent bacteria from attaching to the membrane. Biofouling, the microbial growth or attachment on to membranes, reduces the lifespan and efficacy of membranes due to the blockage of pores. The active biopolymeric composites detailed in this review would prevent biofouling with the controlled release of natural antimicrobials. This method would increase the efficiency of water filtration membranes and reduce the frequency of replacements. Moreover, active packaging technology for this application may reduce material consumption and waste production in the water purification industry. Similarly, the controlled release of active agents has been thoroughly researched for application in medical wound-healing covers. The natural, antimicrobial and biopolymeric films may also provide a sustainable alternative for this sector.

6.5. Perspectives on Commercial Viability for Active Packaging. Active release packaging has applications on many different types of food due to the versatility of biopolymer choice, active agent choice, and film-formation method. Nonetheless, there are developments required in order to achieve good commercial viability of a variety of composite materials. Experimental tests on the application of real food rather than liquid food simulants and studies on the effect of storage and distribution would benefit the research field. However, these experiments and processes may be expensive. As described, adhering to strict safety regulations is vital in the development of active packaging. Therefore, safety studies on the effects of nanofillers is essential. Relating to this, controlled release studies are imperative when the active agent can diffuse and make direct contact with the food. These studies should determine the concentrations of active agents released into the packaging headspace.

One hindrance to development is the temperature instability of some active compounds, leading to a loss of the active compound during film-forming processes. New production processes and the use of more stable active compounds may overcome these development and processing issues. On this topic, the gap between research and application must be bridged for active packaging to be able to compete with conventional plastics in performance and cost. There needs to be synergy between academia, industry, and government

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incentives in order to achieve this. For example, waste infrastructure and waste management industries need government funding in order to allow for the feasible widespread use of bioplastic packaging. These investments are required to develop more tailored waste-management facilities.

6.6. Future Trends in Active Packaging: Synergistic Approaches and Controlling Release. There are many aspects of the AP technology field that currently display promising prospects. Particularly, nanomaterials and the general use of encapsulation methods provide a good potential for future studies on controlled release materials. Synergistic approaches including stimuli-responsive active packaging also holds promise for the future directions of the field of research. In this example, the controlled release of the active agent may be realized through mechanisms triggered by changes in temperature or microorganism activity. Future research must endeavor to achieve release rates suitable for a wide range of food packaging applications. For their application in active packaging, biopolymers must be able to compete with traditional plastics. Therefore, bioplastics should have excellent mechanical and barrier properties, use renewable resources, have good biodegradability, and their use should be economic. It is evident from the examples utilized in this review that this technology may serve as a high potential replacement for ubiquitous petroleum-based plastics. However, the hurdles discussed must be addressed by future research in order to achieve commercialization success. Overall, this review has discussed the use of natural active agents and encapsulation methods to achieve the desired controlled release in active release packaging.

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Notes

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