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Hybrid nanoencapsulation systems: integrating natural polymers with synthetic nanomaterials for enhanced delivery of bioactive compounds in functional foods

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Hybrid nanoencapsulation systems fuse the inherent biocompatibility and functional versatility of natural polymers with the structural precision and tunable properties of synthetic nanomaterials to create next-generation delivery platforms for bioactive compounds. This review provides a comprehensive overview of hybrid nanoencapsulation systems and innovative platforms that merge the biocompatibility and biodegradability of natural polymers (*e.g.*, chitosan, alginate, starch) with the structural precision and tunable functionality of synthetic nanomaterials (*e.g.*, PLGA, PEG, mesoporous silica). We examine key fabrication strategies including self-assembly, layer-by-layer assembly, electrospinning, and nanoprecipitation, emphasizing how each method enhances encapsulation efficiency, physicochemical stability, and controlled release of sensitive bioactives. The role of chemical and enzymatic modifications such as phosphorylation, esterification, hydrolysis, and Maillard conjugation in tailoring interfacial activity and retention of nutraceuticals is highlighted. Recent developments in smart, stimuli-responsive composites are discussed for their ability to enable site-specific, on-demand release. Notable improvements in bioavailability, oxidative resistance, and environmental resilience across diverse food matrices are demonstrated. Remaining challenges include scalable manufacturing, rigorous safety and efficacy validation, regulatory compliance, and consumer acceptance. We propose future research priorities around green synthesis, food-grade material innovation, and comprehensive risk assessment to accelerate translation into commercial functional foods.

1 Introduction

The modern food industry is increasingly driven by the demand for health promoting products that deliver functional benefits beyond basic nutrition. Bioactive compounds such as polyphenols, vitamins, antioxidants, probiotics, and omega-3 fatty acids, are widely incorporated into food systems to support immune health, metabolic function, and disease prevention. However, their practical application is significantly limited by low water solubility, instability during processing and storage, and rapid degradation under gastrointestinal conditions. These issues reduce the efficacy, shelf life, and bioavailability of functional ingredients, ultimately compromising their intended health benefits. Traditional encapsulation systems, though widely used, often fall short in achieving optimal protection and targeted delivery of these sensitive compounds.

Recent advances in nanotechnology and materials science have catalyzed a paradigm shift in food formulation, moving from passive carriers to intelligent, targeted delivery systems.[1] Natural polymers, such as chitosan, alginate, starch, pectin, and whey protein, are biodegradable, biocompatible, and often bifunctional, nevertheless they suffer from inconsistent source quality, poor mechanical strength, and limited encapsulation capacity for hydrophobic molecules. Synthetic nanomaterials, including poly(lactic-*co*-glycolic acid) (PLGA), polyethylene glycol (PEG), polycaprolactone (PCL), and mesoporous silica, offer tunable physicochemical properties, high encapsulation efficiency, and structural precision. However, they raise concerns regarding biodegradability, cytotoxicity, and regulatory approval in food-grade systems. This dichotomy underscores the need for integrated, multifunctional encapsulation platforms that can meet safety, performance, and clean-label requirements while being scalable for industrial application.

In response, hybrid nanoencapsulation systems have emerged as a next-generation solution that synergistically combines natural and synthetic materials to harness the advantages of both. These systems merge the environmental

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Table 1 Comparative advantages and limitations of natural and synthetic polymers used in hybrid nanoencapsulation systems

Aspect	Natural polymers	Synthetic polymers	References
Source & composition	Derived from renewable biomass: plants (cellulose, starch, alginate, pectin), animals (chitosan, gelatin, whey, casein), microbes (pullulan) and gums (gum arabic, carrageenan)	Chemically synthesized monomers: polyesters (PLA, PLGA, PCL), polyethers (PEG), polyvinyls (PVA), polyurethanes, and others	8 and 9
Biocompatibility & safety	Generally recognized as safe (GRAS) for food and pharma use, with minimal toxicity or immunogenicity Low risk of adverse reactions upon ingestion	Many (*e.g.* PLGA, PEG) are FDA-approved for drug delivery but require rigorous purification to remove residual solvents or catalysts; some cationic polymers (PEI) and metal NPs can induce cytotoxicity or immune responses	10 and 11
Biodegradability	Biodegrade into non-toxic byproducts (sugars, amino acids) under physiological or environmental conditions, supporting sustainability	Biodegradable polyesters (PLGA to lactic/glycolic acid), (PCL to 6-hydroxycaproic acid); non-biodegradable polymers (*e.g.*, some PEGs) can persist; environmental accumulation concerns	12 and 13
Functional tunability	Limited intrinsic tunability, requires chemical (crosslinking, phosphorylation, Maillard conjugation) or enzymatic modifications to tailor mechanical strength, solubility, and release profiles	Highly tunable *via* monomer selection, copolymer ratios, molecular weight control, end-group chemistry, precise control over degradation rate and payload release profile	8, 14 and 15
Solubility & bioavailability	Improve water dispersibility of hydrophobic bioactives *via* inclusion complexes (cyclodextrin) or hydrophilic coatings (maltodextrin)	Enhance solubilization through surface modification (PEGylation), emulsifiers, or amphiphilic block copolymers; facilitate incorporation into clear beverages and nanoemulsions	16 and 17
Sensory attributes	Mask undesirable tastes and odors of bioactives (essential oils, polyphenols) to improve palatability in foods	Limited direct impact on sensory quality; polymer matrix is typically flavor-neutral but may require additional surfactants or stabilizers that could affect mouthfeel	18
Mechanical & structural stability	Poor tensile strength and film integrity under harsh processing; prone to swelling and rupture in aqueous media unless reinforced	High mechanical robustness, structural integrity under shear, heat, and varied pH; less prone to premature rupture	19
Environmental sensitivity	Highly responsive to pH, ionic strength, and enzymatic degradation-advantageous for targeted release but can cause uncontrolled payload loss	More stable against environmental fluctuations; controlled degradation under designed triggers (*e.g.*, hydrolysis of ester linkages) but may require external stimuli or enzymes for breakdown	20 and 21
Batch variability & reproducibility	Source-dependent variability in molecular weight, degree of substitution, and purity impacts reproducibility and scale-up	High batch-to-batch consistency due to defined chemical synthesis; stringent quality control possible but cost of high-purity polymers can be significant	22
Scalability & cost	Extraction and purification (green methods) can be energy-intensive and costly; complex fabrication (electrospraying, ionotropic gelation) presents scale-up challenges	Well-established industrial processes (emulsion polymerization, microfluidics) exist but require specialized equipment; high-grade polymers and solvent recovery add to production costs	23 and 24
Regulatory & environmental impact	GRAS status simplifies regulatory approval for food use; fully biodegradable with low ecological footprint	Regulatory clearance more complex for food applications; potential ecological persistence of non-biodegradable polymers; solvent residues and nanoparticle fate must be assessed	25 and 26

responsiveness, edibility, and biodegradability of natural biopolymers with the mechanical strength, customizability, and stability of synthetic nanostructures. The result is a robust delivery matrix capable of protecting bioactives under harsh food processing and digestive conditions while enabling site-specific, stimuli-responsive release. Depending on the design, these hybrids can be engineered to respond to pH, temperature, enzymatic activity, or ionic changes, enabling on-demand release in targeted regions of the gastrointestinal tract.[2]

The novelty of this review lies in its comprehensive synthesis of recent developments in material selection, chemical and enzymatic modifications (*e.g.*, phosphorylation, esterification, hydrolysis, Maillard conjugation), and nano-fabrication techniques such as self-assembly, layer-by-layer deposition, electrospinning, and nanoprecipitation. It uniquely emphasizes how these fabrication methods and structural modifications are employed to enhance encapsulation efficiency, stability, and bioactive retention under dynamic food processing and physiological conditions. Furthermore, emerging hybrid systems incorporating smart, stimuli-responsive components are critically reviewed for their potential in precision nutrient delivery.

In addition to showcasing these innovations, the review explores the practical applications of hybrid nanoencapsulation across functional food categories such as fortified beverages, dairy products, and bakery goods and examines current challenges in scalability, regulatory compliance, safety validation, and consumer acceptance. By identifying gaps in current knowledge and outlining priorities for green synthesis, food-grade material innovation, and systematic risk assessment, this review aims to guide future research at the intersection of nanotechnology, material science, and food innovation.

2 Natural polymers and synthetic polymers in nanoencapsulation

Natural biopolymers are macromolecules derived from renewable biological sources such as plants (*e.g.*, cellulose, starch, alginate, pectin), animals (*e.g.*, chitosan, gelatin, casein, whey protein), and microbial exudates (*e.g.*, pullulan, xanthan gum). These materials are extensively employed in nanoencapsulation systems due to their excellent biocompatibility, inherent biodegradability, and Generally Recognized As Safe (GRAS) status.[3] Their natural origin ensures minimal immunogenicity and high acceptability in food and nutraceutical applications. Additionally, they are capable of forming colloidal dispersions, hydrogels, or particulate systems that offer physical protection to bioactive compounds against environmental stressors such as oxidation, heat, and light. Some, like alginate and chitosan, also exhibit responsiveness to gastrointestinal pH variations, facilitating targeted release in specific regions of the digestive tract.[4] However, their use is sometimes constrained by limitations such as source-dependent variability in purity and molecular weight, limited mechanical robustness under processing conditions, and poor encapsulation efficiency for hydrophobic compounds without prior modification. These shortcomings have led to a growing interest in combining natural polymers with complementary materials to improve functionality.

Synthetic polymers have become pivotal in nanoencapsulation due to their exceptional design flexibility, structural consistency, and capacity to form well-defined, stable nanocarriers. Commonly used materials including poly(lactic acid) (PLA), poly(lactic-*co*-glycolic acid) (PLGA), polyethylene glycol (PEG), polycaprolactone (PCL), and polyvinyl alcohol (PVA) which offer precisely controllable degradation profiles, mechanical integrity, and favorable safety qualifications in food and pharmaceutical applications.[5] Their synthetic composition allows for tailored molecular weight, hydrophilicity/hydrophobicity, and functional end-groups, leading to enhanced encapsulation efficiency and finely tuned release kinetics. For example, PLGA and PEG-based systems are well documented for protecting labile compounds such as polyphenols, vitamins, and antioxidants, delivering prolonged and site-specific release to improve bioavailability and functional outcomes.[6] Moreover, the reproducibility and scalability of synthetic polymer manufacturing is often using established solvent evaporation or emulsion methods to make them attractive for commercial applications, with many materials already approved by regulatory agencies.[7] Nonetheless, concerns remain regarding the use of organic solvents and surfactants in their production, which necessitate stringent purification to meet food-grade standards and avoid cytotoxicity. Additionally, synthetic polymers often lack intrinsic bioactive or environmental responsiveness unless further functionalized or paired with natural polymers. Despite these limitations, their structural precision and functional versatility continue to render synthetic polymers indispensable for next-generation nanoencapsulation platforms in functional foods and nutraceuticals.

A comprehensive comparison of the advantages and limitations of natural and synthetic polymers used in nanoencapsulation, highlighting their respective roles, strengths, and challenges in functional food applications is mentioned in Table 1.

To harness the complementary advantages of both natural and synthetic polymers, hybridization can be achieved by strategically combining them within a single nanoencapsulation system. In such hybrid constructs, the structural precision, mechanical strength, and controlled release properties of synthetic polymers are integrated with the biocompatibility, biodegradability, and environmental responsiveness of natural biopolymers. This synergistic combination allows for the development of advanced delivery vehicles that overcome the individual limitations of each material class such as poor mechanical stability in natural polymers or lack of biological functionality in synthetic ones. Hybrid systems, including chitosan-coated PLGA nanoparticles or electrospun fibers composed of natural and synthetic blends, have demonstrated enhanced encapsulation efficiency, improved protection of bioactive compounds, and targeted, stimuli-responsive release. As a result, hybrid nanoencapsulation platforms represent a promising approach for optimizing the delivery of functional ingredients in complex food systems.

Fig. 1 Self-assembled amphiphilic chitosan–curcumin (ACS–Cur) nanomicelles; (A) critical micelle concentration determination *via* pyrene fluorescence; (B) Tyndall effect in ACS–Cur suspension indicating nanomicelle formation; (C) TEM image showing spherical morphology (scale bar = 50 nm). (*Note*: Reproduced from ref. 36, *Molecules*, **29**, 2693 (CC BY 4.0).)

3 Methods for preparing hybrid systems

The fabrication of hybrid nanoencapsulation systems involves the integration of both natural and synthetic components into highly organized structures that enhance the stability, bioavailability, and controlled release of encapsulated bioactive compounds. Several advanced methodologies have been developed to prepare these complex systems, with prominent techniques including self-assembly, layer-by-layer (LbL) assembly, emulsion-based methods, and sol–gel processes. These approaches offer precise control over the composition, structure, and properties of the hybrid systems, allowing for customization based on specific application needs in functional foods and pharmaceuticals.

3.1 Self-assembly

Self-assembly is a bottom-up approach in which natural and synthetic molecules spontaneously organize into well-defined nanostructures by exploiting intrinsic properties such as hydrophobicity, hydrophilicity, and electrostatic affinity. In hybrid nanoencapsulation, these non-covalent forces such as hydrophobic interactions, van der Waals forces, hydrogen bonding, and π–π stacking drive the formation of micelles, vesicles, and nanoparticle complexes that encapsulate and protect bioactive compounds.[27] For instance, lipid-based carriers (*e.g.*, nanostructured lipid carriers) self-assemble in aqueous media to form vesicles that improve the solubility and stability of hydrophobic nutraceuticals.[28,29] Likewise, block copolymers combining polysaccharides with polyethylene glycol form micellar or vesicular assemblies, offering controlled release and enhanced retention of active payloads.[30]

In electrostatic complexation, oppositely charged biopolymers and synthetic polyelectrolytes form stable hybrid nanoparticles through charge neutralization. Poly(acrylic acid) (PAA) is anionic in neutral pH, whereas chitosan is cationic, mixing them causes electrostatic complexation and coacervation. Anthocyanins (flavonoid pigments) can be incorporated into such complexes. The PAA/chitosan forms a polyion network whose assembly is pH-sensitive, trapping the anthocyanins electrostatically. The resulting nanoparticles swell or shrink with pH, thereby protecting the anthocyanin at low pH (stomach) and releasing it in mild pH (intestine). In some studies, anthocyanin/cisplatin-loaded PAA–chitosan nanoparticles showed improved stability of anthocyanin and pH-triggered release.[31]

Additionally, hydrophobic interactions and π–π stacking, amphiphilic hybrids utilize hydrophobic domains for sequestering lipophilic actives. Inulin is a hydrophilic polysaccharide (fructan) that can be chemically modified with hydrophobic moieties to become amphiphilic. These modified inulins self-assemble into nanomicelles in water and can encapsulate curcumin (a hydrophobic polyphenol). For instance, the synthesized a curcumin–thioketal–inulin conjugate spontaneously formed ∼70–80 nm micelles that solubilized curcumin with high efficiency.[32] Notably, the curcumin-loaded inulin micelles produced a clear, transparent dispersion, whereas free curcumin precipitated quickly. Thus, the hydrophobically modified inulin greatly enhanced curcumin's aqueous solubility and stability. Such inulin-based nanoassemblies protect curcumin from rapid degradation/precipitation, improving bioavailability, while releasing it under target conditions (*e.g.* ROS-responsive thioketal cleavage in inflammatory sites).

Hydrogen bonding plays a pivotal role in the self-assembly of hybrid nanoencapsulation systems, offering structural integrity and enhanced protection of sensitive bioactives. Folic acid, due to its planar aromatic rings and polar functional groups, can self-assemble into nanotubular structures through intermolecular hydrogen bonding and π–π stacking. These folic acid nanotubes act as biological templates for the *in situ* reduction of platinum salts, forming platinum-decorated hybrid nanostructures with catalytic and antimicrobial properties.[33] Similarly, cellulose nanocrystals (CNCs) and polyvinyl alcohol (PVA) form robust hydrogel matrices *via* strong hydrogen bonding between hydroxyl groups. It is demonstrated that CNC–PVA hydrogels could encapsulate *Lactiplantibacillus plantarum* with ∼92% efficiency and maintain >8 log CFU g^{-1} probiotic viability after simulated digestion, showcasing improved resilience to gastrointestinal conditions and storage.[34] These examples

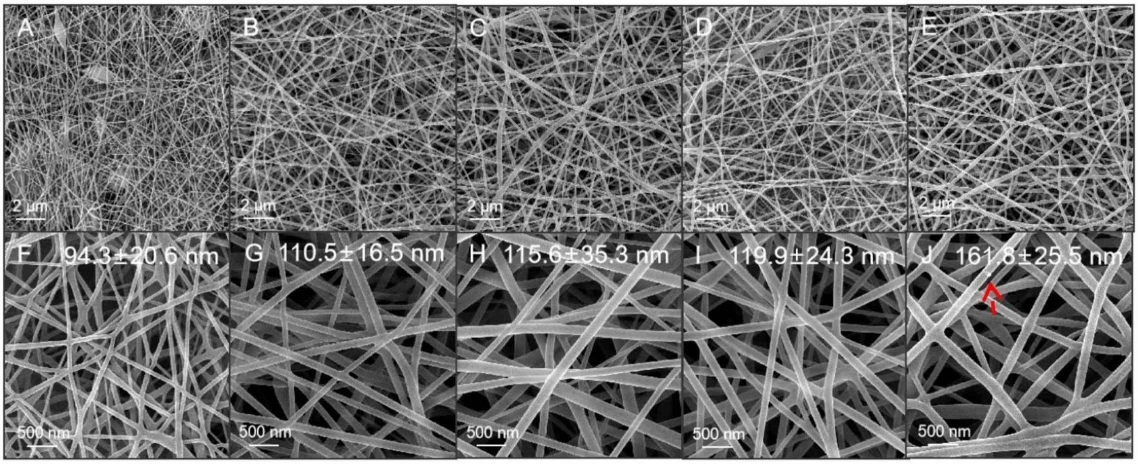

Fig. 2 Scanning Electron Microscopy (SEM) images and fiber diameter distribution of electrospun nanofibers prepared from pullulan and citrus pectin blends; (A and F) PUL-N (pure pullulan), (B and G) PUL-1CP (pullulan with 1% citrus pectin), (C and H) PUL-3CP (pullulan with 3% citrus pectin), (D and I) PUL-5CP (pullulan with 5% citrus pectin), (E and J) PUL-5CP-A (pullulan with 5% citrus pectin and astaxanthin encapsulation). Images (A–E) show fiber morphology at low magnification, while (F–J) show corresponding high-magnification views highlighting fiber surface and structure. (*Note*: Reproduced from ref. 47, *Food Chemistry: X*, **24**, Article 101990, licensed under CC BY-NC-ND 4.0.)

underscore the versatility and functional importance of hydrogen bonding in engineering stable, protective, and biocompatible delivery matrices for food-grade and therapeutic bioactive compounds. Furthermore, curcumin was encapsulated in self-assembled nanoparticles by dissolving lecithin in ethanol was injected into chitosan aqueous solution, forming stable, spherical nanoparticles (120–150 nm) by electrostatic interactions which improved curcumin's solubility, stability, and antioxidant activity, and remained stable under various pH and storage conditions.[35] An example of self-assembled hybrid nanoencapsulation is demonstrated by ref. 36, where amphiphilic chitosan derivatives were used to encapsulate curcumin. The self-assembly behavior of amphiphilic chitosan derivatives is well illustrated in Fig. 1A–C. As shown in Fig. 1A, amphiphilic chitosan molecules, containing both hydrophilic and hydrophobic segments, spontaneously self-assemble into polymeric nanomicelles with a core–shell structure in aqueous environments once their concentration exceeds the critical micelle concentration (CMC). This assembly is driven by hydrophilic–hydrophobic interactions. The CMC, determined using pyrene as a fluorescence probe, was found to be 0.093 mg mL^{-1}, indicating efficient micelle formation at low concentrations. Fig. 1B illustrates the macroscopic appearance of the Amphiphilic Chitosan–Curcumin (ACS Cur) nanomicelles, which were yellow, uniformly dispersed, and showed a distinct bright path when exposed to a laser beam, confirming the presence of colloidal micelles. Fig. 1A presents the TEM image of the nanomicelles, revealing spherical, vesicle-like morphology with consistent particle size, affirming the effectiveness of self-assembly in forming stable hybrid nanostructures.

3.2 Layer-by-layer (LbL) assembly

Layer-by-layer assembly creates multilayered hybrid nanostructures by sequentially depositing oppositely charged materials, enabling precise control over composition, thickness, and functional performance.[37] LbL assembly uses alternating deposition of oppositely charged materials *via* electrostatic and other interactions, forming precise multilayered films or capsules at the nanoscale.

In the context of functional foods, LbL assembly has been employed to enhance the stability, bioavailability, and controlled release of bioactive compounds. For instance, it was developed composite nanoparticles using zein and hyaluronic acid through LbL assembly for the co-delivery of curcumin and quercetagetin which enhanced encapsulation efficiency and sustained release profiles.[38] Moreover, LbL assembly has been utilized to encapsulate probiotics, where it was encapsulated with zein nanoparticles and pectin *via* LbL assembly exhibited improved survival rates during storage and simulated digestion, suggesting a promising approach for delivering live beneficial microbes in functional foods.[39] LbL assembly enables precise hybrid structures with tunable release and enhanced physicochemical stability.[40] Despite challenges like complex multi-step preparation, time-intensive, and environmental sensitivity, future developments in biodegradable polyelectrolytes, automation, and integration with 3D printing may improve scalability and functionality.[41]

3.3 Electrospinning

Electrospinning is an electrohydrodynamic technique that converts polymer solutions or melts into ultrathin fibrous matrices.[42,43] When a strong electric field is applied to a polymer solution at a charged nozzle, the meniscus is drawn into a conical Taylor cone and a fine charged jet is ejected.[44] The jet undergoes whipping instabilities as the solvent evaporates, stretching into continuous nanofibers that collect on a grounded surface.[45] Fiber *versus* droplet formation is determined largely by solution viscosity: higher viscosity yields continuous

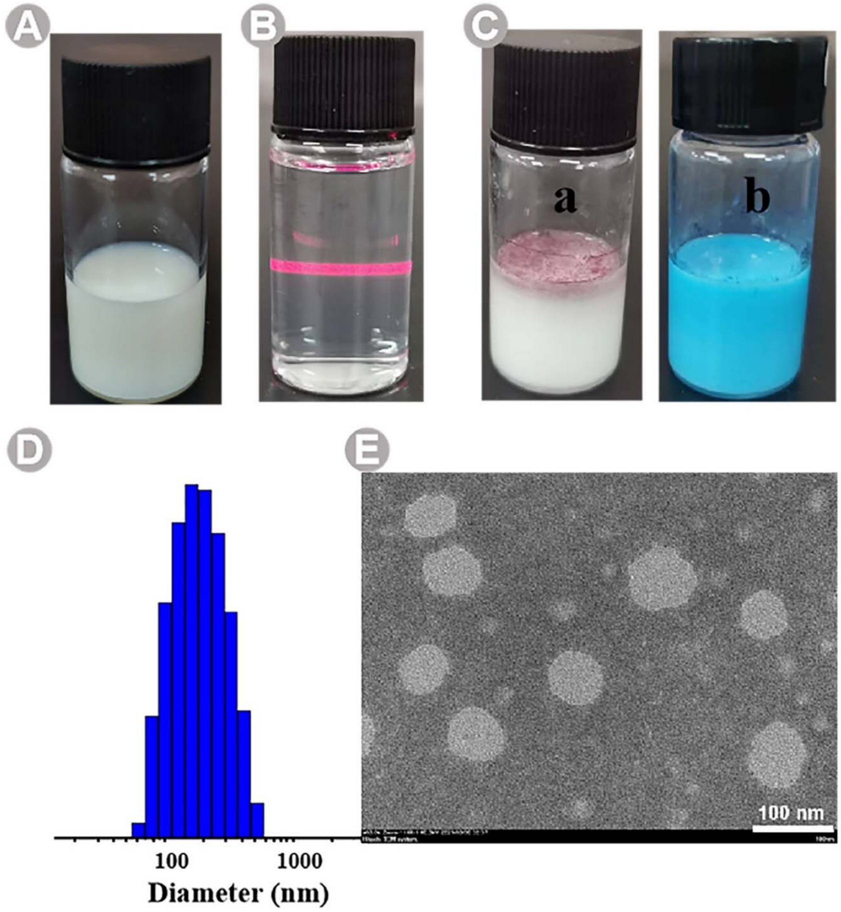

Fig. 3 Physicochemical characterization of BB-TTO nanoemulsions (NEs): (A) appearance and shape; (B) Faraday–Tyndall effect after dilution; (C) oil-in-water type identification using (a) Sudan red and (b) methylene blue; (D) particle size distribution (~160 nm); (E) TEM image showing spherical, smooth, well-dispersed droplets. (*Note*: Reproduced from ref. 58, *Molecules*, **28**, 5889, licensed under CC BY 4.0.)

fibers (electrospinning), whereas low-viscosity solutions break into particles (electrospraying). Process parameters (voltage, tip-to-collector distance, flow rate) and solution properties (polymer molecular weight, conductivity and surface tension) thus control fiber diameter, porosity and morphology.[46] The resulting nonwoven mats typically have uniform nanometer-scale diameters (often 50–500 nm) and highly porous, interconnected structures. Such high surface-area, high porosity fibers afford extensive contact with encapsulated bioactives and are mechanically flexible, features that enhance protection and tunable release of sensitive food ingredients. Hybrid electrospun nanofibers composed of pullulan and citrus pectin were developed by ref. 47 to enhance fiber morphology and functionality for bioactive encapsulation. Increasing citrus pectin (CP) content reduced bead formation and yielded smooth, uniform nanofibers, as shown in the SEM images (Fig. 2). Fig. 2A demonstrates pure pullulan fibers exhibit bead-like defects due to low polymer entanglement while Fig. 2B–E displays increasing citrus pectin content reduces bead formation, improving fiber uniformity and Fig. 2F–I illustrates high magnification images of CP containing fibers reveal smooth, cylindrical nanofibers with uniform surfaces. These changes reflect enhanced molecular interactions and higher viscosity from CP's branched structure, leading to increased fiber diameters (~94 nm to ~162 nm) and better morphology. These hybrid nanofibers successfully encapsulated astaxanthin, improving its antioxidant stability and mechanical properties, highlighting their potential for food preservation and delivery applications.

Electrospinning enables the formation of hybrid nanofibers using food-grade polymers like zein, gelatin, and polysaccharides, often blended with synthetic polymers for strength. Nanofillers such as graphene oxide have been embedded in chitosan/PVA fibers[48] and alginate or starch fibers loaded with ZnO, enhance antimicrobial activity and UV protection.[49] Other additives like silver, TiO_2, carbon nanotubes, clay, or silica can be incorporated *via* blending or coaxial methods. These nanofillers are stabilized within natural polymer matrices (*e.g.*, chitosan, starch), yielding hybrid fibers with improved mechanical strength, barrier function, and added functionality. These mats encapsulate vitamins, flavors, antioxidants, vitamins or probiotics with high efficiency.[50] For instance, higher loading and protection form UV and heat degradation was resulted when encapsulated of folic acid into corn zein or modified starch fibers. Applications include edible coatings[51] using essential oils and bioactives, probiotic bacteria encapsulated in polysaccharide nanofibers for improved survivability and in active packaging.[52] Recent innovations have addressed some issues through green electrospinning with aqueous or solvent-free systems, needleless and multi-jet devices for scale-up, coaxial spinning for core–shell architectures, and incorporation of functional nanoparticles and it advances electrospinning for integrating natural and synthetic components in next generation food delivery systems.

3.4 Emulsion-based techniques

Emulsion-based methods encapsulate hydrophobic bioactives by emulsifying natural polymers with synthetic carriers. The bioactive compounds are then dissolved or dispersed in the oil phase, and the emulsion is stabilized by surfactants or stabilizing agents, such as polysorbates or polyvinyl alcohol. The emulsion is subsequently solidified or crosslinked through various methods, including solvent evaporation, temperature-induced gelation, or chemical crosslinking, to form stable nanoencapsulation systems. The size, morphology, and stability of the resulting particles can be controlled by adjusting parameters such as the emulsification technique, polymer type, and stabilizer concentration used.[53] High-pressure homogenization and ultrasonication generate shear and cavitation forces to reduce droplet size. Natural emulsifiers (proteins, polysaccharides) provide stabilization *via* steric and electrostatic repulsion.[53] Incorporating synthetic nanomaterials (*e.g.*, silica, lipid nanoparticles) enhances stability, bioavailability, and controlled release, making these systems ideal for delivering bioactives in functional foods.

Hybrid nanoemulsions combine natural polymers with synthetic nanoparticles to enhance stability and functionality. Fe_3O_4 embedded in a chitosan/agarose shell for pH-responsive, magnetically responsive curcumin delivery.[54] Pickering nanoemulsions using protein–polysaccharide particles have also been developed.[55] These systems rely on optimized emulsification conditions to promote proper assembly of polymers and nanomaterials at interfaces or within droplets. Nanoemulsion-based hybrid carriers enhance protection, stability, and bioavailability of lipophilic bioactives. Nano-sized droplets shield compounds from oxidation and hydrolysis, while high surface area promotes rapid absorption.[56] Hybrid matrices enable controlled, pH-responsive release, as shown with curcumin–Fe_3O_4/chitosan/agarose systems.[57] Those studies revealed that inorganic cores offer added functionalities, and polymers improve mucoadhesion. Natural stabilizers also ensure robustness; quillaja saponin and whey protein-stabilized nanoemulsions showed strong stability under thermal, storage, and dilution stress.

Researchers studied the physicochemical characterization of the oil-in-water nanoemulsion stabilized by glycyrrhizic acid

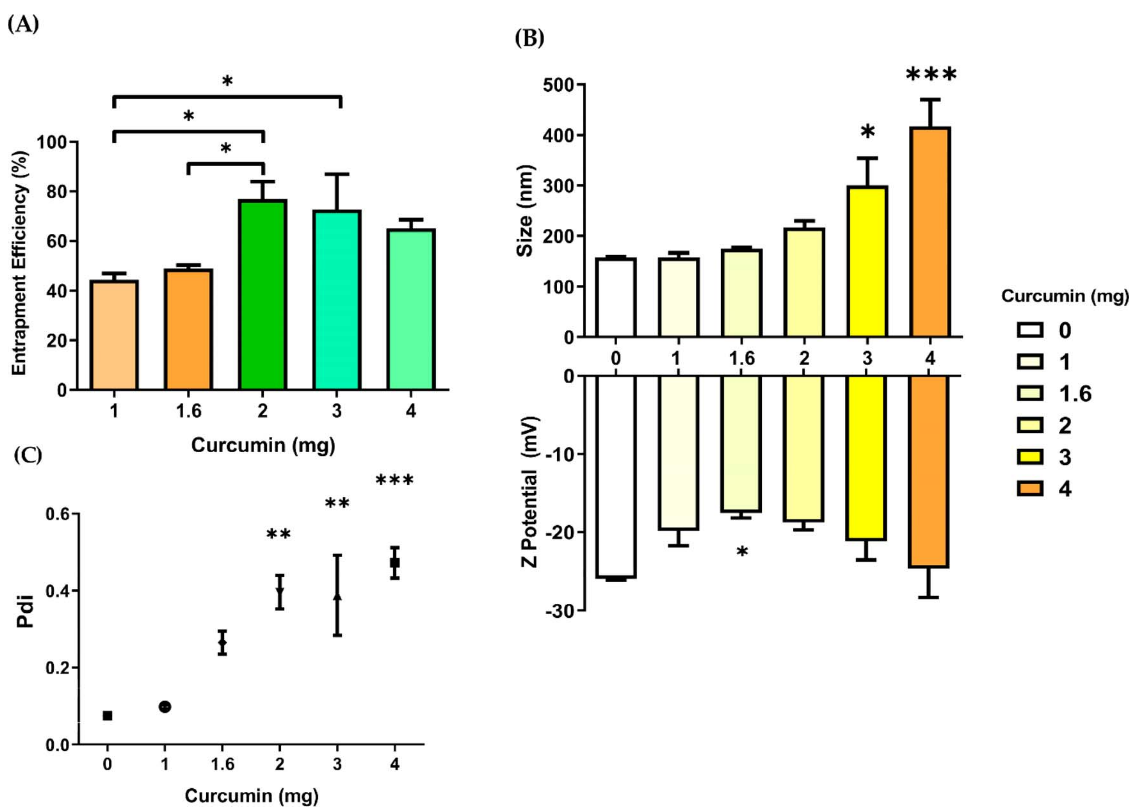

Fig. 4 Curcumin entrapment efficiency and its effect on nanoparticle physicochemical properties in PLGA nanoparticles prepared *via* nanoprecipitation: (A) entrapment efficiency (% EE) of curcumin at different loading concentrations (B) influence of curcumin loading on particle size and zeta potential. (C) Effect on polydispersity index (Pdi) at varying curcumin loads. (*Note*: Reproduced from ref. 67, *Pharmaceutics*, **15**, 1594. CC BY 4.0.)

and composed of *Blumea balsamifera* and tea tree oils.[58] As shown in Fig. 3A nanoemulsion exhibits a uniform milky-white appearance and confirms the presence of nanoscale particles through a prominent Faraday–Tyndall effect after dilution (Fig. 3B). Dye diffusion studies (Fig. 3C) indicate that the nanoemulsion is of oil-in-water type. Dynamic light scattering analysis reveals a narrow particle size distribution with an average droplet size around 160 nm (Fig. 3D). Transmission electron microscopy (TEM) images (Fig. 3E) show spherical, smooth, and well-dispersed nanoemulsion droplets without aggregation, demonstrating controlled size and morphology essential for stable encapsulation.

Nanoemulsion-based systems face challenges such as coalescence, Ostwald ripening, and instability under various environmental conditions such as pH, ionic strength or temperature shifts. Concerns over synthetic emulsifiers and nanoparticles demand thorough safety evaluation. Advances include food-grade, biodegradable stabilizers from proteins and polysaccharides, and low-energy methods incorporating bioactives like essential oils for enhanced antimicrobial effects. These innovations improve stability and shelf life, supporting their functional food use while emphasizing the need for ongoing research and safety validation.[59]

3.5 Sol–gel process

The sol–gel process is a versatile method for creating hybrid nanoencapsulation systems in functional foods. It transforms a liquid sol into a solid gel *via* hydrolysis and polycondensation of precursors like tetraethoxysilane (TEOS). This technique enables the incorporation of bioactives and biopolymers, offering protection and controlled release.[60] Operating under mild conditions, it preserves bioactivity and yields highly pure materials, which can be tailored into films, fibers, or powders for specific food applications.

The sol–gel process forms a three dimensional network *via* hydrolysis and condensation of metal alkoxides, entrapping bioactives and polymers for enhanced stability and controlled release.[61] Adjusting pH, temperature, and precursors customizes properties, while adding natural polymers improves biocompatibility for functional food applications. Sol–gel derived hybrid materials are used in functional foods to encapsulate vitamins, antioxidants, and probiotics, offering protection against light, oxygen, and pH changes and improving bioavailability.[62] Their controlled release enables targeted delivery in the gastrointestinal tract. Applications extend to biosensing and biocatalysis with cell-loaded matrices. However, challenges include costly precursors and drying-related defects such as cracking or shrinkage of the material. Recent advances focus on biofriendly, ambient-condition sol–gel methods that eliminate harsh solvents and simplify processing for better scalability and cost-effectiveness.

3.6 Nanoprecipitation

Nanoprecipitation, or solvent displacement, is an effective method for creating hybrid nanoencapsulation systems, particularly for hydrophobic bioactives in functional foods due to its simplicity, scalability, and precise particle control.[63] It involves mixing a polymer–bioactive solution in a water-miscible solvent (acetone/ethanol) with water, triggering spontaneous nanoparticle formation without high energy or surfactants.[64] Combining natural polymers like chitosan with synthetic ones like PLGA enhances particle stability, biocompatibility, and functional performance.[65]

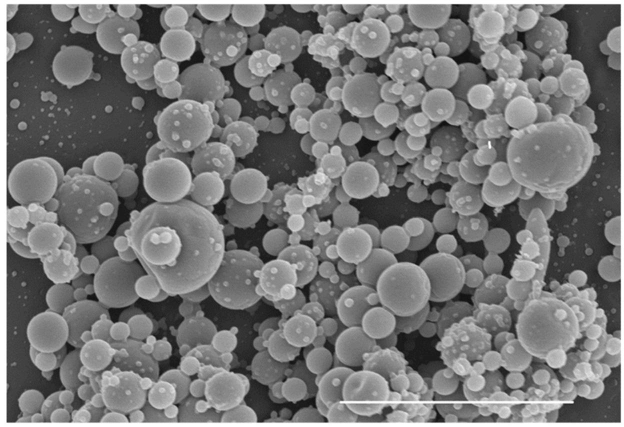

Fig. 5 SEM image of electrosprayed agar nanocapsules loaded with 5 wt% chlorophyllin sodium copper salt (CHL) relative to agar content. Scale bar: 4 μm. (*Note*: Reproduced from ref. 76, *Foods*, **11**, 2093. CC BY 4.0.)

Nanoprecipitation improves solubility, stability, and bioavailability of hydrophobic bioactives like curcumin and β-carotene in functional foods.[66] It produces uniform nanoparticles with high encapsulation efficiency and allows integration of natural (*e.g.*, chitosan) and synthetic (*e.g.*, PLGA) polymers for enhanced performance. However, limitations include solvent removal and food matrix instability. Advances focus on novel biopolymers and hybrid systems to enable targeted release and protect sensitive compounds effectively.

Researchers systematically investigated the nanoprecipitation-based synthesis and optimization of curcumin-loaded PLGA nanoparticles, emphasizing parameter effects on encapsulation efficiency and physicochemical attributes critical for hybrid nanoencapsulation systems.[67] Fig. 4 shows that entrapment efficiency increases up to ∼70% with higher curcumin amounts (Fig. 4A), while nanoparticle size and zeta potential (Fig. 4B) indicate stable, uniform particles below 200 nm with more negative surface charge. Correspondingly, polydispersity index values (Fig. 4C) remain low (<0.2), reflecting narrow size distributions. These findings underscore the ability of nanoprecipitation to precisely control physicochemical characteristics, producing stable, efficient hybrid nanoencapsulation systems suitable for enhancing the delivery of hydrophobic bioactives in functional foods.

3.7 Supercritical fluid technology

Supercritical fluid technology (SCFT) is a green approach for fabricating hybrid nanoencapsulation systems in functional foods. It combines natural polymers with synthetic materials to enhance stability and controlled release of bioactive compounds. Using supercritical CO_2 (SC-CO_2), methods like Rapid Expansion of Supercritical Solutions (RESS), Supercritical Anti-Solvent (SAS), and Particles from Gas Saturated Solutions (PGSS), SC-CO_2 acts either as a solvent or anti-solvent to facilitate the formation of nanoparticles.[68] For example, SAS rapidly precipitates particles by spraying solutions into SC-CO_2 leading to rapid supersaturation and precipitation of nanoparticles, eliminating harmful solvents.[69]

SCFT has been applied to encapsulate bioactives like vitamins, antioxidants, and essential oils using techniques such as SAS and PGSS. Examples include β-carotene in soy lecithin,[70] curcumin in chitosan, and lime oil in fortified foods.[71] SC-CO_2 preserves thermolabile compounds (*e.g.*, polyphenols and omega-3 fatty acids) while eliminating solvent residues.[72] Biopolymer matrices (*e.g.*, alginate, chitosan) improve controlled release and gut delivery as demonstrated in probiotic-loaded edible films.[70] SCFT's scalability and use of agro-waste support sustainability, with growing promise in multi-component delivery systems.[73] For instance, polyphenols encapsulation using SCFT has enhanced solubility and antioxidant retention, bioavailability which are crucial in developing health beneficial functional foods.[74] SCFT is a solvent-free, eco-friendly method enabling precise nanoparticle formation while preserving heat-sensitive bioactives. Though limited by equipment cost and poor polar compound solubility, advances in green co-solvents and hybrid formulations improve encapsulation efficiency and functionality in food-grade polymer nanocarriers.

3.8 Electrohydrodynamic atomization

Electrohydrodynamic atomization (EHDA), including electrospraying and electrospinning, integrates natural polymers with synthetic materials to produce hybrid nanoencapsulation systems under mild conditions.[75] It operates by applying a high-voltage electric field to a polymer solution, forms particles or fibers based on solution viscosity, with coaxial setups enabling core–shell structures for protecting sensitive bioactives, enhancing stability and controlled release. EHDA enhances the stability and bioavailability of encapsulated compounds like polyphenols, vitamins, and essential oils. Applications include electrosprayed agar nanocapsules and zein-based carriers for thermally sensitive açaí polyphenols.

EHDA has been employed to encapsulate a variety of bioactive compounds, including polyphenols, vitamins, and essential oils, enhancing their stability, bioavailability, and controlled release in functional food products. For instance, electrosprayed agar nanocapsules have been developed as edible carriers for bioactives and zein-based electrosprayed particles have been used to improve the thermal stability and bioaccessibility of fruit polyphenols. EHDA enables precise fabrication of particles and fibers at ambient temperatures, offering high encapsulation efficiency and protection for heat-sensitive bioactives. While limited by scalability and solvent residue concerns, advances in coaxial EHDA, food-grade polymers, and parameter optimization enhance core–shell structures, integration of food-grade biopolymers with synthetic materials improving stability and controlled release in functional food applications.

Electrosprayed agar nanocapsules have been developed as edible carriers for bioactives, using acetic acid to solubilize agar and prevent gelation during processing.[76] Optimized electrospraying conditions produced spherical nanocapsules between 50 and 400 nm, with an encapsulation efficiency of ∼40% for

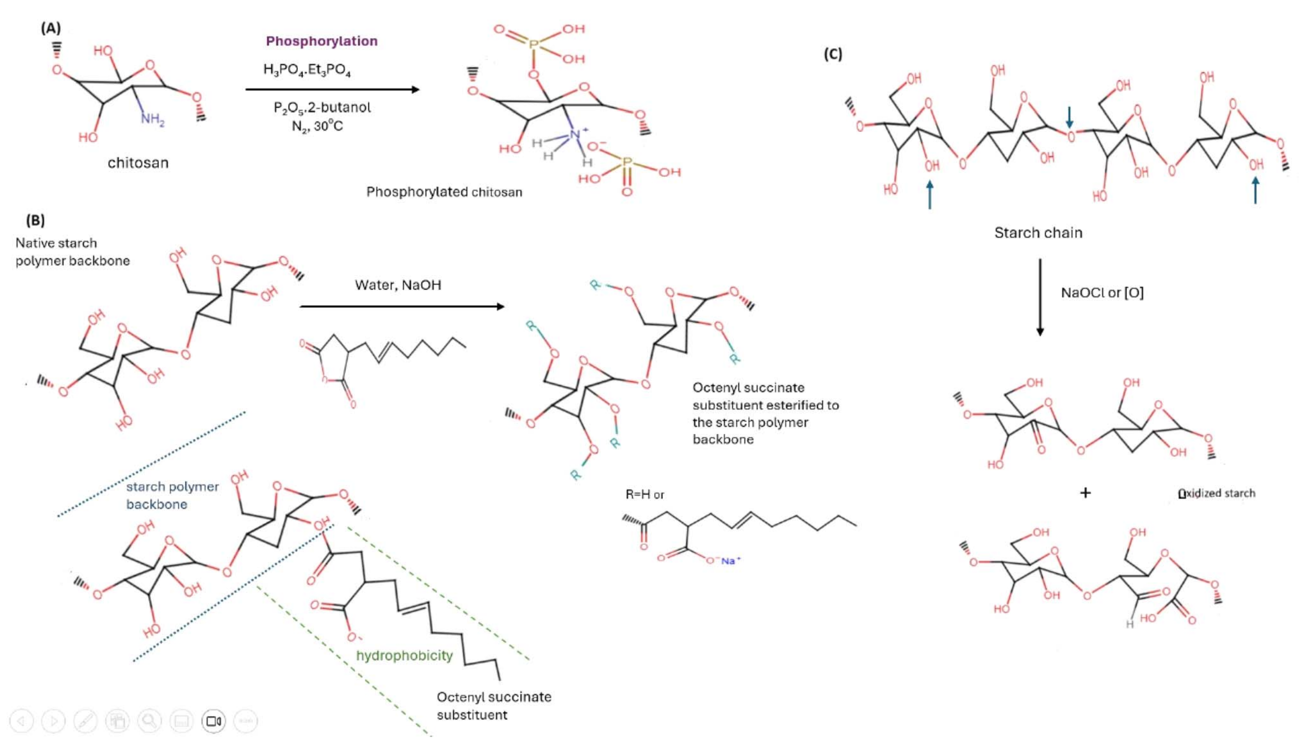

Fig. 6 Diversification of biopolymers by (A) phosphorylation,[83] (B) esterification,[84] (C) oxidation.[85]

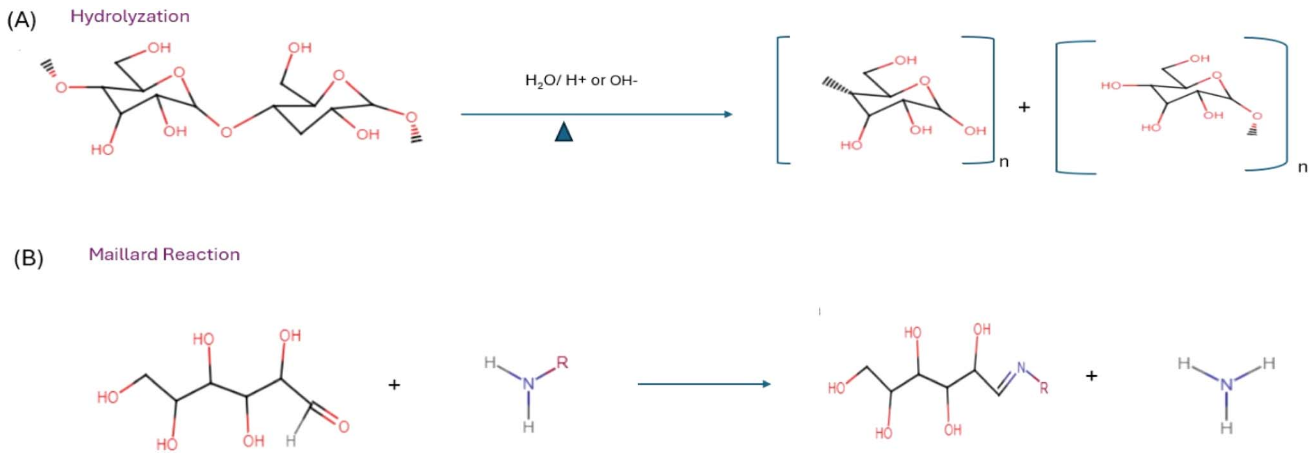

Fig. 7 Diversification of biopolymers by (A) hydrolysis,[86] (B) Maillard conjugation.[87]

chlorophyllin sodium copper salt (CHL). Release studies showed minimal CHL release in hydrophilic media and sustained release in lipophilic simulants, supporting controlled delivery potential in functional foods. As shown in Fig. 5, SEM images confirm the uniform size and morphology of the agar nanocapsules, demonstrating EHDA's capability to fabricate stable, food-grade hybrid nanoencapsulation systems. Advances in EHDA offer promising avenues for encapsulating sensitive bioactives under mild conditions with high efficiency.

4 Recent advances in material selection for hybrid systems

The evolution of hybrid nanoencapsulation systems has been driven by the strategic selection and design of constituent materials, blending the inherent benefits of both natural and synthetic components. These materials are engineered not only to protect and deliver bioactive compounds efficiently but also to interact dynamically with complex food matrices and physiological environments. Recent years have witnessed a significant expansion in the spectrum of materials used, alongside advances in their functionalization, structuring, and integration into responsive and sustainable hybrid systems.

4.1 Diversification of biopolymeric matrices

Natural biopolymers remain foundational to hybrid systems due to their abundance, biocompatibility, and functional versatility. Starch, chitosan, pectin, gelatin, cellulose derivatives, alginate, and proteins (*e.g.*, casein, whey, soy, zein) are frequently employed. Recent developments have focused on tailoring their chemical structure to enhance physicochemical stability, bioactive retention, and interaction with synthetic counterparts.

Chemical and enzymatic modifications of polysaccharides and proteins are pivotal for enhancing their functional performance in nanoencapsulation systems. These modifications improve emulsifying capacity, surface activity, stability under physiological conditions, and compatibility with nanoparticles and making them more suitable for advanced delivery systems in functional foods. Polysaccharides like starch, pectin, and cellulose derivatives are widely used as stabilizers and wall materials due to their biodegradability and non-toxicity. However, their native forms may exhibit limited emulsifying properties under varying environmental conditions (*e.g.*, pH, ionic strength). To address this, several advanced chemical modifications are employed.

4.1.1. Phosphorylation. Phosphorylation introduces phosphate groups, increasing the hydrophilicity and charge density of polysaccharides, which enhances their emulsifying and stabilizing behavior. Chitosan is phosphorylated for enhancing their functional properties such as antioxidant and antimicrobial activity, preservation of food by inhibiting growth microbes and oxidation.[77] This is illustrated in Fig. 6A.

4.1.2. Esterification. This process introduces hydrophobic ester groups, improving amphiphilicity and allowing the polysaccharide to adsorb more effectively at oil–water interfaces. Octenyl succinic anhydride (OSA)-modified starch is a well-known emulsifier used in nanoemulsion systems due to its superior surface activity and stability in acidic and ionic environments[78] as shown in Fig. 6B. OSA modified starch can be used enhance bioaccessibility of β-carotene.[79]

4.1.3. Oxidation. Oxidized polysaccharides, such as sodium periodate-modified starch or cellulose, contain reactive aldehyde groups that form covalent Schiff base crosslinks with amino groups in proteins or chitosan.[80] This is depicted in Fig. 6C. This crosslinking enhances the mechanical strength, water resistance, and film-forming ability of biopolymer matrices, thereby improving retention and controlled release of hydrophobic bioactives in delivery systems.

4.1.4. Hydrolysis. Protease treatment reduces protein molecular size and increases flexibility, allowing better interfacial coverage and co-assembly with nanoparticles. Hydrolyzed pea protein and casein hydrolysates have shown enhanced emulsifying activity index (EAI) and antioxidant properties in lipid-based delivery systems. Hydrolysis of starch involves the enzymatic or acid-mediated cleavage of glycosidic bonds (as shown in Fig. 7A), reducing its molecular weight and enhancing its solubility, emulsifying capacity, and film-forming properties. This modification produces maltodextrins, glucose syrups, or resistant dextrins, which exhibit improved physicochemical characteristics for encapsulating sensitive bioactives.

4.1.5. Maillard conjugation. Through the Maillard reaction, proteins are covalently linked to polysaccharides under controlled heating, improving solubility, emulsifying capacity, and oxidative stability. For example, whey protein–dextran conjugates formed *via* Maillard reaction showed enhanced stability in nanoemulsions loaded with curcumin.[81] Similarly, soy protein–pectin Maillard conjugates provided better resistance to gastric digestion and pH shifts, improving the delivery of lipophilic nutrient.[82] An overview of this approach is provided in Fig. 7B

4.2 Integration with nanoparticles and food matrices

Chemically modified biopolymers have been integrated into hybrid nanoparticle systems to improve encapsulation and stability of bioactive compounds. For example, curcumin-loaded nanoparticles prepared using hydrophobic rice proteins demonstrated enhanced solubility and stability, highlighting the potential of protein-based nanocarriers for hydrophobic bioactives.[88] Similarly, curcumin encapsulated in solid lipid nanoparticles composed of cetyl palmitate and Tween 80 exhibited high encapsulation efficiency, improved photostability, and sustained antimicrobial activity, making them suitable for food and therapeutic applications.[89] Additionally, ovalbumin–alginate nanocomplexes have been shown to increase curcumin bioaccessibility and antioxidant activity through improved stability during simulated digestion.[90]

4.3 Functional synthetic materials and their customization

Synthetic polymers and nanostructures like PLGA, PEG, PLA, PCL, dendrimers, and mesoporous silica are integral to hybrid nanoencapsulation due to their tunable size, surface chemistry, and controlled release profiles. A major advancement is the use of stimuli-responsive polymers (smart polymers) which undergo reversible or irreversible structural changes in response to environmental triggers such as pH, temperature, enzymatic activity, or redox potential.[91,92] Smart coatings such as polydopamine and zwitterionic polymers enhance adhesion, reduce nonspecific interactions, and trigger disassembly in specific conditions.[93] Additionally, functionalized surfaces with ligands or peptides facilitate active targeting and improved absorption. For example, chitosan-grafted liposomes or PLGA particles improve mucosal adhesion and stability in food systems.[94] These innovations significantly enhance the performance, adaptability, and efficacy of synthetic components in hybrid delivery systems for functional food applications.

4.4 Hybrid nanocomposites and multiphase systems

An emerging strategy in hybrid nanoencapsulation is the use of multiphase or composite materials combining organic and inorganic components to achieve synergistic functional properties. Protein–polysaccharide complexes enhance encapsulation and protection of sensitive bioactives such as polyphenols and probiotics.[95] Chemically modified rice starch and Sanxan–protein complexes improve Pickering emulsion by enhancing protein–polysaccharide interactions and providing better oxidative resistance stability.[96] Inorganic–organic hybrids such as calcium phosphate–chitosan and silica–protein composites offer structural strength and targeted release. Additionally, MOFs and nano-clays provide high surface area and tunable porosity for effective bioactive loading.[97]

5 Advantages of hybrids for bioactive compound delivery

Encapsulation of bioactive compounds with hybrids enhances their stability against environmental stressors such as pH, temperature, and light by tailoring the material properties and microenvironment (Table 2).

Encapsulated materials are also protected *via* microenvironment buffering, moderating internal pH by limiting ion diffusion through controlled charge, pore size, or hydrophobicity.[98] Carbohydrates, gums, and proteins resist thermal stress *via* crosslinked networks, while chitosan and alginate hydrogels enhance mechanical stability. Ionic crosslinking in chitosan microspheres protects compounds from environmental stress. Stimuli-responsive hydrogels expand or contract under pH, temperature, or light changes; micro- and nanogels respond faster, enabling precise control and regulation.[104] Additionally, UV-absorbing additives mitigate photodegradation and encapsulated bacteria in pH-responsive nonwovens retained viability ≥2 months, extending shelf life.[103]

Hybrids enhance the systematic delivery of poorly water soluble compounds by overcoming solubility limitations. An increase of gemcitabine solubility was reported in nano gels that are synthesized from dendritic polyglycerol-*co*-polycaprolactone (PG-*co*-PCL) *via* pH-responsive covalent conjugation and achieving tumor-specific release.[105] Chitosan-modified nano gels loaded with paclitaxel use hydroxypropyl-β-cyclodextrin acrylate to improve its lymphatic uptake and encapsulation efficiency, bypassing first-pass metabolism.[106] According to previous study, traditional oral formulations often demand higher doses due to low dissolution rates and erratic absorption.[107] Nanoencapsulation increases the bioaccessibility of lipophilic nutrients such as β-carotene present in aqueous food matrices. Moreover, chitosan-TPP nanoparticles improve their dispersibility by 40% compared to non-hybrid carriers.[108]

Hybrids provide significant spatiotemporal control over bioactive release *via* stimuli-responsive mechanisms. It was found that pH-sensitive chitosan/poly(γ-glutamic acid) complexes release insulin preferentially in the intestinal lumen, avoiding breakdown in the stomach.[109] Furthermore, bacterial-powered microrobots such as advanced delivery systems exploit chemotaxis and natural motility to navigate physiological barriers, to achieve targeted delivery of doxorubicin directly to lung metastases and reported a sevenfold increase in tumour uptake than their passive carriers.[110] Off-target toxicity often associated with traditional intravenous methods happens due to the lack of such high precision. Furthermore, remote

Table 2 Enhanced stability of hybrid-encapsulated bioactive compounds against environmental stressors

Environmental stressor	Affected bioactive compound	Protection mechanism	Hybrid system	Example	Reference
Harsh acidic pH	*Corynebacterium glutamicum*	pH responsive materials	poly(butadiene)-*block*-poly(2-vinyl pyridine) (PB-*b*-P2VP)	*Corynebacterium glutamicum* encapsulated in pH-responsive fibers degraded phenol at pH 4, whereas free bacteria failed due to low survival	99
	Phenolic antioxidants	Structural stability	Xanthan gum/chitosan–alginate composite	The antioxidant activity of the *Eugenia punicifolia* extracts encapsulated in xanthan gum was retained at pH 4.5 due to gum's unique characteristic of double helix confirmation and bonding with hydrogen at lower pH	100
Gastric pH degradation	Peptides	Controlled release	Zein–chitosan	Peptides encapsulated with nanoparticles of zein–chitosan improve bioavailability by resisting the gastric pH degradation and enabling the controlled release at the intestine	101
Direct heat exposure	Lipid vesicles	Physical barriers	AuAgCl NPs	lipid vesicles in hybrids reduced heat-induced degradation of photosynthesized gold–silver chloride nanoparticles (AuAgCl NPs) during characterization tests	102
Moist heat	Ascorbic acid	Crosslinked networks	Alginate based microcapsules	Improved moist heat resistance of ascorbic acid (AA) by up to 82% during steaming at 95 °C	103
Ultra-high temperature processing		Thermal buffering/absorbing heat energy	Egg yolk	EY-enhanced microcapsules retained >70% vitamin C stability after ultra-high-temperature (UHT) processing at 143 °C	

Table 3 Emerging applications of hybrid nanoencapsulation systems in enhancing the functionality, stability, and delivery of bioactives in functional foods

Compound	Hybrid/composite	Functional advantage	Reference
Lipophilic antioxidants such as curcumin and resveratrol	Lipid based carriers stabilized with chitosan	Improve solubility, gastrointestinal absorption, and stability	113
Probiotics	Chitosan–calcium phosphate hybrid systems	Improve the survival in acidic gastric medium and enable targeted intestinal release	114
Lactobacillus species	Chitosan–calcium phosphate hybrid	Enhances their survival in acidic yoghurt ensuring targeted delivery at the intestine	115
Oregano and thyme essential oils	Chitosan–silica nanoparticles	Used as antimicrobial agents in meat and cheese, masking strong odours while maintaining shelf life	
Vitamin C	Lipid-based or polymeric nano-carriers	Improve shelf life and retain potency	65
Polyphenols	Lipid-based or polymeric nano-carriers	Improve shelf life and retain potency	118
Anthocyanins	Zein–pectin nanoparticles	Preserve colour in yoghurt and beverages	117

triggering techniques based on magnetic fields or light improve drug release control, as demonstrated by thermoresponsive nanogels that release antibiotics on demand.[91] These capabilities also provide sustainable co-delivery of incompatible compounds, including iron and ascorbic acid, by isolating them within compartmentalized hybrid frameworks.[104] The unique characteristic of adaptability has revolutionized the hybrid systems especially, bioactive fortified functional foods. Lipid-based nanocarriers are capable of protecting omega-3 fatty acids from oxidation effectively while masking undesirable flavours that occur in snacks and dairy alternatives and enhancing product stability and consumer acceptability.[111] Enzyme induced release mechanisms in hybrid matrices interact with nutrient bioavailability during digestive processes. For example, fortified beverages have resulted in increased iron absorption by up to 60%.[108] Moreover, hybrid micelles co-encapsulating piperine and curcumin improve dispersibility in aqueous media and resolve the solubility problems often encountered in ready-to-drink formulations.[112] These advancements aid in resolving the drawbacks associated with conventional spray-drying techniques, often resulting degradation of heat-sensitive compounds such as polyphenols during processing and leading loss of their functional efficacy.

6 Applications of hybrid nano-encapsulation in functional foods

Hybrid nano-encapsulation systems, which synergistically combine natural polymers with synthetic nanomaterials, have emerged as versatile and effective platforms for enhancing the delivery, stability, and bioavailability of a wide array of bioactive compounds in functional foods (Table 3). Their design is often tailored to meet the unique physicochemical and biological challenges posed by different bioactive classes.

6.1 Hydrophobic antioxidants and polyphenols

Many potent antioxidants like curcumin, resveratrol, and various polyphenols suffer from poor water solubility, low bioavailability, and susceptibility to oxidative degradation. Hybrid nano-carriers such as PLGA nanoparticles coated with chitosan or alginate, enhance aqueous dispersion, provide physical and chemical protection, and enable controlled release. For example, curcumin-loaded PLGA nanoparticles prepared *via* nanoprecipitation demonstrate high encapsulation efficiency (∼70%), stable nanoscale size (<200 nm), and favorable surface charge, optimizing delivery in complex food matrices.[67] Such formulations enhance the functional performance of hydrophobic bioactives in food applications.[113]

6.2 Vitamins

Vitamins such as C and E are highly sensitive to heat, light, and oxygen, leading to significant nutrient loss during food processing and storage. Incorporation into hybrid systems comprising proteins (*e.g.*, whey, zein) and polysaccharides (*e.g.*, chitosan, alginate) affords physical barriers that preserve vitamin integrity, improving shelf life and potency retention.[65,103] These carriers also allow controlled release at targeted gastrointestinal sites, enhancing bioavailability in fortified foods and beverages.

6.3 Probiotics

Probiotic microorganisms face survival challenges during food processing and gastric transit. Hybrid encapsulation with natural polymers like chitosan combined with synthetic materials (*e.g.*, calcium phosphate) improves probiotic viability and facilitates targeted intestinal release. Such systems promote the development of innovative synbiotic foods through the co-encapsulation of probiotics and prebiotics, thereby enhancing gut health and colonization efficacy.[114,115]

6.4 Essential oils and volatile bioactives

Essential oils provide antimicrobial and antioxidant benefits but suffer from volatility, strong odors, and susceptibility to oxidation. Encapsulation within hybrid matrices such as chitosan–silica nanoparticles stabilizes these oils, masks off-flavors, and enables controlled release, expanding their application range in functional foods like cheeses and meats without compromising sensory quality.[115,116]

6.5 Peptides sand functional protein

Peptides and bioactive proteins are prone to enzymatic degradation and pH-induced denaturation in the digestive system. Hybrid composites such as zein–chitosan nanoparticles protect these biomolecules during gastrointestinal transit and enable controlled release, improving bioavailability and therapeutic efficacy while reducing dosing frequency.[101,117]

Hybrid nanoencapsulation can significantly extend the shelf life of perishable foods by integrating natural biopolymers and synthetic nanomaterials into protective delivery or coating systems. The hybrid nanostructures act as multifunctional barriers that limit oxygen and moisture diffusion, retard lipid oxidation, and inhibit enzymatic degradation of sensitive ingredients. Moreover, many hybrid matrices such as chitosan–zinc nanoparticle based coatings and cellulose nanofiber, nanoparticle composites, possess inherent antimicrobial and antioxidant properties that suppress microbial growth and oxidative spoilage. For example, chitosan/zinc complex nanoparticle based carboxymethyl cellulose coatings were shown to reduce weight loss, preserve acidity and ascorbic acid, and reduce microbial load in strawberries stored at both ambient and refrigerated temperatures.[119] Similarly, nanocellulose stabilised coatings with Ag NPs and thyme essential oil in konjac glucomannan matrices exhibited prolonged quality retention in fruit preservation trials.[120] In lipid-rich foods or oils, nano-encapsulation of plant phenolic antioxidants markedly improves oxidative stability, slowing rancidity.[121] In edible coatings for fresh produce, nanocellulose-based systems continue to show suppression of microbial/fungal decay, reduced weight loss, and delayed browning, thereby extending shelf life under storage.[122] Additionally, pH- or temperature-responsive hybrid capsules can release antimicrobial or antioxidant agents in response to early spoilage conditions, offering

Table 4 Examples of market available nanoencapsulation systems and their uses

Product/brand	Encapsulated bioactive compound	Nanoencapsulation system/technology	Functional application and key findings	Reference
Theracurmin®	Curcumin	Colloidal submicron curcumin dispersion prepared as a highly water-dispersible submicron particle formulation	In a double-blind, three-way crossover study in healthy adults, the Theracurmin® drinkable formulation produced markedly higher plasma curcumin concentrations than conventional curcumin, demonstrating substantially improved oral absorption for use in functional beverages and supplements	128
Meriva®	Curcumin	Curcumin is complexed with lecithin phospholipids to improve bioabsorption and prevent self-aggregation	In a 6 month supplementation study in chronic kidney disease patients, Meriva® significantly reduced circulating inflammatory mediators (*e.g.*, CCL-2, IFN-γ, IL-4) and lipid peroxidation, and was well tolerated with no reported adverse events. The product is marketed as a food-grade curcumin supplement	129
Longvida®	Curcumin	Solid Lipid Curcumin Particle (SLCP™) technology, where curcumin is embedded in a protective lipid matrix to enhance stability and absorption	Human and translational studies summarized in Pharmaceutics report that Longvida® increases levels of free (unconjugated) curcumin in plasma and has been investigated for anti-inflammatory and cognitive/neuroprotective benefits; animal studies also show delivery of free curcumin to brain tissue. The product is sold internationally as a nutraceutical ingredient	130
NovaSOL®	Curcumin	Liquid micellar curcumin formulation produced by Aquanova; curcumin is solubilized in amphiphilic micelles to create a highly dispersible oral liquid	In a controlled crossover trial in 23 healthy adults, this Aquanova liquid micelle formulation achieved ∼185-fold higher plasma curcumin AUC and >400-fold higher C_{max} compared with unformulated curcumin powder, supporting its use in high-bioavailability liquid nutraceuticals and softgels	130
BCM-95®	Curcuminoids + turmeric essential oils	A patented self-emulsifying curcumin–turmeric essential oil complex designed to improve curcumin absorption and metabolic stability using only turmeric-derived constituents	Clinical studies summarized in Pharmaceutics describe BCM-95®/Curcugreen™ as a commercially available curcumin formulation that yields several-fold higher plasma curcumin exposure than standard curcumin and demonstrates anti-inflammatory benefits in human use	131
Q10Vital®	Coenzyme Q10 (ubiquinone)			132

Table 4 (*Contd.*)

Product/brand	Encapsulated bioactive compound	Nanoencapsulation system/ technology	Functional application and key findings	Reference
		Water-soluble nano-dispersed syrup formulation; stabilized micellar CoQ10 system for enhanced solubility	In a randomized crossover study in healthy adults aged 65–74 years, single-dose ingestion of the syrup resulted in ∼2.4-fold higher bioavailability than standard crystalline CoQ10 capsules, with maintained redox stability and good tolerability	

dynamic protection and contributing to smart preservation. Collectively, these mechanisms not only improve the physicochemical stability of food components but also enhance microbial safety and extend the storage life of perishable food products without synthetic preservatives. In addition to that, the examples of market available nanoencapsulation systems for enhanced delivery of bioactives in functional foods and nutraceuticals are summarized in Table 4.

Bioactive compounds such as vitamins, polyphenols, and carotenoids play pivotal roles in preventing and managing chronic diseases including cancer, cardiovascular dysfunction, and neurodegenerative disorders.[123,124] Vitamins C and E, curcumin, resveratrol, and catechins exhibit potent antioxidant and anti-inflammatory actions that can mitigate oxidative stress and cellular damage key contributors to carcinogenesis and neuronal degeneration.[125,126] However, the clinical translation of these effects is limited by poor solubility, instability, and low bioavailability when administered in conventional forms. Advanced nanoencapsulation strategies enhance targeted delivery, stability, and bioefficacy of these bioactives, allowing them to act as adjuncts to conventional therapies. For instance, curcumin and resveratrol nanoformulations have demonstrated improved cytotoxicity against cancer cells and neuroprotective outcomes in Alzheimer's and Parkinson's models.[127] Thus, developing efficient nano-delivery systems for vitamins and phytochemicals can substantially strengthen supportive or preventive approaches in chronic disease management.

7 Sustainability and environmental impact of hybrid nanoencapsulation systems

Hybrid nanoencapsulation systems, which combine natural polymers with synthetic nanomaterials, present a sustainable alternative to conventional synthetic materials commonly used in food packaging and delivery. Unlike fossil-fuel-derived plastics, hybrids often utilize renewable, biodegradable components, reducing environmental persistence and ecological toxicity.[133] Recent reviews highlight that hybrid nanocomposites can achieve comparable or superior functional performance while offering improved biodegradability and reduced carbon footprint compared to traditional synthetic polymers.[134] This aligns with the growing consumer and industry demand for eco-friendly materials in functional foods.[135]

The incorporation of natural polymers such as proteins, polysaccharides, and biopolymers into nanoencapsulation matrices enhances biocompatibility and biodegradability. Gelatin-based nanocarriers and plant protein-based nano-delivery systems have demonstrated effective encapsulation and controlled release of bioactives with minimal toxicity concerns.[136] These hybrid systems leverage the amphiphilic and functional group diversity of natural polymers to stabilize bioactives while ensuring safe degradation in the environment and the human body.

Life cycle assessments of hybrid materials indicate a lower environmental impact relative to purely synthetic counterparts, especially when renewable feedstocks and green synthesis routes are employed.[137] However, challenges remain regarding the cost-effectiveness of large-scale production due to complex fabrication processes and material heterogeneity. Advances in process automation, green chemistry, and scalable nano-fabrication techniques are critical to reducing costs and improving commercial viability.

Future research is expected to focus on developing food-grade, biodegradable polyelectrolytes and integrating advanced manufacturing technologies such as microfluidics and 3D printing to enhance throughput and reproducibility. Additionally, regulatory frameworks and consumer education will play vital roles in the adoption of sustainable hybrid nanoencapsulation systems in the functional food industry.

In addition to environmental considerations, safety concerns related to the use of synthetic nanomaterials in food packaging also require careful evaluation. The main safety concern associated with synthetic nanomaterials in food packaging is the potential migration of nanoparticles or their ionic residues from the packaging matrix into food, leading to possible ingestion and bioaccumulation. Migration behaviour depends on particle size, surface charge, matrix compatibility, storage temperature, and the nature of the food.[138,139] Experimental studies confirm that TiO_2 nanoparticles can migrate under simulated food-contact conditions, while ZnO-based composites exhibit lower migration due to stronger polymer interactions.[140] Such migration can induce cytotoxicity and oxidative stress through the generation of reactive oxygen species (ROS), especially at high nanoparticle concentrations. To reduce migration, nanoparticles are increasingly embedded within natural biopolymer matrices such as chitosan, cellulose, and xanthan gum, which act as physical barriers and improve biocompatibility.[141] For instance, chitosan–ZnO and chitosan–xanthan nanocomposite films demonstrated strong antimicrobial activity with minimal nanoparticle release.[142] Comparative studies on nano- *vs.* micro-TiO_2 migration from chitosan films also showed significantly lower migration for nanoscale forms due to tighter matrix confinement.[143] Recent reviews emphasize that adopting hybrid and green-synthesized nanocomposites can improve safety, reduce environmental persistence, and maintain packaging performance.[140]

8 Regulatory landscape for hybrid nanomaterials in food applications

The increasing application of hybrid nanomaterials in food nanoencapsulation has created new opportunities for improving solubility, stability, and targeted delivery of bioactive compounds. These systems often combining natural biopolymers (*e.g.*, chitosan, alginate, starch) with synthetic nanocarriers (*e.g.*, PLGA, PEG, silica nanoparticles) pose unique regulatory challenges due to their complex composition and behavior in biological systems.[144,145] The EU-JRC (2012) report emphasizes that effective regulation of hybrid nanomaterials in food nanoencapsulation requires harmonized EU-OECD testing standards, safe-by-design principles, and integrated testing strategies combining *in vitro*, *in vivo*, and *in silico* models.[146] It highlights the importance of life-cycle-based risk assessment, standardized physicochemical characterization, and predictive modeling to evaluate toxicity, transformation, and exposure, ensuring that innovation in nanoencapsulation progresses alongside robust consumer protection and transparent nanosafety governance.[147]

The U.S. Food and Drug Administration (FDA) regulates nanoencapsulated food substances under existing laws, including the Federal Food, Drug, and Cosmetic Act. According to its Guidance for Industry (2014), FDA evaluates whether a product involves nanotechnology by considering: (1) if a material is engineered to have structures between 1–100 nm, or (2) if it exhibits dimension-dependent properties affecting biological performance. FDA applies a case-by-case, product-specific assessment focusing on safety, bioavailability, and public health implications, encouraging early industry consultation to address nanospecific behavior and ensure compliance with established safety standard.[148]

Within the European Union (EU), nanomaterials in food—including encapsulated nutrients and functional ingredients are regulated under Regulation (EU) 2015/2283 on *Novel Foods* and Regulation (EU) 1169/2011 on food information, which require premarket authorization and labeling of engineered nanomaterials.[149,150] The European Food Safety Authority (EFSA) provides comprehensive guidance (2021) specifying data requirements for nanoencapsulated food substances, such as physicochemical characterization, gastrointestinal degradation, and *in vitro* bioavailability testing. EFSA applies a case-by-case approach for complex or composite nanostructures, recommending integrated testing strategies combining *in vitro*, *in silico*, and *in vivo* methods to evaluate transformations during digestion.[151]

9 Challenges in hybrid nanoencapsulation

The integration of natural polymers with synthetic nanomaterials often leads to complex physicochemical interactions that can compromise the stability of hybrid systems. Phase separation, aggregation, and premature release of encapsulated bioactives may occur due to incompatibility between hydrophilic natural polymers and hydrophobic synthetic components or due to environmental stressors such as pH, ionic strength, and temperature fluctuations.[152] For example, polymeric nanoparticles may face aggregation-caused quenching effects that reduce functional stability and complicate *in vivo* tracking. Achieving a stable, homogeneous dispersion while preserving bioactivity requires precise control over surface chemistry and formulation parameters.[153]

Although hybrid systems generally exhibit improved biocompatibility compared to purely synthetic nanocarriers, concerns remain regarding potential cytotoxicity, immunogenicity, and long-term accumulation of inorganic nanomaterials such as gold, silver, or silica nanoparticles. The toxicity profile depends on particle size, shape, surface charge, and degradation products. Regulatory agencies demand comprehensive toxicological evaluations, including *in vitro* and *in vivo* studies, to ensure food safety and consumer protection.[154] Furthermore, the biological fate and clearance mechanisms of hybrid nanomaterials in the human body are not yet fully understood, complicating risk assessment.

Scaling up hybrid nanoencapsulation from laboratory to industrial production remains a significant bottleneck. Complex multi-step fabrication processes, such as layer-by-layer assembly or sol–gel synthesis, are often time-consuming and require precise environmental control, limiting throughput. Additionally, batch-to-batch variability in natural polymer sources and synthetic nanomaterial quality can affect product consistency. The lack of facile, reliable, and cost-effective manufacturing methods hinders commercialization. Emerging technologies like microfluidics, 3D printing, and automated layer deposition show promise but require further development for industrial application.[155] Effective application of hybrid nanoencapsulation in functional foods and biomedicine demands real-time monitoring of nanocarrier fate, stability, and release kinetics in complex biological environments. Current bioimaging techniques face limitations in resolution, sensitivity, and specificity, especially for hydrophobic or aggregated nanocarriers.

The introduction of novel hybrid nanomaterials into food systems requires navigating complex regulatory landscapes that vary globally. Regulatory frameworks are evolving to address nanoscale materials but often lack specific guidelines for hybrid systems combining natural and synthetic components. Transparency in safety data and clear labeling are essential to gain consumer trust. Moreover, consumer acceptance hinges on perceptions of naturalness, safety, and environmental impact, emphasizing the need for clean-label hybrid formulations and effective communication strategies. The fabrication of stable, reproducible hybrids at a large scale remains one of the most significant challenges in advancing the use of hybrid nanoencapsulation systems, particularly in applications for functional foods, nutraceuticals, and pharmaceuticals. While laboratory-scale experiments have shown promising results, scaling up these systems for industrial production introduces a range of complexities, including issues related to material compatibility, incompatibility between natural and synthetic components, control over biopolymer modification, process optimization, stability and shelf life regulatory compliance, cost and economic viability and consumer acceptance.

10 Future prospects and innovations

The horizon for hybrid nanoencapsulation in food science is defined by increasingly sophisticated architectures that marry the tunable chemistry of natural polymers with the robustness of inorganic nanomaterials. Future research will likely emphasize hierarchical nanoassemblies, for instance, multilayer core–shell constructs that incorporate sequential release triggers (*e.g.*, pH, enzymes, redox potential) to orchestrate site-specific delivery along the gastrointestinal tract. By leveraging advances in microfluidic synthesis and droplet templating, investigators can achieve unparalleled control over particle monodispersity, enabling predictable digestion kinetics and reproducible functional performance in complex food matrices.

In the food industry, the use of nanobiohybrid materials and composites as functional nanomaterials that interact with biological systems is rapidly developing with a focus on utilizing these materials to give increased antibacterial activity, better nutrition delivery, and longer shelf life to food products. Significant developments include the use of nanofibrillar proteins and nanocomposites to alter food texture and functionality, the incorporation of antimicrobial nanoparticles (such as silver or zinc oxide) to prevent microbial growth, and the nanoencapsulation of nutraceuticals to enhance bioavailability and controlled release. These developments provide scalable solutions for industrial applications while addressing important issues in nutrient delivery and food preservation.[156]

Concurrently, the integration of artificial intelligence and machine-learning algorithms offers a transformative route to accelerate formulation design. Predictive models trained on experimental databases of polymer–bioactive interactions will facilitate rapid screening of candidate materials, optimizing parameters such as encapsulation efficiency, particle stability, and release profiles without exhaustive empirical iteration. This data-driven paradigm will be particularly valuable for tailoring nanosystems to emerging bioactives, including plant-derived peptides, carotenoids, and probiotic consortia, whose behavior under nano-encapsulation remains underexplored.

On the packaging front, self-powered nanosensors that harvest energy from ambient light or thermal gradients are anticipated to underpin next-generation intelligent packaging solutions. Such devices could not only monitor spoilage markers in real time but also communicate status *via* wireless protocols, integrating seamlessly into Internet of Things (IoT) ecosystems for end-to-end supply-chain transparency. In parallel, the drive toward eco-friendly materials will catalyze the development of fully biodegradable nanohybrids that constructed from food grade biopolymers and naturally occurring clays that degrade harmlessly after use, closing the loop on circular economy objectives. Despite these exciting prospects, several critical barriers must be addressed to translate laboratory innovations into commercial reality. Scalability remains a formidable challenge; methods such as high pressure homogenization and spray drying must be adapted to preserve nanoscale features at industrial throughput. Likewise, rigorous toxicological and environmental impact assessments are essential to ensure the long term safety of ingested nanomaterials and their eventual release into ecosystems. Harmonized regulatory frameworks spanning nanoparticle characterization, migration testing, and labeling will be pivotal to foster consumer trust and to guide responsible commercialization.

Ultimately, the fusion of hybrid nanoencapsulation with personalized nutrition, smart packaging, and sustainable materials science promises a new era of functional foods that are precisely engineered, environmentally conscious, and seamlessly integrated into digital food-supply networks. As interdisciplinary collaborations deepen between food scientists, materials engineers, toxicologists, and data scientists, the next decade is likely to witness the emergence of bespoke nanoformulations that not only enhance nutrient delivery and preservation but also anticipate and adapt to consumer needs in real time. Food safety and quality control are being revolutionized by the combination of smart packaging and nanohybrids. Nanoscale biosensors and nanocomposites are currently used in smart packaging systems to track environmental conditions, identify microbial contamination, and offer real-time information on food freshness. These systems combine interactive features like color-changing indicators to notify stakeholders of weakened food quality, use embedded nanosensors to detect pathogens, gases, or spoilage indicators, and use nanocomposite materials for enhanced barrier qualities.[157] This multidimensional integration not only enhances food safety but also optimizes supply chain management, reduces waste, and improves consumer trust through transparent quality monitoring.[158]

The nanohybrid systems also offer a significant promise of covering global food security and health issues as their ability to extend shelf life, spoilage reduction, and ensuring food safety directly addresses food loss and waste, a major barrier to food security. These systems also combat malnutrition improving public health outcomes by enabling the targeted delivery of nutrients and functional ingredients.[159] Further, the antimicrobial and contaminant-detection capabilities of nanohybrid packaging reduce the risk of foodborne illnesses, supporting safer food distribution in both developed and developing regions.

Looking forward, several advancements are expected in the field of nanohybrid materials for food applications such as enhanced biosensors with greater sensitivity for detecting contaminants and markers of spoilage that are under development, leveraging advances in nanomaterial engineering. Sustainable materials, such as biodegradable nanocomposites, are gaining enhanced attention to address ecological concerns about nanoparticle migration.[160] Personalized nutrition systems using nanohybrids for customized nutrient delivery are being explored, with potential applications in managing dietary needs for specific populations. Additionally, regulatory frameworks are evolving to ensure the safe commercialization of these technologies, with ongoing research focused on mitigating risks associated with nanoparticle toxicity.

11 Conclusion

Hybrid nanoencapsulation heralds a new chapter in functional food design by seamlessly marrying the biocompatibility and responsiveness of natural polymers with the precision and robustness of synthetic nanomaterials. These hybrid constructs not only shield delicate vitamins, antioxidants and probiotics from harsh processing and digestive environments, but also enable programmable, stimuli-responsive release that maximizes bioefficacy at the right site and time. Cutting-edge fabrication methods, ranging from electrospinning and microfluidic templating to layer-by-layer assembly offer unprecedented control over particle size, surface chemistry and release dynamics, tailoring each delivery system to specific nutritional or sensory goals. Beyond ingredient protection, hybrid systems unlock transformative possibilities in smart packaging and personalized nutrition. Biodegradable nanocomposites and embedded nanosensors pave the way for real-time freshness monitoring, while AI-driven formulation platforms accelerate the discovery of bespoke nano-carriers for emerging bioactives. Yet, realizing this vision hinges on overcoming key hurdles: scalable manufacturing that preserves nanoscale fidelity, rigorous safety and environmental impact assessments, and clear regulatory pathways that inspire consumer confidence. By addressing these challenges through interdisciplinary collaboration uniting materials scientists, food technologists, toxicologists and data experts the hybrid nanoencapsulation paradigm is set to deliver next-generation functional foods that are not only more nutritious and stable, but also smarter, more sustainable and profoundly attuned to individual health needs.

Author contributions

Maheshika Sethunga: writing-original draft, visualization, conceptualization. S. C. Rangani: writing-original draft, visualization. Imalka Munaweera: conceptualization, supervision, visualization, writing-review and editing. K. K. D. S. Ranaweera: supervision, visualization, writing-review and editing.

Conflicts of interest

The authors declare that there is no conflict of interest.

Data availability

No primary research results, software or code have been included and no new data were generated or analysed as part of this review.

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