RESEARCH PAPER

Protein-Polysaccharide Complexes as Delivery Systems for Quercetin: Mechanisms, Microstructure, and Applications in High-Protein Beverages

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ABSTRACT

Quercetin is a dietary flavonol, which has been reported with antioxidants, anti-inflammatory and anti-cancer properties. In food application, its use is limited due to low aqueous solubility, susceptibility to thermal degradation and low bioavailability. To overcome these limitations, protein-polysaccharide complexes are a biocompatible, biodegradable and edible solution. This review summarises the available literature in this field but provides new information regarding the application of protein-polysaccharide complex to deliver quercetin in a new environment (high protein beverages) with physicochemical and sensory issues. Another significant contribution of this review is that it incorporates recent developments and highlights the need to translate molecular-level mechanisms of complex formation from bench research to food and nutrition innovation. Specifically, this review examines and systematically analyse the mechanisms for non-covalent complexation due to electrostatic, hydrogen bonding, and hydrophobic interactions, as well as covalent interactions (Maillard reactions, carbodiimide cross-linking and enzymatic complexation) and correlate these interactions with advanced microstructural characterisation methods on a molecular level. Thereafter, the review discusses how these interactions affect measurable functional properties such as encapsulation efficiency, loading capacity, stability, and bioavailability enhancement. Moreover, it compares various delivery architectures like nanoemulsions, Pickering emulsions, HIPEs and stimuli-responsive hydrogels to both technical and sensory constraints of high-protein beverages and contrasts their behaviours, particularly when using whey protein, and other polysaccharides. Finally, a detailed discussion of the barriers to scale up, batch consistency, cost-effectiveness and regulatory aspects of the industry and a summary of the emerging research areas such as advanced cross linking, personalised and stimuli responsive systems, sustainable green processing and clinical translation. Overall, this review shows that protein-polysaccharide complexes have great importance at the functional ingredient delivery and commercial beverage formulation interface. Thus, it proposes an innovation strategy that advances both scientific understanding and practical application.

Keywords: Quercetin delivery, protein-polysaccharide complexes, bioavailability, high-protein beverages, encapsulation efficiency, nanoparticles, emulsions, microstructure characterisation

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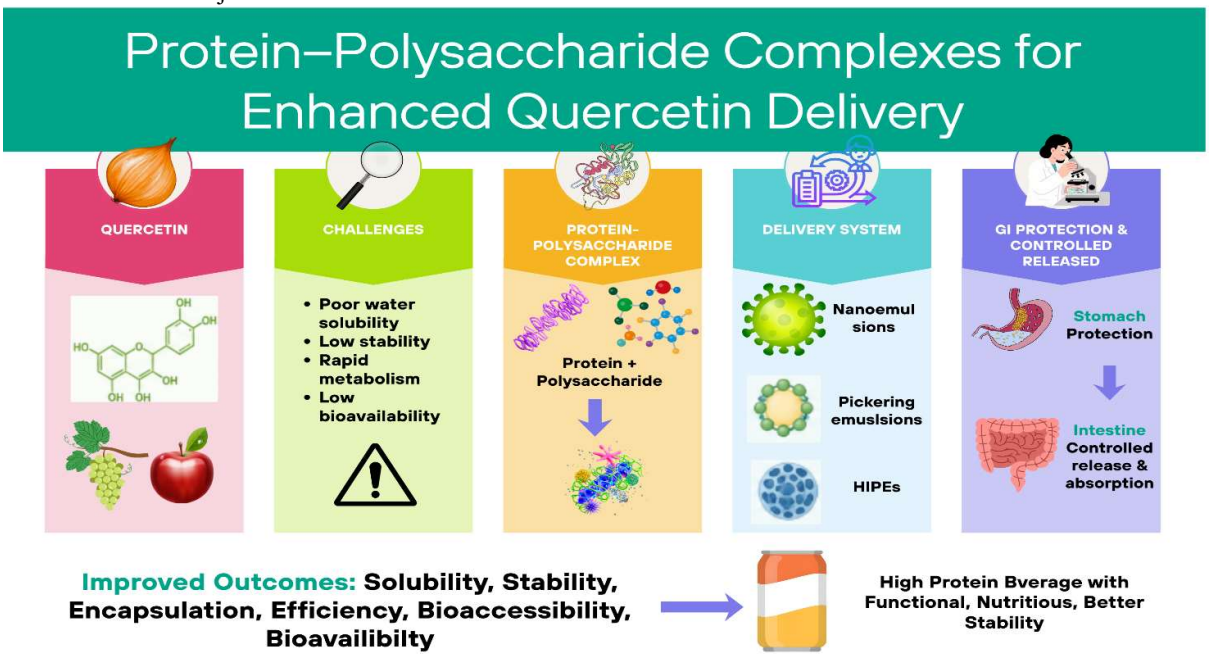

I. INTRODUCTION

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The global functional beverage market is currently undergoing a period of unprecedented expansion, driven by a projected compound annual growth rate of 7.5% as consumer preferences shift toward health-centric, nutrient-dense products (De La Fuente-Carmelino *et al.,* 2025; Gupta *et al.,* 2023). According to De La Fuente-Carmelino et al. (2025) and Kessler et al. (2019), this industrial evolution is a response to the wellness revolution, where consumers increasingly seek food products that provide physiological benefits beyond basic nutrition, such as immunomodulation, improved cognitive function, and chronic disease prevention. Within this dynamic landscape, high-protein beverages have emerged as a dominant segment, particularly those designed for muscle recovery, weight management, and healthy ageing. However, incorporating sensitive hydrophobic phytonutrients into aqueous, protein-rich beverages remain challenging because it can affect physical stability and sensory quality (Li *et al.,* 2025; Qu *et al.,* 2025; Xiao *et al.,* 2025).

Among the various bioactive compounds under investigation for beverage fortification, quercetin (3,3',4',5,7-pentahydroxyflavone) stands out as a molecule of significant therapeutic and commercial interest (Shabir *et al.,* 2022; Wang *et al.,* 2026). A common dietary flavonol found in onions, apples, and berries, is known for its wide range of health benefits. These include strong antioxidant effects, anti-inflammatory properties, as well as neuroprotective and anticancer activities (Aghababaei *et al.,* 2023; Lu *et al.,* 2026; Zhu *et al.* 2026). Although quercetin offers these benefits, its use in industry is limited by its natural physicochemical characteristics. Additionally, it falls under Class II of the Biopharmaceutical Classification System, indicating that while it readily passes through membranes, it has very poor solubility in water (Bai *et al.*, 2025; Kurniawan *et al.,* 2024). As reported by Bai et al. (2025) and Lai and Wong (2021), in native aqueous environments, quercetin exhibits negligible solubility, which leads to poor distribution and potential precipitation within beverage formulations.

In addition to poor initial solubility, quercetin is chemically unstable when exposed to typical food-processing and storage conditions (Zhao *et al.,* 2025). Also, the molecule's chemical structure, characterized by multiple hydroxyl groups, makes it highly susceptible to oxidative degradation, particularly when subjected to ultraviolet radiation, elevated processing temperatures (such as pasteurization or UHT treatments), and alkaline pH shifts (Zhu *et al.,* 2026). Due to its sensitivity, the beverage loses a significant portion of its original antioxidant strength before reaching the consumer, leading to a gap in stability. Furthermore, even when quercetin remains chemically stable, its pharmacokinetic behaviour presents another major hurdle because it undergoes extensive first-pass metabolism in the gastrointestinal tract and liver (Jihwaprani *et al.,* 2023). Consequently, oral absorption of free quercetin typically remains under 10%, which is insufficient to provide notable clinical benefits for humans (Jihwaprani *et al.,* 2023; Liu *et al.*, 2025). Thus, addressing this bioavailability hurdle is essential for the development of effective functional foods.

Quercetin fortification becomes even more challenging in high-protein beverages, which typically contain over twenty grams of protein per serving. In these dense biopolymer environments, non-specific protein-polyphenol interactions are common (Xiao *et al.,* 2025). As stated by Xiao et al. (2025) quercetin molecules bind to food proteins through a combination of hydrophobic effects and hydrogen bonding, which lead to the formation of insoluble protein-quercetin aggregates. Such interactions frequently result in undesirable turbidity, sedimentation, and a significant increase in astringency, all of which compromise the sensory profile and perceived quality of the beverage (Li *et al.,* 2025). This creates a critical shelf-life verses bioavailability challenge for the food industry: the high concentration of bioactive compounds required for health efficacy often destabilizes the food matrix (Qu *et al.,* 2025).

To address these combined solubility, stability, and bioavailability challenges, protein-polysaccharide complexes have emerged as a clean-label and biocompatible encapsulation strategy (Cao *et al.,* 2025; Qu *et al.,* 2025). Thus, by synergizing the unique functional properties of two distinct biopolymer classes, these systems provide a robust delivery vehicle for hydrophobic ligands. Proteins, such as whey protein isolate, soy protein isolate, or pea protein, provide excellent interfacial activity and the ability to form hydrophobic cores that can trap quercetin (Babu *et al.,* 2024; Guo *et al.,* 2025; Wang *et al.,* 2024). Meanwhile, polysaccharides, ranging from inulin and pectin to gellan and xanthan gums, provide steric and mechanical stabilization, creating a protective barrier against environmental stressors and preventing droplet coalescence (Babu *et al.,* 2024; Cao *et al.,* 2025; Umar et *al.,* 2025). At the molecular level, these systems are mainly stabilized by non-covalent interactions such as electrostatic attraction, hydrogen bonding, and hydrophobic interactions. These interactions can be adjusted by changing environmental factors like pH and ionic strength (Alrosan *et al.*, 2025; Wang, 2020; Zhong *et al.*, 2021). For instance, recent studies have demonstrated that the formation of whey protein isolate-inulin complex emulsions can increase the aqueous solubility of quercetin by an astounding 389-fold (Chen *et al.,* 2025).

In addition to non-covalent assembly, recent advancements in glycoprotein engineering through covalent conjugation have significantly improved the thermal resilience of these delivery systems (Sun et *al.,* 2022). From the findings of Cabrera-Ramírez et al. (2024) and Setiowati et al. (2020) Maillard-type conjugates, formed between food proteins and polysaccharides through dry-heat treatment, exhibit superior emulsifying performance and heat stability compared to their non-covalent counterparts. These conjugates are particularly relevant for beverages undergoing thermal sterilization, as they prevent the development of protein aggregates, and preserve the integrity of the encapsulated quercetin (Setiowati *et al.,*

2020). Furthermore, researchers are also considering alternative forms of emulsions, such as Pickering emulsions and High Internal Phase Emulsions (HIPEs), to deliver considerable amounts of quercetin successfully, and achieve a rich and creamy mouthfeel akin to fat (Du *et al.,* 2022; Yang *et al.,* 2024; Zhang *et al.,* 2025). Indicatively, the encapsulation efficiencies have been up to 98.19% with soy protein isolate-dextran HIPEs, which ensure the quercetin is not degraded in the rapid storage at 60°C (Du *et al.,* 2022).

The ultimate test of the effectiveness of such delivery systems is their action in gastrointestinal digestion (Brodkorb *et al.,* 2019). Du et al. (2022) and Herranz et al. (2018) through their standardized in vitro models of digestion, have shown how Protein-polysaccharide complex encapsulation confer protection to quercetin against the highly acidic conditions in the stomach, and release quercetin, specifically in the small intestines.

Li et al. (2022) have demonstrated methoxy nanocomplexes of pea protein to raise the bioaccessibility of quercetin at the baseline level up to over 60%. On the other hand, Wu et al. (2025) reported protein-nanofiber conjugates to possess bioaccessibility values of more than 43% which is a tremendous step in comparison to free quercetin. These enhanced gastrointestinal fate increases are linked to enhanced cellular uptake and biological functionality (Ayala-Fuentes *et al.,* 2023; Chen *et al.,* 2022).

Building on these developments, this review critically analyses protein-polysaccharide complexes as delivery vehicles specifically tailored for high-protein functional beverages. We consider the molecular mechanisms that determine the formation of these complexes and the fact that the more detailed description of microstructures can be utilized to create stable preparations. Finally, the review discusses how these systems improve quercetin solubility and bioavailability while addressing industrial challenges related to scale-up, sensory quality, and regulatory constraints. This review integrates the outputs of 2016-2026, thus outlining a strong guide on how to produce reliable, bioactive enhanced functional drinks. The main aim is to connect theory and practice, so that these new delivery systems can be smoothly adopted into large-scale food production.

PROTEIN-POLYSACCHARIDE COMPLEX FORMATION: PRINCIPLES AND MECHANISMS

After establishing the relevance of these systems for quercetin delivery, it is necessary to examine the molecular forces that govern protein-polysaccharide complex formation, structural integrity, colloidal stability, and delivery performance. These interactions are broadly categorised into non-covalent and covalent processes, with non-covalent forces, driven by environmental parameters such as pH and temperature being the primary mediators of spontaneous biopolymer assembly in encapsulation systems (Umar *et al.,* 2025; Wei and Huang, 2019).

A. Non-Covalent Interaction Mechanisms

1. **Electrostatic Interactions**

Electrostatic attraction is the predominant driving force for the complexation of proteins and polysaccharides (Sponton *et al.,* 2017). These interactions occur between the oppositely charged functional groups on the biopolymer backbones, specifically the cationic amino groups of proteins and the anionic carboxyl or sulphate groups of polysaccharides (Wang, 2020). As reported by Ribeiro et al. (2021) and Sponton et al. (2017), this process is extremely sensitive to environmental pH, which modulates the net charge of the biopolymers relative to the protein's isoelectric point (pI).

When the pH is set between the polysaccharide's characteristic level and the protein's isoelectric point, the protein gains an overall positive charge, while the anionic polysaccharide stays negatively charged (Sponton *et al*., 2017). Such complementarity in charge will lead to complex coacervation, a liquid-liquid separation of phases where biopolymers are neutralized aggregates dissociating with the aqueous phase (Sponton *et al.,* 2017; Zhang *et al.,* 2024). On the other hand, segregative phase separation takes place due to electrostatic repulsion when the biopolymers have similar net charge and share a pH value (Gentile, 2020; Sponton *et al.,* 2017). Figure 1 is a schematic representation of the electrostatic attraction, hydrogen bonding as well as hydrophobic interactions that take place during the formation of protein-polysaccharide complexes to encapsulate quercetin.

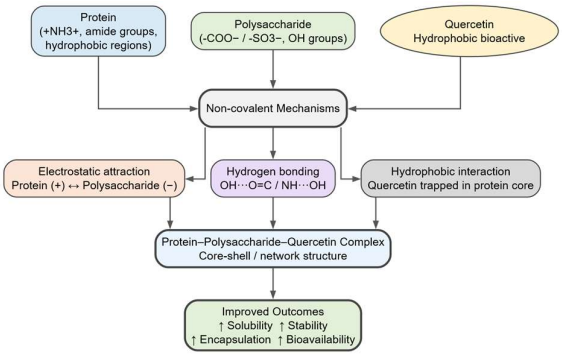

Figure 1. Schematic illustration of non-covalent mechanisms involved in protein-polysaccharide complex formation for quercetin encapsulation

2. Hydrogen Bonding

Hydrogen bonding is essential for the stabilization of internal matrix of biopolymer complexes and to reinforce their mechanical characteristics (Gentile, 2020). These are the interactions between the hydroxyl groups that contain large numbers of polysaccharide chains and the amide groups or polar side chains on the protein backbone (Liu *et al.,* 2023; Lv *et al.,* 2025). Alone, the hydrogen bonds are weak but when combined, they greatly increase the structural strength of delivery systems (Saleem *et al.,* 2025).

These interactions are verified by spectroscopic analysis with the Fourier Transform Infrared that shows typical

shifts in Amide I and Amide II bands (Liu *et al.,* 2026; Liu *et al.,* 2023). As stated by Lv et al. (2025) the three-dimensional network of whey protein-polysaccharide hydrogels is enhanced by hydrogen bonding, resulting in a dramatic increase in storage modulus (G'): pure protein gels have approximately 256.5 Pa, whereas composite systems can reach 7,500 Pa.

3. Hydrophobic Interactions

Hydrophobic interactions are thermodynamically controlled processes, which become relevant when non-polar amino acid residues (leucine, isoleucine, and phenylalanine) form clusters to reduce the interactions with water (Kazemi-Taskooh and Varidi, 2024). Such interactions are especially essential when it comes to the encapsulation of lipophilic ligands such as quercetin as they promote the development of a hydrophobic core in the protein-polysaccharide assembly (Du *et al.,* 2022; Umar *et al.,* 2025).

Isothermal Titration Calorimetry studies by Du et al. (2022) and Wang (2020) have demonstrated that hydrophobic interactions tend to dominate the complex formation of protein like soy protein isolate-dextran with positive enthalpy and entropy changes. Moreover, the inclusion of polysaccharides leads to protein unfolding, opening of internal hydrophobic patches and subsequent co-assembly of the biopolymers surrounding the hydrophobic bioactive compound (Kazemi-Taskooh and Varidi, 2024; Yang *et al.,* 2022).

B. Covalent Conjugation Mechanisms

While non-covalent interactions dominate spontaneous assembly, covalent conjugation provides greater resistance under harsh environmental conditions such as high ionic strength and thermal treatment (Akhtar and Ding, 2017; Yiasmin *et al.,* 2024). The most noticeable one is the Maillard reaction, a non-enzymatic glycation, in which the epsilon-amino groups of the protein lysine residues react with the reducing carbonyl groups of the polysaccharides under controlled dry-heat conditions (Setiowati *et al.,* 2020; Gentile, 2020).

These glycoproteins or covalent conjugates are better emulsifiers as long-range steric stabilisation is provided by the attached polysaccharide chains and the droplets do not form aggregates or merge even in unsuitable conditions (Setiowati *et al.,* 2020). Other covalent interactions, including enzymatic cross-linking (via transglutaminase) and chemical grafting (via carbodiimide chemistry), allow the control of structure closely. These methods have shown improvement of quercetin bioaccessibility, to a maximum of 43.65% (Sulaiman *et al.,* 2022; Wu *et al.,* 2025).

C. Factors Influencing Complex Formation

The binding and stability of protein-polysaccharide complexes are highly sensitive to the environmental and compositional factors. These aspects are essential to understand when it comes to making the shift between bench-top synthesis and the industrial implementation (Babu *et al.,* 2024; Gentile, 2020).

1. pH and Ionic Strength of the environment.

The pH of the environment has the largest influence on non-covalent complexation because it determines the ionization state of the biopolymers (Sponton *et al.,* 2017; Wang, 2020). Wang (2020), determine some important pH transition values: pHc (solvation of complexes), phi (coacervation of insoluble complexes), and pHd (dissolution of complexes). Although the pH-dependency can be exploited to release stimuli, this is a critical drawback to oral delivery vehicles, in which complexes tend to dissociate prematurely in the highly acidic gastric environment (Umar *et al.,* 2025; Wei and Huang 2019).

This stability is further complicated by ionic strength. Complexation can be promoted by low salt concentrations neutralizing superfluous surface charges, whereas the high ionic strengths (usually> 0.1M) screening the charges, and thus efficiently protecting the functional groups, so that electrostatic attraction is inhibited (Gentile, 2020; Wang, 2020). According to Akhtar and Ding (2017), this is a main weakness of non-covalent coacervates over covalent conjugates since the former are very susceptible to salt, thus not able to withstand a change in the surrounding electrolyte concentration.

2. Biopolymer Mixing Ratio and Concentration

The size and the net charge of particles are determined by the mass ratio of protein and polysaccharide (Wang, 2020). To obtain electrical neutrality, a perfect ratio is needed; excess of either of the biopolymers cause overcharging, which forms small, soluble complexes that cannot effectively encapsulate large loads of bioactive (Sponton *et al.,* 2017). Conversely, the ratios used inappropriately cause inappropriate flocculation, where a single chain of polysaccharide is bound to several protein molecules that result in large-scale aggregation and deposition. This downside has been turned into an advantage in more recent studies of high-internal-phase emulsions, which use high concentrations of soy protein-dextran complexes to create gel-like networks that can stabilise oil volume fractions up to 75% (Du *et al.,* 2022).

3. Thermal Processing and Order of Addition.

The thermodynamic equilibrium of the system will be influenced by temperature. Though mild heating might be beneficial in promoting hydrophobic interactions and protein unfolding, which are necessary to encapsulate lipophilic compounds such as quercetin, high heating may cause irreversible protein denaturation and undesired macro-aggregation (Du *et al.,* 2022; Kazemi-Taskooh and Varidi, 2024). The relatively recent controlled dry-heat treatment (the Maillard reaction) is, on the contrary, a relatively new process of covalent conjugate production (Setiowati *et al.,* 2020; Gentile, 2020). These glycoproteins are more thermostable; one is whey protein-polysaccharide conjugates which resist heating sterilisation grade and would otherwise cause pure protein emulsions to break up (Setiowati *et al.,* 2020).

4. Protein and Polysaccharide Molecular weight

The strength of interaction and the properties of the protein-polysaccharide complex is dependent on the molecular weight of both components. Generally, the higher the molecular weight of the polysaccharide, the

more stable the complexes will be, because higher avidity means that more binding sites will provide stronger overall complexes (Sun *et al.,* 2022). Likewise, the molecular weight of proteins affects the appearance of the hydrophobic surface and interaction capability, but too high molecular weight can compromise flexibility and adversely affect the complex microstructure (Cao *et al.,* 2020; Zhang *et al.,* 2022).

The protein-to-polysaccharide mass ratio is the most important factor in determining the composition of a complex, its particle size, surface charge, and encapsulation properties (Wang *et al.,* 2025). There are certain ratios which have been shown through systematic investigations to produce desired properties (Liu *et al.,* 2026).

II. MICROSTRUCTURE CHARACTERISATION OF PROTEIN-POLYSACCHARIDE-QUERCETIN COMPLEXES

Because delivery performance depends strongly on structure, protein-polysaccharide complexes must be examined across multiple scales, from molecular interactions between biopolymers to macroscopic colloidal morphology (Babu *et al.,* 2024; *Guo et al.,* 2025). The system of quercetin entrapment requires to be completely characterised by the complementary analytical methods to understand the mechanism of the system and to predict the stability of the system in complex food matrixes (Ren *et al.,* 2026).

A. **Morphological and Topographical Visualization**

These supramolecular assemblies can be directly observed by advanced microscopy, which provides direct evidence of the systems as delivery systems. The internal organisation of the complexes is revealed using Transmission Electron Microscopy (TEM) often with negative staining with phosphotungstic acid (0.5%) or uranyl acetate (2%) (Blancett *et al.,* 2017; Fang *et al.,* 2024). Protein-polysaccharide-quercetin systems usually exhibit a core-shell or layered structure; for example, quercetin-containing polymer nanoparticles with a three-layer structure have been developed by modifying the polymer nanoparticles with a polymer shell, with a core containing quercetin, and with a surface coating (Saha *et al.,* 2016).

Surface topography can be seen with the use of Scanning Electron Microscopy which complements findings. The drug loaded surface modified particles usually display a rough surface, which is a sign of the successful surface modification with the drug, quercetin, in this instance. Saha et al. (2016) reported that the sizes of these complexes vary greatly depending on the biopolymer ratio and preparation method: pea protein-mesquite gum complexes have hydrodynamic diameters of ~333 nm (Cuevas-Bernardino *et al.,* 2018), whereas zein-polysaccharide nanoparticles range from 165 to 463 nm (Yang *et al.,* 2022). SEM shows the presence of strong three-dimensional gel networks in extremely concentrated systems such as High-Internal-Phase Emulsions, which compartmentalize the oil droplets with high efficiency of quercetin encapsulation (98.19%) (Du *et al.,* 2022).

B. **Spectroscopic Fingerprinting and Molecular Interactions**

Molecular driving forces are studied by spectroscopic shifts, which are mainly due to hydrogen bonding, electrostatic attraction and hydrophobic interactions.

- FTIR Spectroscopy: Successful quercetin encapsulation is evidenced by the attenuation or shifting of characteristic bands, such as the quercetin hydroxyl group (3200–3600 cm^{-1}) and carbonyl group (1664 cm^{-1}) (Kurniawan *et al.,* 2025; Li *et al.* 2023). Protein secondary structural changes are tracked via shifts in the Amide I and Amide II regions (Liu *et al.,* 2023; Lv *et al.,* 2025). Simultaneous rheology-FTIR has recently enabled real-time monitoring of these transitions, revealing that hydrogen-bond reinforcement increases the storage modulus (G') of composite hydrogels from 256.5 Pa to over 7,500 Pa (Lv *et al.,* 2025).
- Fluorescence and UV-Vis: The intrinsic fluorescence of proteins (like tryptophan residues) is typically quenched upon binding with quercetin, allowing for the calculation of binding constants (Ka) and the number of binding sites (n) via Stern-Volmer analysis (Qiu *et al.,* 2023). For pea protein-quercetin complexes, binding constants have been reported at 25°C (Cuevas-Bernardino et al., 2018). Furthermore, UV-Vis spectroscopy reveals characteristic absorption bands at 257 nm and 373 nm for quercetin, with bathochromic shifts indicating the transition of the flavonol into a different chemical environment within the biopolymer matrix.

C. **Crystalline State and Thermodynamic Properties**

The solubility and bioaccessibility of quercetin in the complex are a major factor that depends on the physical form of quercetin. From the studies of Li et al. (2023) and Wang et al. (2020), the X-ray diffraction results clearly show that free quercetin shows strong crystalline diffraction peaks, while the encapsulated quercetin shown a completely. The change from a crystalline form to an amorphous state show that quercetin is uniformly dispersed at the molecular scale within the biopolymer matrix. This dispersion is of great significance for enhancing its dissolution in gastrointestinal fluids (Wang *et al.,* 2020; Zhou *et al.,* 2025).

These complexes are also evaluated for their thermal stability by Differential Scanning Calorimetry. Addition of polysaccharides such as inulin or dextran has been demonstrated to enhance protein denaturation temperature, for example, in a whey protein system, increasing it from 86.38 °C to 103.58 °C, which can help prevent the denaturation of the protein during high-temperature food processing processes such as pasteurization or UHT treatment (Chen *et al.,* 2025; Sun *et al.,* 2026).

D. **Colloidal Stability and Surface Charge**

The kinetic stability of the complexes is determined with Dynamic Light Scattering and Electrophoretic Light Scattering. One of the most important parameters to determine the electrostatic stability is the zeta potential: In the case of high absolute values of the zeta potential (-18 to -38 mV), the inter-particle repulsion is intense, and the bridging flocculation and sedimentation are averted (Yang *et al.* 2022). As an example, the zeta potential of SPI-dextran HIPEs is also -21.73 mV that enables it to stay stable in long-term storage as well as prevents the premature release of quercetin at varying ionic strengths (Du *et al.,* 2022).

IV. QUERCETIN ENCAPSULATION EFFICIENCY AND LOADING CAPACITY

Following structural characterization, encapsulation efficiency and loading capacity become key indicators of the practical performance of protein-polysaccharide delivery systems (Qiu *et al.,* 2023). Although high EE (>90) is often cited in optimized biopolymer systems, a high loading capacity (LC) is a key challenge since the binding sites of proteins backbones are finite and steric constraints are present in the polysaccharide network (Cuevas-Bernardino *et al.,* 2018; Wang *et al.,* 2020).

A. **Performance of Binary and Ternary Delivery Systems**

According to existing studies, binary protein-polysaccharide complexes have always shown a higher ability to sequester quercetin than single-protein carriers do (Wang *et al.,* 2020). When using zein-based delivery systems, dextran sulphate sodium (DSS) as a polysaccharide stabilizer was found to be very effective relative to zein alone (Wang *et al.,* 2020). For instance, as DSS concentration in a Zein-Quercetin-DSS system increased, the EE (at a 120:6:125 ratio) and the peak Loading Capacity (LC) (at a 120:6:75 ratio) started to increase to 72.59% and 3.15%, respectively (Wang *et al.,* 2020). This is credited to the establishment of a stronger complex that affords more hydrophobic pockets and electrostatic shielding, eliminating the untimely leakage of the flavonoid (Wang *et al.,* 2020).

Additionally, colloidal architectures in specialized designs have attained even greater efficiencies. Soy protein isolate-dextran complexes have an extraordinary EE of 98.19 ± 0.14% in the high- internal-phase emulsions (Du *et al.,* 2022). The systems take advantage of the development of a strong interfacial gel network that is effective in compartmentalizing lipophilic compounds and enhances bioaccessibility in an in vitro digestion (Du *et al.,* 2022). Likewise, oxidized fucoidan nanocomplexes of soybean protein isolate have attained EE of 94.80 percent, and a loading of 16.96 μg/mg, which is covalently bound through imine bonds between biopolymers, thus giving the complex improved structural integrity (Yang *et al.,* 2024).

B. **Thermodynamics of Binding and Molecular Limitations**

The thermodynamic affinity of quercetin and the protein component is the basic determinant of the loading capacity of these systems (Cuevas-Bernardino *et al.,* 2018). A flora of fluorescence quenching of pea protein isolate-mesquite gum complexes (PPI-MG) at pH 5.0 showed a high binding constant (Cuevas- Bernardino *et al.,* 2018). This high affinity also guarantees that the loss of the ligand of the nanocarrier is minimal with time (Ghayour *et al.,* 2018).

Nevertheless, one of the significant constraints is the number of binding sites (n) that was estimated to be 1.095 in the case of the PPI-MG system (Cuevas-Bernardino et al., 2018). This limitation is the reason why the LC generally levels off at low weight contents in most biopolymer structures (Cuevas-Bernardino *et al.,* 2018; Wang *et al.,* 2020). In addition, although proteins such as casein are intrinsically highly bound with quercetin, the payload retention might be delicate to the pH of the environment, leading to complex dissociation (Ghayour *et al.,* 2018).

C. Factors Influencing Encapsulation Success

A complex synergy of thermodynamic affinity, structural architecture and environmental constraints control the encapsulation of quercetin within protein-polysaccharide matrices. Recent discoveries synthesised show that even though high encapsulation efficiency is not uncommon, the efficiency of a delivery system measured by its stability and loading capacity is highly dependent on certain formulation parameters (Cuevas-Bernardino *et al.,* 2018; Du *et al.,* 2022; Wang *et al.,* 2020).

The mixing ratios and molecular interactions of biopolymers are studied in the first section.

EE and LC are largely dependent on the mass ratio of the protein and polysaccharide. It is repeatedly demonstrated that binary systems do a better job than single-protein carriers, offering a more robust protective shell and a larger number of binding sites (Wang *et al.,* 2020; Yang *et al.,* 2024). As an example, in zein-dextran sulphate sodium complexes, the EE increased significantly to a maximum of 72.59% with an increase in the DSS concentration, but the LC levelled off at 3.15% (Wang *et al.,* 2020). Likewise, when producing soybean protein isolate-oxidized fucoidan nanocomplexes, covalent imine bonds were formed between the biopolymers, leading to an exceptionally high EE of 94.80% and a loading amount of 16.96 mg of protein/mg (Yang *et al.,* 2024).

One of the trends that have been identified to be the most useful across the literature is the optimum ratio requirement; too much polysaccharide may cause the overcharging of the particles, giving rise to small, soluble complexes which might have reduced retention of the hydrophobic payload (Wang *et al.,* 2020). On the other hand, when there is inadequate polysaccharide, the bridging flocculation can be observed where the chain itself is attached to several protein molecules to result in macro-aggregation and lower the colloidal stability.

2. Thermodynamic Binding Affinity

The binding constant (Ka) and the number of binding sites (n) of quercetin to the biopolymer backbone restrict the basic success of quercetin sequestration (Cuevas-

Bernardino *et al.,* 2018). Cuevas- Bernardino et al. (2018) analysed pea protein isolate-mesquite gum complexes using fluorescence quenching and found a high binding affinity and quercetin tightly bound in the core. Nevertheless, the small population of binding sites is still a significant drawback towards high loading capacities in non-covalent systems (Cuevas-Bernardino *et al.,* 2018; Ghayour *et al.,* 2018).

3. Environmental and Structural Factors

- pH and Ionic Strength: Since most protein-polysaccharide complexes are driven by electrostatic forces, their success is intrinsically tied to the pH-pI relationship (Sponton *et al.,* 2017; Wang, 2020). While this allows for pH-triggered release, it can be a limitation for gastric stability, where low pH induce complex dissociation and premature leakage of quercetin (Ghayour *et al.,* 2018). Furthermore, high ionic strength cause charge screening, effectively neutralizing the attractive forces required for encapsulation (Wang, 2020).
- Colloidal Architecture: The transition from simple nanoparticles to more complex architectures like High-Internal-Phase Emulsions or Pickering emulsions represents a significant advancement (Du *et al.,* 2022; Yang *et al.,* 2024). HIPEs stabilised by SPI-dextran complexes have demonstrated an exceptional EE of 98.19%, leveraging a robust three-dimensional interfacial gel network that provides maximum protection against environmental stressors (Du *et al.,* 2022; Shen *et al.,* 2021).
- One of the important parameters in this context is Crystalline to Amorphous Transition: Physical condition of the payload. The XRD results of different systems (zein-DSS, SPI-fucoidan) show that the successful encapsulation of quercetin from its native crystalline to amorphous form. This molecular dispersion plays a key role in improving the solubility and bioaccessibility of the flavonoid in an aqueous food system (Wang *et al.,* 2020; Zhou *et al.,* 2025).

V. BIOAVAILABILITY AND IN VITRO DIGESTION STUDIES

However, its low aqueous solubility (< 10 µg/mL), chemical instability under physiological pH, and fast first-pass metabolism (Kurniawan *et al.,* 2025; Qiu *et al.,* 2023) limit the use of quercetin in clinical practice. To overcome these obstacles, protein-polysaccharide complexes are created to offer protection during stomach passage and promote micellarization within the small intestine (Chen *et al.,* 2025; Yang *et al.,* 2024). Schematic representation of the protection effect of quercetin in the gastric condition, the control release in the intestinal environment and its improvement of bioaccessibility and bioavailability Figure 2.

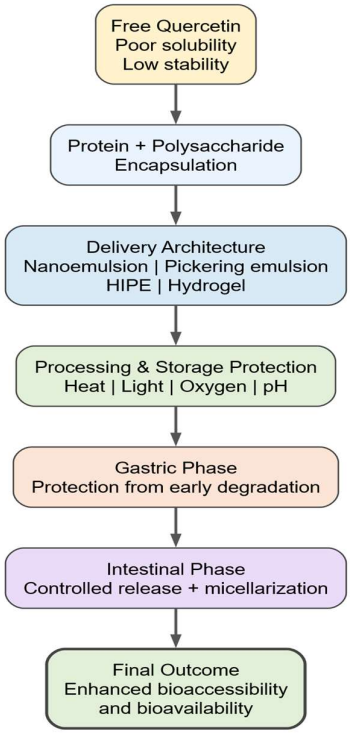

Figure 2. Mechanism of quercetin protection and release in protein polysaccharide delivery systems

A. Gastrointestinal Fate and Release Kinetics

The breakdown of these complexes usually consists of two steps in simulated gastrointestinal tract models:

1. **Gastric Phase:** Due to the presence of pepsin, protein-based carriers in the stomach (pH=2) can be proteolytically degraded (Chen *et al.,* 2025; Ghayour *et al.,* 2018). But the addition of polysaccharides such as pectin or dextran gives a sacrificial protective shell to slow the hydrolysis of protein (Du *et al.,* 2022; Kurniawan *et al.,* 2025). For instance, the pectin-based microspheres derived from peel of red dragon fruit have shown good resistance to the gastric conditions which resulted in the high percentage of quercetin being delivered to the intestinal phase (Kurniawan *et al.,* 2025).
2. **Intestinal Phase:** When the complexes arrive in the small intestine (pH 6.8-7.4), they come into contact with pancreatin and bile salts (Chen *et al.,* 2025; Wu *et al.,* 025). This may be because the dissociation of electrostatic complexes is promoted in the alkaline environment, and the presence of bile salts promotes the extraction of quercetin from the biopolymer matrix into the mixed micelles (Du *et al.,* 2022; Yang *et al.,* 2024). Covalently grafted systems like zein-cellulose nanofibers also have improved controlled release profiles over simple physical mixtures where a burst release may be observed for non-covalently coacervated systems (Wu *et al.,* 2025).

B. In Vitro Gastrointestinal Digestion Models in Food Science

To accurately predict the physiological fate of protein-polysaccharide-quercetin complexes, researchers use

standardised *in vitro* gastrointestinal models, most notably the INFOGEST static consensus protocol (Chen *et al.,* 2025). This sequential model simulates the oral, gastric, and intestinal phases by precisely controlling the pH, electrolyte concentration, and enzymatic activity of simulated digestive fluids (Chen *et al.,* 2025; Du *et al.,* 2022). During the gastric phase, the acidic environment (pH approx. 2.0) and pepsin activity evaluate the structural integrity of the biopolymer shell (Ghayour *et al.,* 2018). While proteins are susceptible to proteolysis, the presence of polysaccharides, such as pectin from red dragon fruit peel, creates a protective barrier that significantly reduces premature quercetin leakage, ensuring that most of the payload transitions into the small intestine (Kurniawan *et al.,* 2025).

C. Bioaccessibility Assessment

The transition from gastric stability to intestinal release marks the most critical stage of the delivery process: the assessment of bioaccessibility. Bioaccessibility is defined as the fraction of the total quercetin that is released from the food matrix into the aqueous micellar phase and is thus available for absorption (Du *et al.,* 2022; Yang *et al.,* 2024). This is typically quantified by centrifuging the intestinal digesta to isolate the micellar fraction, followed by HPLC or UV-Vis analysis (Du *et al.,* 2022; Wang *et al.,* 2020). High-internal-phase emulsions and Pickering emulsions have emerged as superior architectures in this regard; for example, soy protein isolate-dextran complexes have demonstrated an exceptional ability to facilitate quercetin micellarization, largely due to the high surface area of the stabilized lipid droplets which promotes efficient bile salt interaction (Du *et al.,* 2022; Li *et al.,* 2024). Consequently, bioaccessibility values in these optimized systems can reach 40% to 65%, a significant improvement over traditional delivery formats (Wu *et al.,* 2025; Yang *et al.,* 2024).

D. Comparison with Free Quercetin

To clarify the advantage of encapsulation, the performance of these delivery systems should be compared with free, unencapsulated quercetin. In its native crystalline form, free quercetin exhibits negligible aqueous solubility (< 10 μg/mL) and is highly susceptible to chemical degradation in the alkaline environment of the small intestine (Kurniawan *et al.,* 2025; Qiu *et al.,* 2023). During *in vitro* digestion, free quercetin often fails to achieve meaningful micellarization, resulting in bioaccessibility values that are often 3 to 5 times lower than those of encapsulated versions (Du *et al.,* 2022; Yang *et al.,* 2024). Furthermore, while free quercetin undergoes rapid autooxidation and structural modification at physiological pH, protein-polysaccharide complexes preserve its antioxidant capacity by providing a physically shielded environment (Liu *et al.,* 2023; Qiu *et al.,* 2023). This comparative advantage confirms that the biopolymer matrix not only serves as a vehicle for transport but also acts as a critical stabiliser that ensures the bioactive molecule remains chemically potent until it reaches the site of absorption (Ghayour *et al.,* 2018; Wang *et al.,* 2020).

VI. TYPES OF DELIVERY SYSTEMS FOR QUERCETIN IN HIGH-PROTEIN BEVERAGES

Multiple delivery system architectures can be constructed from protein-polysaccharide complexes for quercetin incorporation into high-protein beverages, each offering distinct advantages for specific food applications and processing requirements. Emulsion gel systems combining protein-polysaccharide complexes with strategic oil incorporation represent an innovative platform for food science applications, addressing the stability-versus-functionality trade-off central to commercial beverage formulation while enabling clean-label product development (Hashemi *et al.,* 2025). These systems demonstrate exceptional versatility in food processing, supporting applications ranging from traditional beverages to advanced 3D-printed functional foods (Farias *et al.,* 2025).

A. Emulsion-Based Systems

Emulsions represent the most widely applied delivery systems for lipophilic bioactive in commercial food and beverage applications, with protein-polysaccharide complexes serving as food-grade stabilizers to prevent droplet coalescence and improve long-term shelf-life stability (Li *et al.,* 2024). Natural fat-mimicry approaches using protein-polysaccharide composites successfully replicate the sensory and textural attributes of traditional fat-based formulations in food matrices while simultaneously providing enhanced bioactive protection (Zhang *et al.,* 2025). In the context of the food industry, these systems enable the development of reduced-fat or fat-free functional beverages that maintain consumer-acceptable mouthfeel and texture profiles (McClements, 2020).

Conventional Emulsions**:** Traditional oil-in-water (O/W) emulsions stabilized by protein- polysaccharide complexes offer well-established preparation methods, predictable stability, and consumer familiarity. These systems employ oil as a reservoir for quercetin solubilisation, with complex surfactants adsorbing at the oil-water interface to form protective interfacial films. According to Ai (2023) emulsion preparation can employ high-energy methods (high-speed homogenisation, sonication, microfluidization) or low-energy methods, with energy input level dramatically affecting particle size, stability, and encapsulation efficiency.

Nanoemulsions: Nanoemulsions, featuring droplet sizes below 200 nm, offer enhanced solubility, increased bioavailability, and superior long-term stability compared to conventional emulsions (Algahtani *et al.,* 2022). As reported by Ai (2023), the high interfacial area of nanoemulsions improves quercetin solubility and facilitate transepithelial transport via mechanisms such as lymphatic uptake or direct transcytosis of nano-sized lipid droplets. Advanced self-nanoemulsifying drug delivery systems (SNEDDS) demonstrate promise for quercetin, achieving 8-9-fold improvements in plasma bioavailability compared to

free quercetin through improved gastrointestinal solubility and reduced first-pass metabolism (Mathew and Varkey, 2022).

Pickering Emulsions: These are new emulsions in which the protein-polysaccharide complexes are used as the solid particle stabilizers. These particles are irreversibly strongly adsorbed at oil-water interfaces to create strong interfacial barriers against coalescence (Li *et al.*, 2024; Yang *et al.,* 2024). Emulsion type and stability are related to the three-phase contact angle of the particles that stabilise the emulsion, which have an optimum value of approximately 90° when the emulsion is an optimal Pickering emulsion (Li *et al.,* 2024). Hordein-whey protein isolate complexes were used to prepare Pickering emulsions, and the contact angles varied from 70.2°; the EE% (quercetin) of the Pickering emulsions was 97.8%, with the bioaccessibility of quercetin being 35% (compared to free quercetin) (Yang *et al.,* 2024).

The internal phase volume fraction of HIPEs is more than 70% (Bascuas *et al.,* 2021) and they are continuous gel-like networks (Bascuas et al., 2021) that provide excellent protection for oil-solubilized compounds (Zhu *et al.,* 2025). The HIPEs made using soy protein isolate-dextran complex-stabilized achieved 98.19±0.14% quercetin EE%, and the particles in the HIPEs were 3000.33±201.22 nm with -21.73±1.10 mV zeta potential (Du *et al.,* 2022). From the work of Du et al. (2022) in vitro digestion showed that the bioavailability of quercetin was higher, and the release of free fatty acid was significantly lower than that of the conventional emulsions, demonstrating the excellent protection for lipid and targeted small intestinal release of quercetin. The increased stability is due to the formation of a large network of proteins and polysaccharides that link many oil droplets together to create mechanical reinforcement which is resistant to coalescence during shear and thermal stress (Zhu *et al.,* 2025).

B. Hydrogel and Nanogel Systems

Protease-labile peptide linkages exploited to achieve temporal specificity for targeted bioactive delivery by designing enzyme-responsive hydrogels (Yang *et al.,* 2023). The caseinate-reinforced pectin hydrogels have been proven to be effective by hydrogen-bond reinforcement between caseinate and pectin, which not only ensures the highest efficiency in polyphenol encapsulation but also does not allow for any chemical modification during storage (Yang *et al.,* 2023).

Protein-polysaccharide complexes are also utilised in the development of hydrogels with tunable gelation properties, where the kinetics of quercetin release can be controlled, and maintained the integrity of the complexes during the storage process (Saleem *et al.,* 2025; Yang *et al.,* 2023).

The most significant among the hydrogels in this class are the whey protein-polysaccharide hydrogels, which are formed through the denaturation and aggregation of protein molecules when heated, and then hydrogen-bonded and hydrophobic interactions occur between these molecules and the polysaccharide molecules (Lv *et al.,* 2025). The storage moduli (G') of these hydrogels ranged from 100-10,000 Pa, depending on the type and concentration of polysaccharides, with Armillaria mellea polysaccharide-enhanced hydrogels demonstrating the highest mechanical properties (*Sun et al.,* 2026). The thermal analysis using DSC showed that incorporation of polysaccharides resulted in the increase of denaturation temperatures of the Armillaria mellea systems from 86.38°C to 103.58°C, which meant that the polysaccharides had high thermal stability and were suitable for high-temperature processing or long storage (Sun *et al.,* 2026).

Alginate-based nanogels prepared via ionic gelation with divalent cations (Ca^{2+}, Zn^{2+}) exhibit pH and enzyme-responsive release properties suitable for targeted intestinal delivery (Zhang *et al.,* 2021)

VI. TYPES OF DELIVERY SYSTEMS FOR QUERCETIN IN HIGH-PROTEIN BEVERAGES

Protein-polysaccharide complexes can be built for different delivery systems to incorporate quercetin in high protein beverages, with different properties for different food applications and processing needs. The emulsion gel system that combines protein-polysaccharide complexes with strategic oil incorporation is a novel matrix for food science applications, balancing between stability and functionality, and allows developing clean labelled products for commercial beverage formulations (Hashemi *et al.,* 2025). They illustrate high versatility in food processing, including the production of traditional beverages and the development of 3D printed food with functional properties (Farias *et al.,* 2025).

A. Emulsion-Based Systems

In commercial food and beverage products, emulsions are the most used delivery systems for lipophilic bioactive, while protein-polysaccharide complexes are food-grade stabilizers that prevent coalescence of droplets and ensure long-term stability of the product (Lavlinskaya *et al.,* 2024). According to Zhang et al. (2025) natural fat-mimicry methods based on protein-polysaccharide (PS) composites have proven to be effective in mimicking sensory and textural properties of the fat-based formulation in food matrices while also offering increased bioactive. In the food industry, these systems can be used for creating reduced-fat or fat-free functional beverages with acceptable mouthfeel and texture for consumers (Zhou and McClements, 2021).

Typical Emulsions: Oil-in-water (O/W) emulsions stabilized with protein-polysaccharide complexes have been known for a long time and have been prepared with proven technique, are relatively stable and consumer-friendly. These systems use oil as a reservoir for solubilisation of quercetin and complex surfactants with the ability for adsorption at the oil-water interface, producing a protecting interfacial film. Two types of emulsion preparation are possible: high-energy methods (high-speed homogenisation, sonication, microfluidisation) and low-energy methods, the energy input into which is a factor of vital importance for the

size and stability of particles and for the encapsulation efficiency (Ai, 2023).

Nanoemulsions: Nanoemulsions, which have a droplet size of less than 200 nm, have the advantage of higher solubility, improved bioavailability, and better stability than conventional emulsions (Algahtani *et al.,* 2022). The high interfacial area of these nanoemulsions contributes to its increased solubility of quercetin, which might enhance the transepithelial transport of the particles through other routes like the lymphatic uptake or the direct transcytosis of the lipid droplet of the size of nanometer (Ai, 2023). Much better gastrointestinal solubility and a lower first-pass metabolism have been shown to improve the plasma bioavailability of quercetin by 8-9-fold in advanced self- nanoemulsifying drug delivery systems (SNEDDS) (Mathew and Varkey, 2022).

Pickering Emulsions: The Pickering emulsions are based on a new idea; the colloidal particles themselves being used as stabilisers instead of molecular surfactants and using a protein-polysaccharide complex as the solid particle stabilizer. The irreversible adsorption of these particles at oil-water interfaces creates strong barriers at the interface, hindering coalescence (Li *et al.,* 2024; Yang *et al.,* 2024). Emulsion type and emulsion stability are defined by the three-phase contact angle of the stabilising particles, which is related to their wetting properties (Li *et al.,* 2024) contact angle with values around 90° results in optimal stability of Pickering emulsions. Hordein-whey protein isolate was able to stabilize Pickering emulsion at oil volume fraction up to 70% with 97.8% of quercetin EE% and significantly enhance 35% bioaccessibility compared to pure quercetin (Yang *et al.,* 2024).

High Internal Phase Emulsions (HIPEs): HIPEs with internal phase volume fractions higher than 70% (Bascuas *et al.,* 2021) provide continuous gel-like networks (Bascuas *et al.,* 2021) and have excellent protection for oil-solubilised compounds (Zhu *et al.,* 2025). The HIPEs with particles of 3000.33±201.22 nm yielded 98.19±0.14% quercetin EE% and had a negative zeta potential of -21.73±1.10 mV (Du *et al.,* 2022). From the research of Du et al. (2022) the bioavailability of quercetin and the amount of free fatty acid (FFA) in the digestive fluid was compared and the in vitro digestion showed that the bioaccessibility was better when using the emulsions compared to the conventional emulsions, while the amount of released FFA was significantly lower when using the in vitro digestion, suggesting exceptional lipid protection and targeted small intestinal release. The protein-polysaccharide network formation is more pronounced, which is responsible for the improved stability by creating a network of interlinked oil droplets that gives mechanical strength against coalescing during shear and thermal stresses (Zhu *et al.,* 2025).

B. Hydrogel and Nanogel

Protease-labile peptide linkages-based enzyme-responsive hydrogels achieve temporal specificity for targeted delivery of bioactive agents by responding to intestinal enzyme activity (Yang *et al.,* 2023). The caseinate-reinforced pectin hydrogels have shown potential because of the hydrogen-bond reinforcement of the protein and polysaccharide, which not only enhances polyphenol encapsulation efficiency but also prevents chemical modification during storage (Yang *et al.,* 2023).

Protein-polysaccharide complexes produce hydrogels with some benefits, such as tunable gelation, control of quercetin release kinetics, and the maintenance of the complex internal structure during storage (Saleem *et al.,* 2025; Yang *et al.,* 2023).

A significant type of hydrogels is the heat-induced whey protein-polysaccharide hydrogels where whey protein is denatured and aggregated by heat and linked to polysaccharides by hydrogen bonding and hydrophobic interaction (Lv *et al.,* 2025). Depending on polysaccharide types and concentrations, the storage moduli (G') of these hydrogels varied between 100 and 10,000 Pa, with Armillaria mellea polysaccharide-enhanced systems reaching their highest mechanical strength (Sun *et al.,* 2025). The thermal analysis by DSC showed that the incorporation of the polysaccharide increased the denaturation temperatures of the Armillaria mellea systems between 86.38°C and 103.58°C, indicating high thermal stability, which is suitable for high-temperature processes or long storage times (Sun *et al.,* 2025).

The alginate-based nanogels, formed by ionic gelation using divalent cations, such as Ca^{2+} and Zn^{2+}, are pH and enzyme responsive and can be used for targeted delivery into the intestine (Zhang *et al.,* 2021).

C. Case Studies: Whey Protein and Plant-Based Proteins

Whey Protein Systems in Food Applications.

Commercial functional beverages and food formulations include a high nutritional value whey protein isolate (Cava *et al.,* 2024). Bioactivity and direct applicability in food industry have been shown by whey protein-polysaccharide-quercetin complexes (Guo *et al.,* 2025). The Armillaria mellea in polymerized whey protein (PWP) could be applied as a hydrogel and used to produce bioactive food products like yogurt, fermented beverage, that had good thermal stability during food processing, mechanical gel properties and antioxidant activity (Sun *et al.,* 2025). PWP-polysaccharide systems were particularly noted to have improved sensory properties (creaminess and smoothness) of yogurt products and improved bioactivity (Lv *et al.,* 2025) in beverage processing applications. These systems are functional during normal food processing operations, for instance pasteurisation and homogenisation (Cui *et al.,* 2024).

Plant-Based Protein Systems in Food Formulations.

Plant proteins (soy, pea, corn zein) offer sustainable, cost-effective, and allergen-reducing alternatives to animal proteins for high- protein beverage development while maintaining superior functionality. Soy protein isolate (SPI)-xanthan gum complexes, prepared through

standard food processing techniques, formed stable Pickering emulsions with significantly enhanced quercetin bioaccessibility compared to SPI-alone formulations (Li *et al.,* 2024), demonstrating commercial feasibility. The synergistic combination of plant proteins enables the development of beverages with a complete amino acid profile while improving emulsion stability (Tong *et al.,* 2024). Corn zein, an industrially available alcohol-soluble prolamin protein, self-assembled into nanoparticles providing excellent hydrophobic bioactive encapsulation suitable for beverage manufacturing; zein-polysaccharide complexes achieved 92.8% quercetin encapsulation efficiency with anti-inflammatory activity superior to free quercetin, while maintaining food-grade safety status (Yang *et al.,* 2022). Advanced food processing methods, including high-pressure homogenisation, significantly enhance the functionality of plant protein-polysaccharide complexes in beverage systems (Qayum *et al.,* 2023).

D. Textural and Sensory Properties Improvement

Whey protein fibrils complexed with amphiphilic polysaccharides exhibit exceptional improvements in foaming capacity, with complex ratios optimized for egg white replacement in foam-dependent applications (Zhao *et al.,* 2025). These fibril-based systems achieve foaming performance that is equal to or superior to that of conventional systems (Zhao *et al.,* 2025).

Sensory acceptance critically determines beverage commercial success. Protein-polysaccharide-quercetin complexes improve mouthfeel through polysaccharide-thickening effects, creating a creamy texture without excessive viscosity or grittiness. In vivo sensory studies of protein-polysaccharide hydrogel-containing yogurts demonstrated significantly improved sensory attributes, including improved creaminess, smoothness, and overall liking scores (Sun *et al.,* 2025). Simultaneous rheology-FTIR analysis revealed direct correlations between molecular interactions (hydrogen bonding, electrostatic forces) and macroscopic textural properties, enabling rational design of beverages with targeted sensory profiles (Lv *et al.,* 2025).

E. Shelf-Life and Stability Considerations in Commercial Beverages

Beyond digestion performance, long-term shelf-life stability is also critical for commercial beverage development because it directly affects market viability and consumer acceptance. Protein polysaccharide complexes enhance quercetin stability through multiple complementary mechanisms in food matrices: physical isolation from dissolved oxygen through complex encapsulation, reduced light penetration due to opaque complex particles, and protection from endogenous hydrolytic and oxidative enzymes present in food systems (Cao *et al.,* 2025). Practical shelf-life extensions from 3-6 weeks for free quercetin-containing beverages to 6-12 months for protein-polysaccharide complex-stabilized beverages have been demonstrated in commercial food processing conditions (Du *et al.,* 2022). Storage stability at 4°C extends product viability, with minimal quercetin degradation observed over 3-month refrigerated storage periods (Chuo *et al.,* 2021). Critical for food industry adoption, accelerated stability testing conducted at 25°C (simulating distribution conditions) revealed that complex-stabilized quercetin exhibited significantly lower degradation rates (5-10% over 8 weeks) than free quercetin formulations (40-60% over 8 weeks; (Liu *et al.,* 2025). Advanced polysaccharide-based stabilization strategies, including polyphenol modifications and pH optimization during beverage formulation, further enhance protective effects (Cao *et al.,* 2021).

VII. Mechanisms of Quercetin Stabilization and Protection

Advanced protective strategies leverage multiscale structural design integrating molecular interactions with macro-scale fabrication architectures to achieve unprecedented quercetin stabilisation (Zhang *et al.,* 2025). These include protein-polysaccharide composite design approaches that mimic fat-related functionalities while providing bioactive protection through sophisticated interfacial engineering.

A. Protection Against Oxidative Degradation

Quercetin's multiple hydroxyl groups and conjugated aromatic system render it susceptible to oxidative degradation, particularly at elevated temperatures, high pH, or in the presence of pro-oxidative metal ions. Protein-polysaccharide complexes provide multi-layered oxidative protection. The hydrophilic polysaccharide shell creates a diffusion barrier limiting oxygen penetration to quercetin. Proteins containing sulphur amino acids (example, cysteine, methionine) that exhibit antioxidant capacity through their thiol groups; these amino acids preferentially react with ROS, sparing quercetin from oxidative attack (Xiao, 2022).

Polysaccharides themselves often possess intrinsic antioxidant capacity through phenolic acid constituents and reducing sugar residues, further contributing to overall system antioxidant performance. Studies of Armillaria mellea polysaccharide-whey protein complexes revealed that quercetin radical scavenging capacity (DPPH assay) increased from baseline to 75.40% after complex encapsulation (Sun *et al.,* 2025), suggesting synergistic antioxidant interactions among complex components.

B. Thermal Stability Enhancement

Quercetin exhibits thermal instability, with significant degradation occurring above 40°C, particularly in aqueous solutions. Free quercetin encapsulation in HIPEs or hydrogels reduces temperature-induced compartmentalization in hydrophobic domains or in hydrogel networks slows down the rate of degradation. When free quercetin and HIPE encapsulated quercetin were heated at 60°C for 30 minutes, respectively, the free

quercetin completely degraded, while HIPE encapsulated quercetin maintained the integrity of >70% (Du *et al.,* 2022). Increased thermal stability allows for beverage pasteurisation (usually 65-75°C) and is required to inactivate pathogenic microorganisms without reducing the activity of quercetin.

Additionally, polysaccharide-induced protein stabilisation protects quercetin by minimizing potential protein aggregation events which could lead to exposure or degradation of protected quercetin. For instance, Sun et al. (2025) studied whey protein-Armillaria mellea polysaccharide complexes and showed that the denaturation temperature rose from 86.38°C to 103.58°C when the polysaccharide was incorporated into the complexes, showing that the complexes possessed greater thermal stability with higher incorporation temperature and could withstand high-temperature processing without damage to quercetin.

C. pH and Ionic Strength Effects

The number of phenolic hydroxyl groups on the quercetin molecule have pKa values of 7.4-9.8; at a high pH (>7), the increase in ionization may favor hydrolysis or oxidation due to enhanced nucleophilicity. When pH is below 3, quercetin is protonated and in acidic aqueous solutions, it undergoes C-ring opening and degradation to smaller phenolic molecules. Quercetin is stabilized by protein-polysaccharide complexes via compartmentalisation over a wide range of pH's. The microenvironment is acting to buffer extremes of pH to which the quercetin is present in the hydrophobic protein domains.

The complex structure and the releasing rates of quercetin are modulated by the ionic strength. High ionic strength (0.1-0.5 M) favors weak electrostatic protein-polysaccharide interactions that result in thin interfacial layers and higher release of quercetin. At high ionic strength (0.1-0.5 M), strong electrostatic protein-polysaccharide interactions are formed, which lead to dense interfacial layers and lower release of quercetin. The ionic screening or electrostatic attraction is adequate at moderate ionic strength (0.15–0.3 M) but exceeds the attractive forces that are needed for stability. High ionic strength (>0.5 M) decreases the electrostatic interaction, lowering the complex stability and promoting the release of quercetin, which could be beneficial for the targeted delivery but not for the long-term storage (Zhong *et al.,* 2021).

D. Protection During Food Processing and Storage

Several processing operations such as homogenisation, heat treatment, ultrasonication and storage under different temperature and light conditions may affect the quercetin structure. Protein-polysaccharide complexes are also shown to be resilient during various processing steps (Xiao *et al.,* 2025). In complex formulations, minimal degradation of quercetin was observed during microfluidization up to 500bars. However, there was significant degradation in free quercetin formulations (Wu *et al.,* 2025). In the study, quercetin loss in SPI-dextran complexes was less than 5%, whereas it was between 25- 35% when the quercetin was free, after 30 minutes of homogenization at 12,000 rpm (Du *et al.,* 2022).

Another important storage risk is related to light exposure, where quercetin is found to be photodegradable due to direct absorption of UV-Vis photons. Opaque complex particles will decrease the passage of light and will decrease the amount of degradation of quercetin through the photo process. The photo-stability study under simulated sunlight revealed that the degradation of free quercetin was 60% after 48 hours; while HIPE-encapsulated quercetin had 10-15% degradation under the same conditions (Du *et al.,* 2022).

VII. Specific Protein-Polysaccharide Combinations for Quercetin Delivery

A. Soy Protein Isolate (SPI) with Various Polysaccharides.

The fungal polysaccharide extracted from commercially available fruiting bodies of Ganoderma lucidum and Auricularia auricula-judae is a promising alternative polysaccharide source which has improved emulsifying properties compared with traditional polysaccharide sources and synergy bio-functionality (Dai *et al.,* 2025). These systems are biocompatible and enhance the hydrophobic interaction, leading to the reduction of emulsion droplet size, and are suitable for the efficient encapsulation of quercetin.

The most economical and sustainable source of a complete protein profile (80% 7S and 11S globulins) is soy protein isolate. As a moderately hydrophobic compound, with high binding capacity and certified food grade, SPI can be used for the delivery of quercetin.

SPI-Dextran Systems.

Thermodynamic analysis shows that the $\Delta H > 0$ and $\Delta S > 0$ values indicate that the interaction between Dextran and SPI is dominated by hydrophobic interactions (Du et al., 2022). The SPI-dextran complexes are stable HIPEs which achieved 98.19% quercetin EE% and demonstrate excellent bioaccessibility, with minimal FFA release during the simulated digestion process (Du *et al.,* 2022). SPI-dextran system shows promise for use in beverages because it is tasteless, and because it can be used to enhance beverage texture, but with minimal water absorption (Du *et al.,* 2022).

SPI-Xanthan Gum Systems.

Xanthan gum, a microbial polysaccharide, interacts with SPI primarily through electrostaticattractionsbetweenanionicxanthangumcarboxylgroupsandcationicprotein regions (Nalewajski, 2020; Rahmati *et al.,* 2018). Pickering emulsions stabilized by SPI-xanthan gum complexes demonstrated superior quercetin bioaccessibility compared to SPI-alone controls, with enhanced performance attributed to improved interfacial organization and a thicker gel network (Li *et al.,* 2024).

SPI-Pectin Systems. Pectin, a complex polysaccharide rich in galacturonic acid, forms strong electrostatic complexes with SPI (Xie *et al.,* 2024). The combination

creates gel structures with intermediate moduli suitable for beverage applications (Xie *et al.,* 2024; Zhou *et al.,* 2026). SPI-pectin complexes stabilize high-internal-phase-emulsions while maintaining appropriate flow properties for beverages (Wen *et al.,* 2025).

B. Whey Protein with Polysaccharide Partners

Whey protein, which primarily contains β-lactoglobulin, α-lactalbumin, and lactoferrin, exhibits excellent emulsifying capacity and high nutritional value (Jovanović *et al.,* 2005; Kim *et al.,* 2002). The hydrophobic surface and ability to form stable interfacial films make whey protein an excellent choice for emulsion stabilization, and the stability of the emulsion can be further improved with a combination of polysaccharides, which also improves delivery of quercetin (Chen *et al.,* 2025; Chen *et al.,* 2018). Controlled protein denaturation and aggregation during thermal treatment of lactoferrin improves its functionality in ternary complexes without affecting the antioxidant and antimicrobial properties suitable for functional beverages (Zhou *et al.,* 2026).

Whey Protein-Hyaluronic Acid Systems. Among the anionic polymers, hyaluronic acid, a polymer of N-acetylglucosamine and glucuronic acid, can form electrostatic complexes with whey protein which exhibit good pH responsiveness. It has a pH of complete dissociation of 1.6-1.8 and forms a complex in the pH range of 4.4-4.6 which allows the pH triggered release for intestinal-targeted delivery (Zhong *et al.,* 2021). Rheological properties revealed that the WPI-HA complexes exhibited shear-thinning behaviour, and the elastic moduli indicated good gel network formation (Zhong *et al.,* 2021).

Whey Protein-Polysaccharide from Natural Sources. In recent studies, whey protein and polysaccharides from natural sources (Armillaria mellea, Polygonatum sibiricum, Grifola frondosa and Dendrobium officinale) were investigated where the protein-polysaccharide complexes showed greater functionality than the synthetic polysaccharides. These natural polysaccharides impart additional functionality (antioxidants, anti-inflammatory and immunomodulatory) and texture and physical stability. The thermal stability (its denaturation temperature) and antioxidant activity (DPPH scavenging activity) of PWP-Armillaria mellea polysaccharide complexes were of the order of 86.38°C and 37.73%, respectively (Sun *et al.,* 2025).

C. Plant-Based Proteins (Pea, Corn Zein) with Polysaccharides

Plant-based proteins offer sustainable, allergen-reduced alternatives increasingly desired by consumers. Emerging protein sources combine the sustainability advantages of plant proteins with enhanced polysaccharide functionality. Structural modification of plant proteins through pH shifting and heat treatment significantly enhances electrostatic complexation with polysaccharides by altering conformation, exposing tryptophan/tyrosine residues while maintaining protein ionization properties essential for complex formation (Zhang *et al.,* 2026).

Zein-Polysaccharide Systems. Corn zein, an alcohol-soluble prolamin protein, exhibits exceptional hydrophobicity, making it ideal for encapsulating hydrophobic bioactives. In polysaccharide combinations, including zein Mesona chinensis polysaccharide nanoparticles, achieved 92.8% quercetin EE% with excellent anti-inflammatory activity (Yang *et al.,* 2022). More advanced systems combining zein with cellulose nanofibers via covalent grafting achieved the highest reported quercetin bioaccessibility (43.65%) by leveraging the exceptional interfacial stability conferred by covalent conjugation (Wu *et al.,* 2025).

Pea Protein-Polysaccharide Systems. Pea protein isolates, sourced from legumes, offer a reasonable cost and a favourable nutritional profile. Pea protein-κ-carrageenan cold-set emulsion gels demonstrated enhanced water-holding capacity and mechanical properties with delayed lipid and protein hydrolysis during in vitro digestion (Zhang *et al.,* 2024).

D. Novel Protein Sources and their Combinations

Emerging protein sources, including camel whey proteins, sesame protein isolate, and others, are being explored for quercetin delivery. Two types of covalent conjugates (Camel whey protein-quercetin, WQ) and non-covalent complexes (Camel whey protein-starch, WQS) at micron and nano size, exhibited greater emulsion stability than the traditional formulations (Baba *et al.,* 2025). The coacervates of sesame protein isolate and Tragacanth gum exhibited strong gel-like structure at the optimum pH (5.0) and protein/polysaccharide ratio (5/1), implying that they may serve as bioactive encapsulants (Ghorbani *et al.,* 2025).

VIII. Antioxidant and Bioactive Properties

The combination of quercetin with proteins and polysaccharides results in a synergism, which means that the bioactive properties of the final formulation are greater than the sum of its individual parts, with complex molecular interactions that boost the antioxidant and functional effects of these components (Du *et al.,* 2026). The edible Pickering emulsifier effect of protein-polysaccharide-polyphenol ternary complexes is established by pH responsive assembly of natural byproducts; the complexes serve as delivery systems that are benign to the environment.

A. Antioxidant Capacity of Quercetin in Complexes

The antioxidant activity of quercetin, measured by DPPH radical scavenging, ABTS radical scavenging, ferric reducing antioxidant power (FRAP) and oxygen radical absorbance capacity (ORAC) is frequently enhanced after complex entrapment. This seemingly paradoxical improvement (because physical entrapment should not affect the intrinsic molecular antioxidant capacity) is due to several reasons: first, quercetin aggregation normally lowers the individual antioxidant potential and second, the molecules undergo fewer

damages molecule reactivity; enhanced accessibility of quercetin functional groups; and synergistic interactions with complex component antioxidants. Armillaria mellea polysaccharide-whey protein complexes containing quercetin demonstrated DPPH scavenging rates of 37.73% and ABTS scavenging rates of 75.40% (Sun *et al.,* 2025), exceeding the summed individual component contributions.

B. Anti-inflammatory Effects

Quercetin exhibits potent anti-inflammatory activity by suppressing pro-inflammatory cytokines and modulating signalling (Ahn *et al.,* 2020). Complex encapsulation often enhances anti-inflammatory effects compared to free quercetin (Yang *et al.,* 2022). Quercetin-loaded zein-Mesona chinensis nanoparticles significantly downregulated lipopolysaccharide-induced expression in macrophages with superior anti-inflammatory activity compared to free quercetin (Yang *et al.,* 2022). The mechanism involves enhanced cellular uptake and intracellular delivery of intact quercetin, permitting superior access to target signalling cascades.

C. Cellular Uptake and Bioactivity Enhancement

Endocytic uptake pathways involving clathrin and caveolin-mediated mechanisms are enhanced through protein-polysaccharide complex structuring, with evidence suggesting lymphatic uptake or direct transcytosis of nano-sized complexes bypasses first-pass metabolism for improved systemic availability (Hao *et al.,* 2026). Nano-sized systems (<200 nm) demonstrate particularly enhanced transcellular transport through intestinal epithelial barriers.

The bioavailability of bioactive compounds is an important factor that determines cellular uptake. Protein-protein complexes with polysaccharide-quercetin improve the uptake by cells through various mechanisms: a decrease in particle size, an increase in endocytotic capacity, a modification in the surface charge hydrophobicity which optimises membrane interactions, protein components as possible ligands for cellular uptake and polysaccharides as modulators of cellular internalisation pathways. Intestinal epithelial cell (Caco-2) monolayer studies have consistently shown that complex increases the accumulation of quercetin in cells by 2-3-fold relative to free quercetin in cells, indicating a gain in cellular accessibility (Ayala-Fuentes *et al.,* 2023).

D. Synergistic Effects with Other Bioactives

The use of quercetin loaded complexes in the formulation of multicomponent functional beverages, in combination with other bioactives such as Vitamin C, Vitamin E, polyphenols from tea/coffee, carotenoids,may lead to the presence of bioactive synergisms. The synergistic co-encapsulation of curcumin and quercetin in casein nanoparticles demonstrated a significant increase in quercetin bioaccessibility, reaching up to 53% compared to formulations with curcumin alone, indicating that structurally distinct polyphenols might benefit from each other's protective effects and potentially different metabolism, highlighting a potential for greater stability and bioavailability when combined (Li, 2026).

VIII. Challenges and Limitations

Despite the advantages of protein-polysaccharide systems, several limitations remain, and emerging alternatives such as metal-organic frameworks and graphene derivatives have been explored to overcome some drawbacks of traditional polymer-based nutraceutical delivery systems (Senanayake and Munaweera, 2025). These advanced nanomaterials, however, have their own specific advantages such as stimulus responsive release and inherent antimicrobial activity, but there are major scientific challenges that need to be addressed before they can be used. In particular, regulatory guidance for using these materials is scarce, and the long-term toxicological effects of these materials are poorly understood (Senanayake and Munaweera, 2025). The available literature underscores the need for further critical research, including chronic toxicity, bioaccumulation potential, environmental fate and biocompatibility, to ensure their safety in the context of their incorporation into food systems. However, the potential for using these nanomaterials in the manufacture of commercial nutraceutical and food products is uncertain due to the lack of systematic risk assessment and regulation specifically designed for such nanomaterials.

A. Manufacturing Scale-Up Issues in Food Production

Protein-polysaccharide-quercetin complexes exhibit excellent functionality, but their commercial use in the food and beverage sector is still technically and economically challenging (Cao *et al.,* 2025). Some key food-industry specific matters are:

Batch-to-Batch Consistency.

The sources of natural proteins/ polysaccharides vary in composition in each batch and with the supplier, leading to unpredictable delivery of bioactives and complex formation (Cao *et al.,* 2025). The Standardization processes involve protein characterisation, polysaccharide molecular weight/composition check and specification of the complex properties along the entire supply chain, which lead to manufacturing costs.

Processing Equipment Compatibility. Advanced microfluidization and ultrasonication methods of preparation are the best methods of forming a complex but require capital intensive equipment. To scale these processes to bench-top instruments (processing volumes of 10-100 mL) to pilot-scale (1-10 L) or industrial scale (100-1000 L) instruments requires engineering challenges, such as heat generation, energy efficiency, and ensuring uniform mixing.

Consistency of Particle Size and Encapsulation. To realize narrow particle size distributions and reproducible encapsulation efficiencies in large scale batches of production, multiple variables need to be tightly controlled: pH, temperature, mixing rate,

surfactant concentration and order of addition. Any variation in any parameter will lead to distorted outcomes and will require advanced process control mechanisms and real-time monitoring functionalities.

B. Batch-to-Batch Variability

In addition to the variability of raw materials, the parameters of the manufacturing process also have a significant impact on the final product properties, a change of 5-15 percent in encapsulation efficiency due to a change in pH by 0.3 units or more (Liu *et al.,* 2025). The changes in temperature within the range of 2 °C alter the strength of protein-polysaccharide interactions and hydrophobic interactions and influence the degree of complex formation (Wang, 2020). Varying mixing speeds lead to changes in particle size; e.g., doubling homogenization speed (10,000 to 15,000 rpm) can decrease particle size (500 nm to 250 nm) to change bioavailability and shelf-life stability (An *et al.,* 2023).

C. Cost-Effectiveness Considerations in Food Markets

However, the market penetration of protein-polysaccharide-quercetin complexes is still restricted because of the relative higher cost, which does not occur in the more price-sensitive market segments of the beverage industry where the market demand of functional components is still low (Jiang *et al.,* 2023). Technological maturation, growing competition among suppliers and manufacturing automation are slowly helping to drive costs down in the food industry, but the price premium is offsetting the costs and is currently in the range of 100-200%.

D. Regulatory and Safety Concerns

New food delivery systems are not well established in many places and are shrouded in uncertainty about their commercialization timelines and compliance requirements. Some of the key challenges in regulation are:

Novel Food Classification

The protein source, polysaccharide source, and methods of preparation may lead to new food regulations that require extensive safety studies, efficacy testing, and toxicity testing (Cao *et al.,* 2025). Interspecific commercialization is complicated by the different novel food regulatory requirements in different regions (EU, USA, China).

Allergenicity Assessment

Processing (heating, enzymatic, chemical) may change the protein structure and consequently its allergenicity (Deng *et al.,* 2026; Rahaman *et al.,* 2016). The allergenicity assessment should be comprehensive, which involves purified protein characterization, epitope mapping and animal allergy model these are significant time and cost investments (Zhou *et al*., 2021; Zhou *et al.,* 2025).

Labelling and Claims Substantiation

There is a need for clinical study support for health claims for quercetin bioavailability. The majority of the areas need human intervention studies with controlled bioavailability improvement and/or bioactivity enhancement and/or health effects better than controls (Laville *et al.,* 2017).

E. Long-Term Stability and Storage

Whereas protein-polysaccharide-quercetin complexes can be more stable than free quercetin, they might be susceptible to degradation during prolonged storage or under unsuitable conditions:

Protein Oxidation and Cross-linking

Protein oxidation occurs with extended storage, especially at higher temperatures (>20°C) or in the presence of oxygen, due to modification of residues (methionine to methionine sulfoxide, cysteine to disulfide formation). The reactions change the structure of proteins which may result in the release of encapsulated quercetin or formation of protein-quercetin complexes with new functionality due to protein oxidation.

Polysaccharide Degradation

Polysaccharides may be degraded by microbial contamination or by endogenous plant enzymes, as well as any bacterial enzymes, during prolonged storage leading to the loss of complexes. Additions of preservatives (sodium benzoate, potassium sorbate) can be used to stop microbial degradation but can also lead to the addition of preservatives which may clash with clean label preferences.

Quercetin Crystallization.

Prolonged storage may allow quercetin to crystallize in complexes, decreasing absorption by changing the structure from an amorphous to a more crystalline state which has less aqueous solubility. Prevention strategies are low storage temperatures (4°C), moisture control, and removal of oxygen via nitrogen flushing.

IX. Future Perspectives and Emerging Technologies

A. Advanced Cross-linking Strategies

Future research may benefit from advanced cross-linking techniques that improve complex stability, provide controlled release, and enhance quercetin protection. Precision engineering of particle size, surface properties and stimulus-responsiveness is achieved by multi-layer electrostatic self-assembly (ESA) of oppositely charged polyelectrolytes with 94.5% encapsulation efficiency and significant bioaccessibility enhancement during simulated digestion (Wang *et al.,* 2025).

Click Chemistry Cross-linking.

The specificity, reaction yield, and mild reaction conditions of click chemistry reactions (Huisgen cycloaddition, thiol-ene reactions) facilitates the formation of well-defined covalent conjugates without causing denaturation of proteins or degradation of

quercetin (Cao *et al.,* 2025). By conjugating a polysaccharide-azide group and alkyne-modified proteins or the other way around, covalent networks with known structures are formed, allowing the rational design of quercetin-loaded complexes with ideal characteristics (Xiao, 2019; Zhou *et al.,* 2025).

Enzymatic Cross-linking

Transglutaminase-catalyzed ε-(γ-glutamyl) lysine cross-linking offers clean, food-grade alternatives to chemical cross-linking while permitting enzyme-degradation through catalysis during digestion to release under control (Yan *et al.,* 2023). Integrating enzymatic cross-linking with chemical modification of polysaccharides (such as coupling through oxidation) forms hybrid approaches that exploit the strengths of each method.

B. Stimuli-Responsive Delivery Systems

Continuing the trends, the focus of developments in the future is on the delivery systems which are responsive to physiological stimuli (pH, enzymes, redox conditions) and allow targeted release of quercetin at the locations in the gastrointestinal tract (Yan *et al.,* 2023).

pH-Responsive Systems. Designing complexes with dissolution pH-thresholds enables gastric protection with intestinal release. Incorporating acid-labile linkages (acetal bonds, acetals) or employing polysaccharides with pH-dependent ionization (e.g., alginate with pKa ~3.5) creates systems releasing quercetin at intestinal pH (>6) while remaining intact at gastric pH (<2) (Lu *et al.,* 2026). Such systems may improve quercetin bioavailability by minimising gastric degradation and optimizing small intestinal residence time (Kurniawan *et al.,* 2025; Lee *et al.,* 2017).

Enzyme-Responsive Systems.

Incorporating protease-labile peptide linkers between proteins/polysaccharides and quercetin enables release triggered by intestinal proteases. Similarly, polysaccharides susceptible to α- amylase or β-glucosidase enable carbohydrate-enzyme-triggered release at specific colonic sites where particular microbial enzyme populations predominate. Such approaches may enable prebiotic benefits through enzyme-responsive quercetin delivery, promoting beneficial microbiota.

Redox-Responsive Systems.

Incorporating disulfide bonds between proteins/polysaccharides and quercetin creates systems that respond to reducing environments (enhanced in cancer cells, inflamed tissues, and reduced intestinal epithelium). Redox-triggered release enables preferential accumulation of quercetin in target tissues, potentially enhancing therapeutic effects in disease-specific applications.

C. Personalized Nutrition Applications:

Coffee and tea polyphenol co-administration with quercetin demonstrates synergistic antioxidant interactions through complementary radical scavenging mechanisms and altered metabolism patterns (Shang and Hu, 2025). These multi-compound delivery approaches enable optimisation of individual phenolic compound bioavailability while reducing effective dosages required for therapeutic benefit.

Emerging personalized nutrition paradigms leverage individual genetic, microbiota, and metabolic characteristics to tailor supplement formulations, optimising bioavailability, and efficacy for specific individuals.

Microbiota-Responsive Systems.

Individual variations in intestinal microbiota composition (particularly the Firmicutes/Bacteroidetes ratio and the abundance of Faecali bacterium/Roseburia) influence polysaccharide fermentation and metabolite production. Prebiotic effects could be optimized by designing complex polysaccharide components that align with the fermentation and short-chain fatty acid production capabilities of individual microbiota to optimize prebiotic effects and enhance quercetin bioavailability.

Genetic Polymorphism Adaptation.

The metabolism of quercetin entails cytochrome P450 enzymes (specifically CYP3A4) and sulfotransferases with genetic polymorphisms influencing metabolic ability. Individualised recipes might be used to categorise the consumers into metabolic groups to maximise the results (Ghareeb *et al.,* 2024; Jihwaprani *et al.,* 2023).

D. Sustainability and Green Processing in Food Manufacturing

The ecological sustainability and clean-label consumer needs are behind the creation of sustainable and green technology-based food-grade complex preparation processes (Guo *et al.,* 2024).

Supercritical Fluid Processing. Supercritical CO_2 and other green solvents clean the extraction of quercetin out of the plant sources as well as aiding the formation of protein- polysaccharide-quercetin complex under mild conditions. These methods prevent organic solvent contamination, lessen energy consumption and cut down on the environmental impact than conventional antisolvent precipitation processes (Campone *et al.,* 2018; Zêzere *et al.,* 2021).

Enzymatic Preparation Methods. Enzyme-catalysed protein-polysaccharide cross-linking and quercetin incorporation reduce the need for chemical reagents and generate biodegradable products. Laccase-catalysed oxidative polymerisation and transglutaminase-catalysed cross- linking represent clean technology alternatives to EDC/NHS chemical cross-linking (Alavarse *et al.,* 2022; Heck *et al.,* 2012).

E. Clinical Translation Opportunities

Translation of protein-polysaccharide-quercetin complexes from food applications to pharmaceutical/nutraceutical markets requires a comprehensive clinical evaluation demonstrating bioavailability enhancement and health benefits

superior to free quercetin or standard pharmaceutical alternatives.

Obesity/Metabolic Syndrome. Quercetin demonstrates anti-obesity activity by activating AMPK and promoting white adipose-to-brown adipose tissue conversion (Jiang *et al.,* 2020; Zhang *et al.,* 2019). Complex encapsulation enhancing quercetin bioavailability could improve efficacy in weight management applications. Phase II clinical trials assessing the effects of complex-delivered quercetin on body composition, lipid profiles, and insulin sensitivity represent important near-term opportunities.

Cardiovascular Disease Prevention. Quercetin's capacity to enhance vascular endothelial function and its potential to stabilize atherosclerotic plaques suggest cardioprotective effects (Ermawan *et al.,* 2025; Qian *et al.,* 2023). Clinical trials evaluating the effects of quercetin complex on endothelial function (flow-mediated vasodilation), inflammatory markers (hsCRP, IL-6), and cardiovascular event rates could establish clinical utility and justify pharmaceutical marketing.

X. Conclusion

Overall, the reviewed literature suggests that protein-polysaccharide complexes provide an effective approach for enhancing quercetin delivery in high-protein beverage systems, which can always be encapsulated with percentages of 90 and above and increase bioaccessibility up to 30-55 percent, as opposed to 10-20 percent of free quercetin. Such systems also provide significant enhancements in thermal and oxidative stability which is in line with commercial beverage processing and storage specifications. These complexes offer a synergistically optimised delivery platform, by incorporating the emulsifying, ligand-binding, and thickening properties of proteins with the stabilizing, texturising and prebiotic properties of polysaccharides. Therefore, this method is not only a solution to the low bioavailability of quercetin, but also the practical and technological needs of quercetin as a high-protein beverage.

Use in high-protein drinks presents a direct response to huge commercial market needs of functional foods that promote health and wellness without compromising on consumer demands of natural, clean-label ingredients and sustainable production methods. Currently, whey protein-polysaccharide systems are prevailing in commercial uses of beverages because of a well-established food-grade status and demonstrated compatibility with manufacturing, whereas new plant-based protein systems are sustainable, allergen-reducing alternatives that are environmentally friendly and may be used to broaden market segments. Plant-based emulsion gels have been accepted by the food industry as an option to existing fat-based emulsions, moving the industry towards healthier product options. Future studies ought to focus on how to maximise the formulation parameters of various sources of proteins and polysaccharides, the long-term stability of bioactive quercetin under real world storing and processing conditions and the development of personalised delivery systems that can be altered to personalised nutrition. Therefore, rigorous clinical trials and consumer research are needed to support health-related claims and ensure broader acceptance. To handle these research priorities, there is need to have a multidisciplinary approach that involves food scientists, protein chemists, clinicians, and sensory experts to come up with holistic solutions to high-protein beverage innovation.

Protein-polysaccharide-quercetin complexes therefore represent promising nutraceutical and functional food ingredients for improving quercetin bioavailability in health-oriented beverages.

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