THE PARALLEL LIVES OF POLYSACCHARIDES IN FOOD AND PHARMACEUTICAL FORMULATIONS

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Abstract

The present opinion article discusses how polysaccharide structures can be used in both food and pharmaceutical formulations. We distinguish two regions depending on moisture content where polysaccharides form structures with distinct functional properties. Some trends in key areas of active research are assessed and in particular edible films, encapsulation, polycrystalline polysaccharides, protein-polysaccharide coacervation and fluid gels. We unveil that the physicochemical principles that are shared across the food and pharmaceutical disciplines provide a great opportunity for cross-disciplinary collaboration. We finally argue that such co-operation will help tackling polysaccharide functionality issues that are encountered in both areas.

1. Introduction

Polysaccharides are carbohydrate polymers that are extracted from various natural sources including plants, algae, bacteria, fungi and arthropods. The structural complexity and variability of their fine structure provides a toolbox with a wide spectrum of chemical and physical functionalities to address technological issues in both food and pharmaceutical industries for a range of applications. Established applications include viscosity enhancement of fluid formulations or stabilization of dispersions such as emulsions or suspensions of colloidal solid particles (Figure 1). The ability of polysaccharides to undergo sol-gel transition and structure aqueous solutions is also exploited in both fields. This process results in soft solids that are in a jammed metastable state [1]**. The food industry utilizes gelation events to replace, for instance, fat in low-fat formulations or generate new structures with distinct textural properties. The pharmaceutical industry also employs gelation to fabricate, for example, sustained release drug delivery systems [2] or wound dressings to assist healing [3]. Furthermore, various concepts from material science (e.g., glassy state, phase diagrams, non-equilibrium dynamics, etc.) are frequently employed in both disciplines to analyze and interpret the behavior of polysaccharides when they occur as condensed matter. Apart from established applications that are used in both fields, encapsulation and delivery of compounds is another area, which has advanced at fast pace in the last ten years or so. This technology usually involves engineering the interface of a dispersed system to make it responsive or resistant to the operating environment. For instance, encapsulation of edible oils can be achieved to protect them from environmental parameters (e.g., oxygen) [4]. Similarly, it is feasible by intelligent manipulation of polysaccharides to prepare

systems that are responsive to environmental parameters (e.g., pH). Such systems can be used for drug delivery at locations where pH discrepancies may occur (e.g., along the gastrointestinal tract) [5]. Controlling the particle size of the delivery system is one of the most important and challenging factors that need to be addressed when designing such systems. [6]

Figure 1 illustrates the various theoretical concepts and their implementations that are encountered in both food and pharmaceutical disciplines of science. Interaction occurs at multiple levels as the underlying physics or chemistry share common characteristics. For instance, emulsification or encapsulation of either a hydrophobic drug or a flavor compound is governed by exactly the same physical principles, as hydrophobicity is the fundamental quality that determines behaviour. Furthermore, the environment that these systems are required to be functional is remarkably intricate. For example, a drug may be required to withstand the chemically aggressive environment of stomach. Similarly, a flavor compound should resist the processing conditions and chemical environment of the usually complex food matrices.

Present work identifies some common current trends in polysaccharide research in food and pharmaceutical areas and argues that the two seemingly distant scientific areas have common grounds for utilization of these intricate biopolymers.

2. Low moisture polysaccharide systems

The level of solids to promote polysaccharide gelation rarely exceeds 2%. In the solid polysaccharide state water is usually below ~10% thus failing to sufficiently hydrate the chains resulting in restricted molecular mobility and conformational rearrangements.

Such a state of affairs precipitates in a material with distinct structural and physicochemical properties than its high-moisture counterparts. The formed amorphous solid-state structure has the characteristics of glass and it usually forms on cooling or rapid water removal. The solid state of polysaccharides is mostly amorphous although crystalline state may also be observed within the same system (*e.g.,* amylose or cellulose crystals).

2.1 Edible films and coatings

Edible films consist of a thin layer of polysaccharide in the glassy state that provides barrier to moisture, oxygen and aroma diffusion in foods. The main advantage over the synthetic polymer films is their sustainability, as they minimize the need for synthetic packaging. Edible films and coatings can be fabricated using a diverse range of biopolymers including proteins, polysaccharides, waxes or mixtures thereof resulting in composite materials. Antimicrobial agents [7], flavours [8]* or drugs [9] can be also added in the film depending on the application. In the last few years, nanotechnology is exploited to enhance the functionality of the films and create composite materials using nanoparticles from various sources, as for instance, inorganic fillers, [10, 11] chitosan nanoparticles, [12] cellulose nanocrystals, [13] nanoemulsions [14] or drug nanoparticles [15].

2.2 Encapsulation

Polysaccharides can be also used to encapsulate active ingredients such as flavours, pigments, nutrients or drugs. This technology protects the encapsulated compound from oxidation, light, loses due to volatility or interactions with other ingredients in food or pharmaceutical formulations. In the operating environment (*e.g.*, mouth, stomach or

packaging) the active component will be released in a controlled manner from the matrix or be protected from environmental perturbations for the duration of the shelf life. Encapsulation usually proceeds with immobilization of the desirable component into a glassy polysaccharide matrix. This is most commonly achieved with spray drying [6, 16] or electrospinning [17, 18] where fine particles or fibers are generated with the active compound entrapped a glassy matrix.

2.3 Polycrystalline materials

Polycrystalline materials are those that are composed of aggregated small crystals of different size and orientation. In polysaccharides and some synthetic polymer systems these materials also include amorphous regions in their structure. In cellulose and chitin for instance, acid hydrolysis of the amorphous regions results in fabrication of a new materials that consist of aggregates of cellulose or chitin crystals at various length scales. Typical polysaccharides that acquire a polycrystalline character during their biosynthesis are starch [19], cellulose [20, 21] and chitin [22] that find applications in food and pharmaceutical industries as fat substitutes, texture modifiers, tablet binders or additives to reinforce biopolymer composites.

3. High moisture polysaccharide systems

On the other side of the spectrum when water molecules are abundant, hydration of the chains is facilitated and promotes interactions that result in distinct structures compared with their low moisture counterparts. Gelled structures and protein-polysaccharide coacervates are the most notable examples of such molecular embrace.

3.1 Polysaccharide - protein complexes

Active agents often need to be incorporated into aqueous-based products to be protected during storage prior to controlled release of, for example, lipophilic drugs, antimicrobials or flavours [23]**. Biopolymer complexes, such as those formed by protein and polysaccharide interactions, form micro- or nano- capsules, particles and hydro-gels and are used in both the pharmaceutical and food industries in the encapsulation of active ingredients [24]. Therefore, a fundamental understanding of the factors underpinning the formation of these materials is essential to optimise their functionality. When polysaccharides are mixed with proteins (Figure 2) there are three possible results:

(i) a homogeneous solution

(ii) a two-phase system where both macromolecules are essentially separated from one another (simple coacervation)

(iii) a two-phase system where both macromolecules are concentrated in the same phase (complex coacervation). This is more common if the biopolymers are oppositely charged thus forming two phases. One phase is the so-called "coacervate phase" composed of electrostatically or non-specifically stabilised polymer complexes and the other is a dilute phase containing large amounts of solvent [25].

Complexes can be soluble or insoluble in aqueous solvent depending on biopolymer concentration(s), ionic strength, pH and temperature [23**, 26-30] as well as the physicochemical properties of biomacromolecules such as the charge on the polysaccharide chains and distribution of surface charge in proteins [31]. Therefore, these complexes have great potential as a bioresponsive material for controlled release [23**,

24, 27, 32] or in the reduction of salt, sugars or fats in foods, as the sensory perception of taste and flavour can be altered by tuning the microstructures [33-35]. Protein-polysaccharide complexes have also been shown to exhibit "better" functional properties than proteins and polysaccharides alone, for example, hydration and interfacial properties [25]. There are two alternative procedures for emulsion formation using polysaccharide–protein complexes in emulsion stabilisation [36]*. The first consists of preparing a solution of both biopolymers, and using the resulting protein–polysaccharide complex for the emulsification. The second method, that is named layer-by-layer (LBL) electrostatic deposition technique [36]*, consists in forming a primary protein-stabilized emulsion followed by addition of the polysaccharide. This leads to the formation of a secondary interfacial layer that frequently results in surface-charge reversal. Polyelectrolyte complexes of β-lactoglobulin and alginate formed using this approach have been shown to suppress lipid digestion in model systems [37].

Ternary systems containing a third biopolymer in the complex may result in a wider range of functionalities and greater resistance to changes in, for example, ionic strength or pH [38]. At least in synthetic systems ternary complexes maintain similar characteristics to binary coacervates; however the choice of the third polymer has an influence on both the material properties and (bio)responsiveness [38]. Finally, many polysaccharides are mucoadhesive (interaction with mucous or mucin) but the effect of complexation with proteins on mucoadhesion has not been fully explored yet.

3.2 Fluid Gels

Subjecting a gel forming biopolymer to a shear field during gelation can result in the formation of particulate micro gels that can be prepared to behave in bulk, as

viscoelastic liquids. Microgels exhibit fluid-like behavior while having a cross-linked gel microstructure. These microgels, often referred to as fluid gels (or sheared gels), were first described in the 90's and were produced using polysaccharides, proteins or even synthetically produced polymers [39, 40]. The mechanism by which these gel particles form, was originally described as nucleation and growth process with the molecular ordering limited to within individual gel by the shear imposed on the system. The shear forces that are applied physically are thought to enable the gel nucleation sites to remain distinct from one another resulting in the formation of microgel particles [41]. These fluid gels have received renewed interest recently within food and pharmaceutical systems as a relatively simple method to structure liquid formulations and impart additional functionality. Furthermore, the wide variety of gelling biopolymers to choose from and their different material properties opens up several potential applications with physiologically responsive biopolymers of particular interest. The microstructure of fluid gels can be easily controlled by adjusting processing parameters [42]*. Indeed, changes in the concentration of the polymer, rate of cooling in thermally gelling biopolymers, and/or shear rate during fluid gel formation, controls their particle size and shape (Figure 3) [43-45*]. Moreover, the ability to change the particle size and shape allows the bulk rheology to be tuned and facilitate the application (pouring, spreading spraying etc.). Fluid gels tend to have a significant yield stress and once this stress is exceeded pseudoplastic flow occurs. The bulk viscosity also increases with an increase in the gel strength of the particles due to its greater capacity to resist deformation and subsequent flow [46].

Fluid gels produced from acid insoluble polysaccharides such as alginate [44, 47] and gellan gum have been of most recent interest with gellan gum fluid gels in particular finding applications in both food [48] and pharmaceutical formulations [45]*. In pharmaceutical applications low acyl gellan gum has been investigated as a modified release oral liquid and demonstrated to have the potential to be formulated with a similar viscosity profile to that of a marketed pediatric oral liquid. In addition, it was shown that due to the acid insolubility of gellan gum, it was possible to modify the release of a model drug entrapped in the fluid gel. The drug release, however, was dependent on the acidity and exposure time in simulated gastric fluids [45]*. The acid gel behaviour of low acyl gellan gum and of blends of high and low acyl fluid gels have been explored in food systems as a method to increase satiety [48, 49]. Currently, in our laboratories are under investigation blends of high acyl and low acyl gellan gum fluid gels as a mucoadhesive nasal spray formulations. Incorporating high acyl gellan appears to improve mucoadhesion compared with using low acyl gellan fluid gels alone. Additionally, a further advantage of forming a fluid gel is that the bulk viscosity is sufficiently reduced to enable spraying from a mechanical nasal spray device which was not possible with the non-crosslinked quiescently produced high acyl/low acyl blend.

Fluid gels have also been investigated as a potential fat replacement in low calorie foods as the microgels can be produced to mimic the some of the physical properties of fat droplets [50]. Furthermore, fluid gels have been investigated to deliver enhanced sensory attributes to foods improving mouth feel and textural properties. These properties have been modeled using thin film rheology (tribology) [51] and were influenced by the physical properties of particles such as size and elasticity [46, 52]. Controlling the

particle properties, therefore, not only impacts on bulk rheological behaviour but also allows lubrication properties to be manipulated, which may also have potential advantages in topical pharmaceutical formulations.

4. Conclusions

In the present review some current theoretical and applied aspects of polysaccharide research have been discussed. We have identified that polysaccharide structures can be divided into two distinct classes depending on the moisture content of the matrix. Structures that are formed in the high or low moisture regimes of the systems present an opportunity for cross-disciplinary investigation. This holds true, as similar theoretical and technical approaches are shared between food and pharmaceutical disciplines to tackle functionality issues. Understanding and exploiting the underlying molecular mechanisms that govern polysaccharide functionality will result in further integration of these two outwardly distant areas of science.

5. References and recommended reading

1. van der Sman RGM: **Soft matter approaches to food structuring**. Advances in Colloid and Interface Science 2012 **176-177**: 18-30.

   ****** This review article outlines the opportunities that arise from approaching food structuring from the perspective of soft matter physics. The same concepts can be used for matrix structuring in pharmaceutical applications.

2. Shedden AH, Laurence J, Barrish A, Olah TV: **Plasma timolol concentrations of timolol maleate: timolol gel-forming solution (TIMOPTIC-XE) once daily versus timolol maleate ophthalmic solution twice daily**. Doc Ophthalmol 2001 **103**: 73-79.
3. Miraftab M, Masood R, Edward-Jones V: **A new carbohydrate-based wound dressing fibre with superior absorption and antimicrobial potency**. Carbohydr Polym 2014 **101**: 1184-1190.
4. Carneiro HCF, Tonon RV, Grosso CRF, Hubinger MD: **Encapsulation efficiency and oxidative stability of flaxseed oil microencapsulated by spray drying using different combinations of wall materials**. Journal of Food Engineering 2013 **115**: 443-451.
5. Li L, Ni R, Shao Y, Mao S: **Carrageenan and its applications in drug delivery**. Carbohydr Polym 2014 **103**: 1-11.
6. Fathi M, Martin A, McClements DJ: **Nanoencapsulation of food ingredients using carbohydrate based delivery systems**. Trends in Food Science & Technology 2014 **39**: 18-39.
7. Zhang L, Li R, Dong F, Tian A, Li Z, Dai Y: **Physical, mechanical and antimicrobial properties of starch films incorporated with ε-poly-L-lysine**. Food Chem 2015 **166**: 107-114.
8. Marcuzzo E, Sensidoni A, Debeaufort F, Voilley A: **Encapsulation of aroma compounds in biopolymeric emulsion based edible films to control flavour release**. Carbohydr Polym 2010 **80**: 984-988.

   ***** Carrageenan films have been used as encapsulating matrixes of polar aroma compounds. Similar technology could be used to encapsulate medicinal compounds.

9. Hermans K, Van den Plas D, Kerimova S, Carleer R, Adriaensens P, Weyenberg W, Ludwig A: **Development and characterization of mucoadhesive chitosan films for ophthalmic delivery of cyclosporine A**. Int J Pharm 2014 **472**: 10-19.
10. Shojaee-Aliabadi S, Mohammadifar MA, Hosseini H, Mohammadi A, Ghasemlou M, Hosseini SM, Haghshenas M, Khaksar R: **Characterization of nanobiocomposite kappa-carrageenan film with Zataria multiflora essential oil and nanoclay**. International Journal of Biological Macromolecules 2014 **69**: 282-289.
11. Moreira FKV, De Camargo LA, Marconcini JM, Mattoso LHC: **Nutraceutically inspired pectin-Mg(OH)2 nanocomposites for bioactive packaging applications**. J Agric Food Chem 2013 **61**: 7110-7119.
12. Antoniou J, Liu F, Majeed H, Zhong F: **Characterization of tara gum edible films incorporated with bulk chitosan and chitosan nanoparticles: A comparative study**. Food Hydrocolloids 2015 **44**: 309-319.
13. Pereda M, Dufresne A, Aranguren MI, Marcovich NE: **Polyelectrolyte films based on chitosan/olive oil and reinforced with cellulose nanocrystals**. Carbohydr Polym 2014 **101**: 1018-1026.
14. Otoni CG, Pontes SFO, Medeiros EAA, Soares NDFF: **Edible films from methylcellulose and nanoemulsions of clove bud (Syzygium aromaticum) and oregano (Origanum vulgare) essential oils as shelf life extenders for sliced bread**. J Agric Food Chem 2014 **62**: 5214-5219.
15. Sievens-Figueroa L, Bhakay A, Jerez-Rozo JI, Pandya N, Romanach RJ, Michniak-Kohn B, Iqbal Z, Bilgili E, Dave RN: **Preparation and characterization of hydroxypropyl**

methyl cellulose films containing stable BCS Class II drug nanoparticles for pharmaceutical applications. Int J Pharm 2012 **423**: 496-508.
16. Dordevic V, Balanc B, Belscak-Cvitanovic A, Levic S, Trifkovic K, Kalusevic A, Kostic I, Komes D, Bugarski B, Nedovic V: **Trends in Encapsulation Technologies for Delivery of Food Bioactive Compounds**. Food Eng Rev 2014: 1-39.
17. Ding F, Deng H, Du Y, Shi X, Wang Q: **Emerging chitin and chitosan nanofibrous materials for biomedical applications**. Nanoscale 2014 **6**: 9477-9493.
18. Maeda N, Miao J, Simmons TJ, Dordick JS, Linhardt RJ: **Composite polysaccharide fibers prepared by electrospinning and coating**. Carbohydr Polym 2014 **102**: 950-955.
19. Perez S, Baldwin MP, Gallant JD, *Structural features of strarch granules I*, in *Starch: Chemistry and Technology*, J. BeMiller and R. Whistler, Editors. 2009, Academic Press: London. p. 149-192.
20. Kargar M, Fayazmanesh K, Alavi M, Spyropoulos F, Norton IT: **Investigation into the potential ability of Pickering emulsions (food-grade particles) to enhance the oxidative stability of oil-in-water emulsions**. J Colloid Interface Sci 2012 **366**: 209-215.
21. Domingues RMA, Gomes ME, Reis RL: **The potential of cellulose nanocrystals in tissue engineering strategies**. Biomacromolecules 2014 **15**: 2327-2346.
22. Zeng J-B, He Y-S, Li S-L, Wang Y-Z: **Chitin whiskers: An overview**. Biomacromolecules 2011 **13**: 1-11.
23. Zhang Z, Zhang R, Decker EA, McClements DJ: **Development of food-grade filled hydrogels for oral delivery of lipophilic active ingredients: pH-triggered release**. Food Hydrocolloids 2015 **44**: 345-352.

****** This work outlines the preparation of hydrogel particles by trapping emulsified lipids within electrostatic complexes formed from two food-grade biopolymers: alginate and casein. The authors then evaluated the ability of hydrogel particles to control the release of encapsulated lipid droplets using simulated oral conditions. Their results showed that filled hydrogel particles could be made to release encapsulated lipid droplets under these conditions, which should be useful in the development of polysaccharide delivery systems.

24. Xiao Z, Liu W, Zhu G, Zhou R, Niu Y: **A review of the preparation and application of flavour and essential oils microcapsules based on complex coacervation technology**. Journal of the Science of Food and Agriculture 2014 **94**: 1482-1494.
25. Evans M, Ratcliffe I, Williams PA: **Emulsion stabilisation using polysaccharide-protein complexes**. Current Opinion in Colloid & Interface Science 2013 **18**: 272-282.
26. Chai C, Lee J, Huang Q: **The effect of ionic strength on the rheology of pH-induced bovine serum albumin- κ-carrageenan coacervates**. LWT - Food Science and Technology 2014 **59**: 356-360.
27. Hirt S , Jones OG: **Effects of chloride, thiocyanate and sulphate salts on β-lactoglobulin–pectin associative complexes**. International Journal of Food Science & Technology 2014 **49**: 2391-2398.
28. Fioramonti SA, Perez A, Aringoli EE, Rubiolo AC, Santiago LG: **Design and characterization of soluble biopolymer complexes produced by electrostatic self-assembly of a whey protein isolate and sodium alginate**. Food Hydrocolloids 2014 **35**: 129-136.
29. Zhang Z, Zhang R, Tong Q, Decker EA, McClements DJ: **Food-grade filled hydrogels for oral delivery of lipophilic active ingredients: Temperature-triggered release microgels**. Food Research International 2015 **69**: 274-280.
30. de Souza CJF, Ramos AV, Camara PBS, Gulao ES, de Campos MF, Garcia-Rojas EE: **Polymeric complexes obtained from the interaction of bovine serum albumin and κ-carrageenan**. Food Hydrocolloids 2015 **45**: 286-290.
31. Li Y, Zhao Q, Huang Q: **Understanding complex coacervation in serum albumin and pectin mixtures using a combination of the Boltzmann equation and Monte Carlo simulation**. Carbohydrate Polymers 2014 **101**: 544-553.
32. Hosseini SMH, Emam-Djomeh Z, Razavi SH, Moosavi-Movahedi AA, Saboury AA, Mohammadifar MA, Farahnaky A, Atri MS, Van der Meeren P: **Complex coacervation**

of β-lactoglobulin-κ-Carrageenan aqueous mixtures as affected by polysaccharide sonication. Food Chemistry 2013 **141**: 215-222.
33. Stieger M , van de Velde F: **Microstructure, texture and oral processing: New ways to reduce sugar and salt in foods**. Current Opinion in Colloid & Interface Science 2013 **18**: 334-348.
34. Koliandris A-L, Morris Cc, Hewson L, Hort J, Taylor AJ, Wolf B: **Correlation between saltiness perception and shear flow behaviour for viscous solutions**. Food Hydrocolloids 2010 **24**: 792-799.
35. Ramirez-Santiago C, Lobato-Calleros C, Espinosa-Andrews H, Vernon-Carter E: **Viscoelastic properties and overall sensory acceptability of reduced-fat Petit-Suisse cheese made by replacing milk fat with complex coacervate**. Dairy Sci & Technol 2012 **92**: 383-398.
36. Bouyer E, Mekhloufi G, Rosilio V, Grossiord J-L, Agnely F: **Proteins, polysaccharides, and their complexes used as stabilizers for emulsions: Alternatives to synthetic surfactants in the pharmaceutical field?** International Journal of Pharmaceutics 2012 **436**: 359-378.

***** This work outlines the potential usage of polysaccharides, proteins and their complexes in the stabilisation of emulsions for pharmaceutical applications. Readers may be particularly interested in Table 1, which outlines a number of important studies and the experimental conditions in which protein–polysaccharide complexes have been used.

37. Li Y , McClements DJ: **Modulating lipid droplet intestinal lipolysis by electrostatic complexation with anionic polysaccharides: Influence of cosurfactants**. Food Hydrocolloids 2014 **35**: 367-374.
38. Priftis D, Xia X, Margossian KO, Perry SL, Leon L, Qin J, de Pablo JJ, Tirrell M: **Ternary, tunable polyelectrolyte complex fluids driven by complex coacervation**. Macromolecules 2014 **47**: 3076-3085.
39. Sworn G, Sanderson GR, Gibson W: **Gellan gum fluid gels**. Food Hydrocolloids 1995 **9**: 265-271.
40. de Carvalho W , Djabourov M: **Physical gelation under shear for gelatin gels**. Rheologica Acta 1997 **36**: 591-609.
41. Norton IT, Jarvis DA, Foster TJ: **A molecular model for the formation and properties of fluid gels**. International Journal of Biological Macromolecules 1999 **26**: 255-261.
42. Fernandez Farres I, Moakes RJA, Norton IT: **Designing biopolymer fluid gels: A microstructural approach**. Food Hydrocolloids 2014 **42**: 362-372.

****** This article gives an overview of the molecular events that occur during fluid gel formation and provides an insight in to recent work on thermally stable fluid gels. In addition sensory and lubrication properties of fluid gels are discussed with a view to designing more complex structures with new functionalities.

43. Gabriele A, Spyropoulos F, Norton IT: **Kinetic study of fluid gel formation and viscoelastic response with kappa-carrageenan**. Food Hydrocolloids 2009 **23**: 2054-2061.
44. Fernandez Farres I , Norton IT: **Formation kinetics and rheology of alginate fluid gels produced by in-situ calcium release**. Food Hydrocolloids 2014 **40**: 76-84.
45. Mahdi MH, Conway BR, Smith AM: **Evaluation of gellan gum fluid gels as modified release oral liquids**. Int J Pharm 2014 **475**: 335-343.

***** This is the first report on the application of fluid gels as a controlled release oral liquid and highlights the advantageous bulk properties for such applications in Figure 3. Readers may also be interested in relationship between onset of drug release at pH 7.4 and preceding exposure time in simulated gastric fluid at pH 1.2 and pH 2.

46. Gabriele A, Spyropoulos F, Norton IT: **A conceptual model for fluid gel lubrication**. Soft Matter 2010 **6**: 4205-4213.
47. Fernandez Farres I, Douaire M, Norton IT: **Rheology and tribological properties of Ca-alginate fluid gels produced by diffusion-controlled method**. Food Hydrocolloids 2013 **32**: 115-122.
48. Bradbeer JF, Hancocks R, Spyropoulos F, Norton IT: **Low acyl gellan gum fluid gel formation and their subsequent response with acid to impact on satiety**. Food Hydrocolloids 2015 **43**: 501-509.
49. Bradbeer JF, Hancocks R, Spyropoulos F, Norton IT: **Self-structuring foods based on acid-sensitive low and high acyl mixed gellan systems to impact on satiety**. Food Hydrocolloids 2014 **35**: 522-530.
50. Chung C, Degner B, McClements DJ: **Development of reduced-calorie foods: Microparticulated whey proteins as fat mimetics in semi-solid food emulsions**. Food Research International 2014 **56**: 136-145.
51. Garrec DA , Norton IT: **Kappa carrageenan fluid gel material properties. Part 2: Tribology**. Food Hydrocolloids 2013 **33**: 160-167.
52. Mills T, Koay A, Norton IT: **Fluid gel lubrication as a function of solvent quality**. Food Hydrocolloids 2013 **32**: 172-177.

Figure Captions

Figure 1: Established and current concepts from engineering, physics and chemistry interact at various levels to interpret the behavior of polysaccharide-based systems across food and pharmaceutical scientific disciplines.

Figure 2: Phase diagram for mixtures of gum arabic (GA) and bovine serum albumin (BSA) as a function of pH and mixing ratio (GA: BSA). Adapted from reference [25] and reproduced with permissions.

Figure 3: Light microscopy images of 0.75% w/v gellan gum loaded with 20 mg/ml ibuprofen prepared at a shear rate of 500 s^{-1} using different cooling rates (a-c). (a) 0.5 °C/min, (b) 2 °C/min, (c) 10 °C/min and different shear rates cooling at 2 °C/min (d-f), (d) 100 s^{-1}, (e) 500 s^{-1} and (f) 1000 s^{-1}. Reproduced from [45] with permissions.

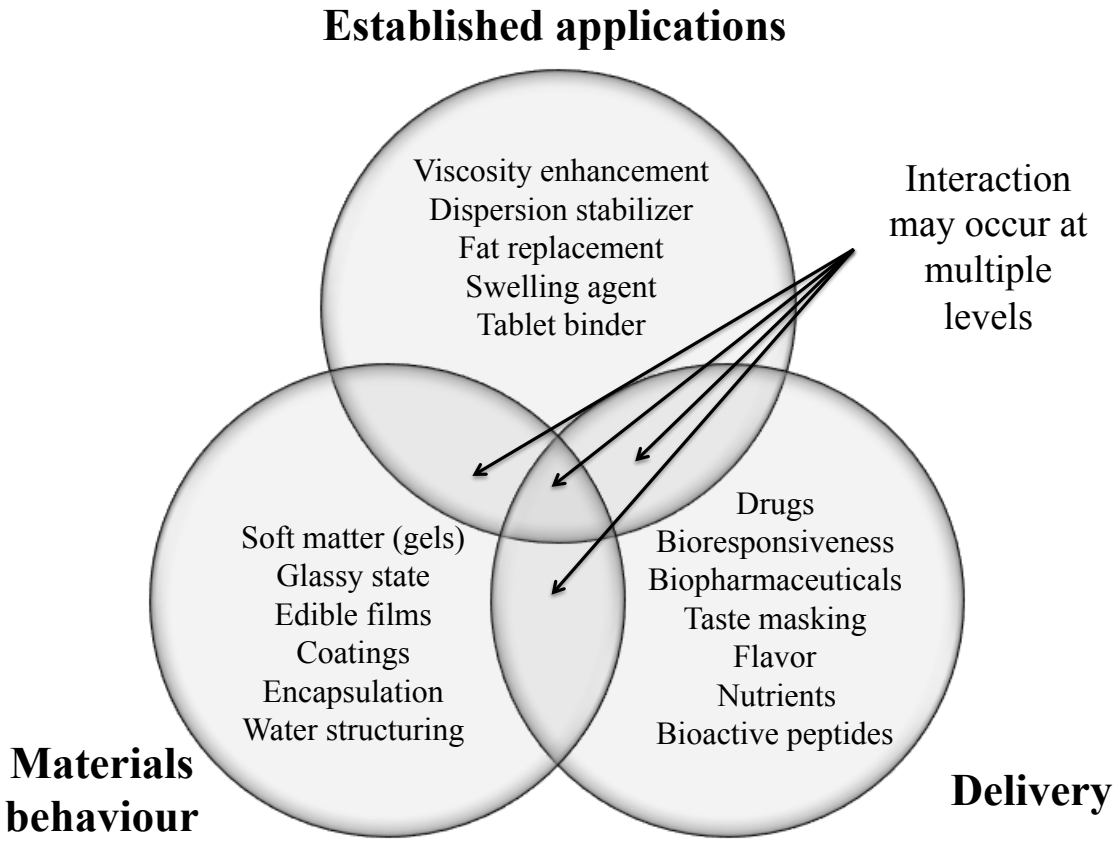
Established applications
Viscosity enhancement
Dispersion stabilizer
Fat replacement
Swelling agent
Tablet binder
Interaction may occur at multiple levels
Soft matter (gels)
Glassy state
Edible films
Coatings
Encapsulation
Water structuring
Drugs
Bioresponsiveness
Biopharmaceuticals
Taste masking
Flavor
Nutrients
Bioactive peptides
Materials behaviour
Delivery

Figure 1

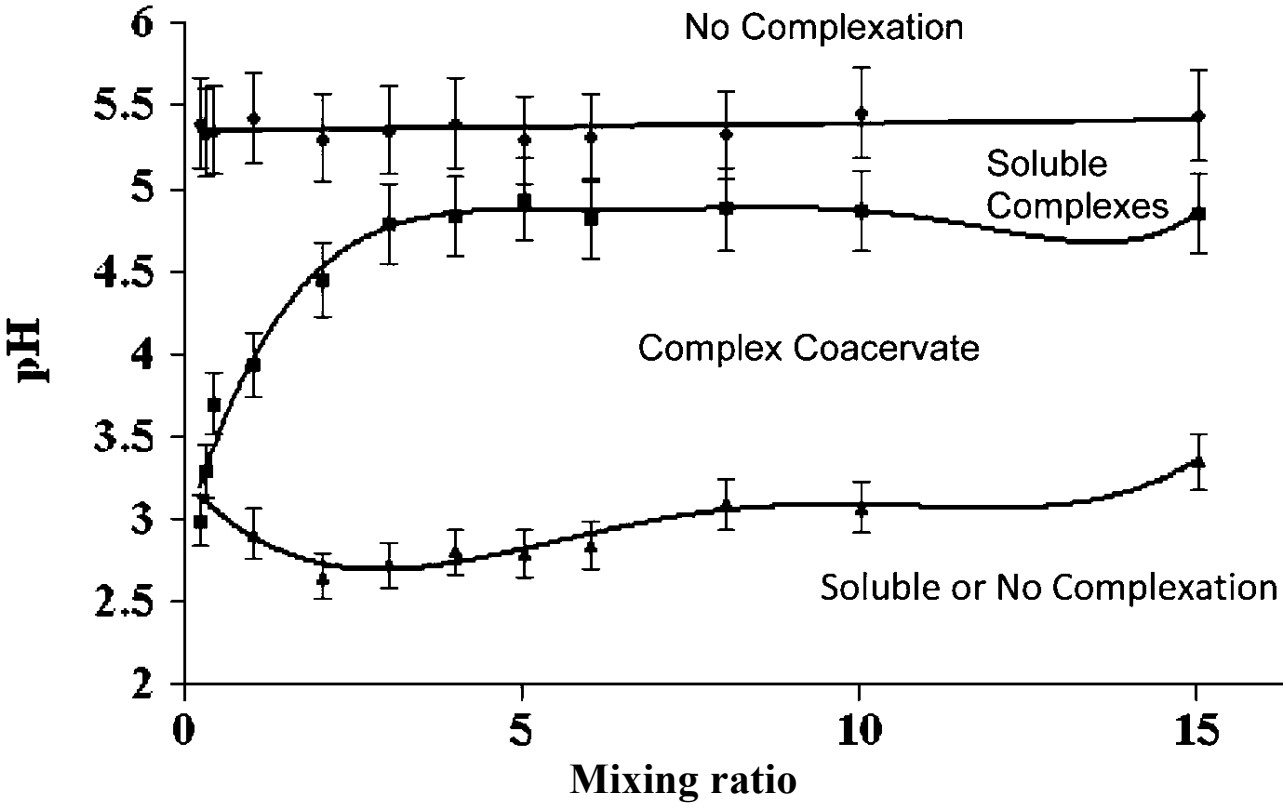
No Complexation
Soluble
Complexes
Complex Coacervate
Soluble or No Complexation
pH
Mixing ratio
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Figure 2

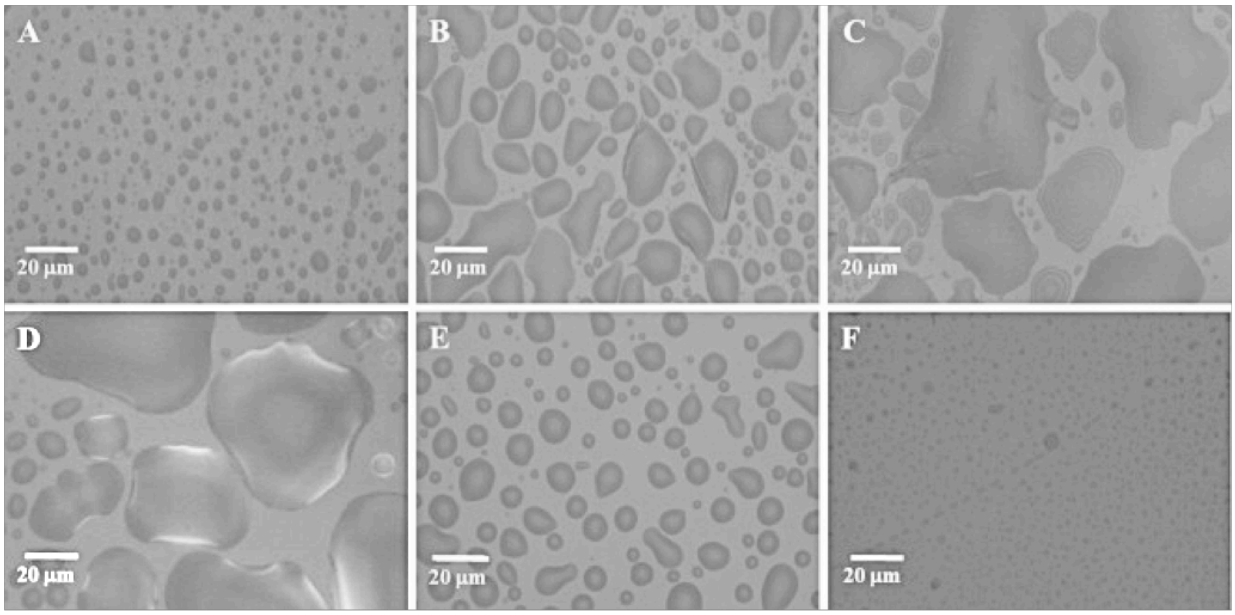

Figure 3