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# The parallel lives of polysaccharides in food and pharmaceutical formulations

Vassilis Kontogiorgos<sup>1</sup>, Alan M Smith<sup>2</sup> and Gordon A Morris<sup>3</sup>



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 cooperation will help tackling polysaccharide functionality issues that are encountered in both areas.

#### Addresses

<sup>1</sup> Department of Biological Sciences, University of Huddersfield, Queensgate, Huddersfield HD1 3DH, UK

<sup>2</sup> Department of Pharmacy, University of Huddersfield, Queensgate, Huddersfield HD1 3DH, UK

<sup>3</sup> Department of Chemical Sciences, University of Huddersfield, Queensgate, Huddersfield HD1 3DH, UK

Corresponding author: Kontogiorgos, Vassilis (v.kontogiorgos@hud.ac.uk)

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For a complete overview see the  $\underline{\mbox{lssue}}$  and the  $\underline{\mbox{Editorial}}$ 

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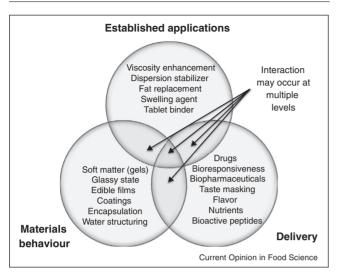
### Introduction

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<sup>••</sup>]. 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 behavior. 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.





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.

#### Low moisture polysaccharide systems

The level of solids to promote polysaccharide gelation rarely exceeds 2%. In the solid polysaccharide state water is usually below  $\sim 10\%$  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).

#### 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], flavors [8<sup>•</sup>] 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].

#### Encapsulation

Polysaccharides can be also used to encapsulate active ingredients such as flavors, 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.

#### **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.

#### 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.

#### Polysaccharide-protein complexes

Active agents often need to be incorporated into aqueousbased products to be protected during storage before controlled release of, for example, lipophilic drugs, antimicrobials or flavors [23<sup>••</sup>]. Biopolymer complexes, such as those formed by protein and polysaccharide interactions, form micro-capsules 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 optimize their functionality. When polysaccharides are mixed with proteins (Figure 2) there are three possible results:

(i) a homogeneous solution

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