Dextrans and dextran derivatives as polyelectrolytes in layer-by-layer processing materials – A review

Aurore Delvart, Céline Moreau, Bernard Cathala, Bernard Cathala

▶ **To cite this version:**

Aurore Delvart, Céline Moreau, Bernard Cathala, Bernard Cathala. Dextrans and dextran derivatives as polyelectrolytes in layer-by-layer processing materials – A review. Carbohydrate Polymers, 2022, 293, pp.119700. 10.1016/j.carbpol.2022.119700 . hal-03714966

HAL Id: hal-03714966
https://hal.inrae.fr/hal-03714966v1

Submitted on 22 Jul 2024

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Distributed under a Creative Commons Attribution - NonCommercial 4.0 International License

Version of Record: https://www.sciencedirect.com/science/article/pii/S0144861722006051
Manuscript_5dbf7914fa0b1e39c92c95e8e1ab7da5

Dextrans and dextran derivatives as polyelectrolytes in layer-by-layer processing materials – a review

Aurore Delvart [a,*], *Céline Moreau* [a] *and Bernard Cathala* [a].

[a] INRAE, UR1268 BIA, F-44316, Nantes, France

Aurore Delvart: aurore.delvart@inrae.fr

Céline Moreau: celine.moreau@inrae.fr

Bernard Cathala: bernard.cathala@inrae.fr

***Corresponding author**

INRAE Centre Pays de la Loire BIA 1268

3 impasse Yvette Gauchois

La Géraudière – CS 71627

44316 Nantes Cedex 3

*E-mail: aurore.delvart@inrae.fr (Aurore Delvart)

*Phone Number: +33(0)624869787 (Aurore Delvart)

© 2022 published by Elsevier. This manuscript is made available under the CC BY NC user license
https://creativecommons.org/licenses/by-nc/4.0/

ABSTRACT

The layer-by-layer technique (LbL) using polysaccharides is receiving increasing interest as the preparation of nano- and micro- multilayer objects composed by natural materials is a promising alternative for actual systems. The use of bacterial polysaccharides and more particularly, dextrans and dextran derivatives, in LbL assemblies allows the simple formation of biodegradable and biocompatible multilayers with engineered functionalities. The choice of dextrans and derivatives along with the assembly conditions can indeed control internal structure and physical, chemical and biological properties. In this review, we describe the use of dextrans and dextran derivatives into multilayers presented in literature, from the method and principles to the key parameters that need to be considered in their formations. We present their valorisation into nanoobjects with specific and stimuli-responsive properties that are mainly exploited for biomedical applications as drug delivery devices.

KEYWORDS

Dextrans, layer-by-layer, thin films, dextran derivatives, capsules, multilayers, nanomaterials

ABBREVIATIONS

LbL, layer-by-layer ; HIV, humain immunodeficiency virus ; DexS, dextran sulfate ; CHI, chitosan ; QCM, quartz crystal microbalance ; PEI, polyethylenimine ; DEAE-Dex, diethylaminoethyl dextran/2-(diethylamino) ethyl dextran ; IEP, isoelectric point ; Dex-HEMA, hydroxyethylmethacrylate-derivatised dextran ; MF, melamine formaldehyde ; HF, hydrofluoric acid ; PLL, poly-L-lysine ; Cat, catalase ; Ins, insulin ; Apr, aprotinin ;

1. INTRODUCTION

Developing alternative materials and systems based on natural polymers is currently challenging and yet, one of the key issues in material chemistry and nanotechnology in reason mainly of current environmental concerns. In the last decades, the scientific community has started to take an interest in polysaccharides due to their biocompatibility, biodegradability and low toxicity (de Belder, 1996; Hernández-Rivas et al., 2020; J. Liu et al., 2015; Rinaudo, 2008). Polysaccharides are a large family of polymers, obtained from biomass (animal, plant, bacterial, algal and fungal), exhibiting various structures and functionalities. They present a wide variety of structures resulting from the absolute configuration of asymmetric carbons, the stereochemistry of linkages as well as the branching pattern of polymers that differ according to their type and their source (J. Liu et al., 2015). Thus, they have been widely studied and used for their functional properties in the pharmaceutical industry, cosmetic formulation, paper industry, food industry, oil extraction and many other applications fields (J. Liu et al., 2015).

Among all polysaccharides, α-glucans are polymers naturally produced by microorganisms, notably dextrans which are the most widely used bacterial α-glucans in many fields, in both industry and research (Mehvar, 2000; Naessens et al., 2005; Yalpani & Hedman, 1985). Dextran family are D-glucose polysaccharides with a large majority of α-(1 → 6) type glycosidic bonds linkages whose structures are dependent on production due to glucose origin and bacteria involved (Taylor et al., 1985). Those bacterial polysaccharides present a great interest to the scientific community and find numerous applications in various areas, especially in the elaboration of bio-based materials: their wide availability, their diverse structures, their different branching patterns, their ‘clean’ production, as well as the possibility of functionalisation with a large variety of groups or active sites. Charged dextrans in particular have been studied as potential alternatives for many synthetic polyelectrolytes in

66 the elaboration of nanomaterials *i.e.* thin films and coatings, capsules, nanoparticles, etc. The
67 occurrence of chemical groups onto their polymer chain promotes formation of electrostatic
68 interactions and facilitates their inclusion with other charged compounds. Pioneering
69 researches on integration of polysaccharides in multilayered films, by well-known methods
70 such as layer-by-layer (LbL) method, have been begun in the middle 1990s (Lvov et al.,
71 1998). The specific integration of dextrans into those thin films, has started in the early 2000s
72 and their applications are gradually growing since then (Hartley et al., 2002; Serizawa et al.,
73 2000).

74 Polyelectrolyte films have become an unavoidable way to functionalise surfaces and to
75 create ordered nanostructures, that found an application range from biomedical devices to
76 environmental field (Boudou et al., 2010; Gribova et al., 2012; Jaber & Schlenoff, 2006;
77 Joseph et al., 2014). The principle commonly used for polyelectrolyte multilayers is the LbL
78 film formation based on the alternate adsorption of polyanions and polycations from aqueous
79 solutions which was investigated firstly by Decher and Hong in the late 1980s. Revised by
80 Decher *et al.* in the 1990, first research generation in the early 1990s allowed an expansion of
81 the method to polyelectrolyte films with various materials as well as film characterisation
82 (Ariga et al., 1997; Decher, 1997; Decher & Hong, 1991a; Lvov et al., 1995). The
83 polyelectrolyte film construction relies mainly on electrostatic interactions between charged
84 polymers and is highly dependent on the charge balance of polyelectrolytes and experimental
85 conditions (Schoeler et al., 2002; Voigt et al., 2002). Indeed, film properties can be controlled
86 by modulating deposition conditions (deposition time, temperature, etc.), characteristics of
87 polyelectrolytes (charge density, molecular weight, etc.) and parameters of polyelectrolyte
88 solution (concentration, pH, ionic strength, etc.) (Dubas & Schlenoff, 1999; Guzmán et al.,
89 2020). In the last two decades, the interest of the research community for bio-based
90 alternatives for LbL assembly from charged polypeptides and polysaccharides, including

dextran derivatives grew significantly (Crouzier et al., 2010; Elbert et al., 1999; Picart et al., 2001, 2002).

General information on dextrans and dextran derivatives (Figure 1) as well as their versatility for applications in various fields (Figure 2) are reported in this study. This review, more precisely, focuses on the use of dextran derivatives into polyelectrolytes multilayers and the elaboration of dextran-based multilayered structures. Reviewing of the extensive use of dextrans as polyelectrolytes for LbL assembly construction, including the main parameters to be controlled, is proposed in this report. Properties and applications of dextran-based multilayered films and other objects as micro- and nano-capsules may give indications for the elaboration of multilayer structures for future works.

2. DEXTRANS

2.1. Dextrans: sources and structures

The primary reports of dextran focused on the studies of "viscous fermentation" by early chemists when fermentative mechanisms understanding was not related to microorganisms yet (Braconnot, 1813). Later on, observations on "viscous fermentation" (dextrans) were done in the 1800s by Desfosses who explained that sugar was able to form a viscous material with carbonic acid and hydrogen emissions. Further analysis suggested that "sugar water" contained a material able to transform sugar into a viscous substance without any gas emission (Desfosses, 1829). A few years later, Gay-Lussac and Pelouze discovered that mannite and lactic acid compounds were the result of viscous fermentation of sugar beet juice (Gay-Lussac & Pelouze, 1833). In 1861, Pasteur had found that slimes on fermented food with plant origins were caused by microbial action that he reported as "viscous fermentation" or "alcoholic fermentation" (Pasteur, 1861). The term "dextran" was first used to name the segregated carbohydrate found in aging sugar juices in 1874 by Scheibler, who

demonstrated that dextran was a carbohydrate with the formula $(C_6H_{10}O_6)_n$ and with a positive optical rotation (Scheibler, 1874). Back in 1878, Van Tieghem named the bacterium responsible, for that mysterious thickening gum that he called "gomme de sucrerie", *Leuconostoc mesenteroides* (Van Tieghem, 1878). Later studies have shown that this family of α-D-glucans can be produced from sucrose by several bacterial strains, mostly gram-positive cocci, including *Leuconostoc*, *Gluconobacter*, *Streptococcus* and *Lactobacillus* strains (Chludzinski et al., 1974; Hehre, 1956; Jeanes et al., 1954). Out of α-D-glucans, bacterial extracellular enzymes, dextransucrases, can commonly form dextrans with their action on sucrose. Those enzymes are synthesised from different mesophilic and thermophilic bacteria such as genera of *Leuconostoc* and *Streptococcus*.

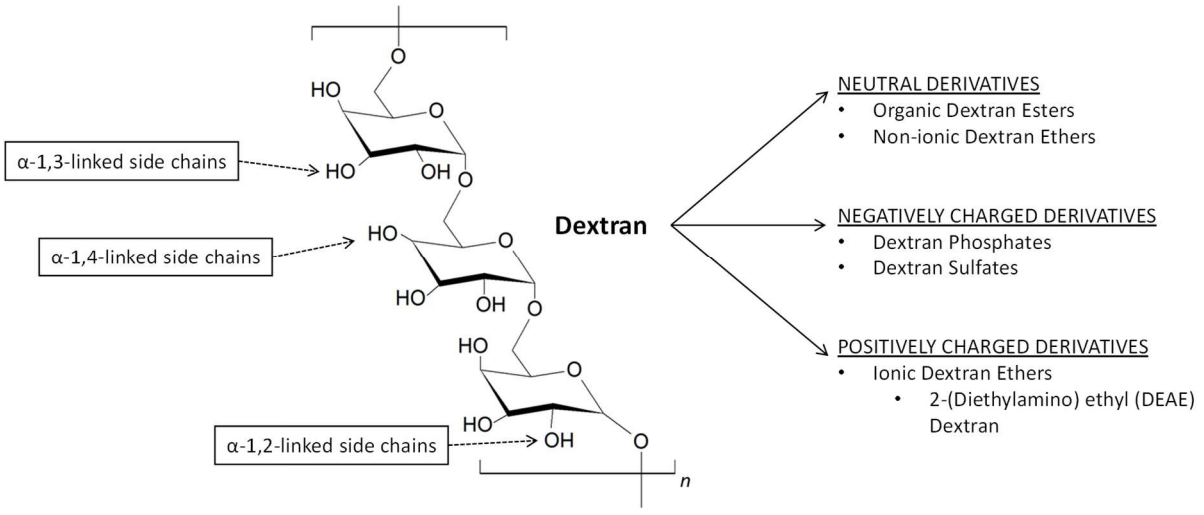


Figure 1. General structure of dextrans with D-glucose main chain linked by α-(1→6) type glycosidic bonds and branches based on α-(1→3), α-(1→4) and α-(1→2) linkages and main derivatives obtained by chemical functionalisation of dextran.

Dextrans are a family of neutral polysaccharides, produced by microorganisms, whose main chain consists of D-glucose units as illustrated by Figure 1. The structure of those α-

glucans is highly dependent on the bacterium strains from which they are produced, which leads to dextrans with various sizes and substitution patterns (Díaz-Montes, 2021). Dextran is a homopolymer of glucose whose backbone chain presents a number of consecutive α-(1→6) linkages that can vary from 50 to 97% of total glycosidic bonds (Leathers, 2002). Side chains of D-glucose units occur in α-(1→3), α-(1→4) and α-(1→2) linkages as indicated on Figure 1. The production of dextran determines the branch density and their nature on polymer backbone as well as its molecular weight (Hehre, 1956; Ruckel & Schuerch, 1967). Dextrans display broad range of average molecular weight (M_w) (10^5 to 10^8 $g.mol^{-1}$) with different polydispersity (M_w/M_n = 1 – 25) that tends to increase with the degree of branching (Antonini et al., 1964; Bovey, 1959; Confer & Logan, 1997; Ioan et al., 2000).

The high content of α-(1→6) linkages leads to important chain mobility as the presence of α-(1→6) linkages between sugar rings provides a considerably wider range of accessible relative orientations of successive sugar rings in dextrans chain (Burton & Brant, 1983; Kadkhodaei et al., 1991). Due to this chain flexibility and occurrence of hydroxyl groups, dextrans display a good solubility in water and most various polar solvents including organic and alcoholic solvents (Heinze et al., 2006; Leathers, 2002; Masuelli, 2013). Most dextrans demonstrate that increasing of the polymer concentration impacts the viscosity of solution that allows the formation of hydrogel (McCurdy, Goff, Stanley, et al., 1994).

2.2. Modification routes of dextrans

Due to the occurrence of hydroxyl groups on the surface of dextrans main chain and branches, the polymer promotes a large possibility of functionalisation to a large variety of neutral and charged dextran derivatives as indicated on Figure 1 (Ahmad et al., 2015; Heinze et al., 2006; Lindenbaum et al., 1977). The two major chemical modifications are esters of dextrans and ethers of dextrans that allow to obtain both neutral and charged dextran

156 derivatives (R. Li et al., 2017). Neutral dextrans represents both organic esters of dextrans and
157 non-ionic ethers. Organic esters of dextrans demonstrate a larger interest as they are used for
158 the coupling with bioactive compounds and for the binding of unsaturated moieties. Among
159 the etherification reactions, about twenty of them are considered as the most frequently used
160 for dextrans modifications and lead to both neutral and charged dextrans (Heinze et al., 2006;
161 Rogovin et al., 1972). Out of the inorganic esters of dextran, mainly negatively charged
162 dextrans, only dextran sulfates (dextran sulfuric acid half esters) and dextran phosphates
163 present a notable interest as they lead to polyelectrolytes presenting interesting biological
164 activity and properties (Bamford et al., 1986; Kagimura et al., 2015; R. Li et al., 2017; Mei et
165 al., 2015). In fact, dextran sulfates have shown anti-inflammatory properties in several
166 studies, anticoagulant capacity as well as anti-viral activity for a few viruses (de Raucourt et
167 al., 1998; Hall & Ricketts, 1952; Jing et al., 2016; Mauzac & Jozefonvicz, 1984; Mitsuya et
168 al., 1988). The introduction of ether-type groups in dextrans structure often results in stable
169 positively charged dextran derivatives such as 2-(diethylamino) ethyl (DEAE) dextrans, with
170 new biological properties such as immunological properties and new physico-chemical
171 properties such as complexing or adhesives properties (Naessens et al., 2005). Even though
172 chemical modifications remained major, cross-linking and grafting are also included in
173 current interest to form esters and ethers of dextrans (R. Li et al., 2017).

174 2.3. Applications of dextrans and its derivatives

175 There is a significant literature on the various uses of dextrans from bacterial origins
176 and their derivatives for medical and industrial applications as summarised on Figure 2.

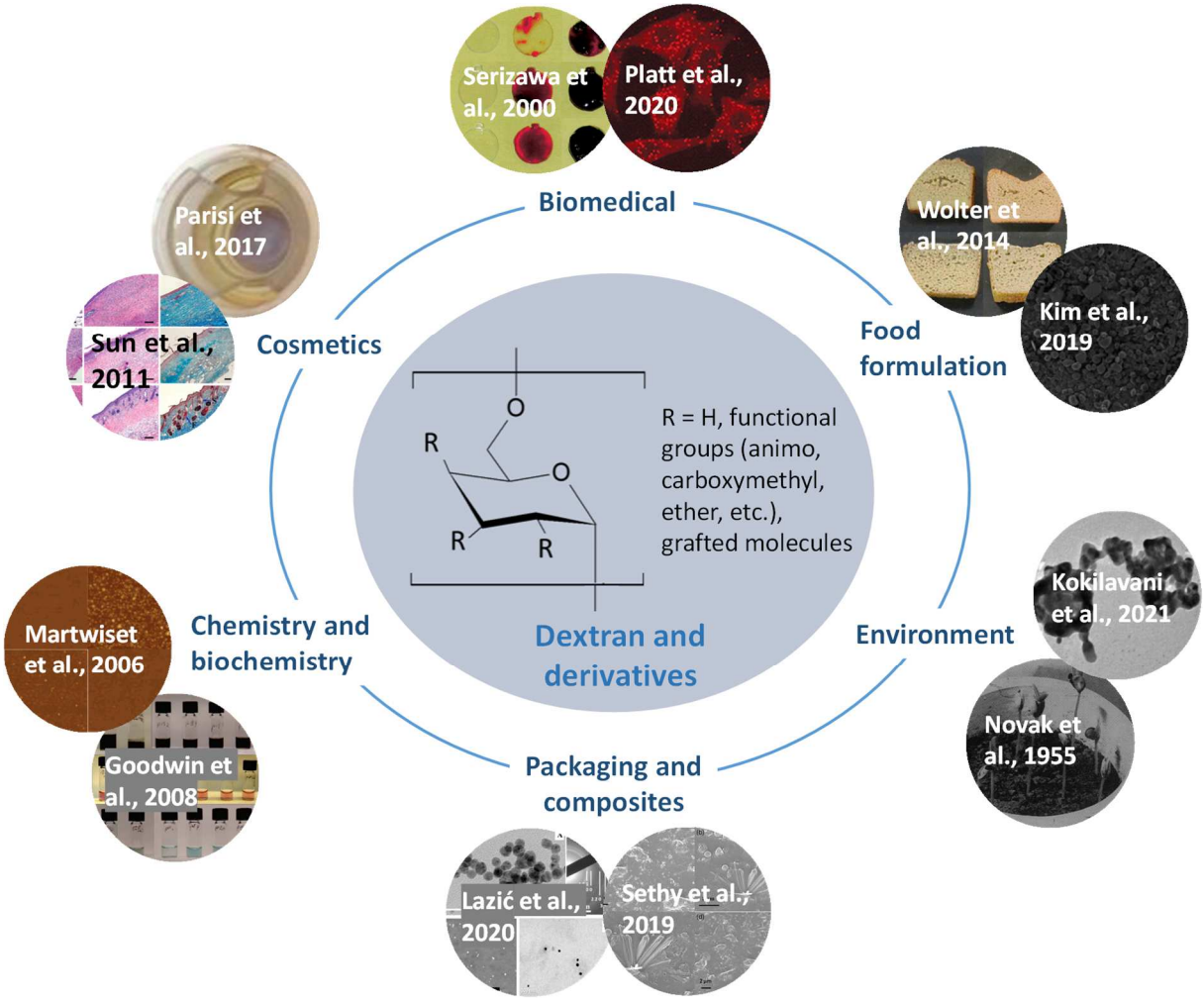


Figure 2. Overview of the most important applications of dextrans and their derivatives in industries. Adapted with permission from (Goodwin et al., 2009), © 2009 American Chemical Society. Adapted with permission from (Martwiset et al., 2006), © 2006 American Chemical Society. Adapted with permission from (Novak et al., 1955), © 1955 American Chemical Society. Adapted with permission from (Serizawa et al., 2000), © 2000 American Chemical Society. Adapted from (Kim et al., 2019; Kokilavani et al., 2021; Lazić et al., 2020; Wolter et al., 2014), with permission from Elsevier. Adapted from (Parisi et al., 2017; Platt et al., 2010; Sethy et al., 2020; Sun et al., 2011).

Dextrans and dextran derivatives have been widely used for years in the biomedical field, as dextrans are physiologically harmless biopolymers. Unlike high molecular weight

native dextran, dextrans with low molecular weight (40 000 – 100 000 Da) are suitable as therapeutic agents in restoring moderate blood volume (Robyt, 1985). The retention of low molecular weight dextrans in plasma is high enough to lead to a volume expansion without causing clogging. In addition, they help to improve blood flow by reducing blood viscosity and inhibiting erythrocyte aggregation (de Belder, 1996). However, sulfate esters of dextrans are mostly used for their anticoagulant properties, similar to the ones of heparin ; by forming complexes with several proteins, dextran sulfates avoid clotting mechanism of blood (de Raucourt et al., 1998; Hall & Ricketts, 1952; Mauzac & Jozefonvicz, 1984; Serizawa et al., 2000). Studies also highlight the use of dextran sulfates as antiviral drugs, laboratory tests showing the possibility of dextrans as anti-HIV (human immunodeficiency virus) agents as well as anti-viral against several other viruses (Mitsuya et al., 1988; Platt et al., 2010).

Beside the medical field, the variety of structures and functionalities found in dextrans and dextran derivatives presents a great interest in numerous industrial domains, mainly in cosmetics formulation and in food formulation. The occurrence of hydroxyl groups and high molecular weights of native dextrans is a source of hydrogen bonds for the formulation of viscous solutions and hydrogels, that are suitable as emulsifiers and as thickening agents (Leemhuis et al., 2013; McCurdy, Goff, & Stanley, 1994). Dextrans and dextran derivatives present a great biocompatibility, moistening properties and excellent solubility, which make them great candidates for the formulation of skin-care products in several cases such as skin regeneration (Sun et al., 2011). In 2017, Parisi *et al.* also highlighted the potential of dextran derivatives as polymeric antioxidants for skin whitening (Parisi et al., 2017).

Moreover, they are often used in the preparation of baked products to improve baking properties and sensory profiles (Lacaze et al., 2007). For instance, dextrans can be used to improve softness, crumb texture and loaf volume in the formulation of gluten-free and wheat breads (Wolter et al., 2014). Dextrans can also find applications as additives to give improved

rheological (gelling, thickening) or physico-chemical (emulsion stabilisation, particle suspension, etc.) properties in several industrial products (Kothari et al., 2014). Recently, more and more studies used dextrans for the elaboration of functional foods such as prebiotics, that can provide health benefits and protection against risk of several diseases (Kim et al., 2019). Since α-(1→6) linkages and α-(1→2) linkages are known to be resistant to human intestinal enzymes, the digestion of dextrans is relatively slow yielding prebiotic activity (Olano-Martin et al., 2000).

Dextran derivatives have potential for the conception of functional materials with great biocompatibility and degradability in the fields of chemistry and biochemistry as they provide a large range of charged or neutral biomacromolecules with different types of substituents, degrees of substitution and molecular weights (Naessens et al., 2005). For example, it was shown that amphiphilic dextrans form stable layers onto surfaces that improve *in vivo* imaging and encapsulation yield (Goodwin et al., 2009). Another study highlighted how grafted dextrans and oxidised dextrans on silicon wafer lead to non-fouling surfaces that can be valorised in the elaboration of biomaterials (Martwiset et al., 2006).

In the environmental applications, charged dextran derivatives are used for separation and detection of particles, soil conditioners, explosives, oil drilling muds, recovery of petroleum or high-viscosity gums. Ionic dextran derivatives have shown potential of flocculants for cleaning of wastewater, as they presented high efficacy for removal of both inorganic and organic particles (Ghimici et al., 2009; Ghimici & Nichifor, 2018). More recently, Kokilavani *et al.* proposed multifunctional materials based on Cu–Ag nanocomposites stabilised with dextrans for selective and sensitive detection of mercury (Kokilavani et al., 2021). Authors also highlighted that this dextran-based nanocomposite presents efficient photocatalytic and anti-microbial behaviour. Dextrans and dextran derivatives also found uses in agriculture as, in the late 1900s, studies proved that inclusion of

238 certain dextrans affects several aspects of soils. Depending on dextran structure, increasing
239 wet-sieve stability of soils studied, percent seedling emergence, rate of plant growth and crop
240 yield for plant used were observed (Novak et al., 1955).

241 Among packaging applications, dextrans and derivatives can be employed in different
242 ways, such as coating for improving compatibility of particles or performance in food
243 packaging as suggested by Lazić *et al.* (Lazić et al., 2020). In this study, dextran used as
244 coating on silver nanoparticles helped to improve barrier properties, *i.e.* oxygen permeability
245 and anti-microbial activity of nanocellulose films. Dextran-composites are also widely studied
246 for elaboration of biocompatible and eco-friendly packaging materials. Sethy *et al.* proposed
247 matrix of dextran-grafted poly(acrylic acid) hybrid nanocomposites and nano-$CaCO_3$ filler to
248 design materials with oxygen barrier, thermal, and antimicrobial properties (Sethy et al.,
249 2020).

250

251 **3. DEXTRAN DERIVATIVES AS POLYELECTROLYTES FOR 2-DIMENSIONAL**
252 **MULTILAYER FILMS**

253 3.1. Principle of layer-by-layer fabrication of multilayers

254 In current technologies, nanostructures and nanomaterials found an important place in
255 the development of ultra-small devices and are mainly prepared by top-down fabrication
256 techniques (Baig et al., 2021; Cheng et al., 2020; Khin et al., 2012; Moon et al., 2011;
257 Pomerantseva et al., 2019; Roduner, 2006; Wang et al., 2021). However due to physical
258 limitations of those techniques, bottom-up techniques are presently gaining in interest and
259 micro- or nano- materials based on self-assembly approaches are becoming more and more
260 present in nanotechnologies (Abid et al., 2022; Lombardo et al., 2020). These methods have

great potential in all fields of research: biomedical (Deng et al., 2010), paper industry (Wu & Farnood, 2014), functional materials (Damasceno Borges et al., 2018), composites (Sher et al., 2010), cosmetics (Yoo et al., 2016), food (Treviño-Garza et al., 2017), electronics (de Oliveira Farias et al., 2015) or even environment (Ma et al., 2011). Among bottom-up approaches, the LbL method is a way to build complex self-assemblies from charged molecules/nanoparticles with controlled architectures. Introduced by Iler in 1966, the LbL method was firstly applied to the alternative deposition of oppositely charged colloidal particles for the electrostatic self-assembly of multilayers (Iler, 1966). In 1991-1992, Decher's group revised the principle for manufacturing polyelectrolyte multilayers on a solid substrate for the first time (Decher et al., 1992; Decher & Hong, 1991a, 1991b). In those studies, the authors presented a simple method to achieve "soft" multilayered films with controlled architectures by adsorption of polyelectrolytes (Decher, 1997). The advantages of the LbL assembly techniques include its simplicity, its versatility but also control of the film architecture (thickness, mass, porosity, etc.) (Figure 3b). The properties of the system are governed to the greatest extent by the choice of polyelectrolytes pair.

Mainly based on Decher group's works, LbL assemblies are traditionally produced by dipping deposition, *i.e.* immersive LbL assembly (Decher et al., 1992; Decher & Hong, 1991a, 1991b; Lvov et al., 1994, 1998). Figure 3a illustrates the formation of LbL films onto a substrate based on the alternate immersion of the substrate in oppositely charged polymer solutions. During immersion, the polymer is adsorbed onto the surface and intermediate rinsing steps allow washing off loosely bound material leading to a layer formation. The dipping procedure is repeated with the opposite charged polymer to form a bilayer. The process is repeated until a multilayer with n bilayers, composed of two layers of polyelectrolytes with opposite charges, is obtained. In addition to the dipping method, there are currently two other deposition processes to form LbL assemblies: spin-coating and

spraying (Richardson et al., 2015). Film fabrication by spin-coating is based on alternative deposition of charged polymer solutions onto a solid substrate immediately followed by a rinsing and drying step, while the substrate undergoes spinning at constant velocity. While polymers are enforced to adsorb during the "classical" spin-coating procedure, spin-assisted LbL assembly of thin films from polyelectrolytes and/or biopolymers have been used in which polymers are allowed to adsorb before spinning steps (Cerclier et al., 2010). During the substrate rotation, the polymer solutions spread onto the surface to obtain layers with complete evaporation of the solvent, generally water. Finally, another alternative of the LbL approach is the consecutive spraying (spray LbL assembly) of polyelectrolytes solutions and rinsing solution on a substrate. This method has been used since the 1970s for the construction of films, but it was introduced into the field of polyelectrolytes in 2000 by Schlenoff, Dubas and Farhat (Félix et al., 2009; Schlenoff et al., 2000).

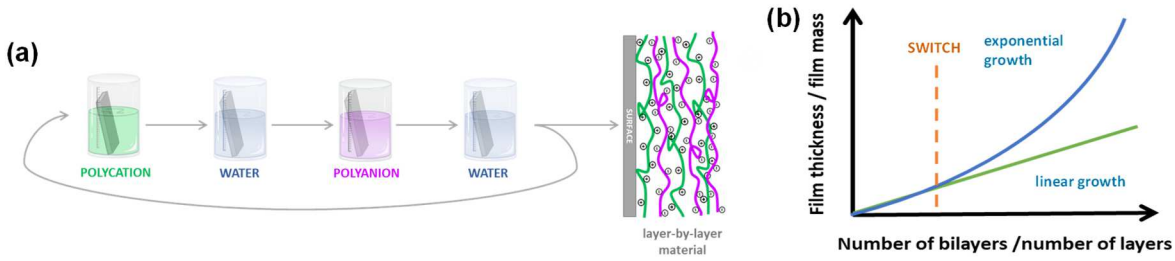


Figure 3. (a) Schematic representation of LbL technique by dipping and (b) graphic representation of film growth behaviour as function of the number of bilayers/layers and the film thickness/film mass.

LbL polyelectrolytes films formation relies on spontaneous adsorption, of at least two species, generally both driven and limited by entropy increase in the system and Coulombic interactions. However, it is important to note that the driving forces involved in multilayers construction are not restricted to electrostatic interactions. More and more multilayer films are exploited for their capacities to form multilayer *via* other interactions than electrostatic ones.

Hydrogen bonds, hydrophobic interactions and van der Waals forces also operate in the formation of the layers and influence the stability of the LbL assemblies (Borges & Mano, 2014; Clark & Hammond, 2000; Kotov, 1999). During deposition, polymers diffuse and adsorb onto the surface and find their equilibrium concentration and configuration. The adsorption process included charge inversion of the surface, indeed adsorption does not yield to surface neutralisation but end with charge overcompensation of the surface that induces repulsive interaction with polymers in solution (Hoogeveen et al., 1996; Schlenoff & Dubas, 2001). The surface charge reversal allows the adsorption of the following layer with composed of oppositely charged polyelectrolyte and thus the growth of the film. From literature, two types of film's growths can be distinguished: linear and non-linear growths. The growth type depends on the polymer couple and experimental conditions and can be identified by the relation between the adsorbed quantity and the number of bilayers differs as presented on Figure 3b (Elzbieciak et al., 2009; Y. Li et al., 2012; Schlenoff & Dubas, 2001). In the first case, polyelectrolyte multilayers growth presents a linear increase of the mass and/or the thickness onto the surface after each bilayer deposition. In the second case, films present a non-linear increase of mass (or thickness) with each adsorbed bilayer, also called supra-linear or exponential growth (Haynie et al., 2011; Picart et al., 2002). Growth mechanisms can be explained by effective charge density of polyelectrolytes, molar mass and are also dependent of characteristics of polymers and the processing parameters (Elzbieciak et al., 2009; Picart et al., 2002; Schlenoff & Dubas, 2001).

More generally, polyelectrolyte multilayer's films and their characteristics are related to the nature of polyelectrolytes and assembly conditions and result in films with different internal structures (morphology, porosity, etc.) and physico-chemical properties (water content, mechanical properties, permeability, etc.) (Borges & Mano, 2014; Dubas & Schlenoff, 1999; Guzmán et al., 2020). Some experimental parameters are crucial for the

assembly of polyelectrolyte multilayers and associated morphologies: physico-chemical characteristics of substrates (roughness, hydrophilicity, charges), physico-chemical characteristics of the polyelectrolytes (charge density, conformation, molecular weight) and the experimental parameters of the deposition procedure (adsorption time, drying step, temperature) and solution parameters (ionic strength, pH, concentration) (Devi et al., 2014; Moreau et al., 2012). The chemistry and structure of polyelectrolytes used in solution have an important role on the formation of LbL films, as they affect the interactions between polymers themselves and with the surface. Charge density of polymer is a key factor that influences the LbL assembly by impacting electrostatic interactions (Calvo et al., 2010; Delvart et al., 2022; Glinel et al., 2002; Schlenoff & Dubas, 2001). While a minimal charge density is necessary to have electrostatic attraction between polyelectrolytes, the adsorption mechanism and the final architecture result from a balance between charge densities of polyelectrolytes employed. An increase or a decrease of charge balance can both evenly lead to complexes formation or absence of LbL assembly (Glinel et al., 2002). Charge density can be tuned by adjusting the pH of the solution for weak polyelectrolytes and charges equilibrium can be switched by further addition of counterions and modification of ionic strength (Dubas & Schlenoff, 2001; Guzmán et al., 2020; Pechenkin et al., 2012). Increasing ionic strength often results in thicker layers due to the screening of charges and changes in polymer conformation (Lundström-Hämälä et al., 2010; McAloney et al., 2001). It can also prevent multilayers formation at some point since it can limit or break the interactions between polyelectrolytes (Dubas & Schlenoff, 2001; Feldötö et al., 2010; Lundström-Hämälä et al., 2010; McAloney et al., 2001). Effects of the counterions types are also of importance: small ions result in lower charge screening and reduced hydration and thickness of the adsorbed layer/film due to weak bonding while larger polarisation of big ions promote thicker layers. Though LbL principle is an easy method,

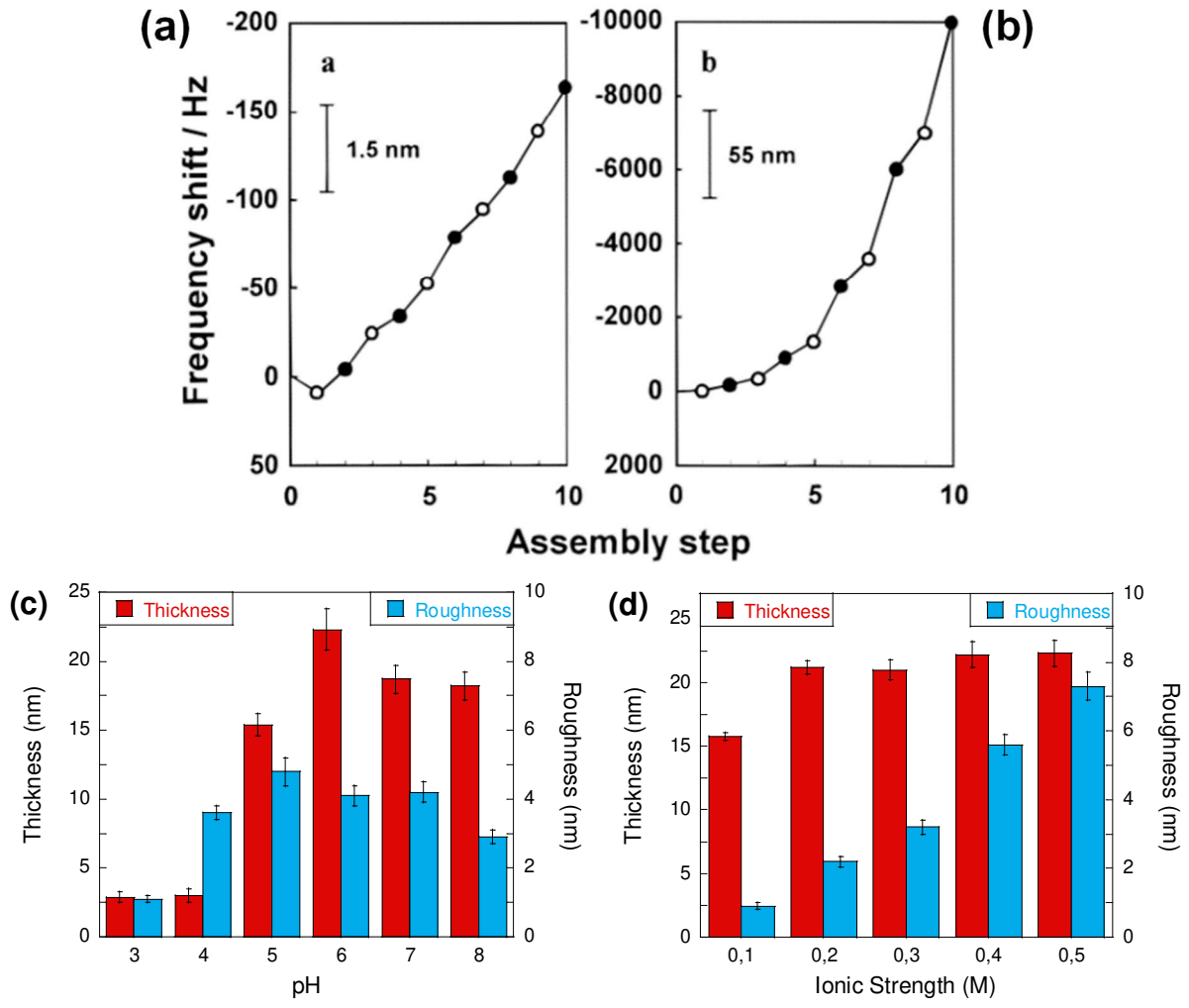
examining all the assembly parameters is critical to control the thickness/growth and the morphology of resulting polyelectrolyte multilayers.

3.2. Dextran sulfates in multilayered films

3.2.1. Dextran sulfates and chitosan multilayered films

Among dextrans used in multilayered materials, dextran sulfates (DexS) are commonly encountered since different molecular weights and sulfate contents are commercially available, expanding the range of materials implementation.

One of the most employed polycation used in combination with DexS is chitosan (CHI), poly[(1→4)-β-linked 2-amino-2-deoxy-D-glucose], a biocompatible and biodegradable anionic biopolymer with NH_2/NH_3^+ groups (pKa between 6 and 7). CHI is prepared by N-deacetylation of chitin extracted from the outer shells of crustaceans or insect wings (Jayakumar et al., 2010; Shukla et al., 2013). The first studies about CHI/DexS based materials were reported by Kikuchi and Fukuda in the 1970s (Fukuda & Kikuchi, 1977, 1978; Kikuchi & Fukuda, 1974). The authors highlight the ability of DexS and CHI to form polyelectrolyte complexes and the water-insoluble complex created was sensitive to the reaction conditions such as pH and concentration of the polyelectrolyte solutions (Fukuda & Kikuchi, 1978). This polyelectrolyte pair was later applied to multilayers for the first time in the 2000s by Serizawa's research group who used LbL principle to build DexS/CHI films (Sakaguchi et al., 2003; Serizawa et al., 2000, 2002, 2003).



375

376

377 **Figure 4.** QCM frequency shift as function of adsorbed layer number up to 10 bilayers of
378 (CHI/DexS) films on silver quartz crystal at pH depending on added salt content, (a) 0 M
379 NaCl and (b) 1M NaCl. Frequency shift and the corresponding thickness is indicated.
380 Reprinted with permission from (Serizawa et al., 2000), © 2000 American Chemical Society.
381 Thickness and roughness of 10 bilayers (CHI/DexS) films grown on silica wafer with (c) pH
382 (at 0.5 M ionic strength) and (d) ionic strength (at pH 6) obtained with ellipsometer analysis
383 respectively, data from (Devi et al., 2014).

384 In 2000, Serizawa *et al.* investigated the assembly process of CHI/DexS films and a
385 key parameter of the construction of multilayers: the impact of salt addition on film growth.
386 Using Quartz crystal microbalance (QCM) to investigate films growth, the authors found out

387 that 10 bilayers of CHI/DexS with no salt addition lead to thin films displaying a thickness of
388 3.7 nm (corresponding to quartz frequency shift of Δf = -163 Hz) while adding 1M NaCl to
389 both polymer solutions leads to an increase of the thickness of the films of 227 nm (Δf = -
390 9946 Hz) as reported on Figure 4a. They explained the low thickness value of no salt film by
391 possible incomplete coverage of the surface and non-accurate QCM values due to the very
392 low thickness and uneven repartition of the polymer on the surface. Nevertheless, results
393 showed a shift from linear film growth at 0M NaCl (figure 4a, left) to an exponential film
394 growth at 1M NaCl (figure 4a, right) as well as a six-fold mass/thickness increase with the salt
395 addition. In 2014, Devi *et al.* studied the formation of 10 bilayers DexS/CHI film on silica
396 using dipping method (Devi et al., 2014). Authors observed an exponential growth in
397 thickness of the CHI/DexS film with increasing number of layers at 0.5M NaCl and explained
398 that after the 4^{th} layer, the film growth changes from linear to exponential showing the
399 influence of the substrate on the first adsorbed layers. This observed exponential growth
400 mechanism is related to the ability of the CHI to diffuse in and out of CHI/DexS film and is
401 often observed for CHI-based multilayered films (Salomäki & Kankare, 2009; Z. Song et al.,
402 2009).

403 Devi *et al.* also investigate the impact of ionic strength and pH on the surface
404 morphology of CHI/DexS films (Devi et al., 2014). By increasing ionic strength, *i.e.*
405 increasing NaCl concentration from 0.1M to 0.5M (Figure 4d), the film thickness increased
406 from 15 nm to 25 nm. The presence of ions induces a screening of the polyelectrolyte charges
407 leading to a decrease of the electrostatic repulsion from identical charges on the polymer
408 chain. Thus, polyelectrolytes display random coil conformation if all charges are screened at
409 high ionic charges allowing more adsorption onto a surface due to the highest compaction and
410 decreased repulsion between polymer coils. At low ionic strength polyelectrolytes are in an
411 extended conformation and higher repulsion between chains occurs. Variation of pH from 3 to

8 at fixed ionic strength (Figure 4c) highlighted a clear dependence of the film growth with pH as well which was observed for other multilayers based on chitosan (Guzmán et al., 2011). As displayed on Figure 4c, average thickness of adsorbed layers increases when increasing pH from 1 to 6, then thickness decreases by increasing pH to 8 with an optimum at 23 nm for 10 bilayers at pH 6. In fact, at high pH (> 6), CHI becomes deprotonated and electrostatic-driven LbL assembly cannot occur between CHI and DexS. At low pH (pH<5), amino groups of chitosan are protonated allowing a successful LbL adsorption. However, at very low pH, authors explained that protonation of chitosan leads to an excess of positive charges from DexS and immediate dissolution of multilayers. The variation of charge equilibrium, here ionic strength and pH, also affects morphology of layers as illustrated on Figure 4c, d, by analysing the roughness and the surface morphologies by AFM. Roughness increases from 3.75 nm to 8 nm by increasing ionic strength from 0.1 M NaCl to 0.5 M NaCl and pH variation induces also significant change of both parameters. Similar effects of the modification of charges ratio/ionic equilibrium was observed on the morphology of DexS-based multilayers, by shifting charges density balance between polyelectrolytes (Delvart et al., 2022).

Table 1. Chitosan and dextran sulfate (CHI/DexS) multilayered films reported in literature and their applications.

Application(s)	Films	Targeted properties	Ref
Biomedical	(CHI-DexS)-CHI $(CHI\text{-}DexS)_{1\ to\ 40}$	Alternating anti- vs procoagulant activity, biodegradability	(Serizawa et al., 2000, 2002)
		Control of blood coagulation, antithrombogenic surface	(Sakaguchi et al., 2003; Yu, Jou, et al., 2007; Yu, Lin, et al., 2007)
		Drug delivery	(Xie et al., 2016; F. Zhang et al., 2019)
Tissue engineering	(CHI-DexS)-CHI $(CHI\text{-}DexS)_{1\ to\ 4}$	Bioactivity, fibroblast cell compatibility	(Kulikouskaya et al., 2018; Serizawa et al., 2003)

By considering the physico-chemical properties of chitosan and dextran sulfate and capacity to form films with controlled architecture, (DexS/CHI) multilayers found potential uses in different fields and mainly in biomedical applications. Table 1 outlines applications and main targeted properties of (CHI/DexS) films found in literature. Thanks to the ability of dextran sulfate to prevent blood coagulation, as seen previously in section 2.1, Serizawa's research group highlighted the potential of CHI/DexS multilayers in blood related devices to control blood coagulation (Sakaguchi et al., 2003; Serizawa et al., 2000; Yu, Jou, et al., 2007; Yu, Lin, et al., 2007). Moreover, integration of chitosan into multilayers films allows to block anticoagulation of DexS and open the possibility to form biodegradable films with both anti-coagulation and pro-coagulation properties (Serizawa et al., 2000, 2002). More recently, the interest of the scientific community in CHI/DexS as potential alternatives as multilayered coating for drug nanocarriers increased. In addition of both polyelectrolytes being biocompatible, their use as surface functionalisation can improve their dispersibility in physiological conditions, as it was observed with graphene oxide nanosheets (Xie et al., 2016; F. Zhang et al., 2019). Moreover, DexS/CHI multilayers were proven to be useful for cell attachment and their growth on surfaces (Kulikouskaya et al., 2018; Serizawa et al., 2003). Cell adhesion seems to depend mainly on the stiffness of the multilayers, which can be related to the growth pattern and thus of the choice of polycations and polyanions and the number of bilayers deposited (Kulikouskaya et al., 2018). Kulikouskaya *et al.* demonstrated that multilayered films are formed by alternating adsorption of negatively charged polysaccharides switched from linear to exponential growth by changing the polycation from polyethyleneimine (PEI) to CHI (Kulikouskaya et al., 2018). Authors also showed that those films built with exponential growth had different properties as the surface roughness increased and the mechanical properties change from elastic to viscous by increasing the number of bilayers.

3.2.2. Dextran sulfates and polyelectrolyte- based multilayered films

Apart from chitosan, other polycations were associated with DexS. These include synthetic and natural polyelectrolytes as well as other dextran derivatives allowing building different film structures. In 1995, Elferink et de Koster introduced diethylaminoethyl dextran (DEAE-Dex), polycation derivate from dextran with physiological effects (antibacterial, antifungal, and antitumor) as a good candidate to substitute synthetic polymers in biomedical applications (Elferink & de Koster, 1995). The use of DEAE-Dex into LbL assembly associated with DexS was proposed later by Benni *et al.* to control surface morphology of films to tune protein adsorption and cell adhesion (Benni et al., 2014). The authors studied $(DEAE\text{-}Dex/DexS)_4$ and $(DEAE\text{-}Dex/DexS)_4$-DEAE-Dex films surface morphology and their properties on glass surface depending on the last layer adsorbed (polycation or polyanion). Comparison between multilayers ending with polycation DEAE-Dex layer and multilayers ending with polyanion DexS layer highlighted significant differences in terms of roughness.

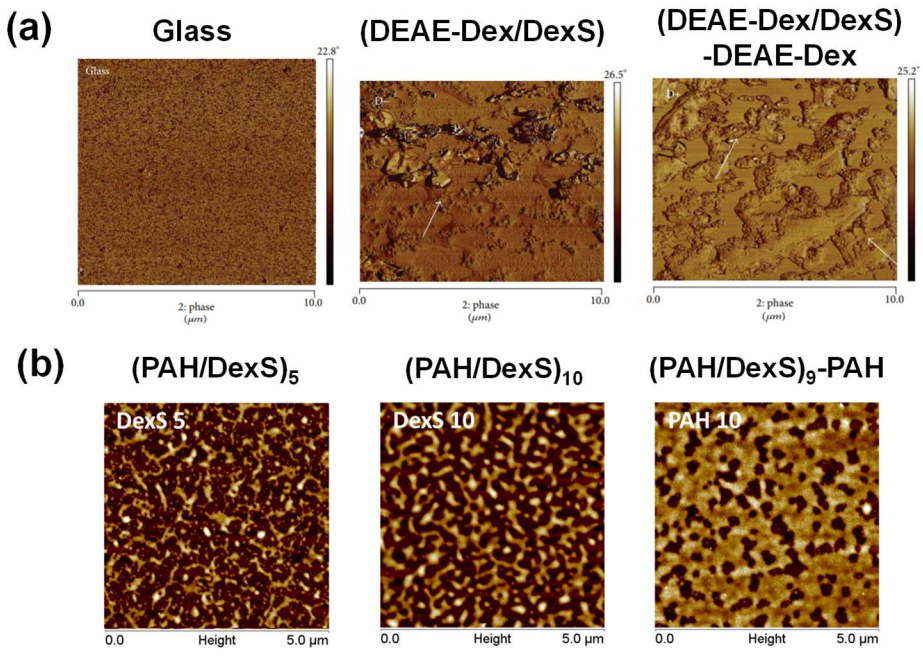


Figure 5. (a) AFM images (10 μm × 10 μm, phase) of bare glass surface, (DEAE-Dex/DexS) multilayer, and (DEAE-Dex/DexS)-DEAE-Dex multilayer adsorbed on glass surfaces (Benni et al., 2014). (b) AFM images (5 μm × 5 μm) of $(PAH/DexS)_5$ multilayer, $(PAH/DexS)_{10}$ multilayer and $(PAH/DexS)_9$-PAH multilayer adsorbed on silica surfaces, reprinted from (Delvart et al., 2022), with permission from Elsevier.

AFM images (Figure 5a) showed that (DEAE-Dex/DexS) and (DEAE-Dex/DexS)-DEAE-Dex multilayers display high coverage of the surface and their topographical morphologies present clusters or granules. Similar morphologies were found with (PAH/DexS) multilayers that are explained by charge equilibrium that led to polyelectrolytes complexes formation and dewatering during adsorption steps (Delvart et al., 2022). Analysis of the multilayers showed an increase of surface roughness with value of 47 nm for (DEAE-Dex/DexS) and 72 nm for (DEAE-Dex/DexS)-DEAE-Dex multilayers while the bare glass roughness range about 3 nm. Advancing contact angles monitoring displays the decrease of hydrophilicity, which may be related to an increase in surface roughness with the number of adsorption steps in general. Also, a higher hydrophobicity of the surface was observed with (DEAE-Dex/DexS)-DEAE-Dex multilayers than for (DEAE-Dex/DexS) multilayers. Consistently, similar surface morphology were obtained with (PAH/DexS) multilayers with also a roughness variation dependent on the last layer as illustrated on Figure 5b (Delvart et al., 2022). In 2019, Jang *et al.* demonstrated similar effect of DEAE-Dex/DexS multilayered coatings on metal stent, both increasing the hydrophilicity and inhibiting cell adhesion of metal stent (Jang et al., 2019). In this study, authors showed an increase of roughness with DEAE-Dex/DexS coating compared to DexS coating. Moreover, water contact angle of (DEAE-Dex/DexS) coated metal stent was significantly higher than water contact angle of the bare metal stent as well, confirming the potential of (DEAE-Dex/DexS) multilayers in tuning surfaces for various applications including protein and cell adhesion.

3.2.3. Dextran sulfates and proteins multilayered films

Proteins were associated with DexS to build multilayers for mainly targeting biomedical applications due to the biocompatibility of dextran sulfates and biological activity of protein. Investigation of interactions between polysaccharides and proteins in multilayers films constitutes a topic of interest in biomedical field in order to build films with controlled organisation of proteins (Brynda & Houska, 1998; J. Zhang et al., 2005). The use of LbL technique and choice of both assembly parameters and nature of polyelectrolyte-protein couple allow building of multilayers structured morphology but also regulation of the conformation of protein within the film (Hong et al., 1993; Lvov et al., 1994, 1995). Similarly to usual encountered polyelectrolytes, processing parameters (pH, salt concentration, compound concentrations, temperature, etc.) are of importance for polyelectrolyte-protein multilayers film construction as well as the nature of protein (Müller et al., 2001; vander Straeten et al., 2018, 2020). Overall, pH was found to be a key parameter in the LbL assembly of proteins with polyelectrolyte to promote interactions between proteins and polyelectrolyte, and pH of the protein solution has to be set apart from the isoelectric point (IEP) (Kayitmazer et al., 2013; Lvov et al., 1995; vander Straeten et al., 2018). In general, proteins may be prone to conformation change according to solution conditions and surface properties, which have an important impact on protein adsorption and multilayer formation.

In 1999, Brynda *et al.* used DexS as a building block to fabricate LbL assembly with human b2-microglobulin antibody cross-linked with glutaraldehyde. The resulting flexible film can be used as immunosensor for b2-microglobulin (Brynda et al., 1999). More recently, Damanik *et al.* investigated the growth of collagen/DexS 4 bilayers on PEI/poly(styrenesulfonate) (PSS) 2 bilayers in order to develop high loading efficiency systems for biomedical applications. This study highlights the effect of collagen/DexS multilayers: collagen at pH 7 leads to linear growth while an exponential growth is obtained

521 with collagen at pH 3. At pH 3, collagen used by authors with basal isoelectric point 7.8 may
522 have more electrostatic interactions with DexS, as well as a compact conformation more
523 likely to lead to exponential film growth. Moreover, they were able to optimise the
524 immobilisation of heparin in such multilayer systems, *i.e.* the bioactivity of heparin is retained
525 on $(PEI/PSS)_2$+$(collagen/DexS)_4$ for 14 days by using collagen in acidic pH and exponential
526 growth of collagen/DexS 4 bilayers (Damanik et al., 2020). He and Hu first reported in 2004 a
527 study on the interactions of hemoglobin or myoglobin with DexS presenting more details on
528 the interactions between proteins and the polyelectrolyte. Authors suggested that localised
529 electrostatic interactions are the driving force in protein/polymer LbL assemblies such as with
530 heme proteins (hemoglobin or myoglobin) that have net positive charges or net negative
531 charges depending on the pH solution (He & Hu, 2004). Houska *et al.* published a report on
532 the influence of polyelectrolyte chain length on the LbL formation with proteins, especially
533 albumin. The authors compared multilayers of albumin/DexS with different molecular
534 weights of DexS and they showed that the assembly of globular proteins and linear strong
535 polyanions at pH below the isoelectric point (IEP) of the protein is affected by the chain
536 length of the polyanion (Houska et al., 2004). The study suggested that at lower molecular
537 weights of DexS, competition with adsorbing protein and absorbed protein might lead to
538 resolubilisation of the polyelectrolyte. Interactions between polysaccharides and proteins in
539 LbL process were further investigated by Jourdain *et al.* using caseinate to understand
540 mechanisms at interfaces for emulsion stabilisation (L. Jourdain et al., 2008; L. S. Jourdain et
541 al., 2009). LbL construction of (Caseinate/DexS) layers displays linear increase of shear
542 viscosity with time explained by strong interactions between caseinate and DexS that produce
543 flat conformation of the layer followed by a slow reorganisation of protein and DexS.

544 3.3. Other dextrans derivatives in multilayered films

In the late 2000s, Lee, Choi and Tsutsumi built polyaniline and carboxydextran multilayer films that present an interesting activity for the oxidation of ascorbic acid but also an excellent electron-transfer mediating capability for oxidation of glucose (Lee et al., 2009). Oxidised dextrans were used to form a bilayer with PEI to immobilise biocatalyst of β-1,4-endoxylanase by surface coating for the production of xylooligosaccharides (Romero-Fernandez et al., 2018). PEI was associated with an amine-substituted dextran, aminodextran (AMD), as well as with oxidised dextrans using dipping technique to build multilayers (Heurich et al., 2011; Romero-Fernandez et al., 2018). Heurich *et al.* proposed the use of biointerfaces for increasing cell compatibility while Romero-Fernandez *et al.* proposed to use them as coating to immobilise biocatalyst of β-1,4-endoxylanase for the production of xylooligosaccharides as well. In order to develop bioink for 3-dimensional printing, another dextran derivative, hydroxyethyl-methacrylate-derivatised dextran (Dex-HEMA), was paired with hyaluronic acid (HA) to produce bio-based hydrogels *i.e.* bioink (Pescosolido et al., 2011). In 2019, boronic derivative (the phenylboronic acid-modified alginate) and a diol biopolymer (a dextran derivative) were applied to the fabrication of H_2O_2-responsive microparticles by Mansour, Joukhar and Belbekhouche (Mansour et al., 2019).

4. DEXTRAN AS POLYELECTROLYTES FOR 3-DIMENSIONAL MULTILAYER STRUCTURES

4.1. Dextran-based multilayer objects: fabrication principle and methods

Polyelectrolyte multilayer objects (films or capsules) form an attractive class of materials which can be designed to achieve multiple functions . Multilayer objects also called shell objects consist of polyelectrolytes layers that are formed in the presence of a template produced by LbL assembly leading to a multilayer of an engineered shape. ‘Hollow’ multilayer objects and capsules are mainly fabricated by coating core particles, which served

as sacrificial templates, with a shell using LbL technique described in *3.1* (Antipov et al., 2003; Bao et al., 2016; Hu et al., 2011; Itoh et al., 2004; Parakhonskiy et al., 2014; G. B. Sukhorukov, Volodkin, et al., 2004). As illustrated in Figure 6a,b, the LbL technique is applied to a core template by sequential adsorption of oppositely charged substances onto the core, followed by removal of the core template by dissolution. However, as presented by Figure 6b, multilayer objects can be built by LbL technique directly onto targeted materials without the need of a dissolution step.

As multilayer films, physical and chemical properties of the multilayered capsules are strongly dependent on chemical nature and structure of the polyelectrolytes used in their fabrication and on the template coated (Gil et al., 2008). The size of the microcapsules can be tuned by varying the size of core template while the thickness of the hollow shell can be controlled by LbL technique conditions, nature of adsorbed molecules and numbers of layers adsorbed (Dubas & Schlenoff, 1999; Shiratori & Rubner, 2000; G. B. Sukhorukov, Shchukin, et al., 2004; G. B. Sukhorukov et al., 2005). Thus, appropriate choice of the template type, of the polyelectrolytes pair and of the LbL deposition parameters should be done to control the morphology of such objects and, as a result, their properties such as permeability (G. B. Sukhorukov et al., 1999; Tong et al., 2005). The choice of polyelectrolytes can also provide interesting properties to capsules such as sensitive permeability, with a stimuli-responsive (pH, ionic strength) character, that is a key property for encapsulation and drug delivery (Delcea et al., 2011; G. Sukhorukov et al., 2001).

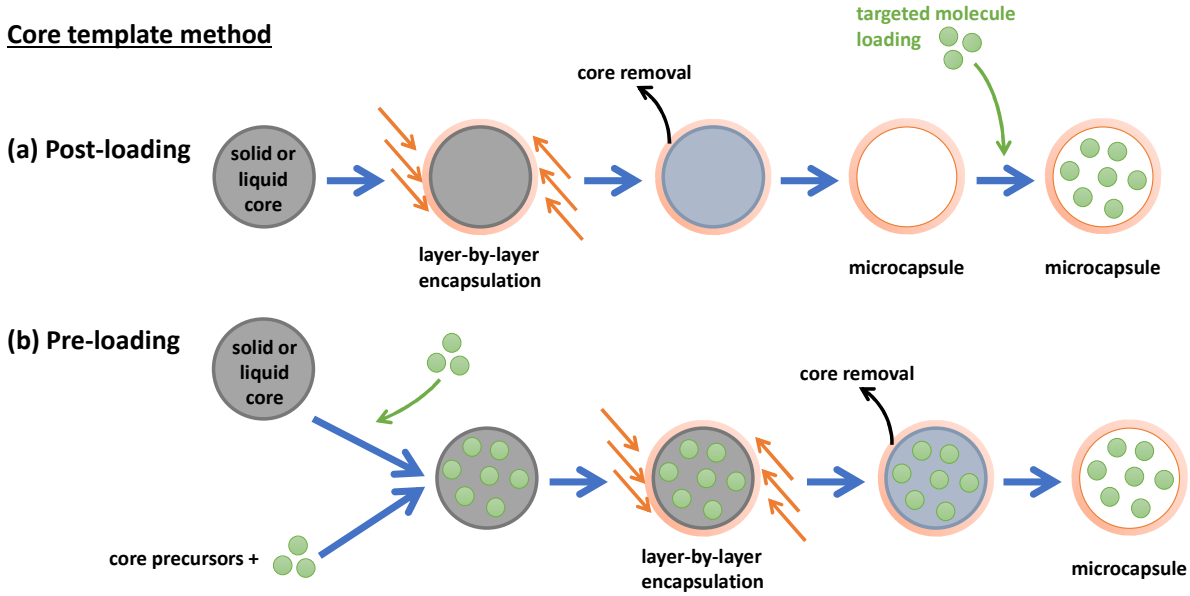


Figure 6. Schematic fabrication of micro- and nano- capsules based on LbL deposition principle onto sacrificial core template with (a) post-loading method and (b) pre-loading method.

Multilayer objects and capsules are mainly used in the biomedical sciences as shown on Table 2 and 3. The scientific community interest is particularly focused on their potential for drug delivery applications that imply loading of active molecules into those objects and their release. The versatility of LbL technique allows the fabrication of micro-objects with various colloid sizes, shapes, compositions and functionalities that answer the problematics of drug delivery devices (Ariga et al., 2011; De Cock et al., 2010; Tong et al., 2012).

A wide range of organic and inorganic molecules/polymers were used as suitable core materials for dextran-based capsules formation and successful formation of microcapsules from the literature is listed in Table 2. Those templates include polymers such as melamine formaldehyde (MF) which has drawbacks concerning production, which involves highly toxic chemicals, and degradation (N. Balabushevich et al., 2005; N. G. Balabushevich & Larionova,

605 2009). In addition to the inherent toxicity of the MF, the dissolution of the MF core at very
606 low pH (< 1.6) or with organic solvent limited their biocompatibility or so their applications.
607 Mineral cores such as SiO_2 or $CaCO_3$ templates are often used for dextran-based capsules
608 (Devi et al., 2015; Gao et al., 2016; Paini et al., 2015; Pawlak et al., 2022; Reibetanz et al.,
609 2011). They have been found to be nontoxic, biocompatible, thermally and mechanically
610 stable (Bao et al., 2016). However, their dissolution step remains a limiting factor since SiO_2
611 cores are dissolved by hydrofluoric acid and carbonates cores are dissolved at low pH (< 3) or
612 with ethylenediaminetetraacetic acid (Antipov et al., 2003; Sudareva et al., 2014; G. B.
613 Sukhorukov, Volodkin, et al., 2004). Moreover, those inorganic cores usually display larger
614 sizes than organic ones (Table 2) which limit their utilisation in some application where
615 capsules with nanometric size are targeted. Dextran microcapsules fabrication can be also
616 formed onto "soft" core templates in order to avoid the removal step (Grigoriev et al., 2008;
617 Tjipto et al., 2006). Preparation of shell capsules are based on emulsions on micro-aggregate
618 procedures of polyelectrolytes and active molecules which act both as the core templates and
619 loaded substances (Averin et al., 2016; Fukui & Fujimoto, 2009, 2011). Less frequent used
620 templates such as metallic silver and gold nanoparticles have also been reported to form
621 'hollow' capsules of dextrans (Anandhakumar et al., 2011, 2012; Livanovich & Shutava,
622 2019).

623 In addition to different sacrificial templates for LbL sequential adsorption, two
624 different approaches for loading active content can be distinguished in literature: pre-loading
625 and post-loading that are illustrated on Figure 6 a and b. With pre-loading procedures, core
626 templates already contain the molecules to encapsulate. It is the case for all the micro-
627 aggregate's precursors, as the first step is the fabrication of the core by complexation of
628 substance of interest with one of the two coating substances (Averin et al., 2016; N. G.
629 Balabushevich et al., 2006, 2016; Crecente-Campo & Jose Alonso, 2019). For example,

630 Averin and co-workers developed doxorubicin containing micro- and nano- particles by
631 preparing insoluble (Doxorubucin-DexS) particles before coating them with
632 $(CHI/DexS/CHI)_1$ (Averin et al., 2016). Pre-loading is also observed with dextran derivatives,
633 using solid templates by adding loaded content directly within the cores during their
634 preparation and keeping/retaining active compounds inside the hollow shell after core
635 dissolution. Selina *et al.* proposed $(DexS/PLL)_3$ biodegradable microcapsules using $CaCO_3$
636 core with entrapped protein (DNA) as template (Selina et al., 2009).

637 4.2. Dextrans and derivatives for multilayer capsules

638 *4.2.1. Overview of dextrans use for micro- and nano- capsules*

639 Table 2 reports the preparation of dextrans-based capsules and their application fields
640 which are mainly dedicated to biomedical, and especially drug delivery. The principal dextran
641 derivatives used, dextran sulfates (DexS) was shown to be suitable for the encapsulation with
642 various macromolecules with control on the quantity and the delivery time of the encapsulate
643 substance. Its availability and its properties in multilayers with various counter-
644 polyelectrolytes opened potential uses for capsules with monitoring capsules releasing and
645 loading by capsule morphology and responsive properties. Although there is a wide of
646 counter-polyelectrolytes, literature overview (Table 2) emphasises that most studies focus on
647 the capsules based on dextrans and bio-based polyelectrolytes (chitosan (CHI), polyarginine
648 including protamine and PLL) for the fabrication of biodegradable and biocompatible objects.

649 **Table 2.** Dextran derivatives as polyelectrolytes for micro– and nano– capsules fabrication
650 reported in literature.

Coating Components	Core Template	Encapsulated species	Size	Applications	Ref
DexS/CHI	SiO_2 cores	FITC-albumin; basic fibroblast	250–350 nm, 3–5 µm	drug delivery	(Devi et al., 2015; Geetha Devi et al.,

		growth factor; vascular endothelial growth factor; rifampicin; ciprofloxacin; ceftriaxone sodium salt; gentamicin sulphate; FITC			2021; Gnanadhas et al., 2013; Itoh et al., 2004, 2006, 2008a, 2008b)
	$CaCO_3$ cores	bovine serum albumin; polyphenol; protein (DNA); antibiotic	3–6 µm	drug delivery	(Ali Said et al., 2020; Ferrari et al., 2017; Paini et al., 2015; Selina et al., 2009)
	Drug-DexS microaggregates	doxorubicin; vitamin E and lecithin	various	drug delivery	(Averin et al., 2016; Crecente-Campo & Jose Alonso, 2019)
	Protein-DexS microaggreagates	N-benzoyl-L-arginine ethyl ester; N-benzoyl-L-tyrosine ethyl ester; insulin	6–12 µm	drug delivery	(N. G. Balabushevich et al., 2006, 2013)
	Emulsion	Phosphate ions; 1-hydroxy pyrene-3,6,8-trisulfonic acid; amphiphilic alendronate; non-ionic glucose	150–250 nm	drug delivery	(Fukui & Fujimoto, 2009, 2011)
	Silver nanoparticles	silver	30–50 nm	catalysis, photonics, pharmaceutics, biotechnology	(Livanovich & Shutava, 2019)
DexS/PAH	Silver nanoparticles	silver	20–50 nm		(Anandhakumar et al., 2011, 2012)
DexS/poly-L-arginine	SiO_2 cores	rhodamine B		drug delivery	(Gao et al., 2016)
	$CaCO_3$ cores	proteins; rhodamine B; messenger RNA; albumin and acid tannic; doxycycline; multikinase inhibitor sorafenib; alpha-2-macroglobulin	4–5 µm, 250–500 nm	drug delivery, cancer therapy, biomedical	(Canova et al., 2015; De Temmerman et al., 2011a, 2011b; Ermakov et al., 2019; Kakran et al., 2015; Karamitros et al., 2013; Kochetkova et al., 2013; W. Liu et al., 2014; Lomova et al., 2015; D. Luo et al., 2016; Novoselova et al., 2020; Poojari et al., 2016)
	Emulsion	acid tannic	150–200 nm	drug delivery	(Kashcooli et al., 2016; Lomova et al., 2010)
DexS/protamine	Melamine formaldehyde core	proteins, enzymes, peroxidases	3–4 µm	food processing, drug delivery, cosmetology	(N. Balabushevich et al., 2005; N. G. Balabushevich & Larionova, 2009)
	SiO_2 cores	kidney cells, various cells	2–4 µm	defoliation, plasmid delivery, drug delivery	(Reibetanz et al., 2006, 2010, 2011)

	$CaCO_3$ cores	proteins, anti-inflammatory, doxorubicin substances	2–5 µm	drug delivery, thermo-induced degradability	(N. G. Balabushevich et al., 2016; Rathmann et al., 2011; Trushina et al., 2018, 2019)
	Insulin-DexS microaggregates	insulin	7–20 µm	drug delivery	(N. Balabushevich & Larionova, 2004)
DexS/PLL	$CaCO_3$ cores	protein (DNA)	2–10 µm	biomedical, DNA vaccines	(Campbell et al., 2021; Selina et al., 2009)
	Erythrocyte carriers	erythrocyte	5–8 µm	drug delivery	(R. Luo, Mutukumaraswamy, et al., 2012)
	Poly(DL-lactide-co-glycolide) nanoparticles	poly(DL-lactide-co-glycolide)	50–100 nm	drug delivery	(R. Luo, Neu, et al., 2012)
	Fe_3O_4 nanoparticles	curcumin	10–20 µm	drug delivery	(Mancarella et al., 2015)
	Emulsion	bioactive compounds	100–200 µm	drug delivery	(Pan & Nitin, 2015)
DexS/DEAE-Dex	$CaCO_3$ cores			antimicrobial agents	(Pawlak et al., 2022)
Animated dextran/ carboxylated nanocellulose	Modified graphene oxide	curcumin	150–200nm	drug delivery, biomedicine, cancer therapy	(Anirudhan et al., 2019)
Carboxymethyldextran/ PLL	CdSe-ZnS cores	quantum dots	150–250nm	drug delivery, biomedicine	(Chen et al., 2003)
Diol dextran/ modified alginate	$CaCO_3$ cores	rhodamine b		drug delivery	(Mansour et al., 2019)

Similarly, for the construction of LbL films, (DexS/CHI) is a common polyelectrolytes couple for the fabrication of micro- and nano- capsules, as reported in Table 2. Since they are biocompatible, biodegradable and pH responsive, (CHI/DexS) capsules present different advantages for drug delivery systems, especially for release control since they offer different possibilities for drug release that can be triggered either by chemical or enzymatic action (Itoh et al., 2004, 2006, 2008a, 2008b).

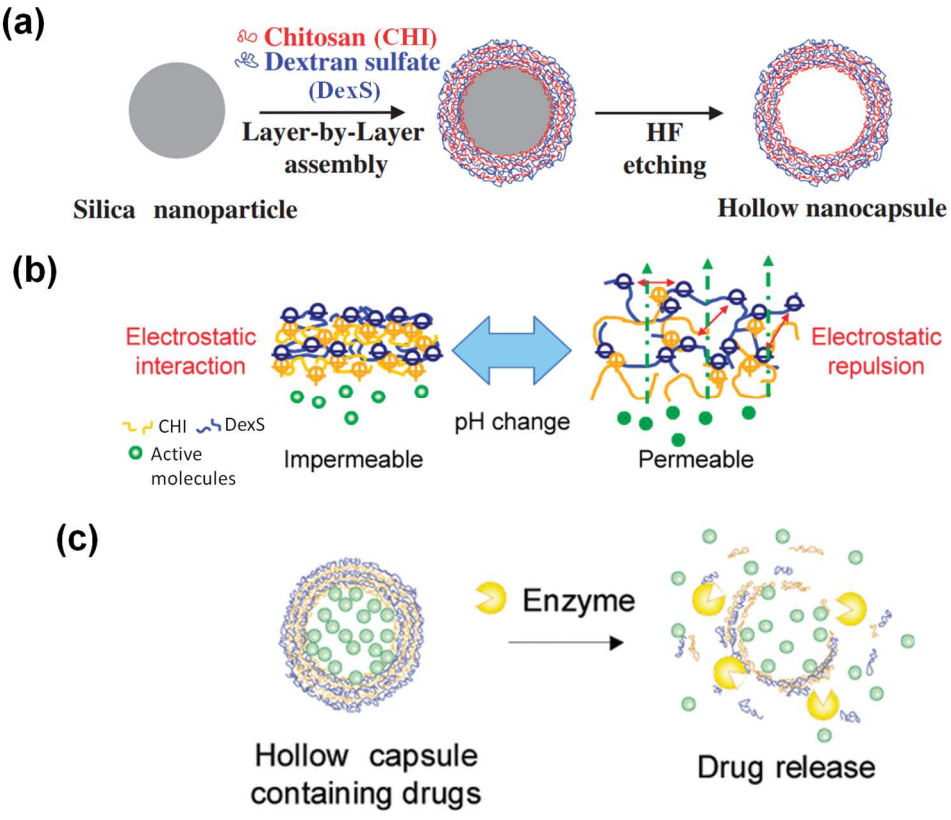


Figure 7. Schematic representations of (a) the fabrication principle of (CHI/DexS) capsules onto SiO_2 cores with dissolution by hydrofluoric acid (HF) (Itoh et al., 2004); (b) sensitive (CHI/DexS) multilayer based on pH changes with the impact on multilayer permeability, reprinted with permission from (Itoh et al., 2008b), © 2008 American Chemical Society; and (c) (CHI/DexS)-based release system of encapsulated drug with enzymatic degradation, adapted with permission from (Itoh et al., 2006), © 2006 American Chemical Society..

Authors designed (CHI/DexS) hollow capsules by LbL assembly on SiO_2 cores before core dissolution, as illustrated by Figure 7a, and obtained capsules with pH-dependent morphology and permeability (Itoh et al., 2008b). They observed a significant change in the permeability of the capsules between pH 6.8 and 8.0. Capsules (CHI/DexS) are impermeable with small pores under pH 6.8 and permeable with larger pores over pH 8.0 due to the pKa of CHI due to the deprotonation of the amine groups of CHI at basic pH as described in Figure 7b. The pH-responsive property of (CHI/DexS) capsules allowed an effective loading of

673 fluorescein isothiocyanate-labelled dextran by switching environmental pH from 8.0 to 5.6
674 but also a release of active molecules triggered by pH change. The advantage of choosing
675 polysaccharides for polyelectrolytes-based structures is their sensitivity to enzymes that allow
676 the elaboration of enzyme-responsive devices (Itoh et al., 2006, 2008a). In those systems, the
677 release is controlled by the selection of the type and amount of enzymes, as illustrated on
678 Figure 7c. Itoh research group demonstrated the biodegradability of (CHI/DexS) capsules by
679 using chitosanase that hydrolysed CHI leading to capsules deformation and degradation (Itoh
680 et al., 2006). Later on, authors also proposed to tune the degradation by building composites
681 multilayer containing other enzyme-sensitive polyelectrolytes such as PLL that can be
682 degraded by α-chymotrypsin. The formation of (CHI/DexS/PLL) allowed the stepwise release
683 of multiple proteins at different time from i) degradation of PLL in a first step and then ii)
684 degradation of CHI. More combinations for a controlled release can be designed based on the
685 choice of polyelectrolyte/enzyme couple and on the characterises of multilayer obtained.

686 Efficiency of dextran sulfates-based capsules and of their release capacity is also
687 dependent on the quantity of targeted molecules encapsulated into the devices. In 2016,
688 Balabushevich *et al.* studied the loading of model proteins: catalase (Cat), insulin (Ins) and
689 aprotinin (Apr) into $(DexS/protamine)_2$-DexS multilayer capsules considering the three
690 approaches (N. G. Balabushevich et al., 2016). 3) Sorption of protein into shell capsules after
691 capsule formation and core dissolution (post-loading), 2) adsorption of protein solution onto
692 pre-made $CaCO_3$ cores before capsule formation (pre-loading and adsorption), 3) co-synthesis
693 of protein with $CaCO_3$ cores before capsule formation (pre-loading and co-synthesis).

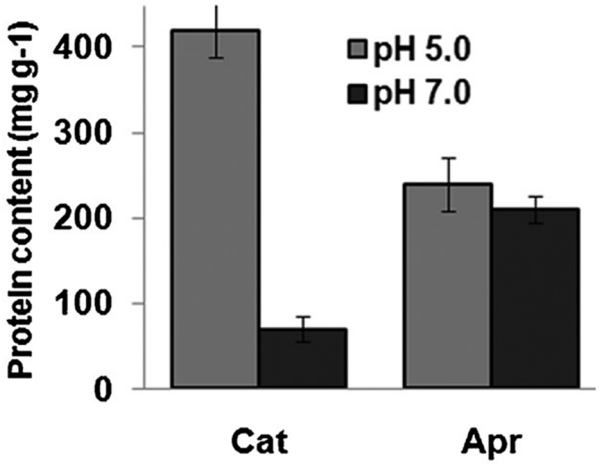


Figure 8. Proteins catalase (Cat) and aprotinin (Apr) contents of (DexS/protamine) capsules obtained by post-loading approach (N. G. Balabushevich et al., 2016).

Pre-loading by adsorption of protein onto $CaCO_3$ cores or by co-synthesis is only based on the electrostatic interaction between proteins and cores at chosen pH while post-loading approach is based on the affinity between proteins and cores. In the post-loading case, it was shown that catalase and aprotinin can be adsorbed into $(DexS/protamine)_2$-DexS capsules at both pH 5 and pH 7 with different efficiency, as illustrated on Figure 8. $(DexS/protamine)_2$-DexS microcapsules have negative charges due to the uncompensated charged groups of DexS, since DexS is a stronger polyelectrolyte than protamine. So, catalase is preferably incorporated at pH 5 (40% by mass) than at pH 7 (7% by mass) as a result of the occurrence of positive charge on catalase at pH 5. For aprotinin, no difference was observed as protein content corresponds to 20 – 25% whatever the pH since the protein is negatively charged at both pH. Those results confirm that loading is mainly driven by electrostatic interactions between loaded molecules and multilayer capsules. Thus, the choice of polyelectrolyte used (charge equilibrium) for multilayers and conditions (pH, ionic strength) are important parameters to consider for controlled loading.

The use of other dextran derivatives remains low compared to dextran sulfates. However, the use of cationic dextrans can increase potential applications for dextran in biomedical due to their use with other polyanion, but it can also add properties to multilayers. In 2019, Anirudhan *et al.* proposed the use of an aminated dextran to create multilayer capsules with stimuli responsive property due to pH sensitivity of both polyanion (oxidised nanocellulose) and polycation (aminated dextran) (Anirudhan et al., 2019). As dextran sulfate is a weak polyanion with high stability in water (pKa ~ 2), the employment of anionic dextran derivatives with a higher pKa can also be useful for the elaboration of stimuli-responsive objects. Dextran derivatives can also be used to substitute synthetic polyelectrolytes in specific applications such as reactive oxygen multilayers. Mansour *et al.* proposed for example the formation of multilayer capsules with hydrogen peroxide sensitivity based on a diol-dextran (Mansour et al., 2019).

5. CONCLUSION

Nanomaterials based on dextran and dextran derivatives built by LbL method present promising applications in biomedical fields due to their biocompatibility and their biodegradability. Dextrans and dextran derivatives have been successfully introduced into multilayer films and structures with control on film growth and characteristics by tuning the processing parameters. Their great compatibility with other polysaccharides (chitosan, cellulose, etc.), polyarginines (poly-L-lysine (PLL), etc.) and proteins (insulin, etc.), allows to form biodegradable multilayers useful for drug delivery systems in particular. Moreover, the versatility and availability of dextrans and derivatives as well as their water-solubility, are key advantages for the exploration of assemblies formed by combining two polysaccharides compared to cellulosic materials (Šimkovic, 2013). The use of different dextrans make possible the formation of LbL films with control over different types of properties (bioactivity, chemical, mechanical) and control over different morphologies to design

736 assemblies and surfaces with specific functionalities (Crouzier et al., 2010). Among
737 derivatives, dextran sulfate seems to present the greater interest for the research community
738 for its many biological properties such as anticoagulant, anti-inflammatory and anti-viral
739 properties.

740 Although studies on the applicability of dextrans and dextran derivatives into
741 multilayers and multilayer objects can be found with various polyelectrolytes, there is a need
742 of deeper understanding of most dextran-based LbL assemblies beside well studied DexS.
743 Works considering other dextran derivatives, such as carboxylmethyl dextran,
744 diethylaminoethyl dextran (DEAE-Dex) or other aminated dextrans, are seldom and dedicated
745 to specific applications so that it is difficult to determine the key parameters controlling the
746 film growth. Commercially available dextran derivatives are still restricted and the chemical
747 functionalisation of dextrans limit the employment of dextran derivatives in the development
748 of innovative structures. Development of new routes of functionalisation of dextrans is
749 promising to extend the panel of dextran derivatives, with a better environmental impact and
750 diversified functional properties. One of them is to explore an enzymatic approach to the
751 custom synthesis of polyelectrolytes based on microbial polysaccharides such as dextrans. In
752 addition to finely controlled structures and molar masses of dextrans, designed enzymes may
753 improve the properties of α-glucans with charged groups (Moulis et al., 2021).

754 Moreover, apart from extensive research on (CHI/DexS) multilayer films and
755 structures, only a few studies have reported LbL assemblies with other polyelectrolyte
756 counterpart than chitosan. Functional groups in dextran derivatives as well as chemical
757 structures provide opening for adsorption. A wider range of other biocompatible and
758 biodegradable functional species from mineral nanoparticles to polypeptides has to be

759 explored in the next years and will open opportunities for controlled elaboration of dextran-
760 based multilayer nanoobjects.

761 Finally, studies and applications mostly focused on biomedical fields with drug
762 delivery applications. The possibility to control the film morphology and the surface pattern
763 of dextran-based multilayer opens opportunities to create specific surfaces or specific objects
764 that can be used in wider application fields. LbL assemblies in general still have room for
765 development in nanoarchitectonics or organized-nanostructures technology from energy
766 applications to life science (Ariga, 2021; Ariga et al., 2022). This includes nano-printing and
767 nano-lithography processes used to fabricate patterns of nanometre scales (Vigneswaran et al.,
768 2014) but also, the possibility to obtain super-hydrophobic coating by tuning hydrophobicity
769 found and developed for cell adhesion and proliferation (Jafari et al., 2019; Sethi & Manik,
770 2018; W. Song et al., 2010).

AUTHOR INFORMATION

Credit authorship contribution statement

Aurore Delvart: Conceptualisation, Investigation, Writing – original draft & editing, Visualisation. **Céline Moreau:** Conceptualisation, Writing – review & editing, Supervision. **Bernard Cathala:** Conceptualisation, Writing – review & editing, Project administration, Funding acquisition.

All authors have given approval to the final version of the manuscript.

Funding

This work has been supported by the French National Agency (ANR) as part of the program ANR-18-CE43-0007 (GRαFTING).

Declaration of Competing Interest

The authors declare no competing financial interest or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgment

The authors gratefully acknowledge the financial support for this study from French National Agency (ARN).

6. REFERENCES

Abid, N., Khan, A. M., Shujait, S., Chaudhary, K., Ikram, M., Imran, M., Haider, J., Khan, M., Khan, Q., & Maqbool, M. (2022). Synthesis of nanomaterials using various top-down and bottom-up approaches, influencing factors, advantages, and disadvantages: A review. *Advances in Colloid and Interface Science*, *300*, 102597. https://doi.org/10.1016/j.cis.2021.102597

Ahmad, N. H., Mustafa, S., & Man, Y. B. C. (2015). Microbial Polysaccharides and Their Modification Approaches: A Review. *International Journal of Food Properties*, *18*(2), 332–347. https://doi.org/10.1080/10942912.2012.693561

Ali Said, F., Bousserrhine, N., Alphonse, V., Michely, L., & Belbekhouche, S. (2020). Antibiotic loading and development of antibacterial capsules by using porous CaCO3 microparticles as starting material. *International Journal of Pharmaceutics*, *579*, 119175. https://doi.org/10.1016/j.ijpharm.2020.119175

Anandhakumar, S., Mahalakshmi, V., & Raichur, A. M. (2012). Silver nanoparticles modified nanocapsules for ultrasonically activated drug delivery. *Materials Science & Engineering C-Materials for Biological Applications*, *32*(8), 2349–2355. https://doi.org/10.1016/j.msec.2012.07.006

Anandhakumar, S., Vijayalakshmi, S. P., Jagadeesh, G., & Raichur, A. M. (2011). Silver Nanoparticle Synthesis: Novel Route for Laser Triggering of Polyelectrolyte Capsules. *ACS Applied Materials & Interfaces*, *3*(9), 3419–3424. https://doi.org/10.1021/am200651t

Anirudhan, T. S., Sekhar, C., V., Shainy, F., & Thomas, J. P. (2019). Effect of dual stimuli responsive dextran/nanocellulose polyelectrolyte complexes for chemophotothermal synergistic cancer therapy. *International Journal of Biological Macromolecules*, *135*, 776–789. https://doi.org/10.1016/j.ijbiomac.2019.05.218

812 Antipov, A. A., Shchukin, D., Fedutik, Y., Petrov, A. I., Sukhorukov, G. B., & Möhwald, H.
813 (2003). Carbonate microparticles for hollow polyelectrolyte capsules fabrication.
814 *Colloids and Surfaces A: Physicochemical and Engineering Aspects*, *224*(1–3), 175–
815 183. https://doi.org/10.1016/S0927-7757(03)00195-X
816 Antonini, E., Bellelli, L., Bruzzesi, M. R., Caputo, A., Chiancone, E., & Rossi-Fanelli, A.
817 (1964). Studies on dextran and dextran derivatives. I. Properties of native dextran in
818 different solvents. *Biopolymers*, *2*(1), 27–34.
819 https://doi.org/10.1002/bip.1964.360020105
820 Ariga, K. (2021). Nanoarchitectonics: what's coming next after nanotechnology? *Nanoscale*
821 *Horizons*, *6*(5), 364–378. https://doi.org/10.1039/D0NH00680G
822 Ariga, K., Lvov, Y., & Decher, G. (2022). There is still plenty of room for layer-by-layer
823 assembly for constructing nanoarchitectonics-based materials and devices. *Physical*
824 *Chemistry Chemical Physics*, *24*(7), 4097–4115. https://doi.org/10.1039/D1CP04669A
825 Ariga, K., Lvov, Y., & Kunitake, T. (1997). Assembling Alternate Dye–Polyion Molecular
826 Films by Electrostatic Layer-by-Layer Adsorption. *Journal of the American Chemical*
827 *Society*, *119*(9), 2224–2231. https://doi.org/10.1021/ja963442c
828 Ariga, K., Lvov, Y. M., Kawakami, K., Ji, Q., & Hill, J. P. (2011). Layer-by-layer self-
829 assembled shells for drug delivery. *Advanced Drug Delivery Reviews*, *63*(9), 762–771.
830 https://doi.org/10.1016/j.addr.2011.03.016
831 Averin, P. S., de Gerenyu, A. V. L., & Balabushevich, N. G. (2016). Polyelectrolyte Micro-
832 and Nanoparticles with Doxorubicin. *Moscow University Chemistry Bulletin*, *71*(2),
833 140–145. https://doi.org/10.3103/S0027131416020012
834 Baig, N., Kammakakam, I., & Falath, W. (2021). Nanomaterials: a review of synthesis
835 methods, properties, recent progress, and challenges. *Materials Advances*, *2*(6), 1821–
836 1871. https://doi.org/10.1039/D0MA00807A

837 Balabushevich, N. G., de Guerenu, A. V. L., Feoktistova, N. A., Skirtach, A. G., & Volodkin,
838 D. (2016). Protein-Containing Multilayer Capsules by Templating on Mesoporous
839 CaCO3 Particles: POST- and PRE-Loading Approaches. *Macromolecular Bioscience*,
840 *16*(1), 95–105. https://doi.org/10.1002/mabi.201500243
841 Balabushevich, N. G., & Larionova, N. I. (2009). Protein-loaded microspheres prepared by
842 sequential adsorption of dextran sulphate and protamine on melamine formaldehyde
843 core. *Journal of Microencapsulation*, *26*(7), 571–579.
844 https://doi.org/10.3109/02652040802518145
845 Balabushevich, N. G., Lebedeva, O. V., Vinogradova, O. I., & Larionova, N. I. (2006).
846 Polyelectrolyte assembling for protein microencapsulation. *Journal of Drug Delivery*
847 *Science and Technology*, *16*(4), 315–319. https://doi.org/10.1016/S1773-
848 2247(06)50056-5
849 Balabushevich, N. G., Pechenkin, M. A., Shibanova, E. D., Volodkin, D. V., & Mikhalchik,
850 E. V. (2013). Multifunctional Polyelectrolyte Microparticles for Oral Insulin Delivery.
851 *Macromolecular Bioscience*, *13*(10), 1379–1388.
852 https://doi.org/10.1002/mabi.201300207
853 Balabushevich, N., & Larionova, N. (2004). Fabrication and characteriation of polyelectrolyte
854 microparticles with protein. *Biochemistry-Moscow*, *69*(7), 757–762.
855 https://doi.org/10.1023/B:BIRY.0000040200.61663.01
856 Balabushevich, N., Sukhorukov, G., & Larionova, N. (2005). Polyelectrolyte multilayer
857 microspheres as carriers for bienzyme system: Preparation and characterization.
858 *Macromolecular Rapid Communications*, *26*(14), 1168–1172.
859 https://doi.org/10.1002/marc.200500141

Bamford, C. H., Middleton, I. P., & Al-Lamee, K. G. (1986). Studies of the esterification of dextran: routes to bioactive polymers and graft copolymers. *Polymer*, *27*(12), 1981–1985. https://doi.org/10.1016/0032-3861(86)90194-1

Bao, Y., Shi, C., Wang, T., Li, X., & Ma, J. (2016). Recent progress in hollow silica: Template synthesis, morphologies and applications. *Microporous and Mesoporous Materials*, *227*, 121–136. https://doi.org/10.1016/j.micromeso.2016.02.040

Benni, S., Avramoglou, T., Hlawaty, H., & Mora, L. (2014). Dynamic Contact Angle Analysis of Protein Adsorption on Polysaccharide Multilayer's Films for Biomaterial Reendothelialization. *Biomed Research International*. https://doi.org/10.1155/2014/679031

Borges, J., & Mano, J. F. (2014). Molecular Interactions Driving the Layer-by-Layer Assembly of Multilayers. *Chemical Reviews*, *114*(18), 8883–8942. https://doi.org/10.1021/cr400531v

Boudou, T., Crouzier, T., Ren, K., Blin, G., & Picart, C. (2010). Multiple Functionalities of Polyelectrolyte Multilayer Films: New Biomedical Applications. *Advanced Materials*, *22*(4), 441–467. https://doi.org/10.1002/adma.200901327

Bovey, F. A. (1959). Enzymatic polymerization. I. Molecular weight and branching during the formation of dextran. *Journal of Polymer Science*, *35*(128), 167–182. https://doi.org/10.1002/pol.1959.1203512813

Braconnot, H. (1813). Expériences Sur un Acide Particulier qui se Développe Dans les Matières Acescentes. *Ann. Chim*, *86*, 84–100.

Brynda, E., & Houska, M. (1998). Preparation of organized protein multilayers. *Macromolecular Rapid Communications*, *19*(4), 173–176. https://doi.org/10.1002/(SICI)1521-3927(19980401)19:4<173::AID-MARC173>3.0.CO;2-S

885 Brynda, E., Houska, M., Brandenburg, A., Wikerstal, A., & Skvor, J. (1999). The detection of
886 human beta(2)-microglobulin by grating coupler immunosensor with three
887 dimensional antibody networks. *Biosensors & Bioelectronics*, *14*(4), 363–368.
888 https://doi.org/10.1016/S0956-5663(99)00013-5
889 Burton, B. A., & Brant, D. A. (1983). Comparative flexibility, extension, and conformation of
890 some simple polysaccharide chains. *Biopolymers*, *22*(7), 1769–1792.
891 https://doi.org/10.1002/bip.360220712
892 Calvo, E. J., Flexer, V., Tagliazucchi, M., & Scodeller, P. (2010). Effects of the nature and
893 charge of the topmost layer in layer by layer self assembled amperometric enzyme
894 electrodes. *Physical Chemistry Chemical Physics*, *12*(34), 10033–10039.
895 https://doi.org/10.1039/C0CP00449A
896 Campbell, J., Abnett, J., Kastania, G., Volodkin, D., & Vikulina, A. S. (2021). Which
897 Biopolymers Are Better for the Fabrication of Multilayer Capsules? A Comparative
898 Study Using Vaterite $CaCO_3$ as Templates. *ACS Applied Materials & Interfaces*,
899 *13*(2), 3259–3269. https://doi.org/10.1021/acsami.0c21194
900 Canova, D. F., Pavlov, A. M., Norling, L. V., Gobbetti, T., Brunelleschi, S., Le Fauder, P.,
901 Cenac, N., Sukhorukov, G. B., & Perretti, M. (2015). Alpha-2-macroglobulin loaded
902 microcapsules enhance human leukocyte functions and innate immune response.
903 *Journal of Controlled Release*, *217*, 284–292.
904 https://doi.org/10.1016/j.jconrel.2015.09.021
905 Cerclier, C., Cousin, F., Bizot, H., Moreau, C., & Cathala, B. (2010). Elaboration of Spin-
906 Coated Cellulose-Xyloglucan Multilayered Thin Films. *Langmuir*, *26*(22), 17248–
907 17255. https://doi.org/10.1021/la102614b

908 Chen, Y., Ji, T., & Rosenzweig, Z. (2003). Synthesis of glyconanospheres containing
909 luminescent CdSe-ZnS quantum dots. *Nano Letters*, *3*(5), 581–584.
910 https://doi.org/10.1021/nl034086g
911 Cheng, L., Wang, X., Gong, F., Liu, T., & Liu, Z. (2020). 2D Nanomaterials for Cancer
912 Theranostic Applications. *Advanced Materials*, *32*(13), 1902333.
913 https://doi.org/10.1002/adma.201902333
914 Chludzinski, A. M., Germaine, G. R., & Schachtele, C. F. (1974). Purification and properties
915 of dextransucrase from Streptococcus mutans. *Journal of Bacteriology*, *118*(1), 1–7.
916 Clark, S. L., & Hammond, P. T. (2000). The Role of Secondary Interactions in Selective
917 Electrostatic Multilayer Deposition. *Langmuir*, *16*(26), 10206–10214.
918 https://doi.org/10.1021/la000418a
919 Confer, D. R., & Logan, B. E. (1997). Molecular weight distribution of hydrolysis products
920 during the biodegradation of model macromolecules in suspended and biofilm
921 cultures. II. Dextran and dextrin. *Water Research*, *31*(9), 2137–2145.
922 https://doi.org/10.1016/S0043-1354(97)00050-X
923 Crecente-Campo, J., & Jose Alonso, M. (2019). Engineering, on-demand manufacturing, and
924 scaling-up of polymeric nanocapsules. *Bioengineering & Translational Medicine*,
925 *4*(1), 38–50. https://doi.org/10.1002/btm2.10118
926 Crouzier, T., Boudou, T., & Picart, C. (2010). Polysaccharide-based polyelectrolyte
927 multilayers. *Current Opinion in Colloid & Interface Science*, *15*(6), 417–426.
928 https://doi.org/10.1016/j.cocis.2010.05.007
929 Damanik, F. F. R., Brunelli, M., Pastorino, L., Ruggiero, C., van Blitterswijk, C., Rotmans, J.,
930 & Moroni, L. (2020). Sustained delivery of growth factors with high loading
931 efficiency in a layer by layer assembly. *Biomaterials Science*, *8*(1), 174–188.
932 https://doi.org/10.1039/c9bm00979e

Damasceno Borges, D., Woellner, C. F., Autreto, P. A. S., & Galvao, D. S. (2018). Insights on the mechanism of water-alcohol separation in multilayer graphene oxide membranes: Entropic versus enthalpic factors. *Carbon*, *127*, 280–286. https://doi.org/10.1016/j.carbon.2017.11.020

de Belder, D. (1996). Polysaccharides in Medicinal Applications. *Marcel Dekker, New York*, 505–524.

de Oliveira Farias, E. A., dos Santos, M. C., de Araujo Dionísio, N., Quelemes, P. V., de Souza Almeida Leite, J. R., Eaton, P., da Silva, D. A., & Eiras, C. (2015). Layer-by-Layer films based on biopolymers extracted from red seaweeds and polyaniline for applications in electrochemical sensors of chromium VI. *Materials Science and Engineering: B*, *200*, 9–21. https://doi.org/10.1016/j.mseb.2015.05.004

de Raucourt, E., Mauray, S., Chaubet, F., Maiga-Revel, O., Jozefowicz, M., & Fischer, A. M. (1998). Anticoagulant activity of dextran derivatives. *Journal of Biomedical Materials Research*, *41*(1), 49–57. https://doi.org/10.1002/(SICI)1097-4636(199807)41:1<49::AID-JBM6>3.0.CO;2-Q

De Temmerman, M.-L., Rejman, J., Grooten, J., De Beer, T., Vervaet, C., Demeester, J., & De Smedt, S. C. (2011a). Lyophilization of Protein-Loaded Polyelectrolyte Microcapsules. *Pharmaceutical Research*, *28*(7), 1765–1773. https://doi.org/10.1007/s11095-011-0411-z

De Temmerman, M.-L., Rejman, J., Grooten, J., De Beer, T., Vervaet, C., Demeester, J., & De Smedt, S. C. (2011b). Lyophilization of Protein-Loaded Polyelectrolyte Microcapsules. *Pharmaceutical Research*, *28*(7), 1765–1773. https://doi.org/10.1007/s11095-011-0411-z

Decher, G. (1997). Fuzzy Nanoassemblies: Toward Layered Polymeric Multicomposites. *Science*, *277*(5330), 1232–1237. https://doi.org/10.1126/science.277.5330.1232

Decher, G., & Hong, J. D. (1991a). Buildup of Ultrathin Multilayer Films by a Self-Assembly Process: II. Consecutive Adsorption of Anionic and Cationic Bipolar Amphiphiles and Polyelectrolytes on Charged Surfaces. *Berichte Der Bunsengesellschaft Für Physikalische Chemie*, *95*(11), 1430–1434. https://doi.org/10.1002/bbpc.19910951122

Decher, G., Hong, J. D., & Schmitt, J. (1992). Buildup of ultrathin multilayer films by a self-assembly process: III. Consecutively alternating adsorption of anionic and cationic polyelectrolytes on charged surfaces. *Thin Solid Films*, *210–211*, 831–835. https://doi.org/10.1016/0040-6090(92)90417-A

Decher, G., & Hong, J.-D. (1991b). Buildup of ultrathin multilayer films by a self-assembly process, 1 consecutive adsorption of anionic and cationic bipolar amphiphiles on charged surfaces. *Makromolekulare Chemie. Macromolecular Symposia*, *46*(1), 321–327. https://doi.org/10.1002/masy.19910460145

De Cock, L. J., De Koker, S., De Geest, B. G., Grooten, J., Vervaet, C., Remon, J. P., Sukhorukov, G. B., & Antipina, M. N. (2010). Polymeric Multilayer Capsules in Drug Delivery. *Angewandte Chemie International Edition*, *49*(39), 6954–6973. https://doi.org/10.1002/anie.200906266

Delcea, M., Möhwald, H., & Skirtach, A. G. (2011). Stimuli-responsive LbL capsules and nanoshells for drug delivery. *Advanced Drug Delivery Reviews*, *63*(9), 730–747. https://doi.org/10.1016/j.addr.2011.03.010

Delvart, A., Moreau, C., D'Orlando, A., Falourd, X., & Cathala, B. (2022). Dextran-based polyelectrolyte multilayers: Effect of charge density on film build-up and morphology. *Colloids and Surfaces B: Biointerfaces*, *210*, 112258. https://doi.org/10.1016/j.colsurfb.2021.112258

981 Deng, Y., Wu, Y., Qian, Y., Ouyang, X., Yang, D., & Qiu, X. (2010). ADSORPTION AND
982 DESORPTION BEHAVIORS OF LIGNOSULFONATE DURING THE SELF-
983 ASSEMBLY OF MULTILAYERS. *BioResources*, *5*(2), 1178–1196.
984 Desfosses. (1829). Observations sur la fermation visqueuse et sur le mutisme. *Journal de*
985 *pharmacie et des sciences accessoires*, *15*(series 2), 602.
986 Devi, M. G., Dutta, S., Al Hinai, A. T., & Feroz, S. (2014). Surface Morphology Study of
987 Chitosan-Dextran Sulphate Multilayer Thin Films. *Journal of Chitin and Chitosan*
988 *Science*, *2*(4), 245–258. https://doi.org/10.1166/jcc.2014.1069
989 Devi, M. G., Dutta, S., Al Hinai, A. T., & Feroz, S. (2015). Studies on encapsulation of
990 Rifampicin and its release from chitosan-dextran sulfate capsules. *Korean Journal of*
991 *Chemical Engineering*, *32*(1), 118–124. https://doi.org/10.1007/s11814-014-0161-9
992 Díaz-Montes, E. (2021). Dextran: Sources, Structures, and Properties. *Polysaccharides*, *2*(3),
993 554–565. https://doi.org/10.3390/polysaccharides2030033
994 Dubas, S. T., & Schlenoff, J. B. (1999). Factors Controlling the Growth of Polyelectrolyte
995 Multilayers. *Macromolecules*, *32*(24), 8153–8160. https://doi.org/10.1021/ma981927a
996 Dubas, S. T., & Schlenoff, J. B. (2001). Swelling and Smoothing of Polyelectrolyte
997 Multilayers by Salt. *Langmuir*, *17*(25), 7725–7727. https://doi.org/10.1021/la0112099
998 Elbert, D. L., Herbert, C. B., & Hubbell, J. A. (1999). Thin Polymer Layers Formed by
999 Polyelectrolyte Multilayer Techniques on Biological Surfaces. *Langmuir*, *15*(16),
1000 5355–5362. https://doi.org/10.1021/la9815749
1001 Elferink, J. G. R., & de Koster, B. M. (1995). The role of calcium ions in DEAE-dextran-
1002 induced stimulation of neutrophil migration. *Chemico-Biological Interactions*, *95*(1),
1003 203–214. https://doi.org/10.1016/0009-2797(94)03360-9
1004 Elzbieciak, M., Kolasińska, M., Zapotoczny, S., Krastev, R., Nowakowska, M., &
1005 Warszyński, P. (2009). Nonlinear growth of multilayer films formed from weak

polyelectrolytes. *Colloids and Surfaces A: Physicochemical and Engineering Aspects*, *343*(1–3), 89–95. https://doi.org/10.1016/j.colsurfa.2009.01.034

Ermakov, A., V., Inozemtseva, O. A., Gorin, D. A., Sukhorukov, G. B., Belyakov, S., & Antipina, M. N. (2019). Influence of Heat Treatment on Loading of Polymeric Multilayer Microcapsules with Rhodamine B. *Macromolecular Rapid Communications*, *40*(5, SI). https://doi.org/10.1002/marc.201800200

Feldötö, Z., Varga, I., & Blomberg, E. (2010). Influence of Salt and Rinsing Protocol on the Structure of PAH/PSS Polyelectrolyte Multilayers. *Langmuir*, *26*(22), 17048–17057. https://doi.org/10.1021/la102351f

Félix, O., Zheng, Z., Cousin, F., & Decher, G. (2009). Are sprayed LbL-films stratified? A first assessment of the nanostructure of spray-assembled multilayers by neutron reflectometry. *Comptes Rendus Chimie*, *12*(1–2), 225–234. https://doi.org/10.1016/j.crci.2008.09.009

Ferrari, P. F., Aliakbarian, B., Zattera, E., Pastorino, L., Palombo, D., & Perego, P. (2017). ENGINEERED CACO(3) NANOPARTICLES WITH TARGETING ACTIVITY: A SIMPLE APPROACH FOR A VASCULAR INTENDED DRUG DELIVERY SYSTEM. *Canadian Journal of Chemical Engineering*, *95*(9), 1683–1689. https://doi.org/10.1002/cjce.22871

Fukuda, H., & Kikuchi, Y. (1977). Polyelectrolyte Complexes of Sodium Dextran Sulfate with Chitosan, .2. *Makromolekulare Chemie-Macromolecular Chemistry and Physics*, *178*(10), 2895–2899.

Fukuda, H., & Kikuchi, Y. (1978). Invitro Clot Formation on Polyelectrolyte Complexes of Sodium Dextran Sulfate with Chitosan. *Journal of Biomedical Materials Research*, *12*(4), 531–539. https://doi.org/10.1002/jbm.820120408

1030 Fukui, Y., & Fujimoto, K. (2009). The Preparation of Sugar Polymer-Coated Nanocapsules
1031 by the Layer-by-Layer Deposition on the Liposome. *Langmuir*, *25*(17), 10020–10025.
1032 https://doi.org/10.1021/la9008834
1033 Fukui, Y., & Fujimoto, K. (2011). Control in Mineralization by the Polysaccharide-Coated
1034 Liposome via the Counter-Diffusion of Ions. *Chemistry of Materials*, *23*(21), 4701–
1035 4708. https://doi.org/10.1021/cm201211n
1036 Gao, H., Goryacheva, O. A., Tarakina, N. V., & Sukhorukov, G. B. (2016). Intracellularly
1037 Biodegradable Polyelectrolyte/Silica Composite Microcapsules as Carriers for Small
1038 Molecules. *ACS Applied Materials & Interfaces*, *8*(15), 9651–9661.
1039 https://doi.org/10.1021/acsami.6b01921
1040 Gay-Lussac, J., & Pelouze, J. (1833). Sur l'acide lactique. *Annales de Chimie et de Physique*,
1041 *52*, 410–424.
1042 Geetha Devi, M., Dutta, S., Al Hinai, A. T., & Feroz, S. (2021). Nano engineered
1043 biodegradable capsules for the encapsulation and kinetic release studies of
1044 ciprofloxacin hydrochloride. *Journal of the Indian Chemical Society*, *98*(8), 100109.
1045 https://doi.org/10.1016/j.jics.2021.100109
1046 Ghimici, L., Morariu, S., & Nichifor, M. (2009). Separation of clay suspension by ionic
1047 dextran derivatives. *Separation and Purification Technology*, *68*(2), 165–171.
1048 Ghimici, L., & Nichifor, M. (2018). Dextran derivatives application as flocculants.
1049 *Carbohydrate Polymers*, *190*, 162–174. https://doi.org/10.1016/j.carbpol.2018.02.075
1050 Gil, P. R., del Mercato, L. L., del_Pino, P., Muñoz_Javier, A., & Parak, W. J. (2008).
1051 Nanoparticle-modified polyelectrolyte capsules. *Nano Today*, *3*(3–4), 12–21.
1052 https://doi.org/10.1016/S1748-0132(08)70040-9

1053 Glinel, K., Moussa, A., Jonas, A. M., & Laschewsky, A. (2002). Influence of Polyelectrolyte
1054 Charge Density on the Formation of Multilayers of Strong Polyelectrolytes at Low
1055 Ionic Strength. *Langmuir*, *18*(4), 1408–1412. https://doi.org/10.1021/la0113670
1056 Gnanadhas, D. P., Ben Thomas, M., Elango, M., Raichur, A. M., & Chakravortty, D. (2013).
1057 Chitosan-dextran sulphate nanocapsule drug delivery system as an effective
1058 therapeutic against intraphagosomal pathogen Salmonella. *Journal of Antimicrobial*
1059 *Chemotherapy*, *68*(11), 2576–2586. https://doi.org/10.1093/jac/dkt252
1060 Goodwin, A. P., Tabakman, S. M., Welsher, K., Sherlock, S. P., Prencipe, G., & Dai, H.
1061 (2009). Phospholipid−Dextran with a Single Coupling Point: A Useful Amphiphile for
1062 Functionalization of Nanomaterials. *Journal of the American Chemical Society*,
1063 *131*(1), 289–296. https://doi.org/10.1021/ja807307e
1064 Gribova, V., Auzely-Velty, R., & Picart, C. (2012). Polyelectrolyte Multilayer Assemblies on
1065 Materials Surfaces: From Cell Adhesion to Tissue Engineering. *Chemistry of*
1066 *Materials*, *24*(5), 854–869. https://doi.org/10.1021/cm2032459
1067 Grigoriev, D. O., Bukreeva, T., Möhwald, H., & Shchukin, D. G. (2008). New Method for
1068 Fabrication of Loaded Micro- and Nanocontainers: Emulsion Encapsulation by
1069 Polyelectrolyte Layer-by-Layer Deposition on the Liquid Core. *Langmuir*, *24*(3), 999–
1070 1004. https://doi.org/10.1021/la702873f
1071 Guzmán, E., Cavallo, J. A., Chuliá-Jordán, R., Gómez, C., Strumia, M. C., Ortega, F., &
1072 Rubio, R. G. (2011). pH-Induced Changes in the Fabrication of Multilayers of
1073 Poly(acrylic acid) and Chitosan: Fabrication, Properties, and Tests as a Drug Storage
1074 and Delivery System. *Langmuir*, *27*(11), 6836–6845.
1075 https://doi.org/10.1021/la200522r

Guzmán, E., Rubio, R. G., & Ortega, F. (2020). A closer physico-chemical look to the Layer-by-Layer electrostatic self-assembly of polyelectrolyte multilayers. *Advances in Colloid and Interface Science*, *282*, 102197. https://doi.org/10.1016/j.cis.2020.102197

Hall, M., & Ricketts, C. R. (1952). The Use of Dextran Sulphate as a Blood Anticoagulant in Biological Research. *Journal of Clinical Pathology*, *5*(4), 366–366. https://doi.org/10.1136/jcp.5.4.366

Hartley, P., McArthur, S., McLean, K., & Griesser, H. (2002). Physicochemical properties of polysaccharide coatings based on grafted multilayer assemblies. *Langmuir*, *18*(7), 2483–2494. https://doi.org/10.1021/la001801i

Haynie, D. T., Cho, E., & Waduge, P. (2011). "In and Out Diffusion" Hypothesis of Exponential Multilayer Film Buildup Revisited. *Langmuir*, *27*(9), 5700–5704. https://doi.org/10.1021/la104516a

He, P., & Hu, N. (2004). Interactions between Heme Proteins and Dextran Sulfate in Layer-by-Layer Assembly Films. *The Journal of Physical Chemistry B*, *108*(35), 13144–13152. https://doi.org/10.1021/jp049974u

Hehre, E. J. (1956). Natural synthesis of low molecular weight (clinical type) dextran by a Streptococcus strain. *Journal of Biological Chemistry*, *222*(2), 739–750.

Heinze, T., Liebert, T., Heublein, B., & Hornig, S. (2006). Functional Polymers Based on Dextran. In D. Klemm (Ed.), *Polysaccharides II* (Vol. 205, pp. 199–291). Springer Berlin Heidelberg. https://doi.org/10.1007/12_100

Hernández-Rivas, M., Guzmán, E., Fernández-Peña, L., Akanno, A., Greaves, A., Léonforte, F., Ortega, F., G. Rubio, R., & Luengo, G. S. (2020). Deposition of Synthetic and Bio-Based Polycations onto Negatively Charged Solid Surfaces: Effect of the Polymer Cationicity, Ionic Strength, and the Addition of an Anionic Surfactant. *Colloids and Interfaces*, *4*(3), 33. https://doi.org/10.3390/colloids4030033

Heurich, E., Zankovych, S., Beyer, M., Schnabelrauch, M., Berg, A., & Jandt, K. D. (2011). A Comparison of the Cell Compatibility of Poly(ethyleneimine) with that of other Cationic Biopolymers Used in Applications at Biointerfaces. *Advanced Engineering Materials*, *13*(9), B285–B295. https://doi.org/10.1002/adem.201080105

Hong, J. D., Lowack, K., Schmitt, J., & Decher, G. (1993). Layer-by-layer deposited multilayer assemblies of polyelectrolytes and proteins: from ultrathin films to protein arrays. In P. Laggner & O. Glatter (Eds.), *Trends in Colloid and Interface Science VII* (Vol. 93, pp. 98–102). Steinkopff. https://doi.org/10.1007/BFb0118482

Hoogeveen, N. G., Cohen Stuart, M. A., Fleer, G. J., & Böhmer, M. R. (1996). Formation and Stability of Multilayers of Polyelectrolytes. *Langmuir*, *12*(15), 3675–3681. https://doi.org/10.1021/la951574y

Houska, M., Brynda, E., & Bohata, K. (2004). The effect of polyelectrolyte chain length on layer-by-layer protein/polyelectrolyte assembly-an experimental study. *Journal of Colloid and Interface Science*, *273*(1), 140–147. https://doi.org/10.1016/j.jcis.2003.12.056

Hu, J., Chen, M., Fang, X., & Wu, L. (2011). Fabrication and application of inorganic hollow spheres. *Chemical Society Reviews*, *40*(11), 5472. https://doi.org/10.1039/c1cs15103g

Iler, R. K. (1966). Multilayers of colloidal particles. *Journal of Colloid and Interface Science*, *21*(6), 569–594. https://doi.org/10.1016/0095-8522(66)90018-3

Ioan, C. E., Aberle, T., & Burchard, W. (2000). Structure Properties of Dextran. 2. Dilute Solution. *Macromolecules*, *33*(15), 5730–5739. https://doi.org/10.1021/ma000282n

Itoh, Y., Matsusaki, M., Kida, T., & Akashi, M. (2004). Preparation of biodegradable hollow nanocapsules by silica template method. *Chemistry Letters*, *33*(12), 1552–1553. https://doi.org/10.1246/cl.2004.1552

1125 Itoh, Y., Matsusaki, M., Kida, T., & Akashi, M. (2006). Enzyme-responsive release of
1126 encapsulated proteins from biodegradable hollow capsules. *Biomacromolecules*, *7*(10),
1127 2715–2718. https://doi.org/10.1021/bm060289y
1128 Itoh, Y., Matsusaki, M., Kida, T., & Akashi, M. (2008a). Time-modulated release of multiple
1129 proteins from enzyme-responsive multilayered capsules. *Chemistry Letters*, *37*(3),
1130 238–239. https://doi.org/10.1246/cl.2008.238
1131 Itoh, Y., Matsusaki, M., Kida, T., & Akashi, M. (2008b). Locally controlled release of basic
1132 fibroblast growth factor from multilayered capsules. *Biomacromolecules*, *9*(8), 2202–
1133 2206. https://doi.org/10.1021/bm800321w
1134 Jaber, J. A., & Schlenoff, J. B. (2006). Recent developments in the properties and applications
1135 of polyelectrolyte multilayers. *Current Opinion in Colloid & Interface Science*, *11*(6),
1136 324–329. https://doi.org/10.1016/j.cocis.2006.09.008
1137 Jafari, R., Cloutier, C., Allahdini, A., & Momen, G. (2019). Recent progress and challenges
1138 with 3D printing of patterned hydrophobic and superhydrophobic surfaces. *The*
1139 *International Journal of Advanced Manufacturing Technology*, *103*(1–4), 1225–1238.
1140 https://doi.org/10.1007/s00170-019-03630-4
1141 Jang, E.-J., Lee, S.-Y., Bae, I.-H., Park, D. S., Jeong, M. H., & Park, J.-K. (2019). Fabrication
1142 and Evaluation of Polyelectrolyte Complexes of Dextran Derivatives for Drug Coating
1143 of Coronary Stents. *Applied Chemistry for Engineering*, *30*(5), 586–590.
1144 https://doi.org/10.14478/ace.2019.1057
1145 Jayakumar, R., Menon, D., Manzoor, K., Nair, S. V., & Tamura, H. (2010). Biomedical
1146 applications of chitin and chitosan based nanomaterials—A short review.
1147 *Carbohydrate Polymers*, *82*(2), 227–232.
1148 https://doi.org/10.1016/j.carbpol.2010.04.074

1149 Jeanes, A., Haynes, W. C., Wilham, C. A., Rankin, J. C., Melvin, E. H., Austin, M. J.,
1150 Cluskey, J. E., Fisher, B. E., Tsuchiya, H. M., & Rist, C. E. (1954). Characterization
1151 and classification of dextrans from ninety-six strains of bacteria1b. *Journal of the*
1152 *American Chemical Society*, *76*(20), 5041–5052.
1153 Jing, Y., Zhang, C., Fu, T., Jiang, C., Ma, K., Zhang, D., Hou, S., Dai, J., Wang, H., Zhang,
1154 X., Kou, G., & Guo, Y. (2016). Combination of dextran sulfate and recombinant
1155 trypsin on aggregation of Chinese hamster ovary cells. *Cytotechnology*, *68*(2), 241–
1156 248. https://doi.org/10.1007/s10616-014-9774-4
1157 Joseph, N., Ahmadiannamini, P., Hoogenboom, R., & Vankelecom, Ivo. F. J. (2014). Layer-
1158 by-layer preparation of polyelectrolyte multilayer membranes for separation. *Polymer*
1159 *Chemistry*, *5*(6), 1817–1831. https://doi.org/10.1039/C3PY01262J
1160 Jourdain, L., Leser, M. E., Schmitt, C., Michel, M., & Dickinson, E. (2008). Stability of
1161 emulsions containing sodium caseinate and dextran sulfate: Relationship to
1162 complexation in solution. *Food Hydrocolloids*, *22*(4), 647–659.
1163 https://doi.org/10.1016/j.foodhyd.2007.01.007
1164 Jourdain, L. S., Schmitt, C., Leser, M. E., Murray, B. S., & Dickinson, E. (2009). Mixed
1165 Layers of Sodium Caseinate plus Dextran Sulfate: Influence of Order of Addition to
1166 Oil-Water Interface. *Langmuir*, *25*(17), 10026–10037.
1167 https://doi.org/10.1021/la900919w
1168 Kadkhodaei, M., Wu, H., & Brant, D. A. (1991). Comparison of the conformational dynamics
1169 of the (1 → 4)- and (1 → 6)-linked α-D-glucans using13C-NMR relaxation.
1170 *Biopolymers*, *31*(13), 1581–1592. https://doi.org/10.1002/bip.360311313
1171 Kagimura, F. Y., da Cunha, M. A. A., Barbosa, A. M., Dekker, R. F. H., & Malfatti, C. R. M.
1172 (2015). Biological activities of derivatized d-glucans: A review. *International Journal*

of Biological Macromolecules, *72*, 588–598. https://doi.org/10.1016/j.ijbiomac.2014.09.008

Kakran, M., Muratani, M., Tng, W. J., Liang, H., Trushina, D. B., Sukhorukov, G. B., Ng, H. H., & Antipina, M. N. (2015). Layered polymeric capsules inhibiting the activity of RNases for intracellular delivery of messenger RNA. *Journal of Materials Chemistry B*, *3*(28), 5842–5848. https://doi.org/10.1039/c5tb00615e

Karamitros, C. S., Yashchenok, A. M., Moehwald, H., Skirtach, A. G., & Konrad, M. (2013). Preserving Catalytic Activity and Enhancing Biochemical Stability of the Therapeutic Enzyme Asparaginase by Biocompatible Multilayered Polyelectrolyte Microcapsules. *Biomacromolecules*, *14*(12), 4398–4406. https://doi.org/10.1021/bm401341k

Kashcooli, Y., Park, K., Bose, A., Greenfield, M., & Bothun, G. D. (2016). Patchy Layersomes Formed by Layer-by-Layer Coating of Liposomes with Strong Biopolyelectrolytes. *Biomacromolecules*, *17*(11), 3838–3844. https://doi.org/10.1021/acs.biomac.6b01467

Kayitmazer, A. B., Seeman, D., Minsky, B. B., Dubin, P. L., & Xu, Y. (2013). Protein–polyelectrolyte interactions. *Soft Matter*, *9*(9), 2553. https://doi.org/10.1039/c2sm27002a

Khin, M. M., Nair, A. S., Babu, V. J., Murugan, R., & Ramakrishna, S. (2012). A review on nanomaterials for environmental remediation. *Energy & Environmental Science*, *5*(8), 8075. https://doi.org/10.1039/c2ee21818f

Kikuchi, Y., & Fukuda, H. (1974). Polyelectrolyte Complex of Sodium Dextran Sulfate with Chitosan. *Makromolekulare Chemie-Macromolecular Chemistry and Physics*, *175*(12), 3593–3596.

Kim, W.-S., Han, G. G., Hong, L., Kang, S.-K., Shokouhimehr, M., Choi, Y.-J., & Cho, C.-S. (2019). Novel production of natural bacteriocin via internalization of dextran

nanoparticles into probiotics. *Biomaterials*, *218*, 119360. https://doi.org/10.1016/j.biomaterials.2019.119360

Kochetkova, O. Y., Kazakova, L. I., Moshkov, D. A., Vinokurov, M. G., & Shabarchina, L. I. (2013). Incorporation of proteins into polyelectrolyte microcapsules by coprecipitation and adsorption. *Russian Journal of Bioorganic Chemistry*, *39*(5), 504–509. https://doi.org/10.1134/S1068162013050087

Kokilavani, S., Syed, A., Thomas, A. M., Elgorban, A. M., Bahkali, A. H., Marraiki, N., Raju, L. L., Das, A., & Khan, S. S. (2021). Development of multifunctional Cu sensitized Ag-dextran nanocomposite for selective and sensitive detection of mercury from environmental sample and evaluation of its photocatalytic and anti-microbial applications. *Journal of Molecular Liquids*, *321*, 114742. https://doi.org/10.1016/j.molliq.2020.114742

Kothari, D., Das, D., Patel, S., & Goyal, A. (2014). Dextran and Food Application. In K. G. Ramawat & J.-M. Mérillon (Eds.), *Polysaccharides* (pp. 1–16). Springer International Publishing. https://doi.org/10.1007/978-3-319-03751-6_66-1

Kotov, N. A. (1999). Layer-by-layer self-assembly: The contribution of hydrophobic interactions. *Nanostructured Materials*, *12*(5), 789–796. https://doi.org/10.1016/S0965-9773(99)00237-8

Kulikouskaya, V. I., Pinchuk, S. V., Hileuskaya, K. S., Kraskouski, A. N., Vasilevich, I. B., Matievski, K. A., Agabekov, V. E., & Volotovski, I. D. (2018). Layer-by-layer buildup of polysaccharide-containing films: Physico-chemical properties and mesenchymal stem cells adhesion. *Journal of Biomedical Materials Research Part A*, *106*(8), 2093–2104. https://doi.org/10.1002/jbm.a.36408

Lacaze, G., Wick, M., & Cappelle, S. (2007). Emerging fermentation technologies: Development of novel sourdoughs. *Food Microbiology*, *24*(2), 155–160. https://doi.org/10.1016/j.fm.2006.07.015

Lazić, V., Vivod, V., Peršin, Z., Stoiljković, M., Ratnayake, I. S., Ahrenkiel, P. S., Nedeljković, J. M., & Kokol, V. (2020). Dextran-coated silver nanoparticles for improved barrier and controlled antimicrobial properties of nanocellulose films used in food packaging. *Food Packaging and Shelf Life*, *26*, 100575. https://doi.org/10.1016/j.fpsl.2020.100575

Leathers, T. D. (2002). Dextran. *Biopolymers*, *5*, 299–321.

Lee, S., Choi, B., & Tsutsumi, A. (2009). Electrochemical properties of polyaniline/carboxydextran (PANI/carDEX) composite films for biofuel cells in neutral aqueous solutions. *Biotechnology Letters*, *31*(6), 851–855. https://doi.org/10.1007/s10529-009-9944-1

Leemhuis, H., Pijning, T., Dobruchowska, J. M., van Leeuwen, S. S., Kralj, S., Dijkstra, B. W., & Dijkhuizen, L. (2013). Glucansucrases: Three-dimensional structures, reactions, mechanism, α-glucan analysis and their implications in biotechnology and food applications. *Journal of Biotechnology*, *163*(2), 250–272. https://doi.org/10.1016/j.jbiotec.2012.06.037

Li, R., Zeng, T., Wu, M., Zhang, H., & Hu, X. (2017). Effects of esterification on the structural, physicochemical, and flocculation properties of dextran. *Carbohydrate Polymers*, *174*, 1129–1137. https://doi.org/10.1016/j.carbpol.2017.07.034

Li, Y., Wang, X., & Sun, J. (2012). Layer-by-layer assembly for rapid fabrication of thick polymeric films. *Chemical Society Reviews*, *41*(18), 5998. https://doi.org/10.1039/c2cs35107b

Lindenbaum, G. M., Mirgorodskaya, O. A., & Moskvichev, B. V. (1977). Chemical modification of water-soluble dextrans. *Pharmaceutical Chemistry Journal*, *11*(6), 806–809. https://doi.org/10.1007/BF00779300

Liu, J., Willför, S., & Xu, C. (2015). A review of bioactive plant polysaccharides: Biological activities, functionalization, and biomedical applications. *Bioactive Carbohydrates and Dietary Fibre*, *5*(1), 31–61. https://doi.org/10.1016/j.bcdf.2014.12.001

Liu, W., Wang, X., Bai, K., Lin, M., Sukhorukov, G., & Wang, W. (2014). Microcapsules functionalized with neuraminidase can enter vascular endothelial cells in vitro. *Journal of the Royal Society Interface*, *11*(101). https://doi.org/10.1098/rsif.2014.1027

Livanovich, K., & Shutava, T. (2019). Influence of Chitosan/Dextran Sulfate Layer-by-Layer Shell on Colloidal Properties of Silver Nanoparticles. *International Journal of Nanoscience*, *18*(3–4, SI). https://doi.org/10.1142/S0219581X19400775

Lombardo, D., Calandra, P., Pasqua, L., & Magazù, S. (2020). Self-Assembly of Organic Nanomaterials and Biomaterials: The Bottom-Up Approach for Functional Nanostructures Formation and Advanced Applications. *Materials*, *13*(5), 1048. https://doi.org/10.3390/ma13051048

Lomova, M. V., Brichkina, A. I., Kiryukhin, M. V., Vasina, E. N., Pavlov, A. M., Gorin, D. A., Sukhorukov, G. B., & Antipina, M. N. (2015). Multilayer Capsules of Bovine Serum Albumin and Tannic Acid for Controlled Release by Enzymatic Degradation. *ACS Applied Materials & Interfaces*, *7*(22), 11732–11740. https://doi.org/10.1021/acsami.5b03263

Lomova, M. V., Sukhorukov, G. B., & Antipina, M. N. (2010). Antioxidant Coating of Micronsize Droplets for Prevention of Lipid Peroxidation in Oil-in-Water Emulsion. *ACS Applied Materials & Interfaces*, *2*(12), 3669–3676. https://doi.org/10.1021/am100818j

Lundström-Hämälä, L., Johansson, E., & Wågberg, L. (2010). Polyelectrolyte Multilayers from Cationic and Anionic Starch: Influence of Charge Density and Salt Concentration on the Properties of the Adsorbed Layers. *Starch - Stärke*, *62*(2), 102–114. https://doi.org/10.1002/star.200900176

Luo, D., Gould, D. J., & Sukhorukov, G. B. (2016). Local and Sustained Activity of Doxycycline Delivered with Layer-by-Layer Microcapsules. *Biomacromolecules*, *17*(4), 1466–1476. https://doi.org/10.1021/acs.biomac.6b00070

Luo, R., Mutukumaraswamy, S., Venkatraman, S. S., & Neu, B. (2012). Engineering of erythrocyte-based drug carriers: control of protein release and bioactivity. *Journal of Materials Science-Materials in Medicine*, *23*(1), 63–71. https://doi.org/10.1007/s10856-011-4485-2

Luo, R., Neu, B., & Venkatraman, S. S. (2012). Surface Functionalization of Nanoparticles to Control Cell Interactions and Drug Release. *Small*, *8*(16), 2585–2594. https://doi.org/10.1002/smll.201200398

Lvov, Y., Ariga, K., Ichinose, I., & Kunitake, T. (1995). Assembly of Multicomponent Protein Films by Means of Electrostatic Layer-by-Layer Adsorption. *Journal of the American Chemical Society*, *117*(22), 6117–6123. https://doi.org/10.1021/ja00127a026

Lvov, Y., Ariga, K., & Kunitake, T. (1994). Layer-by-Layer Assembly of Alternate Protein/Polyion Ultrathin Films. *Chemistry Letters*, *23*(12), 2323–2326. https://doi.org/10.1246/cl.1994.2323

Lvov, Y., Onda, M., Ariga, K., & Kunitake, T. (1998). Ultrathin films of charged polysaccharides assembled alternately with linear polyions. *Journal of Biomaterials Science, Polymer Edition*, *9*(4), 345–355. https://doi.org/10.1080/09205063.1998.9753060

Ma, Y., Zhang, Y., Wu, B., Sun, W., Li, Z., & Sun, J. (2011). Polyelectrolyte Multilayer Films for Building Energetic Walking Devices. *Angewandte Chemie*, *123*(28), 6378–6381. https://doi.org/10.1002/ange.201101054

Mancarella, S., Greco, V., Baldassarre, F., Vergara, D., Maffia, M., & Leporatti, S. (2015). Polymer-Coated Magnetic Nanoparticles for Curcumin Delivery to Cancer Cells. *Macromolecular Bioscience*, *15*(10), 1365–1374. https://doi.org/10.1002/mabi.201500142

Mansour, O., El Joukhar, I., & Belbekhouche, S. (2019). H2O2-sensitive delivery microparticles based on the boronic acid chemistry: (Phenylboronic-alginate derivative/dextran) system. *Reactive & Functional Polymers*, *145*. https://doi.org/10.1016/j.reactfunctpolym.2019.104377

Martwiset, S., Koh, A. E., & Chen, W. (2006). Nonfouling Characteristics of Dextran-Containing Surfaces. *Langmuir*, *22*(19), 8192–8196. https://doi.org/10.1021/la061064b

Masuelli, M. A. (2013). Dextrans in Aqueous Solution. Experimental Review on Intrinsic Viscosity Measurements and Temperature Effect. *Journal of Polymer and Biopolymer Physics Chemistry*, *1*(1), 13–21. https://doi.org/10.12691/jpbpc-1-1-3

Mauzac, M., & Jozefonvicz, J. (1984). Anticoagulant activity of dextran derivatives. Part I: Synthesis and characterization. *Biomaterials*, *5*(5), 301–304. https://doi.org/10.1016/0142-9612(84)90078-4

McAloney, R. A., Sinyor, M., Dudnik, V., & Goh, M. C. (2001). Atomic Force Microscopy Studies of Salt Effects on Polyelectrolyte Multilayer Film Morphology. *Langmuir*, *17*(21), 6655–6663. https://doi.org/10.1021/la010136q

McCurdy, R. D., Goff, H. D., & Stanley, D. W. (1994). Properties of dextran as a cryoprotectant in ice cream. *Food Hydrocolloids*, *8*(6), 625–633. https://doi.org/10.1016/S0268-005X(09)80069-6

McCurdy, R. D., Goff, H. D., Stanley, D. W., & Stone, A. P. (1994). Rheological properties of dextran related to food applications. *Food Hydrocolloids*, *8*(6), 609–623. https://doi.org/10.1016/S0268-005X(09)80068-4

Mehvar, R. (2000). Dextrans for targeted and sustained delivery of therapeutic and imaging agents. *Journal of Controlled Release*, *69*(1), 1–25. https://doi.org/10.1016/S0168-3659(00)00302-3

Mei, J.-Q., Zhou, D.-N., Jin, Z.-Y., Xu, X.-M., & Chen, H.-Q. (2015). Effects of citric acid esterification on digestibility, structural and physicochemical properties of cassava starch. *Food Chemistry*, *187*, 378–384. https://doi.org/10.1016/j.foodchem.2015.04.076

Mitsuya, H., Looney, D., Kuno, S., Ueno, R., Wong-Staal, F., & Broder, S. (1988). Dextran sulfate suppression of viruses in the HIV family: inhibition of virion binding to CD4+ cells. *Science*, *240*(4852), 646–649. https://doi.org/10.1126/science.2452480

Moon, R. J., Martini, A., Nairn, J., Simonsen, J., & Youngblood, J. (2011). Cellulose nanomaterials review: structure, properties and nanocomposites. *Chemical Society Reviews*, *40*(7), 3941. https://doi.org/10.1039/c0cs00108b

Moreau, C., Beury, N., Delorme, N., & Cathala, B. (2012). Tuning the Architecture of Cellulose Nanocrystal–Poly(allylamine hydrochloride) Multilayered Thin Films: Influence of Dipping Parameters. *Langmuir*, *28*(28), 10425–10436. https://doi.org/10.1021/la301293r

Moulis, C., Guieysse, D., Morel, S., Séverac, E., & Remaud-Siméon, M. (2021). Natural and engineered transglycosylases: Green tools for the enzyme-based synthesis of

glycoproducts. *Current Opinion in Chemical Biology*, *61*, 96–106. https://doi.org/10.1016/j.cbpa.2020.11.004

Müller, M., Rieser, T., Dubin, P. L., & Lunkwitz, K. (2001). Selective Interaction Between Proteins and the Outermost Surface of Polyelectrolyte Multilayers: Influence of the Polyanion Type, pH and Salt. *Macromolecular Rapid Communications*, *22*(6), 390–395. https://doi.org/10.1002/1521-3927(20010301)22:6<390::AID-MARC390>3.0.CO;2-B

Naessens, M., Cerdobbel, A., Soetaert, W., & Vandamme, E. J. (2005). Leuconostoc dextransucrase and dextran: production, properties and applications. *Journal of Chemical Technology & Biotechnology*, *80*(8), 845–860. https://doi.org/10.1002/jctb.1322

Novak, L. J., Witt, E. E., & Hiler, M. J. (1955). Soil Conditioners, Dextran and Dextran Products as Soil-Conditioning Materials. *Journal of Agricultural and Food Chemistry*, *3*(12), 1028–1033.

Novoselova, M. V., Loh, H. M., Trushina, D. B., Ketkar, A., Abakumova, T. O., Zatsepin, T. S., Kakran, M., Brzozowska, A. M., Lau, H. H., Gorin, D. A., Antipina, M. N., & Brichkina, A. I. (2020). Biodegradable Polymeric Multilayer Capsules for Therapy of Lung Cancer. *ACS Applied Materials & Interfaces*, *12*(5), 5610–5623. https://doi.org/10.1021/acsami.9b21381

Olano-Martin, E., Mountzouris, K. C., Gibson, G. R., & Rastall, R. A. (2000). In vitro fermentability of dextran, oligodextran and maltodextrin by human gut bacteria. *British Journal of Nutrition*, *83*(3), 247–255. https://doi.org/10.1017/S0007114500000325

Paini, M., Aliakbarian, B., Casazza, A. A., Perego, P., Ruggiero, C., & Pastorino, L. (2015). Chitosan/dextran multilayer microcapsules for polyphenol co-delivery. *Materials*

Science & Engineering C-Materials for Biological Applications, *46*, 374–380. https://doi.org/10.1016/j.msec.2014.10.047

Pan, Y., & Nitin, N. (2015). Effect of layer-by-layer coatings and localization of antioxidant on oxidative stability of a model encapsulated bioactive compound in oil-in-water emulsions. *Colloids and Surfaces B-Biointerfaces*, *135*, 472–480. https://doi.org/10.1016/j.colsurfb.2015.08.003

Parakhonskiy, B. V., Yashchenok, A. M., Konrad, M., & Skirtach, A. G. (2014). Colloidal micro- and nano-particles as templates for polyelectrolyte multilayer capsules. *Advances in Colloid and Interface Science*, *207*, 253–264. https://doi.org/10.1016/j.cis.2014.01.022

Parisi, O., Malivindi, R., Amone, F., Ruffo, M., Malanchin, R., Carlomagno, F., Piangiolino, C., Nobile, V., Pezzi, V., Scrivano, L., & Puoci, F. (2017). Safety and Efficacy of Dextran-Rosmarinic Acid Conjugates as Innovative Polymeric Antioxidants in Skin Whitening: What Is the Evidence? *Cosmetics*, *4*(3), 28. https://doi.org/10.3390/cosmetics4030028

Pasteur, L. (1861). *Expériences et vues nouvelles sur la nature des fermentations*.

Pawlak, A., Michely, L., & Belbekhouche, S. (2022). Multilayer dextran derivative based capsules fighting bacteria resistant to Antibiotic: Case of Kanamycin-Resistant Escherichia coli. *International Journal of Biological Macromolecules*, *200*, 242–246. https://doi.org/10.1016/j.ijbiomac.2021.12.123

Pechenkin, M. A., Möhwald, H., & Volodkin, D. V. (2012). pH- and salt-mediated response of layer-by-layer assembled PSS/PAH microcapsules: fusion and polymer exchange. *Soft Matter*, *8*(33), 8659. https://doi.org/10.1039/c2sm25971k

Pescosolido, L., Schuurman, W., Malda, J., Matricardi, P., Alhaique, F., Coviello, T., van Weeren, P. R., Dhert, W. J. A., Hennink, W. E., & Vermonden, T. (2011). Hyaluronic

Acid and Dextran-Based Semi-IPN Hydrogels as Biomaterials for Bioprinting. *Biomacromolecules*, *12*(5), 1831–1838. https://doi.org/10.1021/bm200178w

Picart, C., Lavalle, Ph., Hubert, P., Cuisinier, F. J. G., Decher, G., Schaaf, P., & Voegel, J.-C. (2001). Buildup Mechanism for Poly(L-lysine)/Hyaluronic Acid Films onto a Solid Surface. *Langmuir*, *17*(23), 7414–7424. https://doi.org/10.1021/la010848g

Picart, C., Mutterer, J., Richert, L., Luo, Y., Prestwich, G. D., Schaaf, P., Voegel, J.-C., & Lavalle, P. (2002). Molecular basis for the explanation of the exponential growth of polyelectrolyte multilayers. *Proceedings of the National Academy of Sciences*, *99*(20), 12531–12535. https://doi.org/10.1073/pnas.202486099

Platt, E. J., Kozak, S. L., Durnin, J. P., Hope, T. J., & Kabat, D. (2010). Rapid Dissociation of HIV-1 from Cultured Cells Severely Limits Infectivity Assays, Causes the Inactivation Ascribed to Entry Inhibitors, and Masks the Inherently High Level of Infectivity of Virions. *Journal of Virology*, *84*(6), 3106–3110. https://doi.org/10.1128/JVI.01958-09

Pomerantseva, E., Bonaccorso, F., Feng, X., Cui, Y., & Gogotsi, Y. (2019). Energy storage: The future enabled by nanomaterials. *Science*, *366*(6468), eaan8285. https://doi.org/10.1126/science.aan8285

Poojari, R., Kini, S., Srivastava, R., & Panda, D. (2016). Intracellular interactions of electrostatically mediated layer-by-layer assembled polyelectrolytes based sorafenib nanoparticles in oral cancer cells. *Colloids and Surfaces B-Biointerfaces*, *143*, 131–138. https://doi.org/10.1016/j.colsurfb.2016.03.024

Rathmann, S., Schoenberg, M., Lessig, J., & Reibetanz, U. (2011). Interaction, Uptake, and Processing of LbL-Coated Microcarriers by PMNs. *Cytometry Part A*, *79A*(12), 979+. https://doi.org/10.1002/cyto.a.21145

Reibetanz, U., Chen, M. H. A., Mutukumaraswamy, S., Liaw, Z. Y., Oh, B. H. L., Donath, E., & Neu, B. (2011). Functionalization of Calcium Carbonate Microparticles as a

Combined Sensor and Transport System for Active Agents in Cells. *Journal of Biomaterials Science-Polymer Edition*, *22*(14), 1845–1859. https://doi.org/10.1163/092050610X528552

Reibetanz, U., Claus, C., Typlt, E., Hofmann, J., & Donath, E. (2006). Defoliation and plasmid delivery with layer-by-layer coated colloids. *Macromolecular Bioscience*, *6*(2), 153–160. https://doi.org/10.1002/mabi.200500163

Reibetanz, U., Lessig, J., Hoyer, J., & Neundorf, I. (2010). Surface Functionalized Colloidal Microparticles for Fast Endocytotic Cell Uptake. *Advanced Engineering Materials*, *12*(9, SI), B488–B495. https://doi.org/10.1002/adem.200980074

Richardson, J. J., Björnmalm, M., & Caruso, F. (2015). Technology-driven layer-by-layer assembly of nanofilms. *Science*, *348*(6233), aaa2491. https://doi.org/10.1126/science.aaa2491

Rinaudo, M. (2008). Main properties and current applications of some polysaccharides as biomaterials. *Polymer International*, *57*(3), 397–430. https://doi.org/10.1002/pi.2378

Robyt, J. F. (1985). Dextran. Encyclopaedia of Polymer Science. *Wiley-Vch*, *4*, 753–767.

Roduner, E. (2006). Size matters: why nanomaterials are different. *Chemical Society Reviews*, *35*(7), 583. https://doi.org/10.1039/b502142c

Rogovin, Z. A., Vernik, A. D., Khomiakov, K. P., Laletina, O. P., & Penenzhik, M. A. (1972). Study of the Synthesis of Dextran Derivatives. *Journal of Macromolecular Science: Part A - Chemistry*, *6*(3), 569–593. https://doi.org/10.1080/10601327208056860

Romero-Fernandez, M., Moreno-Perez, S., Martins de Oliveira, S., Santamaria, R. I., Guisan, J. M., & Rocha-Martin, J. (2018). Preparation of a robust immobilized biocatalyst of beta-1,4-endoxylanase by surface coating with polymers for production of xylooligosaccharides from different xylan sources. *New Biotechnology*, *44*, 50–58. https://doi.org/10.1016/j.nbt.2018.04.007

Ruckel, E. R., & Schuerch, C. (1967). Chemical synthesis of a dextran model, poly-α-(1→ 6)-anhydro-d-glucopyranose. *Biopolymers: Original Research on Biomolecules*, *5*(6), 515–523.

Sakaguchi, H., Serizawa, T., & Akashi, M. (2003). Layer-by-layer assembly on hydrogel surfaces and control of human whole blood coagulation. *Chemistry Letters*, *32*(2), 174–175. https://doi.org/10.1246/cl.2003.174

Salomäki, M., & Kankare, J. (2009). Influence of Synthetic Polyelectrolytes on the Growth and Properties of Hyaluronan–Chitosan Multilayers. *Biomacromolecules*, *10*(2), 294–301. https://doi.org/10.1021/bm8010177

Scheibler, C. (1874). Investigation on the nature of the gelatinous excretion (so-called frog's spawn) which is observed in production of beet-sugar juices. *Z Dtsch Zucker-Ind*, *24*, 309–335.

Schlenoff, J. B., & Dubas, S. T. (2001). Mechanism of Polyelectrolyte Multilayer Growth: Charge Overcompensation and Distribution. *Macromolecules*, *34*(3), 592–598. https://doi.org/10.1021/ma0003093

Schlenoff, J. B., Dubas, S. T., & Farhat, T. (2000). Sprayed Polyelectrolyte Multilayers. *Langmuir*, *16*(26), 9968–9969. https://doi.org/10.1021/la001312i

Schoeler, B., Kumaraswamy, G., & Caruso, F. (2002). Investigation of the Influence of Polyelectrolyte Charge Density on the Growth of Multilayer Thin Films Prepared by the Layer-by-Layer Technique. *Macromolecules*, *35*(3), 889–897. https://doi.org/10.1021/ma011349p

Selina, O. E., Belov, S. Yu., Vlasova, N. N., Balysheva, V. I., Churin, A. I., Bartkoviak, A., Sukhorukov, G. B., & Markvicheva, E. A. (2009). Biodegradable microcapsules with entrapped DNA for development of new DNA vaccines. *Russian Journal of Bioorganic Chemistry*, *35*(1), 103–110. https://doi.org/10.1134/S1068162009010130

1468 Serizawa, T., Yamaguchi, M., & Akashi, M. (2002). Enzymatic hydrolysis of a layer-by-layer
1469 assembly prepared from chitosan and dextran sulfate. *Macromolecules*, *35*(23), 8656–
1470 8658. https://doi.org/10.1021/ma012153s
1471 Serizawa, T., Yamaguchi, M., Kishida, A., & Akashi, M. (2003). Alternating gene expression
1472 in fibroblasts adhering to multilayers of chitosan and dextran sulfate. *Journal of*
1473 *Biomedical Materials Research Part A*, *67A*(3), 1060–1063.
1474 https://doi.org/10.1002/jbm.a.10150
1475 Serizawa, T., Yamaguchi, M., Matsuyama, T., & Akashi, M. (2000). Alternating bioactivity
1476 of polymeric layer-by-layer assemblies: Anti- vs procoagulation of human blood on
1477 chitosan and dextran sulfate layers. *Biomacromolecules*, *1*(3), 306–309.
1478 https://doi.org/10.1021/bm000006g
1479 Sethi, S. K., & Manik, G. (2018). Recent Progress in Super Hydrophobic/Hydrophilic Self-
1480 Cleaning Surfaces for Various Industrial Applications: A Review. *Polymer-Plastics*
1481 *Technology and Engineering*, *57*(18), 1932–1952.
1482 https://doi.org/10.1080/03602559.2018.1447128
1483 Sethy, P. K., Prusty, K., Mohapatra, P., & Swain, S. K. (2020). Nano-CaCO3-embodied
1484 polyacrylicacid/dextran nanocomposites for packaging applications. *Journal of*
1485 *Applied Polymer Science*, *137*(3), 48298. https://doi.org/10.1002/app.48298
1486 Sher, P., Custódio, C. A., & Mano, J. F. (2010). Layer-By-Layer Technique for Producing
1487 Porous Nanostructured 3D Constructs Using Moldable Freeform Assembly of
1488 Spherical Templates. *Small*, *6*(23), 2644–2648.
1489 https://doi.org/10.1002/smll.201001066
1490 Shiratori, S. S., & Rubner, M. F. (2000). pH-Dependent Thickness Behavior of Sequentially
1491 Adsorbed Layers of Weak Polyelectrolytes. *Macromolecules*, *33*(11), 4213–4219.
1492 https://doi.org/10.1021/ma991645q

1493 Shukla, S. K., Mishra, A. K., Arotiba, O. A., & Mamba, B. B. (2013). Chitosan-based
1494 nanomaterials: A state-of-the-art review. *International Journal of Biological*
1495 *Macromolecules*, *59*, 46–58. https://doi.org/10.1016/j.ijbiomac.2013.04.043
1496 Šimkovic, I. (2013). Unexplored possibilities of all-polysaccharide composites. *Carbohydrate*
1497 *Polymers*, *95*(2), 697–715. https://doi.org/10.1016/j.carbpol.2013.03.040
1498 Song, W., Gaware, V. S., Rúnarsson, Ö. V., Másson, M., & Mano, J. F. (2010).
1499 Functionalized superhydrophobic biomimetic chitosan-based films. *Carbohydrate*
1500 *Polymers*, *81*(1), 140–144. https://doi.org/10.1016/j.carbpol.2010.01.041
1501 Song, Z., Yin, J., Luo, K., Zheng, Y., Yang, Y., Li, Q., Yan, S., & Chen, X. (2009). Layer-by-
1502 Layer Buildup of Poly(L-glutamic acid)/Chitosan Film for Biologically Active
1503 Coating. *Macromolecular Bioscience*, *9*(3), 268–278.
1504 https://doi.org/10.1002/mabi.200800164
1505 Sudareva, N., Popova, H., Saprykina, N., & Bronnikov, S. (2014). Structural optimization of
1506 calcium carbonate cores as templates for protein encapsulation. *Journal of*
1507 *Microencapsulation*, *31*(4), 333–343. https://doi.org/10.3109/02652048.2013.858788
1508 Sukhorukov, G., Antipov, A., Voigt, A., Donath, E., & Mohwald, H. (2001). pH-controlled
1509 macromolecule encapsulation in and release from polyelectrolyte multilayer
1510 nanocapsules. *Macromolecular Rapid Communications*, *22*(1), 44–46.
1511 https://doi.org/10.1002/1521-3927(20010101)22:1<44::AID-MARC44>3.0.CO;2-U
1512 Sukhorukov, G. B., Brumen, M., Donath, E., & Möhwald, H. (1999). Hollow Polyelectrolyte
1513 Shells: Exclusion of Polymers and Donnan Equilibrium. *The Journal of Physical*
1514 *Chemistry B*, *103*(31), 6434–6440. https://doi.org/10.1021/jp990095v
1515 Sukhorukov, G. B., Rogach, A. L., Zebli, B., Liedl, T., Skirtach, A. G., Köhler, K., Antipov,
1516 A. A., Gaponik, N., Susha, A. S., Winterhalter, M., & Parak, W. J. (2005).
1517 Nanoengineered Polymer Capsules: Tools for Detection, Controlled Delivery, and

Site-Specific Manipulation. *Small*, *1*(2), 194–200. https://doi.org/10.1002/smll.200400075

Sukhorukov, G. B., Shchukin, D. G., Dong, W.-F., Möhwald, H., Lulevich, V. V., & Vinogradova, O. I. (2004). Comparative Analysis of Hollow and Filled Polyelectrolyte Microcapsules Templated on Melamine Formaldehyde and Carbonate Cores: Comparative Analysis of Hollow and Filled Polyelectrolyte Microcapsules Templated on Melamine Formaldehyde …. *Macromolecular Chemistry and Physics*, *205*(4), 530–535. https://doi.org/10.1002/macp.200300004

Sukhorukov, G. B., Volodkin, D. V., Günther, A. M., Petrov, A. I., Shenoy, D. B., & Möhwald, H. (2004). Porous calcium carbonate microparticles as templates for encapsulation of bioactive compounds. *J. Mater. Chem.*, *14*(14), 2073–2081. https://doi.org/10.1039/B402617A

Sun, G., Zhang, X., Shen, Y.-I., Sebastian, R., Dickinson, L. E., Fox-Talbot, K., Reinblatt, M., Steenbergen, C., Harmon, J. W., & Gerecht, S. (2011). Dextran hydrogel scaffolds enhance angiogenic responses and promote complete skin regeneration during burn wound healing. *Proceedings of the National Academy of Sciences*, *108*(52), 20976–20981. https://doi.org/10.1073/pnas.1115973108

Taylor, C., Cheetham, N. W. H., & Walker, G. J. (1985). Application of high-performance liquid chromatography to a study of branching in dextrans. *Carbohydrate Research*, *137*, 1–12. https://doi.org/10.1016/0008-6215(85)85144-2

Tjipto, E., Cadwell, K. D., Quinn, J. F., Johnston, A. P. R., Abbott, N. L., & Caruso, F. (2006). Tailoring the Interfaces between Nematic Liquid Crystal Emulsions and Aqueous Phases via Layer-by-Layer Assembly. *Nano Letters*, *6*(10), 2243–2248. https://doi.org/10.1021/nl061604p

1542 Tong, W., Dong, W., Gao, C., & Mohwald, H. (2005). Charge-controlled permeability of
1543 polyelectrolyte microcapsules. *Journal of Physical Chemistry B*, *109*(27), 13159–
1544 13165. https://doi.org/10.1021/jp0511092
1545 Tong, W., Song, X., & Gao, C. (2012). Layer-by-layer assembly of microcapsules and their
1546 biomedical applications. *Chemical Society Reviews*, *41*(18), 6103.
1547 https://doi.org/10.1039/c2cs35088b
1548 Treviño-Garza, M. Z., García, S., Heredia, N., Alanís-Guzmán, Ma. G., & Arévalo-Niño, K.
1549 (2017). Layer-by-layer edible coatings based on mucilages, pullulan and chitosan and
1550 its effect on quality and preservation of fresh-cut pineapple (Ananas comosus).
1551 *Postharvest Biology and Technology*, *128*, 63–75.
1552 https://doi.org/10.1016/j.postharvbio.2017.01.007
1553 Trushina, D. B., Akasov, R. A., Khovankina, A. V., Borodina, T. N., Bukreeva, T. V., &
1554 Markvicheva, E. A. (2019). Doxorubicin-loaded biodegradable capsules: Temperature
1555 induced shrinking and study of cytotoxicity in vitro. *Journal of Molecular Liquids*,
1556 *284*, 215–224. https://doi.org/10.1016/j.molliq.2019.03.152
1557 Trushina, D. B., Bukreeva, T., V., Borodina, T. N., Belova, D. D., Belyakov, S., & Antipina,
1558 M. N. (2018). Heat-driven size reduction of biodegradable polyelectrolyte multilayer
1559 hollow capsules assembled on CaCO3 template. *Colloids and Surfaces B-*
1560 *Biointerfaces*, *170*, 312–321. https://doi.org/10.1016/j.colsurfb.2018.06.033
1561 Van Tieghem, P. (1878). On sugar-mill gum. *Ann Sci Nature Bot Biol Veg*, *7*, 180–203.
1562 vander Straeten, A., Bratek-Skicki, A., Jonas, A. M., Fustin, C.-A., & Dupont-Gillain, C.
1563 (2018). Integrating Proteins in Layer-by-Layer Assemblies Independently of their
1564 Electrical Charge. *ACS Nano*, *12*(8), 8372–8381.
1565 https://doi.org/10.1021/acsnano.8b03710

vander Straeten, A., Lefèvre, D., Demoustier-Champagne, S., & Dupont-Gillain, C. (2020). Protein-based polyelectrolyte multilayers. *Advances in Colloid and Interface Science*, *280*, 102161. https://doi.org/10.1016/j.cis.2020.102161

Vigneswaran, N., Samsuri, F., Ranganathan, B., & Padmapriya. (2014). Recent Advances in Nano Patterning and Nano Imprint Lithography for Biological Applications. *Procedia Engineering*, *97*, 1387–1398. https://doi.org/10.1016/j.proeng.2014.12.420

Voigt, U., Khrenov, V., Tauer, K., Hahn, M., Jaeger, W., & Klitzing, R. von. (2002). The effect of polymer charge density and charge distribution on the formation of multilayers. *Journal of Physics: Condensed Matter*, *15*(1), S213–S218. https://doi.org/10.1088/0953-8984/15/1/327

Wang, X., Zhong, X., Li, J., Liu, Z., & Cheng, L. (2021). Inorganic nanomaterials with rapid clearance for biomedical applications. *Chemical Society Reviews*, *50*(15), 8669–8742. https://doi.org/10.1039/D0CS00461H

Wolter, A., Hager, A.-S., Zannini, E., Czerny, M., & Arendt, E. K. (2014). Influence of dextran-producing Weissella cibaria on baking properties and sensory profile of gluten-free and wheat breads. *International Journal of Food Microbiology*, *172*, 83–91. https://doi.org/10.1016/j.ijfoodmicro.2013.11.015

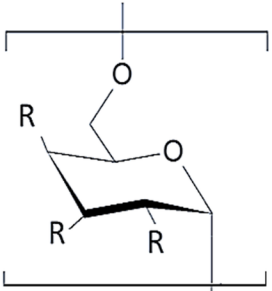
Wu, T., & Farnood, R. (2014). Cellulose fibre networks reinforced with carboxymethyl cellulose/chitosan complex layer-by-layer. *Carbohydrate Polymers*, *114*, 500–505. https://doi.org/10.1016/j.carbpol.2014.08.053

Xie, M., Lei, H., Zhang, Y., Xu, Y., Shen, S., Ge, Y., Li, H., & Xie, J. (2016). Non-covalent modification of graphene oxide nanocomposites with chitosan/dextran and its application in drug delivery. *RSC Advances*, *6*(11), 9328–9337. https://doi.org/10.1039/c5ra23823d

1590 Yalpani, M., & Hedman, P. O. (1985). Preparation and Applications of Dextran-Derived
1591 Products in Biotechnology and Related Areas. *Critical Reviews in Biotechnology*,
1592 *3*(4), 375–421. https://doi.org/10.3109/07388558509150789
1593 Yoo, G., Choi, S. L., Lee, S., Yoo, B., Kim, S., & Oh, M. S. (2016). Enhancement-mode
1594 operation of multilayer MoS2 transistors with a fluoropolymer gate dielectric layer.
1595 *Applied Physics Letters*, *108*(26), 263106. https://doi.org/10.1063/1.4955024
1596 Yu, D.-G., Jou, C.-H., Lin, W.-C., & Yang, M.-C. (2007). Surface modification of
1597 poly(tetramethylene adipate-co-terephthalate) membrane via layer-by-layer assembly
1598 of chitosan and dextran sulfate polyelectrolyte multiplayer. *Colloids and Surfaces B-*
1599 *Biointerfaces*, *54*(2), 222–229. https://doi.org/10.1016/j.colsurfb.2006.10.026
1600 Yu, D.-G., Lin, W.-C., Lin, C.-H., Yeh, Y.-H., & Yang, M.-C. (2007). Construction of
1601 antithrombogenic polyelectrolyte multilayer on thermoplastic polyurethane via layer-
1602 by-layer self-assembly technique. *Journal of Biomedical Materials Research Part B-*
1603 *Applied Biomaterials*, *83B*(1), 105–113. https://doi.org/10.1002/jbm.b.30772
1604 Zhang, F., Xie, M., Zhao, Y., Zhang, Y., Yang, M., Yang, N., Deng, T., Zhang, M., & Xie, J.
1605 (2019). Chitosan and dextran stabilized GO-iron oxide nanosheets with high
1606 dispersibility for chemotherapy and photothermal ablation. *Ceramics International*,
1607 *45*(5), 5996–6003. https://doi.org/10.1016/j.ceramint.2018.12.070
1608 Zhang, J., Senger, B., Vautier, D., Picart, C., Schaaf, P., Voegel, J.-C., & Lavalle, P. (2005).
1609 Natural polyelectrolyte films based on layer-by layer deposition of collagen and
1610 hyaluronic acid. *Biomaterials*, *26*(16), 3353–3361.
1611 https://doi.org/10.1016/j.biomaterials.2004.08.019

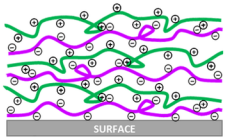
1612

DEXTRAN AND DERIVATIVES

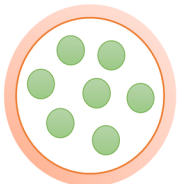


R = H, functional groups (animo, carboxymethyl, ether, etc.), grafted molecules

MULTILAYERS FILMS



MULTILAYERS CAPSULES



APPLICATIONS

pharmaceutics

biodegradable objects

antimicrobial agents

vaccines

photonics

drug delivery

food processing

cell adhesion

hydrophobic surfaces

protein organisation

cancer therapy