colloids and interfaces

MDPI

Review

The Use of Polymer and Surfactants for the Microencapsulation and Emulsion Stabilization

Altynay A. Sharipova [1,*], Saule B. Aidarova [1], Botagoz Z. Mutaliyeva [2], Alpamys A. Babayev [1], Miras Issakhov [1], Assem B. Issayeva [1], Galiya M. Madybekova [3], Dmitry O. Grigoriev [4] and Reinhard Miller [5]

1 Industrial Engineering department, Kazakh National Research Technical University Named after K. I. Satpayev, 22 Satpayev str., Almaty 050013, Kazakhstan; ainano9999@gmail.com (S.B.A.); a_babayev@mail.ru (A.A.B.); mir001@gmail.com (M.I.); isa-asem@mail.ru (A.B.I.)
2 Biotechnology department, M. Auezov South-Kazakhstan State University, 5 Tauke khan, Shymkent 160012, Kazakhstan; mbota@list.ru
3 Chemistry department, South-Kazakhstan State Pedagogical Institute, 13 Baitursynov str., Shymkent 160012, Kazakhstan; galiya56@list.ru
4 Fraunhofer Institute for Applied Polymer Research IAP, Geiselbergstrasse 69, 14476 Potsdam/Golm, Germany; dmitry.grigoriev@iap.fraunhofer.de
5 Max-Planck Institute of Colloids and Surfaces, Am Mühlenberg 1 OT Golm, 14476 Potsdam/Golm, Germany; Reinhard.Miller@mpikg.mpg.de
* Correspondence: a_sharipova85@mail.ru; Tel./Fax: +77017476719

Received: 19 September 2017; Accepted: 18 October 2017; Published: 29 October 2017

Abstract: Polymer/surfactant mixtures have a wide range of industrial and technological applications, one of them being the use in microencapsulation and emulsion stabilization processes. These mixtures are able to form adsorption layers at the surface of oil droplets and so affect the emulsion stability, which depends on the polyelectrolyte/surfactant nature, concentrations ratio, method of the emulsification, etc. Polyelectrolytes alone show low surface activity in contrast to surfactants, which adsorb at the water/oil interface, making the droplets charged, but they are insufficient to stabilize emulsions. When an oppositely-charged polymer is added to the surfactant solution, a steric barrier is formed, which prevents coalescence and enhances the stability. The present review is devoted to the recent studies of the use of polymer/surfactant mixtures for the encapsulation of active ingredients and stabilization of single and double emulsions. Active ingredients are added to the oil phase prior to emulsification so that any subsequent dissolution of the core, like in other encapsulation protocols, can be omitted. By measuring the interfacial tension and dilational rheology it is possible to find optimum conditions for the emulsion formation and hence for encapsulation. Therefore, such systems have become a prominent approach for the encapsulation of active ingredients.

Keywords: polyelectrolyte/surfactant mixtures; encapsulation; O/W; W/O and W/O/W emulsions; complex formation; interfacial tension; dilational rheology

1. Introduction

Polymer/surfactant mixtures (PS) have a wide range of industrial and technological applications and their specific behavior was studied at liquid/gas [1–15], liquid/liquid [16–27], and liquid/solid interfaces [28–30]. In particular, this is clearly seen in metastable micrometer and sub-micrometer heterogenous disperse systems, such as foams [26,31–33], emulsions [22,23,33–35], and dispersions [36–38]. Among them, emulsions stabilized by PS mixtures for microencapsulation of a variety of volatile components, such as perfumes or flavors, in a wide range of applications in home and personal care products, cosmetics, foods, and pharmaceuticals, are a potentially promising route [35].

Due to the electrostatic interaction with oppositely charged ionic surfactants, polyelectrolytes can form complexes which modify the interfacial properties and affect the emulsion stability [17–19]. By changing the PS concentrations ratio, it is possible to change the emulsion droplets' charge which is important for the further steps of the encapsulation procedure.

Despite the large number of systematic studies and reviews of the behavior of PS mixtures at the interfaces and in the bulk [1,2,20,21,26,27,33,39] to the best of our knowledge there is no review of the use of PS mixtures for encapsulation. In the present paper we will review the recent state of the art in encapsulation of active ingredients by single and double emulsions stabilized by PS mixtures.

2. Emulsion Stabilization by Polymers and Surfactants: Interfacial Tension and Dilational Rheology of PS Mixtures at Water/Oil Interface as Key Properties

For the formation of emulsions, mixed PS systems have been intensively studied at different interfaces [4,13,17,27,40,41]. They have an ability to form adsorption layers at the surface of oil droplets and so affect the emulsion stability and, hence, create the possibility to be used as liquid template particles for a further shell formation and finally for the encapsulation of active ingredients [34,35,39,42]. The other important point is that depending on the concentration ratio of the PS mixture, the charge of the initial emulsion droplets can be precisely adjusted, enabling an alternate polyelectrolyte deposition. Thus, the necessity of the core dissolution step, as required in other encapsulation protocols, can be omitted.

Studies of the formation dynamics of mixed PS adsorption layers are essential for the understanding of emulsions, the stability of which depends on the strength and elasticity of adsorption layers thin liquid films. Polyelectrolytes, alone, show low surface activity in contrast to surfactants, which adsorb at the water/oil interface, making the droplets charged, but they do not sufficiently stabilize the emulsion. However, the addition even of small amounts of oppositely charged surfactants to the polymer leads to a sharp decrease in the interfacial tension at the water/oil interface [16,17,19]. The properties and structure of these complexes depend on the molecular characteristics of both the polymer and surfactant [43–45]. The addition of an oppositely charged polymer forms also an extended steric barrier, which prevents coalescence and, hence, enhances stability.

Due to the electrostatic interaction between the oppositely charged polyelectrolyte and surfactant molecules, associates (complexes) with stronger interfacial activity are formed [16], whose attractive features can be exploited in the context of emulsion formation and stability. Obviously, the formation of these complexes results in the strong changes in the interfacial tension and in the dilational rheological properties of this interface.

For the formation of a stable emulsion, not only water-soluble polymers and surfactants [21,22,24,28], but also water-soluble polymers and oil soluble surfactants can be used [23]. Previously, the impact of the surface complex formation in sodium dodecyl sulfate (SDS)/poly(allylamine hydrochloride) (PAH) mixtures at the hexane/water interface was observed using the measurements of the interfacial tension and dilational rheological properties. A minimum in the interfacial tension and a corresponding maximum in the dilational elasticity were attributed to the formation of larger aggregates and their precipitation [16,17,27]. Synergistic effects in the interfacial tension at the water/air and water/oil interfaces in water soluble poly(acrylamide)–surfactant mixtures due to the PS interactions that were also observed in [28].

Alvarez et al. [22] obtained stable oil-in-water (O/W) emulsions (with dodecane and hexadecane) for mixtures of the nonionic surfactant $C_{12}E_4$ (tetraethylene glycol monododecyl ether) and an anionic polyelectrolyte—a hydrophobically-modified poly(sodium acrylate). The enhanced stability was attributed to the formation of PS complexes leading to a viscoelastic interfacial adsorption layer. To obtain such a layer, and consequently a stable emulsion, different parameters can be varied, such as the surfactant chain length, addition of electrolyte, change in pH, etc. [16,17,27,39,46].

Interfacial tension and dilational elasticity are properties which allow for understanding the formation and stability of emulsions. Therefore, such types of experiments are very important as

additional investigations for a dedicated design of emulsions. The measured values of PAH solutions with added alkyl sulfates of different alkyl chain lengths show different mechanisms of adsorption controlled by free surfactant molecules in competition with the PAH/alkyl sulfate complexes at the interface [27]. The difference in the structure of the polycomplexes which changes from a densely packed, particle-like object to a bulky, or even fluffy, associate for large radicals can affect the physical and mechanical characteristics of the interfacial adsorption layers [27].

Emulsion stabilities of two different polyelectrolyte/surfactant mixtures, SDS/polydimethyl diallyl ammonium chloride (poly-DMDAAC) and SDS/polyethylene glycol (PEI), were studied in [35]. It was shown that, for SDS/PEI, the adsorption did not depend on pH and increasing PEI concentration, For SDS/poly-DMDAAC mixtures, the adsorption increased with increasing polymer concentration. The regions of emulsion stability are at both high and low polymer concentrations, leading to the instabilities arising in the regions of low or zero surface charge [16,35].

By measuring the interfacial tension between the liquid phases it is possible to calculate spreading coefficients [47–51], which can give information about the starting point of the capsule formation, to predict the ultimate capsule morphology, as the spreading coefficients are calculated from both the interfacial tensions of the three phases present in the final capsule, core oil, solid PMMA and surfactant solution, and the interfacial tensions for the three phases when the polymer is dissolved in dichlormethane (DCM) [48]. It was found that single chain surfactants give core-shell capsules albeit at higher yields.

Stable O/W emulsions can be obtained by using of oil soluble surfactant, hexadecyl amine, and a high molecular weight (MW) water soluble poly(acrylic acid) [23]. The surfactant adsorbs at the O/W interface, making the droplets positively charged, but it is unable to stabilize the emulsion. Adsorption of a negatively-charged polymer forms a steric barrier, which prevents coalescence and enhances stability [23].

In studies on the surfactant mixed surfactant adsorption at the O/W interface it was shown that for well-defined and stable emulsion droplets that a small angle neutron scattering can be used to determine the adsorbed amounts, compositions, and structure [52]. This approach was also applied to surfactant mixtures on water-in-oil (W/O) emulsion droplets in [53]. Force measurements between emulsion droplets of the weakly interacting poly(vinyl alcohol) (PVA)/surfactant complexes formed at the interface were studied in [54,55]. The addition of SDS to the emulsions sterically stabilized by the PVA resulted in an increase in the repulsive force, which was attributed to a stretching of the polymer in a polyelectrolyte-like behavior due to the SDS adsorption onto the polymer [54,55].

3. Encapsulation Processes

3.1. Encapsulation of Active Ingredients Using O/W Emulsion Stabilized by Surfactants and Polymers

Petrovic et al. [34] have demonstrated for the first time the potential of PS mixtures in microencapsulation. The influence of interactions between hydroxypropylmethyl cellulose (HPMC) and the anionic surfactant sodium dodecylsulfate (SDS) on the properties of 20% *w/w* sunflower oil-in-water (O/W) emulsions and the microcapsules prepared on this basis by spray drying were investigated in [34] (Figure 1).

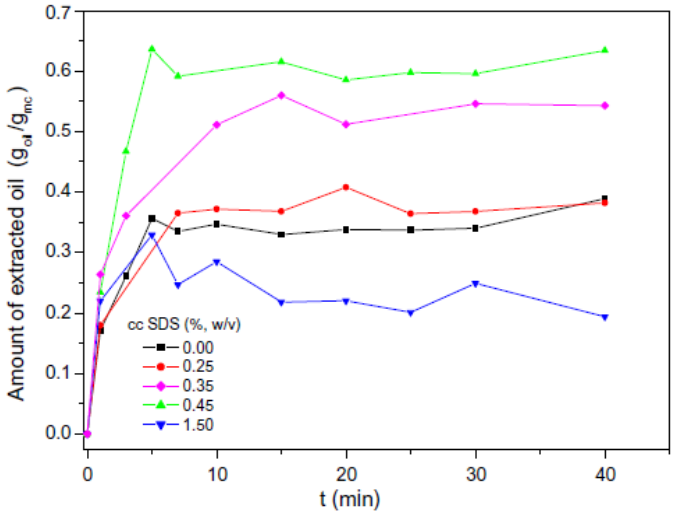

Figure 1. Amount of oil extracted from microcapsules obtained from 20% *w/w* sunflower oil/water emulsions in 1.00% *w/w* HPMC containing different SDS concentrations; redrawn from [34].

The amount of encapsulated oil depends on the SDS concentration, i.e., the HPMC–SDS interactions [34]. The microcapsules prepared without SDS have low encapsulation efficiency, which is a consequence of weak intermolecular bonding between the HPMC molecules [34]. The addition of SDS leads to the formation of HPMC/SDS complexes that have better emulsifying properties, and form more compact adsorption layers at the interface of oil droplets. The maximum amount of encapsulated oil (0.6 g_{oil}/g_{mc}) at 0.45% *w/w* SDS is attributed to the very compact crosslinked interfacial layer formed at the interface of the oil droplets, resistant against breaking during the drying process, while after the saturation with SDS molecules, the interaction becomes more intramolecular in nature, hence, the ability of the interfacial layer formation decreases.

Highly charged microcapsules were obtained via an internal phase separation technique by using ionic dispersants such as poly(methacrylic acid), ionic amphiphilic block copolymers like poly(methyl methacrylate)-poly(sodium (meth)acrylate) and an oil-soluble anionic surfactant, sodium 1,5-dioxo-1,5-bis(3,5,5-trimethylhexyloxy)-3-((3,5,5-trimethylhexyloxy)carbonyl) pentane-2-sulfonate, in combination with a water-soluble polycation, poly(diallyldimethylammonium chloride) [42]. All resulting microcapsules showed sufficient colloidal stabilities, especially for those made of block copolymers whose interaction remains intact even at high ionic strength due to the combination of electrostatic and steric stabilization. However, only weak polyacid- or block copolymer-based microcapsules possessed a core-shell morphology, whereas the microcapsules made with anionic surfactants and polycations had a multicore morphology [42].

Multicore-shell particles consisting of a poly(methyl methacrylate) shell and multiple dodecane cores have been prepared via the internal phase separation method using an oil-soluble anionic surfactant sodium 1,5-dioxo-1,5-bis(3,5,5-trimethylhexylocy)-3-((3,5,5 trimethylhexyloxy)carbonyl)pentane-2-sulfonate (TC4) and the water-soluble polycation PDADMAC in combination as a dispersant pair and studied using SEM, light microscopy, microelectrophoresis, quartz crystal microbalance with dissipation monitoring (QCM-D), and different optical tensiometry methods [50]. TC4 stabilizes, in particular, the polymer/water interface in the presence of PDADMAC instead of the O/W interface in contrast to water-soluble surfactants [50]. In addition, the oil–polymer interface is stabilized by TC4 which prevents coalescence of the oil droplets and leads to a multicore-shell morphology rather than particles with a single core [50]. In contrast, this new surfactant-inspired methodology uses TC4 as an oil-soluble dispersant to anchor the otherwise non-adsorbing water-soluble cationic polyelectrolyte PDADMAC on the O/W emulsion droplets by electrostatic interaction [42,56].

In [57] the encapsulation of coriander essential oil in alginate and alginate (Alg)/chitosan (Chi) microspheres by the emulsification external gelation method was performed. The optimum values of the corresponding parameters for the maximum encapsulation efficiency were: wall material 1.5%, Alg/Chi ratio 1:2, surfactant concentration 1%, oil concentration 30% and sonication time 15 min. The correlation between the swelling degree and the release rate was underlined and the dependence of different conditions of pH and temperature were studied. For pH 4 the release rate grows in close relation with the increase of the chitosan content while for pH 5 it grows together with the increase of the alginate content.

The anionic surfactant Aerosol OT (AOT) and polysaccharide polymer alginate were used for the PS nanoparticle formulation for the sustained release of water-soluble drugs [58]. Due to the size of the nanoparticles in the range of 40–70 nm, weakly basic molecules could be encapsulated efficiently in AOT-alginate nanoparticles [58]. It was shown a sustained release of 60–70% of the encapsulated drug over four weeks, with a nearly zero-order release during the first 15 days.

Microencapsulation of Vitamin E directly from oil-in-water (10% O/W) emulsions was carried out by means of a novel approach [24] where a preformed polyelectrolyte-surfactant complex (sodium polystyrene sulfonate/dodecyl trimethyl ammonium bromide) was simultaneously used as an electrosteric emulsion stabilizer and as a charged precursor for the following build-up of further layers to form microcapsules. The primary emulsions were obtained by ultrasonication, which occurs via common mechanisms including cavitation and shear [59]. Although microfluidization (MF) has been noted to be superior in size reduction and generating emulsions with more narrow size distributions, ultrasonication is deemed to be significantly easier to operate, clean, and maintain systems [60]. With extended duration of processing, ultrasonication has been shown to be able to achieve comparably small emulsion droplets [59]. Leong et al. [61] demonstrated the capability of ultrasound to produce emulsions with particle sizes comparable to MF, provided that the energy density and the surfactant system were optimized.

Subsequently, a layer-by-layer technique was applied to emulsions leading to the formation of core-shell microcapsules with oily cores and polyelectrolyte shells (Figures 2 and 3).

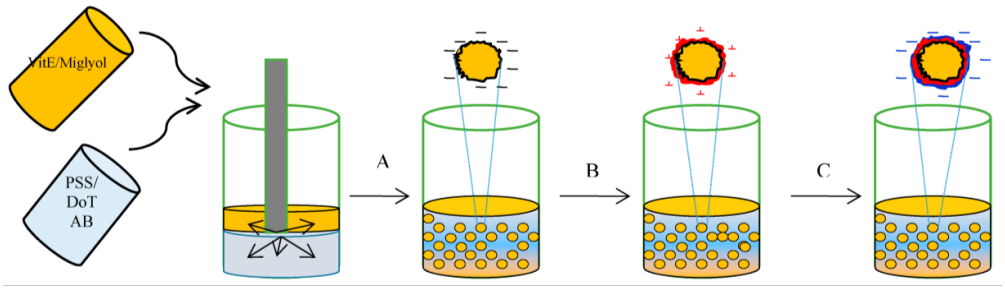

Figure 2. Steps of Vitamin E microencapsulation: A—emulsification; B—LBL (chitosan); C—LBL (PSS); according to [24].

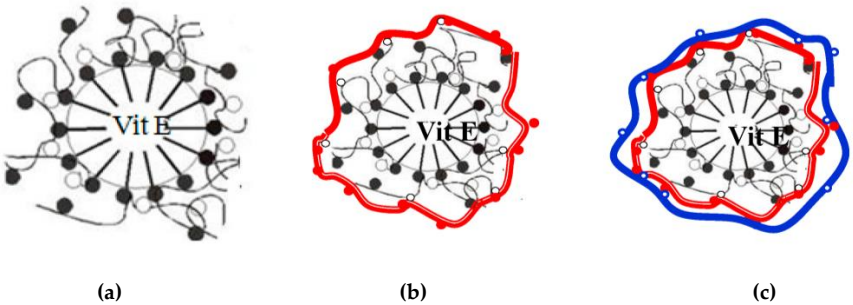

Figure 3. Schematic presentation of initial (PSS-DoTAB, (**a**)), intermediate (PSS-DoTAB/Chitosan, (**b**)) and final (PSS-DoTAB/Chitosan/PSS, (**c**)) capsules with Vitamine E [24].

The effect of the complexes on the process of emulsion formation and on the stability and characteristics of the resulting emulsions was investigated by measurements of dynamic and equilibrium interfacial tension, size distribution (DLS), and interfacial charge (zeta-potential) (Figure 4).

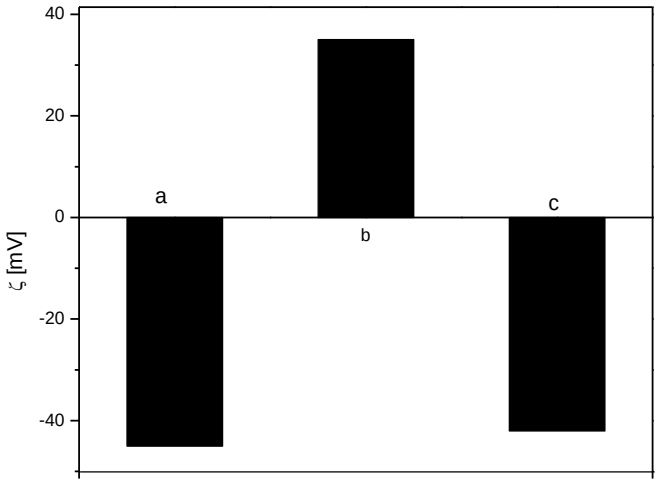

Figure 4. Zeta-potential of the initial (PSS-DoTAB, a), intermediate (PSS-DoTAB/Chitosan, b) and final (PSS-DoTAB/Chitosan/PSS, c) capsules with Vitamine E [24].

It was shown that in each encapsulation step the capsules were recharged and the final capsules revealed the zeta potential value of −40mV. The relatively high values of the zeta potentials in each step of encapsulation (average absolute value of about 40 mV) ensure the good colloidal stability of all of the disperse systems studied (Figure 4).

Via the kinetics of vitamin E a gradual slowing down of the vitamin E release was observed in each stage of the formation of the capsule shells. As can be seen from Figure 5 the final microcapsules showed a sustained release of vitamin E within at least 80 h [24].

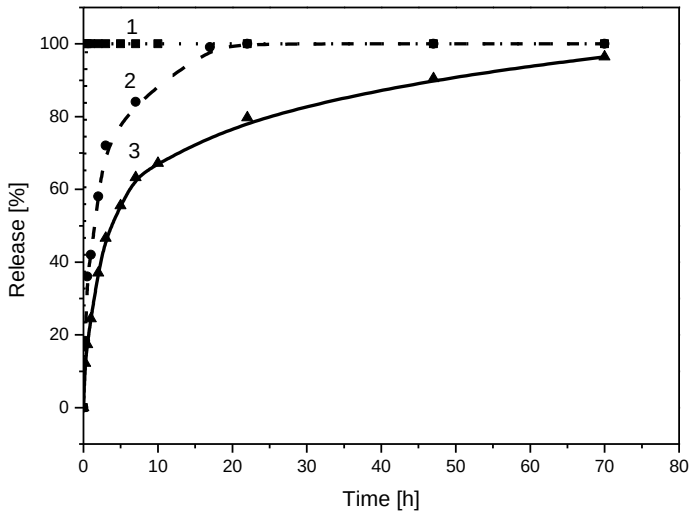

Figure 5. Release of vitamin E from a control emulsion (dotted line 1), intermediate capsules (dashed line 2), and final capsules (solid line 3) into a 50% aqueous ethanol solution [24].

The microencapsulation approach developed is straightforward and economic and could be used for the encapsulation of a variety of bioactive ingredients for cosmetic and food applications

3.2. Encapsulation of Active Ingredients by Double W/O/W Emulsions

A second method of preparing microcapsules is the use of double emulsions, which are "emulsion within an emulsion", i.e., droplets of one fluid encapsulated inside droplets of another fluid. The formation process consists of two steps: (1) the formation of W/O emulsion droplets, and (2) the formation of the final W/O/W emulsion [62–64]. It is known that one surfactant has to have a low HLB to form the primary W/O emulsion, while the other has to have a higher HLB to facilitate the secondary emulsification [65,66]. In W/O/W double emulsions, the internal and external aqueous phases are separated by an oil layer [63].

Several reviews present results on advances in the investigation of many types of pharmaceutical and biopharmaceutical active components used for preparing microparticles by the double-emulsion technique and their controlled release [65–73]. The shell fluid can serve as a barrier between the core droplets and the outer environment. In the double emulsion method, the core droplets can be loaded with many substances to achieve various functions, such as the encapsulation of pesticides, nutrients, drugs or antibodies, so, this method shows great potential in many applications [64,74,75].

However, the formulation and stabilization of these structures is still a challenge and much more difficult than for simple emulsions. The choice of suitable emulsifiers for double emulsions is crucial for their stability and the emulsifier's type, concentration, phase ratio, and homogenization method influence the properties of nano-capsules, such as size, encapsulation efficiency, and drug release. [63,76].

The use of two different emulsifiers creates one of the most serious difficulties—the competition between the lipophilic emulsifier solved in the oil and covering the interface between oil droplets and the inner aqueous droplets, with the hydrophilic emulsifier present in the outer aqueous phase [64,77,78].

Thus, one of the practical problems for the encapsulation of hydrophilic drugs is to get emulsions which provide stable polyelectrolyte complexes capable of maintaining stability over a wide range of external conditions (pH, ionic strength, temperature). At the same time, it should easily and reversibly react on very slight fluctuations leading to changes in the molecular characteristics and the phase state that promotes a controlled release [65]. The restructuring of the complexes can be carried out in an environment that is suitable for the functioning of natural polyions (proteins, enzymes, nucleic acids). It was proposed in [79–84] to use for encapsulation the polymeric drug delivery systems as carriers based on therapeutic proteins and other macromolecules. The use of biopolymers as hydrophilic emulsifiers in W/O/W double emulsions is often advantageous.

The authors in [63,85,86] also describe that the droplets in W1/O/W2 double emulsions are thermodynamically unstable and the formation and stability of double emulsions remains an actual scientific problem because methods of improving the emulsion stability are key factors to yield the final microspheres. Unfortunately, the stability will be severely deteriorated with larger diameters of double-emulsion droplets during the encapsulation and solidification stages. Thus, the formation and stability of double emulsions have been the focus of numerous studies. Additionally, the structures of microcapsules should provide a sustainable release while protecting the material from degradation. However, as described in [87], the conventional techniques such as solvent evaporation, coacervation and spray-drying methods, can be harmful to the substance being encapsulated. Thus, the use of biopolymers as hydrophilic emulsifiers in W/O/W double emulsions often allows to achieve more stable emulsions [64,88–90].

Some works concluded that the combination of surfactants has an enormous importance to provide stability of double-emulsion droplets. [85,91]. The mechanisms of interaction between surfactant and polymers chains used in the formation of emulsion were elucidated in [85]. For example, sucrose as a native carbohydrate mixed with PVA chains, chitosan-alginate microcapsules, and other poly-complexes can serve as an oral delivery carrier for hydrophilic drugs [82,85,91,92]. Large-sized W1/O/W2 double emulsion droplets with uniform wall thicknesses and diameters were prepared by adopting the emulsion microencapsulation method. By visually counting the number of double emulsion droplets online over the observation time, the stability of these droplets solidified in a

constant rotating flow field can be explored. Combining emulsion kinetics of formation and destruction, the adsorption characteristics of polymers, surface tension, and rheological properties of the outer water phase (W2), the influence of surfactant concentration on the stability of double emulsion droplets was systematically investigated. Moreover, the results show that the stability of the double emulsion droplets can be improved when the content of surfactants was less than 1.0 wt%. This is probably due to the proper match between shear forces and surface tension of the W2 phase, and weaker forces were directed inwards caused by the osmotic pressure in dilute surfactant concentrations.

The amphiphilic character is also important for the stability of emulsion droplets stabilized by a surfactant in the W2 phase. It was shown by the authors in [85] who selected polyvinyl alcohol (PVA) as a water-soluble polymer surfactant because of the good water solubility and its amphiphilic character to maintain the stability of double emulsion droplets. It is necessary to note that adding a second substance to the W2 phase increases the life-time of these droplets and gives a better understanding of the mechanism of the emulsion stability. Adjusting the different stripping velocity of the syringe pump used during emulsification influences the diameter and wall thickness of the droplets [63,85].

Moreover, different emulsification methods were applied to study the influence of homogenization on the physicochemical characteristics of double emulsions. The obtained double emulsions were compared in terms of stability and droplet size [63]. It was found that the homogenization method influences the physiochemical characteristics of the double emulsion and the most stable double emulsion with the smallest droplet size was obtained by the high-speed homogenization method. It was also found that the most stable emulsion was produced at high-speed homogenization because of its influence on the stability size distributions of the primary and secondary emulsion of the final double emulsion [63,76,91]. In our earlier work, it was found that at an ultrasound amplitude of 35% the most stable double emulsions with the smallest droplet size were obtained [63], and also the different volume ratios of the aqueous phase with insulin loaded into the oil phase were studied at different concentrations of surfactant, time as well as the regime of sonication (pulse or continuous).

The formulation of double emulsions to be used in food and medical systems were studied and the impact of the W1/O ratios of primary emulsions, and W1/O/W2 ratios of the double emulsions were investigated [63]. Particle size distribution, stability, encapsulation efficiency (EE), rheological properties, and morphology of the double-emulsion droplets were studied. Additionally, the optimum ratio of the liquid phases where double emulsions showed the highest stability were determined. In all cases, high-speed homogenization was used to produce stable double emulsions. The formulation parameters (type of biopolymer, type of oil and stabilizer, and its concentration, volume fraction, and content of internal aqueous phase, time, and regime of mixing), and oil concentration, surfactant concentration, ratio of W1/O/W, etc., were also considered in [63].

As described above, poly-complexes of chitosan (CS) and xanthan gum showed the potential to be used for drug delivery systems [63]. Chitosan solutions were investigated at various pH (2.31; 3.97; 5.01; 6.62; 11.42), and the morphology of the resulting emulsions analysed. Stabilization was possible due to electrostatic interaction with xanthan gum solutions (NH^{3+} group of chitosan and COO^{-} group of xanthan). The results confirm that chitosan mixed with xanthan gum can form double emulsions with a considerably long-term stability. These results testified that the addition of xanthan gum to chitosan solutions allows to reach process yield efficiencies of 65.6–77.5%.

Rheological and release properties of double microemulsions (containing active ingredients) prepared with various polyelectrolytes such as angum gum (AG), arabic gum (GA), whey protein, chitosan, xanthan gum, etc., were investigated in [63,93]. For example, crocin (a bioactive of saffron) is a highly water-soluble carotenoid with several physiological benefits which is sensitive to environmental conditions, such as light, oxygen, and pH. In this study, firstly a W1/O microemulsion containing crocin in the W1 phase was prepared using a spontaneous emulsification method, and then the double emulsion (W1/O/W2) was prepared with AG in the outer aqueous phase (W2). The resulting double emulsions were compared with those obtained by means of whey protein concentrate (WPC) and GA [93]. Emulsions containing AG showed highest viscosity (about 10 times higher) and a gel-like

behavior comparable to GA with an average droplet size of a W1/O microemulsions of approximately 10 nm. In contrast, WPC and GA produced double emulsions with droplet diameters of 429 and 695 nm, respectively, for 5% added biopolymers. Although the highest droplet size was observed for AG stabilized emulsions, they showed the lowest creaming and highest stability which could be attributed to their high viscosity. In terms of a dynamic behavior, for all samples the storage modulus G′ was higher than the loss modulus G″. The sizes of droplets correlated with the results described in [63] where we determined nano-particle formulations that showed a low polydispersity index (PdI) ranging from 0.02 to 0.142, and droplet sizes from 202 to 393 d.nm. This indicates the stability of the obtained emulsions. The outer droplet diameter of the double emulsions was 695–1250 d.nm.

The effect of mixtures of CS and poly(D,L-lactic-co-glycolic acid) (PLGA) on the preparation of double emulsions and microcapsules (MC) was investigated in [94]. MCs were prepared by the W/O/W double emulsion method and characterized in terms of morphology, size, encapsulation efficiency, and physicochemical and thermal properties. The resulting MCs had a spherical shape and different morphology, with sizes ranging from 11 to 20 nm, and encapsulation efficiencies of 40–52%, depending on the CS concentration. In summary, CS/PLGA MCs can be proposed as an attractive delivery system to control the release and long-term protection of resveratrol (RSV).

All the works mentioned here were devoted to microencapsulation and study of release of active ingredients from microcapsules and demonstrated the efficiency of the encapsulation methodology based on the formation of double emulsions. The cumulative release kinetics of insulin from double emulsion microdroplets stabilized by CS is presented in Figure 6. A saline phosphate buffer (PBS) solution at pH 7.4 was chosen as the release medium for insulin to allow the establishment of sink conditions for it [63].

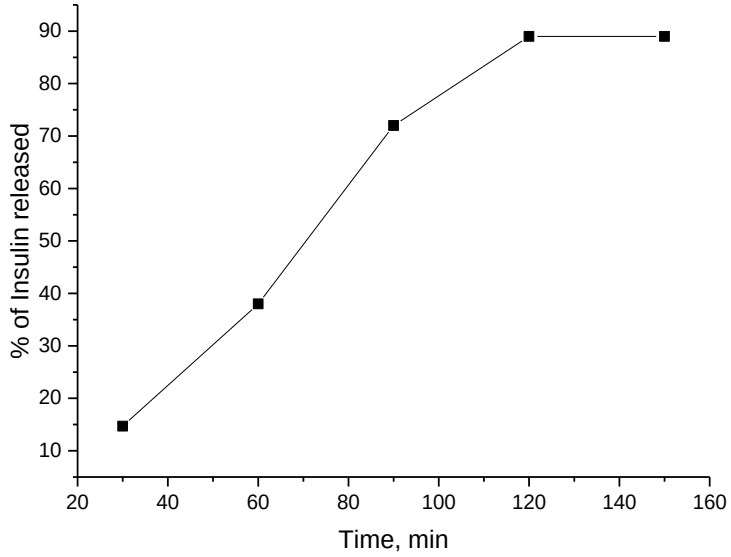

Figure 6. Insulin release profile upon incubation in PBS buffer (pH 7.4) at 37 °C; redrawn from [63].

From the release profile of insulin, it is possible to determine that 15% is released during the first 30 min, 40% within 1 h, and 70% within 1.5 h. Thus, the slow kinetics of the release of the active substances demonstrated the efficiency of the chosen methodology for obtaining double emulsions. Hence, compositions of surfactants with polyelectrolytes provide more stable emulsions and good formulation parameters for microencapsulation of active hydrophilic drugs.

4. Conclusions

The present review aims at describing the recent state of the art in encapsulation of active ingredients using single and double emulsions stabilized by PS mixtures. It was shown that by

measuring of interfacial tension and dilational rheology of PS mixtures it was possible to find optimal conditions for the emulsion stabilization and encapsulation.

Due to their ability to form adsorption layers at the surface of oil droplets because of their surface activity (low interfacial tension values due to the adsorption of surfactants, steric barrier due to the polyelectrolyte adsorption, and high dilational elasticity measurements due to the adsorption of PS complexes) the emulsion stability is enhanced and the use of such systems becomes a prominent approach for encapsulation. As the active ingredients were added to the oil phase prior to emulsification, the core dissolution step required in other capsule preparation protocols can be omitted here.

It was shown that the direct and double emulsions stabilized by PS mixtures have a good potential to be used for the encapsulation of active ingredients in various fields of application, such as pharmaceuticals, foods, and cosmetics.

Acknowledgments: The work was financially supported by German Academic Exchange program DAAD and a project 1395GF4 of the Ministry of Education and Science of the Republic of Kazakhstan.

Author Contributions: All authors (A.A. Sharipova, S.B. Aidarova, B.Z.Mutaliyeva, A.A. Babayev, M. Issakhov, A.B. Issayeva, G.M. Madybekova, D.O. Grigoriev and R. Miller) contributed in equal parts to the search and analysis of literature data, writing the text and designing the graphs. A.A. Sharipova is the leading author additionally responsible for the coordination of work and correspondence with the journal.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Langevin, D. Polyelectrolyte and surfactant mixed solutions. Behavior at surfaces and in thin films. *Adv. Colloid Interface Sci.* **2001**, *89*, 467–484. [CrossRef]
2. Taylor, D.J.F.; Thomas, R.K.; Penfold, J. Polymer/surfactant interactions at the air/water interface. *Adv. Colloid Interface Sci.* **2007**, *132*, 69–110. [CrossRef] [PubMed]
3. Nizri, G.; Lagerge, S.; Kamyshny, A.; Major, D.T.; Magdassi, S. Polymer-surfactant interactions: Binding mechanism of sodium dodecyl sulfate to poly(diallyldimethylammonium chloride). *J. Colloid Interface Sci.* **2008**, *320*, 74–81. [CrossRef] [PubMed]
4. Noskov, B.A.; Grigoriev, D.O.; Lin, S.Y.; Loglio, G.; Miller, R. Dynamic surface properties of polyelectrolyte/surfactant adsorption films at the air/water interface: Poly(diallyldimethylammonium chloride) and sodium dodecylsulfate. *Langmuir* **2007**, *23*, 9641–9651. [CrossRef] [PubMed]
5. Tonigold, K.; Varga, I.; Nylander, T.; Campbell, R.A. Effects of aggregates on mixed adsorption layers of poly(ethylene imine) and sodium dodecyl sulfate at the air/liquid interface. *Langmuir* **2009**, *25*, 4036–4046. [CrossRef] [PubMed]
6. Noskov, B.A.; Loglio, G.; Miller, R. Dilational Viscoelasticity of Polyelectolyte/Surfactant Adsorption Films at the Air/Water Interface: Dodecyltrimethylammonium Bromide and Sodium Poly(styrenesulfonate). *J. Phys. Chem. B* **2004**, *108*, 18615–18622. [CrossRef]
7. Ibragimova, Z.K.; Kasaikin, V.A.; Zezin, A.B.; Kabanov, V.A. Non-stoichiometric complexes of polyacrilic acid with cationic surfactants. *Vysokomolekulyarnie soedineniya Seriya A* **1986**, *28*, 1640.
8. Monteux, C.; Williams, C.E.; Meunier, J.; Anthony, O.; Bergeron, V. Adsorption of Oppositely Charged Polyelectrolyte/Surfactant Complexes at the Air/Water Interface: Formation of Interfacial Gels. *Langmuir* **2004**, *20*, 57–63. [CrossRef] [PubMed]
9. Noskov, B.A.; Loglio, G.; Miller, R. Dilational surface visco-elasticity of polyelectrolyte/surfactant solutions: Formation of heterogeneous adsorption layers. *Adv. Colloid Interface Sci.* **2011**, *168*, 179–197. [CrossRef] [PubMed]
10. Babak, V.G.; Desbrieres, J. Dynamic surface tension and dilational viscoelasticity of adsorption layers of alkylated chitosans and surfactant–chitosan complexes. *J. Colloid Polym. Sci.* **2006**, *284*, 745–754. [CrossRef]
11. Piculell, L.; Lindman, B. Association and segregation in aqueous polymer/polymer, polymer/surfactant, and surfactant/surfactant mixtures: Similarities and differences. *Adv. Colloid Interface Sci.* **1992**, *41*, 149–178. [CrossRef]

12. Benjamins, J.; Lyklema, J.; Lucassen-Reynders, E.H. Compression/expansion rheology of oil/water interfaces with adsorbed proteins. Comparison with the air/water surface. *Langmuir* **2006**, *22*, 6181–6188. [CrossRef] [PubMed]
13. Nylander, T.; Samoshina, Y.; Lindman, B. Formation of polyelectrolyte-surfactant complexes on surfaces. *Adv. Colloid Interface Sci.* **2006**, *123*, 105–123. [CrossRef] [PubMed]
14. Pacios, I.E.; Lindman, B.; Thuresson, K. Polyelectrolyte–surfactant complexes with long range order. *J. Colloid Interface Sci.* **2008**, *319*, 330–337. [CrossRef] [PubMed]
15. Bain, C.D.; Claesson, P.M.; Langevin, D.; Meszaros, R.; Nylander, T.; Stubenrauch, C.; Titmuss, S.; von Klitzing, R. Complexes of surfactants with oppositely charged polymers at surfaces and in bulk. *Adv. Colloid Interface Sci.* **2010**, *155*, 32. [CrossRef] [PubMed]
16. Sharipova, A.; Aidarova, S.; Fainerman, V.B.; Stocco, A.; Cernoch, P.; Miller, R. Dynamics of adsorption of polyallylamine hydrochloride/sodium docecyl sulphate at water/air and water/hexane interfaces. *Colloids Surf. A* **2011**, *391*, 112–118. [CrossRef]
17. Sharipova, A.; Aidarova, S.; Mucic, N.; Miller, R. Dilational rheology of polymer/surfactant mixtures at water/hexane interface. *Colloids Surf. A* **2011**, *391*, 130–134. [CrossRef]
18. Wang, H.; Wang, Y.; Yan, H.; Zhang, J.; Thomas, R.K. Binding of Sodium Dodecyl Sulfate with Linear and Branched Polyethyleneimines in Aqueous Solution at Different pH Values. *Langmuir* **2006**, *22*, 1526–1533. [CrossRef] [PubMed]
19. Fang, H.B. Dilational viscoelasticity of anionic polyelectrolyte/surfactant adsorption films at the water–octane interface. *Colloid Polym. Sci.* **2009**, *287*, 1131–1137. [CrossRef]
20. Miller, R.; Ferri, J.K.; Javadi, A.; Krägel, J.; Mucic, N.; Wüstneck, R. Rheology of interfacial layers. *Colloid Polym. Sci.* **2010**, *288*, 937–950. [CrossRef]
21. Kogej, K. Association and structure formation in oppositely charged polyelectrolyte–surfactant mixtures. *Adv. Colloid Interface Sci.* **2010**, *158*, 68–83. [CrossRef] [PubMed]
22. Alvarez, J.G.; Le, K.A.; Sadtler, V.; Marchal, P.; Perrin, P.; Tribet, C.; Marie, E.; Durand, A. Enhanced stability of nanoemulsions using mixtures of non-ionic surfactant and amphiphilic polyelectrolyte. *Colloids Surf. A* **2011**, *389*, 237–245. [CrossRef]
23. Stamkulov, N.S.; Mussabekov, K.B.; Aidarova, S.B.; Luckham, P.F. Stabilisation of emulsions by using a combination of an oil soluble ionic surfactant and water soluble polyelectrolytes. I: Emulsion stabilisation and Interfacial tension measurements. *Colloids Surf. A* **2009**, *335*, 103–106. [CrossRef]
24. Sharipova, A.A.; Aidarova, S.B.; Grigoriev, D.O.; Mutalieva, B.Z.; Madybekova, G.M.; Tleuova, A.B.; Miller, R. Polymer–surfactant complexes for microencapsulation of vitamin E and its release. *Colloids Surf. B* **2016**, *137*, 152–157. [CrossRef] [PubMed]
25. Penfold, J.; Tucker, I.; Thomas, R.K.; Taylor, D.J.F. The Interaction between Sodium Alkyl Sulfate Surfactants and the Oppositely Charged Polyelectrolyte, polyDMDAAC, at the Air−Water Interface: The Role of Alkyl Chain Length and Electrolyte and Comparison with Theoretical Predictions. *Langmuir* **2007**, *23*, 3128–3136. [CrossRef] [PubMed]
26. Musabekov, K.B.; Aidarova, S.; Abdiev, K. Adsorption of polyelectrolyte associates at the interfaces. In *Progresses of Colloid Chemistry*; L. Chemistry: Leningrad, Russia, 1991; pp. 209–223, (Russ); ISBN 5-7245-0765-X.
27. Sharipova, A.; Aidarova, S.; Cernoch, P.; Miller, R. Effect of surfactant hydrophobicity on the interfacial properties of polyallylamine hydrochloride/sodium alkylsulphate at water/hexane interface. *Colloids Surf. A* **2013**, *438*, 141–147. [CrossRef]
28. Zhang, J.Y.; Zhang, L.P.; Tang, J.A.; Jiang, L. Interactions between poly(acrylamide) and surfactants of different headgroup charge. *Colloids Surf. A* **1994**, *88*, 33–39. [CrossRef]
29. Kundu, S. Polyelectrolyte–surfactant complexes on solid surface. *J. Colloid Interface Sci.* **2010**, *344*, 547–555. [CrossRef] [PubMed]
30. Terada, E.; Samoshina, Y.; Nylander, T.; Lindman, B. Adsorption of Cationic Cellulose Derivative/Anionic Surfactant Complexes onto Solid Surfaces. II. Hydrophobized Silica Surfaces. *Langmuir* **2004**, *20*, 6692–6701. [CrossRef] [PubMed]
31. Aidarova, S.; Musabekov, K.; Ospanova, Z.; Guden, M. Foaming binary solution mixtures of low molecular surfactant and polyelectrolyte. *J. Mater. Sci.* **2006**, *41*, 3979–3986. [CrossRef]

32. Monteux, C.; Fuller, G.G.; Bergeron, V. Shear and Dilational Surface Rheology of Oppositely Charged Polyelectrolyte/Surfactant Microgels Adsorbed at the Air−Water Interface. Influence on Foam Stability. *J. Phys. Chem. B* **2004**, *108*, 16473–16482. [CrossRef]
33. Langevin, D. Influence of interfacial rheology on foam and emulsion properties. *Adv. Colloid Interface Sci.* **2000**, *88*, 209–222. [CrossRef]
34. Petrovic, L.B.; Sovilj, V.J.; Katona, J.M.; Milanovic, J.L. Influence of polymer–surfactant interactions on O/W emulsion properties and microcapsule formation. *J. Colloid Interface Sci.* **2010**, *342*, 333–339. [CrossRef] [PubMed]
35. Tucker, I.M.; Petkov, J.T.; Jones, C.; Penfold, J.; Thomas, R.K.; Rogers, S.E.; Terry, A.E.; Heenan, R.K.; Grillo, I. Adsorption of Polymer–Surfactant Mixtures at the Oil–Water Interface. *Langmuir* **2012**, *28*, 14974–14982. [CrossRef] [PubMed]
36. Espinosa, G.; Langevin, D. Interfacial Shear Rheology of Mixed Polyelectrolyte−Surfactant Layers. *Langmuir* **2009**, *25*, 12201–12207. [CrossRef] [PubMed]
37. Tadros, T.F. *Rheology of Dispersions: Principles and Applications*; Wiley and Sons: New York, NY, USA, 2010; ISBN 978-3-527-32003-5.
38. Dukhin, A.S.; Goetz, P.J. Characterization of Liquids, nano- and microparticulates, and porous bodies using ultrasound. In *Studies in Interface Science*; Möbius, D., Miller, R., Eds.; Elsevier: Amsterdam, The Netherlands, 2010; Volume 24.
39. Aidarova, S.; Sharipova, A.; Krägel, J.; Miller, R. Polyelectrolyte/surfactant mixtures in the bulk and at water/oil interfaces. *Adv. Colloid Interface Sci.* **2014**, *205*, 87–93. [CrossRef] [PubMed]
40. Penfold, J.; Tucker, I.; Thomas, R.K.; Zhang, J. Adsorption of Polyelectrolyte/Surfactant Mixtures at the Air−Solution Interface: Poly(ethyleneimine)/Sodium Dodecyl Sulfate. *Langmuir* **2005**, *21*, 10061–10073. [CrossRef] [PubMed]
41. Langevin, D. Complexation of oppositely charged polyelectrolytes and surfactants in aqueous solutions. A review. *Adv. Colloid Interface Sci.* **2009**, *147*, 170–177. [CrossRef] [PubMed]
42. Trojer, M.A.; Li, Y.; Abrahamsson, C.; Mohamed, A.; Eastoe, J.; Holmberga, K.; Nyden, M. Charged microcapsules for controlled release of hydrophobic actives. Part I: Encapsulation methodology and interfacial properties. *Soft Matter.* **2013**, *9*, 1468–1477. [CrossRef]
43. Akiyama, E.; Kashimoto, A.; Fukuda, K.; Hotta, H.; Suzuki, T.; Kitsuki, T. Thickening properties and emulsification mechanisms of new derivatives of polysaccharides in aqueous solution. *J. Colloid Interface Sci.* **2005**, *282*, 448–457. [CrossRef] [PubMed]
44. Lindman, B.; Thalberg, K. *Polymer-surfactant interactions-recent developments. Interactions of Surfactants with Polymers and Proteins*; Goddard, D.E., Ed.; CRC Press: Boca Raton, FL, USA, 1993; p. 203.
45. Goddard, D.E. *Interactions of Surfactants with Polymers and Proteins*; Goddard, D.E., Ed.; CRC Press: Boca Raton, FL, USA, 1993; 448p.
46. Aidarova, S.B.; Fainerman, V.B.; Aksenenko, E.V.; Bekturganova, N.E.; Tarasevich, Y.I.; Miller, R. Effect of electrolyte on adsorption of polyallyl amine hydrochloride/sodium dodecyl sulphate at water/tetradecane interface. *Colloids Surf. A* **2014**, *460*, 11–17.
47. Tasker, A.L.; Hitchcock, J.P.; He, L.; Baxter, E.A.; Biggs, S.; Cayre, O.J. The effect of surfactant chain length on the morphology of poly(methyl methacrylate) microcapsules for fragrance oil encapsulation. *J. Colloid Interface Sci.* **2016**, *484*, 10–16. [CrossRef] [PubMed]
48. Loxley, A.; Vincent, B. Preparation of Poly(methylmethacrylate) Microcapsules with Liquid Cores. *J. Colloid Interface Sci.* **1998**, *208*, 49–62. [CrossRef] [PubMed]
49. Feczkó, T.; Kardos, A.F.; Németh, B.; Trif, L.; Gyenis, J. Microencapsulation of n-hexadecane phase change material by ethyl ccellulose polymer. *J. Polym. Bull.* **2014**, *71*, 3289–3304. [CrossRef]
50. Trojer, M.A.; Mohamed, A.; Eastoe, J. A highly hydrophobic anionic surfactant at oil–water, water–polymer and oil–polymer interfaces: Implications for spreading coefficients, polymer interactions and microencapsulation via internal phase separation. *J. Colloids Surf. A* **2013**, *436*, 1048–1059. [CrossRef]
51. Trongsatitkul, T.; Budhlall, B.M. Multicore–Shell PNIPAm-co-PEGMa Microcapsules for Cell Encapsulation. *Langmuir* **2011**, *207*, 13468–13480. [CrossRef] [PubMed]
52. Staples, E.; Penfold, J.; Tucker, I.J. Adsorption of Mixed Surfactants at the Oil−Water Interface. *Phys. Chem. B* **2000**, *104*, 606–614. [CrossRef]

53. Bumajdad, A.; Eastoe, J.; Nave, S.; Steytler, D.C.; Heenan, R.K.; Grillo, I. Compositions of Mixed Surfactant Layers in Microemulsions Determined by Small-Angle Neutron Scattering. *Langmuir* **2003**, *19*, 2560–2567. [CrossRef]
54. Philip, J.; Gnana Prakash, G.; Jaykumar, T.; Kalyanasundaran, P.; Mondian-Monvial, O.; Raj, B. Interaction between Emulsion Droplets in the Presence of Polymer−Surfactant Complexes. *Langmuir* **2002**, *18*, 4625–4631. [CrossRef]
55. Philip, J.; Gnana Prakash, G.; Jaykumar, T.; Kalyanasundaran, P.; Mondian-Monvial, O.; Raj, B. Three Distinct Scenarios under Polymer, Surfactant, and Colloidal Interaction. *Macromolecules* **2003**, *36*, 9230–9236. [CrossRef]
56. Trojer, M.A.; Li, Y.; Wallin, M.; Holmberg, K.; Nyden, M. Charged microcapsules for controlled release of hydrophobic actives Part II: Surface modification by LbL adsorption and lipid bilayer formation on properly anchored dispersant layers. *J. Colloid Interface Sci.* **2013**, *409*, 8–17. [CrossRef] [PubMed]
57. Dima, C.; Gitin, L.; Alexe, P.; Dima, S. Encapsulation of coriander essential oil in alginate and alginate/chitosan microspheres by emulsification external gelation method. In Proceedings of the Inside Food Symposium, Leuven, Belgium, 9–12 April 2013.
58. Chavanpatil, M.D.; Khdair, A.; Patil, Y.; Handa, H.; Mao, G.; Panyam, J. Polymer-surfactant nanoparticles for sustained release of water-soluble drugs. *J. Pharm. Sci.* **2007**, *96*, 3379–3389. [CrossRef] [PubMed]
59. Maa, Y.F.; Hsu, C.C. Performance of sonication and microfluidization for liquid-liquid emulsification. *Pharm. Dev. Technol.* **1999**, *4*, 233–240. [CrossRef] [PubMed]
60. Jafari, M.S.; He, Y.; Bhandari, B. Nano-Emulsion Production by Sonication and Microfluidization—A Comparison. *J. Food Prop.* **2006**, *9*, 475–485. [CrossRef]
61. Leong, T.S.H.; Wooster, T.J.; Kentish, S.E.; Ashokkumar, M. Minimising oil droplet size using ultrasonic emulsification. *Ultrason. Sonochem.* **2009**, *16*, 721–727. [CrossRef] [PubMed]
62. Che, Z.; Wong, T.N.; Nguyen, N.-T. A simple method for the formation of water-in-oil-in-water (W/O/W) double emulsions. *Microfluid. Nanofluid.* **2017**, *21*, 8. [CrossRef]
63. Mutaliyeva, B.; Grigoriev, D.; Madybekova, G.; Sharipova, A.; Aidarova, S.; Saparbekova, A.; Miller, R. Microencapsulation of insulin and its release using W/O/W double emulsion method. *Colloids Surf. A* **2017**, *521*, 147–152. [CrossRef]
64. Schuch, A.; Helfenritter, C.; Funck, M.; Schuchmann, H.P. Observations on the influence of different biopolymers on coalescence of inner water droplets in W/O/W (water-in-oil-in-water) double emulsions. *Colloids Surf. A* **2015**, *475*, 2–8. [CrossRef]
65. Giri, T.K.; Choudhary, C.; Amit Alexander, A.; Badwaik, H.; Tripathi, D.K. Prospects of pharmaceuticals and biopharmaceuticals loaded microparticles prepared by double emulsion technique for controlled delivery. *Saudi Pharm. J.* **2013**, *21*, 125–141. [CrossRef] [PubMed]
66. *The HLB SYSTEM: A time-Saving Guide to Emulsifier Selection*; ICI Americas Inc.: Wilmington, DE, USA, 1984; p. 22.
67. Chang, L.C.; Yang, C.Y.; Chua, A.C.; Lin, Y.J.; Lai, S.M. Sustained release of transgenic human factor IX: preparation, characterization, and in vivo efficacy. *Mol. Pharm.* **2011**, *8*, 1767–1774. [CrossRef] [PubMed]
68. Lu, T.L.; Sun, W.G.; Zhao, W.; Chen, T. Preparation of amifostinepolylactide-co-glycolide microspheres and its irradiation protective to mouse through oral administration. *Drug Dev. Ind. Pharm.* **2011**, *37*, 1473–1480. [CrossRef] [PubMed]
69. Karal-Ylmaz, O.; Serhat, M.; Baysal, K.; Baysal, B.M. Preparation and in vitro characterization of vascular endot helialgrowth factor (VEGF) loaded poly(D,L-lactic-co-glycolic acid)microspheres using a double emulsion/solvent evaporation technique. *J. Microencapsul.* **2011**, *28*, 46–54. [CrossRef] [PubMed]
70. Dalmoro, A.; Lamberti, G.; Titomanilo, G.; Barba, A.A.; Amore, M. Enteric microparticles for targeted oral drug delivery. *Pharm. Sci. Tech.* **2010**, *11*, 1500–1507. [CrossRef] [PubMed]
71. Forster, S.; Plantenberg, T. From self-organizing polymers to nanohybrid and biomaterials. *Angew. Chem. Int. Ed.* **2002**, *41*, 688–714. [CrossRef]
72. Sheshala, R.; Peh, K.K.; Darwis, Y. Preparation, characterization, and in vivo evaluation of insulin-loaded PLA-PEG microspheres for controlledparenteral drug delivery. *Drug Dev. Ind. Pharm.* **2009**, *35*, 1364–1374. [CrossRef] [PubMed]

73. Bao, W.; Zhou, J.; Lui, J.; Wu, D. PLGA microspheres with high drug loading and high encapsulation efficiency prepared by a novel solvent evaporation technique. *J. Microencapsul.* **2006**, *23*, 471–479. [CrossRef] [PubMed]
74. Akhtar, N.; Yazan, Y. Formulation and in-vivo evaluation of a cosmetic multipleemulsion containing vitamin C and wheat protein. *Pak. J. Pharm. Sci.* **2008**, *21*, 45–50. [PubMed]
75. Garti, N.; Lutz, R. Recent progress in double emulsions. *Interface Sci. Technol.* **2004**, *4*, 557–605.
76. Yildirim, M.; Sumnu, G.; Sahin, S. The effects of emulsifier type, phase ratio, and homogenization methods on stability of the double emulsion. *J. Dispers. Sci. Technol.* **2017**, *38*, 807–814. [CrossRef]
77. Kanouni, M.; Rosano, H.L.; Naouli, N. Preparation of a stable double emulsion (W1/O/W2): Role ofthe interfacial films on the stability of the system. *Adv. Colloid Interface Sci.* **2002**, *99*, 229–254. [CrossRef]
78. Dickinson, E. Double emulsions stabilized by food biopolymers. *Food Biophys.* **2011**, *6*, 1–11. [CrossRef]
79. Peppas, N.A. Devices based on intelligent biopolymers for oral protein delivery. *Int. J. Pharm.* **2004**, *227*, 11–17. [CrossRef] [PubMed]
80. Jones, M.C.; Leroux, J.C. Polymeric micelles: A new generation of colloidal drug carrier. *Eur. J. Pharm. Biopharm.* **2000**, *48*, 101–111. [CrossRef]
81. Zielinski, B.A.; Aebischer, P. Chitosan as a matrix for mammalian cell encapsulation. *Biomaterials* **2002**, *15*, 1049–1056. [CrossRef]
82. Kim, H.J.; Lee, H.C.; Oh, J.S.; Shin, B.A.; Oh, C.S.; Park, R.D.; Yang, K.S.; Cho, C.S. Polyelectroylte complex composed of chitosan and sodium alginate for wound dressing application. *J. Biomater. Sci. Polym. Ed.* **2000**, *10*, 543–556. [CrossRef]
83. Lee, B.R.; Lee, K.H.; Kang, E.; Kim, D.S.; Lee, S.H. Microfluidic wet spinning of chitosan-alginate microfibers and encapsulation of HepG2 cells in fibers. *Biomicrofluidics* **2011**, *5*, 222–308. [CrossRef] [PubMed]
84. Pays, K.; Giermanska-Kahn, J.; Pouligny, B.; Bibette, J.; Leal-Calderon, F. Double emulsions: How does release occur? *J. Control. Release* **2002**, *79*, 193–205. [CrossRef]
85. Li, J.; Su, L.; Li, J.; Liu, M.-F.; Chen, S.-F.; Li, B.; Zhang, Z.-W.; Liu, Y.-Y. Influence of sucrose on the stability of W1/O/W2 double emulsion droplets. *RSC Adv.* **2015**, *5*, 83089–83095. [CrossRef]
86. Wang, G.; Su, L.; Chen, S.; Yao, H.; Deng, Y.; Li, B.; Wei, J. Stability of large diameter W1/O/W2 emulsion particles. *High Power Laser Part. Beams* **2012**, *24*, 389–393. [CrossRef]
87. Montazeri, L.; Bonakdar, S.; Taghipour, M.; Renaud, P.; Baharvand, H. Modification of PDMS to fabricate PLGA microparticles by a double emulsion method in a single microfluidic device. *Lab Chip* **2016**, *16*, 2596–2600. [CrossRef] [PubMed]
88. Pays, K.; Giermanska-Kahn, J.; Pouligny, B.; Bibette, J.; Leal-Calderon, F. Coalescence in surfactant-stabilized double emulsions. *Langmuir* **2001**, *17*, 7758–7769. [CrossRef]
89. De Araújo, T.M.; Teixeira, Z.; Barbosa-Sampaio, H.C.; Rezende, L.F.; Boschero, A.C.; Durán, N.; Höehr, N.F. Insulin-loaded poly(ε-caprolactone) nanoparticles: Efficient, sustained and safe insulin delivery system. *J. Biomed. Nanotechnol.* **2013**, *9*, 1098–1106. [CrossRef] [PubMed]
90. Schmidts, T.; Dobler, D.; Nissing, C.; Runkel, F. Influence of hydrophilic surfactants on the properties ofmultiple W/O/W emulsions. *J. Colloid Interface Sci.* **2009**, *338*, 184–192. [CrossRef] [PubMed]
91. Altuntas, O.Y.; Sumnu, G.; Sahin, S. Preparation and characterization of W/O/W type double emulsion containing PGPR–lecithin mixture as lipophilic surfactant. *J. Dispers. Sci. Technol.* **2017**, *38*, 486–493. [CrossRef]
92. Fahad, M.; Almutairi, T.E.; Adams, G.G.; Hayes, M.; McLoughlin, P.; Kök, M.S.; Mackie, A.R.; Rowe, A.J.; Harding, S.E. Hydrodynamic characterisation of chitosan and its interaction withtwo polyanions: DNA and xanthan. *Carbohydr. Polym.* **2015**, *122*, 359–366.

93. Mehrnia, M.-A.; Jafari, S.-M.; Makhmal-Zadeh, B.S.; Maghsoudlou, Y. Rheological and release properties of double nano-emulsions containing crocin prepared with Angum gum, Arabic gum and whey protein. *Food Hydrocoll.* **2017**, *66*, 259–267. [CrossRef]
94. Sanna, V.; Roggio, A.M.; Pal, N.; Marceddu, S.; Lubinu, G.; Mariani, A.; Sechi, M. Effect of chitosan concentration on PLGA microcapsules for controlled release and stability of resveratrol. *Int. J. Biolog. Macromol.* **2015**, *72*, 531–536. [CrossRef] [PubMed]