Journal of Medicinal and Chemical Sciences 6 (2023) 2228-2233

Journal of Medicinal and Chemical Sciences

Journal homepage: http://www.jmchemsci.com/

Original Article

Microcapsules of Protein-Polysaccharide Complexes Produced on a Variety of Matrices

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ARTICLE INFO

Article history

Receive: 2023-01-01
Received in revised: 2023-03-11
Accepted: 2023-04-16
Manuscript ID: JMCS-2301-1918
Checked for Plagiarism: **Yes**
Language Editor:
Dr. Fatima Ramezani
Editor who approved publication:
Dr. Sami Sajjadifar

DOI:10.26655/JMCHEMSCI.2023.9.27

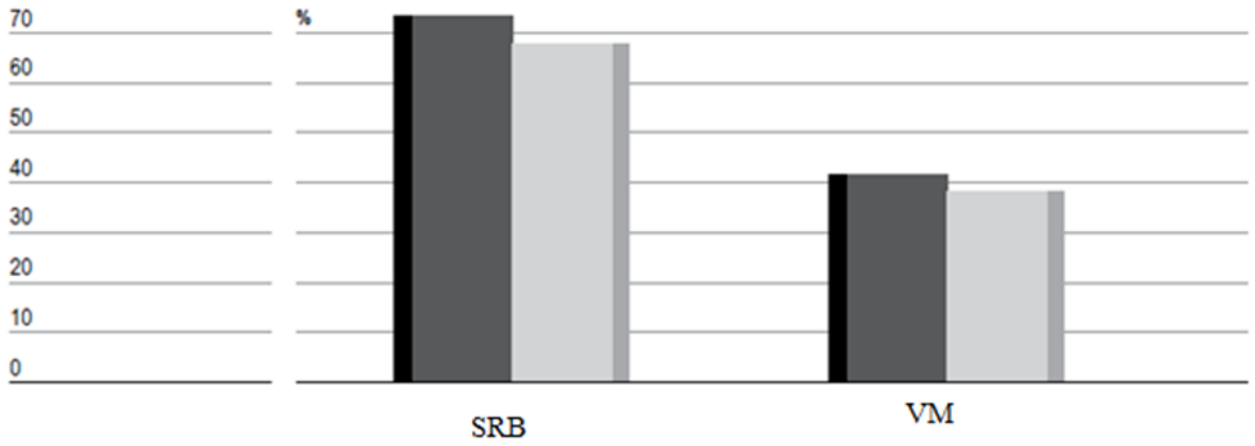
KEYWORDS

Fucoid
BSA
Microcapsules
Layer-By-Layer Adsorption

ABSTRACT

In this work, the chance of the microcapsules development by layer-by-layer adsorption of biopolyelectrolytes was investigated on the cores of inorganic (particles $CaCO_3$) and polymer nature (polystyrene particles). We have assessed the size of got microcapsules, their shape, and quantitative yield. Fucoid (F) was utilized as a high atomic weight polyanion, and ox-like serum egg whites (BSA) was utilized as a high subatomic weight polycation. The cores expulsion was completed by bringing down the pH of framework to 4, on account of a carbonate grid, or by cleaning out using tetrahydrofuran, on account of polystyrene transporters. It was tracked down that the idea of network used to frame microcapsules influences the level of protein fuse and the yield of polyelectrolyte particles.

GRAPHICAL ABSTRACT



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Introduction

Today, in the pharmaceutical industry, the problem of developing new technologies for creating drugs with desired properties to increase the efficiency of their action and reduce side effects is becoming more urgent. One of the promising and popular development methods is the microencapsulation method.

Microencapsulation allows you to enhance the therapeutic effect, improve the pharmacokinetic profile, increase bioavailability, and at the same time, reduce the side effects of pharmaceuticals, as well as increase chemical and conformational stability. Synthetic (polyacrylates, polydioxanones, and polycaprolactones) or natural polymers (lipids, proteins, and polysaccharides), or a combination thereof, are used as material for the microcapsules formation. The physicochemical characteristics of the created microcapsules (size, stability, and number of layers) depend on a number of factors, including the pH of the medium, surfactant, temperature, etc. Interest in natural polymers is due to the fact that they are not toxic, do not cause allergic reactions, their decay products do not accumulate in the body, and can be removed from it or participate in further metabolism. Biopolymers effectively interact with cells, which increases the productivity of their action. In addition, naturally occurring polyelectrolytes have reactive functional groups that easily enter into chemical reactions.

Fucoid is a sulfated heteropolysaccharide isolated from brown algae that are widespread in the seas of polar and temperate latitudes. Fucoid has a number of important characteristics such as the prevalence and availability of polysaccharide source. This polysaccharide is isolated from brown algae that are widespread in the seas of the polar and temperate latitudes. In addition, it has a wide range of biological activity and is anticoagulant [1], antitumor, immunomodulatory [2], antibacterial, antiviral [3], and anti-inflammatory [4] agents. A number of scientific studies [5-7] showed that the polysaccharide induces apoptosis and inhibits angiogenesis, metastasis and invasion of various cancer cells, i.e. it is a potent antigenic and anticancer agent, promising for cancer therapy .Thus, under the action of fucoid, a significant decrease *in vitro* viability of B16 melanoma and carcinoma cells inhibits their growth.

But at the same time, from viewpoint of the physics of solutions, fucoid has the ability to gel formation, self-organization, and can act as a stabilizer and emulsifier. With a deeper study of the properties of fucoid, its fields of application are also expanding. It is possible to single out such areas as therapy of infectious diseases, therapy of diabetic retinopathy, etc. Microcapsules formed with the use of fucoid can be used for the delivery of biologically active substances. There is further a high probability of an increase in the biological activity of polysaccharide itself, due to the fact that in solution, it is in a free state and can easily change its conformation, while in microcapsules, the structure is fixed and can contribute to a more effective interaction with the studied objects [8]. There are many works aimed at studying the conditions for the formation of protein/polysaccharide complexes [8-10], and only a small number of them investigate BSA/fucoid conjugates [11, 12]. The driving force behind the formation of polyelectrolyte protein/polysaccharide complexes is the electrostatic interaction between oppositely charged biopolymers. The completeness of formation of complexes, their solubility depends on pH, ionic strength of the medium, and the protein/polysaccharide ratio [2]. Microstructure Fucoid tourism facilities can be used to deliver a variety of substances, with few restrictions on their chemical nature, properties, and molecular size, which provides a unique opportunity to solve many medical problems. In this work, the formation possibility of microcapsules by layer-by-layer adsorption of biopolyelectrolytes on carriers of inorganic and polymeric nature is considered as the obtained microcapsules, shape, and quantitative yield of formed particles. Fucoid was used as a high molecular weight polyanion, polycation-bovine serum albumin (BSA), matrices were $CaCO_3$, and polystyrene microparticles.

The degree of protein inclusion (SRB) and the yield of the obtained microparticles (BM) were calculated using the formulas, the quantitative protein content was determined

spectrophotometrically using the Bradford method:

$$SRB = \frac{m1 - m2}{m1} * 100\%$$

Where, m1 is the initial mass of the protein, m2 is the mass of the unincorporated protein. VM was calculated as a percentage of the polymers weight used for their formation:

$$VM = \frac{m2}{m1} * 100\%$$

Where, m1 is the initial mass of polymers in solution, m2 is the mass of microparticles that do not contain a nucleus. Microparticles were visualized using a Motic optical microscope.

Results and Discussion

The polysaccharide used in this work is a weakness with a lie electrolyte and the degree of its dissociation strongly depends on the pH of medium. It is known that a fucoid solution has a maximum negative charge at pH 7. Therefore, a polysaccharide solution with an appropriate pH was prepared. Polyelectrolyte microcapsules were obtained by sequential adsorption of negatively charged F and positively charged BSA on carbonate and polystyrene microparticles due to the surface of carbonate matrices has a positive charge [13], and polystyrene ones - negative [14], and then BSA was applied in the first layer at pH 7.4, and then F with the formation of a polyelectrolyte complex. The sequential application was repeated until the required number of layers was reached. Removal of the nucleus from the microcapsules formed on the $CaCO_3$ matrix was carried out using 0.1 M HCl, due to which, in addition to dissolve the core, the pH of the system was lowered to 4, which led to the formation of a denser F/BSA complex. Thus, a gradual decrease in the pH of the system initially leads to the interaction of amino groups of the protein and the side chains of fucoid with the formation of a soluble protein/polysaccharide complex, a further decrease in pH leads to charge neutralization, and an insoluble complex is formed. When pH 4 is reached, the structure of the complex is densified due to the maximum interaction of protein-polysaccharide [15]. The polystyrene core was removed by treating the resulting particles with THF. The resulting microcapsules and microparticles had a shape close to spherical. Removing the core resulted in a resizing the multilayer particles (Figure 1).

Therefore, the size of microparticles formed on polystyrene matrices, before removal of the core was within 3.65 ± 0.8 μm, and the diameter of the microcapsules was 2.79 ±0.5 μm. When using a carbonate matrix up to and after removing the core, the diameter of the obtained multilayer microcapsules did not change significantly and amounted to 4.10 ± 0.9 μm and 3.98 ± 0.6 μm.

Determination of SRB protein was carried out spectrophotometrically according to the Bradford method. The yield of polyelectrolyte complex was determined by weight method. It was found that the nature of matrix used for their formation affects the yield of multilayer microcapsules. Thus, microcapsules formed by layer-by-layer adsorption on a carbonate matrix had a higher yield (47.73 ± 0.33%) than microcapsules formed on a polystyrene matrix (38.26 ± 0.13%). Likewise, the degree of protein incorporation depends on the type of carrier. The use of the $CaCO_3$ matrix led to a more efficient incorporation of the protein and amounted to 73.33 ± 0.43%. The observed increase in the yield of microcapsules, formed on a carbonate matrix, as well as a higher degree of protein inclusion can be associated with the porosity of surface of carbonate particles and associated sorption processes.

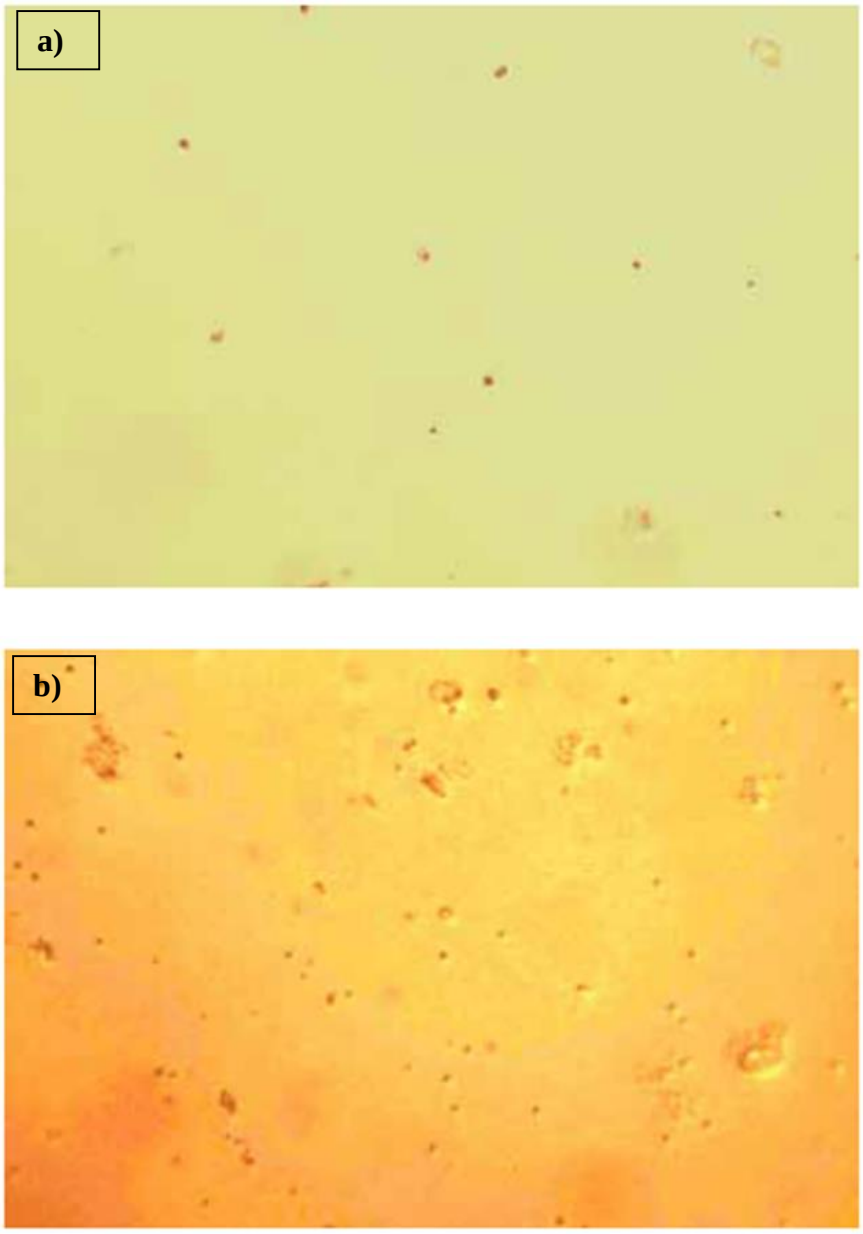

Figure 1: (a) Microcapsules formed on a carbonate matrix (microcapsules I) and (b) microcapsules formed on a polystyrene matrix (microcapsules II)

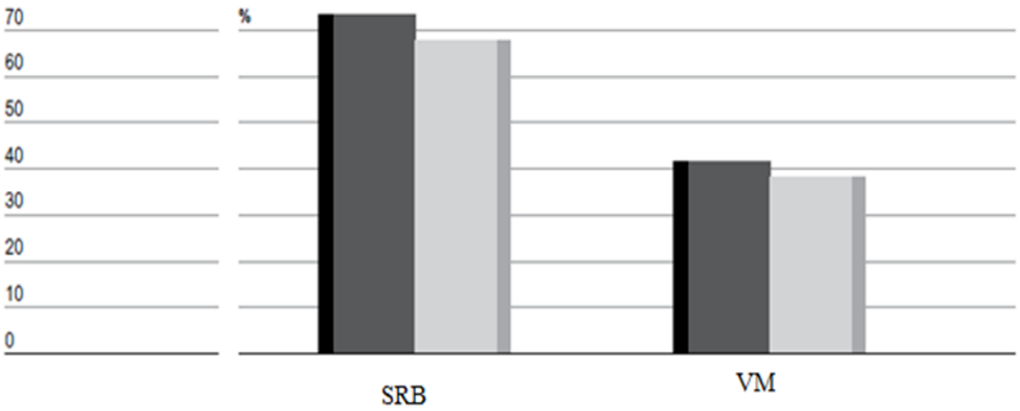

Figure 2: The degree of protein incorporation (SRB) and the yield of microcapsules (BM) when using matrices of different nature

Conclusion

As a result of the work, multilayer microcapsules were used based on natural polymers (BSA/F) using inorganic and organic matrices. The resulting microcapsules had a shape close to spherical, with varying sizes before and after the removal of nucleus, which was proved using the method of dynamic light scattering. In addition, the quantitative yield of microcapsules was studied as well as the degree of protein inclusion. It was found that the considered parameters are significantly influenced by the nature of the matrix applicable for the formation of microcapsules, which may be associated with the porosity of the surface of inorganic nuclei and associated sorption processes.

Disclosure Statement

No potential conflict of interest was reported by the authors.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors' Contributions

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

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HOW TO CITE THIS ARTICLE
Ali L Alfalluji, Fadhel Omran Essa. Microcapsules of Protein-Polysaccharide Complexes Produced on a Variety of Matrices. *J. Med. Chem. Sci*., 2023, 6(9) 2228-2233
DOI: https://doi.org/10.26655/JMCHEMSCI.2023.9.27
URL: http://www.jmchemsci.com/article_170278.html