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Current Opinion in Pharmacology

Capsules with external navigation and triggered release

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Encapsulation is an important technology for pharmaceutical industry, food production, *et cetera*. Its current level of development requires capsule functionalization. One of the interesting ideas to provide new functionality to the microcapsule and nanocapsule is layer-by-layer deposition of functional species. This technique provides step-by-step adsorption of various species (polyelectrolytes, nanoparticles, proteins) when the layer growth is controlled by electrostatic, hydrogen bonding, hydrophobic forces and forming multilayer shells with nanometer precision. This review article introduces recent achievements of layer-by-layer technique attaining external navigation ability and release properties the capsule shell.

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Current Opinion in Pharmacology 2014, **18**:42–46

This review comes from a themed issue on **New technologies**

Edited by **Gleb B Sukhorukov**

For a complete overview see the Issue and the Editorial

Available online 16th September 2014

http://dx.doi.org/10.1016/j.coph.2014.09.002

Introduction

Delivery vehicles modified in order to respond to a certain external triggers in a defined manner have major role in a new generation of intelligent materials, which enable fine spatial and temporal control in 3D environment and replicate natural events during materials' exploitation time. This is very challenging task with requirements, which depend on the application area, such as encapsulation of molecules keeping of their pharmaceutical or other activity during the encapsulation and storage, controlled and sustained release, release at selected target sites.

Different methods for the design of capsule depot systems have specific advantages and drawbacks concerning the upscaling possibility, performance, feasibility to employ different active materials. Capsules with LbL assembled polyelectrolyte shell were used for encapsulation and release of drugs, DNA, sensor dyes and enzymes [1••]; inorganic halloysite nanotubes were demonstrated to be suitable for loading of ferments and inorganic nanoparticles [2]. Mesoporous nanoparticles with polypeptide multilayer shell were used for encapsulation and delivery of enzymes [3]. Hydrogels were used for encapsulation of phospholipids, drugs, as liposome reactors and plant growth media [4]. There are numerous publications on the application of micelles and microemulsions in delivery systems and we would address several recent reviews to provide better understanding of the current achievements in this area [5,6].

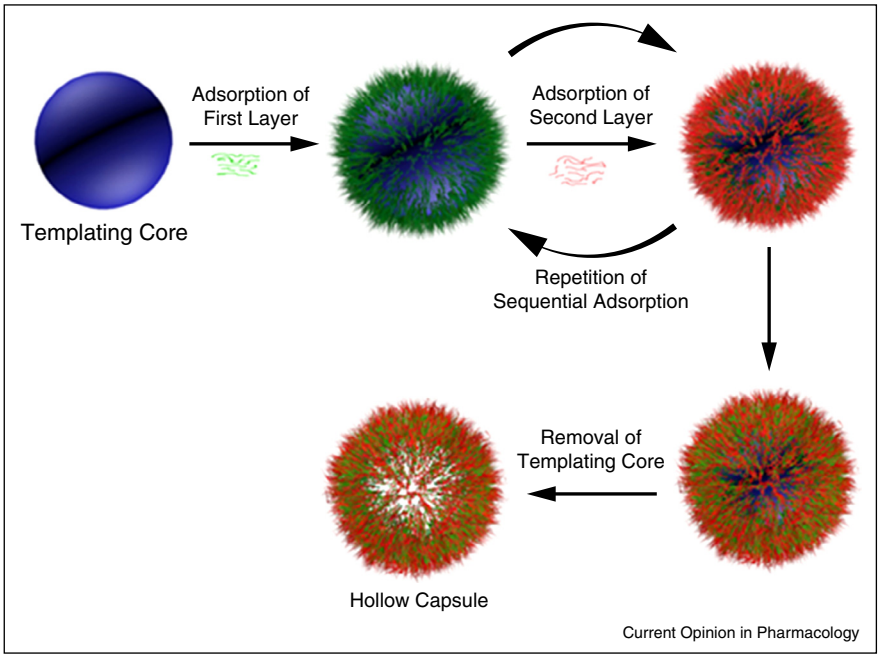
LbL capsules can be fabricated under mild conditions both from water solutions and organic solvents. Moreover, the availability of different polyelectrolytes and other charged materials used as building blocks of LbL assembly, offers interesting prospects for engineering capsules tailored for targeted applications [7].

As depicted in Figure 1, the template core can be dissolved after applying LbL layers resulting hollow LbL capsules. Initially, organic templates based on polystyrene or melamine formaldehyde were used for capsule fabrication. After deposition of polyelectrolyte multilayers, templates were dissolved by organic solvents and aqueous acidic solutions, respectively, to obtain hollow capsules. However, acidic solutions should be avoided for capsules to be employed for delivery of bioactive material due to the possible inactivation of the latter. Therefore, inorganic template materials were used: silica and carbonates [8,9].

Capsules with external navigation

The best way to receive the external control over capsule movement is to include magnetic nanoparticles inside LbL shell as one or several monolayers. In most cases, chemically inert magnetite and γ-Fe_2O_3 are used [10–12]. These oxide nanoparticles possess very good magnetic susceptibility and, at the same time, inert enough to withstand changes of local pH between 3 and 11. Typical method of shell functionalization with magnetic nanoparticles is as follows. The capsules are firstly modified with several layers of polyelectrolytes to provide a positively charged surface that provokes subsequent adsorption of magnetic nanoparticles (usually stabilized with acids like citric acid and have, therefore, negative surface charge) from their colloidal solutions. Additional positive polyelectrolyte layer is deposited at the last stage to stabilize Fe_3O_4 nanoparticles in the capsule shell. Figure 2a presents the initial solution containing the suspension of magnetic capsules. When a magnet is placed close to the vial, as shown in Figure 2b, the capsules are forced to the wall of the vial close to the magnet.

Figure 1



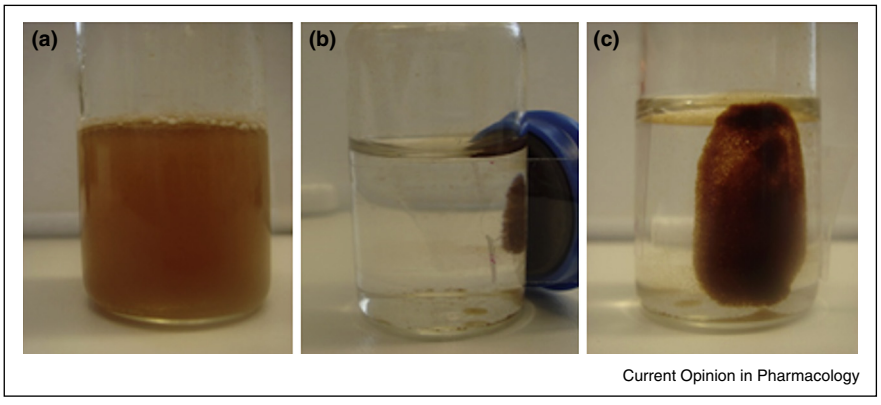
Scheme of the polyelectrolyte capsule formation (from Master Thesis of Simona-Vyara Kolarova, 2014, The University of Liverpool).

So, capsules with magnetic nanoparticles in the shell can be moved by an external magnet in a desired direction. After removal of magnet, magnetic capsules can be easily redispersed in the solution by gentle agitation. When a magnet is placed on the vial again, the precipitates forms againdemonstrating the ability of magnetic containers can be redirected without loss of the magnetic property. Another way to get magnetic properties is to in situ synthesize magnetic nanoparticles inside capsules. Fe_3O_4 nanoparticles were in situ synthesized inside nanoporous poly(L-glutamic acid)/chitosan (PGA/CS) microcapsules [13,14]. The carboxylate groups of PGA in the shell could be used as binding sites for the absorption of iron ions for the synthesis of magnetic nanoparticles [15•]. Unlike earlier reported 'magnetic backpacks' (microconfinements carrying magnetic properties) attached to the cell membrane, the capsules reported here are internalized by cells and could transport a cargo.

Triggered release of encapsulated species

Since LbL method provides high versatility in the shell components, it is possible to fit capsule shell to the certain trigger(s), which remotely and sometimes reversibly open

Figure 2



The prepared magnetic capsules in aqueous solution and their targeted movement under external magnetic stimuli [13].