Glucose-responsive layer-by-layer microcapsules as self-regulated insulin delivery system

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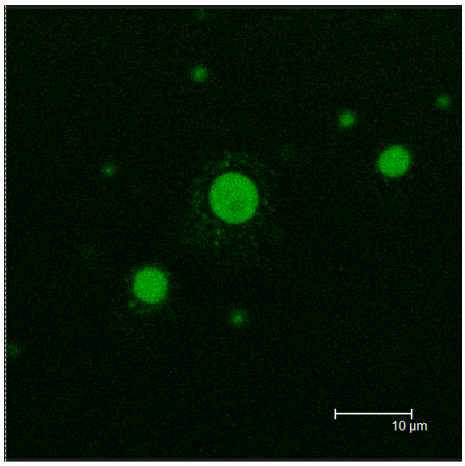
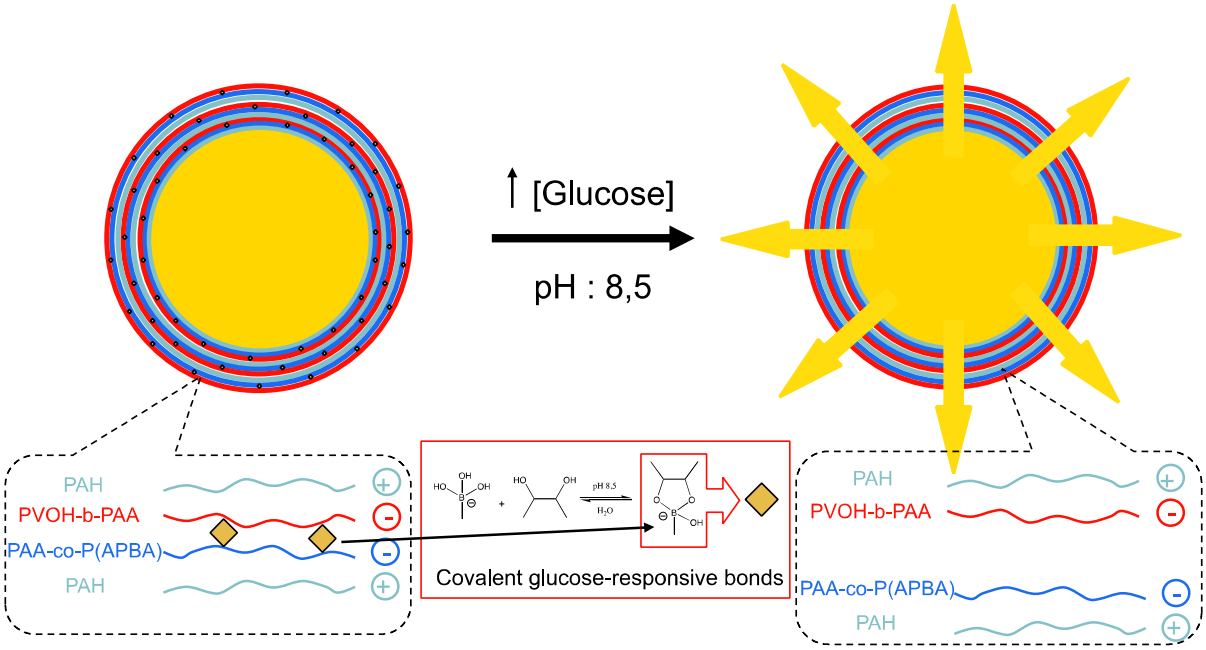
Diabetes is a disorder of glucose regulation, characterized by an accumulation of glucosein the blood. The breakdown of glucose regulation can be attributed to the pancreas's inability to secrete insulin or to the body's inability to properly use it. The usual treatment for type 1 diabetesconsists in multiple subcutaneous insulin injections,daily administered using needles, insulin pen or insulin pump. However, this method doesn't maintain normoglycemia and can lead to complications such as limb amputation, blindness, and kidney failure. To avoid such abnormal episodes, scientists imagined smart systems which are able to regulate the glucose level by themselves.

During the past decades, a large variety of micro- and nanocarriers have been developed in order to improve efficiency, availability and toxicity profiles of drugs. In this field, stimuli-responsive polymer multilayers have attracted great scientific interest because of their potential applications as controlled delivery or release systems, for chemicals and drugs. A category of stimuli-responsive materials is able to sense glucose and respond to it by a modification of their porosity, leading to a release of insulin.

The objective of this work was to investigate the formation of glucose responsive hollow microcapsules (5 microns) made of polyelectrolyte copolymers. These copolymers are composed of carbohydrate-sensitive functions, such as boronic acid and diols (PVOH), known for forming reversible covalent ether bond. In presence of carbohydrates such as glucose, the ether bonds will be reversibly broken and, consequently, the porosity of the glucose particles will change. Therefore, polyelectrolyte copolymers were synthesized by control radical polymerization, i.e. reversible addition-fragmentation chain transfer (RAFT, polyboronic acid) and cobalt-mediated radical polymerization (CMRP, PVOH). Using these polyelectrolytes as polyanions and poly(allylamine) (PAH) as a polycation, we undertook the formation of layer-by-layer capsules starting with a template of $CaCO_3$microparticles which can be dissolved with EDTA leading to the formation of hollow microcapsules. Bovin serum albumin isothiocyanate (BSA-FITC) was used to fill the $CaCO_3$microparticles and to determine the porosity of the resulting capsules in function of the glucose concentration. The sugar-dependent porosity is investigated by following the release of encapsulated BSA-FITC by spectro-fluoroscopy.


10 µm


[Glucose]
pH : 8,5
PAH
PVOH-b-PAA
PAA-co-P(APBA)
PAH
Covalent glucose-responsive bonds
PAH
PVOH-b-PAA
PAA-co-P(APBA)
PAH