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Surface molecularly imprinted organic-inorganic polymers having affinity sites for cholesterol

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ABSTRACT

Novel granular organic-inorganic molecularly imprinted polymers (MIPs) based on 2-hydroxyethyl methacrylate (HEMA) and ethylene glycol dimethacrylate (EGDMA) were prepared by co-polymerization on the surface of selenium (Se) nanoparticles stabilized with poly(vinyl pyrrolidone) (PVP) at different concentrations of cholesterol as a template molecule. The synthesis occurred in Pickering microemulsion. The obtained compounds are intended for use as selective hemosorbents in efferent therapy of hypercholesterolemia. The sorbents were characterized by scanning electron microscopy (SEM), Fourier transform infrared spectroscopy (FTIR) and sorption experiments. It was revealed that MIPs possess more pronounced porous structure as compared to that of the reference non-imprinted polymer (NIP). The influence of the amount of introduced cholesterol template on physico-chemical and sorption properties of MIPs was investigated. FTIR spectroscopy and thermodynamic studies showed that the affinity of MIPs towards cholesterol is related to multi-point polyfunctional binding of adsorbate in complementary cavities or imprint sites; hydrogen bonds play the key role in recognition of the target molecule. The Langmuir, Freundlich, Temkin and BET model isotherms were used for interpreting the experimental data on the equilibrium sorption experiments. The maximum adsorption capacities increased for the MIP synthesized at the highest molar concentration of the template. Cholesterol adsorption proceeded in the monolayer within a wide concentration range, and the data obtained in these experiments better conformed to the Langmuir isotherm. Formation of the surface sorption layer in the MIPs facilitates availability of imprint sites and enhances the efficiency of specific cholesterol binding from blood plasma *in vitro*.

1. Introduction

Atherosclerosis (chronic inflammatory disease that occurs within the artery wall) is one of the basic causes of vascular complications such as myocardial infarction, stroke, and peripheral vascular disease [1]. The factors associated with atherosclerosis include high levels of cholesterol, triglycerides, low-density lipoproteins (LDL) and low levels of high-density lipoproteins in blood. It was found that diet and taking lipid-reducing drugs result in significant reduction of blood levels of cholesterol and LDL and, therefore, in regression of atherosclerosis [2]. However, oral lipid-lowering drugs, such as statins, are risky and may cause liver damage; their efficiency is relatively limited, even when they are taken in association with a strict diet. Moreover, this treatment is not sufficiently effective in case of patients who have familial hypercholesterolemia (FH), a rare form of genetic dyslipidaemia with an incidence of about 1:500 in general population [3]. The genetic mutations underlying FH affect the production and processing of cell surface LDL receptors resulting in impaired hepatic clearance of circulating LDL particles, which leads to their accumulation in bloodstream [4]. The cornerstone of therapy for high cholesterol level in FH patients is plasmapheresis, especially LDL-apheresis based on electrochemical principles. This method allows selective removal of apolipoprotein B-containing lipoproteins through extracorporeal precipitation on the affine sorbents; heparin (Heparin-induced Extracorporeal LDL Precipitation or HELP) [5], dextran sulfate (Liposorber) [6,7], or monoclonal antibodies [8] are used in the procedure. LDL-apheresis can lead to sharp decrease in LDL cholesterol level (by 70–80%), but a rapid rebound to baseline levels occurs within approximately 2 weeks [9].

Thus, monitoring and removal of LDL cholesterol on-demand with the use of polymeric systems are highly desirable; molecularly imprinted polymers (MIPs) can potentially be used for these purposes. As a new class of synthetic receptors, MIPs have shown great potential in many applications due to their good specific recognition ability, high stability, and easy preparation [10]. An ultimate goal of molecular imprinting is to obtain MIPs that can be routinely used as an alternative

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to natural antibodies and receptors and serve as a competitive replacement to the affinity sorbents for LDL-apheresis.

One of the goals of molecular imprinting is to generate sorbents that would eventually replace biological receptors in practical applications. The majority of the developed imprinting protocols can be successfully used to produce MIPs for recognition of a large number of guest molecules, including cholesterol, predominantly in organic solvent-based media, while they often fail to generate MIP for use in pure aqueous environments [11–14]. In addition, biological components, such as proteins and lipids, are strongly adsorbed on polymeric surfaces and thus affect their recognition properties. Therefore, in order to obtain MIPs capable of performance in aqueous media (*e.g.*, biological fluids or environmental waters), these non-specific interactions should be weakened or prevented [15]. In recent years, many efforts have been

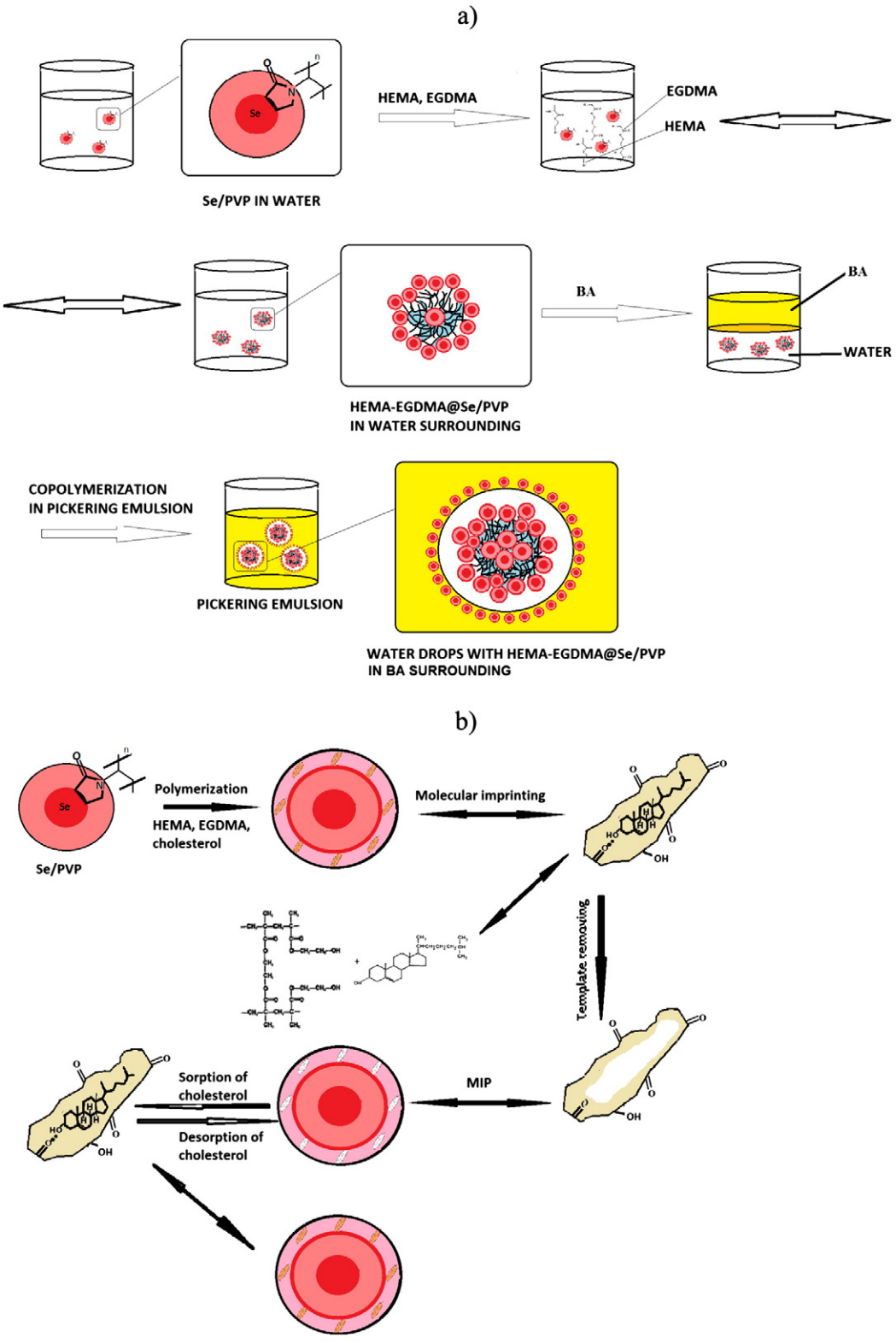

Fig. 1. Scheme of HEMA–EGDMA@Se/PVP copolymerization process in the Pickering emulsion (a), and the formation of imprint sites in the MIP (b).