Synthesis of radiolabeled microspheres

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The vascular embolization objective is to reduce a tumor region by occluding a feeding blood vessel. The limited supply of nutrients shrinks the tumor, allowing tissue recovery. To promote this occlusion, polymeric microspheres are injected through a catheter in the target blood vessel. Polyvinyl alcohol (PVA) particles are commonly used as embolic agents, being vinyl acetate (VNA) of its precursor monomer. The vascular embolization is applied, for example, to treat uterine fibroid and inoperable tumors [1]. For this technique, magnetic resonance, computed tomography (CT), and ultrasound images provide the mapping of an arterial blood supply target, its neighboring tissues and veins, however these imaging techniques are used only for preoperative planning [2]. During embolization procedure, the radiologist can only estimate the devascularization through angiography. Pathological examination shows the precise site of blockade and location of microspheres [3].

Considering *in vivo* imaging techniques, positron emission tomography (PET) and single-photon emission computed tomography (SPECT) provide high-resolution functional imaging and are well-established methods in Nuclear Medicine. In addition, when combining PET or SPECT with CT technique, functional and anatomical information can be achieved simultaneously, improving the location and quantification of radioactive substance distribution in the target tissue. Radiopharmaceuticals are the radioactive substances used for this purpose [4]. By incorporating radioisotopes in PVA polymer structure, e.g., fluorine 18 (^{18}F) or iodine 123 (^{123}I), radioactive embolic agents are obtained and become new tools for embolization procedure. Therefore, the use of PET and SPECT imaging techniques can improve embolization technique with real time imaging, leading to a more precise, faster and safer procedure.

Our goal is to radiolabel a monomer that will be copolymerized with the VNA monomer through catalyzed suspension reaction. This synthesis route not only improves final product specificity, but also reduces radioactivity impurities level. A remaining free radioisotope can be trapped in the copolymer structure and released further when in contact with blood fluid, causing undesirable patient exposure to radiation and undefined images.

^{123}I was first selected to develop this study. This radioisotope is commonly used for SPECT imaging due to its physical characteristics and availability in high level of radionuclidic purity. In addition, iodoaromatic and iodovinylic compounds exhibit higher *in vivo* and chemical stability [5]. Cinnamic acid (CMA) structure exhibits aromatic ring for iodine incorporation and unsaturated aliphatic chain for polymerization (Figure 1).

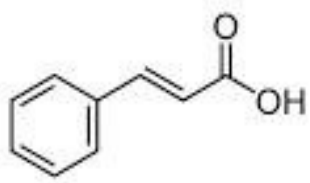

Figure 1: Chemical structure of CMA.

Preliminary studies on I^+ generation through oxidizing agents showed good yields for the iodination of the CMA aromatic ring. Non radioactive iodination occurred to avoid unnecessary exposure to radiation and to synthesize enough product mass for characterization. CMA and VNA mass copolymerization resulted in a chemically stable material. The radioiodination of CMA through isotopic exchange and copolymerization between iodinated CMA and VNA will be further performed.

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