Enzymatic Synthesis of Sorbitan Methacrylate: Effect of Acyl donor and Molar ratio

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Abstract

Sugar polymers have been considered as biomaterial. Biomaterials are widely utilized for a medical applications in direct contact with living tissue Clearly, biomaterials must be carefully and microscopically fabricated for optimal acceptance within the living organism, in both functional and structural senses. In this study, the enzymatic synthesis of sorbitan methacrylate from 1,4-sorbitan via the manipulation of an immobilized biocatalyst (Novozym 435) and acryl donors (methacrylic acid and vinyl methacrylate) was evaluated.

Introduction

"Biomaterials"is a generic term which refers to a variety of medical materials which are designed to be in direct contact with living tissue. Therefore, biomaterials must be carefully and microscopically fabricated for optimal acceptance in living organisms, in both the functional and structural senses. Biomaterials also encompass the materials relevant to the manufacture of catheters, contact lenses, and artificial human hearts. Recently, it has been reported that even drug-delivery systems in the human body could be developed using biomaterials. Medical devices constitute yet another class of-material.

Sugars, as a group of multifunctional compounds, appear to be quite attractive for biomaterial research. They are biologically relevant, and harbor multiple hydroxyl groups. Recently, several applications for sugar-containing polymeric materials, synthesized from sugar esters, have been reported by a host of researchers. Sugar esters, or esters

containing sugar molecules, have been attracting increasing interest, and have been used in a number of industrial fields, as flavorings, emulsifiers, lubricants, detergents, and cosmetic additives. These sugar esters are biodegradable, biocompatible, and non-toxic.

Esterification is the principal process by which sugar esters are synthesized. This process has been studied extensively with regard to the chemical and enzymatic phenomena involved. The chemical process is characterized by low regioselectivity, which results in poor selectivity, undesirable side reactions, and low yields. However, the enzymatic process can also be applied to the regioselective transformations of mono- and disaccharides, without any untoward complications. In this study, two distinct esterification schemes have been applied: acylation and alcoholysis. Acylation refers to the esterification of a carboxylic acid (eq. methacrylic acid) with the hydroxyl group in the acyl acceptor (eq. 1,4-sorbitan), which produces an ester and a water by-product. Alcoholysis, however, refers to the esterification of an ester (eq. vinyl methacrylate) with the hydroxyl group in the acyl acceptor (eq. 1,4-sorbitan). Alcoholysis produces another ester, but yields alcohol as a by-product.

This study was undertaken in order to characterize the processes inherent to the chemical and enzymatic synthesis of sorbitan methacrylate, the basic material used in the manufacture of contact lenses.

Materials and Methods

1,4-Sorbitan preparation

All dehydration reactions (sorbitol cyclization) for the synthesis of 1.4-sorbitan using *p*-toluenesulfonic acid (*p*-TSA) in a solvent-free process wereperformed as was previously reported. The dehydration reaction wasconducted for 2 hours at 130±1℃, under a reduced pressure of 200 mmHg. The reactor volume was 50 mL. The reaction temperature was controlled using an oil bath which was equipped with a PID temperature controller. Agitation was performed with a magnetic bar, spinning at about 200 rpm. During the reactions, 0.1 mL of sample was withdrawn at set intervals, and monitored by HPLC and TLC.

Enzymatic esterification

In this study, two of esterification schemes were carried out: acylation and alcoholysis.

All esterification reactions for the synthesis of 1,4-sorbitan esters using immobilized lipase (Novozym 435) were performed in the apparatus. The reaction temperature was controlled with a water bath which was equipped with a PID temperature controller. Mixing was carried out with a magnetic stirrer, spinning at about 200 rpm. The condenser prevented the evaporation of the reactant (*t*-butanol). Results are expressed as the mean values of at least two independent measurements. To investigate the effect of molar ratio, prepared 1,4-sorbitan was added in bottle, and subsequently MMA, EMA, and VMA were added to meet the molar ratios (1,4-sorbitan:acyl donor) of 0.5:1 to 1:5. *t*-Butanol was inserted to the mixtures to achieve the total volume of 20L. The reaction was initiated by adding 3% (w/v) Novozym 435 at 50℃.

Results and Discussion

This study was performed to research chemo-enzymatic synthesis of sorbitan methacrylate. It was to find the optimum conditions for sorbitan methacrylate synthesis using immobilized lipase (Novozyme 435) in *t*-butanol from 1,4-sorbitan. In this study, alcoholysis was applied by esterification of sorbitan. Alcoholysis is the esterification of a vinyl methacrylate with the hydroxyl group in 1,4-sorbitan that produces sorbitan methacrylate and vinyl alcohol as a by-product. All esterification reactions for the synthesis of 1,4-sorbitan ester using immobilized lipase (Novozyme 435) were investigated with MMA, EMA and VMA as acyl donor.

As shown in Fig. 1, the enzymatic synthesis of sorbitan methacrylate catalyzed by Novozym 435 in *t*-butanol was reached approximately 50% conversion yield at 50 g/L of initial 1,4-sorbitan concentration, 3% (w/v) of enzyme content, 1:5 of molar ratio of sorbitan to EMA, 50℃ of reaction temperature for 36 hours using EMA as acyl donor. The application of high enzyme concentration leads to shorter reaction periods, but the operation cost increases. The process will be optimized between productivity and enzyme concentration. As shown in Fig. 2, during reaction periods, the conversion of 1,4-sorbitan to sorbitan methacrylate was about 68% at 36 hr and 5% (w/v) enzyme concentration. Enzyme concentration slightly influenced the conversion yield. However, ahigh enzyme concentration can cause economic problems.

Using MMA as acyl donor, sorbitan methacrylate was synthesized around 78%

conversion at 50 g/L of initial 1,4-sorbitan concentration, 7% (w/v) of enzyme content, 1:5 of molar ratio of sorbitan to MMA, 50℃ of reaction temperature for 36 hours. The synthesis of sorbitan methacrylate using VMA as acyl donor was expected superior conversion yield at 3% (w/v) of enzyme content, 1:3 of molar ratio and 100 g/L of initial 1,4-sorbitan concentration. VMA was applied to obtain higher yield than EMA and MMA as acyl donor in esterification reaction catalyzed by Novozym 435 in organic solvents.

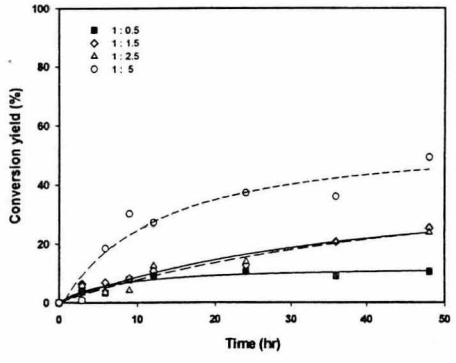

Fig.1. Effect of molar ratio on conversion of sorbitan methacrylate in lipase-catalyzed glycosylation using ethyl methacrylate.

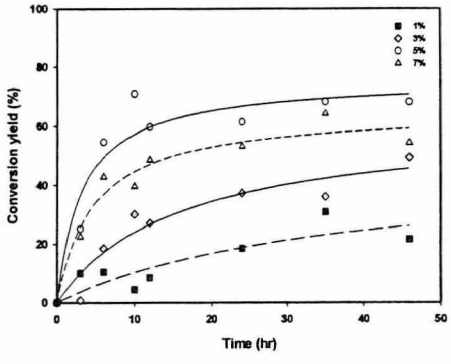

Fig. 2. Effect of enzyme content on conversion of sorbitan methacrylate in lipase-catalyzed glycosylation using ethyl methacrylate.

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