Three Step Chemo Enzymatic Continuous Flow Cascade Synthesis of 1-Monoacylglycerol.

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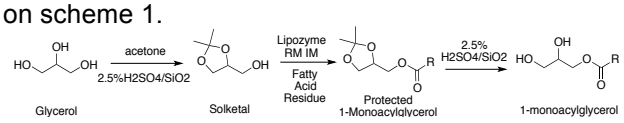
INTRODUCTION

Monoacylglycerols (MAGs) represent 70% of all synthetic emulsifiers used in industry[1]. The use of chemical methods for the synthesis of these esters presents several disadvantages, including poor selectivity towards 1-monoesters and harsh conditions, leading to colored products and poor yields. Lipases have also been applied to overcome these issues, achieving good yields and improving selectivity. Recently, much attention has been given to continuous flow protocols in which reactions can be performed in a cascade sequence without or within isolation of intermediates. The main advantage of the use of continuous flow approach based on packed bed reactor is the improved mass transfer and recyclability of the solid catalyst[2]. In this work we reported our results on a three-step chemo enzymatic cascade reaction starting from glycerol derived from biodiesel synthesis and arriving at 1-monoacylglycerols.The three steps are summarized on scheme 1.



Scheme 1. Strategy to the cascade monoacylglycerol synthesis

RESULTS AND DISCUSSION

The first studied reaction was the glycerol acetalization, catalyzed by a 2.5% H_2SO_4/SiO_2 catalyst packed in a Omnifit column of 2,41 mL of volume. Results showed that there was not significative differences on conversions of solketal towards 0,1 (87%) and 0,2 mL/min (86%) of flow.We also investigated the esterification of solketal with stearic acid, applying optimal conditions according to our previous works[3]. Studies of high concentrations of starting material as well as the recycling of biocatalyst(figure 1), demonstrated that 90% of conversion could obtained under 60°C and 0,1mL/min, with 2M of substrates (figure 1A). Besides, around 15 recycles could be performed.

The ketal cleavage were performed with the same H_2SO_4/SiO_2 catalyst. According to figure 2, there are four possible products to these reaction.

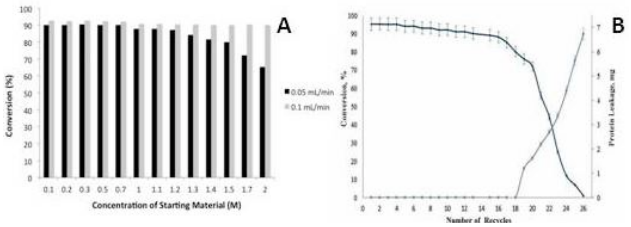
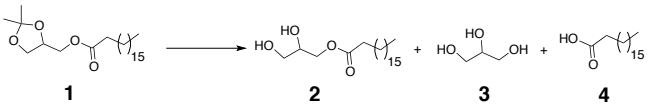


Figure 1: A. Relation between concentration of starting material and conversion on esterification reaction immobilized lipase from *Rizhomucor miehei*.**B**: recycle of biocatalyst.

Studies relating the flow and selectivity for the desired 1-MAG demonstrated that at 0,2mL/min, high selectivity was achieved (figure 2).



1 **2** **3** **4**

Entry	Flow (mL/min)	Conversion (%)			
		1	2	3	4
1	0.1 mL/min	n.d	65	29	5
2	0.2 mL/min	n.d	87	0	12
3	0.3 mL/min	19	70	0	10

Figure 2. Possible products and selectivity according to the flow.

This flow were chosen to be used in the next study, where all steps were telescoped, and the final product obtained in around 2h, with precipitation in n-heptane.

CONCLUSION

We have successfully developed a three-step chemo-enzymatic continuous flow process for obtaining 1-monoacylglycerol in high conversions and high purity.

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