**Immobilization of lipase onto micro tubular reactor for efficient production of (S)-ibuprofen.**

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**Highlights**

* The activity of lipase on (S)-ibuprofen was confirmed by batch system.
* The immobilized lipase onto micro tubular has been prepared by multi-layer deposition.
* The reactivity of immobilized lipase was well conserved during repeated uses.

**1. Introduction**

Ibuprofen is an important drug material of NSAIDs and is sold as a racemate in the market. (S)-Ibuprofen has been reported to be 160 times more reactive than the (R)-ibuprofen. Currently established (S)-ibuprofen production methods involve complex organic synthesis. Lipases have been paid attention to lipid modifications [1]. They catalyzed hydrolysis, alcoholysis, acidolysis, amidolysis, and esterification in food and pharmaceutical industry. Some studies reported lipase reactivity for enantio synthesis of (S)-ibuprofen from racemate [2]. In spite of interesting performance of lipases, their application in industrial level is limited because of their cost and requires reuse of lipase for a practical process. We focused on immobilizing lipase onto micro tube and aimed to develop the reactivity of lipase for (S)-ibuprofen producing.

**2. Methods**

The polydopamine layer was used as a primer layer in polytetrafluoroethylene (PTFE) micro tube to provide inner surface of micro tube reactable groups. Polyethylenimine and *Candida rugosa* lipase were adsorbed on the PTFE surface by the layer-by-layer method. (S)-Ibuprofen production was initiated to introduce ibuprofen ester racemate as substrate into PTFE micro tubular reactor (Fig.1). The (S)-ibuprofen produced was analyzed quantitatively with HPLC.



**Figure 1.** The experimental apparatus of (S)-ibuprofen production by immobilized lipase.

**3. Results and discussion**

The amount of loading lipase kept increasing as the number of layers increased by the 8th layer (Fig.2). The production yield of immobilized lipase on micro tubular reactor was developed than the yield prediction of batch system. The reactivity of immobilized lipase on tubular reactor (loading 3400 μg lipase) was determined by repeated reactions. The reactivity was well conserved during 8th repeated uses. It retained almost 80% of that of first reaction. The results successfully demonstrated that the immobilized lipase on PTFE inner surface was stable throughout the repeated uses.



**Figure 2.** The amount of loading lipase by the multi-layer deposition on PTFE. The lipase loading kept increasing as the number of layers increased by the 8th layer.

**4. Conclusions**

The immobilized lipase onto micro tubular reactor has been successfully prepared by multi-layer deposition. Efficient performance of immobilized micro tubular reactor for production of (S)-ibuprofen was developed.

**References**

1. Masakazu Naya, Masanao Imai, Journal of Chemical Technology and Biotechnology, 91, Issue 10 (2016) 2620-2630.
2. Ozlem Sahin et al. Applied Cat A:General, 369 (2009) 36-41.