**Thermomyces lanuginosus** lipase-catalyzed synthesis of natural flavor esters in a continuous flow microreactor

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**Abstract** Enzymatic catalysis is considered to be among the most environmentally friendly processes for the synthesis of fine chemicals. In this study, lipase from *Thermomyces lanuginosus* (Lecitase Ultra™) was used to catalyze the synthesis of flavor esters, i.e., methyl butanoate and methyl benzoate by esterification of the acids with methanol in a microfluidic system. Maximum reaction rates of 195 and 115 mM min⁻¹ corresponding to catalytic efficiencies (k<sub>cat</sub> / K<sub>M</sub>) of 0.30 and 0.24 min⁻¹ mM⁻¹ as well as yield conversion of 54 and 41 % were observed in methyl butanoate and methyl benzoate synthesis, respectively. Catalytic turnover (k<sub>cat</sub>) was higher for methyl butanoate synthesis. Rate of synthesis and yield decreased with increasing flow rates. For both esters, increase in microfluidic flow rate resulted in increased advective transport over molecular diffusion and reaction rate, thus lower conversion. In microfluidic synthesis using *T. lanuginosus* lipase, the following reaction conditions were 40 °C, flow rate 0.1 mL min⁻¹, and 123 U g⁻¹ enzyme loading found to be the optimum operating limits. The work demonstrated the application of enzyme(s) in a microreactor system for the synthesis of industrially important esters.

**Keywords** Lipases · Microreactor · Lecitase Ultra™ · Esterification · Flavor esters · Biocatalysis

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**Abbreviations**

- k<sub>cat</sub>/K<sub>M</sub> Catalytic efficiency (min⁻¹ mM⁻¹)
- k<sub>cat</sub> Catalytic turnover (min⁻¹)
- v Initial reaction rate (mM min⁻¹)
- K<sub>M</sub> Michaelis constant (mM)
- V<sub>max</sub> Maximum reaction rate (mM min⁻¹)
- Pe Péclet number (dimensionless)
- Da Damköhler numbers (dimensionless)
- Re Reynolds number (dimensionless)
- D Diffusivity coefficient (cm² s⁻¹)
- D<sub>eff</sub> Effective diffusivity (cm² s⁻¹)
- U Superficial Velocity (cm s⁻¹)
- q<sub>v</sub> Volumetric flow rate (cm³ min⁻¹)
- V<sub>S</sub> Molar volume of solvent (cm³ mol⁻¹)
- V<sub>r</sub> Molar volume of reactant (cm³ mol⁻¹)
- η<sub>S</sub> Dynamic viscosity of solvent (mPa s)
- t<sub>r</sub> Characteristic reaction time (s)
- l Channel characteristic length (cm)
- r Radius of the channel (cm)
- P Circumference of the channel (cm)

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**Introduction**

Naturally occurring flavor esters are commonly used in pharmaceutical, food, fragrance, and cosmetics industries as aroma agents. Increasing industrial demand for flavor and fragrance esters is evidenced by their current global markets that stand at $21.8 billion (BBC Research 2012). This figure is projected to exceed $30 billion in 2017, with an estimated annual growth rate of 5.6 % from 2012 to 2017 (BBC Research 2012). Although these types of esters

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