

## Kinetics and optimization of lipophilic kojic acid derivative synthesis in polar aprotic solvent using lipozyme RMIM and its rheological study

### ABSTRACT

The synthesis of kojic acid derivative (KAD) from kojic and palmitic acid (C16:0) in the presence of immobilized lipase from *Rhizomucor miehei* (commercially known as Lipozyme RMIM), was studied using a shake flask system. Kojic acid is a polyfunctional heterocycles that acts as a source of nucleophile in this reaction allowing the formation of a lipophilic KAD. In this study, the source of biocatalyst, Lipozyme RMIM, was derived from the lipase of *Rhizomucor miehei* immobilized on weak anion exchange macro-porous Duolite ES 562 by the adsorption technique. The effects of solvents, enzyme loading, reaction temperature, and substrate molar ratio on the reaction rate were investigated. In one-factor-at-a-time (OFAT) experiments, a high reaction rate ( $30.6 \times 10^{-3} \text{ M} \cdot \text{min}^{-1}$ ) of KAD synthesis was recorded using acetone, enzyme loading of 1.25% (w/v), reaction time of 12 h, temperature of 50 °C and substrate molar ratio of 5:1. Thereafter, a yield of KAD synthesis was optimized via the response surface methodology (RSM) whereby the optimized molar ratio (fatty acid: kojic acid), enzyme loading, reaction temperature and reaction time were 6.74, 1.97% (w/v), 45.9 °C, and 20 h respectively, giving a high yield of KAD (64.47%). This condition was reevaluated in a 0.5 L stirred tank reactor (STR) where the agitation effects of two impellers; Rushton turbine (RT) and pitch-blade turbine (PBT), were investigated. In the STR, a very high yield of KAD synthesis (84.12%) was achieved using RT at 250 rpm, which was higher than the shake flask, thus indicating better mixing quality in STR. In a rheological study, a pseudoplastic behavior of KAD mixture was proposed for potential application in lotion formulation.

**Keyword:** Immobilized lipase; Impeller design; Response surface methodology; Rheology; Organic synthesis; Kojic acid derivative