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 ($30.6 \times 10{-}3$ M·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