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REVIEW

Enzymatic synthesis of kojic acid esters and their potential industrial applications

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In this paper, enzymatic methods for the synthesis of 5-hydroxy-2-(hydroxymethyl)-4*H*-pyran-4-one (kojic acid) esters are reviewed. Important process parameters related to the synthesis of kojic acid esters such as the type of immobilized lipase, solvent, temperature, initial water activity, water content, pH, metal salts, enzyme loading, substrates mole ratio, and acyl donors are highlighted and discussed. The properties of kojic acid esters related to their solubility, stability, cytotoxicity, depigmenting activity, tyrosinase inhibitory, metal-chelating, anti-oxidant, and other biological activities are also highlighted. At present, kojic acid and its esters are widely used in cosmetic and skin health industries as skin whitening agents. The advantages and disadvantages of various kojic acid esters are compared and possible industrial applications of these derivatives are also discussed.

Keywords: kojic acid, kojic acid esters, esterification, depigmenting, tyrosinase, immobilized lipase

Introduction

Large scale production of 5-hydroxy-2-(hydroxymethyl)-4*H*-pyran-4-one (kojic acid, KA), a fungal secondary metabolite and a naturally occurring organic acid, has been studied intensively by several researchers (Ariff et al., 1997; Wan et al., 2005; El-Aasar, 2006; Mohamad & Ariff, 2007; Terabayashi et al., 2010). KA is an iron and copper chelator capable to prevent oxidation, photodamage, hyperpigmentation, and skin wrinkling (Mitani et al., 2001; Briganti et al., 2003). As natural organic acid, KA is biodegradable. This organic acid also possesses some other valuable and potent biological activities such as the ability to reduce mustard toxicity (Smith & Lindsay, 2001), potential to be used in therapeutic drugs (Sudhir et al., 2005), as an inducer of microphage activation (Rodrigues et al., 2011), and metal chelating agent (Stenson & Cioffi, 2007). Potential industrial applications of KA have been reviewed by Mohamad et al. (2010). KA and KA derivatives are widely used as skin whiteners in cosmetic creams. Antimicrobial activities of KA and KA derivatives against bacteria and fungi have been reported (Dowd, 1990). KA and KA derivatives possess also other biological activities such as antioxidant, anti-inflammatory, and metal-chelating ones (Kobayashi et al., 2001; Rho et al., 2007). However, prominent commercial applications of kojic acid and its esters are in the cosmetic and skin health industries.

The hydrophilicity of KA has restricted its application in cosmetic, oily food, and pharmaceutical products. Moreover, there are concerns about its toxicity (Burdock et al., 2001), irritancy (Nakagawa et al., 1995), carcinogenicity, mutagenicity (Wei et al., 1991), hepatocarcinogenicity (Chusiri et al., 2011; Moto et al., 2006), genotoxicity, and tumor-initiating activity (Nohynek et al., 2004; Nawarak et al., 2008; Tamura

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