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Glyceric Prodrug of Ursodeoxycholic Acid (UDCA): Novozym 435-Catalyzed Synthesis of UDCA-Monoglyceride

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Abstract

Bile acids (BAs) are a family of steroids synthesized from cholesterol in the liver. Among bile acids, ursodeoxycholic acid (UDCA) is the drug of choice for treating primary biliary cirrhosis and dissolving cholesterol gallstones. The clinical effectiveness of UDCA includes its choleretic ac tivity, the capability to inhibit hydrophobic bile acid absorption by the intestine under cholestatic conditions, reducing cholangiocyte injury, stimulation of impaired biliary output, and inhibition of hepatocyte apoptosis. Despite its clinical effectiveness, UDCA is poorly soluble in the gastro-duo deno-jejunal contents, and pharmacological doses of UDCA are not readily soluble in the stomach and intestine, resulting in incomplete absorption. Indeed, the solubility of 20 mg/L greatly limits the bioavailability of UDCA. Since the bioavailability of drug products plays a critical role in the design of oral administration dosages, we investigated the enzymatic esterification of UDCA as a strategy of hydrophilization. Therefore, we decided to enzymatically synthesize a glyceric ester of UDCA bile acid to produce a more water-soluble molecule. The esterification reactions between UDCA and glycerol were performed with an immobilized lipase B fromCandida antarctica (Novozym 435) in solvent-free and solvent-assisted systems. The characterization of the UDCA-monoglyceride, enzy matically synthesized, has been performed by 1H-NMR, 13C-NMR, COSY, HSQC, HMBC, IR, and MS spectroscopy

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Biography

Stefania Costa was born in Ferrara, Italy, in 1984. She received his master's degree in medical-pharmaceutical biotechnology in 2009 from University of Ferrara and obtained his PhD degree in Pharmaceutical Sciences in 2014. University. Since 2010 she has been a research fellow at the Department of Life Sciences and Biotechnology of the University of Ferrara. To date, she is a lecturer in the Chemistry of Fermentation of the Degree in Biotechnology at the University of Ferrara. He is co-author of 2 publications and 1 patents. His research activity is focused on the field of fermentation and biotransformations using whole cells or enzymes.