## Nonconventional Method for Separation of Rosmarinic Acid: Synergic Extraction

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Abstract: Rosmarinic acid, an ester of caffeic acid and 3-(3,4-dihydroxyphenyl) lactic acid, is considered a valuable compound for the pharmaceutical and cosmetic industries due to its antimicrobial, antioxidant, antiviral, anti-allergic, and antiinflammatory effects. It can be obtained by extraction from vegetable or animal materials, by chemical synthesis and biosynthesis. Indifferent of the method used for rosmarinic acid production, the separation and purification process implies high amount of raw materials and laborious stages leading to high cost for and limitations of the separation technology. This study focused on separation of rosmarinic acid by synergic reactive extraction with a mixture of two extractants, one acidic (acid di-(2ethylhexyl) phosphoric acid, D2EHPA) and one with basic character (Amberlite LA-2). The studies were performed in experimental equipment consisting of an extraction column where the phases' mixing was made by mean of a perforated disk with 45 mm diameter and 20% free section, maintained at the initial contact interface between the aqueous and organic phases. The vibrations had a frequency of 50 s<sup>-1</sup> and 5 mm amplitude. The extraction was carried out in two solvents with different dielectric constants (n-heptane and dichloromethane) in which the extractants mixture of varying concentration was dissolved. The pH-value of initial aqueous solution was varied between 1 and 7. The efficiency of the studied extraction systems was quantified by distribution and synergic coefficients. For calculating these parameters, the rosmarinic acid concentration in the initial aqueous solution and in the raffinate have been measured by HPLC. The influences of extractants concentrations and solvent polarity on the efficiency of rosmarinic acid separation by synergic extraction with a mixture of Amberlite LA-2 and D2EHPA have been analyzed. In the reactive extraction system with a constant concentration of Amberlite LA-2 in the organic phase, the increase of D2EHPA concentration leads to decrease of the synergic coefficient. This is because the increase of D2EHPA concentration prevents the formation of amine adducts and, consequently, affects the hydrophobicity of the interfacial complex with rosmarinic acid. For these reasons, the diminution of synergic coefficient is more important for dichloromethane. By maintaining a constant value of D2EHPA concentration and increasing the concentration of Amberlite LA-2, the synergic coefficient could become higher than 1, its highest values being reached for n-heptane. Depending on the solvent polarity and D2EHPA amount in the solvent phase, the synergic effect is observed for Amberlite LA-2 concentrations over 20 g/l dissolved in n-heptane. Thus, by increasing the concentration of D2EHPA from 5 to 40 g/l, the minimum concentration value of Amberlite LA-2 corresponding to synergism increases from 20 to 40 g/l for the solvent with lower polarity, namely, n-heptane, while there is no synergic effect recorded for dichloromethane. By analysing the influences of the main factors (organic phase polarity, extractant concentration in the mixture) on the efficiency of synergic extraction of rosmarinic acid, the most important synergic effect was found to correspond to the extractants mixture containing 5 g/l D2EHPA and 40 g/l Amberlite LA-2 dissolved in nheptane.

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