

**Dicarboxylic Acids as Acyl Donors for the Biocatalytic Synthesis of
Lipophilic Derivatives of Natural Antioxidants:
Anti-tumor and Anti-angiogenic potential of the Novel Analogues
Studied on K562 Human Leukemia Cells.**

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Diets rich in naturally occurring antioxidants have been shown to be associated with the reduced incidence of various human cancers. Several flavonoids including silybin have been reported to possess an angiopreventive effect that could be helpful in controlling the development of cancer at earlier stages. Due to their biological activity, the use of flavonoids in pharmaceutical and food preparation seems very attractive. However, the hydrophilic nature of flavonoids limits their stability and solubility in lipidic matrices and lipophilic media.

In the present work, the enzymatic synthesis of lipophilic derivatives of silybin and rutin, using non toxic organic solvents as media, has been described. The effect of various reaction parameters, such as the nature of organic solvents, as well as the nature and the concentration of substrates, which affect the reaction rate, the conversion yield and the regioselectivity of the biocatalytic process were investigated. Furthermore, in order to study the potential anti-tumor and anti-angiogenic properties of the novel silybin analogues we examined their effects on K562 human leukemia cells relative to cell proliferation, induction of apoptotic cell death and release of an essential regulator of the angiogenic process, Vascular Endothelial Growth Factor.