PHARMACOCHEMICAL STUDY OF CINNAMIC HYBRIDS WITH BIOLOGICAL INTEREST

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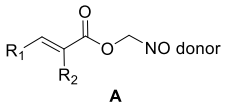
Inflammation is the body's defense mechanism in cases of histological lesions and is divided into acute and chronic. Cyclooxygenases (COXs) and lipoxygenases (LOXs) are important enzymes involved in the onset of the inflammation in correlation to the important role of reactive oxygen species. Chronic inflammation, which results from the constant activation of these enzymes, can lead to a variety of multifactorial diseases, including cardiovascular disease, cancer, diabetes, and Alzheimer's disease. Nitric oxide (NO) produced in the body, plays an important role in diseases with multifactorial etiology, as it is involved in the inflammatory process. At low concentrations, it regulates the oxidation of COX's iron, while at higher concentrations it forms stable nitrosylated complexes, which inhibit its function. In addition, in the presence of NO peroxides, LOX appears to be inhibited too (Pontiki, E., Hadjipavlou-Litina, D., Litinas, K., Nicolotti, O., Carotti, A., 2011).

Due to the multifactorial nature of these diseases, multiple drugs combinations are usually used for treatment. During the last decade molecular hybridization technique seems to be advantageous as a dynamic alternative solution to face therapeutically complex diseases. The hybridization approach is supported by the presence of two or more bioactive compounds which are covalently or via a linker combined to a molecule.

Cinnamic acid and its derivatives have been studied for a variety of biological activities including anti-inflammatory activity. At the same time, many hybrid compounds of cinnamic derivatives with other bioactive molecules have been synthesized and evaluated, including hybrid compounds carrying a NO donor group (Tsopka, I. C., & Hadjipavlou-Litina, D., 2021).

Prompted by these data, the current study is focused on the molecular design, druglikeness, synthesis and biological evaluation of new cinnamic acid-NO donor hybrid molecules with the general structure A, as COX, LOX inhibitors and anti-inflammatory agents. The design of the new compounds is based on previous QSAR studies and models.



A

The new cinnamic hybrids have been synthesized through esterification of the cinnamic acids and identified with spectrometric methods. The *in vitro* results underline the role of lipophilicity of the molecules and the presence of furoxan ring was found to be crucial for better activity of the new hybrids as LOX inhibitors.

References

Pontiki, E., Hadjipavlou-Litina, D., Litinas, K., Nicolotti, O., & Carotti, A. (2011). *Eur.J.Med.Chem. 46*(1), 191-200.

Tsopka, I. C., Hadjipavlou-Litina, D. (2021).*IJMS*, *22*(18), 9788.