Synthesis of novel azole derivatives of cinnamic acid with possible antioxidant and lipoxygenase inhibitory activity

Konstantinos Theodoridis and Eleni Pontiki*

*** Department of Pharmaceutical Chemistry, School of Pharmacy, Aristotle**
University of Thessaloniki, Thessaloniki 546 36, Greece ,

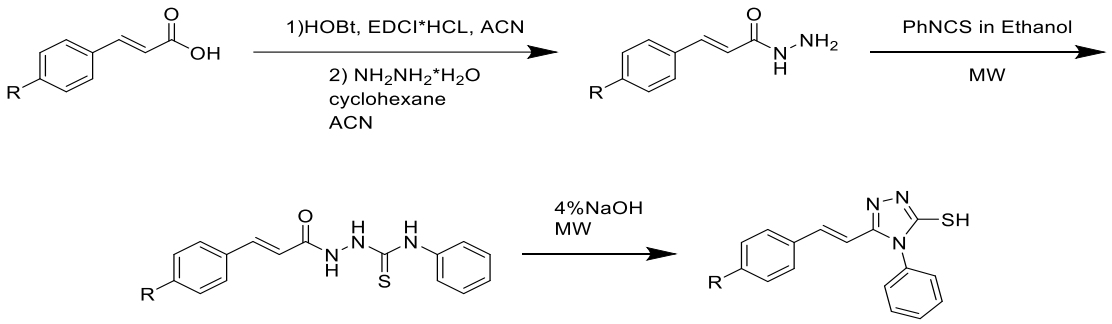
Research studies have reported that cinnamic acid derivatives exhibit a wide variety of therapeutic effects such as anti-inflammatory, anti-microbial and anti-cancer.[1] Moreover 1,2,4-triazol derivatives play a vital role in the same biological fields and additionally seem to act as anticonvulsants and pain relievers. Reactive oxygen species (ROS) are commonly produced from oxidative stress, that is a state of organism that responds to environmental stimulation and takes part in oxidative and antioxidative systems. Also, ROS not only take part in carcinogenesis from DNA damage but also in lipid peroxidation of polyunsaturated fatty acids. Moreover, this procedure is catalyzed by lipoxygenases (LOXs) in order to form hydroperoxides from linoleic acid and arachidonic acid (AA). LOXs generate ROS as by-products during the oxidation of AA.[2] It is well known that chimeric molecules combining two or more pharmacophores are able to interact with multiple targets achieving their therapeutic effects.

Based on the above studies a series of novel azole derivatives of cinnamic acid have been designed and synthesized[2] and studied for their antioxidant properties and soybean lipoxygenase inhibition.

The general synthetic procedure of the novel derivatives is depicted in Scheme 1.

It comprises of three synthetic steps starting from the appropriate substituted cinnamic acid reacting with hydrazine monohydrate in acetonitrile with cyclohexane resulting in the formation of hydrazides. Consequently, the hydrazide reacted with phenylisothiocyanate under microwave irradiation. Then cyclization proceeds to the 1,2,4-triazol after the addition of NaOH solution and microwave irradiation.

All the synthesized derivatives have been studied for their ability: a) to interact with the free radical DPPH, b) to inhibit lipid peroxidation through AAPH and c) to inhibit soybean lipoxygenase.



Scheme 1. General synthetic procedure

1. O. H. Oladimeji, P. O. Owere and P. C. Anthony (2021), DOI: 10.26717/BJSTR.2021.39.006260

2. M. Amir, K. Saifullah & W. Akhter (2011) J Enz Inh, 26:1, 141148, DOI:10.3109/14756366.2010.481622