DESIGN AND SYNTHESIS OF PYRAZOLE DERIVATIVES AS POTENTIAL LIPOXYGENASE INHIBITORS WITH ANTIOXIDANT ACTIVITY

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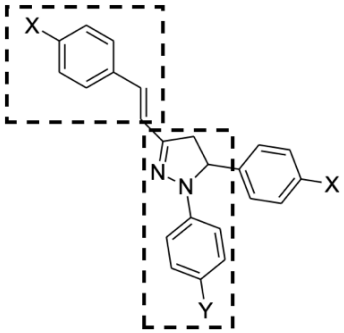
Multifactorial disorders such as cancer, cardiovascular diseases, or diabetes do not have a clear pattern of inheritance and are particularly difficult to determine. For these reasons, science turned their attention towards alternative treatments. The most effective method was found to be the design of hybrid molecules, integrating different pharmacophores together to generate new bioactive molecules. The novel hybrids present improving activities and polypharmacological effects in multiple targets [1].

Inflammation is usually defined as a defence reaction of the immune system aiming to protect the internal environment from various factors, physical, chemical, or even biological. Extensive inflammation leads to the formation of free radicals attacking and damaging organism cells. Disturbance in the balance between the production of reactive oxygen species (free radicals) and antioxidant defences leads to “oxidative stress” [2].

The most important enzymic systems associated with inflammation and by extension with causal diseases such as cancer or chronic diseases, are the cyclooxygenase and the lipoxygenase. Lipoxygenase is responsible for catalysing the peroxidation of arachidonic acid resulting in the formation of leukotrienes. Arachidonic acid metabolites act both as mediators of inflammation and hold a key role in the emergence and progression of frequent diseases such as cancer, obesity, diabetes and cardiovascular disease.

This work aimed at the design, synthesis and physicochemical study of pyrazole derivatives with known anti-inflammatory and antioxidant activities. The synthesis of the novel derivatives was optimized with microwave irradiation using the appropriate substituted dibenzacetones and phenylhydrazines.



The novel derivatives are studied in terms of their physicochemical properties, their antioxidant activities and soybean lipoxygenase inhibition. Many of the pyrazole derivatives showed potent antioxidant properties and significant inhibition of soybean lipoxygenase as a result of their physicochemical features.

References

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