

Bioisosterism: Evaluation of aromatic alkynes as non-classic bioisosters of aromatic amides

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Bioisosterism is a strategy of Medicinal Chemistry for the rational design of new drugs, applied to a lead compound as a special process of molecular modification [1].

The coining of the term bioisosterism goes back to the pioneer work of Friedman and Thornber during the early 50s. Friedman [2], recognizing the usefulness of the concept isosterism to design bioactive molecules, defined bioisosters as compounds which fit the definitions of isosteres and which exercise their biological activity of bioreceptor, whether through agonist or antagonist actions.

Among the most recent numerous examples used in the strategy of bioisosterism for designing new pharmaco-therapeutically attractive substances [3-5], there is a significant predominance on non-classic bioisosterism, distributed in distinct therapeutic categories. Several findings are indicating that aromatic alkynes may be considered as bioisosters for aromatic amides. However, considering the huge number of drugs situated in the worldwide market, it is striking that only very few substances involving the oral contraceptive ethynylestradiol and the CNS active MAO inhibitor Selegiline contain a carbon-carbon triple bond.

We would therefore explore potential of aromatic alkyne to replace aromatic amide in several known drugs or drug candidates. We are also interested in evaluating physico-chemical and pharmacological (ADME) profile of aromatic alkyne bioisosters of these novel compounds in order to benchmark true value of such a replacement.

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