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ACETILPYRAZOLINE OBTAINED FROM (2E)-3-(4-BROMOPHENYL)-1-(2-HYDROXPHENYL) PROP-2-EN-1-ONE

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INTRODUCTION

Medicinal chemistry has contributed to the development of new drugs through the valuable information of the modern technological tools and disseminated information obtained from studies with miscellaneous chemical classes. Among the classes of interest in this work, there are the chalcones and pyrazolines.

MATERIAL AND METHODS

Initially, the chalcone was synthesized by an adaptation of the general method of the Claisen-Schmidt condensation. In this method, an equimolar mixture of 4-bromobenzaldehyde and 2-hydroxyacetophenone was dissolved in ethanol, in the presence of 10 % sodium hydroxide. The solution was kept under mechanical stirring for until the point at which it was no longer possible to stir the mixture (due to product precipitation). To realize a molecular modification, the chalcone obtained was kept a reflux or microwave method with hydrazine hydrate and acetic acid and the product formation was analyzed by thin-layer chromatography. All compounds obtained were characterized by proton and carbon nuclear magnetic resonance. Absorption and permeation were predicted according to the Lipinski Rule parameters, as well as intestinal absorption and blood-brain barrier permeation. Virtual screening was also performed to identify potential biological targets and toxicological prediction in silico.

RESULTS

The proposed compound (1-[5-(4-bromophenyl)-3-(2-hydroxyphenyl)-4,5-diidro-1H-pyrazol-1-il]ethanone) was obtained from the conventional and microwave methods however, both showed no significant differences in the conditions used. The compounds obtained were satisfactorily characterized by spectroscopic techniques (1H and 13C NMR). The acetylpyrazoline derivative showed good intestinal absorption, strong binding to plasma protein with lower blood-brain barrier permeation compared to the prototype. For toxicity, both have mutagenic, carcinogenic in rats and the medium potential risk to the locks of the hERG channel type, only the carcinogenic in mice was negative differently from the prototype, however, the molecular changes were not enough to change all the toxicological profile of the prototype.

CONCLUSIONS

The derivative has an advantage over the prototype when it comes to toxicity and also because it has a positive Druglikeness result. The derivative synthesized show that it is a good option for possible drugs to be administered orally.

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