SYNTHESIS AND EVALUATION OF THE LARVICIDIC ACTIVITY OF QUINOLINE-4-CARBOXYLIC ACIDS

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ABSTRACT

Dengue, Zika, and Chikungunya are arboviruses transmitted by the Aedes aegypti mosquito, causing symptoms such as fever and headache and, in some cases, can be fatal. These diseases represent a public health problem, both in Brazil and in other countries. The fight against these diseases is based on controlling the mosquito population since vaccines are not yet fully effective. Some biologically active compounds, which have been reported in the literature as new insecticides and repellents, contain fluorine atoms in their structure. Fluorinated compounds have significantly boosted the development of the pharmaceutical industry, arousing great interest from these companies. Their chemical, physical, electronic, and biological properties, in addition to their high reactivity, have made the incorporation of fluorine atoms into molecules an essential step in the creation of new drugs. One class of compounds that have a wide range of biological activities is quinoline-4-carboxylic acids (Q4CAs). These can be obtained through the Pfitzinger reaction involving isatin and an α-methylene carbonyl compound. This work aimed to synthesize, characterize, and evaluate the larvicidal activity of 11 quinoline-4-carboxylic acids, 4 of which are new, derived from 5-fluoro-isatin and acetophenones substituted with electron-donating and withdrawing groups. The Q4CAs were obtained through the proposed methodology, using a basic potassium hydroxide solution (KOH 30% m/v) in a reflux system, at a temperature of 100°C in an oil bath, in a period that varied from 4 to 24 hours, with yields that were in the range of 70%-98%. All synthesized compounds had structural confirmation by physical characterization methods such as ^{13}C and ^{1}H nuclear magnetic resonance, infrared spectroscopy, and high-resolution mass spectrometry. The larvicidal activities of Q4CAs against Aedes aegypti mosquito larvae in the L2-L3 stage were investigated, and obtained from the Moscamed Brasil Breeding Unit, located in Juazeiro-BA, Brazil. Solutions in different concentrations of the investigated compounds were used and the IC_{50} was obtained after 72h of exposure. Thus, the most expressive values for which the average mortality of the negative control did not exceed 20% correspond to compounds 6c, with an IC_{50} value of 61.66 ppm, 9d with an IC_{50} of 34.67 ppm, and 11e presenting an IC_{50} of 53.70 ppm, which have the substituents *p*-F, *p*-OH and dioxymethylene, respectively. Analyzing a possible structure-activity relationship, it was observed that substituents in the para position cause a more pronounced effect than in other positions. Furthermore, there is a preference for less bulky substituents, as bulky substituents or those with a longer chain are unfavorable for larvicidal activity.

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