

Evaluation of Cytotoxic Potential of synthetic sesquiterpene lactones in leukemia cell lines

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Introdução

According to World Health Organization (WHO), cancer is a disease that affects more than seven million people worldwide each year. As a result, new anticancer drugs have been developed. However, cytotoxic agents have very little or no specificity which leads to systemic toxicity, causing undesirable side effects. Therefore, the development of innovative and efficacious tumor-specific drugs delivery protocols or systems is urgently needed.^{1,2}

Sesquiterpene lactones have been identified to the active constituents of medicinal plants several used in traditional medicine. These represent a wide spectrum of biological activities as anti-inflammatory, phytotoxic, antimicrobial, antiprotozoal, and, cytotoxicity against several tumor cell lines.³ It was recently found that a sesquiterpene lactones, can selectively kill leukemia cells without affecting primitive normal stem and hematopoietic progenitor cells.⁴

The objective of this study is to evaluate the cytotoxicity of synthetic sesquiterpene lactones in leukemic cell lines (K562 and Jurkat).

Resultados e Discussão

The cytotoxic analyses were performing by MTT (3 - (4,5-dimethyl-2-thiazolyl) -2,5-diphenyl-2H-tetrazolium bromide). The synthetic compounds tested, derived from α -Santonin, were: isofotosantonin acid (1), 10 α -acetoxy-3-oxo-1,7 α H,6,11 β H-guai-4-en-6,12-olide (2), 10 α -hydroxy-3-oxo-1,7 α H,6,11 β H-guai-4-en-6,12-olide (3) (Figure 1).

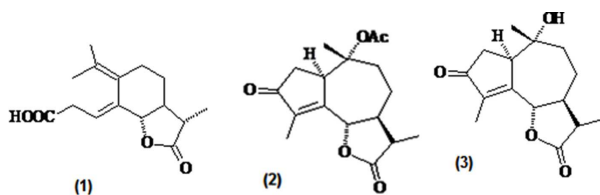


Figure 1. Sesquiterpene lactones derived from α -santonine.

The results show that the more effective compound against K562 cells was 2 with IC₅₀ of 393.4 μ M. The resistance of this cell line to the protocols of cancer chemotherapy can be one of the reasons for the high value of IC₅₀. Against Jurkat cells, the compound 3 were more efficient with IC₅₀ of 221.1 μ M. The precise mechanism of action of sesquiterpene lactones as inhibitors of cell growth is still unclear. It is believed that the bigger activity of compounds 2 and 3 is due to the presence of group α -methylidene- γ -butyrolactone. Therefore, the presence of such a structural motif has significant role in the mechanism by which these compounds exert their biological activities.

Conclusões

Thus, sesquiterpene lactones may present a promising class of anticancer drugs and different lactones derived from α -Santonin can be synthesized to increase the cytotoxic activity.

Agradecimentos

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