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Abstract

Enhancement of the antiproliferative effect of the abietane diterpenoid ferruginol by amination of position 18†

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Abstract: The family of abietane-type diterpenoids has long attracted natural product researchers, biochemists, organic and medicinal chemists with endless discoveries in terms of isolations, characterization, pharmacology, biosynthesis, chemical synthesis and medicinal chemistry. In our group, we have developed over the last decade a number of studies towards the semisynthesis of a variety of aromatic abietanes as well as biological screenings. The diterpene ferruginol is a very simple phenolic abietane which has demonstrated a plethora of promising biological and pharmacological properties. Some years ago, we developed a multigram semisynthetic procedure to obtain ferruginol itself from the commercially available (+)-dehydroabietylamine, also called leelamine. Over the years, we have investigated ferruginol and related analogues synthesized by us, with the aim of extending the pharmacological knowledge of this unique molecule and characteristic carbon framework and unveil their potential application. In this communication, we disclose how a simple modification in the carbon skeleton of ferruginol such as the introduction of an amino group can lead to a more potent analogue, 18-aminoferruginol or 12-hydroxydehydroabietylamine, in human breast cancer and melanoma cell lines and also changes in the mechanism of action as compared to the parent molecule. This outcome may set a platform for the development of novel anticancer agents based on natural products.

Keywords: Diterpene; abietanes; ferruginol; dehydroabietylamine; melanoma; breast cancer.

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