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Design and synthesis of potential ribonucleotide reductase enzyme (RNR) inhibitors as antileukemic and/or antiviral 2'-deoxymethylene nucleosides

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In order to improve the antitumor and/or antiviral activities of existing nucleoside analogs, eight new compounds (9a, b, 14a, b, 15a, b and 16a, b) were designed and synthesized. Halogen atom were incorporated at the 2-position of the purine base to render the amino group at the 6-position less susceptible to metabolism by adenosine deaminase. A methylene group was introduced at the 2'-position following the lead of nucleoside antibiotics angustmycin A and neplanocin A. The two key intermediates 9a and 9b were prepared from guanosine after protection of the 3' and 5' hydroxyl groups and oxidation of the 2' hydroxyl group to the corresponding carbonyl group using Swern method. The conversion of the carbonyl group to the methylene function was carried out by applying Wittig reaction conditions. The final compounds 14 a, b, 15 a, b, 16a, b was prepared by means of non-aqueous diazotization of 9a and 9b. The prepared compounds were subjected to *in vitro* antileukemic and antiviral activity upon a new L1210 cell line that is doubly resistant to both hydroxyurea and deoxyadenosine which was grown and characterized. The new compounds showed potent antileukemic activity.

Biography

Khairia M Youssef is a Professor of Organic Chemistry since 1999. She has completed her Bachelor of Pharmaceutical Sciences, Master degree and PhD in Organic Chemistry from Faculty of Pharmacy, Cairo University. In 1992, she was on a Peace Fellowship for Post Doctoral Research at the University of Southern California, USA under the supervision of Dr. Eric J. Lien. She is interested in drug design, synthesis and evaluation of certain pharmacologically active compounds. She has published 62 papers in national and international journals and supervised many researchers and teaching assistants.

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