This article was downloaded by:

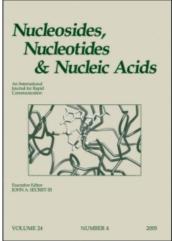
On: 27 January 2011

Access details: Access Details: Free Access

Publisher Taylor & Francis

Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-

41 Mortimer Street, London W1T 3JH, UK



Nucleosides, Nucleotides and Nucleic Acids

Publication details, including instructions for authors and subscription information: http://www.informaworld.com/smpp/title~content=t713597286

Anticancer Activities of 7-, and 9-Substituted 3-Deazaguanine Derivatives

Tasneem A. Khwaja^a; Sumitra Roy-burman^a; Stephanie Pentecost^a

^a Dept. of Pathology and USC Cancer Center, Los Angeles, California, U.S.A.

To cite this Article Khwaja, Tasneem A., Roy-burman, Sumitra and Pentecost, Stephanie(1985) 'Anticancer Activities of 7-, and 9-Substituted 3-Deazaguanine Derivatives', Nucleosides, Nucleotides and Nucleic Acids, 4: 1, 253

To link to this Article: DOI: 10.1080/07328318508077876 URL: http://dx.doi.org/10.1080/07328318508077876

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: http://www.informaworld.com/terms-and-conditions-of-access.pdf

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

ANTICANCER ACTIVITIES OF 7-, AND 9-SUBSTITUTED 3-DEAZAGUANINE DERIVATIVES

Tasneem A. Khwaja*, Sumitra Roy-Burman and Stephanie Pentecost
Dept. of Pathology and USC Cancer Center,
1303 N. Mission Road,
Los Angeles, California 90033, U.S.A.

Summary: Interesting differences in anticancer activities of 7- and 9-substituted derivatives of 3-deazaguanine are described.

3-Deazaguanine (DG) is a potent inhibitor of a variety of experimental mammary tumors and is about to undergo clinical trial in USA. The antitumor activity of DG has been ascribed to its incorporation into tumor cell DNA as its 2'-deoxyriboside. Syntheses of 7- and 9-substituted ribosides (7-DGR and 9-DGR, respectively) and 7- and 9-substituted 2'-deoxyribosides (7-DGR and 9-DGdR, respectively) of DG has been reported. 3,4 DG, 9-DGR and 9-DGdR, at concentrations of 7.5, 6.0 and 8.0 μM caused a 50% inhibition in the growth of leukemia L1210 cells in culture. DG and 9-DGdR also were active against C3H/16C mammary adenocarcinoma system in B6C3F $_1$ female mice; 9-DGR was toxic and lacked therapeutic activity in this system. 7-DGR and 7-DGdR at concentrations of 2000 and 900 μM , respectively, caused 50% inhibition of the growth of L1210 cells in culture; both of these derivatives were inactive in C3H/16C tumor system, in vivo. The apparent lack of antitumor activity of 7-DGR and 7-DGdR was ascribed to the inability of the mammalian nucleoside phosphorylase to degrade these derivatives to DG.

Recently we have found that the 7-tetrahydropyranyl-3-deazaguanine (7-THPDG) is active (ED $_{50}$, 45 μ M) in leukemia L1210 system, in vitro, and in C3H/16 tumor system, in vivo. The 9-tetrahydropyranyl-3-deazaguanine (9-THPDG) was inactive, in vitro (ED $_{50}$, 3000 μ M), as well as, in vivo. The studies on mechanism of action of these analogs are in progress.

REFERENCES

- 1. Khwaja, T.A., Cancer Treat. Rep. 1982, <u>66</u>, 1853-1858.
- Khwaja, T.A., Momparler, L., Varven, J.C. and Mian, A.M., Proc. Am. Assoc. Cancer Res. 1979, 20, 152.
- 3. Cook, P.D., Allen, L.B., Streeter, G., Huffman, J.H., Sidwell, R.W. and Robins, R.K., J. Med. Chem., 1978, 21, 1213-1218.
- 4. Mian, A.M., Khwaja, T.A., J. Med. Chem., 1983, 26, 286-291.