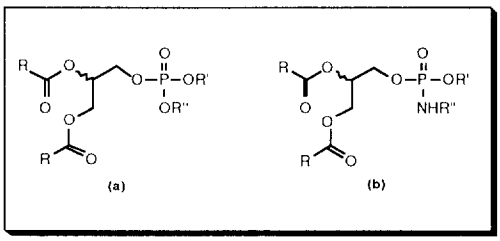
43

The Synthesis of Novel Phospholipids with Potential Antineoplastic and Antiviral Activity.

MS. Wilson, C. McGuigan, AJ. Hay[1], N. Mahmood[1], J. Balzarini[2], E. De Clercq[2], A. Postle[3] and PA. Riley[4]. *Welsh School of Pharmacy, UWCC, Redwood Building, King Edward VII Avenue, Cardiff, CF13XF, Wales, UK.* [1] *U.K.MRC Collaborative Centre, UK/NIMR, London, UK.* [2] *Rega Institute, Leuven, Belgium.* [3] *Child Health, Southampton General Hospital, Southampton, UK.* [4] *University College London Medical School, London, UK.*

Phosphotriesters are often used as intermediates in the synthesis of phospholipid diesters. The use of phospholipid triesters themselves as bioactive moieties has been little studied. The 'masked' phosphodiester approach used successfully in our group for the synthesis of nucleotides with excellent anti-HIV activity has been applied to phospholipids.



Thus, phosphotriesters of diacyl glycerols **(a)** have been prepared and tested for their antineoplastic and antiviral activity. These triesters contain one labile group and thus act as 'masked' phosphodiesters. A similar series of diacyl glyceryl phosphoramidates **(b)** has also been synthesised. Novel, structurally interesting phospholipid dimers have also been prepared and their biological activity is currently being evaluated.

44

ON THE BIOISOSTERIC POTENTIAL OF THE PYRIDAZINE CORE IN THE SYSTEMATIC STRUCTURAL MODIFICATION OF ANTIVIRAL AGENTS

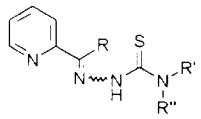
G. HEINISCH, J. EASMON, and B. MATUSZCZAK

Institute of Pharmaceutical Chemistry, University of Innsbruck, Innrain 52a, A-6020 Innsbruck, Austria

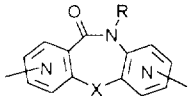
Whereas the pyridine system represents an important substructure in a variety of antiviral agents, the effect of replacing this azine system by pyridazine (1,2-diazine) so far remained largely unexplored. This *N*-heteroaromatic is unique considering its weak basicity together with its extremely high dipole moment. Due to this physicochemical characteristics one may expect altered pharmacokinetic behaviour together with improved solubility when incorporating the pyridazine nucleus into bioactive molecules. Here we want to report on the chemistry and on the results of preliminary investigations of antiviral properties of 1,2-diazine congeners of ribonucleotide reductase inhibitors of type **A** and reverse transcriptase inhibitors of type **B**.

pyridazine

pK_a: 2.33
μ: 3.95 D



A



X= O, NR'

B

The authors are very grateful to Univ.-Doz. Dr. W. Holzer, V. Hartmann, and R. Planer for their contribution to the chemical part and to Prof. Dr. M. Dierich, Prof. Dr. B. Rosenwirth, Dr. H. Stoiber, and I. Schöpf for antiviral screening.