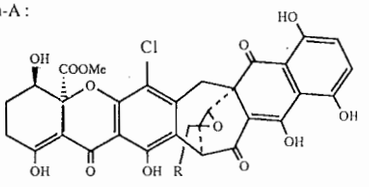
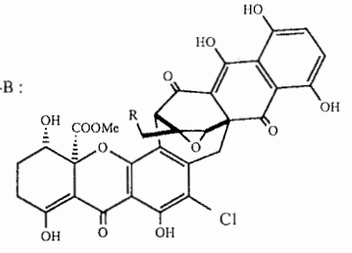
chlorinated Xanthone/Anthraquinone skeleton. Most of these toxins belong to the two families of Beticolin A and B (figure). Both types of toxins differ mainly by the way the two anthraquinone and xanthone moieties are attached together. Beticolin 1 (R=H) and Beticolin 3 (R=OH), part of the beticolin A familly, were crystallized from $CHCl_3$/methanol mixture as $CHCl_3$ solvates (the structures are isomorphous) while Beticolin 2 (B type, R=H) and Beticolin 4 (B type, R=OH) were identified by NMR (Millat et al., 1993) to share the cebetin A structure (Jalal et al, 1992).
The structure of Beticolin 1 was easily solved by direct methods. In the case of Beticolin 3, the crystals so far obtained were too small (max. size : 0.15mm) to produce enough data for direct methods. The structure was solved by Molecular Replacement technique.

	Beticolin 1	Beticolin 3
Xtal size (mm) :	0.25x0.25x0.5	0.05x0.05x0.15
nb. of Fobs observed :	2480	1027
R factor (%) :	6.0	9.4

Beticolin-A :



Beticolin-B :



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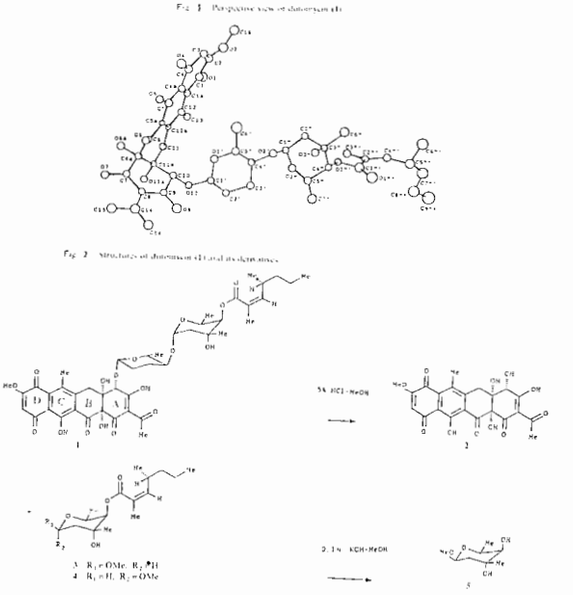
-M.A.F. Jalal, M.B. Bilayet Hossain, D.J. Robeson, D. van der Helm (1992) J. Amer. Chem. Soc, 114, 5967-5971.
-M.L. Millat, J.P. Blein, J. Einhorn, J.C. Tabet, P.H. Ducrot, J.Y. Lallemand (1993) Tetrahedron Lett., submitted.

PS-04.01.25 THE STRUCTURE OF DUTOMYCIN. Ming-Qin Chen* and Jie Liu, Research Center of analysis & Measurement, Fudan University, Shanghai, P.R.China, 200433. Li-Jiang Xuan, Sao-Hua Xu, Hai-Lin Zhang and Ya-Ming Xu, Shanghai Institute of Materia Medica, Academia Sinica, P.R.China.

Dutomycin, a new antitumor antibiotic, has been found in the culture of Streptomyces SP1725 (Ya-Ming Xu and Ming-Qin Chen, et al.(1992) J.Antibiotics, 45, 715). The antibiotic was active against leukemia P388 and 100% inhibition was acheived as a concentration of 1 μg/ml. We report herewith its molecular structure and absolute configuration.
The empirical formula was established as $C_{44}H_{71}O_{17}\cdot 2C_1H_1$ on the basis of X-ray diffraction analysis and reconfirmed by elemental analysis, NMR spectral analysis and chemical degradation. The compound crystallized in the orthorhombic space group $P2_12_12_1$ with a=18.045(3), b=18.963(3), c=15.611(3)Å, V=5341.8Å^3, Z=4. Based on 5223 unique and 1612 observed reflections ($I>3\sigma(I)$), the structure was solved by direct methods and refined by full matrix least squares to the final R value of 0.0773. The molecule has a naphthacene carbon skeleton which is structurally related to the tetracycline and Anthracycline antibiotics, such as SF2575 (Masahiro Hatsu, et al.(1992) J. Antibiotics, 45, 325), and is unique by bearing glycosides and 2,4-dimethylheptene-2 acid moieties and containing many carbonyl groups which may relate to its biological activity as shown in Fig. 1.
In the aglycone moiety intramolecular hydrogen bonding between the exocyclic oxygen atoms on neither rings B and C nor C and D has been observed. However, the intramolecular hydrogen bonding $O_{13}\cdots H_{11}\cdots O_{12}$ may exist. This differs from that observed in most anthracycline antibiotics. The rings B, C, D are nearly coplanar (except C_{11} atom) because of the configuration among these atoms. It resembles the shape observed in all the anthracycline antibiotics.
The absolute configuration of Dutomycin was elucidated by subsequent chemical degradation (See Fig. 2). Methanolysis of 1 with methanolic hydrochloric acid gave the aglycone 2 and a pair of anomeric isomers 3 and 4. 3 was further methanolized in alkaline methanol and L-axenose methyl glycosides 5 was obtained (Arcamone,F. et al. (1973) J.Am.Chem.Soc., 95,2008). Since the configuration of 5 was known and consistent with that found in Dutomycin, the determined structure was thus implied absolute meaning due to the retention of the configuration during degradations. The chiral carbon atoms C_{11}, C_{12}, C_{13}, $C_{1'}$, $C_{3'}$, $C_{5'}$ and $C_{5''}$ thus have the configuration of (S,S,R,R,R,S,R).



PS-04.01.26 THE PROTOTYPES OF THE ENNIATIN B CHANNELS IN THE CRYSTAL STRUCTURE OF THIS MEMBRANE-ACTIVE ANTIBIOTIC

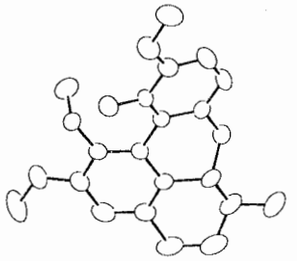
By G.N.Tishchenko*, N.E.Zhukhlistova, V.I.Andrianov, Institute of Crystallography, Russian Academy of Sciences, Moscow, Russia and P.Main, Department of Physics, University of York, York, England.

The crystal structure of the title compound has been determined by a single-crystal three-dimensional X-ray diffraction study. The compound crystallised from heptane in the space group $P2_1$ with four $C_{33}H_{57}N_3O_9$ molecules in one asymmetric unit. The unit cell dimensions are a=29.178(15), b=28.294(15), c=10.840(5)A, g=121.12(5)°. The structure was solved by direct

method using the program Multan 84 and refined by the block full-matrix "cascade" technique to a conventional R value of 0.0714 for 8468 independent reflections with F>4s(F). The enniatin B molecules resemble each other in common features, but differ in detail. Two molecules, designated C and D, are in slightly distorted conformations compared with those in the crystallohydrate and the Na, Ni complex (P-conformation). The conformations of the two other molecules, A and B, are quite different and have not been previously seen in either crystal form or in solution. All molecules are asymmetric with a pseudo-equatorial trans or gauche-orientation of the isopropyl radicals and with various arrangements of the carbonyl groups - up, down, inside or outside the ring. The N-methylamide and ester groups have nearly planar trans configurations. The bond lengths and angles in all the molecules do not differ very much from those found in other cyclic depsipeptides. The changes in the geometrical parameters of the enniatin B molecule between the present structure and the crystalline complexes with water and with Na, Ni ions are discussed. The conformational flexibility of the enniatin B molecule, important for its biological activity, is adduced. The molecules pack in two somewhat distorted hexagonal layers, separated by approximately c/2 and with alternate disposition of the polar molecular discs. This results in the appearance of non-crystallographic symmetry elements and in the possibility, after a shift of the two layers, of the formation of enniatin B channels running through the crystal.

PS-04.01.27 THE CRYSTAL AND MOLECULAR STRUCTURE OF N-METHYL-11-HYDROXY-1,2,10-TRIMETHOXY APORPHINE. By A. Hamid Othman* and Ikram M. Said, Department of Chemistry, Universiti Kebangsaan Malaysia, 43600 Bangi, Malaysia.

The above mentioned compound, an alkaloid was extracted from fresh leaves and bark of *Dehassia incrassata* and its crystal and molecular structure has been determined from three dimensional X-ray diffraction data for 2914 unique reflections taken on a CAD-4 diffractometer. Crystal data: $C_{20}H_{23}NO_4$, M_r= 340, orthorhombic $P2_12_12_1$, a = 7.549(2), b = 9.937(3), c = 23.376(6), V = 1753.5 A^3, $\lambda(MoK_\alpha)$ = 0.7107 A, D_c = 1.29 g cm^{-3}, μ = 0.964 cm^{-1}, Z = 4. The structure was solved by direct method and refined by full matrix least-squares procedures. All calculations were done using XTAL 3.0 program system (Hall, S.R. and Stewart, J.M., (1990) Eds. *Xtal3.0 Reference Manual*, Universities of Western Australia and Maryland) on a PC-AT microcomputer. The final R value was 0.064 and R_w = 0.071 for 1884 $I > 3\sigma(I)$ reflections. The final cycle of refinement gave R = 0.089, for all the 2914 reflections. The molecule contains two planar aromatic rings with inter-planar angle of 32.8°. The bonds and angles and intermolecular contact distances all have regular and acceptable values.



04.02 – Structure of Nucleic Acids and Nucleic Acid Complex

MS-04.02.01 Structural study of DNA/RNA and their complexes with antitumor drugs by x-ray crystallography
Andrew H.-J. Wang, Division of Biophysics and Department of Cell & Structural Biology, University of Illinois at Urbana-Champaign, Urbana, IL 61801, USA

Our lab has been investigating the problems associated with the structure and dynamics of DNA/RNA and their complexes with antitumor drugs. We are particularly interested in the unusual DNA structures, possibly preferred by certain sequences. In addition, we have studied the interactions of several types of antitumor drugs (including minor groove binder, intercalator, nucleoside analog) with DNA oligonucleotides. In this paper, I will focus on the structural analyses of several complexes of anthracycline drugs and DNA. For example, the interactions of cyanomorpholinyladriamycin, a promising potent adriamycin derivative, with DNA have been analyzed using the structure obtained from the high resolution (better than 2 Å) x-ray diffraction analysis. We also study the binding of other anthracyclines (e.g., aclacinomycin A and nogalamycin) with DNA oligonucleotides by NMR. The structures derived from the solid state and solution state are then compared carefully to understand the forces that are used to stabilize the structure and the mechanism of the drug binding. (Supported by NIH.)

MS-04.02.02 Structural Studies on DNA Minor-Groove Recognition by Drugs.
C.M. Nunn, N. Spink, D.G. Brown, K.J. Edwards and **S. Neidle**.
CRC Biomolecular Structure Unit, Institute of Cancer Research, 15 Cotswold Road, Sutton, Surrey SM2 5NG, UK.

Compounds that interact in the minor-groove of B-form DNA, primarily at AT-rich regions, have usage in both animal and veterinary medicine. For example, the bis-phenylamidinium compound pentamidine, is one of the agents of choice in the treatment of *pneumocystis carinii*, the opportunistic infection that affects about 70% of AIDS patients. We have been studying the interactions of this and other compounds with DNA sequences, in part to provide a rational basis for the discovery of new more effective agents, and in part to develop building blocks for the recognition of specific DNA sequences. A number of structure analyses of such drugs complexed with DNA sequences have now been performed by us. Several of these have been reported by us in the recent literature. These structures are currently forming the basis of molecular modelling studies which are resulting in the rational design of new analogues with defined sequence recognition properties.

The X-ray analyses of the drug-oligonucleotide complexes have revealed a number of new aspects of minor-groove recognition.

(i) Water molecules can play an active role in drug-DNA recognition, mediating between them. They can also help to maintain the drug in its bound state; a novel type of "spine of hydration" has recently been observed in one of these complexes.

(ii) The hydrophobic nature of the minor groove walls plays an important role in drug binding.

(iii) The effects of sequence on structure are important for defining the nature of a drug complex. In particular, the effects of changes in parameters such as roll and propeller twist can determine which particular base pairs are recognised by a drug.