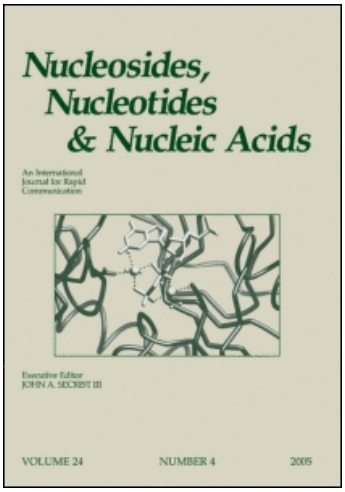

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Two-Dimensional ^{1}H-N.M.R. Assignment of Short Duplex Oligodeoxyribo-Nucleotides Which May Be Used as Potential Targets for Anticancer Drugs

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TWO-DIMENSIONAL ^{1}H-N.M.R. ASSIGNMENT OF SHORT DUPLEX OLIGODEOXYRIBONUCLEOTIDES WHICH MAY BE USED AS POTENTIAL TARGETS FOR ANTICANCER DRUGS

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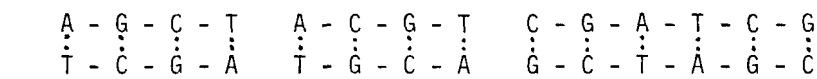
Summary High-field NMR, methods have been developed for assigning proton resonances of duplex oligodeoxyribonucleotides which may be applied to the analysis of their complexes with anticancer agents.

The self complementary oligomers which have been examined by ^{1}H-



nmr spectroscopy include the above. The duplex nature of the oligomers under the ^{1}H-NMR conditions was confirmed by labelling the 5'-end with ^{32}P-phosphate using T4 polynucleotide kinase and butt-end joining employing the absolute specificity of T4 ligase for double stranded DNA. Analysis was done by running the samples on polyacrylamide electrophoretic gels with visualisation of the spots by autoradiography.

Complete nmr assignment of the ^{1}H chemical shifts and coupling constants was achieved. The assignments were secured using NOE difference measurements, and two dimensional COSY and INADEQUATE experiments. Spectrum simulation confirmed the experimental values of chemical shifts and coupling constants. The techniques for the assignment outlined together with ^{31}P and 2-D heteronuclear shift correlation permit an approach to a systematic analysis of more complex single strand and duplex oligodeoxyribonucleotides.

The complexation of the oligomer $d(CG)_4$ with the anticancer drugs mitoxantrone and ametantrone was examined using the above techniques. The spectra provided evidence for intercalative binding complementing our previous studies with electron microscopy.

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