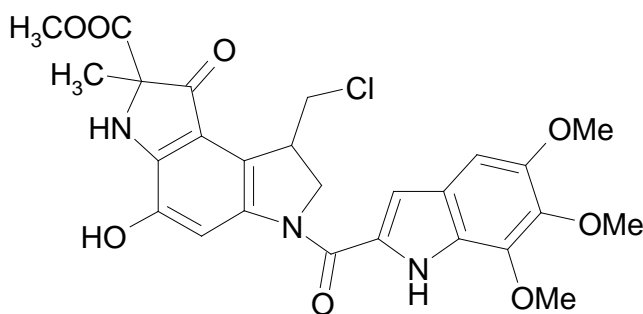


INVESTIGATION OF PYRINDAMYCIN A BINDING TO OLIGONUCLEOTIDES

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The binding of the antitumour antibiotic pyrindamycin A (PyA) to the oligonucleotides 5-CGGTAATTACC-3, 5-CGCGAATTCGCG-3, 5-GGTAATTACC-3, 5-CGTACG-3 and 5-GGTATAACC-3 was studied by HPLC, ESI-MS and nano ESI-MS/MS. The ligand, pyrindamycin A, is a minor groove binding agent which alkylates the N3 position of adenine. Data from other work has shown that the bound ligand spans 3.5 base pairs from the site of alkylation and as such it is seen that the sequence of three bases yields the preferred binding sites, i.e. 5-AAA-3 > 5-TTA-3 > 5-TAA-3 > 5-ATA-3. The formation of the intact PyA plus oligonucleotide adduct was only directly observed by ESI-MS for the oligonucleotide 5-GGTATAACC-3, suggesting that the identity of the fourth base may also effect the stability of the resulting adducts formed. The product resulting from depurination, i.e. the [(PyA-HCl)+Adenine] adduct, was observed for all oligonucleotides studied. The depurination was especially rapid for the oligonucleotides which did not contain a preferred binding site.



Pyrindamycin A