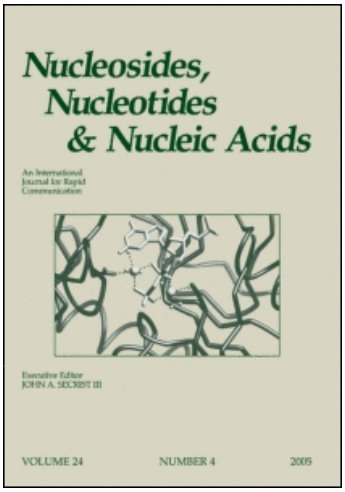

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Sequence Preference of Acridine Interaction with Single and Double Stranded Octadeoxyribonucleotides

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SEQUENCE PREFERENCE OF ACRIDINE INTERACTION WITH SINGLE AND DOUBLE STRANDED OCTADEOXYRIBONUCLEOTIDES

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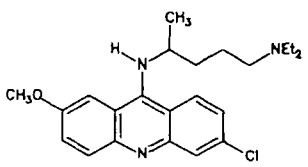
Abstract: Binding of three derivatives of 9-aminoacridine to octadeoxyribonucleotides and their duplexes was studied by visible spectroscopy. Scatchard plot analysis of the binding data permitted determination of apparent binding constants and number of binding sites.

Understanding the mode and specificity of acridine binding to nucleic acids is crucial for the design of anti-AIDS agents consisting of acridines tethered to anti-sense oligonucleotides. Several important questions need to be addressed including: (1) Do acridines bind to single strands?; (2) Is there sequence specificity in this binding?; and (3) Do acridines show sequence specificity in binding to duplexes?

Previous studies have investigated the binding of acridines to double stranded DNA[1,2] but little is known about the nature of acridine binding to single strands. Four non-self-complementary octadeoxyribonucleotides $^{5'}$TCACGTCA$^{3'}$ (SS_1), TGACGTGA (SS_2), TCACCTCA (SS_3), and TGAGGTGA (SS_4) were chemically synthesized by the modified phosphotriester method and purified by anion exchange HPLC[3]. These oligonucleotides were used to study the binding of three acridines, quinacrine 1, 9-[4-(*N*,*N*-diethylamino)-1-methylbutyl]aminoacridine 2 and AMSA 3 to each



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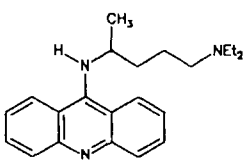

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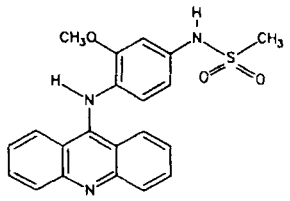

3

TARGET[a]	LIGAND[a] 1 K[b]	n[c]	2 K	n	3 K	n
TCACGTCA (SS_1)	6.2×10^6	0.12	ONLY WEAK BINDING			
TGACGTGA (SS_2)	9.8×10^5	0.29	ONLY WEAK BINDING			
TCACCTCA (SS_3)	NO SIGNIFICANT BINDING					
TGAGGTGA (SS_4)	8.9×10^5	0.30	3.7×10^5	0.28	4.9×10^6	0.30
TCACGTCA / AGTGCAGT (DU_I)	4.0×10^6	0.69	6.3×10^5	0.88	2.8×10^6	0.32
TCACCTCA / AGTGGAGT (DU_{II})	2.0×10^6	0.62	7.1×10^5	0.46	1.9×10^6	0.30

[a] Ligand concentration was 30-36 μM; final target concentrations ranged from 200 to 430 μM.
[b] Observed specific intrinsic binding constant, 1/M.
[c] Number of binding sites per mmole of target.

single strand and to duplexes formed between SS_1/SS_2 (DU_I) and SS_3/SS_4 (DU_{II}). The visible absorption spectrum (350-540 nm) of each acridine was measured in the presence of increasing concentrations of the oligonucleotide until further increases in nucleic acid concentration failed to alter the absorption of the acridine. The changes in absorbance of the acridine with respect to oligonucleotide concentration were analyzed using Scatchard plots in order to determine the number of binding processes (strong and weak), the binding constants, and number of binding sites. The results for strong (intercalative) acridine binding to single strands and duplexes are summarized in the following table.

All of the acridines bind to the G-rich single strand SS_4 and to the duplexes of the octanucleotides. Only quinacrine, 1, binds to the single strands of SS_1 and SS_2. Our results show that these acridines appear to have a slightly greater affinity for duplexes with a central CG·CG binding site (DU_I) *vs* a GG·CC binding site (DU_{II}).

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REFERENCES

1. Wilson,W.R., Baguley,B.C., Wakelin,L.P.G., and Waring,M.J.; (1981) Mol. Pharmacol., 20:404
2. Denny,W.A., Atwell,G.J., and Baguley,B.C.; (1983) J. Med. Chem., 26:1625-30
3. Lawson,T.G., Regnier,F.E., and Weith,H.L.; (1983) Anal. Bchm., 133:83-93