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Drug-Nucleic Acid Structures: Thirty Years On. Stephen Neidle, CRUK Biomolecular Structure Group, The School of Pharmacy, Univ. of London, London WC1N 1AX, UK.

The recognition of nucleic acids by small molecules is of importance in the action of an extraordinarily wide range of drugs active against bacterial and fungal infections, viruses, human cancers and a number of parasitic diseases.. These molecules have been mostly targeted against double-helical DNA, and their discrimination for particular sequences is based in large part on hydrogen-bonding to base-pair edges; the more subtle and detailed sequence-dependent differences in backbone geometry and base morphology are probably of lesser importance. All this has been revealed by single-crystal studies of drug-nucleic acid complexes and some of this information has been useful in drug design studies. More recently, it has become apparent that some DNA sequences, notably those within guanine-rich tracts, can form a wide diversity of higher-order quadruplex structures. These present altogether much more selective drug targets.

This lecture will review the progress of drug-DNA crystallography during this period, taking as exemplars a number of complexes with acridine-based drugs.