

P015 NMR studies of the binding of *peptidyl transferase* inhibitor antibiotics to conserved secondary structural motifs of 23S ribosomal RNAs

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We have successfully carried out the NMR structure determination of the RNA binding, *peptidyl transferase* inhibitor antibiotics Amicetin, Blasticidin S and Gougerotin in native solution state. The structures of the antibiotics exhibit a stable and well folded conformation, stabilised by intramolecular hydrogen bonds, and are distinctly different from the linear, extended conformation previously determined by X-ray crystallography. The interaction of a highly conserved 29mer RNA motif of *H. halobium* and *E. coli* 23S ribosomal RNAs with amicetin antibiotic has been investigated by NMR and molecular modelling. The NMR spectra of the 29mer RNA motifs revealed features characteristic of a stable, well folded A-RNA type tertiary conformation, including resolved resonances assigned to unpaired bases located in the middle of the motif strongly implicated in amicetin binding. Addition of amicetin to the RNA samples was accompanied by discrete changes to the spectra which can be qualitatively interpreted to the changes induced to the local conformation of the RNA motifs arising from the formation of a specific complex with amicetin. These results are also supported by the unconstrained molecular model of RNA-amicetin complex which highlights potential interactions between the two molecular components.