Alkaloid fagaronine and its interaction with non-canonical DNA structures

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Fagaronine is a rare member of the benzo[c]phenanthridine alkaloid family that can be extracted from the roots of the *Fagara zanthoxyloïdes* plant or produced synthetically. Several benzo[c]phenanthridine alkaloids have already been shown to have a stabilizing effect on non-canonical structures, in particular on g-quadruplexes, which are secondary DNA structures occurring on guanine-rich sequences, especially at the ends of telomeres. Increasing the stabilization of these structures can inhibit DNA replication or transcription, which can result in a significant reduction in cell division. For this reason, g-quadruplexes have become a popular target in the search for new anticancer drugs.

In this work, the interactions of fagaronine with parallel, antiparallel and hybrid g-quadruplexes were measured, some of which occur on human telomeres. We measured that fagaronine significantly stabilized all 3 types of g-quadruplexes, while parallel G4s were stabilized by up to 30 °C, which is our highest stabilizing effect measured so far.