Comparison between synthetic and natural G4-ligands and the effects of their binding to DNA

P-01.1-34

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Among local and non-canonical DNA structures are G-rich sequences that can form G-quadruplex (G4) sequences widespread among prokaryotic and eukaryotic kingdoms and are an increasingly used targets for regulatory proteins. There are evidence from more than three decades of research confirm their function in important cell processes such as transcription and replication. G-quadruplexes have become targets for anticancer drugs because of their ligands high specificity and affinity. We focused on the differences between binding of G4-ligands to DNA and their subsequent effect on cells. In the present study, the effects of G4-ligands on tumor (MCF-7) and non-tumor cell lines (HEK293ft) were studied in relation to binding to the DNA and connected mechanisms. Concentration and time-dependent studies were performed to study different effects of these compounds. Mentioned cell lines were used to study cell viability after exposure to G4-ligands. Morphological alterations were observed by fluorescent-based studies as confocal microscopy or ThT assay (Thioflavin T) supplemented by electromobility shift assay (EMSA). Apoptotic and anti-apoptotic genes were studied, and a strong effect derived from the binding of our tested molecules was observed. Our study propose that natural G4-ligands were used preferentially due to their significant lower toxicity to non-cancer cell lines, and with the same specificity as designed synthetic ligands, that even at low concentrations cause significant cell damage. In conclusion, treatment with natural G4-ligands leads to comparable effects to what we obtained with synthetic ligands and holds a great potential as future cardio-oncological therapeutics. Another possible approach could be to use G4-ligands to protect cell from subsequent chemotherapy.

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