Effects of glycosylation in the human α_1-Acid glycoprotein (AGP) conformation

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The AGP is an abundant human plasma glycoprotein that plays an important role in drug-binding. It has a large content of carbohydrates (ca 45%), N-linked, and its plasma concentration can rise up to fivefold during inflammatory events. Its glycan content is highly variable, depending on cellular events. The structure of the unglycosylated human AGP has been recently described, but no 3D information on its glycan content was reported until now. In this context, the current work intends to describe the complete glycosylated human AGP considering its different glycan compositions. The molecules were described employing the GROMACS package and GROMOS96 force field, added by Löwdin HF/6-31G** derived atomic charges for the carbohydrate residues. The AGP was described both in its unglycosylated and glycosylated forms, considering different glycan compositions and fucosylation patterns, as reported by previous works. Such glycan structures were built based on its most prevalent conformations on aqueous solutions, following a protocol already established by the group. The so obtained data indicate that the crystallographic conformation and secondary structure content may not be retained in biological solutions. Additionally, the presence of glycosylation is capable to influence the dynamics and residue exposition of AGP, suggesting a role of its glycan moiety on the protein biological functions and, possibly, in the complexation to specific ligands.

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