Computational Analysis of Beta-Lactam Stabilization in the N-Terminal Domain of Silk Fibroin

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An important area of pharmaceutical research is the formulation of a stabilized antibiotic that does not require cold storage, which holds promise of reducing costs and providing much needed relief to poverty and disease stricken areas of the world. Recently, researchers have concluded that a silk protein biomaterial is capable of stabilizing antibiotics within silk fibroin's ß-sheet structure. Characterizing the interactions between antibiotics and fibroin could shed light upon compound binding interactions to fibroin. It was proposed that there would exist a correlation between the molecular weight of a beta-lactam antibiotic and the docking energy (?G) of its interaction with silk fibroin. In addition, other parameters studied included compound volume, surface area, hydrogen bonding to fibroin, partition coefficient, and apolar and polar desolvation energies. Through the use of a computational chemistry analysis and simulation to characterize the binding sites, molecular interactions between the silk protein and antibiotic were quantified and visualized using SwissDock, ZINC, and Chimera software. Seventy-five different antibiotics were grouped together based upon specific fibroin residues that were shared through hydrogen bonding. Three distinct binding sites were discovered that had in common the ARG66, LYS79, or ILE73 residues respectively. Moreover, out of the parameters studied, specific trends supporting correlation were found between both molecular weight and ?G and between polar desolvation energy and ?G, with up to 50% of the variation in ?G being statistically attributable to antibiotic molecular weight and up to 56% of the variation in ?G being statistically attributable to polar desolvation energy.

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