Enzyme Dynamics of Biofilm-Breaking Dispersin B

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Biofilm-based infections pose two major problems: extreme resistance to antibiotics and many other conventional antimicrobial agents and extreme capacity for evading the host defenses. Dispersin B is a glycoside hydrolase that hydrolyzes the linear polymers in poly-β-1,6-N-acetylglucosamine, considered the main component of the biofilm. Thus, understanding the enzyme dynamics of biofilm-breaking Dispersin B and the nature of the substrate transition state would be important to develop effective antibiotic strategies. To obtain thermodynamic activation parameters, assays of Dispersin B and a biofilm from Staphylococcus aureus were conducted. Dispersin B successfully disturbed biofilm formation due to its cleaving abilities. Additionally, various concentrations of glucose were added to bacteria media, and addition of glucose was found to improve the biofilm formation. Using the optimal concentration of 8 mg/L glucose, independent temperature-controlled assays were performed with varying degrees of substrate concentration to determine the rate constant, which was input in the Arrhenius and Eyring equations. From the resulting thermodynamic values, the Gibbs free energy of activation was determined to be 62.9 kJ/mol at 37 degrees Celsius. Molecular dynamics simulations were performed to predict the transition state structure. After chemically drawn and optimized using the program Avogadro, the substrate analog (4-Nitrophenyl N-acetyl-β-D-glucosaminide) and the potential transition state structure were docked in the active site of Dispersin B. After 1ns molecular dynamics simulations, the potential transition state was observed. This computational method could yield better models of transition-state inhibitors for drug design.

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