Chemistry and biology: the structure and catalytic mechanism of the mannuronan C-5-epimerase AlgE4 from *Azotobacter vinelandii*

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Abstract

Alginate is a family of linear copolymers of (1→4)-linked β-D-mannuronic acid and its C-5 epimer α-L-guluronic acid (G). The polymer is first produced as polymannuronic acid and the G-residues are then introduced at the polymer level by mannuronan C-5-epimerases. The structure of the catalytic A-module of the *Azotobacter vinelandii* mannuronan C-5-epimerase AlgE4 has been determined by X-ray crystallography at 2.1 Å resolution. AlgE4A folds into a right-handed parallel β-helix structure originally found in pectate lyase C and subsequently in several polysaccharide lyases and hydrolases. The β-helix is composed of four parallel β-sheets, comprising 12 complete turns, and has an amphipathic α-helix near the N-terminus. The catalytic site is positioned in a positively charged cleft formed by loops extending from the surface encompassing Asp152, an amino acid previously shown to be important for the reaction. Site-directed mutagenesis further implicates Tyr149, His154, and Asp178 as being essential for activity. Modeling of a substrate in the active site suggests that Tyr149 acts as the proton acceptor, while His154 is the proton donor in the epimerization reaction.


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