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### Archaeal hyperthermostable mannitol dehydrogenases: A promising industrial enzymes for D-mannitol synthesis

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Sugars is a source of energy, despite the close relation of added sugars to some diseases such as obesity, diabetes, etc. As a result, the sweetener market has flourished, which has led to increased demand for natural sweeteners such as polyols, including D-mannitol. Various methods have been developed to produce D-mannitol to achieve high productivity and low cost. In particular, metabolic engineering for D-mannitol considers one of the most promising approaches for D-mannitol production on the industrial scale. To date, the chemical process is not ideal for large-scale production because of its multistep mechanism involving hydrogenation and high cost. The study highlights and presents a comparative evaluation of the biochemical parameters affecting Dmannitol synthesis from *Thermotoga neapolitana* and *Thermotoga maritima* mannitol dehydrogenase (MtDH) as a potential

contribution for D mannitol biosynthesis. These species were selected because purified mannitol dehydrogenases from both strains have been reported to produce D-mannitol with no sorbitol formation under high temperatures (90–120 °C). Recombinant DNA techniques for these thermal enzymes are recommended for D-mannitol industrial synthesis due to some advantages including, enzyme activity, cost-effectiveness, excellent stability under moderate pH and temperature, low toxicity levels of the catalytic process, distinct thermodynamic signature, and the end product purity. Replacing the added sugars with polyols is not an easy task, mainly due to economic reasons. Now, the challenge is to improve the total production of D-mannitol sorbitol free via genetic engineering tools.

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