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A structural classification of carbohydrate epimerases: from mechanistic insights to practical applications

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Abstract
In recent years, carbohydrate epimerases have attracted a lot of attention as efficient biocatalysts that can convert abundant sugars (e.g. D-fructose) directly into rare counterparts (e.g. D-psicose). Despite the increased research activities, no review about these enzymes has been published in more than a decade, meaning that their full potential is hard to appreciate. Here, we present an overview of all known carbohydrate epimerases based on a classification in structural families, which links every substrate specificity to a well-defined reaction mechanism. The mechanism can even be predicted for enzymes that have not yet been characterized or that lack structural information. In this review, the different families are discussed in detail, both structurally and mechanistically, with special reference to recent examples in the literature. Furthermore, the value of understanding the reaction mechanism will be illustrated by making the link to possible application and engineering targets.

Keywords
Carbohydrate epimerases; Classification; Mechanisms; Rare sugar synthesis; Engineering opportunities; GalE; Structural family

1. Introduction

Carbohydrates and derivatives exhibit a wide variety of functions that are essential for all living organisms. Indeed, they can serve as a source of energy or as structural elements, play a part in molecular recognition processes, and can be used as precursors for the biosynthesis of other molecules like aromatic amino acids (Trp, Phe, Tyr) (Englyst et al., 2007; Stallforth et al., 2009; Beerens et al., 2012; Maeda and Dudareva, 2012). Several types of enzymatic reactions are involved in the metabolism of carbohydrates, including dehydrogenation, oxidation, reduction, acetylation, isomerization, and epimerization. In this review, we will focus on the group of enzymes that catalyse an epimerization reaction, which can be defined as the inversion of stereochemistry in molecules with more than one chiral center (Tanner, 2002) (Figure 1).

Insert Figure 1

In the case of carbohydrate epimerases (CEP, EC 5.1.3), epimerization can theoretically occur on every stereocenter of the sugar molecule, although not all of these reactions have been observed in nature. Some epimerase members can even