

SUGAR THE DRUG

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Carbohydrates comprise the most abundant group of natural products and they are present in all living organisms. Traditionally, the carbohydrate moieties of bioactive compounds have been implicated in the control of drug pharmacokinetics such as absorption, distribution and metabolism. Recent growing evidence has produced a change in this dogmatic view. The sugar components are often involved in the interaction between the drug and the cellular target and their presence is therefore important for the biological activity of many natural products [1]. Thus carbohydrate-containing metabolites show many different biological activities and are of great interest.

A growing number of natural products produced by bacteria consist of oligosaccharide chains (Fig.1). These chains are mostly made up of deoxysugars which are very often further modified by methylation or amination. The biosynthesis of these oligosaccharides is catalyzed by sugar biosynthetic enzymes and glycosyltransferases (GTs). GTs transfer a sugar from an activated sugar donor to an acceptor molecule and as such are involved in the transformation of huge number of compounds in the biosphere. In recent years the biosynthetic gene clusters from several oligosaccharide antibiotics produced by actinomycetes have been isolated, sequenced and characterized [2, 3, 4]. Genes encoding GTs have been found and investigated by gene deletion- and gene expression. Molecular biological engineering of glycoside moieties has been shown to be a promising tool for the rational design of natural products and a steadily increasing number of new “unnatural” antibiotics has been generated based on these attempts [5, 6, 7].

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