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Commentary

Classifying Sulfotransferases: Families, Functions, and Substrate Specificities

Vincenzi Cass*

Department of Chemistry, Federal University of São Carlos, São Carlos, Brazil

DESCRIPTION

Sulfotransferases (SULTs) are a vital group of enzymes that play a crucial role in the metabolism and detoxification of numerous endogenous and exogenous compounds by transferring a sulfonate group from 3'-Phosphoadenosine-5'-Phosphosulfate (PAPS) to various substrates. This enzymatic process, known as sulfation, alters the chemical structure and properties of molecules, affecting their solubility, biological activity, and elimination from the body. Understanding the functions, classifications, significance, and clinical implications of sulfotransferases sheds light on their importance in human physiology and pharmacology.

Function and mechanism

Sulfotransferases are a part of phase II metabolism, catalyzing the transfer of a sulfonate group (-SO3) from the universal sulfate donor PAPS to an acceptor substrate. This conjugation reaction leads to the formation of sulfated compounds [1]. The sulfation process plays a critical role in regulating the biological activities of various endogenous substances, drugs, hormones, xenobiotics, and environmental compounds [2]. Sulfonation alters the physicochemical properties of compounds, increasing their water solubility and facilitating their excretion from the body via urine or bile. Moreover, it can modify the biological activity of substrates, influencing their potency, duration of action, and interactions with target molecules or receptors [3].

Classification of sulfotransferases

Sulfotransferases are classified into families and subfamilies based on amino acid sequence similarities and substrate specificities. In humans, thirteen functional SULT genes have been identified and categorized into several families:

SULT1 family: The largest family, encompassing enzymes involved in the metabolism of numerous endogenous compounds like steroids, neurotransmitters, and drugs. Subfamilies within SULT1 include SULT1A and SULT1E.

SULT2 family: Primarily involved in the sulfation of steroid hormones such as Dehydroepiandrosterone (DHEA) and bile acids.

SULT3 family: Limited information is available on this family, but it is believed to be involved in the sulfation of various small molecules.

SULT4A1: This is a distinct gene encoding a protein that may not have canonical sulfotransferase activity.

Significance in drug metabolism

Sulfotransferases significantly impact drug metabolism and pharmacokinetics [4]. They often catalyze the inactivation or activation of drugs and xenobiotics, affecting their bioavailability, elimination, and therapeutic efficacy. Some drugs undergo sulfation as part of their metabolism, leading to the formation of more water-soluble metabolites that are readily eliminated from the body [5].

Conversely, the sulfation of prodrugs can activate them into their pharmacologically active forms. For example, the activation of minoxidil, a drug used to treat hypertension and stimulate hair growth, occurs *via* sulfation [6].

Clinical implications and research

Understanding the role of sulfotransferases in drug metabolism is crucial for predicting and managing drug interactions, variations in drug response among individuals, and potential adverse effects. Genetic variations in SULT genes can lead to interindividual differences in enzyme activity, affecting drug efficacy and toxicity [7,8].

Ongoing research focuses on uncovering the genetic polymorphisms in SULT genes and their implications in personalized medicine and drug development. Identifying variations in sulfotransferase activity among different populations can help tailor drug dosages and treatments to maximize therapeutic benefits while minimizing adverse reactions [9,10].

Correspondence to: Vincenzi Cass, Department of Chemistry, Federal University of São Carlos, São Carlos, Brazil, E-mail: cassvincenzi@ufscar.br

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CONCLUSION

Sulfotransferases are integral enzymes involved in the metabolism and regulation of a diverse array of compounds, influencing their bioavailability, biological activities, and elimination. Their role in drug metabolism underscores their significance in pharmacology and therapeutics. A deeper understanding of sulfotransferases, their classifications, and their impact on drug metabolism holds immense promise in refining drug development, optimizing treatments, and advancing personalized medicine. Continued research in this field promises to unveil further insights into the intricate workings of these enzymes and their clinical relevance.

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