SUPPLEMENTARY MATERIAL

Article

Inhibitory Effect of Coumarins and Isocoumarins Isolated from the Stems and Branches of *Acer mono* Maxim. against *Escherichia coli β*-Glucuronidase

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1. Drug-likeness properties of compound 1

An optimal drug candidate must satisfy the requirements for absorption, distribution, metabolism, excretion, and toxicity (ADMET) properties, afford full and rapid absorption from the gastrointestinal tract, precise target distribution, stimulate metabolic activity, and safe excretion [1]. Orally active drugs must follow Lipinski's rule of five: molecular weight (MW) <500, hydrogen bond acceptor (HBA) ≤10, hydrogen bond donor (HBD) ≤5, predicted octanol/water partition coefficient (ClogP) <5, and the number of rotatable bonds ≤10 [2]. The rule of five was established following a study conducted by Pfizer in the late 1990s, according to which a molecule is considered inactive if it violates two or more rules [2]. The drug-likeness properties of active compound **1** were analyzed and visualized using the SwissADME web tool [3].

Based on the predicted results presented in Table **S1**, the drug-likeness properties indicate that compound **1** did not violate Lipinski's rule of five. A drug with weak solubility and dissolution rate is excreted upon oral administration. Drug solubility is represented as log S, where S is the concentration of the drug in a saturated aqueous solution (mol/L) and is determined by three methods: ESOL, ALI, and SILICOS-IT. The log S values for 85% of drugs range between −1 and −5 [4]. Furthermore, based on BOILED-Egg method [5], compound **1** does not penetrate the blood-brain barrier; a blue dot indicates that compound **1** is predicted to be a P-glycoprotein 1 substrate (Figure **S1**).
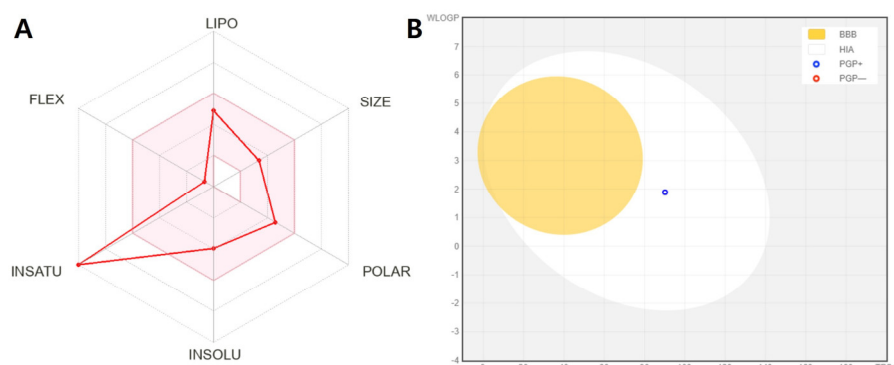

Figure S1. Bioavailability radar of compound **1** (**A**; LIPO: Lipophilicity, SIZE: Molecular size, POLAR: Polarity, INSOLU: Insolubility, INSATU: Instauration, FLEX: Flexibility) and the analysis of compound **1** by the BOILED-Egg method (**B**).

Table S1. Drug-likeness properties of compound **1**.

Properties	1
Physicochemical properties	
MW (g/mol)	272.25
HBAs	5
HBDs	4
ClogP	1.62
No. rotatable bonds	1
Solubility	
Log S (ESOL)	−3.15 (Soluble)
Log S (Ali)	−3.50 (Soluble)
Log S (SILICOS-IT)	−2.71 (Soluble)
Pharmacokinetics	
GI absorption	High
CYP enzymes inhibitors	No
Log K_p (skin permeation, cm/s)	−6.55

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