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An abstract should describe the background, methods used, central findings, and conclusions. References to any published work should be avoided. When deemed necessary, please place the reference in the text and use a shortened form, e.g., Black et al.: J. Biol. Chem. 269 (1964) 1238.

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**ABSTRACT TEMPLATE**

**Inhibition of cytochrome P450 3A4 and P-glycoprotein transporter by *2*-hydroxytriazolo[4,*5*-b]pyridine**

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 (The main text, Times New Roman font, 12 points) The analgesic effects of opioids are mediated through four known receptors: mu-(MOR), kappa-(KOR), delta-(DOR), and the opioid receptor-like 1 (ORL-1). Of the opioid analgesics, mu-opioid agonists (MOAs) are the most commonly used. *2*-hydroxytriazolo [4,*5*-b]pyridine was synthesized as a potentialMOA. Pyridines are potent inhibitors of P-glycoprotein and are compounds that reverse the multidrug resistance phenomenon in cancer cells. Besides, pyridines are known to inhibit rodent Cyp3a enzymes (Black et al.: J. Biol. Chem. 269 (1964) 1238).

We examined if *2*-hydroxytriazolo[4,*5*-b]pyridine inhibits cytochrome P450 3A4 (CYP3A4) enzyme and P-glycoprotein transporter.

For this purpose, we use human liver microsomes and MDCKII cells with artificial expression of human P-glycoprotein transporter (ABCB1 gene). Midazolam was used as a CYP3A4 substrate. Digoxin was used as a P-glycoprotein substrate in transport assays.

We found efficient inhibition of P-glycoprotein transporter but not CYP3A4 by 2-hydroxytriazolo[4,*5*-b]pyridine with IC50 0.03 and 25.2 μM, respectively. Despite this fact, CYP3A4 inhibition by the compound appeared as a mechanism-based (irreversible) interaction.

We can conclude that the novel pyridine compound is a potent P-glycoprotein inhibitor. Since CYP3A4 is responsible for the metabolism of more than 50% of medicines, we propose/hypothesize that *2*-hydroxytriazolo[4,*5*-b]pyridine may also inhibit CYP3A4 after high doses with significant consequences for drug-drug interactions.

*Supported by the University Agency, grant No. 1234.*