národní
úložiště
šedé
literatury

**Organoruthenium glycomimetics as selective galectin-1 inhibitors**

Hamala, Vojtěch
2023

Dostupný z http://www.nusl.cz/ntk/nusl-526201

Dílo je chráněno podle autorského zákona č. 121/2000 Sb.

Tento dokument byl stažen z Národního úložiště šedé literatury (NUŠL).

Datum stažení: 03.06.2024

Další dokumenty můžete najít prostřednictvím vyhledávacího rozhraní nusl.cz .

# Organoruthenium glycomimetics as selective galectin-1 inhibitors

*Student: Ing. et Ing. Vojtěch Hamala*
*Supervisor: Ing. Tomáš Strašák, Ph.D.*
*Supervising Expert: Mgr. Jindřich Karban, Ph.D.*

Galectins are a type of lectins that have the ability to bind to β-galactosides. Human galectin-1 (Gal-1) and galectin-3 (Gal-3) have been linked to tumor progression, with Gal-1 contributing to cell migration and tumor immune escape, while elevated levels of Gal-3 are associated with increased invasiveness, metastatic spreading, immunosuppression, and angiogenesis. The natural ligands of galectins include galactose, lactose, *N*-acetyllactosamine (LacNAc), as well as their glycosylated and sulfated forms. Modifications of these carbohydrate ligands can lead to the creation of glycomimetics, thus enhancing binding to galectins and can serve as potent inhibitors. A common method of modification involves replacing carbohydrate hydroxyls with an aromatic substituent, which enhances binding to galectins.

Several Gal-3 inhibitors are already in clinical trials against illnesses connected with galectin overexpression, yet selective galectin-1 inhibitors are still lacking.[1] To address this, we conducted a project in which we replaced the aromatic substituent in known galectin in-

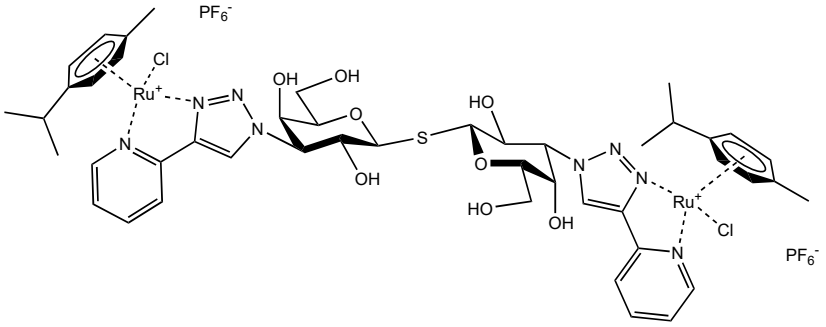


**Figure 1:** A structure of prepared organoruthenium highly selective galectin-1 inhibitor.

hibitors based on LacNAc, phenylthiogalactoside, and thiodigalactoside scaffolds with arene-containing ruthenium *"piano-stool"* complexes. We discovered that the unique geometry of the ruthenium ligands in these complexes creates additional favorable interactions in the binding site of Gal-1 while disrupting the inhibitor's affinity to Gal-3.

The prepared organoruthenium glycomimetics demonstrated single unit nanomolar affinity to Gal-1 and over four orders of magnitude higher selectivity to Gal-1 in comparison to Gal-3. The organoruthenium galectin inhibitors were found to be nontoxic to both cancer and noncancerous cell lines. Selected complexes showed an in vitro antimigratory effect against invasive cancer cell lines MDA-MB-231 and SK-OV-3.

This work was supported by The Czech Science Foundation (grant 23-06115S). This work was also supported by the Martina Roeselová Memorial Fellowship granted by the IOCB Tech Foundation.

*References*

1. Sethi, A.; Sanam, S.; Alvala, R.; Alvala, M. *Expert Opin. Ther. Pat.* **2021**, *31* (8), 709-721.
2. Kacsir, I.; Sipos, A.; Ujlaki, G.; Buglyó, P.; Somsák, L.; Bai, P.; Bokor, É. *Int. J. Mol. Sci.* **2021**, *22* (19), 10454.