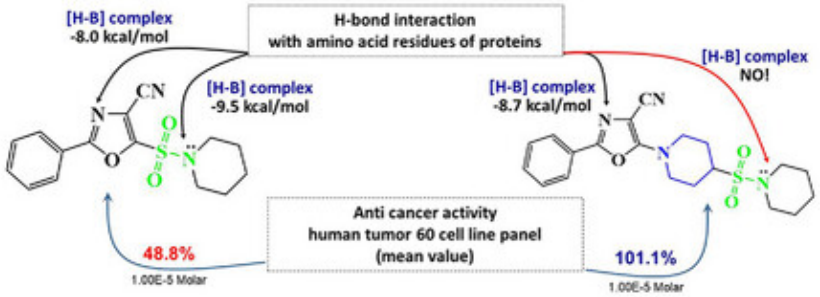
A Comparative In Vitro Anticancer Evaluation and In Silico Study of New 1-(1,3-Oxazol-5-yl)piperidine-4-sulfonylamides

Oleksandr Severin, Dr. Nataliya Obernikhina, Dr. Stepan Pilyo, Dr. Maryna Kachaeva, Dr. Olexiy Kachkovsky, Dr. Oleksandr Kozachenko ... See all authors

First published: 28 October 2024 | https://doi.org/10.1002/slct.202403531

Graphical Abstract

This study scrutinizes the biological activity of new and known sulfanylamide containing 1,3-oxazoles employing in vitro and in silico methods. It shows previously unknown effects of the proximity of the sulfanylamide group toward the 1,3-oxazole on the anticancer activity and purported complexation of the derivative products with low molecular weight biomolecular fragments under varied mechanisms of action.



Abstract

In this work, we synthesized a series of new 1,3-oxazole derivatives comprising the sulfonylamide group and tested their activity against the human tumor cell line panel. This study further explores the stereoelectronic characteristics of 1,3-oxazol-5-sulfonylamides and new 1-(1,3-oxazol-5-yl)piperidine-4-sulfonylamides to connect their anticancer activity to the molecular structure. Combining in vitro and in silico methods, we analyzed how the proximity of the sulfonylamide group to the heterocyclic ring affects the structure–activity interplay. Herein, our assessment is based on the purported complexation of 1,3-oxazoles with targeted biomolecular fragments involving the π-stacking interaction and hydrogen bonding within the prospective complexes. Defining the probability of the prospective drug–target interactions, we detail conformational properties, donor/acceptor capabilities, electronic characteristics, and thermodynamic preference of produced sulfanylamide group containing 1,3-oxazoles toward biomolecular fragments, identifying the nature of variations in anticancer activity.