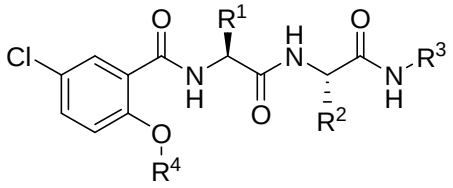
SYNTHESIS AND ANTICANCER ACTIVITY OF NOVEL SALICYLAMIDE DERIVATIVES

Pratibha Magar[a], Aleš Imramovský[a,*], Radek Jorda[b], Vladimír Kryštof[b], Deisa Hendrychová[b]

[a]Institute of Organic Chemistry and Technology, Faculty of Chemical Technology, University of Pardubice, studentská 573, 53210 Pardubice, Czech Republic
ales.imramovsky@upce.cz
[b]Laboratoty of Growth Regulators, Palacky University and Institute of Experimental Botany, The Czech Academy of Sciences, Šlechtitelů 27, 78371 Olomouc, Czech Republic

Salicylic acid amides are compounds with diverse pharmacological activities and can be classified according to the bounded amine. Salicylanilide (attached with an aromatic amine) are a group of compounds having a wide range of biological activities against microbial pathogens [1], these compounds also possess antiviral activities [2], antimycobacterial activities [3]. Latest studies described the aliphatic salicylamides as epidermal growth factor receptor tyrosine kinase inhibitors [4]. In addition, antiproliferative properties of salicylanilide were described as an important marker for protentional anticancer treatment.



R^1, R^2 = (*S*)-CH_2-CH-$(CH_3)_2$
or (*S*)-CH_2-phenyl in combinations
R^3 = aromatic, alicyclic, heterocyclic
R^4 = -CH_2-phenyl or H

Figure. Triamide derivates of salicylamide

Our previous study shows interesting biological properties of salicylamides. A series of variously substituted 2-hydroxy-*N*-(arylalkyl)benzamides were prepared and screened for antiproliferative and cytotoxic activity in cancer cell lines [5]. Salicylamides terminated with aliphatic chain possess antiproliferative activity [6]. We introduce here the synthesis and biological characterization of 32 novel salicylamides bearing the combination of optically pure amino acids, namely aromatic phenylalanine or aliphatic leucine. All derivatives display antiproliferative activity in tested cancer cell lines and eight of them reach up single-digits micromolar GI_{50}.

The authors acknowledge the financial support from the SG project Faculty of Chemical Technology, University of Pardubice and from the Grant Agency of Czech Republic project No.: *GA 18-03847S*.

[1] Imramovský, A. *et.al*.; *Mini-Reviews in Organic Chemistry* **2011**, *8*, 211-220.

[2] Krátký, M. *et.al*.; *Mini Rev. Med. Chem.* **2011**, *11*, 956-967.

[3] Waisser, K. *et.al*.; *Arch. Pharm. Med. Chem*. **2003**, *336*, 53-71.

[4] Liu, Y. *et.al*.; *Lett. Drug Des. Discov*. **2016**, *13*, 314-323.

[5] Imramovský, A. *et.al*.; *Eur. J. Med. Chem*. **2013**, *68*, 253-259.

[6] Dušek J. *et.al*.; *Lett. Drug Des. Discov*. **2017**, *14*, 662-671.