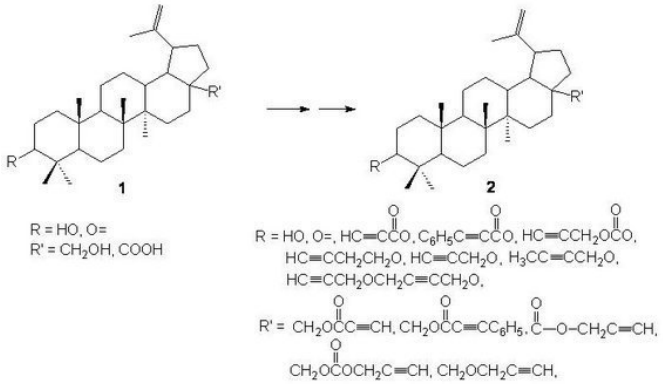
As an extension of our work on the development of anticancer agents, we synthesized the series of new derivatives of betulin **2** possessing one or two acetylenic functions. Betulin was isolated from the birch bark and then was oxidized to betulonic acid (R= O=, R'=COOH) and betulinic acid (R=OH. R'=COOH). Compounds **1** in the reactions with acetylenecarboxylic acids or acetylenehalides were converted into the corresponding mono- and diesters or ether derivatives **2**.



The obtained compounds were tested for their anticancer activity *in vitro* against the cells of human and murine cancer cell lines.

[1] T.G.Tolstikova, I.V.Sorokina, G.A. Tolstikov, O.B.Flekhter, *Russ.J.Bioorg.Chem*., **32** (2006) 37-49.

[2] Y.Bi, J.Xu, X.Wu, W.Ye, S.Yuan, L.Zhang, *Bioorg.Med.Chem.Lett*., **17** (2007) 1475-1478.

[3] S.F.Vasilevsky, A.I.Govdi, E.E.Shults, M.M.Shakirov, I.V.Sorokina, T.G.Tolstikova, D.S.Baev, G.A.Tolstikov, I.V.Alabugin, *Bioorg.Med.Chem*., **17** (2009) 5164-5169.

17:00 Poster 12

Synthesis of long-chain arylpiperazine theophylline derivatives as potential 5-HT$_7$ and 5-HT$_6$ receptors ligands

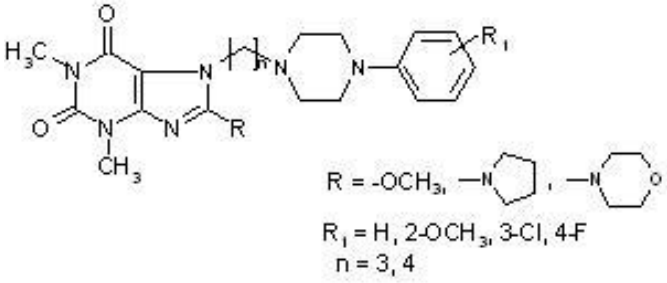
Grażyna Chłoń-Rzepa[1], Małgorzata Harłacz[1], Paweł Żmudzki[1], Maciej Pawłowski[1], Andrzej J. Bojarski[2], Beata Duszyńska[3], Aneta Kozioł[3]

1. *Jagiellonian University, Collegium Medicum, Department of Pharmaceutical Chemistry, Medyczna 9, Kraków 30-688, Poland* **2.** *Polish Academy of Sciences. Institute of Pharmacology, Smętna 12, Kraków 31-343, Poland* **3.** *Institute of Pharmacology Polish Academy of Sciences, Department of Medicinal Chemistry, Smętna 12, Kraków 31-343, Poland*

e-mail: mfchlon@cyf-kr.edu.pl

The role of 5-HT$_{1A}$ and 5-HT$_{2A}$ receptors in the pathogenesis of neuropsychiatric disorders is well known. However the most recently identified serotonin receptor subtypes: 5-HT$_6$ and 5-HT$_7$ are also reported to have importance in the control of many CNS functions (thermoregulation, circadian rhythms) and dysfunction like migraine, epilepsy and depression [1]. It has been postulated that 5-HT6 ligands may afford useful therapies for the treatment of obesity, as well as cognitive enhancement in schizophrenia and Alzheimer's disease [2].

In the field of serotonergics we have concentrated on the development of long-chain arylpiperazines (LCPs) theophylline derivatives which were active at 5-HT$_{1A}$, 5-HT$_{2A}$ and 5-HT$_7$ receptors [3, 4]. Among them the 8-alkoxy derivatives of 1,3-dimethyl-7- (4-arylpiperazinylalkyl)-3,7-dihydropurine-2,6-dione proved to be potent ligands for these receptors and showed anxiolytic and antidepressant activities *in vivo* models [4]. To continue our research and extend the study on 5-HT$_6$ receptors we designed and synthesized series of the new analogues by modification of the substituent in position 8 of the purine-2,6-dione core. Additionally the *p*-fluoro substituent was introduced into the phenyl ring.



The new analogues are under evaluation for their affinity to the 5-HT$_7$ and 5-HT$_6$ receptors. The structure-activity relationship (SAR) will be discussed.

This study is partly supported by a grant PNRF-103-AI-1/07 from Norway through the Norwegian Financial Mechanism.

References:

[1] Hedlund P.B., Sutcliffe J.G.: Trends Pharmacol. Sci., 2004, 25, 481.

[2] Singer J.M. et al. Bioorg. Med. Chem. Lett., 2009, 19, 2409.

[3] Chłoń G., Pawłowski M., Duszyńska B., Szaro A., Tatarczyńska E., Kłodzińska A., Chojnacka-Wójcik E.: Pol. J. Pharmacol., 2001, 53, 359.

[4] Chłoń-Rzepa G., Żmudzki P., Zajdel P., Bojarski A.J., Duszyńska B., Nikiforuk A., Tatarczyńska E., Pawłowski M.: Bioorg. Med. Chem., 2007, 15, 5239.

17:00 Poster 14

HPLC Methods for Stress Testing of ZL-S Drug Substances

Ewelina Czerniec-Michalik, Maria Puchalska, Tatyana Gilevska, Magdalena Kossykowska, Katarzyna Badowska-Rosłonek

Pharmaceutical Research Institute (IF), Rydygiera 8, Warszawa 01-793, Poland

e-mail: e.michalik@ifarm.waw.pl

ZL-S, namely the 4-({3-[2-(dimethylamino)ethyl]-1*H*-indol-5-yl}-methyl)-1,3-oxazolidin-2-one is very potent serotonine receptor inhibitor. The primary objectivev ot this research was to study the degradation behaviour ofZL-S under different stress conditionsby HPLC with UV detection and to establish stability of this drug substance. The secondary was to establish the stability indicating HPLC methods for assessment of purity and content of ZL-S.