NEW SERT INHIBITORS WITH ANTINEOPLASTIC ACTIVITY

Jarosław Walory\textsuperscript{a}, Miroslawa Koronkiewicz \textsuperscript{a}, Andrzej J. Bojarski\textsuperscript{b}, I. Sylte\textsuperscript{c}, Małgorzata Jarończyk\textsuperscript{a}, Zdzisław Chilmonczyk\textsuperscript{a}

\textsuperscript{a}National Medicines Institute, 30/34 Chełmska Street, 00-725 Warsaw, Poland
\textsuperscript{b}Institute of Pharmacology PAS, 12 Smętna Street, 31-343 Cracow, Poland
\textsuperscript{c}Medical Pharmacology and Toxicology, Department of Medical Biology, Faculty of Health Science, University of Tromsø, N-9037 Tromsø, Norway

It was previously observed that some antagonists of the 5-HT\textsubscript{1A}, and 5-HT\textsubscript{1B} and certain serotonin reuptake inhibitors may inhibit the \textit{in vitro} growth of prostate cancer cells - PC-3 (androgen-insensitive), DU-145 and LNCap (androgen-sensitive).\textsuperscript{1,2}

In the present study the effects of some known 5-HT\textsubscript{1A} antagonists and agonists as well as several known and new serotonin transporter inhibitors (6-nitroquipazine derivatives) on the PC-3 cell line proliferation \textit{in vitro} were examined. It was found that new nanomolar SERT inhibitors exhibited substantial cytotoxic against PC-3 cancer cell line. The cytotoxic activity of new compounds was higher than that observed for fluoxetine. It was also found that atypical 5-HT\textsubscript{1A} receptor agonist S 14506 exhibited similar activity. The compounds influenced mitochondrial membrane potential (OMMP) suggesting the internal apoptotic pathway involving apoptosome formation.


Acknowledgements: The paper was supported by the Polish-Norwegian Research Program Pol-Nor/198887/73/2013.