NEW SERT INHIBITORS WITH ANTINEOPLASTIC ACTIVITY

Jarosław Walory[a], Mirosława Koronkiewicz [a], Andrzej J. Bojarski[b], I. Sylte[c], Małgorzata Jarończyk[a], Zdzisław Chilmonczyk[a]

[a]*National Medicines Institute, 30/34 Chełmska Street, 00-725 Warsaw, Poland*
[b]*Institute of Pharmacology PAS, 12 Smętna Street, 31-343 Cracow, Poland*
[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_{1A}, and 5-HT_{1B} and certain serotonin reuptake inhibitors may inhibit the *in vitro* growth of prostate cancer cells - PC-3 (androgen-insensitive), DU-145 and LNCaP (androgen-sensitive).[1,2]

In the present study the effects of some known 5-HT_{1A} antagonists and agonists as well as several known and new serotonin transporter inhibitors (6-nitroquipazine derivatives) on the PC-3 cell line proliferation *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_{1A} receptor agonist S 14506 exhibited similar activity. The compounds influenced mitochondrial membrane potential (OMMP) suggesting the internal apoptotic pathway involving apoptosome formation.

[1]S.C. Hsiung, H. Tamir, T.F. Franke, K.-p. Liu. Roles of extracellular signal-regulated kinase Akt signaling in coordinating nuclear transcription factor-κB-dependent cell survival after serotonin 1A receptor activation. J. Neurochem. 95(6) (2005) 1653-1666.

[2]Emad J Siddiqui, Majid Shabbir, Dimitri P Mikhailidis, Cecil S Thompson, Faiz H Mumtaz: The Role of Serotonin (5-Hydroxytryptamine1A and 1B) Receptors in Prostate Cancer Cell Proliferation. J Urol 176:1648-53, 2006.

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