

The development of 5-HT6 receptor ligands as potential cognition enhancers	
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In silico selection of target-focused compounds from commercial repositories and in vitro screening of compound libraries are often the first steps in new drug development projects. With the use of both these approaches several hits with affinity for 5-HT6 receptor were identified. Since its discovery in 1993 the 5-HT6 receptor has received increasing attention due to its involvement in learning and memory processes, and recently it became a promising target for improving cognition. From the selected hits different groups of 5-HT6 receptor ligands were developed as potential cognition enhancers.

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Towards experimental pharmacology of endothelium	
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Vascular endothelium, is presently looked upon as an important autocrine/paracrine/endocrine organ that regulates number of cardiovascular functions and there are number of pharmacotherapeutic mechanisms of endothelium and vascular wall that could be exploited therapeutically. For example, COX-2/PGI₂ pathway represent an important defensive mechanisms of vascular wall that could be stimulated by 1-methylnicotinamide (MNA), a major metabolite of nicotinamide (vitamin PP, vitamin B₃). Indeed, we described anti-thrombotic, anti-inflammatory and vasoprotective activity of MNA *in vivo*.

In turn, we demonstrated that NO-based therapy targeted to the liver with the use of V-PYRRO/NO therapy improved liver steatosis and postprandial glucose tolerance in mice model of NAFLD, while V-PROLI/NO was ineffective. Today, decades after the discoveries of vasoprotective endothelial mediators such as prostacyclin (PGI₂), and nitric oxide (NO), we have learn to stimulate their vasoprotective activity with pharmacological tools. Still, further development of experimental and clinical pharmacology of endothelium is needed to translate these endeavours into organ-selective therapeutics.

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 [3] Chlopicki S et al., *Br. J. Pharmacol.*, **2007**, 152, 230-239