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CONTENT

2-Oxindole as privileged structure for antiglaucomic and antidiabetic drug design: synthesis and biological activity

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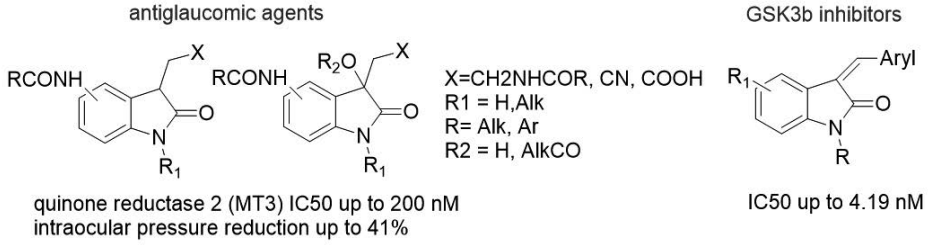
New amide-substituted oxindoles were synthesized using catalytic hydrogenation of corresponding nitro-derivatives and their biological activity was investigated [1]. The synthesis of new ligands of quinone reductase 2 (QR2, proposal MT3 receptor) [1-4] and kinase-3β glycogen synthase (GSK3β) [5] based on 2-oxindole scaffold was performed using condensation of isatin and 2-indolinone derivatives with appropriate compounds. The ability of oxindole-based QR2 ligands to reduce the intraocular pressure (IOP) was studied in vivo in normotensive rabbits. The lead compound was found to reduce IOP at 41% (more, then reference drug timolol (32%)) and had the long-lasting hypotensive effect (>6h). It was shown that 3-arylidene-substituted 2-oxindoles were effective inhibitors of kinase-3β glycogen synthase and exhibit pronounced anti-diabetic activity under conditions of the glucose-tolerant test in vivo [5]. The lead compound showed moderate cytotoxicity in the micromolar range which creates a sufficient therapeutic window for the design of potential antidiabetic drugs based on this compound.



References

[1] Zaryanova E.V., Ignatov A.A., Lozynskaya N.A. *Tetrahedron,* **2017***, Vol. 73, P. 6887–6893*

[2] Volkova M.S., Jensen K.C., Lozinskaya N.A., Sosonyuk S.E., Proskurnina M.V., Mesecar

A.D., Zefirov N.S. *Bioorganic and Medicinal Chemistry Letters,* **2012,** *Vol. 22, no.5, P. 7578–7581*
[3] Zaryanova E.V., Lozinskaya N.A., Beznos O.V., Volkova M.S., Chesnokova N.B., Zefirov N.S. *Bioorganic and Medicinal Chemistry Letters,* **2017***, Vol. 27, P. 3787–3793.*
[4] Chesnokova N.B., Beznos O.V., Lozinskaya N.A., Volkova M.S., Zaryanova E.V., Zefirov N.S. Grygor'ev A.V. *Biochemistry, Supplemental Series B,* **2017***, Vol. 11, no. 3, P. 272–278*
[5] Lozinskaya N.A., Babkov D.A., Zaryanova E.V., Bezsonova E.N., Efremov A.M., Tsymlyakov M.D., Anikina L.V., Zakharyascheva O.Yu., Borisov A.V., Perfilova V.N., Tyurenkov I.N., Proskurnina M.V., Spasov A.A., *Bioorganic and Medicinal Chemistry,* **2019**, *in press*

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