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CONTENT

Synthesis and biological evaluation of 3- arylidene 2-oxindole derivatives as new agents for treatment of diabetes mellitus

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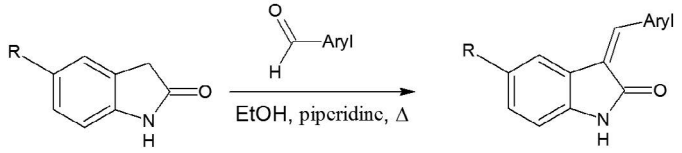
2-Oxindole scaffold was used for targeted design and synthesis of a number of novel compounds with pronounced antidiabetic activity[1]. Condensation of 2-oxindoles with 2-substituted heteroaromatic aldehydes was E/Z selective and resulted in one isomer predominancy.



43 - 99 %

R = H, BzNH, (2-furoyl)NH, $CH_3C(O)NH$, MeOC(O)NH, Br, NO_2
Aryl = 2-pyridyl, 4-Br-Ph, 4-OH-Ph, 3,4,5-tri-MeO-Ph, 3-OH-Ph, 4-NO_2-Ph, 3-pyridyl, 4-pyridyl, 2-thienyl, 2-furyl, 3,4-dimethyl-pyrazol-4-yl

The inhibitory activity of obtained compounds was tested *in vitro* on two molecular targets for diabetes mellitus therapy, glycogen synthase kinase 3β (GSK-3*β*) and α-glucosidase [2,3,4]. The lead compounds were shown to inhibit GSK-3*β* and *α*-glucosidase with IC_{50} 4.19 nM and IC_{50} 6.78 *μM* respectively. Even though GSK-3*β* ligands and α-glucosidase inhibitors share similar scaffold, lead compounds in screenings on these two molecular targets were structurally different which suggests a possibility for further structural optimization and search for selective ligands based on 2-oxindole scaffold for both enzymes. Lead compounds for each of two enzymes displayed significant antidiabetic effect in oral glucose tolerance test in rat model of type 2 diabetes mellitus.

References

[1] N.A. Lozinskaya, E.V. Zaryanova, E.N. Bezsonova, M.D. Tsymlyakov, A.M. Efremov, L.V. Anikina, D.A. Babkov, O.Yu. Zakharyascheva, D.R. Prilepskaya, A.A. Spasov, *Bioorganic & Medicinal Chemistry,* in print
[2] G.W. Cline, K. Johnson, W. Regittnig , *Diabetes*, 2002, 51, 10, 2903-2910
[3] H. Bischoff, *European Journal of Clincal Investigation,*1994, 24, 3, 3-10
[4] F. Takahashi-Yanaga, *Biochemical Pharmacology,* 2013, 86, 2, 191-199

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