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Synthesis and evaluation of novel indole derivatives as AKT inhibitors

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We described the discovery and synthesis of a new series of 1,2,4,7-tetra-substituted indole derivatives as novel AKT inhibitors by optimization of a weak hit methyl 4-(2-aminoethoxy)-1H-indole-2-carboxylate. Both representative compounds 8a and 8o showed the most potent inhibitory activity against AKT 1 with inhibition rates of 72.5% and 78.6% at 10 nM concentrations, respectively. Moreover compounds 8a and 8o also potently inhibited the phosphorylation of downstream GSK3 protein and displayed strongly anti-proliferative activity in prostate cancer cell line.

Keywords: AKT inhibitors, GSK3β, Inhibition rate, Tetra-substituted indoles.

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