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Computational drug design in the search of protein tyrosine phosphatase 1B inhibitors as potential antidiabetic agents

Computational approaches, including both indirect and direct designs have been used in the search of novel small molecules as potential biologically active agents. The protein tyrosine phosphatase 1B (PTP1B) is been considered is potential targets for designing for antidiabetic agents as PTP1B inhibition results both in increased insulin sensitivity and resistance to obesity, with no abnormalities in growth or fertility or other pathogenetic effects. Thus in search of small molecule as potential PTP1B inhibitors, the indirect drug design approaches like CoMFA, CoMSIA and pharmacophore modeling resulted in the design and synthesis of a series of 2-[(4-methoxyphenyl) ethyl] acetamide derivatives including a promising PTP1B inhibitor (IC_{50} = 69µM) and another series of substituted phenoxy-3-piperazin-1-yl-propan-2-ols where one compound showed 40.3% normalization of plasma glucose levels at 100mg/kg in sugar-loaded model (SLM) and 32% activity in streptozocin model (STZ). In continuation of this work using computer assisted pharmacophore modeling and direct drug design approaches like docking led to the identification and synthesis of substituted sulfonamides and carboxamides where the best compound of the sulfonamides and carboxamides series showed very high activity with IC_{50} values 7.54 and 5.8µm respectively. Both the compounds improved in vivo activity in STZ model and restored the insulin level and the serum lipid profile by significantly improving the insulin signaling and insulin resistance. Altogether, both compounds present excellent profile for development as candidate for future PTP1B targeted drug discovery.

Speaker Biography

Anil K Saxena is actively involved in the domain of medicinal chemistry, including CADD, drug discovery and development research. He has more than 49 years of research experience with 206 research publications, 24 reviews/articles in books and/monographs, 72 patents and has delivered more than 180 invited lectures and chaired more than 48 sessions. He is a Fellow of Royal Society of Chemistry, UK, Editorial Board Member of different prominent journals like Medicinal Chemistry Research, SAR and QSAR in Environmental Research, online International journal ARKIVOC and Patent Evaluator: Current Drugs, UK. He is also series editor for book series "Topics in Medicinal Chemistry" published by Springer Verlag.

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