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Synthesis of some new 1-(4-(4,6-dimethyl-6*H*-1,3-thiazin-2-yl)phenyl-sulfonyl)-1,3-disubstituted-urea scaffolds as potential antidiabetic agents

Sathish Kumar Mittapalli[1], Deepesh Parashar[2]*, S. Roshan[3], Hero Khan Pathan[2], Adarsh[2], Sagar Pamu[4] and M. V. Neethu[2]

[1]Department of Pharmaceutical Chemistry, Parul Institute of Pharmaceutical Education and Research, Parul University, Vadodara, Gujarat, India
[2]Department of Pharmaceutical Chemistry, Amity Institute of Pharmacy, Amity University, Gwalior, Madhya Pradesh, India
[3]Department of Pharmacognosy, Deccan School of Pharmacy, Hyderabad, Telangana, India
[4]Department of Pharmacy Practice, Institute of Pharmacy, Nirma University, Ahmedabad, Gujarat, India

ABSTRACT A series of 4-(4,6-dimethyl-1,3-thiazin-2-yl)-*N*-phenylsulfonylurea analogs **(6a-6z)** were synthesized by a multistep route starting from 4,6-dimethyl-2-phenyl-2*H*-1,3-thiazine (**2**). Compound **2** was prepared according to the literature procedure from acetylacetone with benzaldehyde **(1)** in the presence of ammonium thiocyanate. The docking studies were performed toward α-glucosidase, aldose reductase, and α-amylase along with some standards. The results demonstrated that sulfonamide derivatives **6o, 6k, 6m**, and **6h** had strong inhibitory effects against α-glucosidase and α-amylase inhibitory activity. Compounds **6m, 6k**, and **6h** showed enhanced glucose uptake as compared to berberine with EC50 values of 19.03, 21.38, and 30.82 µM, respectively. An integrated approach combining molecular docking with experimental validation provides more reliable and accurate predictions in drug discovery.

KEYWORDS *In silico* screening, Toxicity, Binding affinity, α-glucosidase, α-amylase, glucose uptake, ProTox-II.

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