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THE DESIGN, SYNTHESIS AND PHARMACOLOGICAL EVALUATION OF PYRAZOLE CONTAINING SULFONYLUREA DERIVATIVES AS POTENT GSK3B INHIBITOR FOR BLOOD GLUCOSE LOWERING EFFECT

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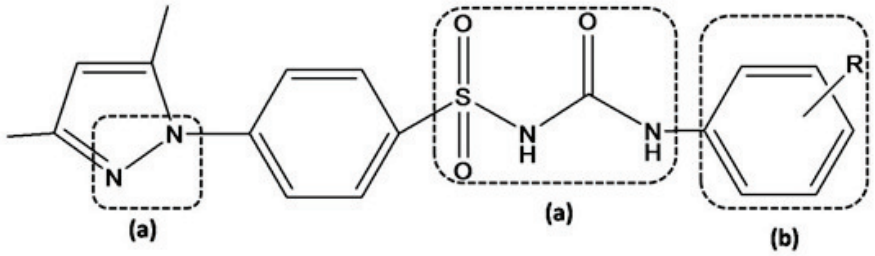
ABSTRACT A series of pyrazole containing sulfonylurea derivatives have been design, synthesized and evaluated for the glycogen synthase kinase (GSK3β) inhibition to achieve the blood glucose lowering activity in type-2 diabetic patient. All the designed derivatives were bind very efficiently with GSK3β without any toxic interpretation revealed under in silico study profile. Structural activity relationship (SAR) study is suggested the use of chloro derivative **(3c)** for exhibiting most suitable orientation to bind with GSK3β cascade. The use of pyrazole ring along with sulfonylurea justified its role after formation of hydrogen bond by nitrogen heteroatom with the arginine residue of GSK3β. The developed scheme has yielded targeted analogs are characterized by spectroscopic and elemental analysis. Under the bioassay study by oral glucose tolerance test (OGTT) in rats, analog **3c** found the most suitable to reduce level of glucose in blood plasma at the dose of 50 mg/kg and 10 mg/kg shown by area under curve (AUC) and blood glucose lowering plot.



Test Molecule

KEYWORDS GSK3β; OGTT; pyrazole; sulfonylurea; AUC.