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DESIGN, SYNTHESIS, PHARMACOLOGICAL SCREENING, MOLECULAR DOCKING AND TOXICITY STUDIES ON 7-(2-(BENZO[D]THIAZOL-2-YLAMINO) ETHOXY)-4-METHYL-2H-CHROMEN-2-ONE DERIVATIVES FOR ATYPICAL ANTIPSYCHOTIC ACTIVITY

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Typical antipsychotics are used to treat a mental, baffling, severe disorder called Schizophrenia. The present study focuses on design and synthesis of some novel derivatives. The novel series 7-(2-(benzo[d]thiazol-2-yl-amino)ethoxy)-4-methyl-2H-chromen-2-one (4a-4k) was designed and synthesized by refluxing 2-amino benzothiazole substituted derivatives (3a-3k) with 7-(2-chloroethoxy)-4-methyl-2H-chromen-2-one(2) in dry pyridine. All the synthesized compounds were screened and evaluated for their dopamine D2 and serotonin 5HT2 antagonistic activity as a measure of typical antipsychotic property. Compounds 4b, 4c, 4e, 4g and 4i have shown good preliminary pharmacological activity. Some of the better activity compounds were selected for determination of acute toxicity (LD50) studies by OECD guidelines and also for effective dose (ED50) determination by probit log scale method. The therapeutic index (TI) of the selected compounds was determined for selection of safer and better compounds. These synthesized derivatives were screened by molecular docking method. The compounds were sketched using ChemBioDraw Ultra 12 and subjected for all possible conformation of compounds interacting with receptors. Molecular docking was performed with the Glide 7.6, Maestro 11.3 of Schrodinger 2017. PDB for Dopamine receptor 6CM4 and for serotonin 5TUD were obtained from Brookhaven Protein database. The ligand-protein hydrogen bond network was obtained and total energy was minimized by employing OPLS 2005 force field. The docking poses were ranked according to GlideScore. From all above data results, compounds with electron withdrawing substitution like 4e and 4b has shown better atypical antipsychotic profile.

BIOGRAPHY

Ashish A Gawai is an Associate Professor at Department of Pharmaceutical Chemistry at Anuradha College of Pharmacy, India. He had completed his Master of Pharmacy in Pharmaceutical Chemistry from Bharti Vidyapeeth University, Poona College of Pharmacy, India and PhD in Pharmaceutical Sciences at Department of Pharmaceutical Sciences, Dibrugarh University, India. He has 12 years of teaching, 1.5 years of industrial experience and having more than 30 research papers and 50 research publications. He has also crashed Maharashtra Public Service Commission and Union Public Service Commission examination for Pharmacy post. He has attended to the invited conference at South Korea as well as several in India also. He has one published book entitled "A TEXTBOOK OF MEDICINAL CHEMISTRY" in his credit also. He is a potential reviewer for prestigious research journals like *Bentham Science, Indian Journal of Pharmaceutical Sciences* and many more. 24 students were completed Post-Graduation under his guidance. His research area is drug synthesis, drug design (Molecular modeling and docking study), toxicity studies and quality assurance.

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