DISCOVERY OF THE NOVEL PI3K/mTOR DUAL INHIBITOR BALOVAPTAN (RO-5285119) THROUGH STRUCTURE-BASED DRUG DESIGN FOR AUTISM TREATMENT

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Abstract:

Autism spectrum disorder (ASD) refers to a broad range of condition characterized by challenges with social skills, repetitive behaviour, speech and non-verbal communication. ASD is difficult to treat and a very less number of drugs are currently available in the market for example the first discovered anti-psychotic drugs are Respirodone and Ariprazole. PI3k and mTOR are the key kinase signaling pathways involved in cancer and many neurodegenerative disorders such as Autism and Schizophrenia. Recent evidences also demonstrated that disruption of several pi3k/mTOR elements causes Autism. In search of structurally different back up candidate to balovaptan (RO-5285119) which is currently approved in Phase-I /II clinical trials for treating ASD.The present study is aimed to carry out the lead optimization on the tricyclic benzodiazepines-triazole series. The lead optimization for the tricyclic series leads to potent anti-autistic analogues with an improved efficacy. The optimization of balovaptan analogues was carried out using molecular docking approach as PI3k/mTOR dual targets for ASD. Our results conclude that lead optimization was carried out successfully and new lead compounds having a good potency against ASD were identified.

Keywords: Autism, PI3k and mTOR, balovaptan, molecular docking