[P31] Computer aided drug design towards new inhibitors of Kynurenine Aminotransferase

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Kynurenine aminotransferase (KAT) is a promising target for the development of future central nervous system(CNS) medication. KAT is an enzyme catalyzing the transformation of kynurenine into kynurenic acid, a metabolite implicated in CNS disorders including schizophrenia. A limited amount of inhibitors of KAT are known but they suffer from drawbacks such as low chemical diversity, potential toxicity and difficulty of preparation. In this study, in silico methods were used to predict new distinct chemotypes that inhibit KAT. Candidate inhibitors were selected, refined and scored using pharmacophore modeling of known inhibitors, bulk virtual screening and rational drug design. Molecular docking of the candidate inhibitors and comparison with binding modes of known inhibitors were used to cross-validate the novel compounds. This resulted in a list of highly promising drug candidates. The obtained molecules have superior qualities such as chemical diversity and synthetic and commercial availability and thus facilitate the development of superior, modern therapies for CNS disorders.