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RESEARCH ARTICLE

IN SILICO PHARMACOPHORE VALIDATION OF ANTICONVULSANT ACTIVITY OF (*E*) (±)-3-MENTHONE DERIVATIVES

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In an endeavor to pursuit new strategies beyond conventional ones, energetically optimized, structure based pharmacophore was used for *in silico* anticonvulsant screening in present investigation. The study combines pharmacophore perception with protein-ligand interactions (docking) computed by *BioPredicta* and *MolSign* of VLife Molecular Design Suite 4.3.0. We derived energy-optimized pharmacophoric features for six anticonvulsants relevant to (*E*)-(±) 3-menthone derivatives (J_6, J_{14}, J_{25}, J_{30}, J_{32}, J_{33}) to access novel and potent GABA-AT inhibitors. Docking produced the most cases (5/6) with score greater then Vigabatrin, a well known GABA-AT inhibitor with proven clinical anticonvulsant efficacy. The docking results suggest the probable mechanism of anticonvulsant action that leverages the strong H-bonding (LYS329A, ARG192A) and *π*-stacking interactions (PHE189A) with GABA-AT receptor.

Key words: Pharmacophore, Anticonvulsant, Menthone, GABA-AT, Docking.

INTRODUCTION

Target and lead discovery constitute the main components of today's early pharmaceutical research (Bansal *et al* 2011; Sharma *et al* 2011; Kumar, 2011). Today, there is a urgent need for new antiepileptic drugs, since long established antiepileptic drugs control seizures in 50% of patients developing partial seizures and in 60-70% of those developing generalized seizures (Duncan, 2002; Kulandasamy *et al* 2009a, b). During past decade numerous new drugs were approved but despite the advances, approved antiepileptic drugs have dose related toxicity and idiosyncratic side effects (Ghogare *et al* 2010). The field of antiepileptic drug development (AED) has become quite dynamic, affording many promising research opportunities. Mechanistic approaches are increasingly being facilitated by the wave of research in the epileptics (Eadie and Tyrer, 1989). The search continues for the ideal drug that should be potent, selective in raising seizure threshold and preventing seizure spread without causing serious side effects. Structural features of most of the currently used antiepileptic have indicated presence of hydrazones (=N-NH-), amides (-$CONH_2$), carbamides (-NHCONH-) and semicarbazido groups (=NNHCONH-). Majority of active compounds were found to contain large hydrophobic group in close proximity to two