

## Suven Research Publications upto June 2014

### 1. J Enzyme Inhib Med Chem. 2014 Mar 25. [Epub ahead of print]

**Design, synthesis and pharmacological evaluation of indolylsulfonamide amines as potent and selective 5-HT<sub>6</sub> receptor antagonists.**

**Nirogi RV, Bandyala TR, Reballi V, Konda JB, Daulatabad AV, Khagga M.**

Abstract

Abstract A series of N'-[3-(indole-1-sulfonyl) aryl]-N,N-dimethyl ethane-1,2-diamines and N'-[3-(indole-1-sulfonyl) aryl]-N,N-dimethyl propane-1,3-diamines was designed and synthesized as 5-HT<sub>6</sub> receptor ligands. These compounds, when screened in a functional reporter gene-based assay, displayed potent antagonistic activity with K<sub>b</sub> values in the range of 1.8-60 nM. The lead compound 9y has shown good ADME surrogate properties, acceptable pharmacokinetic profile and is active in animal models of cognition like novel object recognition test and Morris water maze. It was selected for detailed profiling.

PMID: 24666297 [PubMed - as supplied by publisher]

### 2. Pharmacol Rep. 2014 Jun; 66(3):394-8. doi: 10.1016/j.pharep.2013.10.007. Epub 2014 Apr 13.

**Role of glutamate and advantages of combining memantine with a 5HT<sub>6</sub> ligand in a model of depression.**

**Abraham R, Nirogi R, Shinde A.**

Abstract

BACKGROUND:

It is a well-known fact that 5HT<sub>6</sub> ligands increase glutamate levels. In the current study we investigated whether a 5HT<sub>6</sub> antagonist, SB399885 would show antidepressant like property at a dose which would significantly increase the glutamate levels. Further we studied if the combination of a 5HT<sub>6</sub> antagonist and N-methyl-D-aspartate (NMDA) antagonist, memantine would restore the antidepressant property. As dementia and depression are co-morbid, we evaluated if this combination would have an effect on cognition.

METHODS:

The antidepressant like property of SB399885 alone and in combination with memantine was investigated using the forced swim test (FST). Object recognition task (ORT) was used to investigate the combination therapy on cognition. Additionally, glutamate levels in prefrontal cortex and corresponding brain concentration of SB399885 were determined.

RESULTS:

Brain concentrations of SB399885 equal to or greater than 553nM significantly increased brain glutamate levels and reduced immobility time in FST. When combined with memantine, glutamate levels and immobility time in FST was reduced. A dose dependent increase in the discriminative index was observed in ORT.

CONCLUSION:

Loss of antidepressant like property seen at the highest tested dose of SB399885 could be due to increased glutamate levels which was reversed by memantine. Combining memantine and SB399885 offers the advantage of extending the therapeutic window of antidepressant like property of SB399885 as well as having procognitive effect. The combination therapy holds promise in treatment of dementia associated with depression.

PMID: 24905514 [PubMed - in process]