ABSTRACT OF THE REVISED THESIS ENTITLED “SYNTHESIS AND BIOLOGICAL EVALUATION OF INDOLE AND THIENOPYRIMIDINE DERIVATIVES AS 5-HT₆ RECEPTOR LIGANDS.”

The theme of the research work is design and synthesis of novel molecules which have potent affinity towards 5-HT₆ receptors. Based on this concept, design and synthesis of novel 5-(N-substituted piperazinyl)-N¹-aryl (sulfonyl, carbonyl and methylene) indole derivatives and fused thieno pyrimidine derivatives were undertaken and evaluated the in-vitro activity of these derivatives. 5-(N-substituted piperazinyl)-N¹-arylsulfonyl indoles were found to have potent affinity towards 5-HT₆ receptors. So these derivatives were further taken up for their evaluation in in-vivo studies. They have good selectivity over other receptors and no CYP liabilities. These derivatives were further profiled in animal models of cognition like Novel Object Recognition Test (NORT) and Morris water maze. Oral administration of these compounds has shown improvement in performance of rats in NORT and significantly reversed scopolamine induced special memory deficit in Morris water maze test indicating improvement in cognitive potential of the compounds.

The revised thesis is divided into seven chapters and a simplified overview of these chapters was presented below.
**Present Work:**

It is evident from the literature that 5-HT₆R area is currently the hottest topic for the identifying potent therapeutic agents as for cognitive disorders. So, we considered the 5-HT₆R research area as an area of immense importance and worthwhile to study. Accordingly, we have designed and synthesized a few novel series of molecules and subjected them to *in-vitro* and *in-vivo* activity studies targeting 5-HT₆R.

**CHAPTER - 1:**

This chapter deals with the introduction to G-protein couple receptors with special reference to serotonin 5-HT₆ receptors and their drug action.

**CHAPTER - 2:**

This chapter deals with the synthesis of 5-(*N*-substituted piperazinyl-*N*¹-arylsulfonyl-1H-indole derivatives using Leimgruber method of indole synthesis which involves the condensation of substituted ortho nitro toluenes with *N*,*N*-dimethylformamide dimethyl acetal followed by reductive cyclization of the resulting trans-β-dimethylamino-2-nitrostyrene derivatives.

**CHAPTER - 3:**

This chapter deals with the synthesis of 5-(*N*-substituted piperazinyl methyl-*N*¹-arylsulfonyl-1H-indoles using reductive amination of indole-5-carboxaldehyde derivatives with *N*-substituted piperazines in presence of sodium triacetoxy borohydride.
CHAPTER - 4:

This chapter deals with the synthesis of 3-chloro-5-(N-substituted piperazinylmethyl)-N\textsuperscript{1}-arylsulfonyl-1\textsubscript{H}-indoles using N-chlorosuccinimide as a chlorinating reagent.

CHAPTER - 5:

This chapter deals with the synthesis of 5-(N-substituted piperazinyl methyl)-N\textsuperscript{1}-arylcarbonyl and 5-(N-substituted piperazinylmethyl)-N\textsuperscript{1}-arylmethyl-1\textsubscript{H}-indoles using reductive amination method followed by acylation or aralkylation of indole nitrogen.

CHAPTER - 6:

This chapter deals with the synthesis of fused thienopyrimidines using Gewald’s reaction, involving the condensation of a ketone (or aldehyde) with α-cyanoester in the presence of elemental sulfur and a base to obtain substituted 2-aminothiophene derivatives. The latter compounds were converted into fused thienopyrimidine derivatives subsequently.

CHAPTER - 7:

This chapter deals with the \textit{in-vitro} results and the structure activity relationships of novel 5-(N-substituted piperazinyl)-N\textsuperscript{1}-arylsubstituted indole derivatives and fused thienopyrimidine derivatives, whose synthesis was discussed in Chapter - 2 to Chapter - 6, as 5-HT\textsubscript{6} receptor ligands.