SECTION-II

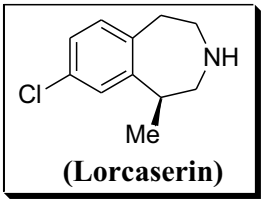
CHAPTER 2.
RESEARCH ENVISAGED

2. RESEARCH ENVISAGED

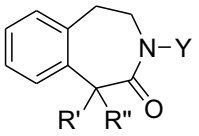
A guileless literature survey revealed that substitution at benzene ring in 3-benzazepine moiety has been sufficiently explored to throw open the following SAR points:

1. Substitution of chlorine, bromine, or trifluoromethyl at the 8-position or chlorine at the 7-position shows good 5-HT_{2C} potency.
2. Substitution of methoxy, fluorine, or hydrogen at only the 7 and 8 positions reduces potency.
3. Substitution of chlorine at either the 6- or 9-position shows lower potency.
4. Addition of a second substituent to the 8-chlorobenzazepine, regardless of the substituent (Cl, F, or OMe) or position, generally result in potent compounds.
5. For 8-chlorobenzazepines substitution at the 1-position with methyl or ethyl, all show good 5-HT_{2C} potency.

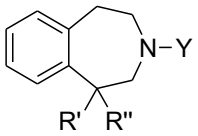
The search for potent and selective 5-HT_{2C} agonists has identified lorcaserin, recently approved by US-FDA for the treatment of obesity.



(Lorcaserin)



(A)



(B)

In light of the above observations, it was planned to initiate a hit-to-lead research program with the objective of seeking potent 5-HT_{2C} agonistic activity.

Considering lorcaserin as a lead molecule, target compounds **A** and **B** were planned for synthesis. Basic emphasis was given on the following points:

1. As the substitutions on 6, 7 and 8 positions in benzene ring has been well explored and reported, it was aimed to explore C_1 position, for mono- and di-alkyl substitutions.
2. It was also planned to explore the activity of di and tri-substituted 3-benzazepin-2-one compounds.