3. RESEARCH ENVISAGED

Lamotrigine and Oxcarbazepine, the drugs chosen in the present study, belong to Biopharmaceutics Classification System (BCS), Class II (Amidon et al., 1995), have poor water solubility (0.17mg/ mL (Neil MJO, 2006) and 0.084 mg/ mL (Stahl, 1972) at 25 °C respectively) which is a major hurdle in making these drugs bioavailable in the body. Thus, there is a need to develop alternative forms of lamotrigine and oxcarbazepine with improved solubility which can significantly enhance the oral absorption of these drugs in the gastro-intestinal tract.

The lamotrigine framework is comprised up of four acidic amino hydrogen bond donors along with two basic hydrogen bond acceptors i.e. amino-pyridine nitrogen atoms giving rise to a variety of hydrogen bonding donor/ acceptor sites for an approaching coformer to bind, thus making it a potential target for both co-crystal and salt formation. These features of lamotrigine along with the availability of vast number of coformers of GRAS status for co-crystallization provided a motivation to explore this multicomponent approach in an attempt to improve the biopharmaceutical parameters of this anticonvulsant drug.

Oxcarbazepine is a derivative of carbamazepine, which is of considerable structural interests as a model compound for studying polymorphs (four anhydrous crystalline forms known) (Florence et al., 2006; Harris et al., 2005), solvates (Rager and Hilfiker, 2010) and co-crystals (Childs et al., 2008; Fleischman et al., 2003; Jayasankar et al., 2006; Seefeldt et al., 2007; Porter et al., 2008; Ter Horst et al., 2009). Although, the basic backbone of oxcarbazepine has also been proved to be a polymorphophore (Lutker and Matzger, 2010), only two reports on polymorphism in oxcarbazepine have been reported while none is available on its co-crystals till date.

Keeping in mind, the above mentioned facts on these drugs, following objectives were set to be achieved.
Research Envisaged

1. To prepare various crystals (solvates/hydrates/polymorphs) of the above mentioned drug molecules using pure solvents or solvent mixtures and slow evaporation or solvent-antisolvent addition method.

2. To prepare co-crystals of the lamotrigine and oxcarbazepine with various co-crystal formers on a trial and error basis by solution crystallization method using slow evaporation technique and fast evaporation method (by utilizing rota-vapor).

3. To characterize the crystals and co-crystal forms by various thermo-analytical techniques (DSC, TGA and HSM), X-Ray Diffractiometry (PXRD and SCXRD), spectroscopic techniques (FT-IR and SS-NMR).

4. To investigate any improvement in pharmaceutical properties of these APIs by carrying out the solubility and dissolution studies in water and other appropriate medium.

5. To investigate the stability of identified crystals and co-crystal forms in solid state, under ambient and varying relative humidity conditions using various analytical techniques.

6. To evaluate the efficacy of selected crystals/co-crystals in vivo, using maximal electroshock (MES) model in mice.