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# Microemulsion of Lamotrigine for Nasal Delivery

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Epilepsy is a neurological disorder which requires quick management of seizures in order to avoid the risk of permanent brain damage. Intranasal administration allows transport of drugs to the brain circumventing BBB, thus providing a unique feature and better option to target drugs (for example lamotrigine) to the brain with quick onset of action in case of emergencies such as epilepsy. We have already reported microemulsion (ME) of lamotrigine for nasal delivery[1]. Further, previous studies on ME of tamoxifen citrate (hydrophobic drug) have demonstrated a dramatic increase in solubility with micellar and ME despite poor solubility of drug in oily phase[2]. This finding can be utilized in formulation of nasal ME of hydrophobic drugs. Improved solubilization by virtue of ME can exploited to accommodate higher drug concentration per unit nasal ME as nasal anatomy pose severe constraints on volume of formulation to be administered. This can aid reduction of dosage volume of nasal ME ultimately resulting in high patient compliance. The objective of present study was to evaluate the role of ME components in solubilization of lamotrigine. Ascertaining the role of ME components would create better understanding of the system for further formulation development.

## MATERIALS AND METHODS

Formulation components are listed in Table 1 with equilibrium solubility data. ME and micelles (MI) were formulated using surfactant - cosurfactant mixtures, Solutol HS 15 and Transcutol P in the ratio of 1:2 and Solutol HS 15: soluphor P in the ratio of 1:1, with and without oil phases, respectively. Solubilization by ME and MI was determined by adding excess of lamotrigine and concentration of solubilized drug was determined by UV spectrophotometry (307 nm) after 48 h of equilibration.

## RESULT AND DISCUSSION

The observed solubilization capacity of ME and MI systems was much lower than the predicted solubility calculated from the summation of contribution of each component of the system (Table 2). Furthermore the improvement in solubilization capacity of ME over MI was not high in relation to the equilibrium solubility data for lamotrigine in the three oil phases. Also the solubilization capacity of the ME did not increase with

**TABLE 1: FORMULATION COMPONENTS AND EQUILIBRIUM SOLUBILITY OF LAMOTRIGINE**

| | Formulation components (mg/ml ± SE) | Lamotrigine solubility |
|---|---|---|
| Oily phases | Capmul MCM | 45.13 ± 0.1821 |
| | Peceol | 18.04 ± 0.3564 |
| | Captex 355 | 0.93 ± 0.1245 |
| Surfactant | Solutol HS 15 | 67.06 ± 0.7189 |
| Co surfactants | Transcutol P | 133.39 ± 0.7726 |
| | Soluphor P | 13.46 ± 0.3834 |
| Aqueous phase | Water | 0.17 ± 0.678 |

**TABLE 2: COMPARISON OF PREDICTED AND OBSERVED SOLUBILIZATION CAPACITIES OF ME AND MI**

| Oil phase | Concentration of oily phase (% w/w) | Solubility (mg/ml) Predicted | Solubilization (mg/ml±SE) capacity observed |
|---|---|---|---|
| Capmul MCM | 3.5 | 68.32 | 34.01±0.034 |
| | 8.5 | 70.67 | 34.07±0.9596 |
| Peceol | 3.5 | 67.38 | 29.87±0.685 |
| | 7 | 68.1 | 30.02±0.1555 |
| Captex 355 | 3.5 | 66.78 | 28.57±0.1619 |
| | 5 | 66.79 | 28.55±0.448 |
| Micelles | - | 66.75 | 26.33±0.125 |

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increase in concentration of the oil phase irrespective of solubility in oil.

Solubilization capacity of ME of lamotrigine was significantly lower than predicted. Moreover no appreciable difference was seen in solubilization capacity of MI and ME formulation. This observation though contrary to our previous study with tamoxifen, where marked increase in solubilization was observed, was in accordance with reports on steroid ME[3]. Though the oil phase is known to play a significant role in generation of the interface it may not always play a major role in drug solubilization. Moreover, cosurfactants may affect the micelle structure[3] thereby causing significant reduction in solubilization by MI and ME despite high solubility of drug in cosurfactant. The decreased solubilization of lamotrigine by ME compared to the predicted could be due to interaction of the drug with ME components. This however needs to be explored and confirmed. However adequate solubilization was observed to enable design of ME [5 mg lamotrigine per actuation (100 µl)] for nasal delivery.

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