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Oxcarbazepine: Preformulation Studies of Authoritative Part of Formulation Design

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Abstract: Preformulation research is a stage that is started before the novel molecule is seeded. In a larger sense, it connects with studies of a molecule's physical, chemical, analytical, and medicinal properties and offers ideas about appropriate modifications that could be made to improve performance. The analysis of preformulation characteristics can contribute to the development of pharmaceutical formulations that are efficient, safe, dependable, and stable. Oxcarbazepine is an antiepileptic drug. It controls seizures or fits by declining the abnormal and excessive activity of the nerve cells in the brain.

Keywords: Preformulation study, Oxcarbazepine, Solubility & analytical methods.

Research Paper

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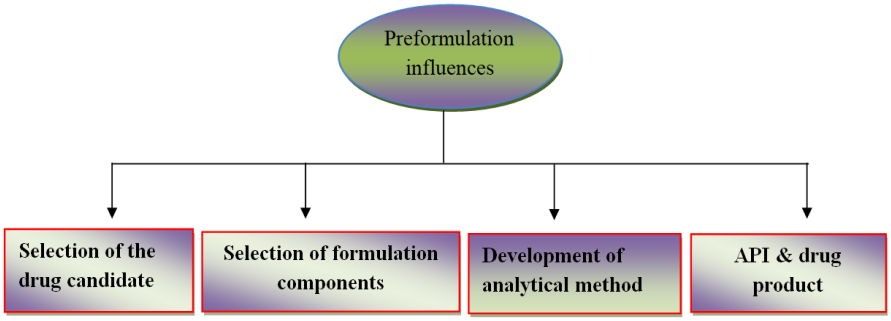
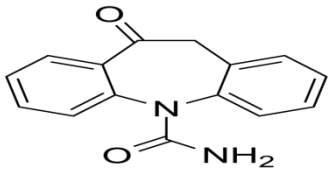
INTRODUCTION

The primary step in the logical development of dosage forms for a medicinal substance is preformulation research. The study comprises a review of the drug substance's physical and chemical characteristics both by itself and when paired with an excipient. The main goal of preformulation testing is to produce data that will aid the formulator in creating stable, bioavailable dosage forms that can be mass produced. Preformulation studies are made to provide the relevant information, particularly on the physicochemical, physico-mechanical, and biopharmaceutical properties of medicinal ingredients, excipients, and packaging materials [1]. These investigations should concentrate on the novel compound's physicochemical characteristics that may have an impact on medication performance and the creation of an efficient dosage form. A rationale for formulation design could someday be provided by a systematic study of these features [2, 3]. Oxcarbazepine is a new anticonvulsant with an active metabolite. It is approved as mono- or adjunctive therapy for partial seizures in adults and children older than 4 years of age and as adjunctive therapy in children 2 years and older. Its spectrum of anticonvulsant activity is comparable to carbamazepine, but it has an improved pharmacokinetic profile, is better tolerated and is associated with few clinically significant drug-drug interactions [4, 5].



Drug (Oxcarbazepine) description [6, 7]	
IUPAC Name	5-oxo-6*H*-benzo[b][1]benzazepine-11-carboxamide
Structure	
Molecular formula	$C_{15}H_{12}N_2O_2$
Molecular Weight	252.27 g/mol
Solubility	Slightly soluble in chloroform, dichloromethane, acetone, and methanol and practically insoluble in ethanol, ether, and water.
Therapeutic category	Anticonvulsant drug

In the present works a challenge was made to study preformulation parameters of Oxcarbazepine which helps to produce information useful in developing stable and Bioavailable dosage forms.

MATERIAL AND METHODOLOGY

Procurement of Drug

Oxcarbazepine was obtained as gift sample from Psycho remedies limited, Ludhiana.

Organoleptic Properties

Organoleptic properties of the drug sample were studied by visual inspection.

Preformulation Studies [8-16]

Identification of Drug

Melting Point Determination

To determine the M.P. of drug powder, it was filled in a capillary tube with one end open and the other end closed and then the capillary was placed in a digital melting point apparatus.

Solubility

The solubility of oxcarbazepine in different solvent like distilled water, methanol, dimethylsulfoxide and phosphate buffer pH 6.8.

Partition Coefficient

About 50mg of drug was dissolved in 50ml of distilled water and n-octanol separately and both the solution was mixed together by using wrist watch shaker for 30 min. Then the solution was kept in a separating funnel until two phases separated. The aqueous phase was then filtered through the filter paper and was diluted 100 times. The absorbance of both the solutions was taken at 234nm by using UV spectrophotometer. The concentration of drug was determined with the help of standard curve and partition coefficient was determined by following formula:

$$\text{Partition coefficient} = \frac{\text{Concentration of drug in organic phase}}{\text{Concentration of drug in aqueous phase}}$$

FTIR Spectroscopy Studies

FTIR (ATR Bruker, Germany) was used. The IR spectrum was obtained by scanning it in the range 4000-500nm and compared with the reference pharmacopoeia (IP-2014).

Analytical Method

100 mg of oxcarbazepine was taken in 100 ml volumetric flask, the drug was dissolved in ethanol and volume was making up to the 100 ml with (stock solution A). 10 ml of stock solution was taken in another 100 ml volumetric flask and volume was make up to 100 ml with ethanol (stock solution B i.e., 100 µg/ml solution was obtained). From the solution, aliquots of 0.5 ml, 1.0 ml, 1.5 ml, 2.0 ml, were taken and diluted up to 10 ml in order to get concentration ranging from 5-100 µg/ml. These concentrations were used to conclude absorbance at λ_{max} 372 nm against blank (ethanol) using UV-VIS spectrophotometer. The calibration of oxcarbazepine was done in ethanol and phosphate buffer.

Table 1: Preformulation Characteristics

S. No.	Characteristics	Results
1.	Colour	Yellowish
2.	Odour	Odourless
3.	Taste	Slightly bitter
4.	Partition coefficient	1.31
5.	M.P.	215^0C

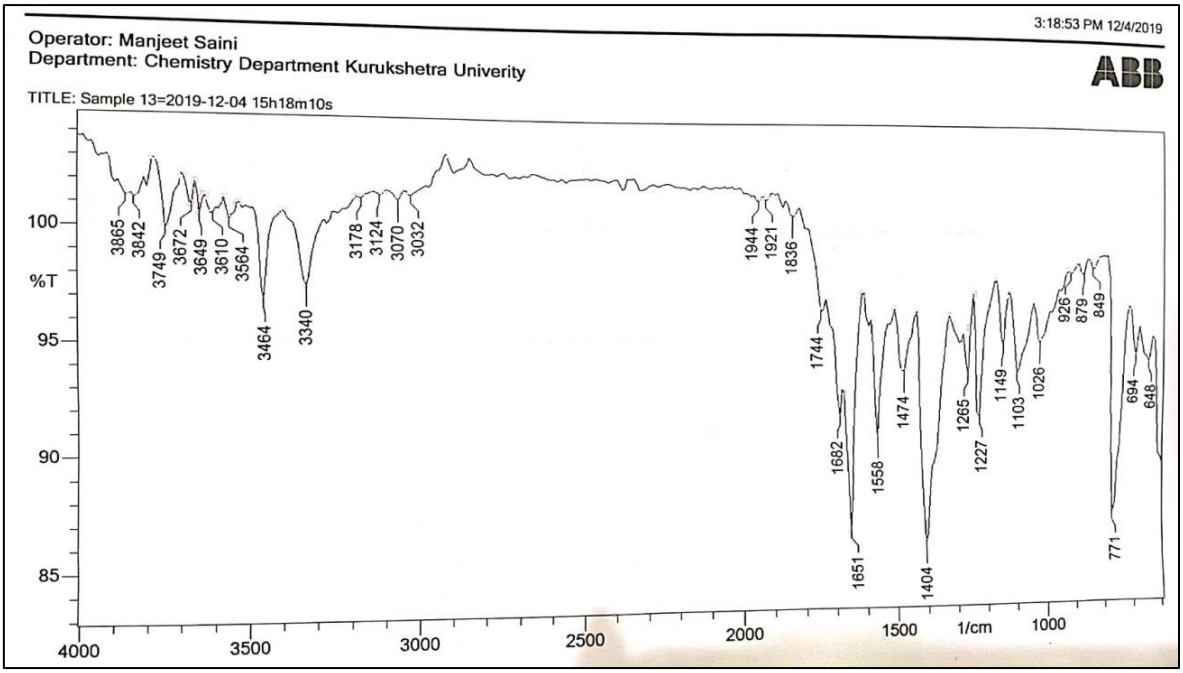


Figure 1: FTIR of oxcarbazepine

Table 2: Interpretation of Oxcarbazepine [FT-IR]

Oxcarbazepine		
Sr. No.	**Peaks**	**Functional group**
1.	3467	NH and hydrogen bond
2.	3340	NH
3.	1685	C=O
4.	1407	C-N
5.	1558	(-C=C),NH deformation

Table 3: Calibration data of oxcarbazepine in ethanol

S. No.	Concentration	Absorbance
1.	0	0.000
2.	10	0.252
3.	15	0.482
4.	20	0.741
5.	25	0.947
6.	30	1.172

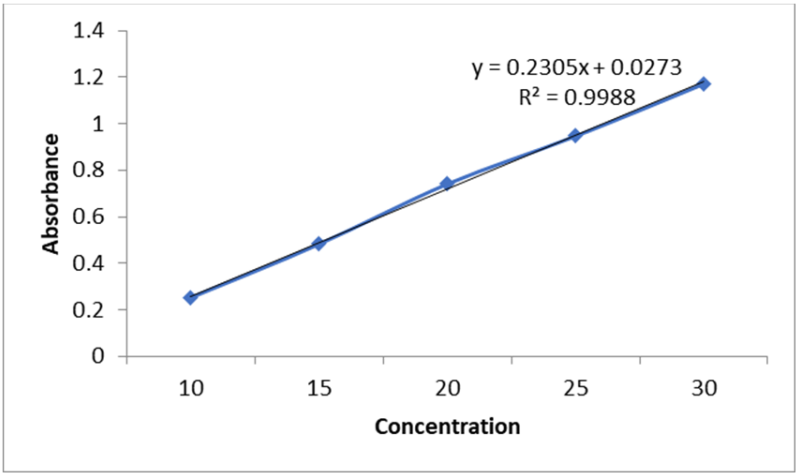


Figure 2: Calibration data of oxcarbazepine in ethanol

Table 4: Calibration data of oxcarbazepine in phosphate buffer $_{P}$H6.8

Sr. No.	Concentration	Absorbance
1.	0	0
2.	10	0.095
3.	15	0.194
4.	20	0.346
5.	25	0.465
6.	30	0.575

Calibration data of oxcarbazepine in phosphate buffer $_{P}$H6.8

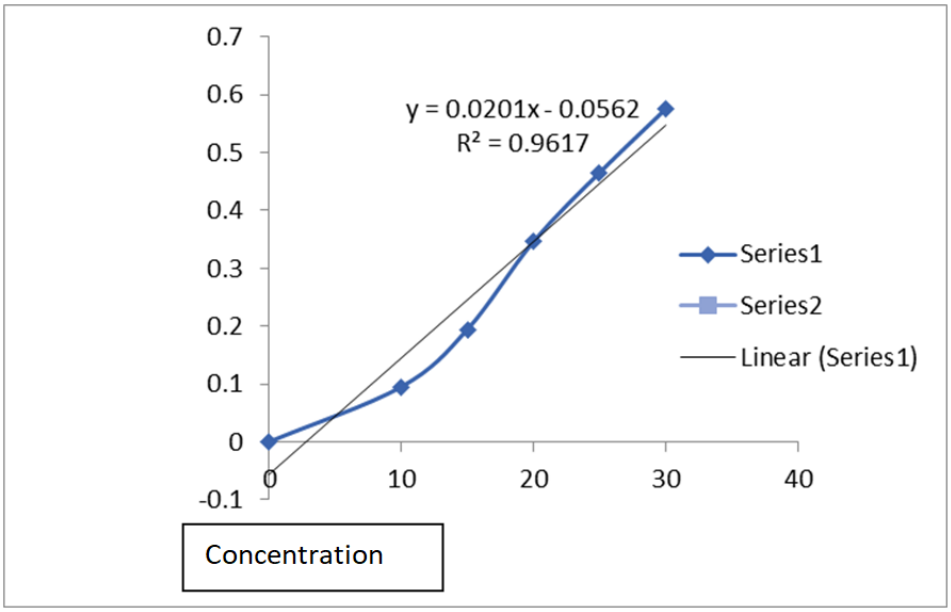


Figure 3: Calibration data of oxcarbazepine in phosphate buffer $_{P}$H6.8

Table 5: Solubility of oxcarbazepine in different solvents

Sr. No.	Solvent	Interpretation
1.	Distilled water	Practically insoluble
2.	Acetic acid	Soluble
3.	Ethanol	Soluble
4.	Phosphate buffer 6.8	Practically insoluble

RESULTS AND DISCUSSION

The in general purpose of the present work was to investigate preformulation studies of new antiepileptic drug oxcarbazepine is to generate information useful in developing stable and Bioavailable dosage forms. Preformulation studies of drug were undertaken concerning melting point, solubility analysis, UV-spectrophotometric analysis and FTIR analysis to identify and assessment of purity of drug. Various Preformulation Characteristics were tabulated in table 1. The partition coefficient of oxcarbazepine was found 1.31, which confirms the lipophilicity of the drug. The drug was found to be freely soluble in acetic acid and in ethanol, practically insoluble in dist. Water and phosphate buffer 6.8, which matches the existing reference. The analytical method for determination of drug was UV spectroscopy. The absorption spectral analysis showed the λ_{max} of oxcarbazepine at 372 nm in ethanol and phosphate buffer pH 6.8 respectively (table 3-4 & Fig. 2-3). The FTIR spectrum, there was no variation in the oxcarbazepine peaks from the standard spectrum of IP 2014(fig 1). The result of interpretation of IR spectra was tabulated in table 2. Preformulation studies revealed the purity of the drug. UV-spectrophotometric analysis of drug in ethanol and phosphate buffer pH 6.8 ($y = 0.2305x + 0.0273$, $R^2 = 0.9988$ in ethanol and $y = 0.0201x + 0.0562$, $R^2 = 0.9617$ in phosphate buffer pH 6.8) revealed the suitability of the standard curve for further calculation.

CONCLUSION

The preformulation step is a fundamental fraction in establishing the properties of drug that will allow suitable risk assessment for development. Usually, it begins all through the lead optimization

phase, continues through predomination, and on into the early on phases of development. Hence, it is necessary that preformulation should be performed as carefully as possible to facilitate coherent decisions to be made. The preformulation study of oxcarbazepine is to make information useful in developing stable and Bioavailable dosage forms.

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