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ORIGINAL RESEARCH ARTICLE

Physicochemical Properties of Lamotrigine and its Compatibility with Various Inactive Ingredients to Formulate Lamotrigine Orally Disintegrating Tablets

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ABSTRACT

The aim of the present study was to understand physicochemical properties of Lamotrigine and its compatibility with various inactive ingredients (excipients) which are suitable to formulate Lamotrigine Orally Disintegrate Tablets. Each excipient selected was individually mixed with Lamotrigine and this blend was stored in a closed vial at accelerated stability condition, 40°C±2°C/75% ±5% RH for one month. The samples were analyzed for Related Compounds to determine the drug excipients compatibility.

Key words: Lamotrigine, excipients, Orally Disintegrate Tablets.

INTRODUCTION

Due to the growing complexity of drug substances and formulations, developing a quality drug product and a process that manufactures it in a reproducible manner becomes increasingly challenging and costly [1]. Proper understanding of drug substance properties is essential for pharmaceutical development to maintain the critical quality attributes throughout the product shelf life. A detailed understanding of the properties of the drug substance helps to minimize formulation problems in later stages of drug development and reduce drug development costs.

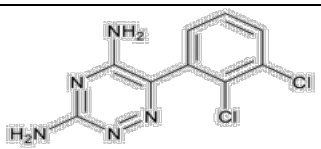
Important part in developing orally disintegrating tablets is proper understanding of drug substance properties and excipient selection. It is preferable to use excipients that are compatible with the drug substance to maximize drug-product stability and to have desired bioavailability. It is critical to understand the physicochemical properties of the drug substance, and preformulation compatibility studies will help identify incompatibilities so that certain excipients can be avoided during pharmaceutical development of drug product for better drug product stability.

The orally disintegrating products are designed to disintegrate or dissolve rapidly on contact with saliva by placing them on the tongue, thus eliminating the need to chew the tablet, swallow an intact tablet, or take the tablet with liquids [2]. This mode of administration is beneficial to pediatric and geriatric patients, to people with conditions related to impaired swallowing, and for treatment of patients when compliance may be difficult (e.g., for psychiatric disorders).

EXPERIMENTAL

1. Physicochemical Properties of Lamotrigine:

Lamotrigine is an antiepileptic drug (AED) indicated for Epilepsy - adjunctive therapy in patients ≥2 years of age: partial seizures; primary generalized tonic-clonic seizures; generalized seizures of Lennox-Gastaut syndrome [3].

Physicochemical Properties of Lamotrigine	
Chemical Name	1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)
Chemical Structure	
Formula	$C_9H_7Cl_2N_5$
Molecular weight	256.09

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Appearance	A white to pale cream-colored powder
General Solubility	Slightly soluble in 0.1 N hydrochloric acid, in acetone, in methanol, and in water.
Melting Range	214°C to 220°C
pKa	5.7
Partition Coefficient:	1.19 at pH 7.6
Polymorphism	Solvated forms and hydrated forms are reported in the literature.
Stereochemistry	Lamotrigine does not show any Stereochemistry
Hygroscopicity	Lamotrigine is not hygroscopic

Solubility as a function of pH

Medium	Solubility (mg/mL)	Solubility (mg/250ml)	Remarks
0.1 N HCl	2.87	717.50	Soluble
0.01 N HCl	2.74	685.00	Soluble
0.001 N HCl	0.44	110.00	Insoluble
pH 4.5 Acetate buffer	1.44	360.00	Soluble
Purified Water	0.20	50.00	Insoluble
pH 6.8 phosphate buffer	0.21	52.50	Insoluble
pH 7.2 phosphate buffer	0.19	47.50	Insoluble

Based on above pH solubility data, Lamotrigine is found to be demonstrating pH dependent solubility. Lamotrigine having low solubility and high permeability categorized as Class II drug as per BCS Classification.

2. Compatibility of Lamotrigine Drug Substance with Inactive Ingredients:

Excipients compatibility studies were carried out to study the compatibility of various excipients selected in the formulation with Lamotrigine. Each excipient selected was individually mixed with Lamotrigine and this blend was stored in a closed vial at accelerated stability condition, 40°C±2°C/75% ±5% RH for one month. The samples were analyzed for Related Compounds to determine the drug excipients compatibility. The results are provided in (**Table 1**).

RESULTS AND DUSCUSSION

Table 1: Excipients Compatibility with Lamotrigine

Drug:Excipient	Impurity	Initial	1 month
Lamotrigine: Mannitol	Impurity B Impurity C Impurity D Unknown Impurity Total Impurities	Not Detected	Not Detected
Lamotrigine: Micro Crystalline Cellulose -102		Not Detected	Not Detected
Lamotrigine: Pregelatinised starch		Not Detected	Not Detected
Lamotrigine: Aspartame		Not Detected	Not Detected
Lamotrigine: Crospovidone		Not Detected	Not Detected
Lamotrigine: Colloidal Silicon Dioxide		Not Detected	Not Detected
Lamotrigine: Sodium Chloride		Not Detected	Not Detected
Lamotrigine: Magnesium Stearate		Not Detected	Not Detected
Lamotrigine: Peppermint Flavor		Not Detected	Not Detected

Impurity B: 2,3-Dichlorobenzoic acid
Impurity C: 3-Amino-6-(2,3-dichlorophenyl)-1,2,4-triazin-5(4H)-one
Impurity D: N-[5-Amino-6-(2,3-dichlorophenyl)-1,2,4-triazin-3-yl]-2,3-dichlorobenzamide

CONCLUSION

A review of the above data shows that there is no increase in the quantity of the known related compounds of Lamotrigine in the presence of the above excipients for a period of one month at accelerated stability conditions of 40^{O}C and 75% Relative Humidity. It was also observed that the unknown impurities and total impurities for Lamotrigine with all excipients were well within the specifications. It was therefore concluded from above experiment that the tested excipients are compatible with Lamotrigine and were acceptable for use in the drug product, Lamotrigine Orally Disintegrating Tablets.

REFERENCES

1. Martin, A., Swarbrick.j., and Commarata,A.: Physical Pharmacy: Physical Chemical Principles in the Pharmaceutical sciences. 3rd ed. Lea and Febiger, Philadelphia, 1983.
2. Chien Y W, "Novel Drug Delivery Systems," ed. By Chien Y. W., Marcel Dekker, Inc., New York, U.S.A., 1992.
3. Prescribing Information for LAMICTAL® (lamotrigine) orally disintegrating Tablets dated November 2011.
4. USP35–NF30 Page 3635 Pharmacopeial Forum: Volume No. 34(3) Page 617.