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Stability Study of Enalapril Maleate in Tablet Form Using High Performance Liquid Chromatography Techniques.

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ABSTRACT

This paper demonstrates the stability studies of Enalapril Maleate. The results observed from the stability during the storage of Enalapril Maleate tablets give better result with alkali compounds e.g. sodium bicarbonate. The influence of various parameters such as heat, moisture was investigated. The degradation of Enalapril Maleate has been followed by using an HPLC. Enalapril Maleate is much stable when it is prepared in form of Enalapril sodium salt. Enalapril Maleate alone showed high stability for temperature under dry and humid conditions, however it became unstable when mixed with the drug-matrix in its tablet formulations and exposed to the same conditions. The pathway of degradation of Enalapril Maleate was found to be pH dependent. The Enalapril Maleate show better stability in pH range 2.00 – 7.00. Enalapril Maleate shows the incompatibilities with various excipients silicon dioxide, lactose, microcrystalline cellulose & magnesium stearate.

Keywords: Enalapril Maleate, Stability, HPLC, Excipients, Enalaprilat.

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INTRODUCTION

Enalapril Maleate is the ethyl ester of long acting angiotensin-converting enzyme inhibitor. It is indicated for the treatment of essential and renovascular hypertension. Enalapril is a prodrug followed by oral administration; it is bioactivated by hydrolysis of the ethyl ester to enalaprilat, which is the active angiotensin-converting enzyme inhibitor. [1]

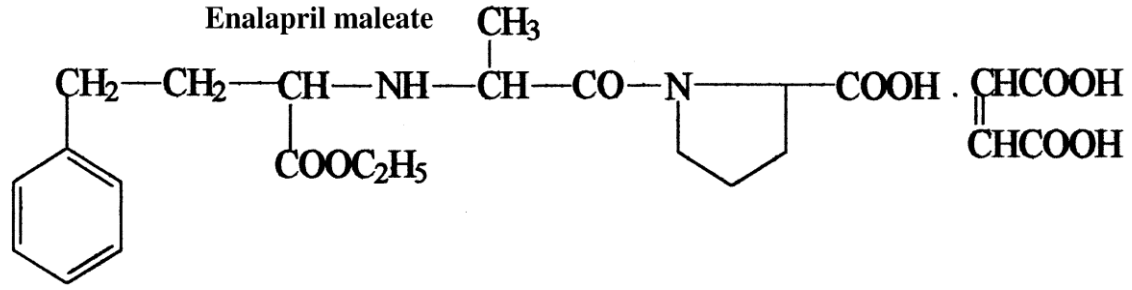

Fig a): Enalapril Maleate.

It is reported that the Enalapril degrades two major degradation products Enalaprilat (Below pH 5) & Diketopiperazine (Above pH 5).[2] The objective of this study to validate the chemical stability of Enalapril Maleate drug substance under stress testing in salt form using High Performance Liquid Chromatography. Thermo analytical methods are commonly used for pharmaceutical problem. Chemical degradation of active drug creates a problem and causes the loss in potency. As per many pharmaceutical preparation 90% of labeled potency is required as minimal potency level. Many factors are responsible for the degradation of the active drug substance. Enalapril Maleate tablet form when mixed with lactose, magnesium stearate as he lubricant it will causes degrades into Diketopiperazine and enalaprilat at high temperature in accelerated study and also responsible for the change in appearance of tablet. [3] The reaction between Enalapril Maleate and Sodium bicarbonate increases the thermal stability of the drug. Stoichiometrically, one mole of Enalapril Maleate reacts with 3 moles of NaHCO3 which is 252.0g. For 1.0 gram of Enalapril Maleate, the amounts required are 0.512 g of sodium bicarbonate. [4]

MATERIAL AND METHOD

Enalapril Maleate and excipients pharmaceutical grade. They were donated by a Sinochem mingbo ltd., China Company. The excipients were Sodium bicarbonate (AVA Chemicals), Isopropyl alcohol (China), Stearic acid, Maize starch, Pvpk-30, Starch 1500, Mannitol, Talcum Stearic Acid, and Crospovidone.

Enalapril Maleate and sodium bicarbonate were carried out using mixtures of drug and excipients. Excipient was mixed with the drug and $NaHCO_3$ and stay for some time period until the reaction is completed. The two products were reacted separately after that all excipients

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mixed with drug and $NaHCO_3$. Once the reactions were completed, the resulted products were dried in fluid bed dryer. Lubrication was done with the stearic acid and talcum.

Table 1: Enalapril Maleate tablet physical parameter.

Parameter	Specifications	Results
Weight	204±2%	204mg
Diameter	8.7±0.1mm	8.68mm
Thickness	2.7±0.2mm	2.71mm
Hardness	Not less than 2.0kg/cm^2	2.0kg/cm^2
Disintegration	Not more than 15 minutes	7 minutes
Friability	Not more than 1.0%w/w	0.36%w/w

REAGENT AND CHEMICAL

Enalapril Maleate standard, Acetonitrile HPLC grade (Rankem), Potassium hydrogen phosphate, Hydrochloric acid.

INSTRUMENTATION AND CHROMATOGRAPHIC CONDITIONS

Liquid Chromatography (Waters), Automatic injector and a 50 µl injection volume. Stainless steel column 20cm x 4.6mm, packed with octylsilane bonded to porous silica 3 to 10µm (Waters). Column temperature 50^{0}c, flow rate was 2.0ml/min. The mobile phase consisted of acetonitrile – phosphate buffer pH 2.0 (25:75v/v). The UV detection was made at 215nm.

SAMPLE PREPARATION

Weigh and powder 20 tablets. A portion equivalent to 50 mg of Enalapril Maleate was accurately weigh, add 150ml of phosphate buffer pH 2.0, disperse with the aid of ultrasonic sound for 15 minutes and shake for 30 minutes and diluted with buffer to 250.0 ml volume, mix and filter. [6]

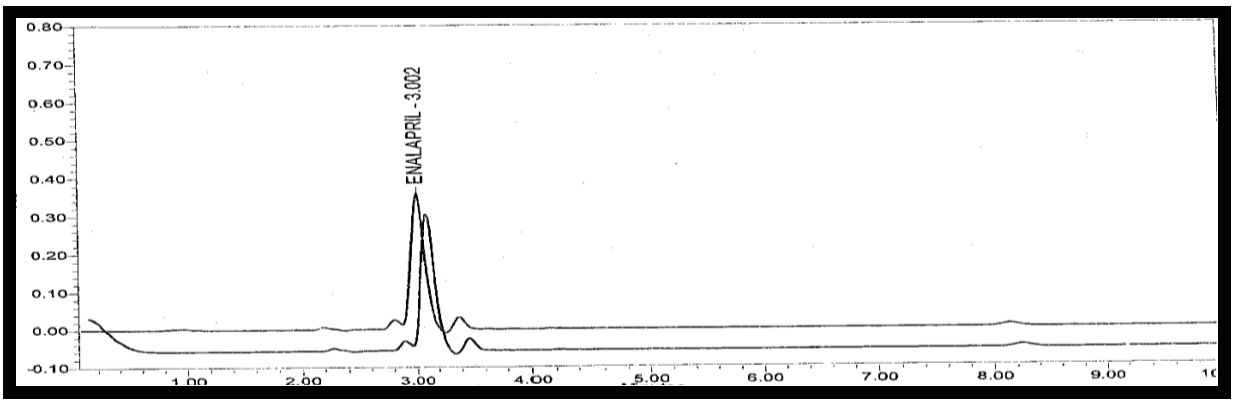

Fig 2:- HPLC chromatograms for Enalapril Maleate tablets.

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RESULT

Table 2:- Table represents the percentage of drug recovered.

Storage Condition	Amount of Enalapril Recovered
Enalapril Maleate tablets initial.	98.80%
Enalapril Maleate Powder	98.62%
Enalapril Maleate tablets 15 days open at room temp.	97.96%
Enalapril Maleate tablets 15 days open at 40^0c /75%.	97.72%
Enalapril Maleate tablets one month at 40^0c /75%. (Strip Packing)	98.73 %
Enalapril Maleate tablets Two month at 40^0c /75%. (Strip Packing)	98.42 %
Enalapril Maleate tablets Three month at 40^0c /75%. (Strip Packing)	97.20%

CONCLUSION

Enalapril Maleate tablet stability study can be studied by an HPLC method. Enalapril Maleate powder form is much stable as it's in active form at higher temperature. But it can show a degradation pattern when it is mixed with the formulation excipients of preparation. But the problem is resolving by converting the Enalapril Maleate to Enalapril Sodium salt. The Enalapril Sodium salt is stable in wider range in form of tablet by mixing with the excipients. However it there are various excipients which show the incompatibility with Enalapril Maleate, Like Colloidal silicon dioxide, Magnesium stearate, Lactose, & Cellulose derivative. Tablet is stable against moderate heat and humidity without using these excipients mention above. However, in tablet formulations, hardness problem are arising which is also solve by maize starch granules. Enalapril Maleate tablet formulations with an acidic matrix would have a better stability against humidity, environmental factor, & temperature as compared to basic matrix. Strip packing, pH, drug matrix, environmental conditions are major factors that affect the stability of the drug in its tablet formulations. [7]

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