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STABILITY STUDY OF ESOMEPRAZOLE PREPARATIONS IN DIFFERENT PACKAGING MATERIAL USING STABILITY INDICATING VALIDATED HPLC METHOD

Issa Al-Salloum[1*] and Bashar Al-Sabti[2]

[1]Faculty of Pharmacy, University of AL-Hawash, Syria.

[2]Faculty of Pharmacy, University of Damascus, Syria.

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***Corresponding Author**
Issa Al-Salloum
Faculty of Pharmacy,
University of AL-Hawash,
Syria.

ABSTRACT

A stability study of esomeprazole was carried out in accordance with the guideline for Industry Q1A(R2): Stability Testing of New Drug Substances and Products.[1] Esomeprazole is sensitive to heat, humidity, and light, consequently, accelerated tests for stability evaluation were performed at 40°C±2°C and 75±5% relative humidity (RH), according to the current official guideline. The samples were kept in a climatic chamber for 6 months in the conditions described above. The samples were withdrawn from the climatic chamber and analyzed periodically (0,1,2,3,6 months) by an HPLC method with UV detection. A standard statistical methodology was used to calculate the expiration date based on the analytical results obtained in the studied samples. Long-term stability tests were also performed at 25°C±2°C and 60±5% relative humidity (RH), according to the current official guideline. The samples were kept in a climatic chamber for 3 years in the conditions described above. The samples were withdrawn from the climatic chamber and analyzed periodically (0,3,6,9,12,18,24,36 months) by the previous method mentioned above. Also, many samples are put in different conditions of temperature and humilities and analysis after that. The purpose of this study was to select the best packaging and container for esomeprazole products and to use the results obtained in stability testing in order to estimate the expiration date in normal room temperature conditions (25°C±2°C).

KEYWORDS: Stability, accelerated, long-term, Esomeprazole, HPLC.

1. INTRODUCTION

Esomeprazole magnesium trihydrate (ES), bis (5-me thoxy-2- [(S) - [(4-me thoxy-3,5 dime thyl -2- pyridinyl)methyl]sulfinyl-1H-benzimidazole-1-yl) magnesium trihydrate (Figure 1) is the S isomer of racemic omeprazole approved in February 2001 for use as a new pharmacological entity designed to improve the clinical outcome of available proton pump inhibitors in the management of acid-related disorders.[2,3]

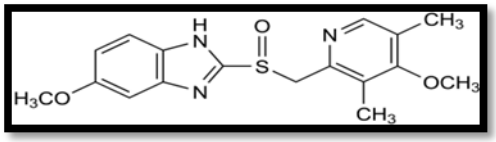

Figure 1: The structure of omeprazole.

Esomeprazole is widely used in the prophylaxis and treatment of gastro-duodenal ulcers and the treatment of symptomatic gastroesophageal reflux. It interacts with H+/K+ ATPase in the secretory membranes of the parietal cells and it is very effective in the treatment of the Zollinger–Ellison syndrome.

Esomeprazole is a lipophilic, weak base with pKa1= 4.2 and pKa2= 9 that may be degraded unless protected against acid conditions. It contains a tricoordinatedsulphur atom in a pyramidal structure and therefore can exist in two different optically active forms, (S)- and (R)-omeprazole.

A HPLC method was developed to determine esomeprazole in presence of its degradation product.

In order to shorten the development period of a pharmaceutical formulation, the chemical stability of pharmaceuticals was evaluated in accelerated storage conditions at high temperature and high relative humidity (RH) by a high-performance liquid chromatographic method.[4,5]

Long-term stability during preservation at room temperature is generally predicted based on the obtained accelerated data, using the Arrhenius equation. Therefore, it is not easy to predict transformations at room temperature from the data obtained at a high temperature.[6] According to our present knowledge, no studies are available for the kinetics of decomposition or activation energy of omeprazole.

2. MATERIALS AND METHODS

2.1. Equipment and instruments

HPLC system with model of Agilent 1100, with G1311A Quaternary Pump, G1313A Autosampler, UV / Vis Detector, and G1379A Vacuum Degasser. Ultrasonic Device for Elma. Filters 0.45 µm of Millipore Millex-LCR. column: C_{18}, (250mmx4.6mm, 5µm). Macherey-Nagel company, analytical Balance model Shimadzu AUW220D, with accuracy 0.1 mg.

2.2. Reagents and solvents

HPLC-Grade solvents are used

Acetonitrile from Panreac and Monobasic potassium Phosphate Extra Pure from sigma-aldrich.

2.3. Samples

2.3.1. Standard Materials

Esomeprazole Standards: Purchased from the European Council of the European Pharmacopoeia (EPH) Strasbourg, France.

2.3.2. Pharmaceutical Products

Esomeprazole capsules were supplied from a pharmaceutical industry in syria, esomeprazole products of many companies, and the trade name product –nexium-were brought.

2.4. Preparation of solutions

2.4.1. Mobile phase: A mixture of acetonitrile and Phosphate buffer 0.05M, pH7,(40:60), v/v.

2.4.2. Stock solution of esomeprazole standard (1 mg / ml):

Weigh 55.5 mg of esomeprazole magnesium trihydrate standard and take it into a 50 mL volumetric flask, dissolve it by adding about 70 ml of mobile phase, sonicate for 15 minutes, add mobile phase to volume.

2.4.3. Standard solution of esomeprazole (100 mcg / ml): Diluent 5.0 ml of stock solution to 50 ml using mobile phase as a diluent.

2.4.4. Sample solutions of esomeprazole: These solutions were prepared to contain a concentration similar to the concentration of the standard solution of esomeprazole.

2.4.5. Chromatographic conditions

Mobile phase: A mixture of acetonitrile and Phosphate buffer 0.05M, pH7,(40:60), v/v.

Flow rate: 1.5 ml / min.

Injection volume: 20 µl.

Column temperature is set at 25 ° C.

Detector: UV at a wavelength of 302 nm.

Table 1: The parameters of peak of esomeprazole

Compound	Retention time (minute)	Asymmetry	Theoretical plates	Area
Esomeprazole	6.124	1.17	2200	6925

3. RESULTS

3.1. Validation of the method

Table 2: Discusses the parameters of method validation.

Parameter		
Retention Time		6.124 min
Linearity (r^2)		0.9998
Accuracy (Recovery %)		100.002
Repeatability (RSD)		1.60
Intermediate Precision (RSD)		0.18
Selectivity (Recovery %)		99.97
Robustness (Relative Retention Time)	1.3 ml/min	0.9994
	1.5 ml/min	1.0054
	1.7 ml/min	1.001
Detection Limit (ng/ml)		69.99
Quantitation Limit (ng/ml)		233.3

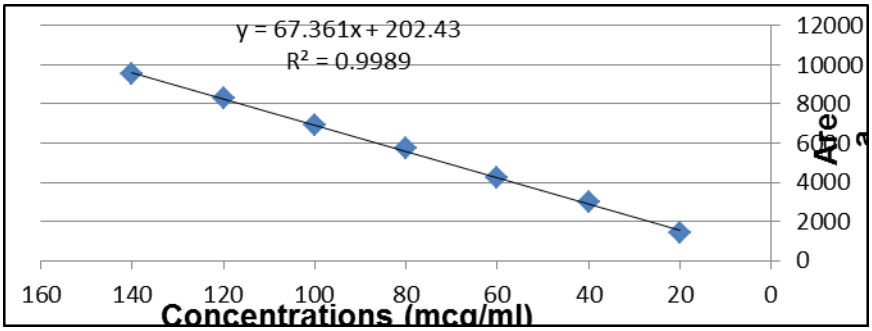

Figure 2: The calibration curve of Esomeprazole.

3.2. Stability study of Esomeprazole Preparations

3.2.1. Stability study of Esomeprazole in P.V.C/ALU packaging

The table (3) shows the percentage of retained esomeprazole in capsules with P.V.C/aluminum (Alu) packaging.

Pharmaceutical Form	Packaging	RH%	T %	0 %	1 %	2 %	3 %	6 %
Ea 20	P.V.C/Alu	100	40	101.2	86.3	77.5	68.6	46.8
Ea 20	P.V.C/Alu	100	25	98.3	96.2	95.1	94.3	91.7
Ea 40	P.V.C/Alu	100	40	100.3	87.2	76.2	67.4	48.2
Ea 40	P.V.C/Alu	100	25	99.6	97.1	95.3	94.8	92.0
Eb 20	P.V.C/Alu	100	40	100.3	92.5	87.5	79.8	58.6
Eb 20	P.V.C/Alu	100	25	101.2	99.7	99.2	98.5	96.2
Ec 20	P.V.C/Alu	100	40	98.7	87.3	75.4	66.2	48.6
Ec 20	P.V.C/Alu	100	25	98.4	79.2	96.1	94.5	88.2

a, b, c: 3 different companies.

3.2.2. Stability study of Esomeprazole in Alu/Alu packaging

The table (4,5) shows the percentage of retained esomeprazole in capsules with Alu/Alu packaging.

Table-4.

Pharmaceutical Form	Packaging	RH%	T	0 %	1 %	2 %	3 %	6 %
Ea 20-1	Alu/Alu	100	40	100.2	98.5	96.4	94.5	91.2
Ea 20-2	Alu/Alu	100	40	99.6	98.2	97.1	95.4	92.1
Ea 20-1	Alu/Alu	100	25	98.7	97.8	97.2	95.7	94.6
Ea 20-2	Alu/Alu	100	25	100.2	98.4	97.5	97.2	95.1
Ea 20-1	Alu/Alu	65	30	101.5	98.5	97.1	96.4	95.5
Ea 20-2	Alu/Alu	65	30	101.4	98.2	97.4	96.6	96.0
Ea 20-1	Alu/Alu	75	40	100.6	98.2	95.2	93.7	91.4
Ea 20-2	Alu/Alu	75	40	100.3	98.4	95.8	93.5	91.6

Table-5.

Pharmaceutical Form	Packaging	RH%	T	0 %	1 %	2 %	3 %	6 %
Ea 40-1	Alu/Alu	100	40	99.5	98.2	96.7	95.2	93.2
Ea 40-2	Alu/Alu	100	40	100.2	98.7	97.0	95.4	93.5
Ea 40-1	Alu/Alu	100	25	101.2	99.5	98.3	96.7	95.6
Ea 40-2	Alu/Alu	100	25	99.7	98.3	97.4	96.4	95.8
Ea 40-1	Alu/Alu	65	30	101.4	99.2	98.6	97.5	96.4
Ea 40-2	Alu/Alu	65	30	102.3	99.7	98.8	97.4	97.1
Ea 40-1	Alu/Alu	75	40	99.7	97.4	96.5	95.1	92.8
Ea 40-2	Alu/Alu	75	40	98.8	97.4	96.4	95.2	93.4

3.2.3. Stability study of Esomeprazole in Plastic Bottles packaging

The table (6) shows the percentage of retained esomeprazole in capsules with plastic bottles packaging.

Table-6.

Pharmaceutical Form	Packaging	RH%	T	0 %	1 %	2 %	3 %	6 %
Ea 20-1	**Plastic Bottles**	65	30	101.2	99.4	99.2	98.2	97.5
Ea 20-2	**Plastic Bottles**	65	30	100.4	99.4	98.9	98.0	98.6
Ea 20-1	**Plastic Bottles**	75	40	99.6	99.1	98.4	97.9	97.4
Ea 20-2	**Plastic Bottles**	75	40	99.4	98.8	97.9	98.1	97.6
Ea40-1	**Plastic Bottles**	65	30	100.6	99.1	98.4	98.5	98.2
Ea40-2	**Plastic Bottles**	65	30	101.4	99.5	98.4	97.8	97.4
Ea40-1	**Plastic Bottles**	75	40	102.3	99.6	98.2	98.4	98.2
Ea40-2	**Plastic Bottles**	75	40	99.8	99.1	98.4	98.1	97.3

4. RESULTS AND DISCUSSION

This study shows that packaging materials (plastic bottles, aluminum - aluminum) are the pest packaging materials for esomeprazole products, while esomeprazole is not stable in P.V.C/ALU packaging.

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