



A Comparative Physiochemical Properties of Esomeprazole Brands

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Abstract

Esomeprazole is the S-isomer of Omeprazole and it is a proton pump inhibitor (PPI). Esomeprazole is used in acid-related disorders and it is available as several brands in the market which makes it difficult for doctors to select the effective, safe and economic one for patients. Therefore we have decided to establish pharmaceutical equivalence among the different brands of esomeprazole available in Karachi, Pakistan. In our present study different brands of esomeprazole are evaluated for weight variation, hardness and dissolution. Disintegration Test shows results for NEX 01, ESS 02, EZI 03 and they disintegrate in 1.35, 1.15 and 2.15 minutes respectively. Dissolution test demonstrate the result as NEX 01, ESS 02, EZI 03 is 100.00% for NEX, 117.87% for ESS and 80.66%. The results showed that all parameters weight-variation, hardness, dissolution of different brands of esomeprazole are in accordance with the USP limits.

Keywords

Esomeprazole, Thickness, Weight Variation, Hardness, Friability

Subject Areas: Analytical Chemistry, Information Science, Public Health

1. Introduction

Omeprazole is a proton pump inhibitor (PPI). It is a substituted benzimidazole and exists as a racemic mixture of the S- and R-isomers. Esomeprazole (**Figure 1**) is the S-isomer of Omeprazole. It is the first (PPI) developed as an optical isomer and is used for the treatment of acid-related disorders. Esomeprazole has shown a similar mechanism of action to Omeprazole. It is also an effective inhibitor of gastric acid secretion [1]. However it differs from Omeprazole, as it is less prone to first-pass metabolism [2]. It also shows slower plasma clearance and results in higher plasma concentrations [3]. This leads to a more effective and long-lasting gastric acid secretion inhibition effect over 24-h dose interval. Moreover Esomeprazole shows less inter individual variations therefore it might show consistent response [2]. A recent study has showed that esomeprazole at a dose of 40 mg

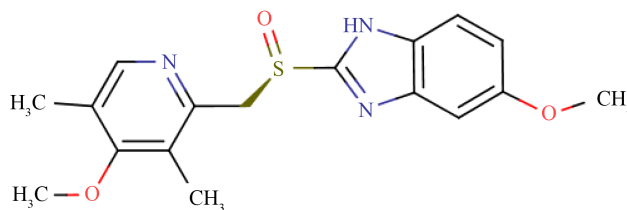


Figure 1. Structure of Esomeprazole.

once daily shows more effective gastric acid control at steady state than 40 mg doses of lansoprazole, rabeprazole and pantoprazole, in patients with symptomatic gastro esophageal reflux disease (GERD [4] [5]. It also shows a higher healing rate for erosive esophagitis and provides a long relief of heartburn in more patients than any other available PPI [6].

Esomeprazole is a competitive inhibitor of the enzymes CYP2C9 and CYP2C19. It may interact with drugs that depend on these enzymes for metabolism, for example warfarin and diazepam; their concentrations may increase if used concomitantly with esomeprazole. Some drugs depend on stomach pH for their absorption and interact with omeprazole. Ketoconazole or atazanavir drugs like drugs that depend on an acidic environment will be hardly absorbed and those drugs that are broken down in acidic environments example erythromycin will be absorbed to an efficiently than normal [7].

PPI may be associated with a greater risk of *Clostridium difficile*-associated diarrhea and hip fractures [8]. By suppressing acid-mediated proteins breakdown, esomeprazole leads to an elevated risk of developing drug and food allergies. This happens due to undigested proteins then passing into the GI tract where sensitization occurs. It is however unknown whether this risk occurs with long-term use or with short-term use [9]. Patients are frequently administered esomeprazole in intensive care as a protective measure against ulcers. This use is also related with a percent increase in occurrence of pneumonia [10]. We have done these types of study on different drugs which is very useful for selection of drug for pharmacist and doctors [11]-[13].

2. Methodology

We have purchased different brands of Esomeprazole capsules (USP) of 20 mg from the local market *i.e.* NEXUM (NEX), ESSO (ESS) and EZIUM (EZI). Physicochemical tests were performed for the comparison of different brands.

2.1. Weight Variation Test

Weight Variation test indicates content uniformity of each dosage form during compression. For this 10 capsules of each brand were weighed on Electronic Balance FX-400 and determined that weight of each capsule must be within BP/USP limits *i.e.* for capsules containing less than 300 mg not more than 2 capsules out of the sample may be outside $\pm 10\%$ of the average and all must be within 20%.

2.2. Disintegration Test

Disintegration apparatus (Curro model no DS-0702) was used to perform disintegration test. Six capsules were placed in the basket and then covered with the disk. Temperature is maintained at 35°C to 39°C using water or another liquid (unless specified) as the immersion fluid. After a specified time examine whether all the capsules have been disintegrated completely. If 1 or 2 capsules do not disintegrate, the test is repeated on 12 capsules. Out of 18 capsules 16 tested are disintegrated the requirements is met. Follow the same procedure for each brand. According to USP, capsule should disintegrate in not more than 30 minutes.

2.3. Dissolution Test

We perform this test on GDT-7L of Galvano Scientific dissolution apparatus. For this we take 900 ml of water in the vessel, assemble the equipment and maintained at temperature 37°C \pm 0.5°C. Put one capsule of each brand of Esomeprazole in a dry basket. Lower the basket into position before rotation, start rotation of the basket at 50 RPM. Withdraw a sample of ten ml at 15, 30, 45 and 60 min intervals from each vessel, sample must be taken from a zone midway between the surface of the dissolution medium and the top of the rotating basket, not

less than 10 mm below the surface and at least 10 mm from the vessel wall. Determine the quantity of esomeprazole dissolved as specified in USP.

3. Results

The physicochemical parameters of different brands of esomeprazole capsules (NEX 01, ESS 02, and EZI 03) were analyzed. The results of average weight of 10 capsules of NEX 01, ESS 02, EZI 03 is 136.9 mg, 138.5 mg, 135.9 mg and their upper & lower limits are 148.07 - 125.2, 143.3 - 128.2, 152.4 - 124.5 respectively which is show in **Table 1** and **Table 2**. Disintegration Test shows following results for NEX 01, ESS 02, EZI 03 and they disintegrate in 1.35, 1.15 and 2.15 minutes respectively shown in **Table 4**. Dissolution test demonstrate the result as NEX 01, ESS 02, EZI 03 is 100.00% for NEX, 117.87% for ESS and 80.66% shown in **Table 5**.

4. Discussion

The aim of this study is to evaluate and compare the quality standards of three brands of esomeprazole capsules (NEX 01, ESS 02, EZI 03) commercially available in Karachi, Pakistan. For comparatively study, physicochemical testing such as weight variation, in-vitro dissolution and disintegration of esomeprazole capsules (20 mg) (NEX 01, ESS 02, EZI 03) were performed and evaluated. Dissolution, disintegration and Uniformity of weight are compendial standards to checks the quality of capsules. The weight variation values of NEX 01, ESS 02, EZI 03 are given in **Table 1**, which shows that ESS 02 has the highest value of mean weight among all the three brands. According to USP the requirements of weight variation are met when out of 20 capsules of each brand the weight of not more than 2 capsules differs from the average weight by more than 10% (**Table 3**). Dif-

Table 1. Statistical weight variation table.

Serial no.	Average weight (mg)	Standard deviation (mg)	Upper Limit (X + 3S)	Lower Limit (X - 3S)
NEX 01	136.9	3.7252	148.07	125.72
ESS 02	138.5	2.558	143.5	128.2
EZI 03	135.9	4.648	152.4	124.5

Table 2. Calculation for weight variation test.

NEX	CAP1	CAP2	CAP3	CAP4	CAP5	CAP6	CAP7	CAP8	CAP9	CAP10
WEIGHT	132	138	130	140	136	138	138	136	138	143
MEAN	136.9	136.9	136.9	136.9	136.9	136.9	136.9	136.9	136.9	136.9
SD	3.7252	3.7252	3.7252	3.7252	3.7252	3.7252	3.7252	3.7252	3.7252	3.7252
UCL	148.07	148.07	148.07	148.07	148.07	148.07	148.07	148.07	148.07	148.07
LCL	125.72	125.72	125.72	125.72	125.72	125.72	125.72	125.72	125.72	125.72
COMMENT	OK	OK	OK	OK	OK	OK	OK	OK	OK	OK
ESS	CAP1	CAP2	CAP3	CAP4	CAP5	CAP6	CAP7	CAP8	CAP9	CAP10
WEIGHT	138	138	141	141	135	138	132	133	141	148
MEAN	138.5	138.5	138.5	138.5	138.5	138.5	138.5	138.5	138.5	138.5
SD	4.648	4.648	4.648	4.648	4.648	4.648	4.648	4.648	4.648	4.648
UCL	152.4	152.4	152.4	152.4	152.4	152.4	152.4	152.4	152.4	152.4
LCL	124.5	124.5	124.5	124.5	124.5	124.5	124.5	124.5	124.5	124.5
COMMENT	OK	OK	OK	OK	OK	OK	OK	OK	OK	OK
EZI	CAP1	CAP2	CAP3	CAP4	CAP5	CAP6	CAP7	CAP8	CAP9	CAP10
WEIGHT	133	133	137	138	140	139	136	135	133	135
MEAN	135.9	135.9	135.9	135.9	135.9	135.9	135.9	135.9	135.9	135.9
SD	2.558	2.558	2.558	2.558	2.558	2.558	2.558	2.558	2.558	2.558
UCL	143.5	143.5	143.5	143.5	143.5	143.5	143.5	143.5	143.5	143.5
LCL	128.2	128.2	128.2	128.2	128.2	128.2	128.2	128.2	128.2	128.2
COMMENT	OK	OK	OK	OK	OK	OK	OK	OK	OK	OK

Table 3. Weight variation test.

Serial no	Result (mg)	USP specification	Deviation from USP
NEX 01	136.9	±10%	Pass
ESS 02	138.5	±10%	Pass
EZI 03	135.9	±10%	Pass

Table 4. Disintegration test.

Serial No.	Disintegration time (min)	Limits	Deviation from USP
NEX 01	1.35	NMT 15 Min	PASS
ESS 02	1.15	NMT 15 Min	PASS
EZI 03	2.15	NMT 15 Min	PASS

Table 5. Dissolution test.

Serial No.	Dissolution at 30 min	USP Spec	Deviation from USP
NEX 01	100.00%	Not less than 80% (Q) of the labeled amount dissolved in 60 min	pass
ESS 02	117.87%		pass
EZI 03	80.66%		pass

ference in weight between these 3 brands (NEX 01, ESS 02, EZI 03) of esomeprazole capsules is due to the non-uniform amount of an API. Disintegration Test shows following results for NEX 01, ESS 02, EZI 03 and they disintegrate in 1.35, 1.15 and 2.15 minutes respectively shown in **Table 4**. Dissolution test demonstrate the result as NEX 01, ESS 02, EZI 03 is 100.00% for NEX, 117.87% for ESS and 80.66% shown in **Table 5**.

These types of comparative studies are very useful for doctors, pharmacist and prescriber because by these studies they can analyze which is the better choice of all brands [14]-[22].

5. Conclusion

It is concluded that the results of all the tests (weight variation, disintegration and dissolution) of selected brands of esomeprazole capsules (20 mg) exhibit some difference but these variations are in specified limits.

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