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A Comparative Study between Legally Imported and Smuggled Brands of Bisoprolol and Esomeprazole Tablets Marketed in Aden, Yemen

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ABSTRACT

Background: While drugs are legally introduced into the Yemeni pharmaceutical market through local agents under supervision of the Ministry of Public Health and Population (MOPHP), the past year has seen a notable increase in the distribution of smuggled drugs.
Objective: The aim of this study was to perform a comparative evaluation of the quality control parameters of both legally imported and smuggled products of bisoprolol (5 mg) and esomeprazole (40 mg) tablets, which are marketed in public pharmacies in Aden, Yemen.
Methods: A hundred tablets from each studied brand were purchased from a community pharmacy, and the quality of the studied brands was assessed through evaluation of weight variation, friability, thickness, diameter, hardness, disintegration, and assay tests, as well as identification of drugs by Fourier Transform Infra-Red spectrophotometer.
Results: The result of this study showed that both legally imported and smuggled tested tablets of bisoprolol conform with quality control standards except the weight variation test of smuggled bisoprolol failed to agree with pharmacopoeias specifications. Furthermore, the legally imported esomeprazole meets the quality control specifications for the tested parameters except the hardness and disintegration tests, while the smuggled esomeprazole complies with all tests but failed to an agreement with specifications for hardness, disintegration, and assay tests, where the result shows a value of 137%.
Conclusion: These results highlight the variability in quality across different sourcing pathways and underscore the importance of stringent regulatory oversight and routine quality assessment to ensure the safety, efficacy, and consistency of marketed pharmaceutical products.

Keywords: Legally imported drugs, smuggled drugs, bisoprolol, esomeprazole, quality control tests.

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INTRODUCTION

A drug is defined as a substance with known biological effects on humans or other animals, utilized in the treatment, cure, prevention, or diagnosis of disease, or to otherwise enhance physical or mental well-being [1]. In Yemen, the pharmaceutical landscape is heavily reliant on imports. The local pharmaceutical industry contributes approximately 10-20% of the total market demand, despite Yemen's membership in the Arab Union of Manufacturers of Pharmaceuticals and Medical Appliances and its 11th ranking among Arabic countries in medicine production [2]. While drugs are legally introduced into the Yemeni pharmaceutical market through local agents under the supervision of the Ministry of Public Health and Population (MOPHP), the past year has seen a notable increase in the distribution of smuggled drugs. These illicit pharmaceuticals bypass crucial quality control tests within the country [2].

Informal studies indicate that smuggled drugs constitute as much as 60% of all imported medicines entering Yemen through illegal channels. Such medicines, often of doubtful quality, origin, and expiry date, pose a serious threat to public health. Their quality is further compromised by exposure to adverse conditions like moisture and light during illicit transport [3]. Given these critical concerns, this project aims to address the issue of drug quality in Yemen by focusing on specific drug models. Bisoprolol is a highly selective β1-adrenoceptor antagonist used in the management of chronic heart failure and hypertension, known to improve left ventricular function and reduce heart rate [4].

Esomeprazole, a proton pump inhibitor (PPI), is primarily used to treat acid-related diseases such as dyspepsia, peptic ulcer disease, and gastroesophageal reflux disease by inhibiting stomach acid formation [5]. The quality of medicine is paramount for both therapeutic efficacy and patient safety [5]. The aim of this research is to perform a comparative evaluation of some quality control parameters for legally imported and smuggled products of Bisoprolol tablet 5 mg and Esomeprazole tablet 40 mg available in Aden, Yemen.

METHODOLOGY

Materials

The tested samples of legally imported bisoprolol, smuggled bisoprolol, legally imported esomeprazole, and smuggled esomeprazole brand were coded as B1, B2, E1, and E2, respectively, and were obtained from a community pharmacy in Aden City, Yemen, as shown in Table 1.

Table 1: General description of the drugs used in study

Code	Strength	Manufactory date	Expiration date	Coating type	Batch number
B1	5 mg	11/2019	10/2022	Film coating	E204522
B2	5 mg	11/2020	11/2024	Film coating	206099
E1	40 mg	2/2021	1/2023	Enteric coating	RT003
E2	40 mg	2021	1/2024	Enteric coated	21D892

Weight Variation Test

Twenty tablets from each tested product were weighed individually with the analytical balance. The average weight and the percent deviation of the tablets for each brand were calculated. Then the % of weight variation was determined by using the following formula: Percentage weight variation = (average weight – individual weight)/individual weight x 100 [6].

As per BP [7], the tablet complies with the test if not more than 2 of the individual masses deviate from the average mass by more than the percentage deviation as shown in Table 2 and none deviates by more than twice that percentage.

Hardness Test

The hardness test is done by the tablet hardness instrument model (PTB 111E) to determine the need for pressure adjustment on the tableting machine. Hardness values differ with the instrument used, allowing values of 8-12 kg. Tablet hardness usually affects drug dissolution and release, and it may affect bioavailability [8]. Oral tablets normally have a hardness of 5 kg to 15 kg [7].

Diameter Test

The procedure was carried out by using a hardness, thickness, and diameter tester on ten tablets of each studied brand. The range of acceptable diameters is shown in Table 3 [9].

Thickness Test

Thickness should be controlled within a ± 5% variation of a standard value [10]. The thickness of ten tablets was measured using a thickness tester [11].

Friability Test

Friability was examined using the Electrolab Friabilator. A number of 10 tablets for each brand were weighed and placed in the friabilator, in which rolling and repeated shocks of tablets are done as they fall 6 inches in each turn within the apparatus. After four minutes of this treatment, or 100 revolutions, the tablets were weighed, and the weight was compared with the initial weight. A maximum weight loss of not more than 1% of the weight of the tablets being tested during the friability test is considered generally acceptable. Then the percentage loss of weight of the tablets was calculated by using the following formula [6]:

Percentage friability= {(Initial weight- Final weight)/ Initial weight} x 100

Disintegration Test of Bisoprolol

Generally, disintegration is the mechanical breakup process of tablets into smaller particles, and the length of time that is required to measure for causing disintegration is known as disintegration time [6]. In this test, according to BP, one tablet was placed in each tube, and the basket rack was positioned in water or the specified liquid medium for 30 min at 37 ± 2°C. Perforated plastic discs are also used in the test, as they are useful for tablets that float [7].

Disintegration Test for Esomeprazole

According to BP, 6 tablets from each tested sample were used for the disintegration test in 0.1 N HCl at 37 ± 2°C for 2 h and then in phosphate buffer (pH 6.8) using a disintegration apparatus. The disintegration time was taken to be the time when no particle remained on the basket [7]. Enteric coated are to point out no proof of disintegration after 1 hour in simulated stomach fluid and are to disintegrate in 2 hours, the time per the monograph, within the intestinal fluid. To be compliant with standards, the tablets should disintegrate, and particles must pass through the 3 in.-long glass tubes and be held against a 10-mesh screen within the time given [5].

Identification Test by FTIR

The identification of the pure drug was established through FT-IR spectrophotometry using a PerkinElmer Spectrum Two, through the identification of different functional groups present in the drug sample. 2 mg of a tested drug was triturated in a glass mortar along with 200 mg of potassium bromide. The mixture was compressed in a hydraulic KBr pellet press at a pressure of 6000 kg/cm^2 to obtain a transparent pellet. This pellet was analyzed under the FTIR spectrophotometer under a scanning range between 4000 cm^{-1} and 400 cm^{-1} at a resolution of 4 cm^{-1}.. The peaks obtained in the spectrum are characteristic of a particular functional group, which was used to establish the identity of sample [12].

HPLC Analysis of Bisoprolol

A simple, precise, and stability-indicating HPLC method was used for the determination of bisoprolol in this study. Ten whole tablets were weighed and disintegrated by shaking for 5 min with 10 mL water in a 100 mL volumetric flask. 30 mL acetonitrile was added. It was sonicated for 10 min, and water was added to make up the volume in the flask. The solution was further diluted 10 times with the diluent to produce test solutions. HPLC (PerkinElmer Flexar) column: a (25 cm x 4.6 mm) 5-micron column with isocratic flow. The mobile phase at a flow rate of 1.0 mL/min consisted of 0.1M potassium dihydrogen phosphate buffer and acetonitrile (70:30, v/v). The UV detection was carried out at 210 nm. A linear response was observed over the concentration range of 2.5-50 µg/mL of bisoprolol fumarate [13].

HPLC Analysis of Esomeprazole

A simple, selective, and rapid reversed-phase high-performance liquid chromatographic (RPHPLC) method for the analysis of esomeprazole has been used in this study. The separation was achieved from an HPLC (PerkinElmer Flexar) column (Prevail C8, 5 µ, 4.6 mm x 150 mm) with a mobile phase consisting

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of HPLC-grade acetonitrile and phosphate buffer solution (35:65) at a flow rate of 1 ml/min with UV detection at 280 nm [14]. The sample solution of Esomeprazole (20 mg) tablets was prepared by transferring 10 tablets into a 1000 mL volumetric flask, followed by an addition of 600 mL of a mixture of 800 mL of methanol and 200 mL of milli-Q grade water and 4 mL of triethylamine and sonication for 30 min with intermediate shaking. After the sonication, the volume was made up with 0.25 N sodium hydroxide. A portion of this solution is centrifuged at 4000 rpm for 10 min. [15]

Table 2: BP limits for weight variation test of tablets

BP average weight (mg)	+or-Weight deviation allowed (%)
80 or less	**10**
81-250	**7.5**
251 or more	**5**

Tablet 3: Diameter test (acceptable ranges)

Diameter (mm)	+or- Allowed deviation (%)
less than 12.5	not exceeding ± 5%
12.5 mm or more	not exceeding ± 3%

RESULTS

Quality Control Tests of Bisoprolol

Weight Variation Test

By performing a weight variation test, we noticed that legally imported bisoprolol was within the acceptable range, with a division range from 0.87% to 6.7%, while the smuggled bisoprolol was out of the acceptable range. The division of smuggled bisoprolol varied from 0.58% to 20.71%, and we noticed seven tablets over 7.5 lead to the failure of the test, according to the BP standards.

Hardness Test

According to the BP 2010 specification, a hardness test value ranging from 5 kg to 15 kg is acceptable. The results showed in Table 4 the mean values of hardness for both legally imported bisoprolol and smuggled bisoprolol are 9.981 kg and 5.18 kg, respectively. These results indicate the hardness values of both legally imported and smuggled bisoprolol tablets were within the allowed limit.

Table 4: Results of hardness test of Bisoprolol

Tablet No.	Legally Imported Bisoprolol (kg)	Smuggled Bisoprolol (kg)
1	10.08	4.93
2	9.90	5.44
3	9.29	5.97
4	10.19	5.89
5	10.72	4.99
6	10.48	5.27
7	9.60	4.94
8	10.06	4.25
9	9.99	4.70
10	9.57	5.45
Mean ± SD	9.98 ± 0.42	5.18 ± 0.53

Diameter Test

The results of the diameter test of legally imported bisoprolol tablets ranged from 6.59 mm to 6.62 mm, while the diameter of smuggled bisoprolol ranged from 6.63 mm to 6.67 mm, as shown in table 5. So that all of the tablets of legally imported and smuggled

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bisoprolol fulfill the specification in which their deviation is not more than ± 5% from the mean value.

Table 5: Results of diameter test of Bisoprolol (mm)

Tablet No.	Legally Imported Bisoprolol		Smuggled Bisoprolol	
	Diameter (mm)	Deviation %	Diameter (mm)	Deviation %
1	6.60	0	6.66	0.60
2	6.6	0	6.63	0.15
3	6.6	0	6.64	0
4	6.61	0.15	6.63	0.15
5	6.59	-0.15	6.63	0.15
6	6.6	0	6.63	0.4
7	6.59	-0	6.64	0.6
8	6.60	0	6.67	1
9	6.62	0.3	6.63	0.5
10	6.61	0.2	6.64	0.6
Mean ± SD	6.60 ± 0.01		6.64 ± 0.01	

Thickness Test

The result of the thickness test of legally imported bisoprolol tablets varied from 2.41 mm to 2.49 mm, while the thickness of smuggled bisoprolol tablets ranged from 2.78 mm to 2.89 mm, as shown in table 6. Therefore, all of the tablets of legally imported and smuggled bisoprolol have a deviation below ± 5%, which is within acceptable limits.

Table 6: Results of thickness test of bisoprolol (mm)

Tablet No.	Legally imported bisoprolol		Smuggled bisoprolol	
	Thickness (mm)	Deviation %	Thickness (mm)	Deviation %
1	2.41	1.23	2.78	-1.4
2	2.44	0	2.82	0
3	2.44	0	2.85	1
4	2.45	-0.41	2.84	0.7
5	2.45	-0.14	2.81	0.4
6	2.48	-1.64	2.86	1.4
7	2.41	-1.23	2.78	1.4
8	2.40	1.64	2.82	0
9	2.49	-2.05	2.83	0.3
10	2.42	0.82	2.81	0.4
Mean ± SD	2.44 ± 0.74		2.82 ± 0.03	

Friability Test

From the results shown in Table 7, it was observed that the friability percent of legally imported and smuggled tested brands of bisoprolol was 0.00% and 0.36%, respectively, which complies with the BP standards.

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Table 7: Friability test of Bisoprolol

Run No.	legally imported bisoprolol			Smuggled bisoprolol		
	Initial weight (g)	Final weight (g)	Friability %	Initial weight (g)	Final weight (g)	Friability %
1	1.7	1.7	0	1.74	1.72	1.14
2	1.7	1.7	0	1.71	1.71	0
3	1.7	1.7	0	1.72	1.72	0
Mean ± SD			0.00 ± 0.00			0.36± 0.63

Disintegration Test

The results from the study of the disintegration time of both legally imported and smuggled tested brands of bisoprolol complied with the compendia requirements. According to table 8, the smuggled brand of bisoprolol disintegrates faster (3.72 min. sec.) than the legally imported one.

Table 8: Disintegration time for Bisoprolol (min. sec)

Run. No	Number of tablets	legally imported bisoprolol (min. sec)	smuggled bisoprolol (min. sec)
1	6 tablets	3.52	3.41
2	6 tablets	4.14	4.28
3	6 tablets	4.50	3.47
Mean ± SD		4.05 ± 0.49	3.72 ± 0.48

Identification Test by FTIR

The individual spectra of the bisoprolol standard, legally imported bisoprolol, and smuggled test brands of bisoprolol are shown in Figures 1-3. The results showed that both smuggled and legally imported tested tablets of bisoprolol had the required functional groups that indicate these products contain the active ingredient in their formulation, consistent with the reference standard spectrum, as listed in Table 9.

Table 9: IR spectroscopy absorption frequencies and corresponding functional group of bisoprolol

Functional group	Absorption frequency (cm -1)
N-H group	3100 – 3500
O-H	2500 – 3300
-CH2	2927 – 2935
C=O	1628 – 1650
C=O (ester)	1735 – 1750
C=O (anhydride)	1800 – 1830
CH2	1435
CH bonds	1417
CH bonds	1404
CH3	1346
C-O group	1000 – 1300
-CH-CH	1111 – 1097
C-O	1065 – 1068
Fingerprint region	400 – 1000

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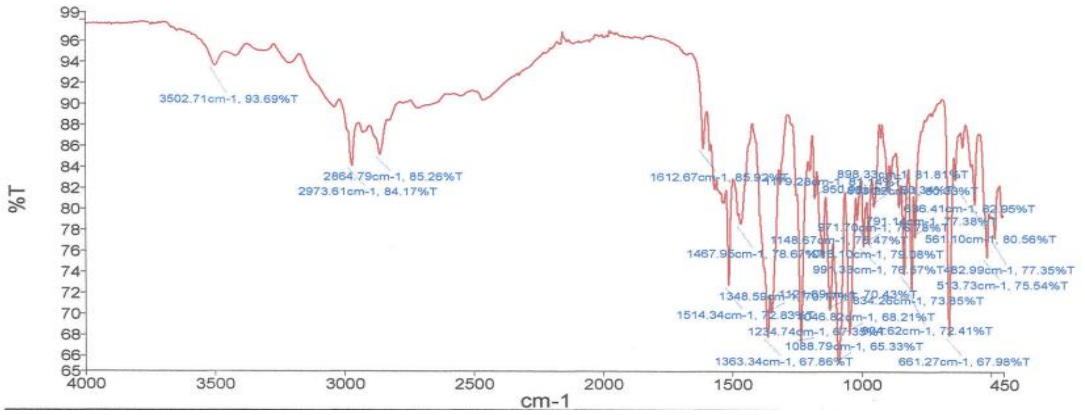

Figure 1: FTIR Spectra of standard Bisoprolol

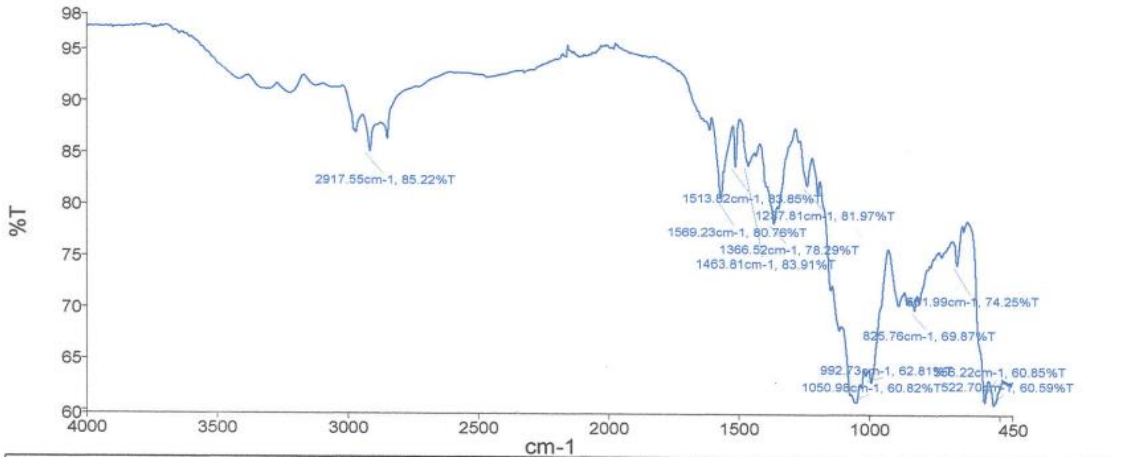

Figure 2: FTIR Spectra of legally imported Bisoprolol

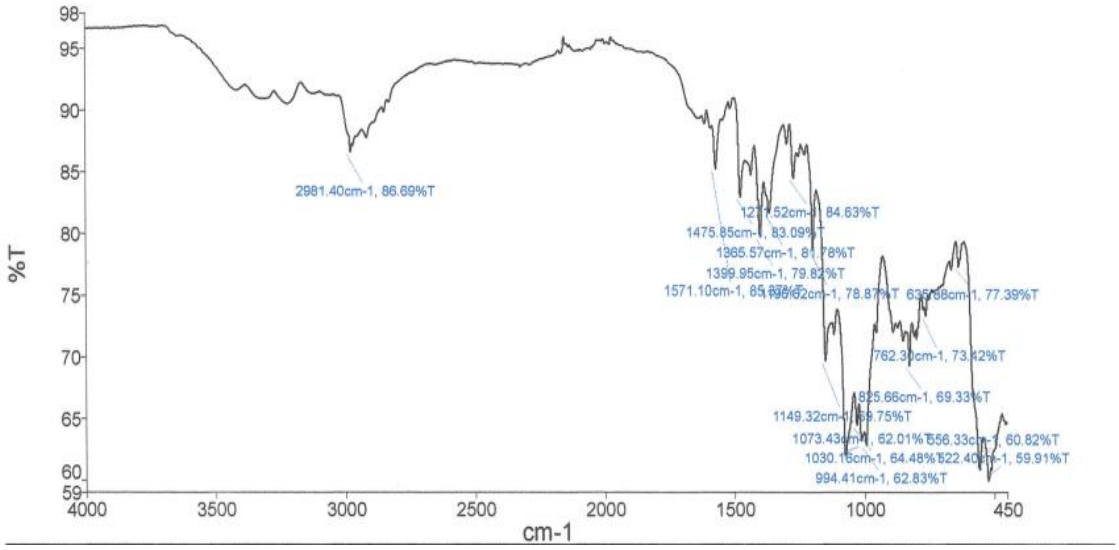

Figure 3: FTIR Spectra of smuggled Bisoprolol

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HPLC Analysis of bisoprolol

According to the result shown in table 10, the result showed that legally imported bisoprolol had an average value of 108%, while smuggled drugs had an average value of 106%. These results confirm that the concentration of active ingredient for both products lies within the acceptable limit, which should be between 90% and 110%.

Table 10: HPLC Analysis of Bisoprolol

Run No	Standard	B1	B2
	Peak area		
1	8071843	8695988	**8289204**
2	8131365	9360352	**9274449**
3	8186775	8178306	**8399681**
4	7910351	8908656	**8344397**
Average	8075083	8785825	**8576932**
Assay %		108%	**106%**

Quality Control Tests of Esomeprazole

Weight Variation Test

As a result, we noticed that both legally imported esomeprazole and smuggled esomeprazole are within the acceptable range. A percent of division for legally imported esomeprazole ranged from 0.17% to 1.86%, which complies with BP Specification (allowed error is 5%). On the other hand, the percent of division for the tested tablets of smuggled esomeprazole varied from 0.34% to 5.09%, which confirms the BP specification, where only one tablet was more than 5%.

Hardness Test

The results presented in table 11 showed the hardness test did not conform to the acceptable limit, with mean values of 26.49438 kg and 19.788 kg for legally imported and smuggled esomeprazole, respectively.

Table 11: Hardness test of esomeprazole

No.	Hardness (Kg) for Legally Imported Esomeprazole	Hardness (Kg) for Smuggled Esomeprazole
1	30.39	**19.32**
2	26.14	**20.42**
3	24.93	**19.07**
4	26.11	**19.13**
5	24.01	**20.48**
6	24.01	**20.72**
7	30.68	**21.18**
8	25.62	**19.97**
9	26.57	**17.61**
10	26.47	**19.52**
Mean ± SD	26.49 ± 2.32	**19.78 ± 6.34**

Diameter Test

The result of the diameter test of legally important esomeprazole tablets ranged from 8.00 mm to 8.17 mm, while that for smuggled esomeprazole tablets ranged from 8.09 mm to 8.13 mm, as shown in Table 12. So that all of the tested tablets of legally imported and smuggled esomeprazole are fulfilling the specification in which their deviation is not more than ± 5% from the mean value.

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Table 12: Results of diameter test of Esomeprazole

Tablet No.	legally imported Esomeprazole		smuggled Esomeprazole	
	Diameter (mm)	Deviation %	Diameter (mm)	Deviation %
1	8.15	-0.2	8.11	0
2	8.14	-0.12	8.11	0
3	8.11	0.25	8.13	0.2
4	8.15	0.25	8.09	0.21
5	8.14	-0.12	8.11	0.2
6	8.13	0	8.11	0
7	8.15	0.25	8.13	0.2
8	8.00	-1.59	8.13	0.2
9	8.17	-0.49	8.11	0
10	8.15	-0.25	8.11	0
Mean ± SD	8.13 ± 0.05		8.11 ± 0.01	

Thickness Test

As shown in table 13, the thickness test for legally imported esomeprazole tablets varied from 5.35 mm to 5.55 mm, while that for smuggled esomeprazole tablets ranged from 5.20 mm to 5.26 mm. Therefore, all of the tested esomeprazole tablets in this study comply with specifications (deviation below ± 5%).

Table 13: Results of thickness test of Esomeprazole

Tablet No.	legally imported Esomeprazole		smuggled Esomeprazole	
	Thickness (mm)	Deviation %	Thickness (mm)	Deviation %
1	5.47	0.3	5.22	-0.2
2	5.45	0	5.20	-0.6
3	5.41	0.7	5.23	0
4	5.39	- 1.1	5.23	0
5	5.44	- 0.2	5.26	0.6
6	5.44	- 0.2	5.23	0
7	5.47	0.3	5.25	0.4
8	5.55	1.8	5.25	0.4
9	5.40	0.9	5.20	-0.6
10	5.45	0	5.22	-0.2
Mean ± SD	5.45 ± 1.64		5.23 ± 0.02	

Friability Test

From the results shown in Table 14, it was observed that both legally imported and smuggled esomeprazole meet the acceptable limits according to BP (a maximum weight loss of not more than 1%), where there is no loss of weight for the tested tablets.

Table 14: Friability test of esomeprazole

Run No.	Legally imported Esomeprazole			Smuggled Esomeprazole		
	Initial weight (g)	Final weight (g)	Friability %	Initial weight (g)	Final weight (g)	Friability %
1	5.82	5.82	0	5.81	5.81	0
2	5.79	5.79	0	5.80	5.80	0
3	5.77	5.77	0	5.87	5.87	0
Mean ± SD			0.00±0.00			0.00±0.00

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Disintegration Test

The result of the study, which is shown in table 15, indicates both legally imported and smuggled esomeprazole were disintegrated rapidly in an acid medium within a few minutes, while the BP specification (no disintegration occurring during 1 hour in 0.1 N HCl) was not.

Table 15: Disintegration time for esomeprazole in acidic media

Run NO.	Number of tablets	Legally imported Esomeprazole (min . sec)	Smuggled Esomeprazole (min . sec)
1	6 tablets	8.20	6.26
2	6 tablets	2.10	2.04
3	6 tablets	2.30	1.48
Mean ± SD		4.2 ± 3.47	3.53 ± 2.36

On the another hand, both legally imported and smuggled esomeprazole were passed the disintegration in the alkaline medium with faster disintegration time for smuggled than legally imported esomeprazole as shown in the (Table 16).

Table 16: Disintegration time for esomeprazole in phosphate buffer

Run NO.	Number of tablets	Legally imported Esomeprazole (min . sec)	Smuggled Esomeprazole (min . sec)
1	6 tablets	7.50	10.59
2	6 tablets	3.45	0.51
3	6 tablets	4.32	0.53
Mean ± SD		5.09 ± 2.13	3.88 ± 5.81

Identification Test by FTIR

The individual spectra of the esomeprazole standard, legally imported esomeprazole, and smuggled esomeprazole are shown in figures 4, 5, and 6, respectively. The results showed that both smuggled and legally imported esomeprazole had the required functional groups that indicate these products contain the active ingredient (esomeprazole) in their formulation consistent with the reference standard spectrum listed in Table 17.

Functional group	Absorption frequency (cm -1)
SO	**1076**
O - CH3	**1199 , 1228**
NH2	**1409**
= CH -	**1569**
C7 H6 N2	**1612, 1588**
Aromatic	**2970**
C2 H5 OH / H2O	**3100 – 2800**

Table 17: IR spectroscopy absorption frequencies and corresponding functional group of esomeprazole

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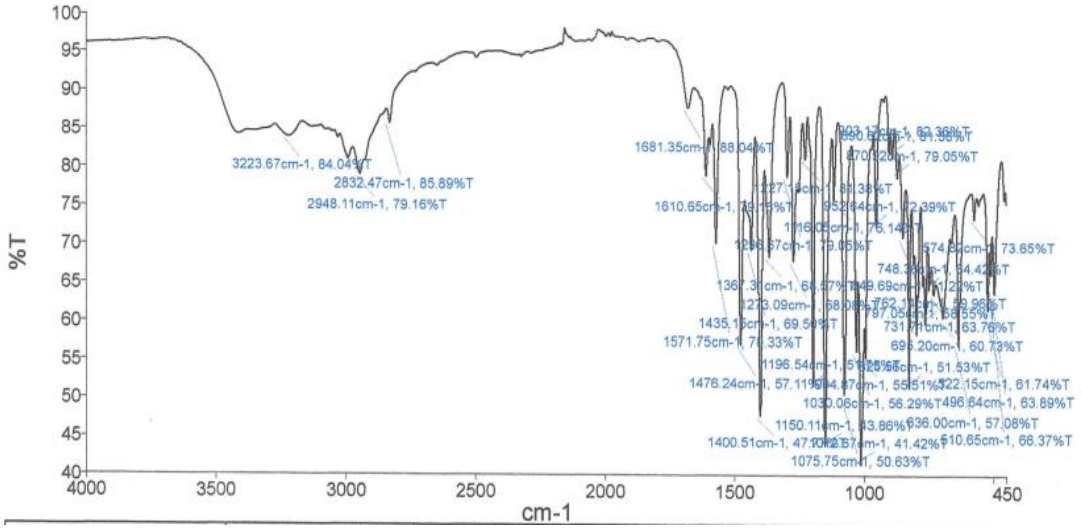

Figure 4: FTIR Spectra of stander esomeprazole

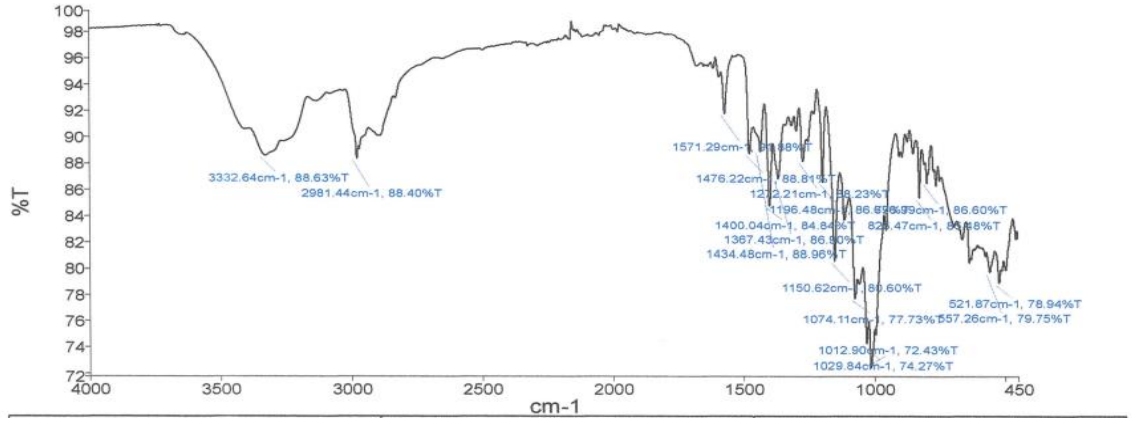

Figure 5: FTIR Spectra of legal esomeprazole

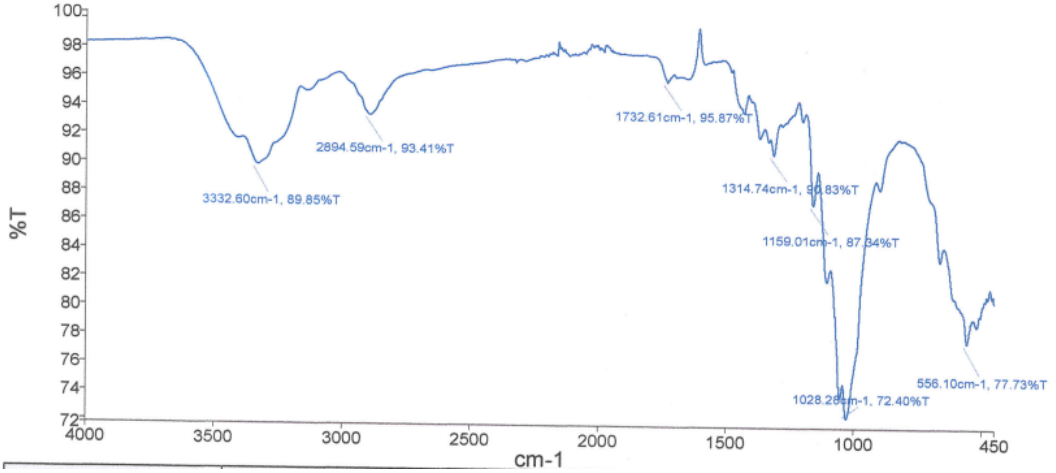

Figure 6: FTIR Spectra of smuggled esomeprazole

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HPLC Analysis of Esomeprazole

The result of the assay test for legally imported esomeprazole was found to be 91%, as shown in Table 18, and confirms the specification (90-110%), while the result of the assay test for smuggled esomeprazole was equal to 137%, which is in an unacceptable range and does not confirm the specification.

Table 18: HPLC assay test for esomeprazole

Run No	Standard	Legally imported Esomeprazole	Smuggled Esomeprazole
		Peak area	
1	2689539	2594124	1187439
2	28425477	2577445	1207049
3	2892072	2492569	1243009
4	2862326	2483782	1048193
Average	2.821621	2.583394	3.887284
Assay %		91%	137%

DISCUSSION

In contrast to our findings, which indicate clear failures in smuggled drug quality, some literature suggests that not all informally distributed medicines are inherently substandard. For example, Dulla et al. [5], in an in vitro comparative quality evaluation of different brands of esomeprazole tablets, reported that the obtained results of all parameters complied with the pharmacopoeial limit. This highlights that the quality of unregulated drugs can be variable and source-dependent and that some channels may inadvertently distribute products of acceptable quality [5].

The extraordinarily high assay result (137%) for the smuggled esomeprazole samples is indicative of production in facilities operating without any adherence to Good Manufacturing Practices (GMP). As documented by the World Health Organization, such gross over-concentration of the active ingredient is a hallmark of falsified medicines, resulting from a complete lack of quality control during the blending and granulation processes [16]. The assay result of 137% for the smuggled esomeprazole samples represents a dangerous deviation exceeding acceptable dosage limits (90-110%). Overdosing on proton pump inhibitors like esomeprazole is associated with an increased risk of adverse drug reactions, particularly with long-term use. Studies indicate that exposure to supratherapeutic levels can exacerbate the frequency and severity of known side effects such as headache, diarrhea, nausea, and abdominal pain. More significantly, long-term use of high-dose PPIs is linked to an elevated risk of vitamin B_{12} deficiency [17].

The failure of both legally imported and smuggled esomeprazole samples to undergo acid solubility testing is a critical indicator of enteric coating damage. While the cause in smuggled samples may be primarily due to faulty manufacturing practices in unregulated facilities, the presence of the same defect in the legal sample points to a common and serious factor, often improper storage and transportation conditions. Prolonged exposure to heat and humidity during the supply chain can degrade the physical properties of drugs, including the enteric coating's ability to resist acid [18].

CONCLUSION

In conclusion, legally imported and smuggled tablets of bisoprolol have values within the acceptable limits in all tests that have been done, except the weight variation test of smuggled tablets that showed values out of the acceptable limit. Furthermore, the legally imported esomeprazole meets the quality control specifications for the tested parameters except the hardness and disintegration tests, while the smuggled esomeprazole complies with weight variation, diameter, hardness, and friability tests but fails to agree with specifications for hardness, diameter, and assay tests.

Recommendations

It is necessary to study other pharmaceutical dosage forms such as injections, syrups, or suspensions. We recommend further studies to be included in vivo

studies to know the extent of the effect and concentration of the drug rather than in vitro studies only. It is necessary to add several tests in addition to the tests that we performed in our research, such as dissolution and leaking tests.

Limitations

This study includes some limitations, such as the potential difficulty in ethically obtaining consistent samples of smuggled medications. Additionally, assessing effectiveness might be limited by resources and ethical constraints. Lastly, the results may not be generalizable to all smuggled or imported drugs in Yemen.

Conflict of Interest

The authors declare that there is no conflict of interest.

REFERENCES

[1] Karman R. Commonly Used Drugs - Uses, Side Effects, Bioavailability and Approaches to Improve It. Nova Science Publishers, Inc.; 2015.

[2] Alshakka M, AlMansoub MA, Babakri M, Qubati S, Alshammri T, Jha N, et al. Current pharmaceutical situation (services) in Yemen and future challenges. Indian J Pharm Biol Res. 2014;2(4):77-81.

[3] Alshami M, Hassali M, Alresheedy A, Altamimi S, Algfri S. The Need of Pharmacovigilance Activities in Yemen. Glob J Med Res (B). 2014;14(4).

[4] Foody JM, Farrell MH, Krumholz HM. β-Blocker therapy in heart failure: scientific review. JAMA. 2002;287(7):883-9.

[5] Dulla O, Sultana S, Shohag Hosen M. In vitro comparative quality evaluation of different brands of esomeprazole tablets available in selected community pharmacies in Dhaka, Bangladesh. BMC Res Notes. 2018;11(1):184.

[6] Al Ragib A, Islam T, Sazib S, Hosain F. Comparative study on quality analysis on marketed diclofenac sodium tablets of different brands available in Bangladesh. Res J Life Sci Bioinform Pharm Chem Sci. 2018;4(4):362-73.

[7] British Pharmacopoeia. Vol. I-II. London: The Stationery Office; 2010.

[8] Ashrafi J. Evaluation of the Quality Control Parameters of Two Different Brands of Combined Atenolol (50mg) & Amlodipine (5mg) Tablets Available in Bangladesh [Dissertation]. Dhaka: East West University; 2014.

[9] Rani B, Dhanalakhmi G, Manuja P, Prathusha M, Meenakshi S. Formulation and evaluation of controlled release matrix tablet of pantaprazole sodium. Int J ; 2013 .

[10] Lachman L, Liberman HA, Kanig JL. The Theory and Practice of Industrial Pharmacy. 3rd ed. Mumbai: Varghese Publishing House; 2008.

[11] Bashar A, Deb P. Evaluation of Different Brands of Pantoprazole Sodium Tablets: A Comparative Study. Int J Pharm Pharm Res. 2017;9(3):134-40.

[12] Kanwar K, Gautam SP. Qualitative Portrayal of Esomeprazole Magnesium by Exploring Diverse Analytical and Investigative Approaches. J Pharm Res Int. 2021;33(41A):52-68.

[13] Joshi SJ, Karbhari PA, Bhoir SI, Bindu KS, Das C. RP-HPLC method for simultaneous estimation of bisoprolol fumarate and hydrochlorothiazide in tablet formulation. J Pharm Biomed Anal. 2010;52(3):362-71.

[14] Bellah SF, Momin MAM, Islam MM, Khan MS, Anisuzzaman SM. Development and validation method for determination of esomeprazole by HPLC. Int Res J Pharm. 2012;3(7).

[15] Reddy PS, Sait S, Vasudevmurthy G, Vishwanath B, Prasad V, Reddy SJ. Stability indicating simultaneous estimation of assay method for naproxen and esomeprazole in pharmaceutical

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https://journals.ust.edu/index.php/yjms

formulations by RP-HPLC. Der Pharma Chemica. 2011;3(6):553-64.

[16] World Health Organization. A study on the public health and socioeconomic impact of substandard and falsified medical products. Geneva: World Health Organization; 2017.

[17] Sheen E, Triadafilopoulos G. Adverse effects of long-term proton pump inhibitor therapy. Dig Dis Sci. 2011;56(4):931-50.

[18] Qiu Y, Chen Y, Zhang GG, Yu L, Mantri RV, editors. Developing solid oral dosage forms: pharmaceutical theory and practice. San Diego: Academic Press; 2016.