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Original Research Article

Assessment of the pharmaceutical quality of various brands of omeprazole capsules

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Abstract

Introduction: Omeprazole is a first-line therapy drug for the treatment of peptic ulcer disease. The availability of numerous generic brands in the market raises doubts about their quality.
Purpose: This study aimed to assess the pharmaceutical quality of various brands of omeprazole capsules marketed in three states of southern Nigeria.
Methods: Organoleptic and physicochemical properties of ten (10) generic brands of omeprazole capsules were assessed according to official and unofficial standards. Quality assurance tests such as weight uniformity, disintegration time and drug content assay were carried out. The dissolution test was done in a double dissolution medium consisting of 0.1 N HCl for 1.0 h and phosphate buffer pH 6.8 for 2.0 h.
Results: Capsules tested were suitably packaged with shells containing evenly coloured white pellets. All capsules were slightly soluble in water, sparingly soluble in ethanol and readily dissolved in alkaline medium. The 10 brands tested met the British Pharmacopeia (BP) specification for weight uniformity. All capsules had drug content within 90 - 110% and an average disintegration time of less than 15 min. All brands retained the drug in acid medium for 1 hour but released more than 75% within 40 min in phosphate buffer pH 6.8.
Conclusion: Brands of omeprazole capsules passed Pharmacopeia tests, exhibited similar *in vitro* drug release profiles and may therefore be used interchangeably for the treatment of peptic ulcer. The study also showed that almost all brands of omeprazole capsules available in Nigeria are imported, hence the need arises for regular post-clinical analysis of imported drugs.

Keywords: Omeprazole, generic brands, quality, analysis

Introduction

Omeprazole is a proton pump inhibitor that has more potent antisecretory activity than H_2 (histamine) blockers. It has been generally used in the treatment of gastric and duodenal ulcers, erosive esophagitis, and gastroesophageal reflux disease (GERD) [1]. Its mechanism of action is by a dose-dependent inhibition of H^+/K^+ ATPase system found on the secretory surface of the gastric parietal cells [2].

Omeprazole is acid labile hence it is formulated as enteric-coated pellets in hard gelatin capsules that release the drug in an alkaline medium from where it is easily absorbed [3]. Pellets may change after storage, primarily in terms of their gastrointestinal performance and release properties [4]. Additional storage-related alterations to the capsule shell may occur after encasing [5,6]. In order to track potential changes that could impact the effectiveness of omeprazole during its storage and use, post-clinical quality study is required.

In Nigeria, omeprazole is commercially available in several generic brands. A generic drug contains the same active pharmaceutical

ingredient(s) as the drug that was originally protected by patent (i.e. brand drug). Generic brands play indispensable roles in public healthcare and their use steadily increases due to their affordability and availability.

Various production factors create tendencies for dissimilarity in the pharmaceutical quality of generic brands of drugs [7]. Factors such as differences in the quality of granule coating as well as types of packaging may account for variations in formulation stability and *in vitro/in vivo* pharmacokinetics between various generic brands of omeprazole [8].

A significant public health issue is the spread of low-quality and counterfeit medications, particularly in underdeveloped nations where there are not enough resources to effectively monitor the occurrence. There are currently no accurate figures available on the prevalence of fraudulent medications in Nigeria [9].

According to earlier surveys, between 25 and 80% of Nigeria's prescription drugs are believed to be substandard [10-14]. Counterfeit products may have the right or incorrect ingredients, no active substances, insufficient amounts of active ingredients, or poor packaging. From a public health perspective, the public's trust in the delivery system for healthcare has been damaged by counterfeit/substandard pharmaceuticals [7].

Treatment failures, organ dysfunction/damage, deterioration of chronic illness states and mortality are few of the negative outcomes that could occur [10]. Morbidity and mortality are expected to rise when typical diseases with high untreated mortality are treated with drugs that have little to no active components [15].

The need to continuously evaluate drugs' quality to safeguard public health and prevent pharmaceutical companies from exploiting patients is thus created. This study aims to assess the pharmaceutical quality of generic brands of omeprazole capsules available in three states of Nigeria using official and unofficial tests.

Materials

Ten generic brands of 20 mg omeprazole capsules (Table 1) were purchased from registered community pharmacies in Edo, Delta and Anambra States. Omeprazole powder was the product of Alpa Laboratory, India. Potassium dihydrogen phosphate, disodium hydrogen phosphate and hydrochloric acid were products of BDH Chemicals (Poole, England). All other chemicals used in the study were of analytical grade.

Methods

Organoleptic properties

The different brands of omeprazole capsules were examined for their organoleptic properties; appearance, colour and odour. These properties aid in the nonspecific identification of the drug and are directly related to the chemistry of the drug [16].

Physicochemical analysis

Solubility test

The drug content in the capsules of each brand was emptied into a mortar, crushed and 250 mg each of the resulting powder was dissolved in 3 beakers containing 25 ml of distilled water, 25 ml of 96% ethanol, and 25 ml of 10% sodium hydroxide solution. The contents in the three beakers were stirred using a glass stirrer for 5 mins each and allowed to stand for 15 mins. This test was carried out for all the brands and the results obtained were recorded.

Quality assurance tests

Weight uniformity test

Ten (10) capsules from each brand were weighed using a digital balance (Kerro BL3002, England) and their weights were recorded. This test was carried out for all the brands and the result was recorded accordingly. The mean weight and standard deviation were then determined.

Assay of omeprazole content

Preparation of stock solution

A 0.1%w/v stock solution of omeprazole was prepared by dissolving 40 mg of omeprazole powder in 40 ml of phosphate buffer (pH 6.8). This was then serially diluted to get working solutions of various concentrations. The sample was scanned within UV range (200 - 400 nm) using a UV/Visible spectrophotometer (T80+ PG instrument Ltd, USA), and peak maxima was observed at 296 nm. Subsequently, the absorbance of all the solutions was measured at 296 nm using phosphate buffer as blank, and the calibration curve was plotted.

Table 1: Label information on omeprazole brands studied

Product code	Product name	Manufacturer	Batch number	NAFDAC number	Manufacturing date	Expiry date	Labeled strength (mg)
C_A	Pramozole	Flourish Pharma, India	885	B4-3917	02/2021	01/2024	20
C_B	Nardson	Merit Organics, India	C05903	C4-1866	12/2022	11/2025	20
C_C	Omefast	Swiss Pharma, India	2074	04-5325	03/2022	02/2025	20
C_D	Pinnazole	Globela Pharma, India	GC21051	B4-0911	07/2021	06/2024	20
C_E	Meprasil	Fidson Healthcare, Nigeria	C0122020	04-3823	10/2022	09/2024	20
C_F	Gastroloc	Alpa Lab, India	CE2006	A4-1296	04/2022	09/2024	20
C_G	Somepra	Theon Pharma, India	EGC210012	A4-7298	02/2021	01/2024	20
C_H	Ralphones	Salud Care Pvt, India	SC22-066	B4-8938	03/2022	02/2024	20
C_I	Omipref	Fredun Pharma, India	CA0050	B4-1860	01/2023	12/2025	20
C_J	Pkn	Surmount Lab, India	GZ217	C4-1908	11/2022	10/2025	20

Content assay

Omeprazole content of each brand was determined using UV spectrophotometric method [8]. One capsule from each brand was selected at random and dissolved in 40 ml of phosphate buffer (pH 6.8). The solution was filtered using a Whatman number 1 filter paper and made up to 40 ml with the phosphate buffer. The resulting solution was suitably diluted and the absorbance was measured spectrophotometrically at 296 nm and phosphate buffer as blank. A triplicate determination was done for each brand then the average drug content and standard deviation were determined.

Disintegration time test

The disintegration time for capsules was carried out following the BP method [16] using Erweka disintegration tester, USA. Disintegration beaker containing 1,000 ml of water maintained at 37 ± 2.0°C was used as immersion fluid. Six (6) capsules from each brand were randomly chosen and placed in each of the cylinder tubes in the basket rack of the disintegration apparatus. The metal mesh base of the basket rack was placed such that it was not less than 1.5 cm below the surface of the disintegration medium. The tubes were moved up and down in the disintegration medium such that the capsules were constantly agitated. The endpoint was taken as the time when all the contents had passed through the mesh. This procedure was repeated for each brand and the mean disintegration time was recorded.

Dissolution test

Dissolution test was carried out using the USP basket apparatus (Caleva dissolution apparatus, UK). Dissolution medium was 900 ml of 0.1 N HCl for the first hour followed by phosphate buffer (pH 6.8) for the next two hours both maintained at 37 ± 1.0°C with an agitation speed of 100 rpm. At intervals of 30 min, 10 ml samples were withdrawn using a pipette and replaced with equal volumes of fresh solution. The withdrawn samples were filtered and analyzed on a UV Spectrophotometer at wavelength of 296 nm. The concentration of omeprazole in each sample was calculated and percentage release were determined.

Statistical analysis

Triplicate determinations of all experimental tests were carried out and results were recorded as mean ± standard deviation (SD).

Results

Physical assessment

On visual inspection of the primary and secondary packaging of the various omeprazole brands used for analysis, they all met British Pharmacopeia specifications for capsule packaging and labeling [16]. Of all the brands analyzed only one was manufactured locally, all others were imported from India. Sampled

brands were all within reasonable shelf-life at the time of sampling and analysis (Table 1).

Organoleptic properties

All capsules were smooth and glossy. Pellets were evenly coloured and whitish, with a characteristic odour.

Physicochemical properties

Solubility test showed all samples were slightly soluble in water, sparingly soluble in 96% ethanol and readily dissolved in 0.1 N NaOH.

Weight uniformity

The results from the weight uniformity test are presented in Table 2. The individual capsule weights of all sampled brands fell between 10% of the average weight.

Drug content

The drug content of each brand sampled is displayed in Table 2. The uniformity of content test as their drug contents were within ±10% of the acceptable range in all brands tested.

Disintegration time

The disintegration time of all brands tested is presented in Table 2. All sampled brands had an average disintegration time of less than fifteen (15) min.

Dissolution test

Dissolution profiles are presented as a percentage (%) of active ingredients dissolved over time (Figure 1 A & B). Less than 10% of the active pharmaceutical ingredient was released from all the brands in acid pH within the first hour. When the dissolution medium was changed to phosphate buffer; 75% omeprazole release was achieved within the next hour from all the brands.

Table 2: Physicochemical parameters of omeprazole capsule brands studied

Product code	Weight (g) ± SD	Drug content (%)	Disintegration time (min) ± SD
C_A	0.331 ± 0.011	108	11.44 ± 1.58
C_B	0.347 ± 0.007	103	13.66 ± 1.80
C_C	0.349 ± 0.008	105	14.27 ± 0.91
C_D	0.330 ± 0.005	101	9.24 ± 1.47
C_E	0.317 ± 0.008	97	11.47 ± 0.55
C_F	0.355 ± 0.005	106	10.55 ± 0.46
C_G	0.340 ± 0.007	109	12.80 ± 1.51
C_H	0.360 ± 0.006	95	9.66 ± 0.72
C_I	0.328 ± 0.005	109	10.36 ± 0.45
C_J	0.344 ± 0.020	94	11.67 ± 1.23

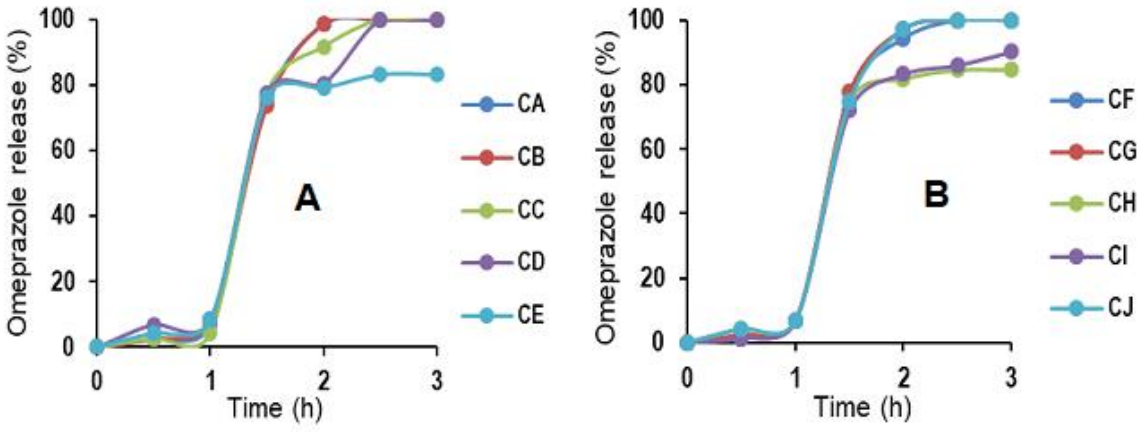

Figure 1: Dissolution profile of the generic brands (A) C_A-C_E and (B) C_F-C_J of omeprazole capsules

Discussion

The need for a uniform amount of medication in each capsule within a batch is an essential requirement for capsules [7]. Minor variations in capsule weight are permissible but should not exceed the standards stipulated in official books. Variance in the weight of individual capsules and the corresponding variation in drug content appear to be directly correlated [3,18]. For a batch of capsules to pass the weight uniformity test, not more than two of the individual capsules' weight should deviate from the average weight by more than 10% and no individual tablet should deviate from the average weight by more than 20% [16].

The USP [19] stipulates that on the assay, the active content of a pharmaceutical dosage form should lie within 90 - 110% of the labeled claim. Possible reasons a sample may fail drug content test include; inaccurate weighing of active ingredients, under or over-incorporation of active ingredients during formulation, ineffective mixing during granulation, and degradation of active ingredients on storage [8].

Disintegration time is an important factor in the release of active pharmaceutical ingredients from dosage forms [16]. The British Pharmacopeia stipulates a maximum disintegration time of sixty (60) min for all gastro-resistant capsules [16]. For omeprazole to be absorbed *in vivo* it should first be released from the capsule within a reasonable time. The type and quality of the polymer used to create the coating for capsule pellets play a key role in a gastro-resistant capsule's ability to pass the disintegration test. The capsules' success or failure in the test is influenced by additional variables such as the size of the pellets' particles and the temperature of the disintegration medium [7].

Dissolution is defined as the process by which a solid substance passes into a liquid known as a dissolution medium or solvent to form a solution [20,21]. Dissolution test is done to evaluate the rate of release of an active pharmaceutical ingredient from the dosage form. It is one of the most critical techniques for predicting *in vivo* bioavailability and some situations, determining guaranteed interchangeability and bioequivalence [22].

A dissolution profile analyzes the proportion of a drug substance that dissolves over time in advance of clinical testing [17]. The results of the study were represented as a percentage (%) of active ingredients dissolved over time. All samples passed the dissolution test for enteric-coated capsules by failing to release the drug in an acidic medium and releasing more than 75% of the drug in 40 min when immersed in an alkaline medium (phosphate buffer pH 6.8). Enteric-coated capsules are formulated to withstand stomach acid and release the active drug in an alkaline medium.

Failure of an enteric-coated capsule to pass the test is attributed to an error in manufacturing operations. Omeprazole capsules showed similar *in vitro* pharmaceutical properties because it is a specialized delivery system targeted to release its content in the intestine (enteric-coated). This technology to a significant extent would be difficult to compromise when compared to conventional capsules as any attempt to compromise the quality will lead to product failure and consequently poor clinical outcomes. This probably explains why omeprazole capsules from foreign companies are prevalent in the country.

Conclusion

All sampled omeprazole brands met the pharmacopeia standard with regard to weight uniformity, drug content, disintegration time and dissolution rate for enteric-coated capsules. The study has shown that the majority of omeprazole capsules sold in Nigeria are imported. There is a need for continuous post-clinical analysis of imported drugs in the country by regulatory agencies, so as to aid early detection and curtailing of substandard drugs.

Conflict of Interest

No conflict of interest is associated with this work.

Contribution of Authors

We declare that this work was done by the author(s) named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. MIA and AOO conceived, designed and supervised the study. NVM and MOI collected, analyzed the data and prepared the manuscript. All the authors read and approved the final draft submitted.

References

1. Colin WH. Clinical pharmacology of omeprazole. Clin Pharmacokinet 1991; 459-520.
2. Bosch ME, Sanchez RAJ, Rojas FS, Ojeda BC. Analytical methodologies for the determination of omeprazole: an overview. J Pharm Biomed Anal 2007; 44(4): 831- 844.
3. El-Sayed A, Boraie NA, Ismail FA, El-Khordagui LK, Khalil SA. Assessment of the pharmaceutical quality of Omeprazole capsule brands marketed in Egypt. Eastern Mediter Health J 2007; 13(6): 1427-1437.
4. Thoma K, Bechtold K. Influence of aqueous coatings on the stability of enteric coated pellets and tablets. Euro J Pharm Biopharm 1999; 47: 39-50.
5. Ofner CM, Zhang YE, Jobeck VC, Bowman BJ. Crosslinking studies in gelatin capsules treated with formaldehyde and in capsules exposed to elevated temperature and humidity. J Pharm Sci 2001; 90: 79-88.
6. Chang RK, Raghavan KS, Hussain MA. A study on gelatin capsule brittleness: moisture transfer between the capsule shell and its content. J Pharm Sci 1998; 87: 556-558.
7. Okorie O, Azaka JE, Amadi CM. Pharmaceutical quality assurance of omeprazole capsule brands commonly used in health institutions in Southern Nigeria. Amer J Pharmacy Pharmacol 2016; 3(4): 33-39.
8. Osei YA, Boakye EO, Bayor MT, Owusu FWA. Physicochemical equivalence and quality assessment of various brands of gastro-resistant omeprazole capsules in the Kumasi metropolis. Sci World J 2022; 10-55.
9. Enoche F, Florence DT, Olayinka F. An assessment of the quality of various brands of Paracetamol tablets sold in the Nigerian capital city. Int J Biol Chem Sci 2010; 4(1): 115-121.
10. Akunyili D. Counterfeit drugs and pharmacovigilance. The study of adverse drug reactions training course held at Uppsala monitoring center, Sweden 2005; 1-64.
11. Erhun WO, Babalola OO, Erhun MO. Drug regulation and control in Nigeria: The challenge of counterfeit drugs. J Health Population Dev Countries 2001; 4(2): 23-34
12. Shakoor O, Taylor R, Behrens R. Assessment of the incidence of substandard drugs in developing countries. Trop Med Int Health 1997; 2(9): 839-845.
13. Morris J, Stevens P. Counterfeit medicines in less developed countries: Problems and solutions. International Policy Network 2006; 1-9.
14. World Health Organization (WHO). Counterfeit Medicines: an update on estimates. News Release WHO/7. 13 March 2007. Accessed on 21 August 2023 at http://www.istm.org/publications/ News share/200805/counterfeit.aspx
15. Mitchel M. Effect of health plan and physician clinic collaboration on increasing Omeprazole use. UBM Medica Network 2009; 14.
16. British Pharmacopeia. British Pharmacopeia Commission. The Stationary Office London 2012; 2: 2293-2296.
17. Oliveira EDFS. Dissolution test optimization for Meloxicam in the tablet pharmaceutical form. Brazil J Pharm Sci 2009; 67-73.
18. Zaid AN, Rowa J, Ramahi A, Ghoush AA, Qaddumi A, Zaaror AY. Weight and content uniformity of Lorazepam half-tablets: a study of correlation of a low drug content product. Saudi Pharm J 2013; 21(1): 71.
19. United States Pharmacopeia. 33rd Revision. US Pharmacopeial Convention, Rockville, MD 2010; 3: 3870-3871.
20. Joshi K, Chandra A, Jain K, Talegaonkar S. Nanocrystalization: An emerging technology to enhance the bioavailability of poorly soluble drugs. Pharm Nanotechnol 2019; 7(4): 259-278
21. Karaźniewicz-Łada M, Bąba K, Dolatowski F, Dobrowolska A, Rakicka M. The polymorphism of statins and its effect on their physicochemical properties. Polim Med 2018; 48(2): 77-82.
22. Mubarak N, Nanda N, Kumar AKG, Perrett D, Tucker A, Johnston A. The differences between the branded and generic medicines using solid dosage forms: *in-vitro* dissolution testing. Elsevier 2012; 2: 1-8.