





Original Research

Comparative Analysis of Different Brands of Ibuprofen Available on the Georgian Pharmaceutical Market

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Abstract

According to the World Health Organization (WHO), 1 out of 10 medical products in developing countries are substandard or falsified. Since Georgia is a developing country and is listed among the countries where substandard and falsified medical products have been discovered and reported to WHO, it is important to explore the quality of medical products available on the Georgian pharmaceutical market. As an initial study, we have chosen one of the most widely used drugs worldwide – ibuprofen, available in the pharmacy network in Tbilisi – the capital of Georgia. We have studied 10 different brands, imported and locally produced, and 2 brand-name ibuprofens (Motrin and Advil). The content of the Active Pharmaceutical Ingredient (API) was determined by a spectrophotometer, in the ultraviolet region. The obtained results showed that all brand ibuprofens contained labeled amounts of API.

Keywords: Ibuprofen, Georgia, Spectrophotometry, Generic drug, Active Pharmaceutical Ingredient.

Introduction

Access to essential medicines still remains a public health problem. As of 2017, according to research conducted by the World Health Organization (WHO), approximately 2 billion people worldwide did not have access to essential medicine [1]. The price of medicine is significantly reduced by their generic analogs but sometimes at the expense

of quality [2]. Based on various studies, WHO states that 10% of medical products (medicines, vaccines, and diagnostic kits) in developing countries are substandard or falsified [3]. A systematic review and meta-analysis reports 13.6% of poor quality medicine [4]. According to some research, this number can be even higher [5,6].



According to WHO, which is based on Appendix 3 to Annex, World Health Assembly document A70/23, 2017, falsified and substandard medical products are defined as follows: “Falsified medical products - Medical products that deliberately/fraudulently misrepresent their identity, composition or source. Substandard medical products - Also called “out of specification”, these are authorized medical products that fail to meet either their quality standards or their specifications, or both” [3]. Anesthetics and painkillers represent 8.5% of all reported falsified and substandard medical products and share third place with lifestyle products after malaria medicine and antibiotics [3]. According to the same report Georgia is listed in the countries where substandard and falsified medical products have been discovered and reported to WHO. Therefore, it is important to explore the quality of medical products available at Georgian pharmaceutical market. To begin testing medical products at the Georgian pharmaceutical markets, we chose Ibuprofen. Ibuprofen is widely used worldwide and is known as one of the safest pain killers, fever reducer, and nonsteroidal anti-inflammatory drug, which is also used

Materials and Methods

Sample collections, selection of solvent, and preparing samples for measurements

10 different brands of Ibuprofen tablets, originated from different countries (including Georgia) were purchased from

for the treatment of rheumatoid arthritis. Ibuprofen has been used as a pain reliever and fever reducer during the covid pandemic, despite the initial hypothesis that ibuprofen might worsen the condition of covid patients [7] – which ultimately was rejected [8,9]. Ibuprofen comes in different forms - tablet, capsule, suspension and intravenous and is mostly available as a generic form. Tests in different countries revealed substandard and falsified medicines including Ibuprofen [10–12]. Therefore it is important that medicines be tested on a regular basis by independent parties, especially in developing countries where mostly generic drugs are available.

The aim of this work was to compare labeled amount of API to our measurements for each brand of ibuprofen tablets purchased at pharmaceutical networks in Tbilisi, the capital of Georgia.

We studied 10 different, 9 imported and 1 domestically produced ibuprofens available at the Georgian pharmaceutical network. We have also studied the brand-name ibuprofens (Motrin and Advil) ordered from the USA. Motrin was used as a standard in this study.

drug stores in Didi Dighomi district, Tbilisi in September 2020. Another two brand-name ibuprofens, Motrin and Advil were ordered from the USA. Motrin was used to plot the standard curve and Advil was tested



along with other brand ibuprofen tablets. Three tablets for each brand of Ibuprofen were randomly selected and weighed. Then each tablet was powdered and dissolved in 0.1N NaOH solution. 0.1N NaOH was selected after testing several different solutions (unpublished data). Brand names with their country of production, labeled

amount of API, and weights are given in **Table 1**. According to the label, some tablets contained 200mg of ibuprofen and some 400mg. Therefore, 200 mg tablets were dissolved in 200 ml 0.1N NaOH and 400mg tablets in 400 ml 0.1N NaOH to make 1mg/ml final concentration. 1mg/ml stock solutions were diluted as needed.

Table 1. Ibuprofen tablets analyzed in this study. Sample ID, Brand name, origin of production, labeled amount of ibuprofen in the tablet, origin of production, labeled amount in the tablet, weights of 3 randomly selected tablets for each brand of ibuprofen and MEAN value with Standard Deviation (SD).

Sample ID	Brand name of samples	Country of origin	Labeled amount (mg)	Tablet weight (mg). Test 1	Tablet weight (mg). Test 2	Tablet weight (mg). Test 3	MEAN ± SD
A	IBUPROFEN	Ukraine	200	523	314	317	384.7 ± 119.8
B	IBUPROFEN	Belarus	200	250	253	256	253.0 ± 3.0
C	IBUPROFEN	Russia	200	446	437	387	423.3 ± 31.8
D	INFORIN	Macedonia	400	656	646	657	653.0 ± 6.1
E	IBUPROFEN DENK 400	Germany	400	692	696	686	691.3 ± 5.0
F	IBUPROFEN NORMON	Spain	400	588	580	585	584.3 ± 4.0
G	IBUPROTEC-400	India	400	726	733	744	734.3 ± 9.1
H	MIGOFEN	Georgia	400	561	550	560	557.0 ± 6.1
I	NUROFEN	Great Britain	200	446	439	432	439.0 ± 7.0
J	IBUPROFEN-GRINDEKS	Latvia	400	675	673	676	674.7 ± 1.5
K	Advil	USA	200	471	477	477	475.0 ± 3.5
L	Motrin	USA	200	335	325	329	329.7 ± 5.0

Spectrophotometric measurements in the UV range and data analysis

The spectrophotometric method was used to perform qualitative and quantitative tests.

Samples were scanned at Spectrophotometer (DRAWELL, UV-VIS SPECTROPHOTOMETER, MODEL: DU-8800RS) in UV range (190-300 nm; scan

interval 5nm) in 1 cm quartz cuvettes. Measurements were repeated three times for each brand of Ibuprofen. To plot standard curves (using Motrin) 6 different concentrations were used: 6.25 µg/ml; 12.5 µg/ml; 18.75 µg/ml; 25 µg/ml; 31.25 µg/ml and 37.5 µg/ml. Stock solutions for Motrin

were made the same way as other brand ibuprofens, described above. Mean values

and standard deviations of concentrations were calculated for each brand of Ibuprofen.

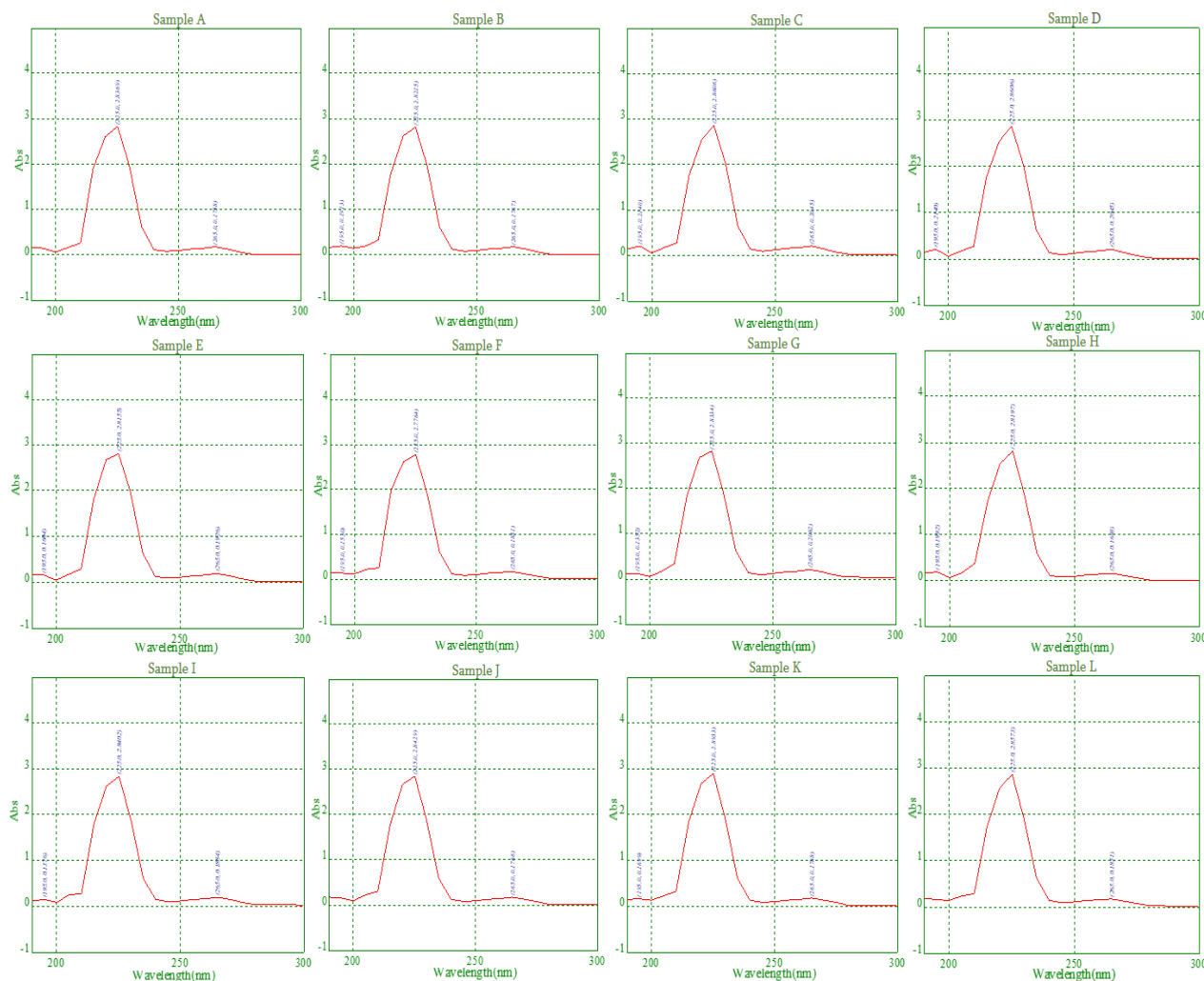


Figure 1. Individual UV spectra for each brand Ibuprofen – samplers A-L. Each sample was scanned in UV range 190-300 nm to identify Active Pharmaceutical Ingredient. ALL samples showed similar results.

Results

To test if tablets contained ibuprofen as API, qualitative studies were performed. UV Spectra with maximum absorbance at 225 nm were detected, which is in concordance with other works [12–14]. All brand ibuprofens showed similar spectra in the UV range (Figure 1), indicating the presence of

an identical substance in each of them. To perform quantitative studies we chose to use the brand name Ibuprofen - Motrin. Another brand name Ibuprofen – Advil was also tested with other brand Ibuprofens. A standard curve (including R-value) with the absorptions of Motrin and other brand Ibuprofens (mostly generics) are shown in Figure 2.

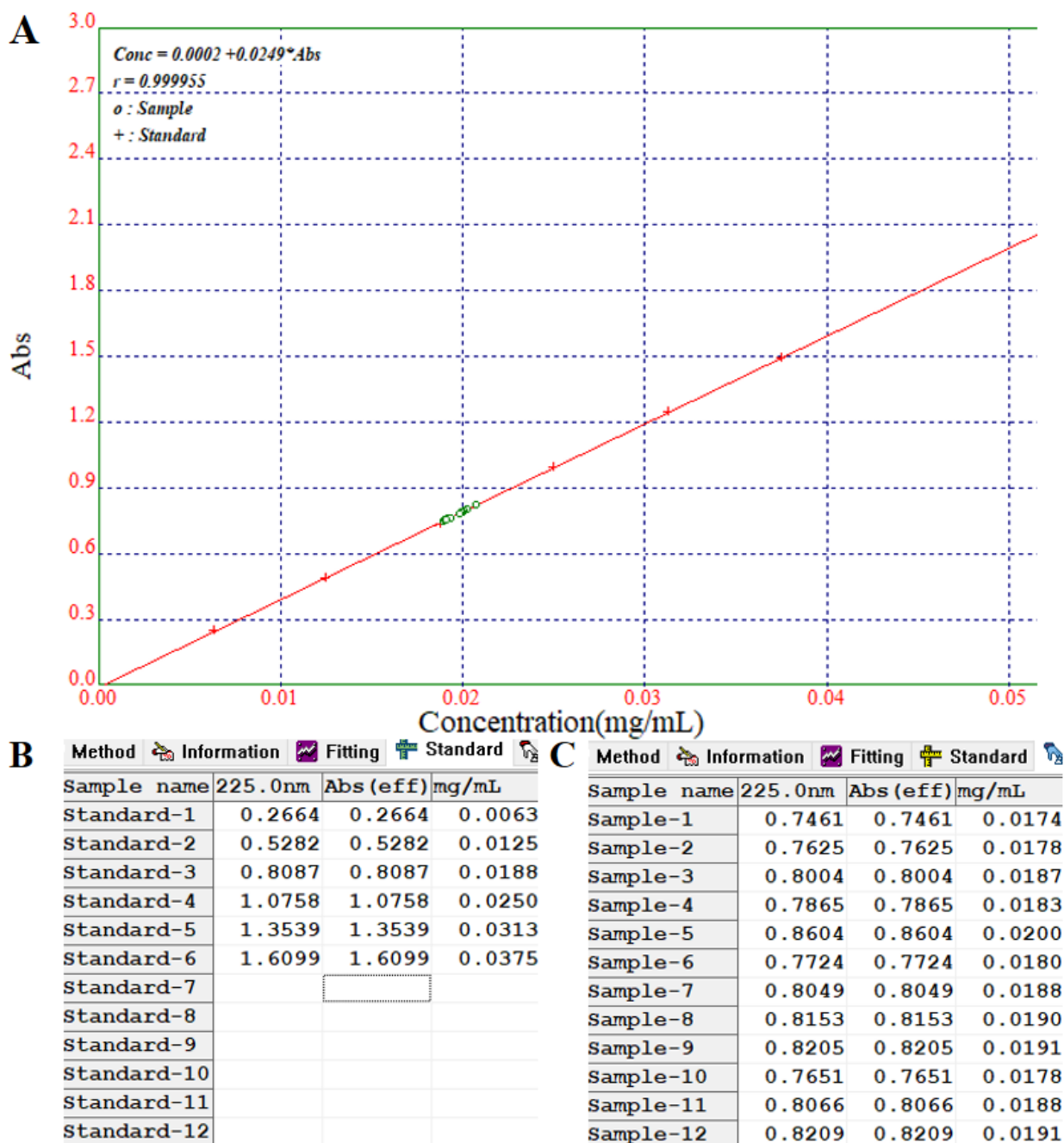


Figure 2. One of the representative of quantitative assay. Standard curve was plotted using Motrin (Brand name Ibuprofen) (A). Concentrations and corresponding absorptions for Motrin (B) Absorptions and concentrations for each samples tested, including Advil and Motrin itself (C). Order of the samples Sample 1-12 are in the same order A-L as shown in **Table 1**.

Similar results were generated in two other tests (not presented in the paper). To better visualize our data we have calculated the ratio of the MEAN value of concentration to

the expected value (MEAN value of concentration for Motrin) for each brand of Ibuprofen and plotted in **Figure 3**.

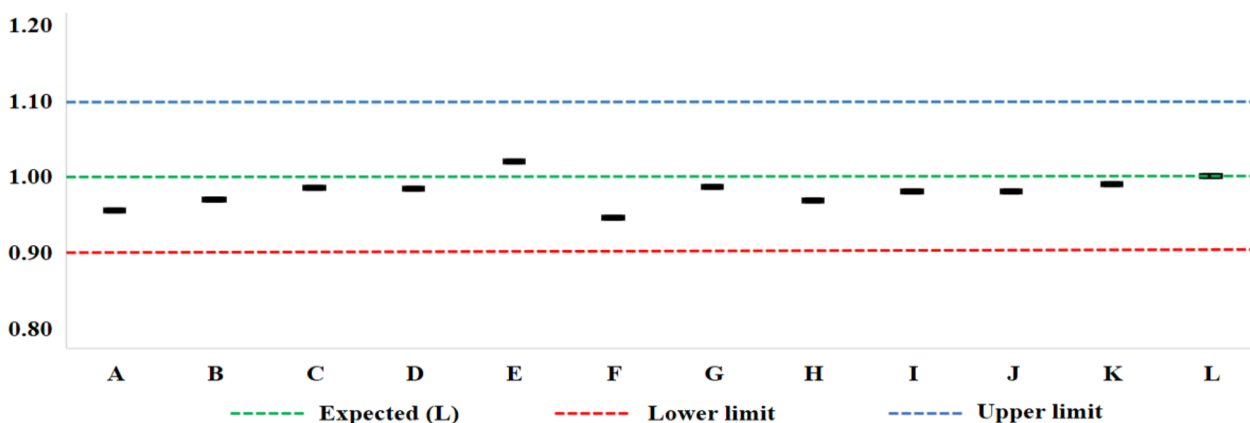


Figure 3. Ratio of MEAN value of concentration to expected amount concentration (Motrin). Mean value of none of the ibuprofens tested did not exceed $\pm 10\%$ range of the MEAN value of standard (Motrin). All brand ibuprofens are within 10% tolerance limits of expected amount of Active Pharmaceutical Ingredient and except one (F), all tested samples were in 5% limits.

This data along with each test MEAN values of concentrations and standard deviations are shown in **Table 2**. We have applied 10% tolerance limits used in other studies [15]. From Figure 3 we can see that all brand ibuprofens are within 10% tolerance limits of

the expected amount of ibuprofen. However, it is worth mentioning that except one, all tested brand Ibuprofens were in the 5% range of the expected amount of API (**Table 2** and **Figure 3**).

Table 2. Quantitative results for ibuprofen tablets analyzed. 3 randomly selected tablets were analyzed on spectrophotometer in UV (SD) was calculated for each brand. Results adjusted to standard ibuprofen (Motrin) by range. MEAN value and Standard Deviation dividing MEAN value of each brand Ibuprofen by MEAN value of Motrin

Sample ID	Results of measurements ($\mu\text{g/ml}$)			MEAN \pm SD	MEAN of Sample/MEAN of Motrin
	Test 1	Test 2	Test 3		
A	17.4	19.9	17.9	18.40 ± 1.32	0.96
B	17.8	20.2	18	18.67 ± 1.33	0.97
C	18.7	20.7	17.5	18.97 ± 1.62	0.98
D	18.3	20.1	18.4	18.93 ± 1.01	0.98
E	20	20	18.9	19.63 ± 0.64	1.02
F	18	18.9	17.7	18.20 ± 0.62	0.94
G	18.8	19.2	19	19.00 ± 0.20	0.99
H	19	19	17.9	18.63 ± 0.64	0.97
I	19.1	19.3	18.2	18.87 ± 0.59	0.98
J	17.8	19.9	18.9	18.87 ± 1.05	0.98
K	18.8	19.8	18.6	19.07 ± 0.64	0.99
L	19.1	19.1	19.6	19.27 ± 0.29	1



Discussion

As the demand for generic drugs worldwide increases, it is important to have affordable, qualitative, and quantitative tests [16]. As we have discussed in the introduction, according to WHO, anesthetics and painkillers represent 8.5% of all falsified and substandard medical products reported to WHO [3], possibly due to the high demand for these types of medical products. The exact amount of ibuprofen sold in Georgia is unknown. However, the variety of ibuprofens found on the website of the Agency for Regulation of Medical and Pharmaceutical Activities in Georgia probably means that this product is highly demanded. Since Ibuprofen is used as a fever reducer or as an anti-inflammatory drug for consuming the medical products not controlled solely by the government agencies. It will also decrease the financial load for families who cannot afford brand-name medical products and consume generic analogs instead. We think that testing other medications at the local market has to be continued and antibiotics should be next in line since they take second place in all falsified and substandard medical products reported to WHO. In addition, according to studies conducted by the University of Edinburgh, it is estimated between 72,000 and 169,000 children may die each year from pneumonia due to antibiotics that do not meet the required standards [3].

rheumatoid arthritis, it is important to have an affordable and simple quality test for this medication. Even though government agencies are involved in the monitoring medical products in Georgia, generally, we think that the involvement of other parties, including academia, and sharing the results to the public will reassure that patients are

Conclusions

Despite the significant price differences (prices are not reported purposely) of different brand ibuprofens produced in different countries, all of them contained labeled amounts of active pharmaceutical ingredient - Ibuprofen. The approach we have used does not require expensive equipment and long-term training of employees and therefore may be used as an affordable method to test ibuprofen on regular basis.

Competing interests

The authors declare that they have no competing interests.

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Authors' Contributions



Conceived and designed the experiments: ZRT MV. Performed the experiments: MV TM MK. Analyzed the data: ZRT MV. Contributed reagents/material/analysis Tools: MP ZRT. Wrote the paper: ZRT

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საქართველოს ფარმაცევტულ ბაზარზე არსებული სხვადასხვა ბრენდის იბუპროფენის შედარებითი ანალიზი

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აბსტრაქტი

ჯანმოს მონაცემებით, განვითარებად ქვეყნებში 10 სამედიცინო პროდუქტიდან 1 უხარისხო ან ფალსიფიცირებულია. ვინაიდან საქართველო იმ ქვეყნებს შორისაა, სადაც ჯანმოს თანახმად უხარისხო და ფალსიფიცირებული სამედიცინო პროდუქტები იქნა აღმოჩენილი, ამიტომ მნიშვნელოვანია საქართველოს ფარმაცევტულ ბაზარზე არსებული სამედიცინო პროდუქტების ხარისხის რეგულარული გამოკვლევა. კვლევისთვის შევარჩიეთ თბილისის სააფთიაქო ქსელში არსებული და მსოფლიოში ერთ-ერთი ყველაზე ფართოდ გამოყენებული პრეპარატი - იბუპროფენი.

შევისწავლეთ იმპორტირებული 10 სხვადასხვა ბრენდის და ადგილობრივი წარმოების 2 ბრენდული დასახელების იბუპროფენი (Motrin და Advil). აქტიური ფარმაცევტული ინგრედიენტის (API) შემცველობას ვსაზღვრავდით ულტრაიისფერ უბანში სპექტროფოტომეტრით. მიღებულმა შედეგებმა აჩვენა, რომ ყველა ბრენდის იბუპროფენი შეიცავდა API-ს ეტიკეტირებულ რაოდენობას.

საკვანძო სიტყვები: იბუპროფენი, საქართველო, სპექტროფოტომეტრი, გენერიკული პრეპარატი, აქტიური ფარმაცევტული ინგრედიენტი.

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