Daffodil International University Journal of Allied Health Sciences. Volume 6, Issue 1&2, January-July 2019

In Vitro Comparative Quality Evaluation of Some Brands of Cephradine Capsules Available in Selected Community Pharmacies in Dhaka City

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Abstract: *: Cephradine is a first-generation cephalosporin antibiotic used to treat infectious diseases caused by bacteria such as upper respiratory infections, ear infections, skin infections, and urinary tract infections.This project involved evaluating the quality of different brands of cephradine capsules available in the local market. Five different brands of marketed samples of cephradine capsules were collected from different retail pharmacy shops of Bangladesh. This study has been conducted by comparing various quality control parameters such as weight variation test, loss on drying, potency test, disintegration,dissolution test, and assay test from top, middle and lower grades pharmaceutical company of Bangladesh using standard techniques. The values were compared with the official specifications.The obtained result for weight variation is 0.58±0.71 to 2.13±3.01% and disintegration time were between 2.30±0.17 and 5.19±0.14 minutes. Loss on drying of all batches were in between 2.09±3.17 and 2.52±2.84% and potency or assay result were 98.08±0.52 to 100.25±0.19%. Moreover, the release rate of different brands of cephradine was satisfactory within 45 minutes where the mean dissolution rate is 93.96±0.13 %. The obtained results of all parameters were complied with the pharmacopoeial limit. By evaluating these parameters, we can ensure the quality of the marketed cephradine capsules.*

Keywords: *: Cephradine, loss on drying, weight variation, disintegration time, dissolution rate*

Introduction

Cephradine is the first generation antibiotic of cephalosporin group[1]. It isa semisynthetic antibiotic which chemical name is 7-[D-2-amino (1, 4- cyclohexadien-1- yl) acetamido] - 3- methyl-8-oxo-5-thia-1-azabicyclo [4.2.0] oct-2-ene2-carboxylic acid[2]. It works on broad-spectrum antibacterial activity against gram-negative as well as gram-positive bacteria[3]. The indication of cephradine is to treat urinary tract infections, respiratory tract infections, staphylococcal infections, streptococcal infections, Escherichia coli infections, skin diseases, soft tissue infections[4]. In Bangladesh,thetotal number of pharmaceuticals companies is almost 300. Only 3% of medicines are imported from different countries and 97% of the medicines come from local companies[6]. Already Bangladesh is exporting pharma products and raw materials in 150 countries including United States which can dramatically increase GDP rate[7,8]. The fundamental parameters for good quality medicines are safety, potency, efficacy and stability which ensures a healthy nation[9]. Counterfeit medicines are pivotal issues of the whole world. In Bangladesh 3.0% of the total medicine supply is counterfeit and it is enlarging rapidly[10]. Fake and substandard medicines as well as millions of patients are exposed death trap of consuming counterfeit drugs are claimed by the drug market.

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The drug makers calculated that Tk 600 crore of counterfeit medicines are traded in Tk 18,000 crore medicine market in Bangladesh per year [11]. According to a survey of Bangabandhu Sheikh Mujib Medical University from 1982 to 1992 found that 2,700 children died due to renal failure after taking toxic syrup. In 1991 child kidney specialist Dr Mohammad Hanif first ranged the alarm over counterfeit drugs. He also found out many children suffering kidney failure and most of them consumed paracetamol syrup[12]. So quality product manufacturing should be focused to reduce the burden of counterfeit medicine.

This study aims to illustrate the overall quality of thecephradine capsules. Hence, general people will get the opportunity to ensuretheir health awareness as well as the health practitioners, so that the drug regulatory authority will force the pharmaceutical companies to improve the quality of their medicines. The study is also beneficial to increase comprehensible knowledge about the weight variation, disintegration, loss on drying, potency or assay,dissolution of cephradine capsules which are manufactured by pharmaceuticals companies of Bangladesh, and the result compared with official specifications.

Materials and Methods

The specified compendial method was followed for their evaluation test. Five brands of cephradine tablets, manufactured by five different pharmaceutical manufacturers of Bangladesh with a label claim of 250 mg were obtained from retail pharmacies of different areas of Dhaka city. All capsules were of the same manufacturing year.

Instruments and Reagents Used in the Study

Laboratory instruments such as dissolution test apparatus USP (Minhua, RC-8),UV–visible spectrophotometer (T60U PG Instruments, England), oven (Bench thermosteric dryer) electronic balance (Ohaus CP213 China) and disintegration test apparatus (Aesico, CAT NO 20066B) 0.1 N HCl (CID 313), distilled water (CID: 962) were used in this study. All the reagents were analytical grade.

Collection of Sample

The samples were properly checked for their physical appearance, name of the manufacturer, batch number, manufacturing data, expiry date, manufacturing license number, D.A.R. number and maximum retail price at the time of purchase. No samples were bought and analyzed whose date of expiry had already been passed. Collected samples also covered various pharmaceutical companies. The samples were then coded for analysis. (CAP 01, CAP 02, CAP 03, CAP 04, CAP 05).

Collection of Standard

The working standard of cephradine was obtained from Incepta Pharmaceuticals Ltd. of Banglades has a gift sample for research. The purity of the reference standard was 99.99%.

In Vitro Quality Control Tests

Weight Variation Test

The weight variation test is a satisfactory method of determining the medicine content uniformity of capsules and does serve as a pointer to Good Manufacturing Practices (GMP) maintained by the manufacturers as well as the amount of active pharmaceutical ingredient (API) contained in the formulation.Twenty tablets from each brand products were weighed individually in a weighing balance. The average weights of the tablet, as well as their percent deviation, were calculated (Table 1) using the following equation [13].

Weight variation = (Iw − Aw)/Aw × 100%

Where, Iw = Individual weight of the tablet and Aw = Average weight of the tablet.

Disintegration Time Test

For disintegration testing, six capsules from each brand were used in 0.1 N HCl at 37 ± 2 °C. The disintegration time was taken to be the time when no particle remained on the basket[14]. Disintegration is the breakdown process of a capsule into smaller particles and is the first step towards dissolution. To comply with USP standards, the capsules should disintegrate, and particles must pass through the 3-inch-long glass tubes and held against a 10-mesh screen within the time given[15]. The capsules ought to be disintegrated within the acceptable time, otherwise, the prescribed course is affected and also the drug might not exert its effect properly. The disintegration time of five brands in distilled water of cephradine is shown in Table 1[16].

Loss on Drying Test

At first, the blank watch glass was measured and the capsule contents were placed in watch glass and weight of capsule contents with watch glass were measured individually. Then all the watch glass was placed in an oven and drying the samples at 60 for 180min. After that, the samples were unloaded from the oven and measured the weight of the sample after drying. Then calculated the initial and final weight of the sample and determined the LOD by the following equation:

Weight loss= Initial weight of Sample-Final weight of sample after drying
Loss on drying % = (Weight loss of sample /Final weight of sample) 100

Preparation of Standard Curve

A series of standard solution of Cephradine standard eg, 5µg/mL, 15µg/mL, 20µg/mL, 25µg/mL, 35µg/mL, 45µg/mL etc were prepared and absorbance was measured at 255nm against a blank for each solution by UV-spectrophotometer. The measured absorbance was plotted against the respective concentration of the standard solutions to check the linearity.

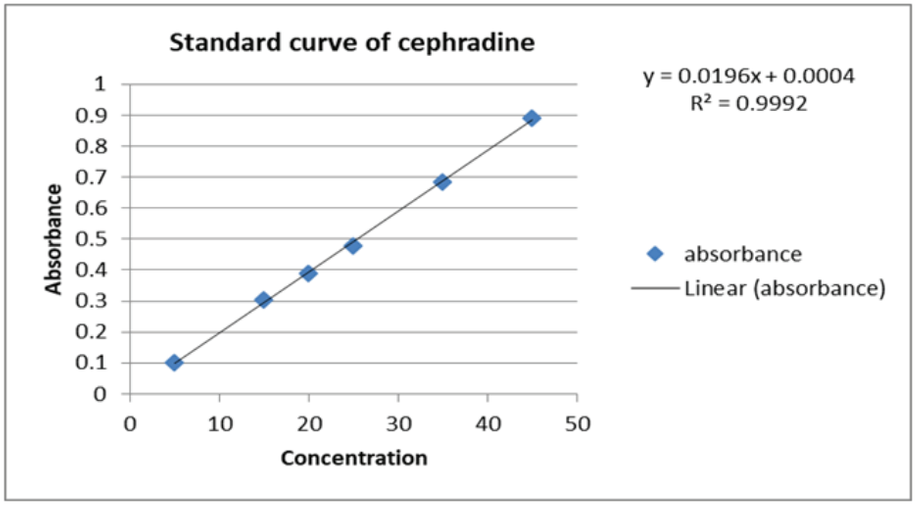

Figure 1: Standard curve of cephradine

Preparation of Assay Solution

At first, the capsule contents were removed from shell. An amount of powder equivalent to 10 mg of cephradine was transferred in a 100-ml volumetric flask. 60 ml of 0.1 N HCL solutions was added and was sonicated for 15 minutes. The volume was made up to the mark with the same solvent and filtered the solution with filter paper and make the solution 10 µg/mL with 0.1N HCL.1.5 ml of the filtered solution was diluted to 10 ml with the distilled water. The absorbance of both standard and sample were measured in a suitable UV-VIS spectrophotometer at 255 nm against blank. Each sample was run in triplicate and the average of the results was taken into consideration. Finally, the assay of the cephradine capsule was determined by the following equation of Beer-Lambert laws [17].

$$\text{Assay of sample} = \frac{\text{Absorbance of sample} \times \text{Weight of standard}}{\text{Absorbance of standard} \times \text{Weight of sample}} \times \text{DF} \times \text{Potency} \times \text{Av. wt}$$

$$\text{Potency of capsule} = (\text{Mean Assay/Amount of capsule API}) \times 100$$

Dissolution test

Dissolution test of capsule was performed by using basket method. About 900 ml of .1N HCL was filled into a 1000 mL basket of dissolution apparatus. One cephradine capsule was placed into each basket. The dissolution medium was heated up to (37±0.5) ˚C by an auto heater and 100 R.P.M was adjusted. 5ml solution was withdrawn from beaker at 10 minutes interval which was replaced with 5ml distilled water & then the withdrawn solution was filtered through filter paper. The withdrawn solution of the sample was suitably diluted &absorbance was measured at 255nm by using a UV-visible spectrophotometer against blank[18].Finally, the percent release of cephradine capsule was determined by the following equation:

% of release drug = (Absorbance of sample ×Concentration of standard× Potency ×Dilution factor ×100)/ (Absorbance of standard × Concentration of sample)

RESULTS AND DISCUSSION

Table 1: Evaluation of different quality control parameter of cephradine

Sample	Weight variation (%)	Disintegration Time (minute)	Loss on drying (%)	Potency (%)
	(Mean ± %RSD)			
CAP 01	2.13±3.01	5.19±0.14	2.52±2.84	100.52±0.19
CAP 02	0.72±0.85	2.30±0.17	2.09±3.17	99.26±0.52
CAP 03	0.65±0.87	2.32±0.11	2.25±6.33	98.18±0.64
CAP 04	0.834±1.31	2.42±0.14	2.25±3.30	98.10±1.53
CAP 05	0.583±0.71	3.3±0.32	2.48±4.25	98.08±0.52
USP specification	NMT ± 5% to ± 7.5%	5–30 min	Near to 7%	95-105%

Weight Variation: The weight variation for all the capsules used in this study ranges from 0.58±0.71 to 2.13±3.01 gm which showed compliance within the official specifications[19]. When the weight variation is within the specifications the tablets are thought to contain a uniform active ingredient to give a desired therapeutic response but when the weight variation is out of the specification the tablets are thought to contain less or more active ingredient to give an ineffective therapeutic response or toxic effect respectively[20]. It may vary due to result from, poor granulation flow properties, resulting in uneven die fill[21,22.] It was obtained that all the brands meet the USP specification which was between 0.58 ± 0.71 to 2.13 ± 3.01% (Table 1).

Disintegration Time: It was seen from the table-1 the disintegration time were between 2.30±0.17 and 5.19±0.14 minutes.So it can be said that the entire marketed sample complied with the specification of disintegration time for capsule.

Loss on Drying (LOD): This test method is used to estimate the amount of volatile materials present in a material.The LOD of five brands of cephradine are shown in Table 1.From this study, we observed that the specification of LOD % varies from product to product for cephradine capsules and it is near to 7.0% [23]. It was seen from the result that none of the marketed cephradine samples exceeded the specification and therefore it can be said that the entire marketed sample complied with the USPspecification for capsules.

Assay Test: The capsule must contain an average amount of active content for their proper therapeutic response. Because the active ingredients of the capsule exert the therapeutic effect. The low content will result in less therapeutic response or even the product may be ineffective.

From this study, we noticed that official specifications or other standards provide an acceptable potency range around the label potency. For highly potent, low dose drugs, this range is usually not less than 90.0% and not more than 110.0% of the labeled amount. For most other larger dose drugs in capsule form the official potency range that is permitted is not less than 95.0% and not more than 105.0% of the labeled amount[24]. From the above result, it is observed that all brands of capsules meet the specification of the assay result (Table 1).

Dissolution Rate Test: The dissolution rate of five brands of cephradine capsule were determined. The percent release of drug was plotted against the times, which give dissolution curve.The observed results were shown in figure 2 where the mean dissolution rate is 93.96±0.13 % within 45 minutes.

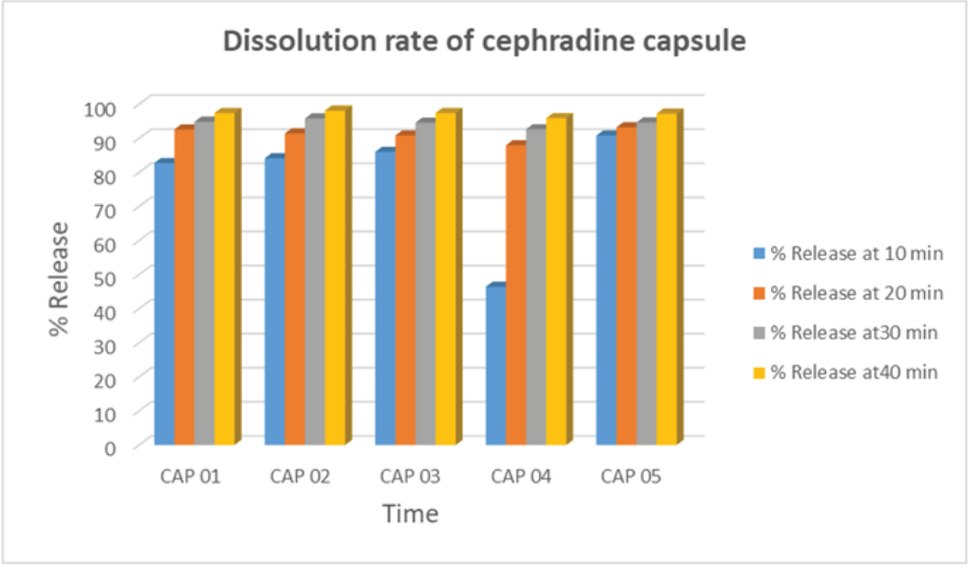

Figure 2: Graphical representation of dissolution rate of various brands of cephradine capsule

Conclusion

This work was done to find out the current status of the quality of the marketed cephradine capsule available in Bangladesh. It will help to create awareness among the common people, health practitioners as well as drug control authority. So that pharmaceutical manufacturers will produce quality medicine and people may not waste their hard-earned money by buying low-quality products. For this purpose, the marketed sample of five brands of cephradine capsule was analyzed by using established methods and apparatus. A comprehensive knowledge about the weight variation, disintegration, dissolution, assay, loss on drying of cephradine capsule preparations can be measured and compared these values with their specifications. Loss on drying of all brands are within the range of specification of USP guidelines. Weight variations are within the limit for all brands, dissolution rate and disintegration time are also within the pharmacopoeial limit for all brands. This study will help both health practitioners and consumers to select quality products. The present study also can provide some information to drug control authority of Bangladesh to evaluate the overall quality status of cephradine preparations.

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