WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 9, Issue 5, 146-157. Research Article ISSN 2277– 7105

A COMPARATIVE STUDY ON QUALITY ANALYSIS ON MARKETED VITAMIN C (ASCORBIC ACID) CHEWABLE TABLETS OF DIFFERENT BRANDS AVAILABLE IN BANGLADESH

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Article Received on
08 November 2019,
Revised on 29 March 2020,
Accepted on 19 April 2020
DOI: 10.20959/wjpr20205-14989

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ABSTRACT

Ascorbic acid is used to treat scurvy, delayed wound and bone healing, urine acidification, used as an antioxidant, and vitamin C deficiency. This study was involved to determine the physical and chemical parameters of different brand tablets of ascorbic acid chewable tablets in Bangladesh. The comparison among the products was done by using of the standard parameters of pharmacopeia specifications. Tablets used in this analysis was collected from the local market. Different popular brands were chosen for the study of different quality control tests involving appearance, hardness, friability, disintegration time, weight variation, dissolution rate & assay were calculated. The result of the hardness was shown between 3-20 kg/N. Friability results were also shown not more than 1 % which is matched with the USP specification for the all samples except Nutrivit C (1.151%). According to in-vitro dissolution of pharmacopeia, Ceevit (77.218%) dissolution profile didn't match with the standard limit and the all other samples meet the acceptance criteria of pharmacopeia. Assay tests result meet the acceptance criteria for all brands. This study is an analysis of between the market products that gives the clear comparison between the products to give the information to the prescriber communities to have the great choice of medicines by choosing the best products among different brands.

KEYWORDS: Ascorbic Acid, Vitamin C, Pharmacopeia, Dissolution rate, Assay.

1. INTRODUCTION

The solid dosage forms are the most commonly used routes of drug administration. It offers one of the safest and most convenient methods of drug administration. Chewable tablet forms is one of the most common forms for administrating ascorbic acid. So, it is necessary to

maintain the perfect quality of each drug for human health. The tablet dosage form is mostly used dosage form all over the world. According to BP chewable tablets have the same specification as immediate-release tablets. The tablet manufacturing process is one of the easiest and safest method of manufacturing pharmaceutical dosage forms.[1] Ascorbic acid is a popular chewable tablet in which [(2R)-2-[(1S)-1, 2-dihydroxyethyl]-3, 4-dihydroxy-2H-furan-5-one] are present as active ingredients in pharmaceuticals are used as vitamin C drugs in the management of scurvy, delayed wound, urine acidification, bone healing, vitamin C deficiency and in general as an antioxidant.[2] Some Excipients are used in this formulation to make the formulation stable. Binders, lubricants, glidants, diluents, or granulating agents, are used to ensure efficient tableting and disintegrate to promote tablet breaking down in the digestive tract. Sweeteners and flavoring agents are used to make the formulation most acceptable. The coloring agent makes the tablets visually attractive.[3] The half-life of ascorbic acid in plasma is 16 days, after ingestion of a plain release tablet plasma ascorbic acid concentration increased 66% ($P<001$) to a maximum concentration of 74.2724.3 mmol/L at 4.0 h (T_{max}).[5] It is available in the various formulations such as chewable tablets, gums, capsules, powdered form, injections.[6] Drug products should be chemically and pharmaceutically equivalent and must be identical in strength, purity, and release profile.[6] Because of the widespread use of this drug, quality control testing should be done for ascorbic acid marketed products to ensure safety, efficacy, accepted quality, the rationality of use of the drug.[7] The objective of this work was therefore to evaluate the pharmaceutical quality of five different brands ascorbic acid chewable tablets available in Bangladesh.

2. MATERIALS AND METHODS

The quality analysis of chewable tablets was studied through the determination of weight variation, friability, hardness, dissolution rate, disintegration time and assay study. The study was performed by doing these various test procedures which are the key factor analyzing the quality of the different brands of various brand tablets.

Collection of Sample

There are more than forty products of ascorbic acid chewable tablets in Bangladesh. Five popular brands were collected from the local retail markets (Malibagh, Dhaka). 30 tablets of each brand were collected for quality analysis. All brands of ascorbic acid chewable tablets contain 250 mg per tablet. The products were finely checked for their physical appearance, the name of the manufacturer, batch number, manufacture date, expiry date, manufacturing

license number, and D.A.R number before purchasing. The physical appearances of different brands were also shown in table 1 and the level information about the sample of the different brand tablets available in Bangladesh is in Table 2.

Reagents, Instruments, and Equipment Used

Distilled water, tablet hardness tester USP-1217 (Electrolab: EH-01P), test tubes, PharmaTest disintegration tester, dissolution tester (PharmaTest: DT70), pipette, volumetric flask, UV-visible spectrophotometer (SHIMADZU UV Spectrophotometer: UV-1800- 240V), analytical precision balance (DENVER Instrument, Model-M 310, Switzerland), single drum friability tester (model: PHARMA TEST-F10E/ER).

Determination of Weight Variation of Tablets

Ten tablets from five different brands of the tablet were taken to determine the weight. Weight of those products were determined by electric balance which is mentioned before. The average weight of the product was determined and the percent deviation of the tablets were calculated carefully.[8]

The formula of percent (%) of weight variation:

Percentage (%) weight variation= (average weight – individual weight)/ individual weight x 100 %

Determination of Hardness of the Tablets

Tablet hardness can be defined as the load necessary to crush a tablet. Hardness denotes the capacity of a tablet to withstand mechanical shocks. The hardness test is necessary because the tablet must be stable during for the tablets during manufacturing, packaging, transportation. The tablets were placed into the center hardness tester and then the pressure increased to determine the strength of the tablet. The average hardness of the tablet was calculated with the standard deviation. The acceptable range of the hardness of a tablet is 4 to 7 kg-f (kilogram of force). In this analysis, the hardness of all different brands of tablets was determined using a tablet hardness tester. Ten tablets of each brand were taken to determine the hardness of the tablets.[9]

Table 1: Physical Appearance Chewable Tablets of Different Brands.

Brand Names	Color	Shape and Others
Ceevit 250mg	Orange	Round, uncoated
VC 250mg	Orange	Round, uncoated
Nutrivit C	Pale-Yellow	Oval, uncoated
Cecon	Orange	Round, uncoated
Vasco	Orange	Unusual, Uncoated

Determination of Friability of the Tablets

The friability test apparatus is made of such a way that a certain number of tablets go through the effects of abrasion and shock. In this apparatus, there is a plastic chamber and the rotation of the chamber is 25 per minute. The tablets were dropping from a distance of 6 inches. Generally, the initial weight of the tablet is placed in the friability tester, which has a rotation of 100 rpm. Then the final weights of the tablets were taken. The acceptance criteria of friability for the tablet is 1%. When friability shows the results more than 1% it indicated the tableting problems and it should not be accepted for commercial use. Friability should be less than 1%. Formula for calculation percentage friability is given below:[10]

Percentage (%) friability= {(Initial weight- Final weight)/ Initial weight} x100

Determination of Disintegration Time on Tablets

After administrating oral dosage forms, the drug does for disintegration. Disintegration can be defined as the breakdown of the solid dosage form into small particles which give the action of active ingredients to the human body. So, the disintegration test is an important test for determining the quality control of the products' bioavailability, the onset of action, and the effectiveness of the tablets. The disintegration process means mechanical break-down of tablets into smaller granular particles. The time taken to breakdown the tablets is known as disintegration time (DT).[7] According to USP the standard disintegration time for an uncoated tablet must be not more than 15 minutes. Tablet disintegration was determined by the tablet disintegration tester (USP, Pharma Test Disintegration Tester).[10] The temperature was maintained in distilled water at 37°C. Six tablets of each brand were selected and placed in each of the cylindrical tubes of the basket and the disc was used.[10,11]

Dissolution Rate Test of Tablets

The definition of dissolution is a process by which the solid dosage forms go into a solution and it's become available at the systemic circulation. There are some factors such as the media in which the drug is dissolving, the temperature of the media, and the solubility of the

drugs to dissolution media. The most rapid absorption is from a solution, most dosage forms are solids, either tablets or capsules. There are also some physical factors for formulating a tablet, such as excipients, coatings, and pH, which have an effect on the rate of dissolution.[12] A dissolution test for each brand of Ascorbic Acid tablet was carried out by USP dissolution type apparatus.[13] In this apparatus, 900 ml distilled water was used as dissolution medium, and the rpm is 75. The process was maintained at 37 ± 0.5°C by a constant temperature bath with a selected speed of 75 rpm by a variable speed motor.[13] In general, a single tablet is placed of each brand in a basket tied to the bottom of the shaft connected to a motor. Samples were withdrawn from the vessel and the amount is 10 ml from the medium in which replacing of an equal volume of the amount of fresh dissolution medium (distilled water) must be immediately done. Diluted filtered samples were suitably analyzed by using UV Spectrophotometer (Shimadzu UV Spectrophotometer: UV-1800-240V) at 295.4 nm. By measuring the absorbance, the percentage release of drug after 30 minutes of various brands was calculated.[10] The obtained data was given (Table 5) and (Figure 2).

Table 2: Label Information about the Sample of Different Pharmaceutical Company.

No	Brand Name	Batch No.	Mfg. Date	Exp. Date	DAR No	Manufactured by
1.	Ceevit 250mg	9BO1582	OCT 2018	OCT 2020	012-0135-078	Square Pharmaceutical Ltd.
2.	VC 250mg	BI0318	DEC 2018	DEC 2020	143-0068-078	Aristo Pharma Limited
3.	Nutrivit C	AL238	OCT 2018	OCT 2020	005-0155-078	ACI Pharma. Ltd
4.	Cecon	T0088029	APR 2018	APR 2020	036-0079-078	Acme Pharma Ltd.
5.	Vasco	TGJ151	OCT 2018	OCT 2020	025-0054-078	Opsonin Pharma Ltd

Assay Determination of Tablets

About 25 mg of standard ascorbic acid was accurately weighed and transferred into a 100 ml volumetric flask. Then dissolved the samples in distilled water up to 100 ml. and was shaken mechanically for 30 min. 5 tablets were weighed & crushed into fine powder from each formulation. An equivalent weight of samples was taken in a 100ml volumetric flask and then the volumetric flasks were filled with distilled water up to 100ml. The absorbance of both standard and sample were measured in a suitable UV-VIS spectrophotometer at 295.4 nm using distilled as blank. Each sample was tested twice and average of the results was taken into consideration.

3. RESULTS AND DISCUSSION

Weight variation

The weight of 10 different brands of Ascorbic Acid tablets was determined with the help of an electronic balance and the observed results have been included in the table below (Mean values ± SD, n=10).

Table 3: Average Weight of Different Brands of Ascorbic Acid Tablets.

Sl. No	Brand Name	Average wt. mg	Weight variation limit
1.	Ceevit 250mg	907.88	-3.01 to +4.60%
2.	VC 250mg	744.49	-3.90 to +4.73%
3.	Nutrivit C	819.76	-3.43 to +4.49%
4.	Cecon	834.99	-4.50 to +2.83%
5.	Vasco	817.25	-3.24 to 4.87%

According to the BP, for the average weight of tablets (mg) are 80 or less the maximum percentage differences allowed ±10 and for the limit 80-250 mg, the percentage difference should be ±7.5 and more than 250mg this should be ±5. Besides, according to USP, for the average weights of tablets (mg) are 130 or less, 130-324 and more than 324 the maximum percentage difference should be ±10, ±7.5, ±5 respectively.[7] From the experiment results (Table 3), it was obvious that weight variation limit values of all branded tablets were within the specification of the official pharmacopeia differences and no abnormality has occurred.

Hardness and Friability of Tablets

Hardness is one of the most important physical features for evaluating tablet.[10] It may affect tablet friability, disintegration time and bioavailability. Too hard tablets may result in a decrease in the release of the drug. A digital hardness tester was used to measure the hardness of 10 different brands (Mean values ± SD, n=10).

Table 04: Friability and Hardness of Different Brands of Ascorbic Acid Tablets.

Sl. No	Brands	Average % of friability	Hardness (kg-f)
1.	Ceevit 250mg	0.156	14.82
2.	VC 250mg	0.043	11.801
3.	Nutrivit C	1.151	02.599
4.	Cecon	0.065	18.201
5.	Vasco	0.092	03.474

The observed results are shown that all different brands of tablets hardness limit 2-18 kg-f (Table 4). In the study, it was found that most of the brands of the ascorbic acid group passed the test of hardness and had acceptable crushing strength of between 2.599 kg-f to 3.474 kg-f

except Cecon brand which was the hardest of all the ascorbic acid tablet brands with a hardness of 18.201 kg-f, indicated that it was above the limit range of between 4 to 7 kg-f stated.[17] On the other hand, VC and Ceevit brands had a crushing strength was 11.801 and 14.820 kg-f respectively which also denoted that those brands were above the standard limit. It may either due to using different granulation techniques or using different excipients. Besides, the friability of the tablets which is determined using friabilator was found between 0.043– 0.151% (Table 4). Most of the samples passed the standard limit of friability (not more than 1%) but Nutrivit C was above the limit due to its different granulation techniques or different excipients.

Calculation of Disintegration Time on Tablets

The rate of drug absorption and therapeutic efficacy and the onset of the action of the drug is dependent upon the disintegration time. If the disintegration time is perfect and matches with the standard we can easily confirm that the effectiveness of the drug is good.[7] The disintegration time was measured according to the above-denoted procedure and the observed results are shown in Table 5 (Mean values ± SD, n=10). According to the BP/ USP specification of disintegration time, it is observed from the results that most of the samples follows specification for disintegration time except Ceevit, VC, Nutrivit C.

Table 5: Disintegration Time (DT) of Different Brands of Ascorbic Acid Tablets.

Serial No.	Sample Name	Average DT
01	Ceevit	53 Min 51 Sec ± 0.003
02	Cecon	15 Min 22 Sec ± 0.010
03	VC	22 Min 32 Sec ± 0.005
04	Vasco	14 Min 02 Sec ± 0.015
05	Nutrivit-C	21 Min 47 Sec ± 0.012

Calculation of Dissolution Test on Tablets

The process by which the drug dissolves from the dosage form and becomes available for absorption from the gastrointestinal tract. The outcomes of the in vitro release of branded tablets were shown in Table 6 and Figure 3. By the finish (30 minutes) of the in-vitro release test, the percentage drug release for most of the brands were showed more than 80% except Ceevit was found 77.21 %. Most of the brands passed the BP/USP general specifications. The graphical representation of this test is below Figure 1.

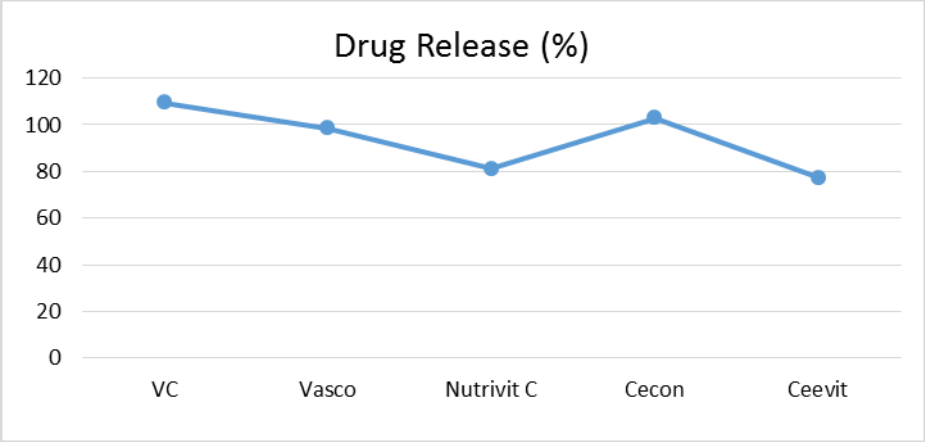

Figure 1: Comparative Drug Release Profile of Ascorbic Acid Tablet at 30 Minutes.

Table 6: The % of Drug Release after 30 Min of Various Brands of Ascorbic Acid Tablets.

Sl. No.	Sample Name	Drug Release (%)
1	VC	109.531
2	Vasco	98.392
3	Nutrivit C	81.198
4	Cecon	102.973
5	Ceevit	77.218

Calibration Curve of Ascorbic Acid (API)

The values of Abs. (absorbance) were plotted against respective concentrations (Figure 2). The conc. (concentration) showed linearity when the curve was plotted indicating it obeyed beers law. The linear equation was y = 0.0286x - 0.0107 and the regression coefficient R^2 was also 0.9913.

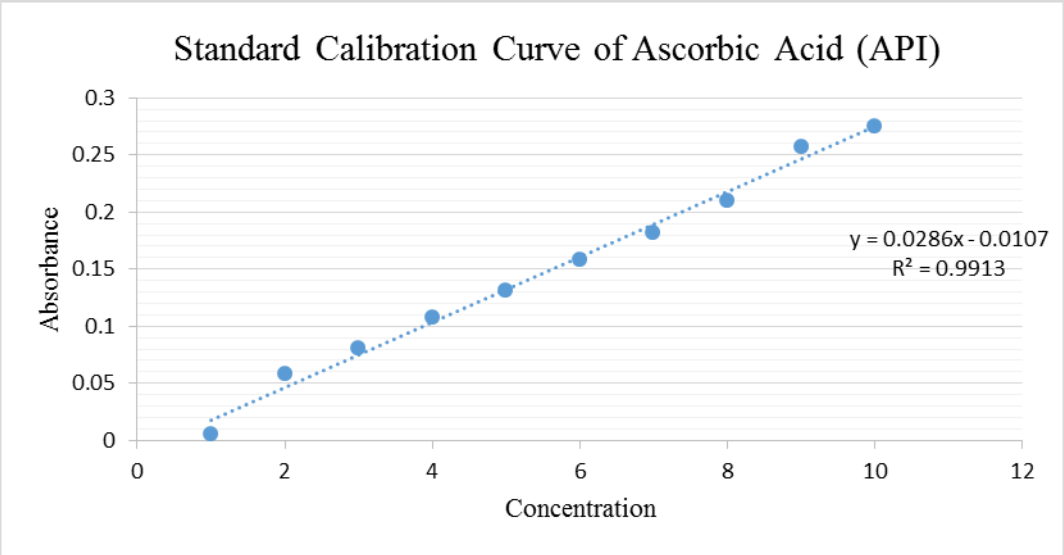

Figure 2: UV Standard Calibration Curve of Ascorbic Acid at 295.4 nm.

Assay Determination of Ascorbic Acid Tablets

Determination of the Assay was performed according to the USP method. The potency value was found to be between 95.89% - 99.51% (Table 7) which is within the USP limit. It denotes the presence of ascorbic acid in all the brands perfectly. These potency values are also expressed in a graphical presentation in Figure 3.

Table 7: Assay of Various Brands of Ascorbic Acid Tablets.

Serial No.	Product Name	% Assay
01	Ceevit	97.40
02	Vasco	95.89
03	Nutrivit C	99.51
04	Cecon	98.31
05	Vc	97.58

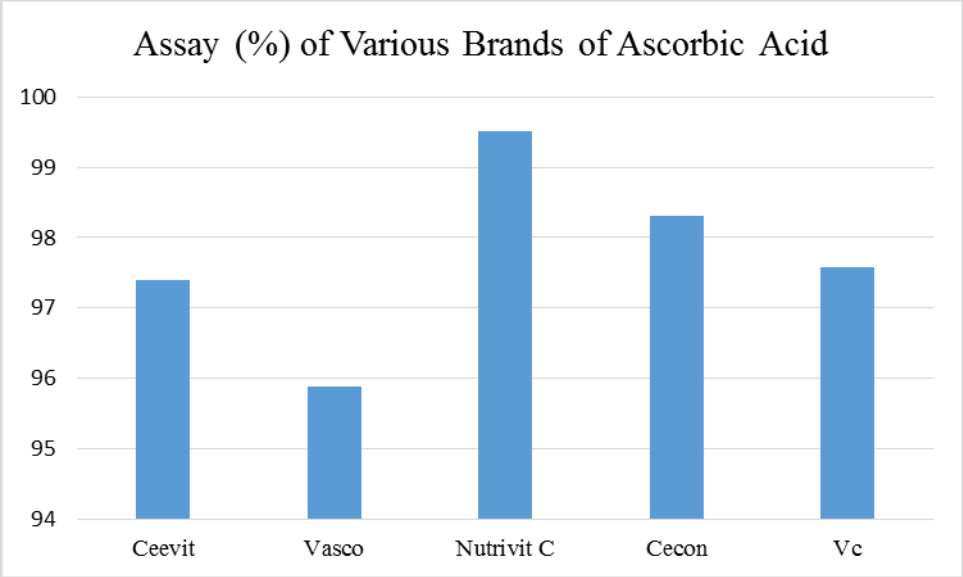

Figure 3: Comparative Assay Profile of Ascorbic Acid Tablets of Different Brands.

4. CONCLUSION

The current pharma market of Bangladesh is flooded with various vitamin C preparations.[18] So it is necessary to justify the perfect quality of this tablet of various brands. The quality parameter, considerable cost, time consumption and scientific expertise of any formulation are important because therapeutic response and safety depends on its quality maintenance.[19] The quality of a drug in a pharmaceutical industry depends on personnel qualifications, active pharmaceutical ingredients quality, validation of the manufacturing process etc.[20,21] Weight variation, hardness, friability, disintegration time, dissolution test, potency profiles of all branded tablets used in the study were within BP/USP specified limits. Most of the samples

showed acceptable disintegration time, assay, friability, hardness and weight variation, dissolution profile. However, Ceevit showed low dissolution profile compared to the other brands and Nutrivit C didn't follow the friability specification and Ceevit, VC, Nutrivit C takes more disintegration time than the pharmacopeia specification. This study is a good analysis for finding compatibilities of the sample formulations with the specifications of the official Pharmacopeia. This study confirms the need for continuing close observation on marketed ascorbic acid tablets within the country to ensure the quality and this quality maintain also directly relates to public health. In addition, public health issue is important for the development of Bangladesh.

ACKNOWLEDGEMENT

The authors are grateful to the Department of Pharmacy, Stamford University Bangladesh for providing the research facility for this investigation.

CONFLICT OF INTEREST

There is no conflict of interest.

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