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Quality assessment of some brands of vitamin C (ascorbic acid) tablets marketed in Uyo, Nigeria

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Abstract

The quality of some brands of vitamin C tablets marketed in the city of Uyo, Nigeria was assessed. All the ten samples passed the uniformity of weight and disintegration time tests as specified in the British Pharmacopoeia and United States Pharmacopoeia for effervescent, uncoated, dispersible tablets. However, the titrimetric evaluations for the content of active ingredient showed that seven samples contained a chemical equivalent of ascorbic acid within the limits of official specification. Finally, the equivalence point (end-point) was very sharp and attained faster when ceric ammonium sulphate was used as the titrating reagent.

Keywords: Ascorbic acid; Quality assessment; Weight uniformity; Disintegration time; Active ingredient.

Introduction

The World Health Organization (WHO) at the International Conference on Primary Health Care, held at Alma-Ata in 1973, identified the supply of good quality essential drugs as one of the basic prerequisites for the delivery of health care (WHO General Reports, 1988). However, the incidence of counterfeiting in drugs [for which many descriptions exist (Pakistani manual of drugs in Nigeria, 1987; WHO, 1992; USFDA, 2004)] has seriously militated against the achievement of this lofty goal especially in developing countries of the world. Basically, counterfeiting in pharmaceutical products may present itself in correct ingredient but not in correct amounts; wrong ingredient and/or without ingredient which results in the reduction of safety, efficacy and quality of such products (WHO, 1992). Also, counterfeiting in drugs could result from poor current Good manufacturing practices (cGMP), stability problems and sometimes purely out of criminal intent. In 1988, the WHO assembly adopted a resolution that governments and Pharmaceutical Manufacturers should co-operate in the detection and prevention of imports/exports and/or smuggling of deceitfully labeled and spurious drug preparations (WHO, 1999). It is alleged that almost every efficacious patent or prescription drug in Nigeria has either a fake or adulterated version, ranging from vitamins,

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antimalarials, analgesics, through antibiotics to drugs for diabetics and hypertension (Midala, 1990; IRIN-WA, 2001). Vitamin C (ascorbic acid) is L-threo-2,3,4,5,6-pentahydroxy-2-hexanoic acid-4-lactone. It occurs in fresh vegetables (lettuce, cabbage, green peppers) liver and fruits (lemon, tomatoes, berries) and is readily absorbed after oral administration, distributed in tissues and excreted from the body (American Society of Hospital Pharmacists-ASHP, 1987). It is useful in the prevention and treatment of cold, flu and scurvy, development of cartilage, bone, teeth and healing of wounds (Martindale, 1989). It is also prescribed as an antioxidant in the treatment of dysentery, ulcers, hay fever, tuberculosis, arteriosclerosis, cancer, osteogenesis, among others (ASHP, 1987). In the light of the multifarious uses of this drug, the present study was undertaken to assess the quality of some brands of vitamin C marketed in the city of Uyo, Nigeria with the aim of confirming the compliance or otherwise of parameters such as weight uniformity, disintegration time and percentage drug content.

Experimental

Materials and reagents. A sample of vitamin C crystals was obtained from Neimeth Pharmaceuticals PLC, Lagos, Nigeria and used to prepare the reference standard. Ten brands of vitamin C tablets were purchased from pharmacy shops in Uyo, Nigeria and coded alphabetically. Analytical reagents; iodine crystals, ceric ammonium sulphate, soluble starch, ferrous sulphate, sodium thiosulphate, silver nitrate, sulphuric acid, nitric acid (BDH Chemicals Limited, Poole, England) and 1,10-phenanthroline (Riedel-De Haen AG Seelze-Hannover, Germany) were purchased prior to the study.

Packaging and product aesthetics. The products were assessed for tablet appearance, aesthetics and packaging quality.

Identification. 0.2mL of 2M nitric acid and 0.2mL of 0.1M silver nitrate solutions were added to 5% w/v of sample solution in a clear test-tube. Observation was made for a grey color precipitate (BP, 1988). The reference sample of vitamin C, which served as a control was also tested.

Melting point. The aqueous solution of sample was filtered and the filtrate evaporated in a water-bath to obtain ascorbic acid crystals. Some of the crystals were then filled to a quarter of the length of a micro-capillary tube and the melting point determined (BP, 1993) using an Electrothermal melting point apparatus (Electrothermal Engineering, Limited, England). The melting point of the reference sample was also determined.

Uniformity of weights. The tablets were randomly selected and separately weighed on a balance (Mettler Toledo GmbH, USA). The mean weights and the standard deviations were then calculated (BP, 1988).

Disintegration time. An Erwerka BDT disintegration test apparatus was used to determine the disintegration time of six tablets. Simulated gastric fluid was used as the medium and maintained at a temperature of 30 ± 0.5^{o}C (BP, 1988).

Content of active ingredient. Ten tablets of each brand of vitamin C were powdered separately.

(i) Powder equivalent to 400mg of sample was accurately weighed and dissolved in a mixture of 100mL carbon dioxide- free water and 25mL of 1M sulphuric acid. 3ml of starch solution was added as indicator and the resultant solution titrated at once against 0.05M iodine solution (which previously had been standardized with sodium thiosulphate solution) until a persistent violet blue color was obtained (Olaniyi and Ogungbamila, 1991).

(ii) Powder equivalent to 150mg of sample was dissolved in a mixture of 30mL of water and 20mL of 1M sulphuric acid. 3 drops of

ferroin sulphate (made by dissolving 700mg of ferrous sulphate and 1.5mg of 1,10-phenanthroline in sufficient water) were added to the solution and was subsequently titrated against 0.1M ceric ammonium sulphate solution until a sharp yellow coloration resulted (Olaniyi and Ogungbamila, 1991). The determinations were repeated and the calculated results averaged.

Results and Discussion

Product aesthetics and packaging. All the vitamin C brands investigated were oval in shape and they came in different colors ranging from white and cream through orange to brown tablets. The tablets were all packed in aluminum/plastic blister packs. The packs were all contained in cardboard boxes with well designed impression of the brand names. The manufacture and expiry dates, batch and NAFDAC registration numbers were ink printed (Table1).

Identification of sample. All the samples tested positive for ascorbic acid (USP, 1995) as can be seen in Table 2.This was reassuring in that, the samples studied all had ascorbic acid in them.

Melting point. The melting point of the reference vitamin C crystals (X) was 190^{o}C. This falls within the official range of 188-190^{o}C (BP, 1993; USP, 1995). This was indication of purity and the suitability of the sample as a reference standard. However, the sample brands gave values which ranged from160^{o}C (J) to 183^{o}C (A) (Table 3). These values were lower than that of the reference standard because of the presence of excipient particles in the dried filtrates used for the determination.

Uniformity of weights. All the tablets from the various brands showed significant weight uniformity with low percentage weight deviations (Table 3). Thus, there was satisfactory consistency in the weights of the tablets. Wide variation in weights of tablets is undesirable as this could militate against dosage uniformity.

Disintegration time. All the samples passed the disintegration test since the tested tablets disintegrated within 30 minutes as specified by USP, 1995.

Percentage drug content. The USP (1995) requires that ascorbic acid tablets contain not less than 90% w/w and not more than 110% w/w ascorbic acid. Iodine and ceric ammonium sulphate were respectfully employed as titrating reagents in this determination. All the brands assayed were found to contain amounts of ascorbic acid within the above stated range except J (82.00% w/w; 80.30% w/w), D (115.75% w/w; 112.53% w/w) and I (119.75% w/w; 112.73% w/w). Brand J failed this determination (having a lesser % w/w value than the lower limit of 90% w/w). This is most probably a manifestation of counterfeiting (WHO, 1992). Similarly, brands D and I also failed the percentage drug content determination (having slightly higher % w/w values than the upper limit of 110% w/w). Ascorbic acid is easily converted to its isomer; dehydroascorbic acid at high temperatures. This could be taken as another indication of poor handling/ counterfeiting (WHO, 1999). Ceric ammonium sulphate was found to be more sensitive and more reliable than iodine as a titrating reagent because the equivalence (end-point) was very sharp and attained faster. This was not surprising as ceric ammonium sulphate is less highly colored (compared with iodine which is brown) hence making meniscus reading less cumbersome. It is also stable in air over long periods, requires no protection from light and maintains constant composition.

Table 1. Some particulars of the vitamin C brands investigated.

Sample	MD	ED	BN	NAFDAC Reg. No	Color of tablet	Manufacturer or address of sample source
A	June, 2005	June, 2008	ASC/105	04-4134	White	SKG Pharma, Lagos, Nigeria
B	Aug, 2005	Aug, 2008	LOTO/55F	04-1847	Cream	Emzor PLC, Lagos, Nigeria
C	July, 2005	July, 2008	0150	04-0170	Orange	New England, USA
D	Feb, 2005	July, 2006	10305	04-3480	Cream	Vietnam
E	Nov, 2004	Oct, 2007	054054	04-2333	Brown	Hamburg, Germany
F	Nov, 2005	Nov, 2007	DM/360	04-3622	Cream	Malaysia
G	Oct, 2005	Oct, 2008	2210/F	04-6705	White	Evans Medical Ltd, Nigeria
H	Dec, 2005	Dec, 2008	5612/H	04-1453	White	Sussex, England
I	Oct, 2005	Oct, 2008	A13/T	04-4997	Orange	Indonesia
J	Sept, 2004	Sept, 2007	N/10181	04-3928	Orange	India

Key: Study was carried out in March, 2005 when samples were within their viable shelf life.
MD = Manufacture Date, ED = Expiry Date, BN = Batch Number, NAFDAC Reg. No. = National Agency for Food, Drug Administration and Control Registration Number.

Table 2. Identification test of vitamin C brands

Sample	A	B	C	D	E	F	G	H	I	J	X
Remark	+	+	+	+	+	+	+	+	+	+	+

Key: X = Reference standard sample of ascorbic acid,
+ = Ascorbic acid present.

Table 3. Some determined quality parameters* of the vitamin C brands investigated.

Sample	% Uniformity of weight	% Drug content (w/w)		Disintegration Time (min. s)	Melting point (^{0}C)
		I_2	Ceric ammonium sulphate		
A	0.37(0.055)	107.50(0.71)	98.80(0.20)	5min. 3s(0.95)	183(0.22)
B	0.30(0.012)	106.75(0.75)	103.52(0.40)	3min(0.10)	163(0.30)
C	035(0.016)	108.50(0.50)	106.70(0.70)	4min.2s(0.20)	173(0.41)
D	0.33(0.012)	115.75(0.74)	112.53(0.38)	7min .3s(0.50)	168(0.23)
E	0.34(0.017)	104.75(0.94)	100.93(0.48)	2min.48s(0.05)	177(0.77)
F	0.32(0.020)	105.75(0.30)	102.06(0.50)	3min.2s(0.20)	164(0.48)
G	0.33(0.018)	106.50(0.50)	101.33(0.98)	2min.12s(0.03)	182(0.64)
H	0.38(0.025)	103.50(0.74)	100.62(0.74)	2min.(0.12)	181(0.31)
I	0.31(0.013)	119.75(0.98)	112.73(0.41)	2min.2s(0.45)	162(0.61)
J	0.36(0.016)	82.00(0.93)	80.30(0.15)	2min.5s(0.72)	160(0.54)
X	ND	109.50(0.30)	107.20(0.35)	ND	190(0.80)

Key: * = Value of each parameter above is the mean with the standard deviation in brackets.
X = Refer to Table 2. ND = Not done.

From the results obtained in this study, it is recommended that authorities like Pharmacists Council of Nigeria (PCN), National Agency for Food, Drug and Administration and Control (NAFDAC) and Standard Organization of Nigeria (SON) should be strict in the monitor and control of drugs circulating in Nigeria with a view to preventing the availability and use of substandard or counterfeit drugs as such do not only fail to give to give the desired therapeutic effect but can also aggravate the disease state of patients.

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