African Journal of Pharmaceutical Research & Development

Vol. 12 No.3; pp. 342-349 (2020)

ORGANOLEPTIC AND PHYSICOCHEMICAL EVALUATION OF BRANDS OF LIQUID MULTIVITAMIN PRODUCTS IN EDO STATE, NIGERIA

ITUA ESTHER OLEIYE [1], ERAGA SYLVESTER OKHUELEGBE[2,*], ARHEWOH MATTHEW IKHUORIA[2]

1. National Agency for Food and Drug Administration and Control (NAFDAC). Benin Regional Office, Federal Government Secretariat, Benin City, Edo State, Nigeria.
2. Department of Pharmaceutics and Pharmaceutical Technology, Faculty of Pharmacy, University of Benin, Benin City, Edo State, Nigeria.

ABSTRACT

Multivitamins accounts for a high percentage of prescribed medicines in tertiary health institution and over the counter (OTC) drugs in pharmacies in Benin City, Edo State. The aim of this study was to determine the organoleptic and physicochemical qualities of some liquid multivitamin products available in Edo State, Nigeria. Fifteen different brands of liquid multivitamin products were purchased from pharmacies across Edo State. The brands were code labelled ML1 to ML15. The organoleptic and physicochemical properties of the products were assessed according to British Pharmacopoeia (BP) and unofficial standards, while the chemical properties of some of the marker vitamins (B1, B2, B6 and folic acid) and the dietary mineral (iron) were analyzed using high-performance liquid chromatography (HPLC) and atomic absorption spectrophotometry (AAS). The presence of lead and manganese as contaminants was also assessed. All the drug samples were within their shelf life at the time of sampling and analyses and were duly assigned registration numbers by National Agency for Food and Drug Administration and Control (NAFDAC). Twelve brands were manufactured in Nigeria while the remaining three in India. The samples had pleasant odour and taste except ML8 that had an unpleasant odour, while ML3 had a bitter-sweet taste. They exhibited no particular standard in pH (4.20 - 6.60) and specific gravity (1.37 - 1.81 g/ml). Content assay showed some discrepancies between labelled claims and actual contents of samples, with variable amounts of the different marker vitamins and dietary minerals. In conclusion, all samples tested except two (ML3 and ML8) had satisfactory organoleptic and physicochemical properties. None of the samples met all official compendial specifications for content in all marker vitamins and dietary mineral assessed.

KEYWORDS: **Multivitamins; Liquid preparations; Pharmaceutical quality; Contaminants.**

INTRODUCTION

A multivitamin formulation is a dietary supplement which contains vitamins, dietary minerals, and other nutritional elements. A multivitamin is defined as a supplement containing three or more vitamins and minerals that does not include herbs, hormones, or drugs, where each vitamin and mineral is included at a dose below the tolerable upper level, as determined by the Food and Drug Agency and does not present a risk of adverse health effects [1]. Multivitamin preparations are used to provide vitamins that are not taken through diet [2]. Such preparations are available in the form of tablets, capsules, pastilles, powders, liquids, and injectable formulations. Other than injectable formulations, which are only available and administered under medical supervision, multivitamins are recognized as a category of food. There are thirteen (13) vitamins universally recognised at present. They are the vitamins A, B (B1, B2, B3, B5, B6, B7, B9 and B12) C, D, E, and K [3].

***Corresponding author:** eragaso@uniben.edu; +2348030884928*

Multivitamins account for about 69.0% of prescribed medicines in a tertiary health institution in Benin City [4]. They also account for over 70% of drugs prescribed for pregnant women in Ghana [5]. Furthermore, between 30 to 40% of over the counter (OTC) drugs displayed for sale in pharmacies and patent medicine shops (PMS) in Egypt are multivitamins [6]. The problem of substandard and falsified drugs has made it necessary to routinely assess the pharmaceutical quality of manufactured drugs all over the world [7]. However, almost all the routine drug assessment tend to focus on other commonly used drugs such as antimalarials [8], analgesics [9], antibiotics [10], antihypertensive [11], antidiabetic [12], etc. Researchers tend to avoid investigating multivitamins for several reasons including the fact that multivitamins have a wide therapeutic window and a high safety margin of use and therefore do not appear to pose immediate danger to prospective users. They are therefore generally regarded as safe medicines since majority of their constituents are similar to endogenous agents and hence side effects from the use of multivitamins are usually rare. This does not however justify the need to ignore the production and monitoring of products to ensure quality standards. Furthermore, they generally contain a number of active ingredients which require that several components should be monitored simultaneously. This makes monitoring of multivitamins expensive since it will require use of highly technical analytical equipments such as high-performance liquid chromatography (HPLC). The aim of this study was to investigate the pharmaceutical quality of some oral liquid multivitamin products found in Edo state, Nigeria.

MATERIALS AND METHODS

Sample collection

On a cross-sectional basis, multivitamin products of different strengths and from different generics were purchased from January to March 2016 from pharmacies across Edo State, Nigeria. No particular sampling procedure was employed other than the researchers posing as a 'customer' purchased the drugs from pharmacies and patent medicine shops. The different brands were obtained from drug stores wherever they could be found until fifteen (15) different samples of oral liquid preparations were collected and their unit price recorded.

Following the purchase, information on brand name, batch numbers, manufacture and expiration dates of each brand, manufacturer's name and address and country of origin of the brand, as well their registration status by the National Agency for Food and Drugs Administration and Control (NAFDAC) were recorded from the product label where available (Table 1). Also recorded were the labelled strength of some essential vitamins and minerals in each formulation (Table 2).

Evaluation of drug samples

Organoleptic properties

Preliminary examination of the organoleptic properties was done for all the samples. The following properties were evaluated; colour, taste and odour. The differences in observations were handled objectively and the decision of a majority (at least 2 out of 3) of assessors was taken. The appropriate definitions for the evaluations were based on the relativity of our findings to the descriptions of British Pharmacopeia for the products of multivitamins [13].

Physicochemical properties

pH determination

This was determined using Jenway digital pH meter (Cole-Parmer, UK). Phosphate buffers (pH 4, and 6.8) were used to calibrate the equipment at room temperature before measurement was taken.

Specific gravity

The specific gravity was determined for the different brands of the liquid dosage forms of the multivitamins by weighing 10 ml of the different brands three times and then the average in weight per millilitre (g/ml) of the three values was determined and taken as the specific gravity of the sample.

Fill volume

The fill volume of the different brands of the liquid dosage forms were determined using a graduated measuring cylinder. The volumes of any three bottles of each brand randomly selected were used and the average value was calculated.

Sealing/resealing integrity

The sealing integrity of the different liquid dosage forms was determined by first turning the sealed or unopened bottles of all the different products upside down for 24 hours. They were then observed to see if there were leakages of any form from the caps of the products. For the resealing integrity, the caps were unscrewed and then re-screwed again. The re-screwed caps were observed to see if the caps continue to turn round without stopping.

Drug analysis

The analyses of the various brands were carried out within one month after their purchase. Pure vitamin samples (Vits. B1, B2, B6, vitamin C and folic acid) and minerals (iron, and manganese) supplied by the NAFDAC zonal laboratory, Agulu, Anambra State, Nigeria were used as internal standards. The standards were used in the generation of calibration plots of the vitamin samples and in the calibration of the analytical equipment. All other chemicals used for the analysis were of analytical grade.

Content assay

The products were assayed for uniformity of content according to the British Pharmacopeia [13] and Codex Alimentarius guideline [14]. Using HPLC (Hitachi, Japan) Column type (C18 250 x 4.6 mm) with a UV/Visible detector. The mobile phases used at flow rate of 1.0 ml/min include: methanol:potassium dihydrogen orthophosphate (20:80) for vitamins B1 and B6, acetonitrile:ammonium acetate (80:20) for vitamins B2 and C and acetonitrile:citrate buffer (10:90) for folic acid. Sample detection was carried out at various wavelengths viz: vitamin B1, 254 nm; vitamin B2, 230 nm; vitamin B6, 280 nm; folic acid, 270 nm and vitamin C, 254 nm.

Atomic absorption spectrophotometry was carried out for the assay of iron, manganese and lead. The instrumental parameters were adjusted according to the manufacturer's recommendations. A lead hollow cathode lamp was used as a radiation source, operated at 5 mA with a slit width 0.2 nm. The air-acetylene flame flow rate was 1.5 l/min. Concentrations of the minerals were determined by using AA990 Atomic Absorption Spectrophotometer (PG Instruments, UK) [15].

Statistical analysis

Experiments were carried out in triplicates and mean values reported with standard deviation. Differences between means were subjected to one-way ANOVA with Dunnett multiple comparison test against the brand that met the BP standard for crushing strength (5.0 - 8.0 kp) at $p \leq 0.05$ using GraphPad InStat 3.10.

RESULTS

Results of preliminary investigation

All the product had labels showing the names of the products, names, addresses and country of the manufacturers, date markings (batch numbers, manufacturing dates and expiry dates) and their NAFDAC registration numbers. Also, they all had caution signs, such as “Keep all medicines out of the reach of children”, direction for use, storage condition, indication for use, date markings, leaflet insert containing all information about the drug (Table 1).

The labels of samples ML1, ML3, ML4, ML5, ML6 and ML11 did not indicate the presence of iron, while vitamins B9, B12, C and elemental iron were absent in ML4 label. Sample ML2 label contained quinine in addition to other minerals and vitamins. Samples ML6 and ML11 label information showed the absence of the B and C vitamins and elemental iron. ML6 label displayed only herbal constituents, while ML11 had ciproheptadine in addition to other minerals. (Table 2)

Cost, organoleptic and physicochemical properties

The most expensive drug in this group was ML6, which contained only herbal constituents that were not listed as either vitamins or not, while the cheapest were samples ML1, ML3 and ML13. All the samples had pleasant odour with the exception of ML7 that had an unpleasant odour (Table 3).

All the samples had one form of sweetness or another with the exception of sample ML2 that had bitter taste. Samples ML7 and ML9 had the least mean fill volume in comparison to their product volume of 200 ml.

The samples were free flowing with specific gravity ranging from 1.35 - 181 g/ml and the lowest and highest values exhibited by samples ML1 and ML5, respectively. Most of the samples were slightly acidic except sample ML12 that was slightly alkaline. All the products had good sealing/resealing properties with the exception of sample ML7 that had bad sealing/resealing property and lumpy sediments.

Content assay and elemental contaminants

The samples exhibited variation in percentage content in comparison with their labelled values especially in vitamin B2 content. There were discrepancies in labelled content and actual content as sample ML5 contained vitamins B1 and B6, but the labelled information did not indicate the presence of these vitamins. Samples ML7 and ML14 indicated on their secondary label that they each contained 1.5 and 1.0 mg of vitamin B2, respectively, but analysis of the sample showed that they did not contain any amount of vitamin B2 (Table 4).

All the liquid products investigated had low amounts of lead and manganese (Table 4). There were slight differences in the amounts present in all the formulations for both contaminants.

Table 1: Label information on the liquid multivitamin products evaluated

Brand Code	Batch number	Date of manufacture	Expiry date	NAFDAC number	Country of manufacture
ML1	L882U	August 2015	August 2018	04-0135	Nigeria
ML2	50504	May 2015	May 2017	04-0847	Nigeria
ML3	L763T	July 2014	July 2017	04-0287	Nigeria
ML4	MB-9697	May 2014	April 2016	A4-4031	Nigeria
ML5	4S21005	August 2014	July 2016	A4-2778	India
ML6	CFAD13	August 2014	January 2017	A4-5994	Nigeria
ML7	LI3311H	September 2013	September 2016	04-0942	Nigeria
ML8	L260U	March 2015	March 2017	04-1450	Nigeria
ML9	FK2021	June 2015	May 2017	04-6398	Nigeria
ML10	2684356	March 2015	February 2018	04-0511	Nigeria
ML11	OAL057	August 2014	July 2017	A4-1647	India
ML12	ARL14036	November 2014	October 2016	04-2551	India
ML13	3914	August 2014	August 2016	04-1155	Nigeria
ML14	1715	July 2015	June 2017	04-1194	Nigeria
ML15	BH-0614	November 2014	October 2016	A4-8261	India

Table 2: Labelled content information on the liquid multi-vitamin products

Brand Code	Contents (mg)							
	Iron	Vit. B1	Vit. B2	Vit. B6	Vit. B12	Vit. C	Folic acid	Others
ML1	-	1.5	10.0	-	0.0025	50	-	Vit. A (1000 IU), Vit. D (200 IU)
ML2	32.18	0.98	3.92	0.39	0.0006	-	-	Liver extract (23.4 mg), quinine HCl (0.15 mg)
ML3	-	5.0	20.0	2	-	-		
ML4	-	5.0	25.0	1.5	-	40	0.75	Amino acids
ML5	-	-	0.003	-	0.0025	40	0.75	
ML6	-	-	-	-	-	-	-	Herbals constituents
ML7	50.0	1.0	1.5	1.5	-	30	2.00	
ML8	14.0	2.0	3.0	2	0.005	-	0.50	
ML9	70.0	2.5	5.0	1	0.005	5	0.50	
ML10	41.0	-	-	-	0.005	-	0.50	
ML11	-	-	-	-	-	-	-	Ciproheptadine, lysine, peptone
ML12	47.0	5.0	25.0	1.5	2.5	40	0.50	
ML13	40.0	-	-	-	0.003	-	0.20	
ML14	18.0	2.0	1.0	1.0	0.001		0.20	
ML15	10.0	5.0	10.0	1.0	0.005	-	0.05	

Table 3: Cost, organoleptic and physiochemical properties of liquid multivitamin products

Brand Code	Cost (₦)	Colour	Volume (ml)	Taste	Odour	Specific gravity (g/ml)	pH	Sealing/ resealing	Additional remarks
ML1	200	Golden Yellow	98	Banana sweet	Pleasant	1.35	4.37	Good	Clear and consistent
ML2	450	Dark Gold	95	Bitter sweet	Slight	1.38	5.11	Good	Clear and consistent
ML3	200	Golden Yellow	100	Syrupy sweet	Slight	1.40	5.57	Good	Clear and consistent
ML4	700	Brownish Gold	195	Metallic sweet	Metallic	1.70	4.57	Good	Clear and consistent
ML5	700	Brownish Gold	200	Honey sweet	Metallic	1.81	4.67	Good	Clear and consistent
ML6	1,250	Darker Orange	190	Very sweet	Pleasant	1.70	4.85	Good	Clear and consistent
ML7	400	Darker Gold	187	Alcoholic sweet	Unpleasant	1.57	4.20	Bad	Lumpy sediment
ML8	400	Darker Gold	196	Sweet	Vanilla	1.51	6.08	Good	Clear and consistent
ML9	300	Darker Gold	189	Slightly sweet	Pleasant	1.54	6.60	Good	Clear and consistent
ML10	300	Darker Gold	203	Slightly sweet	Slight	1.35	6.19	Good	Clear and consistent
ML11	600	Dark Gold	201	Sweet and cool	Pleasant	1.40	4.77	Good	Clear and consistent
ML12	1,200	Darker Gold	200	Boring taste	Metallic	1.60	7.17	Good	Clear and consistent
ML13	200	Darker Gold	290	Metallic sweet	Metallic	1.39	6.30	Good	Clear and consistent
ML14	280	Red	199	Sweet and cool	Pleasant	1.57	5.30	Good	Clear and consistent
ML15	450	Darker Gold	200	Very sweet	Pleasant	1.37	5.11	Good	Clear and consistent

Table 4: Content of vitamins and some elements in the liquid preparations evaluated

Brand code	Quantity (%)						Quantity (ppm ± SD)	
	Iron	Vit. B1	Vit. B2	Vit. B6	Vit. C	Folic acid	Lead	Manganese
ML1	-	120.47	717.27	-	103.5	-	0.003 ± 0.0006	0.011 ± 0.0005
ML2	92.29	99.70	869.74	100.51	-	-	0.003 ± 0.0004	0.013 ± 0.0002
ML3	-	101.60	939.85	102.65	-	-	0.006 ± 0.0002	0.013 ± 0.0008
ML4	-	109.66	675.97	140.13	104.20	110.0	0.005 ± 0.0002	0.009 ± 0.0006
ML5	-	100.56	102.20	-	106.78	113.0	0.006 ± 0.0008	0.009 ± 0.0002
ML6	-	-	-	-	-	-	0.004 ± 0.0004	0.010 ± 0.0006
ML7	132.48	255.00	0	142.4	102.30	-	0.007 ± 0.0005	0.012 ± 0.0003
ML8	375.29	100.05	668.0	99.95	-	94.8	0.006 ± 0.0006	0.008 ± 0.0001
ML9	97.90	103.6	721.2	104.4	113.6	102.6	0.003 ± 0.0004	0.010 ± 0.0002
ML10	150.41		-			111.80	0.002 ± 0.0006	0.012 ± 0.0004
ML11	-	-	-	-	-	-	0.004 ± 0.0008	0.014 ± 0.0004
ML12	212.77	105.3	731.43	105.3	112.00	102.6	0.004 ± 0.0001	0.008 ± 0.0008
ML13	275.00	-	-	-	-	96.00	0.007 ± 0.0003	0.007 ± 0.0009
ML14	241.11	100.30	0	205.80	-	130.0	0.003 ± 0.0004	0.012 ± 0.0004
ML15	571.10	110.52	415.20	250.00	-	-	0.005 ± 0.0003	0.011 ± 0.0005

N=3; ppm = parts per million.

DISCUSSION

The organoleptic and physicochemical evaluations of some liquid multivitamin brands available in pharmacies across Edo State were carried out. The label information regarding the contents of the multivitamin products gives an insight that some of these products should not be marketed as multivitamin brands. This is because they did not fit into the class of products called multivitamins, which are described as formulations containing 3 or more vitamins, dietary minerals and other nutritional supplements but not herbs, hormone or drug [1,16]. A multivitamin product supplies vitamins, dietary minerals and nutritional supplements that may be absent from the normal diet of individuals but needed by the body.

In addition, multivitamins are usually prescribed for people who are recovering from illness, pregnant and nursing mothers, infants, growing children and elderly [17,18]. This is because they contain nutritional supplements that are needed to keep the human body healthy, build blood and strengthen the immune system [17]. Elemental iron is an essential dietary mineral that helps the body to build blood necessary for oxygen transport in the body [19]. Vitamin C (ascorbic acid) helps to strengthen the human immune system, promotes wound healing and is utilised by the bone to produce red blood cells [20]. Vitamins B6 (pyridoxine), B9 (folic acid) and B12 (cyanocobalamin) are also very essential for the formation of red blood cells and also help prevent anaemia [21]. Based on the above, prescribing some of these products may not have the desired benefits since they do not contain the required minerals and vitamins that will help to bring relief. It is commonly known and widely accepted that liquid preparations are mostly prescribed for infants and growing children. As a result, the appearance, odour and taste of liquid preparations are important factors to be considered during formulation. Liquid preparations with sweet taste and pleasant odour are easier to administer to infants and growing children, hence achieving better patients' compliance to dosage regimen. Based on these results, it will be difficult to administer samples ML2 and ML7 to children.

The acidic nature of the multivitamin brands is expected as most of the products contained both vitamin C (ascorbic acid) and folic acid. The high acidic value of sample ML7 may be as a result of its high content of folic acid. Uneven discharge from bulk discharge containers in product filling may be implicated in uneven fill volumes [22]. Lumpy sediments may have resulted from one or a combination of several factors such as the pH of the medium in which the product was formulated, the presence of certain metals like iron, copper, calcium, stabilizers (like antioxidant), the nature of the base and the concentration of water present in the preparation, the conditions of storage such as light, temperature, type of container, humidity etc., or the incompatibility of the vitamins present in the preparation [23,24]. Faulty sealing/resealing property may lead to loss of potency during use, since poor resealing ability will lead to undue exposure to humidity and microorganisms and this would consequently lead to degradation of the product which can manifest in the formation of lumpy sediments, production of foul odour, etc [25].

The percentage contents of the vitamins and/ or minerals present in the brands varied from one product to another to such an extent that none of the fifteen liquid preparations complied with USP requirements for multivitamin products with regards to iron (90 - 125%), vitamins B1 (90 - 250%), B2 (90 - 150%) and B6 (90 - 150%) [26]. This may be attributed to their wide therapeutic window and a high safety margin; hence the manufacturers might not be strict in ensuring the appropriate amounts of each vitamin or mineral are present in their formulation.

The levels of the impurities detected in all the formulations showed that they were within acceptable and tolerable limits of safety [27]. It also showed that adequate care was taken in the selection of raw materials and water purification process. Lead as an impurity is usually used as the index of water purity since lead is a major water contaminant [28].

Most elemental impurities are introduced to bulk powder for drug production via the catalysts or other reagents employed in drug production [29]. The different sourcing of active ingredients/excipients in the bulk powders for the preparation of these products during manufacture and interactions between formulation and packaging materials are ready routes of metallic contamination [30].

CONCLUSION

There were variations in labelled claims and the product contents which should be addressed by the drug regulatory agency. The level of impurities or contaminants was generally low and within official requirements. There is no justification for the wide difference in cost since they did not markedly vary in quality.

ACKNOWLEDGMENTS

The authors acknowledge the technical support received from the laboratory staff of the NAFDAC zonal laboratory, Agulu, Anambra State, Nigeria.

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