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An assessment of the compliance of some essential drugs in Nigeria to pharmacopoeial specifications

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Abstract
The counterfeit drugs phenomenon is a global one. Most developing countries however lack adequate scientific data on the incidence. An attempt has been made to establish the level of counterfeit medicines in Nigeria as at 1993. Sampling and assay of drugs were completed by 1993, prior to the establishment of the National Drug Regulatory Agency. A total of 379 samples were analyzed to determine the percentage content of their active ingredients and the results judged against the British Pharmacopoeia 1988 specifications. The analytical tools employed were those of ultraviolet/visible spectrophotometer and liquid chromatography. A total of 265 (69.9%) drug preparations were found to be outside of BP 1988 specifications of their active ingredients. On application of the Null hypothesis statistical tool to further analyze the data, the overall failure came to 41.4%. Further analysis of the data revealed that of the 379 total samples, 103 (27.2%) were imported while 267 (70.4%) were made in Nigeria. The labels on 9 (2.4%) of the samples did not indicate country of manufacture. 184 (69.4%) of the samples that failed to comply with pharmacopoeia standards were made in Nigeria while the remaining 81 (30.6%) were imported. The study showed that the level of counterfeit drugs in Nigeria as at 1993 was as high as 41.4%.

Keywords: Counterfeit drugs, Pharmacopoeia standards

Introduction

Counterfeiting in goods is as old as man, while counterfeiting in drugs is a fairly recent occurrence. On the African continent, the first open concern was at the Nairobi conference organized by World Health Organization (WHO) in 1985 (WHO, 1999). Various descriptions exist of counterfeit drugs (WHO, 1992, USFDA, 2004, Lahore 1987). These range from that of deliberately and fraudulently mislabeled products with respect to identity and/or source of a drug whose container or labeling is made without authorization to bear the trademark, trade name, or other identifying mark, imprint, or device or any likeness thereof, of a drug manufacturer, processor, packer, or distributor other than the one who in fact manufactured,

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processed, packed or distributed such a drug. Counterfeiting, falsely presents medicinal products with correct ingredients but not in the correct amounts, wrong ingredients and/or without ingredients that result in the reduction of the safety, efficacy and quality of the product. Simply understood, a counterfeit drug is one which is deliberately or fraudulently mislabeled with respect to identity and/or source or with fake packaging, and can apply to both branded and generic products. The WHO's definition of counterfeit pharmaceutical products (WHO 1992), include products with correct ingredients, wrong ingredients, without active ingredients, with the incorrect quantity of active ingredient and/or with fake packaging and labeling.

Counterfeiting in drugs could result from poor current Good Manufacturing Practices (cGMP), stability problems and sometimes purely out of criminal intentions. In 1988, the WHO assembly adopted a resolution that governments and pharmaceutical manufacturers should co-operate in the detection and prevention of the increasing incidence of the export, and/or smuggling of deceitfully labeled and spurious drug preparations (WHO, 1999).

This study was conducted prior to the establishment in 1997 of one of the major Health intervention programs in Nigeria through the petroleum (special) Trust Fund (PTF) and the official take off of the National Agency for Food and Drug Administration and Control (NAFDAC). Prior to PTF intervention of 1997-1999, there existed a huge fall in the supply of drugs to the public health facilities. Thus a big gap existed between drug supply and demand. It was alleged that almost every efficacious patent or prescription drug in Nigeria had either a fake or adulterated version, which ranged from common analgesics, through antibiotics to drugs for ailments such as diabetes and hypertension (IRIN-WA, 2001).

The objective of the study is to establish level of counterfeit drugs in the Nigerian Health System before the Health intervention Programs.

Experimental

Samples. This study was carried out between January 1991 and June 1993 and it involved seven classes of drugs. These drugs were chosen based on their inclusion in the Nigerian list of essential drugs. They included Chloroquine, Cotrimoxazole, Paracetamol, Ampicillin, Sulphadoxine/Pyrimethamine, Metronidazole and Chloramphenicol. The drug preparations were tablets, capsules, syrups, suspensions and injections. The drugs used in the study were obtained from pharmacies, hospitals, Federal Medical Centres and patent medicine vendors in Ganawuri, Kaduna, Onitsha, Suleja, Bida, Minna, Lagos, Barkin-Ladi and Jos; all in Nigeria. 379 samples were collected, 103 of the samples (representing 27.7%) were imported while 267 (representing 70.4%) were made in Nigeria. The labels on 9 of the samples (representing 2.4%) did not indicate the country of manufacture. No attempt was made to authenticate the source of drugs, nor the manufacturers of the products. All label instructions were accepted as such.

Analytical instruments. A Beckman System Gold Liquid Chromatograph (LC) with a reversed phase, C_{18} packed analytical column was used. Various mobile solvent systems were used, some of which were as specified in the official pharmacopoeia. The solvent systems developed in the laboratory for the combination products, sulphamethoxazole and trimethoprim, sulphadoxine and pyrimethamine were validated before use. LC was a preferred method for most of the analysis because of its greater precision and accuracy (Sharma 2002). For the single content drug product, for which pharmacopoeia methods are available,

Shimadzu UV/Visible spectrophotometer was employed for their analysis.

Sample preparation. Each sample underwent some form of preparation before the assay was carried out. The samples were prepared according to the methods described in the BP official monographs (BP, 1988) under the respective formulations. External standard method of quantitation was employed in all cases.

Data treatment. The results were analyzed by simple statistical analysis. Samples drug categories greater than 30 were subjected to d-test while those samples less than 30 were subjected to t-test.

Results

Table 1 presents a summary of the number of samples, stated dosage, average percent content obtained, BP limits for each drug product and the percentage of the samples that failed or passed, while Table 2 shows the statistical analysis of the data.

Discussion

A Total of 379 samples were assayed for percentage content of active ingredient. These samples included chloroquine sulphate tablets, syrup and injection; chloroquine phosphate tablets, syrup and injection; cotrimoxazole tablets and suspension; paracetamol tablets and syrup, ampicillin capsules and suspension; sulphadoxine + pyrimethamine tablets, metronidazole tablets and chloramphenicol capsules. 265 samples (69.9%) did not comply with the standards for percentage content of active ingredient set in the British Pharmacopoeia, (BP 1988) while 114 samples (30.1%) complied (Table 1). Up to 184 (69.4%) of the samples that failed to comply with pharmacopoeia standards were made in Nigeria while the remaining 81 samples (30.6%) that did not comply with pharmacopoeia standards were imported. Some of the samples taken contained higher amounts of the active ingredient(s) while a majority had less than the percentage content specified in the monographs.

From the outcome of the statistical analysis (Table 2), it was evident that the null hypothesis was not accepted 100% and that samples that were few in number were mostly rejected. The null hypothesis (Bolton, 1984) requires that there be no real difference between the sample mean and the population mean, was therefore accepted when the calculated t (d) was less than the tabulated t (d) while it was rejected if the calculated t (d) was more than the tabulated t (d). Two of the combination products, sulfadoxine + pyrimethamine and sulfamethoxazole + trimethoprim tablets had one of the components rejected because these were treated statistically as independent drug candidates and therefore reflected in the overall failure as such.

Since the null hypothesis was rejected for trimethoprim (tablets), trimethoprim and sulphamethoxazole (suspension), ampicillin (capsules), sulphadoxine, metronidazole and chloramphenicol, it follows that the results obtained for these preparations were not statistically significant and were therefore, omitted from the computation of the final failure rate. Thus, the number of samples that failed to comply with the pharmacopoeia standards became 157, giving rise to a total percentage of 41.4% that failed.

Many factors contribute to the high proliferation of fake and substandard drugs today (Wondemagegnehu, 2003). These factors include, attractiveness of drugs for counterfeiting, absence of or weak national drug regulatory authority (NDRA), lack of political will and commitment to establish strong NDRA, lack of appropriate drug legislation, weak enforcement, corruption and conflict of interest, shortage or erratic supply of drugs, inappropriate use of drugs, high prices of drugs, price differentials, inefficient co-operation between stakeholders, lack of

control over export drugs, trade through several intermediaries and trade through free-trade zones/free ports. For the Nigerian made products, the lack of technical know-how, deliberate use of unqualified personnel and lack of laboratory quality control testing facilities are additional factors. These factors have a direct bearing on current Good Manufacturing Practices (cGMP). As at the time this study was conducted, the control of drugs was being administered by a department under the Federal Ministry of Health. Also the National Agency for Food, Drug Administration and Control (NAFDAC) was to be established. Combating counterfeiting requires the involvement of the national governments, national drug regulatory authorities (NDRA), consumers and the international community as drug counterfeiting is a global issue.

This study has shown that the level of substandard drugs in the selected cities in Nigeria as at 1993 was 41.4%

Table 1: Summary of descriptive characteristics of samples collected and the treated data after laboratory analysis

Active ingredient	Dosage forms	No. of samples	Stated dosage	Average percent content obtained	B.P Limit[16]	% Failure	% Passed
Chloroquine sulphate	Tablets	45	200mg	100.7	92.5-107.5%	63.5	36.5
	Syrup	36	50mg/5ml	95.2	90-110%	47.2	52.8
	Injection	28	40mg/ml	104.7	95-105%	71.4	28.6
Chloroquine phosphate	Tablets	16	250mg	109.8	92.5-107.5%	50.0	50.0
	Syrup	21	50mg/5ml	93.7	95-105%	52.4	47.6
	Injection	17	250mg/5ml	109.1	95-105%	71.4	28.6
Trimethoprim	Tablets	32	80mg	61.8	92.5-107.5%	100.0	0.0
Sulphamethoxazole			400mg	90.5		63.6	36.4
Trimethoprim	Suspension	30	40mg	50.8	92.5-107.5%	90.0	10.0
Sulphamethoxazole			200mg per 5ml	66.9		100.0	0.0
Paracetamol	Tablets	50	500mg	90.3	95-105%	68.0	32.0
	Syrup	20	120mg/5ml	97.4	90-110%	45.8	54.2
Ampicillin	Capsules	26	250mg or 500mg	84.2	92.5-107.5%	61.5	38.5
	Suspension	40	250mg/5ml	129.2	80-120%	73.0	27.0
Pyrimethamine	Tablets	6	25mg	87.8	92.5-107.5%	83.3	16.7
Sulphadoxine			500mg	82.2		100.0	0.0
Metronidazole	Tablets	6	200mg or 400mg	89.6	95-105%	100.0	0.0
Chloramphenicol	Capsules	8	250mg	42.9	95-105%	100.0	0.0

B.P = British Pharmacopoeia 1988

Table 2: Statistical analysis of data using t- test and d- test

Active ingredient	Dosage forms	No. of samples	Sample mean	Standard deviation	Test carried out	Calculated d or t	Tabulated d or t (0.05)	Inference
Chloroquine sulphate	Tablets	45	100.7	26.6	d-test	0.026	1.960	Accept
	Syrup	36	95.2	20.4	d-test	0.235	1.960	Accept
	Injection	28	104.7	21.9	t-test	1.136	2.052	Accept
Chloroquine phosphate	Tablets	16	109.8	18.5	t-test	2.119	2.131	Accept
	Syrup	21	93.7	30.4	t-test	0.950	2.086	Accept
	Injection	17	109.1	24.2	t-test	1.550	2.120	Accept
Trimethoprim	Tablets	32	61.8	13.3	d-test	2.872	1.960	Reject
Sulphamethoxazole		32	90.5	10.5	d-test	0.905	1.960	Accept
Trimethoprim	Suspension	30	50.8	20.4	t-test	13.210	2.045	Reject
Sulphamethoxazole		30	66.9	13.6	t-test	13.331	2.045	Reject
Paracetamol	Tablets	50	90.3	22.1	d-test	0.439	1.960	Accept
	Syrup	20	97.4	15.5	t-test	0.038	2.093	Accept
Ampicillin	Capsules	26	84.2	33.0	t-test	2.441	2.060	Reject
	Suspension	40	129.2	49.2	d-test	0.594	1.960	Accept
Pyrimethamine	Tablets	6	87.8	17.4	t-test	1.718	2.571	Accept
Sulphadoxine		6	82.2	3.6	t-test	12.111	2.571	Reject
Metronidazole	Tablets	6	89.6	3.8	t-test	6.704	2.571	Reject
Chloramphenicol	Capsules	8	42.9	31.3	t-test	5.160	2.365	Reject

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References

Bolton, S. (1984); Pharmaceutical Statistics: Practical and Clinical Application. Vol 1. Marcel Dekker Inc, New York pp 107, 162-163.

British Pharmacopoeia (1988); Vol II. Her Majesty's Stationery Office, London pp 524, 552,725, 746, 752, 790, 799.

IRIN-WA (2001); The Menace of Fake Drugs in Nigeria. www.healthyskepticism.org

Lahore (1987); Pakistan Manual of Drugs in Nigeria. Lahore Time Publication

Sharma B. K. (2002); Instrumental Methods of Chemical Analysis. 22nd revised and enlarged edition, GOEL Publishing house pp S-50

USFDA (2004); Federal Food, Drug and Cosmetic Act. www.fda.gov/opacom/laws/fdcact/fdcact1.htm

Wondemagegnehu E. (2003); Counterfeit Medicines Overview. www.who.int

World Health Organization (1992); Counterfeit Drugs: A Report of a Joint WHO/IFPMA Workshop, WHO, Geneva

World Health Organization (1999); Counterfeit and Substandard Drugs in Myanmar and Vietnam: Report of a study carried out in co-operation with the Governments of Myanmar and Vietnam.