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Full Length Research Paper

Quality assessment of three imidazole antiparasitics (albendazole, mebendazole and metronidazole) sold in Benin

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Illicit circuit of medicines disrupts the quality assurance system and the rational use of medicines. Substandard and falsified (SF) medicines present a major risk for the public health, due to lack of active ingredient and/or toxicity of certain components. The purpose of this study was to evaluate the quality of three imidazole antiparasitic medicines (albendazole, mebendazole and metronidazole tablets) sold in Benin, to describe the different forms of non-compliances of the medicines sold in the illicit circuit. The samples were collected in the formal and illicit (informal) circuits. The results appeared as follows: irregularities of packaging (25.5% of samples from the illicit circuit); mass uniformity test (14.7% of samples from the illicit circuit were non-compliant); disintegration test (2.1% of samples from the illicit circuit and 3.5% from the formal circuit were non-compliant); identification (all samples were compliant) and assay (47.1% of samples from the informal circuit were non-compliant among which 26.5% of under-dosing and 20.6% of overdose). In sum, there were respectively 38.3% (i.e. 18/47) and 3.5% (i.e. 2/58) of non–compliance in the illicit and formal circuits.

Keys words: *Substandard and falsified medicines, Quality assurance, Quality control, Albendazole, Mebendazole, Metronidazole.*

INTRODUCTION

The medicinal products are one of the main elements intervening in the chain of sanitary devices for disease control. The availability of medicine, their affordability, quality assurance and rational use represent major challenges for authorities and other actors in the pharmaceutical sector. In 1987, the regional African committee of the World Health Organization (WHO) adopted the Bamako Initiative; it is a reform of the management of health systems in countries facing difficult economic situations. In particular, it aims to promote the health of women and children through the financing and management of essential medicines at the community level (OMS, 1987).

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Since the Bamako Initiative was subscribed in 1989, Benin has opted for the system of cost recovery of medicines. In the same year, the Purchasing Centre for Essential Medicines and Medical Consumables (CAME) was created, this has led to a gradual improvement in the supply of quality, low-cost generic medicines to health facilities (DPM/MSP, 2008).

According to the WHO, the turnover of counterfeit medicines in some African countries could be more than 60% (Delval, 2010). The falsification of medicines affects all countries. In developing countries, the most falsified medicines are basic medicines such as antibiotics, antimalarial and antiparasitics (Leem, 2010, Frimpong et al., 2018, Belewa et al., 2018). Illicit trafficking and falsification of medicines pose a major risk to public health due to the absence of active ingredient(s) or the contents of these medicines which maybe dangerous (wrong dosage, impurities, etc.) (OMS, 2012). This risk is particularly increased by ignorance of the populations and their low purchasing powers. A survey on the purchasing practices of medicines in Cotonou showed that 86% of respondents believe that street medicines are of good quality and 25.9% of them buy their medicines at the market and on the streets (Azondékon et al., 2005).

The fight against illicit trafficking and falsification of medicines requires several joint measures. First, measures should be taken to reveal falsified medicines in the national distribution system and to prevent them reaching populations (OMS, 2012). In 2018, an initiative was launched at the first international Conference on Medicine Quality and Public Health held at Oxford University (Newton et al., 2019). A Statement signed by the participants, calling for investment, policy change and action to eliminate substandard and falsified medical products must be reinforced both at local, regional and internal levels.

In 2009 Benin organized the ‘’Cotonou Appeal’’ against fake medicines which brought together several presidents and several international organizations. The country has ratified the MEDICRIME Convention, the first international legal tool (born in 2011) in the fight against the illicit medicine trafficking (AN, 2017). Despite these efforts, the Benin drug sector is seriously disrupted by illicit trafficking and falsification of medicines. The illicit sale of medicines affects almost all the classes (Assanh, 2013) including the antiparasitics used against the intestinal parasites. This really poses a public health problem. Indeed, several intestinal parasitoses being a part of Neglected Tropical Diseases (NTD) affect particularly the tropical zones disadvantaged of Africa (Hotez, 2009). Estimates show that global burden of NTD would be at least as high as that of malaria and tuberculosis (Hotez, 2009); intestinal nematode infections occupy the first place of NTD in the DALY (Disability-adjusted life year) ranking from GBD (Global Burden of Disease Study) 2010 (Hotez, 2014). Several NTD, in particular ascariasis, trichocephaliasis and ankylostomiasis can be easily stopped by periodic preventive chemotherapy (Hotez, 2009; OMS, 2008); or treated with effective medicines, available at affordable prices in pharmacies and health centers. These medicines are also subject to falsification and illicit sale in various markets and streets of Benin. This raises concerns about the quality of these antiparasitic medicines.

Few studies (*Akole et al., 2010; Assanh, 2013*; *Baba-Moussa et al., 2015a; Baba-Moussa et al., 2015b*) have been conducted on the frequency and types of non-compliances of these medicines in Benin. Of the studies that were conducted, none of them were interested in describing the types of non-compliances (particularly those relating to packaging) encountered in this illicit circuit for the sale of medicinal products. It is therefore important to increase knowledge about the characteristics of these illicit medicines sold in Benin and about their implications for population health. Because of their high frequency of prescription and consumption in self-medication, three of antiparasitic medicines were selected in the present study. The purpose of this study was to evaluate the quality of three imidazole antiparasitic medicines sold in Benin; to describe the different forms of non-compliances encountered in the illicit circuit. These medicines are: albendazole (ABZ), mebendazole (MBZ) and metronidazole (MTZ) tablets.

MATERIAL AND METHOD

Sampling place and collect period

This work is a descriptive and analytical cross-sectional study conducted from April 2015 to March 2016.

For the purpose of describing the specific characteristics of illicit medicines, samples were collected both in the illicit (informal) circuit and in the formal circuit for the sale of medicinal products. In the formal circuit, sampling took place at CAME, public health centers and private pharmacies. In the illicit circuit, these were the following three markets: Dantokpa (Cotonou), Ouando (Porto-Novo) and Cococodji (Abomey-Calavi).

Sampling in the formal circuit was done with the LNCQ team. During sampling in the illicit circuit, the targeted medicines were purchased as a retailer or consumer, to avoid any mistrust of the sellers. In each market, different outlets were randomly visited. Various medicines composed by the molecules of interest (ABZ, MBZ and MTZ) were purchased by anonymous mystery shoppers. Sometimes various medications available to help treat

intestinal worms and diarrhoea were requested from sellers.

Sample size

Since the size of sampling in the illicit circuit could not be determined in advance; in each market, we collected all available batches at the time of sampling. In the formal circuit, sampling was carried out during the periodic rounds of collection of samples by the LNCQ in the four departments chosen. A total of 105 samples were collected: 58 from the formal circuit and 47 from the illicit circuit. We collected 28 samples of ABZ, 42 samples of MBZ and 35 of MTZ. For each sample, 80 to 100 tablets were collected.

Sample analyses

Figure 1 (Baba-Moussa, 2005) shows the successive steps in the analysis of a sample; each of these steps has been performed even if the sample is non-compliant for the previous test.

The preliminary tests carried out are: the study of packaging, the macroscopic checks and the mass uniformity test. The study of packaging (UEMOA, 2010) consists in verifying whether the inscriptions imposed by Good Manufacturing Practices (GMP) are respected and clearly legible; and if there are no anomalies on the package leaflet and/or packaging. The macroscopic checks consist in verifying the organoleptic characteristics, the possible inscriptions on the tablets and for the breakable tablets the score lines. The mass uniformity test (Eu. Ph.1) was carried out on 20 units of tablets taken at random.

The disintegration test (Eu. Ph.1) was carried out on 6 units of tablets taken at random; this test was not done on ABZ and MBZ samples (chewable tablets). ABZ (USP 1) and MTZ (Eu. Ph.2) were identified by UV-visible spectrophotometry while MBZ (USP 2) was identified by thin-layer chromatography.

The determinations of actives ingredients (AI) were carried out by titrimetric techniques adapted from International and European pharmacopoeias (Int. Ph. 1, Int. Ph. 2, Eu. Ph. 2); control tablets (containing known amounts of AI) were used. Samples and controls were treated in the same manner. Solubilisation of tablet powders was done by glacial acetic acid for MBZ and MTZ and by a mixture of formic acid anhydrous and glacial acetic acid (1:10, v/v) for ABZ. Like the samples and the control, the blank (mixture of solubilisation solvent(s) and the coloured indicator) was titrated with the titrant solution (0.1N perchloric acid) to make necessary calculation adjustments.

Procedure

Permission to take samples from the formal circuit was obtained from the Benin Ministry of Health.

Data analysis

Data were processed using Excel® 2016 and Epi info™ 7.2.0.1 software. In each circuit and for each test, the frequency (%) of each type of non-compliance was calculated.

RESULTS AND DISCUSSION

The consideration of the two circuits not only gives an overall idea of the quality of these drugs but also on the ramifications of illicit drug trafficking in the Beninese areas studied. Careful analysis of packaging was carried out for samples collected from the informal circuit.77.6% of all formal circuit samples were manufactured in African countries *(*Table1*)*. African countries, like those in Asia, are increasingly making efforts to produce essential medicines locally. Concerning illicit circuit (Table 2), the main countries are Benin, Nigeria and India. These results are similar to those found in 2013(Assanh, 2013) which placed a manufacturer legally installed in Benin as the main supplier of the illicit circuit.

Besides, we noted that 53.2% of the samples collected in the informal circuit have registered trade names in Benin; 2.1% of samples had registered trade names for which sale is prohibited(Free medical sample) (Table 3). The same phenomenon was observed in the study on antimalarial sold in the informal sector of Porto-Novo (Baba-Moussa et al., 2015a).Weakness in the quality assurance system of the official distribution channel could be one of main factors promoting illicit medicines trafficking in Benin. In addition, the tolerance and/or complicity of certain drug promotion agencies would also be involved in the supply of the informal circuit.

In total,12/47 (*i.e*. 25.5%) samples from the informal circuit did not meet current GMP requirements for the presentation of packaging and leaflets. This percentage is higher than those found by Assanh (Assanh, 2013)and Baba-Moussa et al., (2015b)i.e. 2.18% and 10% respectively. By analysing the results presented in Table 4, it appears that medicines sold illicitly in the studied areas (markets and streets) present a multitude of cases of non-compliance on their packaging and leaflets. Spelling errors(e.g. on Figure 2) accounted for22.7% of the irregularities found on packaging and leaflets, this raises a problem of pharmacotherapeutic information with probable risks of non-compliance with treatment and misuse of the medicine that may result in therapeutic failure. Two cases were of particular interest: the indication

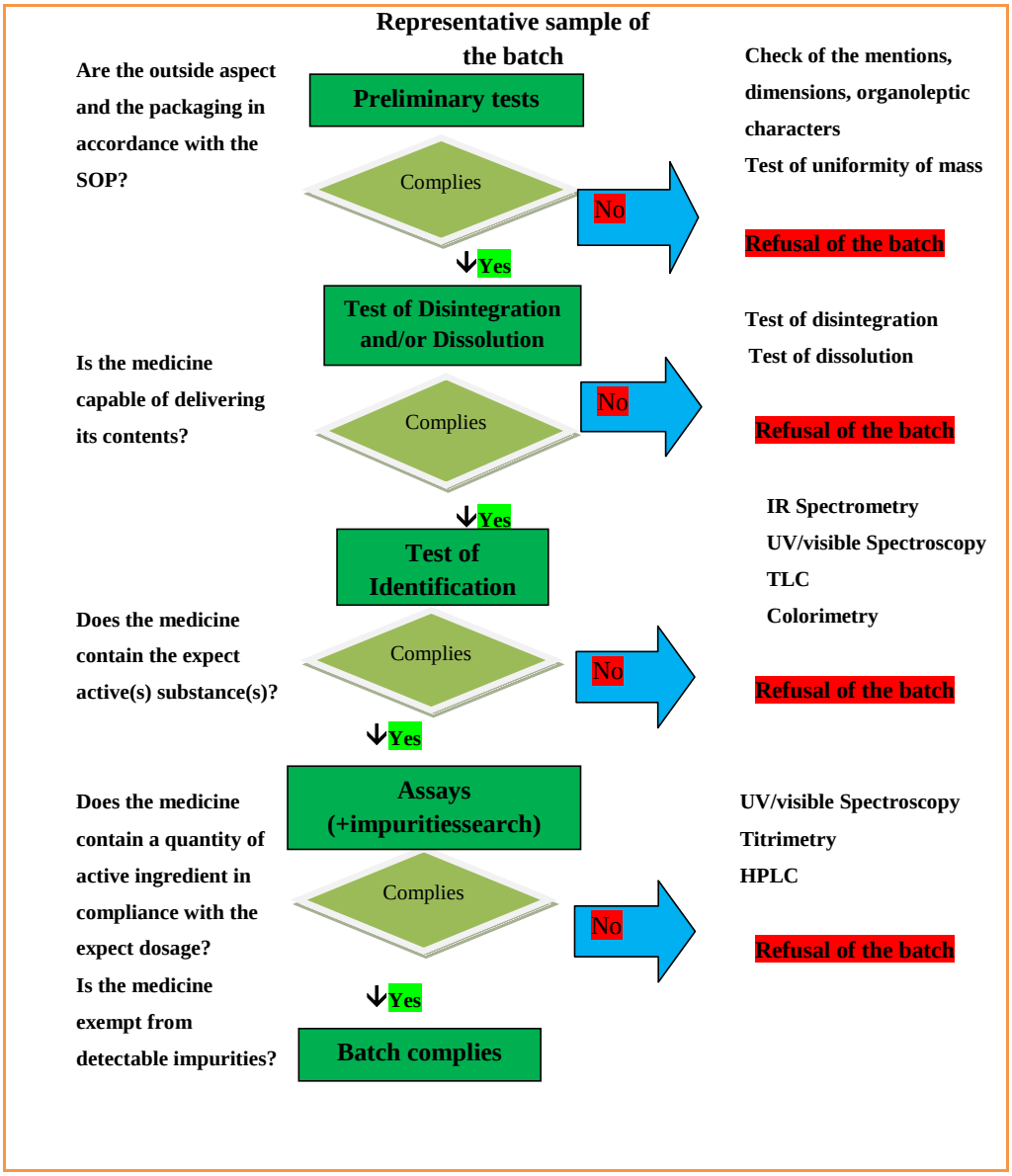


Figure 1. Flowchart of analytical approach as applied at the National Laboratory for Quality Control of Medicinal Products and Medical Consumables (LNCQ).

of a half-tablet dosage for a tablet that is not divisible (no score line on the tablet) and the indication of an oral dosage as a rectal for the single form (tablet) of MTZ.

The percentage of non-compliances in the informal circuit (Table 5) was higher than 19.3% and 28.0% respectively found on the parallel market in Cameroon (OMS, 1995) and in Ivory Coast (Legris, 2005); this difference could be explained by the sample size. However, the same percentage of 38.3% is lower than the percentages found in Benin in 2010 (Akole, 2010) and 2013(Assanh, 2013) which are respectively67.92 % and 56.77%. The difference can be explained by the study on several classes of medicines (antibiotics, antimalarial, analgesic, anthelminthic, etc.).

The percentage of non-compliances in the formal circuit (Table 6) is less than 8% found in Mali in 2003 (Oumarou, 2003). This could be explained by the difference in sample size and the number of molecules involved, but also by the countries of origin of the medicines studied (European and Asian manufacturers).

Fornon-compliance by molecule, ABZ samples represented the highest proportion of non-compliance (60%) followed by MBZ samples (25%) and MTZ samples (15%). All identified non-standard ABZ and MBZ

Table 1. Distribution of formal circuit samples by country of origin of manufacturers.

	Albendazole	Mebendazole	Metronidazole	Total	Percentage
Ghana	8	19	9	36	62.1%
India	3	1	8	12	20.7%
Benin	0	5	0	5	8.6%
Togo	1	0	3	4	6.9%
China	0	0	1	1	1.7%
Total	**12**	**25**	**21**	**58**	**100.0%**

Table 2. Distribution of informal circuit samples by country of origin of manufacturers.

	Albendazole	Mebendazole	Metronidazole	Total	Percentage
Benin	0	11	8	19	40.4%
India	13	3	0	16	34.0%
Nigeria	2	2	3	7	14.9%
Ghana	1	1	0	2	4.3%
France	0	0	1	1	2.1%
Togo	0	0	1	1	2.1%
Chine	0	0	1	1	2.1%
Total	**16**	**17**	**14**	**47**	**100.0%**

Table 3. Official status of samples collected in the informal circuit.

	MA (Authorized for sale)	No MA(not authorized for sale)	Free medical samples (Not for sale)	Total
Mebendazole	11	6	0	17
Albendazole	5	11	0	16
Metronidazole	9	4	1	14
Total	**25**	**21**	**1**	**47**
Percentage	**53.2%**	**44.7%**	**2.1%**	**100.0%**

MA: Marketing Authorization.

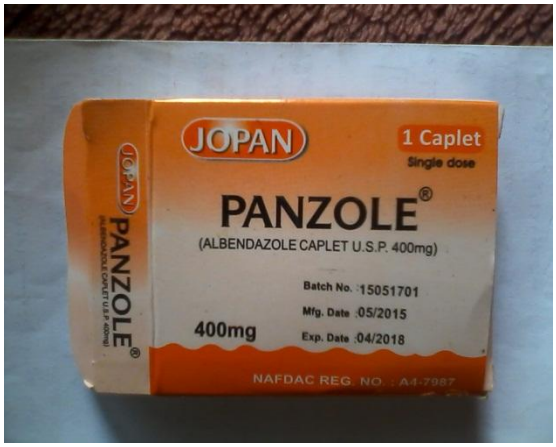
samples came from the informal circuit. Among the non-conforming samples 60% were from India (Asia) and 25 % from Nigeria (Africa). These results are similar to those reported in Mal i(Oumarou, 2003)namely 11.10% non-compliance among the medicines from Asia and 10.30% non-compliance among the medicines from Africa.

The percentage of non-compliance in the informal circuit is statistically different from that in the formal circuit (Homogeneous Chi-squared test:*p*-value = 0.000006126< 0.05).

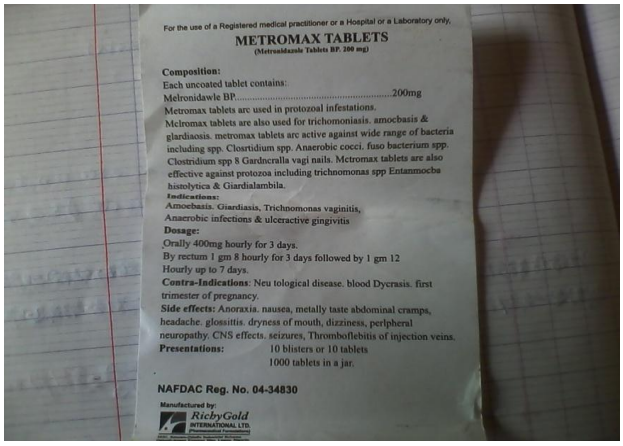
In addition to non-compliances on packaging and organoleptic characteristics; four other types of non-compliances were detected (Table 7): lack of mass

Table 4. Distribution of irregularities on packaging and leaflets of samples collected in the informal circuit.

Irregularities	**Leaflet**	**Manufacturer**	**Batch number**	**Spelling mistakes**	**Inadequate and/or inaccurate information**	**Total**
Size	9	1	2	5	5	**22**
Percentage	40.9%	4.5%	9.1%	22.7%	22.7%	**100%**
Commentaries	Leaflet not written in french	Absence of manufacturer's name	Absence of the batch number on the blister strip of tablets	"*non emballé*" instead of "*non dragéifié*" or "*non pelliculé*". "*caplet*" instead of "*tablet*". "*melronidawle*" instead of "*métronidazole*".	Posology of half-tablet while the tablet is not breakable. Posology indicating the possibility of taking by oral and rectal for the singlepharmaceutical form of metronidazole	



Picture 1: Packaging of sample coded Cc08



Picture 2: Leaflet of sample coded A15

Figure 2. Pictures of secondary package (picture at left) and leaflet (picture at right) of albendazole and metronidazole samples, respectively.

uniformity, high disintegration time, under-dosing and overdose. Regarding identification, all samples contained the declared active ingredients.

The lack of mass uniformity reflects a large difference in individual mass between different units of the same batch. This would result from improper mixing during manufacturing but could also be caused by physical friction of the tablets during transport. A lack of mass uniformity will certainly change the amount of active ingredient in the tablets.

2.1% (i.e. 1/47, Table 5) of samples from the informal circuit presented a high disintegration time. This percentage is similar to that found in Mali (Oumarou, 2003) which was 2.68%. It is lower than the 32.07% found in Benin in 2010 (Akole, 2010). This may be due to the characteristics of the medicines included in our study: the disintegration test was performed only for MTZ samples; ABZ and MBZ chewable tablets were not tested in accordance with LNCQ procedures.

Overdose was for ABZ and MBZ samples from the informal circuit (Table 5). Both molecules are widely used

Table 5. Results of pharmacotechnical and physico-chemical tests of samples collected in the informal circuit

	Mass uniformity		Disintegration		Identification		Assay		Total		Percentage	
	C	NC	C	NC	C	NC	C	NC	C	NC	C	NC
ABZ	14	2	-	-	16	0	5	11	4	12	25.0%	75.0%
MBZ	15	2	-	-	17	0	12	5	12	5	70.6%	29.4%
MTZ	13	1	13	1	14	0	13	1	13	1	92.9%	7.1%
Total	**42**	**5**	**13**	**1**	**47**	**0**	**30**	**17**	**29**	**18**	**61.7%**	**38.3%**

Legend: C: Conform; NC: Not conform.

Table 6. Results of pharmacotechnical and physico-chemical tests of samples collected in the formal circuit.

	Mass uniformity		Disintegration		Identification		Assays		Total		Percentage	
	C	NC	C	NC	C	NC	C	NC	C	NC	C	NC
ABZ	12	0	-	-	12	0	12	0	12	0	100%	0%
MBZ	25	0	-	-	25	0	25	0	25	0	100%	0%
MTZ	21	0	19	2	21	0	21	0	19	2	90.5%	9.5%
Total	**58**	**0**	**19**	**2**	**58**	**0**	**58**	**0**	**56**	**2**	**96.6%**	**3.4%**

Legend: C: Conform; NC: Not conform.

Table 7. Distribution of types of non-compliances on samples collected in the informal circuit.

Types of non-compliances	Size	Percentage
Irregularities on packaging	12	35.3%
lack of mass uniformity	5	14.7%
High disintegration time	1	2.9%
Under-dosing	9	26.5%
Overdose	7	20.6%
Total	**34**	**100,0%**

in family medication for regular deworming. Overdose may be caused by non-compliance with GMP but it would be, according to Akole's conclusions (Akole, 2010), an option made by counterfeiters "to develop loyalty" of consumers of basic products such as analgesics, anti-inflammatory medicines and certain anthelmintics.

Two samples (ABZ and MTZ) showed simultaneously lack of mass uniformity and under-dosing. Two other samples(ABZ and MBZ)showed simultaneously lack of mass uniformity and overdose.

CONCLUSION

The main purpose of this study was to contribute to the description of the quality non-conformities of illegal antiparasitic medicines in Benin. The results have objected serious non-conformities of packaging (25.5% of samples from the informal circuit did not meet GMP requirements for the presentation of packaging and leaflets) and a probable supply of this illicit circuit by certain actors in the formal pharmaceutical sector of Benin.

Consent

As per international standard and university standard, oral consent was obtained from the surveyed if required and preserved by the authors.

Ethical approval

The study had an agreement of the research commission of the Faculty of Health Sciences (University of Abomey-Calavi). Collected samples were coded and anonymised. They were not left available to people possibly involved in the survey.

Competing interests

Authors have declared no interest in the study nor with any involved pharmaceutical companies.

REFERENCES

Akolé C. Lutte contre les médicaments contrefaits: Etude pilote de contrôle de qualité des médicaments du marché illicite béninois. Thèse de doctorat en pharmacie N°058/UFR Pharmacie/FSS/UAC, 2010:6-76.

Assanh JMC. La lutte contre les faux médicaments: contrôle de qualité des médicaments issus des marchés de Parakou, de Cotonou et de Porto-Novo. Thèse de doctorat en pharmacie N°093/UFR Pharmacie/FSS/UAC, 2013: 105.

AN, Assemblée Nationale du Bénin,Loi N°2017-23 du 19 juin 2017. Décision DCC 17-164 du 27 juillet 2017.

Azondékon A, Abdoulaye I, Chastanier H. Enquête sur les pratiques d'achat des médicaments dans la ville de Cotonou. Fondation Pierre Fabre. 2005: 573-76.

Baba-Moussa F. Communication personnelle: consultation sous régionale des laboratoires nationaux de contrôle de qualité/DG-LNCQ; 24-25-26 Mai 2005; Alger.

Baba-Moussa F, Bonou J, Ahouandjinou H, Dougnon TV, Kpavode L, Raimi N et al. Quality Control of Selected Antimalarials Sold in the Illicit Market: An Investigation Conducted in Porto-Novo City (Republic of Benin). Advances in Bioscience and Biotechnology 2015, 6, 637-44.

Baba-Moussa F, Bonou J, Dougnon TV, Ahouandjinou H, Dotou-Sègla R, Loko F et al. Quality control of selected antibiotics from beninese illicit market and their impacts on public health. Asian Jr. of Microbiol. Biotech. Env. Sc. Vol. 17, No. (4) : 2015 : 1037-042.

Belewa S., Suleman S., Wynendaele E., D'Hondt M., Kosgei A., Duchateau L., De Spiegeleer B. (2018). Quality of anthelminthic medicines available in Jimma Ethiopia, Acta Tropica 177, 157–163

Delval P. Le marché mondial du faux. Crimes et contrefaçons. Paris : CNRS éditions ; 2010 : p 153.

DPM/MSP. Politique Pharmaceutique Nationale. 3ème édition, Cotonou, 2008: 57.

Eu. Ph.1, Pharmacopée Européenne, 2013, 8ème édition, Volume 1.

Eu. Ph.2, Pharmacopée Européenne, 2013, 8ème édition, Volume 2.

Frimpong G., Ofori-Kwakye K.,Kuntworbe N., OheneBuabengK.,AsantewaaOsei Y.,El Boakye-Gyasi M.,Adi-Dako O. (2018). Quality Assessment of Some Essential Children's Medicines Sold in Licensed Outlets in Ashanti Region, Ghana, J. Trop. Med., Vol. 2018, 1-14., doi.org/10.1155/2018/1494957

Hotez PJ, Fenwick A, Savioli L, Molyneux DH.Rescuing the bottom billion through control of neglected tropical diseases. *Lancet* 2009 ; 373 : 1570–75.

Hotez PJ, Alvarado M, Basanez MG, Bolliger I, Bourne R,Boussinesq M et al.The Global Burden of Disease Study: Interpretation and Implications for Neglected Tropical Diseases. *PLoSNegl Trop Dis* 2014; 8(7) : e2865. doi:10.1371/journal.pntd.0002865

Int. Ph. 1, Pharmacopée Internationale. OMS Genève 1994, 3ème édition, Volume 3:58-59.

Int. Ph. 2, Pharmacopée Internationale. OMS Genève 1994, 3ème édition, Volume 3:195-96.

Legris C. La détection des médicaments contrefaits par investigation de leur authenticité. Etude pilote sur le marché pharmaceutique illicite de côte d'Ivoire. Thèse de doctorat en Pharmacie, Nancy I.2005: 99-100.

Leem : Les entreprises du médicament. Dossier de presse : Contrefaçon de médicaments. Paris : Leem ; 2010.

Newton P.N., Bond K.C, on behalf of the Oxford Statement signatories (2019). Global access to quality-assured medical products: the Oxford Statement and call to action, The Lancet Global Health, Vol. 7, No. 12, e1609–e1611

OMS. Rapport de la 37ème session du comité régional à Bamako (Mali). Brazzaville : OMS Comité Régional de l'Afrique ; 1987 : 12-14.

OMS. Produits médicaux de qualité inférieure/faux/faussement étiquetés / falsifiés / contrefaits : Aide-mémoire N°275. Genève : OMS ; Mai 2012.

OMS. Chimioprévention des helminthiases chez l'homme. Utilisation coordonnée des médicaments antihelminthiques pour les interventions de lutte : manuel à l'intention des professionnels de la santé et des administrateurs de programmes. Genève : Organisation Mondiale de la Sante ; 2008.

OMS. Programme d'action pour les médicaments essentiels : Qualité des médicaments sur le marché pharmaceutique africain; Etude analytique dans trois pays africains : Cameroun, Tchad, Madagascar. OMS/DAP, 1995.

Oumarou GarbaMamata. Contrôle de qualité de certains antiparasitaires (Métronidazole, Mébendazole, Niclosamide, Praziquantel) au Laboratoire National de la Santé. Thèse de pharmacie N°42 Bamako, 2003: 77.

UEMOA (Union Economique et Monétaire Ouest-Africaine). Guide de bonnes pratiques de fabrication des produits pharmaceutiques à usage humain dans les Etats membres de l'UEMOA. Ouagadougou: Commission de l'UEMOA ; 2010.

USP1. USP, The United States Pharmacopeial Convention. USP 39, Volume 2; 2016.

USP2. USP, The United States Pharmacopeial Convention. USP 39, Volume 3; 2016.