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Research Article

PHARMACOTECHNICAL EVALUATION OF PARACETAMOL ISSUED FROM BOTH LEGAL AND ILLICIT MARKET OF EBOLOWA – SOUTH REGION OF CAMEROON: A PUBLIC HEALTH CONCERN

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Abstract

Introduction: In Cameroon and especially in Ebolowa, the parallel and illicit sale of drugs not only promotes automedication, but also the proliferation of fake medicines. Studies on drug quality control help provide appropriate treatments and avoid the addictions and resistance. Objective: To evaluate the pharmacotechnical quality of paracetamol tablets, generic blister of 10 sold in the legal and illicit markets of the city of Ebolowa. **Materials and methods:** An experimental study was conducted over a period of 5 months according to the standards of current pharmacopoeias. Eight (08) drug samples consisting of 90 blisters of 10 paracetamol tablets, each collected from both legal and illegal sectors, were tested for pharmacotechnical use. The analyzes were carried out at the National Laboratory for the Quality Control of Medicines and Expertise and at the Pharmaceutical Technology Laboratory of the Institute for Medical Research and Studies of Medicinal Plants. Descriptives statistics was realize with IBM SPSS Statistics 22 and XLSTAT 2014 served to execute Student's t test. **Results:** The results obtained from the analyses of 08 batches of paracetamol revealed several nonconformities: hardness (63%) that is 05 lots, labeling (12.5%) with identification of two batches from the same laboratory but with different labeling, control of disaggregation (12.5%), organoleptic character control (25%). 5 samples out of 8 (63%) were non – compliant and 4 of these 5 batches were purchased at underground market. 63% (5/8) of these samples were non-compliant and 80% (4/5) were from the "black market". **Conclusion:** The circulation and sale of illicit and non-compliant drugs remains a major problem in Cameroon. The highest number of detected nonconformities originated from the "black market" and from the Asian continent. The strict control of access zones, drug quality and appropriate conservation and distribution of medicines will help enchance the reduction of this phenomenon.

Keywords: Pharmacotechnical Evaluation, Paracetamol, Illicit Circuit, Public Health.

INTRODUCTION

The parallel market of drugs enhances both self – medication and prolific sale of substandard products. Despite the impossibility to give the exact number of deaths due to this practice, the HO estimates that it causes not less than 800 thousand deceases worldwide and yearly (OMS, 2015). Regarding the field of public health, the history of drugs has been marked by back – to – back successes and failures in Cameroon and is of both socio – political and cultural order. Indeed, medicines are effective pharmaceutical products, a commodity and an operator for a set of socio – economic networks, practices, representations of socio – cultural construction relating with treatment and socially represented disease. As Van Der Geest and Whyte suggest, in Southern Cameroon, drugs bring about significant transformations as far as commercialization of health, well – being and the individualization in relation with health (Van der Geest, 1988).

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For more than two decades, Cameroon has been resolutely involved in the fight against the fraudulent sale of medicines through the setting up, since 2010, regional commissions. Despite intermittent repressive actions, the sale of "street drugs" is becoming more and more prosperous across the country. According to Tanguy, more than 62% of Cameroonians consume street drugs and nearly 40% of the medicines sold in the country are contraband products. The unregulated circuit alone accounts for a quarter of the Cameroonian drug market (Tanguy, 2011). In addition, there is an accelerated growth of cases of chronic renal diseases, strokes and especially liver diseases whose causes cannot be determined with certainty. Although several studies on quality control of drugs have been conducted in Cameroon, those dealing with paracetamol are rare, despite notwithstanding the fact that it is the most sold drug in the informal circuit (Awono Noah, 2015; Pouillot *et al.,* 2007). Although paracetamol is sold over-the-counter and considered harmless even by practitioners, it is not devoid of side effects and could cause unimaginable damage. In Ebolowa, South Cameroon, there is an increasing proliferation of illicit sale of medicines and an

attachment of the population to street drugs (Awono Noah, 2015). Moreover, the sale of the drug in the informal sector is closely linked to the poor functioning of the health system in the South region (Van Der Geest, 1982, 1987 & 2017). In the light of the foregoing, the present study aims at evaluating the pharmaco - technical quality of paracetamol 500 mg generic molecules, blister of 10 tablets from authorized structures and illicit markets in the city of Ebolowa.

Methodology

Framework of the study

The samples of paracetamol used for the study were collected fom the Regional Fund for the Promotion of Southern Health and pharmacies (legal sector) and the street markets (illicit sector) of the town of Ebolowa. The experiments were carried out at the National Laboratory for Drug Quality Control and Expertise (LANACOME) and the Pharmaceutical Technology Laboratory of the Institute for Medical Research and Studies of Medicinal Plants (IMPM), both based in Yaoundé, the capital city of Cameroon.

Duration of the study

It took us one month to collect the samples and four months to conduct pharmaco – technical tests. The study was finally carried out over a period of five months.

MATERIALS AND METHODS

Target

This research focused on the analysis of paracetamol tablets of 500 mg, a generic blister of 10 available in the legitimate sector (pharmacies and Regional Fund for the Promotion of Southern Health) and illicit markets (Nkoo'vos and Ebolowa Si 2 markets).

Selection of collection sites and samples of drugs (paracetamol)

Criterion of the choice of collection sites

Samples were collected from RFPS because it is the official representative in charge of health facilities in the city of Ebolowa. During this collection, only 3 drugstores out of 4 could provide the paracetamol used in this study. The illegal trade of drugs is widespread in the markets of Nkoo'vos and Ebolowa Si 2.

Selection of drugs samples

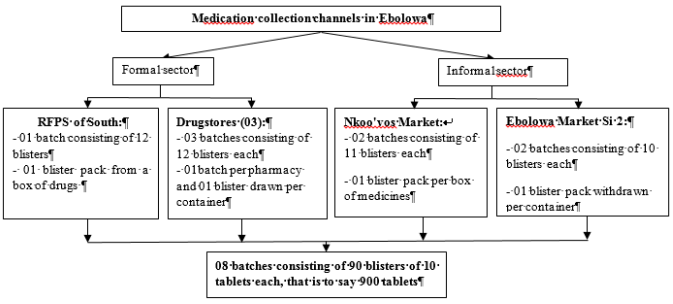

Figure 1. Drug Selection in Both Sectors in Ebolowa

The samples consisted of 08 batches of paracetamol 500 mg (generic blister of 10 tablets) among which 04 were selected in the legal circuit and 04 others in Ebolowa's illicit circuit. Each batch from the formal sector consisted of 12 blister packs, while informal sector packs consisted of 11 blisters for the Nkoo'vos market and 10 blisters for the Ebolowa market Si 2. Boxes of drugs were drawn at random. The paracetamol tablet blisters were also selected per box in the same way. A total of eight (08) batches consisting of 90 blisters of 10 tablets each, that is to say 900 tablets were selected according to the availability of stocks.

SAMPLE ANALYSIS TECHNIQUES

Monographs of pharmacopoeias and books, particularly the British, European, American and International pharmacopoeias were used for the analytical control of the selected paracetamol batches (Pharmacopée Américaine, 1998, 2008 & 2009).

Labeling control: it aimed at identifying the presence of the product and active principle names, its quantity, the number of the batch, dates of manufacture and expiry, dates and the manufacturer's name and address.

Control of organoleptic properties: it consisted of using sensing organs to find out specifications relating to the analyzed products.

- **Modus operandi**

  - Select at random 10 tablets: describe their color, appearance, shape, the possible presence of a coating and a dividing line;
  - The smell: Is there any characteristic odour? if yes, is it compliant with the galenic formula of the analyzed product? if not anomaly;
  - The colour;
  - The appearance;
  - The shape (round, oval ...).

Uniformity of the sizes of the tablets

- **Modus operandi**

  - Take at random 10 tablets;
  - Measure the thickness and diameter of each round tablet using a caliper;
  - For oval or triangular tablets, measure the thickness, the long length and the short length (width), using a vernier caliper.

Average weight and tablets mass uniformity: this checkup required the use of precision balances with a sensitivity corresponding to the degree of precision expected. They were preserved from any moisture or acid vapor and were periodically checked.

- **Modus operandi**

  - Take at random 20 tablets;
  - Weigh each tablet on a precision scale to 0.0001g.

The individual mass of two (02) units of not more than twenty (20) units may deviate from the average mass by a percentage

greater than the one indicated in the following table. However, no mass can exceed the double of this percentage.

Pharmaceutical form	Average mass	Limit gap and average mass percentage
Uncoated tablets and film-coated tablets	80 mg or more	10
	More than 80 mg and less than 250 mg	7,5
	250 mg or more	5

Source: European Pharmacopoeia 6 (2008). Volume 1

Checking of the hardness of the tablets: it intended to test, under defined conditions, the tablets resistance to corrosion. It was measured through the necessary strength to make them by crushing.

- **Modus operandi**

  - Place the tablet between the jaws taking into account, if necessary, its shape, the breaking bar and the engraving. For each determination, direct the tablet in the same way with respect to the direction of application of the force;
  - Take at random 10 tablets;
  - Take a hardness measurement on the 10 tablets with the durometer, caring for the removal of all tablet debris before each operation;
  - Complete the results sheet.

Tablet friability test (abrasion)

Friability is another characteristic that determine the resistance of the tablet, specifically its resistance to erosion. This property is measured thanks to a device based on the following principle: a plexiglass drum with inner blades is operated by a motor at a speed of 25 rpm.

- **Modus operandi**

  - Take at random n tablets whose mass is closest to 650 mg;
  - Dust the tablets and examine / grade their appearance;
  - In a weighing capsule, weigh the mass of all n tablets, to the nearest 0.001g. Note the initial mass (Mi);
  - Place the tablets in the rotating drum with a baffle;
  - Make 100 rotations on the cylinder;
  - Ensure that the tablets are regularly dropped;
  - Withdraw the tablets, dust them off and examine their appearance;
  - Weigh the mass of all the tablets in the capsule close to 0.001 g. Note the final mass (Mf).

Disintegration test: This test was performed to determine compliance with the disintegration standards (limits) in the monographs, except when it is stipulated that the tablets or capsules are intended to be chewed, sucked or to release the active ingredient gradually in body cells.

- **Modus operandi**

Place one unit of the preparation to be examined in each of the 6 tubes of the rack, then add a disc, if their use is prescribed. Operate the apparatus using as immersion liquid the specified milieu maintained at 37 ± 2 ° C. At the indicated time, lift the tube holder out of the liquid and examine the condition of the tested units.

This test is intended to determine the capacity of tablets or capsules to disintegrate in a prescribed time when immersed in the liquid and under well-defined experimental conditions.

Standards and identity tests: Standards and identity tests for pharmaceutical forms must be designed in a way that clearly demonstrates that the samples examined effectively contain the active sample (s) enunciated. The results obtained in the chromatogram or spectrum were compared with the solution to be tested and corresponding to the standard solution.

Standard and test content of active principle (s): the standard is expressed quantitatively by limits of the content of active ingredients per tablet. The test is often carried out according to a suitable quantitative method, following a uniform mixture of the content of several tablets in that respect, the results of the analysis are expressed in in terms of quantity of active principle contained in a tablet of average weight.

Acceptable limits were set by the monograph used. There are several methods of quantification. Spectrophotometry is a method that hinges on the quantitative analysis of molecules and help measure how much a chemical substance absorbs light by measuring the intensity of light as a beam of light passes through sample solution. The basic principle is that each compound absorbs or transmits light over a certain rage of wavelength. It is mainly used to determine the concentration of a know chemical substance.

Protocol for identifying and dosing the active ingredient

- **Modus operandi**

Weigh and crush 20 tablets. Incorporate a quantity of powder containing 0.15 g of paracetamol in 50 ml of 0.1 M sodium hydroxide (NaOH), dilute with 100 ml of water, shake for 15 minutes and add enough water to obtain 200 ml. next mix, filter and dilute 10ml of the filtrate in 100ml with water. After that, add 10 ml of the resulting solution in 10 ml of 0.1 M sodium hydroxide, dilute to 100 ml with water and measure the absorbance of the resulting solution maximally at 275 nm. Appendix II B. Finally calculate the content in C8H9NO2 considering 715 as the value of A (1%, 1cm) with a maximum of 257nm.

Materials

Laboratory glassware

- vials of 100ml, 50ml;
- An Erlen Meyer of 1000 ml;
- A cylinder of 1000 ml;
- Graduated pipettes with 2 lines of 5 ml;
- A 500 ml wash bottle;
- Bottles of 20 ml.

Equipments

- Sliding calipers : SCHIEBLEHRE 155 mm ;
- Precision balance: Explorer OHAUS 1mg of sensibility;

- Analytical balance Metler Toledo XS connected to a printer;
- Durometer: SCHLEUNIGER-2E of precision 2 Newtons;
- Tablet Friabilitor SOTAX FT2 ;
- Tablet Friabilitor ERWEKA TA ;
- Disintegrator : ERWEKA ZT3 ;
- Spectrophotometer Perkin Elmer Lambda 25 ;
- Distillation apparatus ;
- Ultrasonic cleaning bath ;
- Filter papers.

Reagents

- Sodium hydroxyde (NaOH) 0,1 M ;
- EDQM (European Directorate for the Quality Medicines & HealthCare) Chemical Reference Substance (CRS);
- Distilled water.

Data analysis and exploitation methods

The exploitation and analysis of the data derived from the quality control of the drug samples depended on the monographs used for pharmaco - technical tests. The associated statistics were produced with the help of IBM SPSS Statistics 22 and XL Stat 2014 software for parametric comparison tests of averages.

Ethical considerations

The administrative authorizations as well as the ethical clearance N ° 2015/103 / CEIRSH / ESS / MSP were obtained giving the green light to proceed with the research. All sales managers involved in the study were informed about the purpose of drugs purchase.

RESULTS

Paracetamol tablets collected

The drug samples consisted of 900 tablets of paracetamol that is a minimum of 100 tablets per batch. The table below shows that in the street, the price of a paracetamol blister 500 mg ranges from 40 CFA francs to 75 CFA francs while in pharmacies, it varies between 100 CFA francs and 200 CFA francs. This gives a gap of between 25 Frs CFA and 160 Frs CFA. Batches of paracetamol collected in the city of Ebolowa are mainly from the Asian (62.5%) and African (37.5%) continents; no batch (0%) of paracetamol from India was found in the informal sector in Ebolowa and none (0%) from China was found in the formal sector. On the contrary, batches of paracetamol from Togo were found in both circuits, that is to say 25% for the formal and 50% for the informal.

Label control

Formal sector samples were 100% compliant with primary packaging control whereas 25% of non-compliant samples originated from the informal sector (names and addresses of the manufacturer were not listed on the blister but rather on the box of 100 blisters). The scrutiny of the physical appearance of PARA Sprukfield batches labels, from the informal sector and PARA Sprukfield batches labels collected from the formal sector (RFPS of the South region) it revealed some subtle differences as it appears on iconography n° 1. What would show evidence that the generic paracetamol 500 mg is fake

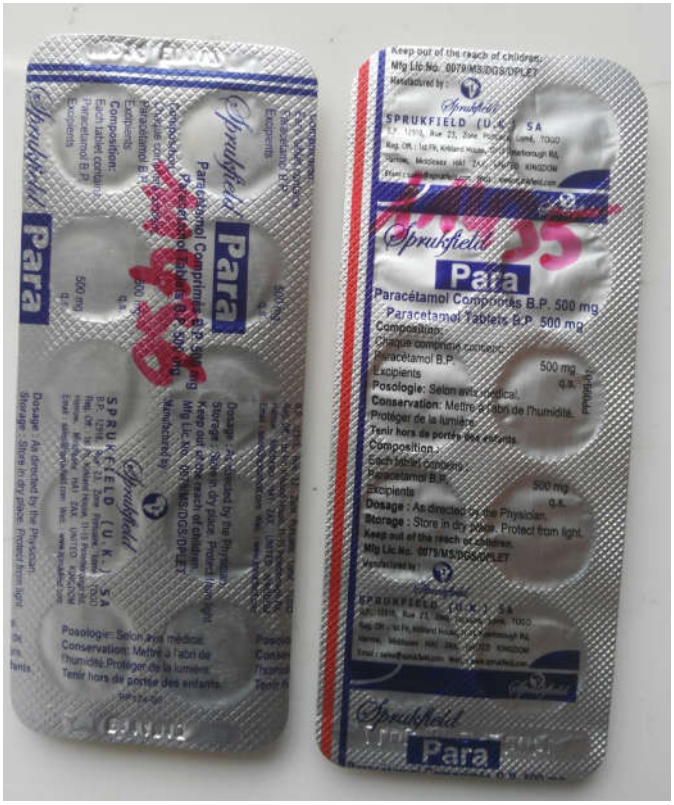

Figure 2. Presentation of Para Sprukfield's "Street vs South FRPS" Primary Packaging

Control of organoleptic properties

For the control of organoleptic properties 100% of the samples from the formal circuit were compliant while 50% of the samples from the informal circuit were non-compliant. The non-compliance was a type of decapping.

Uniformity of the size of tablets

All the samples analyzed were 100% compliant. No batches had tablets smaller than the LCL (Lower Control Limit) or greater than the UCS (Upper Control Limit).

Table 1. Description of the place of purchase and cost of paracetamol blisters

Product Name	Active subtances	Dosage	Blister price (Frs CFA)	Date – per	Bath / Lot	Lab / Country	Purchase places
Paracetamol BP	Paracetamol	500 mg	75 FCFA	10 / 2018	141156	North China Pharmaceutical Qin Huang Dao Co LTD	Street
PARA Sprukfield	Paracetamol	500mg	40 FCFA	05 /17	BC14028	Sprukfield / TOGO	Street
Paracétamol tablets	Paracetamol	500mg	50 FCFA	11 / 2017	141167	Zhejiang Medecines and Products IE Co LTD	Street
PARA Sprukfield	Paracetamol	500mg	50 FCFA	01 / 17	BC14010	Sprukfield / TOGO	Street
Paracetamol	Paracetamol	500mg	150 FCFA	07 / 2017	B1406	Fourrts / INDE	Pharmacy
Paracetamol	Paracetamol	500mg	200 FCFA	02 / 2018	ES5024	Ubithéra / INDE	Pharmacy
Paracetamol	Paracetamol	500mg	100 FCFA	11 / 2017	7750024	Strides Arcolab / INDE	Pharmacy
PARA Sprukfield	Paracetamol	500mg	Donation	04 / 2017	140479	Sprukfield / TOGO	FRPS du SUD

Average weight and mass uniformity

All the samples analyzed were 100% compliant with the European Pharmacopoeia standards as, compared to the authorized maximum limit (5%), no tablet had a mass above the Upper Control Limit (UCL) or below the Lower Control Limit (LCL).

Hardness testing of tablets

Regarding the hardness testing, 25% of the formal sector samples were non-compliant while 100% of the informal sector samples were non-compliant. The tablets had hardness values lower than the LCL (Lower Control Limit) calculated for each batch or higher than the UCL (Upper Control Limit) calculated for each batch.

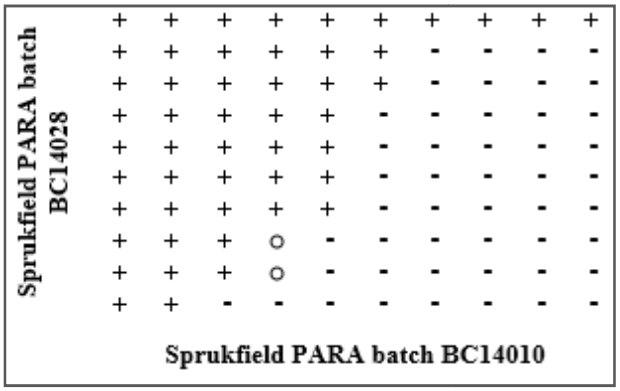

Figure 3. Hardness Dominance Diagram of Streets Sprukfield PARA Tablets

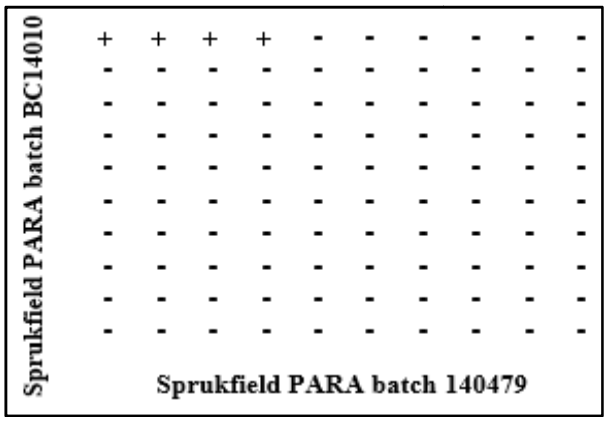

Figure 4. Hardness Dominance Diagram of the Sprukfield PARA Tablets of the Formal vs. Sprukfield PARA Circuit of the Informal Circuit

Furthermore, the parametric comparison tests of the average hardness of the tablets of the PARA Sprukfield batches collected both from the street the South Regional Health Promotion Fund revealed the following patterns of dominance: the average hardness of the tablets from the two street samples are equal. Besides, there is a statistically significant difference (P -Value < 0.0001) between the average hardness of Paracetamol Sprukfield tablets from the South RFPS (batch140479) and those taken from the street (batch BC14010 and batch BC14028).

Tablets friability test (abrasion) tablets

Samples from both sectors were 100% compliant. Indeed, no lot had a mass loss greater than 1%.

Disintegration test

The samples from the formal circuit were 100% compliant whereas those from the informal circuit had 25% of non-compliance (03 units not disaggregated out of 18 units tested, the test durations being respectively 17, 20 and 19 minutes).

Identification and dosage of the active ingredient

All of the samples were identified as paracetamol because the spectra of the samples were superimposable to the spectrum of the standard solution of the EDQM, the European Directorate for the Quality of Medicines and Health Care. The preparations (weighing and dilutions) were well processed because all the FR values (Recovery Factor) for each batch were within the limits of 98% - 102%. All samples (formal and informal) complied with the British Pharmacopoeia standard because the active ingredient levels of these batches were within 95% - 105%. Moreover, the assay coefficient of variation for each batch was less than 2.41%.

Compliance per sector and continent

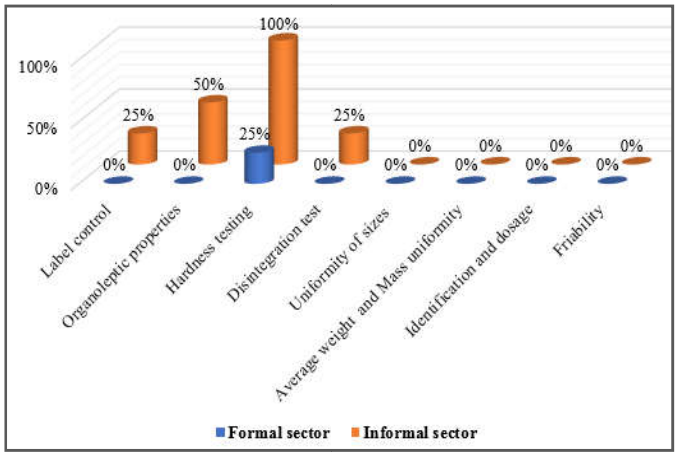

Figure 5. Non-compliance per sector according to analysis carried out

The chart above shows that the non – compliances observed in the batches originating from the illegal markets were analyzed according to the following criteria: label control (25%), control of organoleptic properties (50%), hardness testing (100%) and disintegration test (25%) while the non – compliances determined in the formal sector paracetamol batches were concerning only hardness testing (25%).

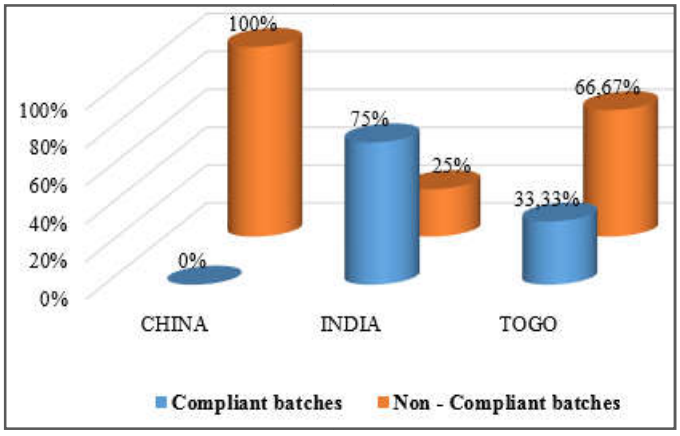

Figure 6. Compliance per country of origin

The previous chart shows that non-compliance affected all countries concerned with the study. 100% of non-compliance for batches from China, 66.67% of non-compliance for paracetamol tablets from Togo and 25% non-compliance for those from India.

DISCUSSION

The samples were tested according to the following parameters:

- Label control;
- Control of organoleptic properties;
- Uniformity of the size of the tablets;
- Average weight and mass uniformity;
- Hardness testing;
- Friability test;
- Disintegration test;
- Identification and dosage of the active ingredient.

The non-compliances identified were related to the following analyzes:

- Label control;
- Organoleptic property;
- Hardness testing;
- Disintegration test.

The analysis of these parameters according to the British, European and international pharmacopoeia standards reveals that the paracetamol tablets 500 mg (generic blister of 10 tablets) of the formal circuit (pharmacies and RFPS of south region) in Ebolowa present 25% of non-conformity against 100% for those from the street.

According to the label control

This analysis consisted of verifying that the mandatory regulatory requirements for labeling in Cameroon (primary and secondary packaging) were met. The control of the immediate packaging focused on the following elements: the name of the product, its pharmaceutical form, its content of active substances (unit doses), the number of the batch, the name and the address of the operator. 25% of the batches found in the street, had neither the name nor the manufacturer's address on the immediate packaging; which does not allow to ensure their traceability. PARA Sprukfield paracetamol batches collected in the street from the street and PARA Sprukfield paracetamol batch from the RFPS had two different labels at the level of the primary packaging. These results are similar to other cases of conditioning abnormalities found in 2001 in Nigeria for Panadol (Naik, 2004) and in 2004 in Ivory Coast for 3 generics of paracetamol (Legris, 2005), A similarity was also observed with the results of Diop *et al.* (2009) who found, in Senegal a case of counterfeit generics of paracetamol at the level of the illicit circuit and those of Akahi *et al.* (2011) who, in their study in Ivory Coast, found abnormalities regarding the secondary packaging of two batches of paracetamol Créat®. These differences in labeling and packaging suggest counterfeiting. Counterfeit medicines are sometimes distinguished from original drugs by minor differences. It may be small modifications on the packaging or differences in the manufacturing process that may affect the galenical parameters, biogalenic and active substance contents.

Regarding organoleptic properties

Two (02) samples of drugs (50%) out of 4 of from the informal circuit were non-compliant with the analysis of the organoleptic characteristics while 100% of the formal circuit samples were compliant. The anormalities detected were associated with the "decapping"; 25% of non-compliance with the analysis of the organoleptic characteristics of the samples were obtained. These results were similar to those of Diop *et al.* who, in their study conducted in Senegal, found 23% of non-conformity to the analysis of organoleptic characters (Diop, 2008). The irregularities detected highlights a manufacturing defect specific to the incriminated batches.

Concerning the hardness test

The hardness test points up the ability of the tablets to withstand a certain pressure force which in turn reveals the stability and bioavailability of the tablets. Given the control limits, the formal circuit samples were 75% compliant compared to 0% compliance in the informal circuit. Globally, five (05) batches out of eight (08) or 62.5%, presented this non-compliance. The reasons could be weather, drug storage conditions or manufacturing problem as all were below the Lower Control Limit. This non-compliance might have an influence on the bioavailability of the active ingredient because the drug will be either quickly or slowly dissolved in the body causing a delay in the release of the active ingredient and its therapeutic action. This result therefore raised up the question of the storage conditions of the tablets analyzed. In addition, the comparison of the hardness of various batches of street-based Sprukfield PARA and South RFPS showed a statistically significant difference (p-value < 0.0001). This significant difference proves that the drugs concerned had different origins. If not, a change might have occurred during the manufacturing process.

According to the disintegration test

The disintegration test makes it possible to evaluate the ability of the tablets to disintegrate under the conditions of temperature and pH corresponding to the conditions in vivo. The tablets of the formal circuit, considering the limits of control, were 100% compliant unlike those of the informal circuit which revealed 25% of non-compliance. This result was contrary to Diop *et al.* survey who found a lower percentage of non-compliance of 6.25% (Diop, 2008). Hence the issue of the bioavailability of tablets coming from the informal circuit.

As far as the identification and dosage of the active ingredient are concerned

The identification and dosage of the active ingredient revealed no irregularities for all the samples tested. In contrast, a survey carried out in Congo on three samples of paracetamol taken from the illicit sector showed a loss in active ingredient of around 12.2% (Henzelin-Nkubana *et al.,* 2006). The study conducted in Cameroon, Madagascar and Tchad by the WHO (OMS, 1995) on the quality of 58 paracetamol samples revealed non-compliance rates of 17.24% or 9.52% for the parallel market in Cameroon (4/42 non-compliant samples); 33.33% for Madagascar (4/12 non-compliant) and 50% for Chad (2/4 non-compliant underdosage: 1 parallel sector, 1 private sector).

Depending on the etiologies of the pharmacotechnical variations observed

Moisture, temperature and light are environmental factors that can influence the pharmacotechnical characteristics of the tablets analyzed. This hypothesis is corroborated by the studies of Cid and Jaminet (Cid *et al.,* 1971) and those of Nyqvist and Lundgren (1982) which showed that the hardness changes of the tablets are related to variations in their water content due to a longer storage life and under high moisture. The temperature may also cause the evaporation of the water contained in the tablet that is to say what is necessary for its good cohesion. Similarly, Niqvist, Nickalsson and Lundgren showed evidence that the increase in disintegration time is due to the decrease in the water content of the tablets, the consequence of a high temperature (Niqvist *et al.,* 1985). For Huber, it is necessary to keep the drugs safe from heat because it is responsible for clumping and a change in the porosity of the tablets resulting in a slow release of the active substance (Huber, 1985). The exposure to sunlight may cause a photodegradation of the active ingredient and lead to a drop in the therapeutic effect, the formation of toxic products which sometimes provoke side effects. Thus, there are alterations of drugs in case of disrespect of conservation rules (Le Hir, 2009). These findings corroborate the results obtained by Awono Noah, who reported a general disregard for the rules of storage of drugs in the illicit markets in Ebolowa (Awono Noah, 2015). Medicines laid up on the counters were not protected from sunlight. In addition, most vendors were keeping drugs in the trunks of cars parked in front of their shops all day long. It was also observed, some mold growth not only on the walls of some retailers' stores but also on secondary packaging of certain drugs.

In accordance with the specificity of the studied molecule

Paracetamol, the leader in analgesic and antipyretic drugs, well tolerated by pregnant women and children, is widely used worldwide; it is the most used analgesic in Europe. France is the biggest consumer (Hider-Mlynarz *et al.,* 2018). It is the most sold molecule in the streets of Ebolowa (Awono Noah, 2015) as well, the daily medication that is kept at the bottom of the bag as a precautionary measure and that is offered without any hesitation to an acquaintance or child. Suffering from headache. The toxicity of paracetamol to the liver being known, in case of abuse, UK scientists carried out research on the consequences of regular and long-term use of paracetamol (Roberts *et al.,* 2014). Based on eight cohort studies, they showed after meta-analysis an increased mortality rate of up to 63% in patients repeatedly consuming large doses of paracetamol (3 grams per day). Indeed, regular intake of paracetamol increases the risk of cardiovascular diseases on the ratio of 68% in case of consumption of more than 15 tablets per week. 20% of paracetamol users are therefore exposed to cardiovascular diseases, including heart attacks and strokes. The risk of developing gastrointestinal and renal problems is also increased with regular consumption. The risk of developing an ulcer would increase by 68% and bleeding by 49%. For kidney problems, the risk would be multiplied by two in case of accumulated intake of more than 500 g of paracetamol in the course of life. As a result, heavy consumers of paracetamol are much more likely to suffer from kidney failure than those who never consume them or that take reasonable doses. The anarchic self-medication of Ebolowa's population, combined with the almost systematic prescription of paracetamol by street vendors will give room to a serious and real problem in the long run namely the high rate of prevalence of chronic diseases in the city.

Conclusion

To sum up, the poor monitoring of supply and distribution channels is responsible for the proliferation of illicit sale of substandard drugs that represent a major health risk for consumers and a proven public health problem. The eradication of this phenomenon remains a complex process as it is part of a long – term rationale of multisectorial approach and permanent repression. The pharmacotechnical evaluation of paracetamol 500 mg, generic blister of 10 sold both in the legal and illegal markets of Ebolowa made it possible to establish that the available drugs were globally non-compliant despite the small number of batches analyzed. In fact, 05 of them (63%) were non-compliant; among them 80% were from the illicit sector that is 100% from the informal sector. This situation is probably due to either a manufacturing problem or non-observance of current pharmaceutical regulations and inadequate storage conditions too. Paracetamol 500 mg generic blister 10 sold in the streets of Ebolowa is essentially of poor quality. Thus, street drugs remain a dangerous panacea for both potential consumers and the economy of the country. A large-scale pharmacotechnical evaluation will make it possible to assess the quality of drugs at the national level. In addition, more deterrent and coercive measures must be taken and implemented at all levels and by all the stakeholders in order to overcome the fight against counterfeiting, circulation and the illicit sale of medicines. A particular attention must be paid to the storage as it precedes the distribution and use of drugs. Good storage conditions are necessary to ensure the integrity of the product and the patient's health. Whether in the pharmaceutical industries stores or in the carrier's trucks as well as in the users medicine cabinets, it is essential to respect the rules. Information regarding the storage of drugs is specified in Good Distribution Practices.

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