Health Sciences and Diseases
The Journal of Medicine and Biomedical Sciences

Origina Article

Quality Assessment of Analgesics Paracetamol and Ibuprofen for Sale in the Douala City (Cameroon)

Évaluation de la qualité des analgésiques paracétamol (500 mg) et ibuprofène (400 mg) en vente dans la ville de Douala au Cameroun

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Keywords : sales, quality, analgesics, Douala central market, Ndokoti.

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ABSTRACT

Background: Base on the findings from the Research Institute Against Counterfeit drugs (RIACD) and the Organization for Economic Cooperation and Development Drugs (OECD), 700,000 cases of death are recorded per year due to malaria and tuberculosis counterfeit drugs. According to the World Health Organization (WHO), roadside drugs kill at least 100,000 people in Africa every year, 1/3 of these drugs are counterfeit. The objective of this study was to evaluate the quality of paracetamol tablets (500 mg) and ibuprofen (400 mg) sold in an illicit manner within Ndokoti and Douala Central Markets in Cameroon. **Materials and methods**: This was an experimental study which was carried out from December, 4th,2013 to June 12th,2014. Samples were randomly selected and The analyzes were focused on the visual, technical and pharmacological tests reported in the International Pharmacopoeia 2018 . Data were analyzed using the Statistical Package for Social Science (SPSS) 20.0 and graphs were mounted using Microsoft excel software. **Results**: Sampling was done on 39 batches of which 24 were ibuprofen and 15 paracetamols Additionally, out of the 39 batches 53.85 percent came from Ndokoti market and the rest (46.15) were obtained from central market. Visual analysis 25 batches out of the 39 were non-compliant this was estimated at 64.10 percent Also, Hardness testing showed non-compliances at 80 and 91.67 percent for paracetamol and ibuprofen samples respectively. We also observed non-compliances of 33.33 and 12.5 percent for paracetamol and ibuprofen batches respectively at the disintegration test. Finally, the mass uniformity test presented a non-compliance of 8.34% of for ibuprofen. The size measurement showed no noncompliance. **Conclusion**: All paracetamol tablets were consistent with the dosage. Visual inspection presented nonconformities paracetamol and lots of ibuprofen. This non-compliance was plausible in the central market.

RÉSUMÉ

Contexte : Sur la base des conclusions de l'Institut de recherche contre les médicaments contrefaits (RIACD) et de l'Organisation de la coopération et du développement économiques (OCDE), 700 000 cas de décès sont enregistrés chaque année en raison de la contrefaçon de médicaments contre le paludisme et la tuberculose. Selon l'Organisation Mondiale de la Santé (OMS), les médicaments vendus illicitement en bordure de route tuent au moins 100 000 personnes en Afrique chaque année. Un tiers de ces médicaments sont contrefaits. L'objectif de cette étude a été d'évaluer la qualité des comprimés de paracétamol (500 mg) et d'ibuprofène (400 mg) vendus de manière illicite sur les marchés centraux de Ndokoti et Douala au Cameroun. **Matériels et méthodes** : Il a s'agit d'une étude expérimentale déroulée du 4 décembre 2013 au 12 juin 2014. Les échantillons ont été choisis au hasard et les analyses ont porté sur les tests visuels, techniques et pharmacologiques rapportés dans la Pharmacopée Internationale 2018. Les données ont été analysées à l'aide du progiciel Statistical Package for Social Science (SPSS) 20.0 et les graphiques ont été montés à l'aide du logiciel Microsoft excel. **Résultats** : L'échantillonnage a été effectué sur 39 lots dont 24 étaient de l'ibuprofène et 15 des paracétamols De plus, sur les 39 lots, 53,85 % provenaient du marché de Ndokoti et le reste (46,15) du marché central. L'analyse visuelle a révélé que 25 des 39 lots étaient non conformes, soit une proportion estimée à 64,10 %. De plus, les essais de dureté ont révélé des taux de non-conformité de 80 % et de 91,67 % pour les échantillons de paracétamol et d'ibuprofène, respectivement. Nous avons également observé des non-conformités de 33,33 % et de 12,5 % pour les lots de paracétamol et d'ibuprofène, respectivement, lors de l'essai de désintégration. Enfin, le test d'uniformité de masse a présenté une non-conformité de 8,34 % pour l'ibuprofène. La mesure de la taille n'a révélé aucune non-conformité. **Conclusion** : Tous les comprimés de paracétamol étaient conformes à la posologie. L'inspection visuelle a révélé des non-conformités pour le paracétamol et les lots d'ibuprofène. Cette non-conformité était plausible dans le marché central.

INTRODUCTION

Pain is a common and important symptom, as is a sign of disease in the broadest sense and diagnostic aid [1], it is the first reason for consultation to the doctor and pharmacy in council. Paracetamol is the analgesic most consumed and widely used analgesic ibuprofen to relieve pain and inflammation. [2,3].

Nowadays, population health needs, rapid financial returns and flaws regulations open the doors to counterfeiting of the drug. [4]

According to the World Health Organization (WHO) the street drugs are the cause of at least 100 000 deaths a year in Africa, 62% of medicines purchased on the Internet are counterfeit, 1/3 of drugs would counterfeit in some countries in Africa, Asia and Latin America and 75% of counterfeit drugs are from China and India. [5]

The work of KUE NGNOTCHOUE in 2013 showed that more than 26.67% of painkillers (Ibuprofen and paracetamol) sold in the illegal sector in the city of Bangante in Cameroon were of poor quality. [6]

The illicit sale endangers the sick, destroyed the economy and threatens the profession of pharmacy. [7]

The function of the inspection and supervision of the market in the pharmaceutical sector is very vulnerable in Cameroon. [8]

Falling wages Cameroonian officials in 1992, the devaluation of the CFA franc in 1994 [9] are obvious causes of the impoverishment of the population, found "refuge" in the consumption of dubious quality drugs. The Ndokoti district is the heart of the city of Douala, it is located in the largest district (3rd) and has 646 347 inhabitants on 2,865,795 of the city. [10] The central market of Douala is one of the largest markets in Central Africa.

The drug is an essential element in the management of the disease. Its marketing requires Pharmacotechnical controls contained in the various statutory instruments that guarantee its quality. For this, we have focused our attention on "quality painkillers purchased at Ndokoti and central markets."

MATERIAL AND METHODS

Period and scope of the study

Our study was experimental type and was held in seven months (December 4, 2013 to June 12, 2014). We conducted the mass uniformity testing, identification and assay in the Laboratory of Analytical Chemistry of the University of Liege in Belgium. Other tests were carried out at the Medical Research Institute of Medicinal Plants and studies of Yaounde in Cameroon.

Reagents

The reagents used were the milli-Q water (Milli-Q plus 185), HPLC grade methanol gradient (JT Baker®; Lot No. 1323912006), hydrochloric acid (international VWR®), ammonium carbonate (Analar NORMAPUR®; lot No. 10I010007), distilled water.

The reference standards used for the study were paracetamol (SCR Fagron®; 12A27-batch B03-268532) and Ibuprofen USP.

Equipment

The equipment used was:

- From a High Performance Liquid Chromatograph (HPLC) Waters alliance PDA 2996 mark;
- On a precision balance (AE163 Metller toledo);
- In an ultrasound bath (Branson 2210);
- In a pH meter (Metller Toledo Seven Easy);
- On a magnetic stirrer (Rotamag 12);
- Of a hardness meter (Schleuniger-2E);
- On the vernier caliper;
- On the disintegration apparatus (Erweka ZT3).

Sampling

Sampling was consecutive non-exhaustive. The sample consisted of tablets coated ibuprofen 400 mg and paracetamol dry tablets, dosed at 500mg.

Sample analysis techniques

Visual inspection of tablets

The analysis involved the control of labeling of tablets by checking whether or not the batch number, manufacturing and expiry dates, trade name and manufacturer of laboratory name on the blister.

We then examined the tablets out of their blister (color, shape, appearance, presence of powder in the blister).

Dimensional inspection

The dimensional control required 10 tablets per lot. Using a caliper, thickness, length and width were measured.

Tear resistance

The measurement of hardness required 10 units. The apparatus, the durometer is composed of two jaws facing each other, one being mobile. Each tablet was placed between the jaws taking into account, if applicable, its shape, the crossbar of breakage and burning. The tablet was oriented in the same way relative to the direction of application of force. The durometer indicated in Newton the force required to rupture of the tablet, the standard being between 40 and 100 N.

Disintegration time

Eighteen tablets were used per batch to determine the disintegration time. The apparatus consists of a basket carrier tubes, a cylindrical vase bottom of 1L (height: 149 ± 11 mm; inner diameter: 106 ± 9 mm) containing distilled water, a thermostatic system (now liquid at a temperature between 35 and 39 ° C), and a device allowing to print to the carrier tubes an alternating vertical movement of constant frequency between 29 and 32 cycles per minute and 55 ± 2mm amplitude in the liquid 'immersion. The disintegration time is the time (in minutes) after which all tablets basket tube holder (six) are completely disintegrated.

Mass uniformity

This test was carried out on 20 tablets per lot. Each tablet was weighed individually using a precision balance and the mass noted. According to the European Pharmacopoeia, the individual weight of 2 to more than 20 units may deviate from the average mass of a higher percentage than the standard 95-105%. But the mass of any unit can differ by more than double that percentage.

Determination of active substances

An HPLC equipped with a column X bridge RP18 3.5µm (4.6 x 100) mm and a UV detector was used.

paracetamol assay in tablets

An initial solution of paracetamol was prepared at 50mg / 25mL, centrifuged, and the supernatant was diluted 40 times in methanol: water (15/85) (V / V) to obtain a final solution of 50µg / mL. Two try independents were well made. The mobile phase consisting of methanol / ammonium hydrogen carbonate buffer 20 mM, pH 6 (15/85) had a flow rate of 1ml / min. injection volume was 10µL. paracetamol was detected at 243nm.

Statistical analysis

Statistical analysis of data was done by SPSS software with a 95% confidence interval.

RESULTS

Sampling

A total of 15 separate batches of tablets of paracetamol and ibuprofen were 24 purchased in Central and Ndokoti markets of Douala.

Table I: Representation of molecules according to the place of sampling

	Central Market	Ndokoti Market	Total
Paracetamol	06	09	15
Ibuprofen	12	12	24
Total	18	21	39

Batch analysis

Visual inspection of tablets

Label

The manufacture date was not mentioned in 20 (83.33%) lots.

The International Nonproprietary was misspelled on 01 (4.17%) lot.

Two (8.33%) had the same batch manufacturer address but had points of differences in the coding of batch number (F303 13576 for one and for the other) and at police level write (darker for one of the two lots).

Organoleptic character

Thirteen (33.33%) items showed various nonconformities.

Table II: Types of non-compliance to the organoleptic characteristics

Type of non-compliance	Non-compliant N(%)
presence of powder in the blister	02 (8.33)
Non-tight closure	01 (4.17)
Tablets irregular outline	06 (25)
Presence of a small fragment of additional drug in a cell	01 (4.17)
blisters soiled	01 (4.17)
Tablets same batch of different colors	01 (4.17)
bad filming	01 (4.17)
Total	13 (33.33)

Dimensional inspection

The dimensions of the tablets were consistent for all lots of the two molecules.

Tear resistant

Twenty-two (91.67%) of ibuprofen lots and 12 (80%) of paracetamol had nonconformities.

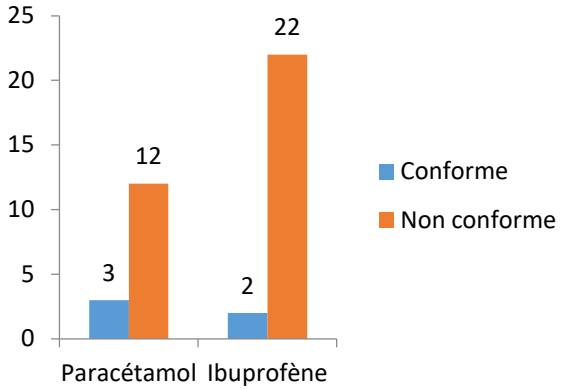

figure 1: Tear resistant

Disintegration time

Five (33.33%) of paracetamol lots and 03 (13.5%) of ibuprofen lots were non-compliant.

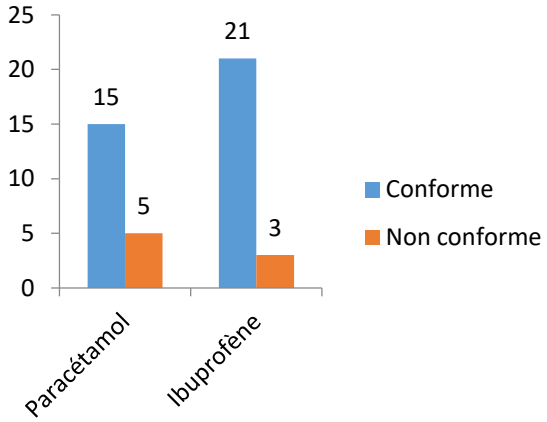

figure 2: Disintegration time

Mass uniformity

Two (8.33%) of ibuprofen lots were non-compliant and zero (0%) set of paracetamol was non-compliant.

Dosage of active substance in tablets

Determination of paracetamol

All lots had a paracetamol amount of active ingredient included in the compliance range is 475-525mg.

Non-conformance

In total 35 (89.74%) batch of the 39 had at least one non-compliance on controls.

Board IIi: non-compliance by country of origin

Country	Conformity N(%)		Total (%)
	Yes	No	
Germany	00 (00)	04 (100)	04 (100)
Cameroon	01 (50)	01 (50)	2 (100)
China	00 (00)	04 (100)	04 (100)
India	02 (8.33)	22 (91.66)	24 (100)
Nigeria	01 (100)	00 (00)	01 (00)
Non identified	00 (00)	01 (100)	01 (100)

Table IV: global non-compliance

Country	Global non compliance N (%)
Germany	04 (10.25)
Cameroon	01 (2.56)
China	04 (10.25)
India	22 (56.41)
Nigeria	00 (00)
Non identified	04 (10.25)
Total(%)	35 (89.74)

DISCUSSION

Although our samples were taken in two markets (Central and Ndokoti), this work has not sought to conduct a comparative study. The goal was to assess the quality of analgesics consumed by a large population of Douala.

The calculated values of p-value of the various parameters studied show a similarity between the medicines in these two markets.

Counterfeit Places

India was the country with the highest non-compliance in our sample with 62.85%, followed by China and Germany which showed 11.43% each. These results are similar to those of WHO which revealed that most counterfeit (75%) were from India[5]. Studies in Côte d'Ivoire by Candice L [11] in 2005, show a greater rate (94%) of counterfeit medicines from India. These results show that the majority of counterfeit medicines originate in India. [12]

Visual inspection of tablets

Visual inspection showed 33.33% of non-compliance. This result differs from Djoko[13] in 2010 in the city of Bangante in Cameroon who found 13.33% of non-conforming lots, but approximates the results of KUE in 2013 [6] which showed 26.67% of non-compliance. The presence of black spot on the pockets of a lot shows poor storage; the absence tablets coloring homogeneity another batch can be explained by re-labeling of probably obsolete tablets.

Mass uniformity

Two (8.34%) lots were inconsistent with the uniformity of mass. It was found inside a cell from one of these lots a little extra fragment may imply a failure to comply with Good Manufacturing Practices. A lack of uniformity of mass reflects poor granulation in the compression process[14] This could influence the distribution of the active ingredient in the tablet and thus the efficacy and safety of the drug. This result differs from KUE [6] which was 13.33% of non-compliance with this same test.

Disintegration time

The disintegration test showed 20.51% of non-compliance with three lots of time indefinite disintegration. These non-conformities translate a default binding agent during compression[14]. Ingestion of such tablets would cause no pharmacological effect, if a delayed effect from the normal time. The results of KUE show a lower percentage, 13.33%. [6] The study by HAMANI in 2005 in Niger showed 4.45% of non-compliance to the disintegration test. [15]

Hardness testing

Eighty percent of paracetamol lots and 91.67% of ibuprofen lots are nonconforming to the hardness test. This can be explained by the high storage temperature on the one hand and on the other hand by a defect of binder in the formulation which results in a greater force of compression and therefore an increase in the tablet hardness[14]. A tablet having a hardness greater than 100N can irritate the stomach, which will struggle to disintegrate.

Identification of active substance

All batches of paracetamol contain the active ingredient. DJOKOfound the same result in 2010 in his study of antibiotics. [13] HAMANI had found in his study of the anti infectives street nonconformity (2.23%) of the 45 items surveyed. [15]

Active substance dosage

The levels of active ingredient are normal for all paracetamol lots. This is different from Candice L. and DJOKOwho found 28% and 53.33% lower or higher content of active ingredient [11,13]. HAMANI found a rate of 28.89% for non-compliance with this test. [15] This can be justified by the fact that these lots come from the legal circuit. However the assay alone does not determine the quality of a tablet. A tablet well balanced and having a very long disintegration time is not consistent, since the disintegration is a prerequisite for the bioavailability of the active principle; is the case of our paracetamol samples.

Measurement of dimensions

The measurement of dimensions is correct for all lots of ibuprofen as paracetamol. This result is similar to studies by DJOKO on antibiotics [13].

The circulation of counterfeit drugs is a big problem caused by the illegal sale of drugs in the sense that their uncontrolled physicochemical nature can be dangerous.

CONCLUSION

The technical tests ensure pharmaco with the physical, chemical and biological tests the quality, effectiveness and safety of drugs. Our work mostly led to unexpected results. This is the case of the hardness (with a percentage of non-compliance very high) which is a parameter influencing disintegration, prior to the dissolution and bioavailability of the active ingredient.

The proliferation of counterfeit drugs can increase the rate of morbidity and mortality users.

Through our work, we wanted to make our modest contribution to the fight against drugs of dubious quality. However, the identification and determination have not been fully carried out. Similarly biological controls tablets have not been addressed. We believe increasing the sampling, perform all controls testing in future studies.

Conflict of interest

No conflict of interest

Training and funding source

This research received no specific grant from the public funding agencies, commercial or nonprofit.

thanks

Our gratitude goes to the place of people below that of some way helped make this work:

Professor Marini of Analytical Chemistry Laboratory of the University of Liege.

Prof. Emmanuel MPONDO MPONDO of the Faculty of Medicine and Pharmaceutical Sciences of the University of Douala

The Medical Research Institute of Medicinal Plant Studies of Yaounde

The Faculty of Medicine and Pharmaceutical Sciences of the University of Douala

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