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Research Article

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Quality control of some antibiotic molecules seized on the Ivorian illicit market by the GPHF-Minilab kit

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Abstract Medicines of lower and falsified qualities (MLFQ) are a real public health problem. They are responsible for some drug resistance to antibiotics and several deaths worldwide. Faced with this scourge, quality control of our country's medicines is essential in order to maintain the quality of medicines and ensure a certain safety for patients. To contribute to the fight against MLFQ, we proposed to use the GPHF-Minilab kit to evaluate the quality of some antibiotic molecules seized on the Ivorian illicit market.

This is a descriptive study with analytical purposes on the quality of illicit drugs seized by the police. Medicinal products presented as containing ceftriaxone or cefixime or ciprofloxacin or ofloxacin were collected and analysed according to the instructions of the GPHF-Minilab.

The analyses carried out on the 24 samples revealed non-conformities, namely unknown origin (12.5%), lack of batch number (12.5%), package leaflet (16.67%), address of manufacturer (58.33%), absence of expiry date (8.33%) and date of manufacture (4.17%), underdosed active ingredients (4%) or over-dosed active ingredients (13%). As these non-conformities are likely to induce misuse, therapeutic failures or even poisoning, the marketing and consumption of such products should be avoided.

The Minilab kit is a relevant, fast, and easy-to-use tool that can contribute to the evaluation of the quality of the drug at checkpoints in our country to fight against this gangrene.

Keywords: MLFQ, illicit market, Minilab, antibiotics

Introduction

Counterfeit medicines are a growing phenomenon worldwide. It represents 10 to 15% of the global drug market. According to the WHO, in poor and developing countries, the problem is more serious because one in ten medicines is said to be of substandard quality or falsified [1]. The problem of substandard and falsified medicines is a serious public health threat. In Côte d'Ivoire, this scourge is in full swing, where this market represents 30% of the drugs in circulation. This is encouraged by the proliferation of illicit markets for the sale of medicines on the streets, the most famous of which is called "Pharmacie ROXY" [2]. According to a report from the IMPACT (International Medical Products Anti-Counterfeiting Taskforce) group of the World Health Organization (WHO), anti-infectives are among the most affected therapeutic classes [3]. The use of such counterfeit products could lead to drug resistance to infectious agents, treatment failures or even poisoning that could lead to the death of the patient [4]. In addition, modelling studies by the London School of Hygiene and Tropical Medicine estimated that 64,000 and 158,000

additional malaria deaths are caused each year in sub-Saharan Africa by substandard or falsified antimalarial drugs [1]. To combat the spread of substandard and falsified medicines, a new approach based on simple and reliable testing methods for the rapid verification of drug quality and the detection of falsified medicines has been initiated by the Global Pharma Health Fund (GPHF), a charitable organization [5]. In this context that we proposed to use the GPHF-Minilab to evaluate the quality of some antibiotic molecules seized on the Ivorian illicit market.

Material and methods

Materials

The controls were carried out using the GPHF-Minilab (**Figure 1**). The GPHF-Minilab is a mini-laboratory in the form of a self-contained kit containing the reference substances, glassware and all the laboratory equipment necessary to carry out physical and visual inspection, disintegration and thin-layer chromatography tests. This kit also contained handling manuals that describe the protocols, the composition of the eluent and the migration time.

Figure 1: Photograph of the GPHF-Minilab [6]

Methods

This is a descriptive study with analytical purposes on the quality of medicines seized by the Narcotics and Drugs Police Directorate (DPSD) located in Abidjan. This study took place from December 2019 and March 2020. Sampling of drugs was carried out randomly from the stock of drugs available at the DSPD. Thus, all drugs presented as containing amoxicillin or ciprofloxacin or ofloxacin were collected. After collection, three tests were carried out on the drug samples taken according to the recommendations of the GPHF-Minilab. These are the visual and physical inspection test, the disintegration test, and the qualitative identification and semi-quantitative thin-layer chromatography (TLC) assay test. The physical and visual inspection made it possible to assess each sample in its entirety, i.e., the description of the primary and secondary packaging, the dosage form of the drug and the information on the manufacturer as well as the dates of manufacture and expiry. As for the disintegration test, it determines the time at the end of which the tablets or capsules placed in a 150 ml bottle containing 100 ± 2 ml of water at 37°C disintegrate. As the bottle is stirred from time to time, the tablet or capsule should completely disintegrate after a maximum of 30 minutes. Qualitative identification of the active ingredient contained in each sample was carried out by thin-layer chromatography compared to the control substances provided in the kit. The active ingredient in the sample will be identical to the control substance, if it has the same frontal ratio as the control. The purpose of the semi-quantitative assay is to assess the active substance content of each sample. To do this, the stain intensities of the sample and the control substances with 80 and 100% active ingredient are compared. After the TLC, samples containing no active ingredients, impurities (more than one task per deposit) and samples with an active ingredient content of less than 80% or more than 100% were considered non-compliant [6].

Results

Sampling

In our study we collected 24 samples, 5 of which are presented as containing ciprofloxacin, 4 as ofloxacin, 6 as cefixime and 9 as ceftriaxone. The various information (trade names, International Nonproprietary Names (INNs), dosage and dosage form) on these samples are presented in **Table I**.

Table I: Characteristics and information on samples collected at the DPSD

Trade Name	International Nonproprietary Name	Dosage	Galenic Form
Cephaloral	Cefixime	200mg	Tablet
Fixim	Cefixime	200mg	Tablet
Melcef	Cefixime	100mg/5ml	Suspension
Mexime	Cefixime	200mg	Tablet
Solexim	Cefixime	200mg	Tablet
Ofiken	Cefixime	100mg/5ml	Suspension
Cefdec	Ceftriaxone	1000mg	Powder for injection
Ceftriaxone(A)	Ceftriaxone	1000mg	Powder for injection
Ceftriaxone(B)	Ceftriaxone	1000mg	Powder for injection
Ceftriaxone(C)	Ceftriaxone	1000mg	Powder for injection
Ceftriaxone(D)	Ceftriaxone	1000mg	Powder for injection
Ceftriaxone(E)	Ceftriaxone	1000mg	Powder for injection
Ceftriaxone(F)	Ceftriaxone	1000mg	Powder for injection
Solicef	Ceftriaxone	1000mg	Powder for injection
Triox	Ceftriaxone	1000mg	Powder for injection
Ciprofloxacine M®	Ciprofloxacine	500mg	Tablet
Serviflox®	Ciprofloxacine	500mg	Tablet
Jubi ciprofloxacine®	Ciprofloxacine	500mg	Tablet
Cipromed®	Ciprofloxacine	500mg	Tablet
Nacipro®	Ciprofloxacine	500mg	Tablet
Lyoflox®	Ofloxacine	200mg	Tablet
Orixo®	Ofloxacine	200mg	Tablet
Quinolox®	Ofloxacine	200mg	Tablet
Oflocet®	Ofloxacine	200mg	Tablet

Physical and Visual Inspection

The physical and visual inspection of the primary and secondary packaging as well as the dosage forms revealed that the samples analyzed had several non-conformities such as the absence of the country of origin, the batch number, the manufacturer's address, a package leaflet in French and the appearance of the tablets (**Figure 2**).

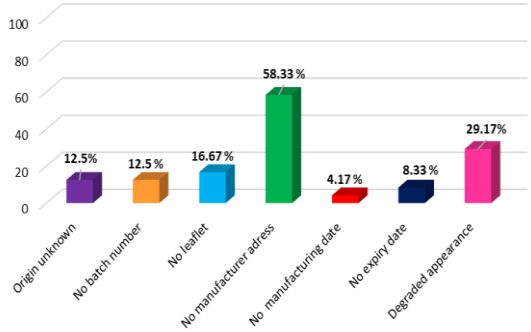

Figure 2: Visual Inspection Results

Disintegration Test

The disintegration test was performed on capsules and tablets only. The results of this test are summarized in the figure below. These results reveal that one sample did not disintegrate within the maximum 30 min as indicated in the kit manual [6].

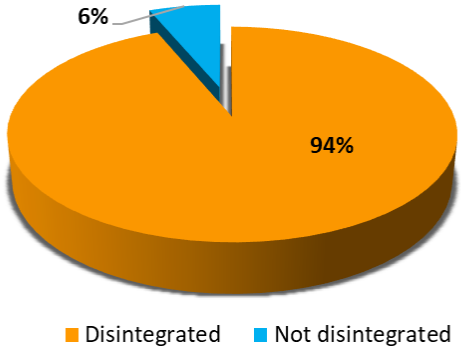

Figure 3: Disintegration Test Results

Qualitative and semi-quantitative analysis

The results of the tests for the identification of the active substance showed that 8% of the sample had different frontal ratios from the reference substance (**Figure 4**). This means the presence of other substances.

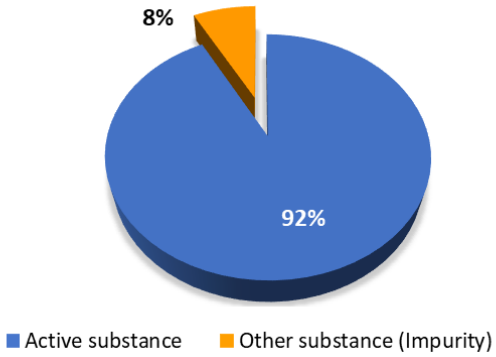

Figure 4: Identification test results

As for the semi-quantitative assay, it revealed the presence of some samples that were overdosed, and others underdosed of active substance (**Figure 5**).

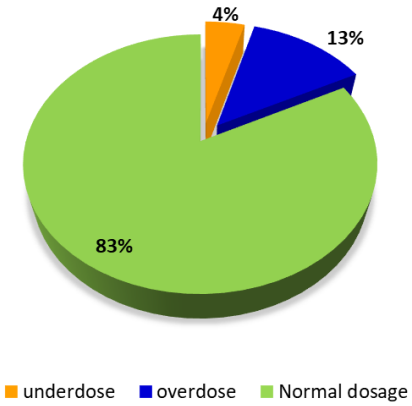

Figure 5: Semi-quantitative assay result

Discussion

Physical and visual inspection

Physical and visual inspection of the 24 samples 24 of ciprofloxacin and ofloxacin, cefixime and ceftriaxone samples revealed numerous non-compliances. It revealed that most of the samples did not give information on the address of the manufacturer (58.33%) and its origin (12.5%), nor a leaflet in French (16.67%), nor a batch number (12.5%). In addition, slightly fewer of the samples did not have the date of manufacture (4.17%), nor an expiry date (8.33%). This information on the primary and secondary packaging of medicines is an important element for the traceability and proper use of the medicine [7]. The absence of the manufacturer 's address could be considered as a deliberate attempt by counterfeiters to evade controls and sanctions by the health authorities of our country. As for the batch number, its absence makes it impossible to verify the conformity of the drugs in a manufacturing batch and to withdraw defective batches in the event of manufacturing anomalies. Non-compliance in relation to the absence of a date of manufacture and/or expiry is an anomaly that does not allow us to know the shelf life of the medicine. This indicates the absence of a quality monitoring system during the production of these drugs [8]. As the quality of the drug is influenced by its stability over time, the presence of the dates of manufacture and expiry date constitute an element of the safety of use of the drug. Such an absence could increase the risk of poisoning of populations through the consumption of expired and degraded medicines. As for the package leaflet, it contains all the information necessary for the correct and safe use of the medicine. Its absence is therefore a serious breach that increases the risk of medication error and reduces consumer protection [9]. In addition, some tablets and capsules showed physical damage such as breakage and cracks (29.17%). This suggests poor conservation and storage practices and poor galenic formulation [10].

Disintegration test

The time of disintegration is a predictive parameter of the bioavailability of drugs in the body |11]. Thus, the tablets or capsules should be strong enough to withstand handling without breaking. But, they should be brittle enough to disintegrate easily in the body so that the drug can be used by the body. In our study, 6% of the samples showed a decay defect after 30 minutes. Such a defect could contribute to a reduction in the bioavailability of the active substance, with the consequence of a delay in the onset of the therapeutic effect or even a therapeutic failure that could lead to the persistence of the patient's morbid state. This disintegration defect could be explained by poor galenic formulation and/or improper storage, tablets, and capsules [12].

Qualitative and semi-quantitative analysis

The qualitative analysis by TLC showed that 8% of the samples analyzed contained substances different from the active ingredient marked on the primary and secondary packaging. These two suspect samples believed to contain ciprofloxacin had different frontal ratios than the reference ciprofloxacin. In addition, they showed traces of impurity in addition to the active ingredient. This impurity was objectified on the TLC by the presence of a second spot on the chromatogram. These impurities could be degradation products of the active ingredient or even unpurified synthetic residues. In any case, the presence of these impurities could lead to serious adverse effects and drug poisoning in populations that use drugs from the illicit circuit.

As for the semi-quantitative analysis by TLC, non-conformities to the type of under- and over-dosing have been highlighted. Underdosing pharmaceutical products is a common practice among fraudsters who favor the search for more profits by reducing the quantity of the active ingredient. Such an attitude is harmful to the health of the population because it can lead to a delay in recovery of the patient or a therapeutic failure that can lead to death. In addition, under-dosing promotes the emergence of resistance phenomena in bacterial germs. Against overdose could promote an increase in adverse effects and serious fatal poisonings. This type of anomaly is more akin to an involuntary suicide of populations that use drugs from the illicit circuit.

Conclusion

The general objective of our work was to evaluate the quality of some antibiotic molecules seized on the Ivorian illicit market by the GPHF-Minilab kit. Visual and physical inspection of the 24 samples, presented as containing ciprofloxacin, ofloxacin, cefixime and ceftriaxone, revealed the absence of origin (12.5%) and address of the

manufacturer (58.33%), batch number (12.5%), package leaflet (16.67%), date of manufacture (4.17%) and expiry date (8.33%). Also 29.17% of the samples had a degraded appearance. In addition, 6% of the samples showed a decay defect after 30 minutes. As for the qualitative and semi-quantitative identification test, it revealed that 8.33% contained a product other than the active substance (ciprofloxacin, ofloxacin, cefixime and ceftriaxone); 4% of the samples were underdosed in active ingredient, 13% were over-dosed and 8% had impurities. The GPHF-minilab kit showed that the antibiotics seized in the Ivorian illicit circuit were of poor quality with several non-compliances that are likely to endanger the health of the population.

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