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# Pharmaceutical equivalence and stability study of levofloxacin tablets commercialized in Europe and Africa

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## 1. Introduction

Tuberculosis (TB) is one of the most severe and deadly infectious diseases in African region, where there is a high prevalence of multi-drug resistant tuberculosis (MDR-TB) too [1]. This resistant has increased in the recent years due to the commercialization of substandard and falsified medicines in low and middle income countries. The quality of the medicines may be affected in the whole steps of its lifecycle. In this sense, many medicines require specific conditions to ensure their quality during storage or shipping. In addition, climatic conditions of African countries are extremely harsh for many medicines, so packaging must be selected for environments with high temperature and humidity. Then, the detection of such poor-quality medicines it is essential to ensure an optimum treatment of TB disease and must be carried out by WHO-accredited reference laboratories [2]. In this way, the ISACAM project (www.isacam.eu) aims to establish a medicine quality assurance system in collaboration with the Laboratoire National de Contrôle de la Qualité des Médicaments (LNCQM) and achieve its qualification.

Levofloxacin (LVFX) is one of the most widely used drugs to treat MDR-TB and its quality assurance is essential to cure the disease and prevent new resistance.

The objective of this work was to evaluate the influence of storage conditions on the quality attributes of 3 LVFX medicines obtained from European and African supply-chain and compare the formulations through the dissolution profiles.

## 2. Materials and methods

500 mg LVFX film-coated tablets were collected: Tavanic® (Tenerife, Spain), Levofloxacino Cinfa® (Pamplona, Spain) and Amesol® (Nouakchott, Mauritania) from distribution company, manufacturer laboratory and an official national program against TB, respectively.

All medicines were collected in December 2019, transported to ULL lab in an isothermal bag, stored at 5 ºC and 11 % of relative humidity (RH) and analysed before their expiration date. Primary and secondary package were checked for imperfections, colour changes and lack of relevant information. Ultra-Performance Liquid Chromatography (UPLC, Waters) was employed

to detect and quantify LVFX. The method used was adapted for UPLC and validated following ICHQ2(R1) guideline [3].

*2.1. Quality Control and Stability study.*

Mass uniformity, disintegration and uniformity of dosage units tests were carried out according to European Pharmacopeia (Eu. Ph.). Dissolution studies were performed according to the procedure recommended by United State Pharmacopeia for Levofloxacin tablets [4]. Then, medicines were stored at climatic zone IV conditions (40 ºC ± 2 ºC / 75 % RH ± 5 % RH) in a climatic chamber ICH 110L (Memmert). Content and dissolution studies were performed for each medicine at 3 and 6 months.

*2.2. Dissolution profiles.*

Samples of 5 mL were withdrawn and replaced with new medium at 5, 10, 15, 20, 30 and 40 minutes to compare their dissolution profiles. The similarity between dissolution profiles were evaluated calculating the similarity factor (f2) according to European Medicine Agency recommendations [5] using Tavanic® as reference medicine.

## 3. Results and Discussion

At initial time, the packaging medicines were checked and all of them were in good condition and contained the required information. 6 months later, the colour of the packaging had changed while the appearance of the dosage form seemed unchanged.

*3.1. Stability study*

Every medicine complied with mass uniformity and disintegration Eu. Ph. tests because no units deviate more than 5 % of average weigh and all tablets were disintegrated before 15 minutes. At 0, 3 and 6 months all formulations met with the requirements for uniformity of dosage units and dissolution tests too. In addition, no degradation products or impurities were detected during the study.

*3.2. Dissolution profiles.*

Figure 1 shows the dissolution profiles of all formulations. As can be seen, the best dissolution result was obtained for Levofloxacino Cinfa®, reaching the asymptotic value before 15 minutes, so f2 estimation is not necessary and could be considered as a quick dissolution. To compare the dissolution profiles of Amesol® and Tavanic®, sampling points at 10, 15 and 20 minutes were used to calculate f2, which was 55.9. Then, the similarity between the dissolution profiles may be accepted.

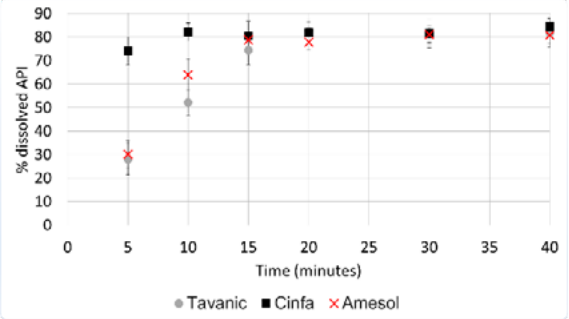


**Fig. 1.** Dissolution profiles of LVFX medicines

## 4. Conclusions

The Mauritanian medicine is a pharmaceutical equivalent of Tavanic® that meets quality requirements and is not affected by storage conditions. However, the sample size should be expanded to include generics commercialized in Mauritania, medicines from more cities where shipping conditions may affect their qualities and other sites of the supply-chain like pharmacy services, hospitals or centres of diagnostic and treatment.

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## References

1. World Health Organization. Global Tuberculosis Report 2020. 2020.

2. World Health Organization. A study on the public health and socioeconomic impact of substandard and falsified medical products. 2017.

3. Kim HJ et al. Simple and accurate quantitative analysis of 20 anti-tuberculosis drugs in human plasma using liquid chromatography–electrospray ionization–tandem mass spectrometry. J Pharm Biomed Anal. 2015;102:9-16. doi: 10.1016/j.jpba. 2014.08.026

4. USP. Levofloxacin tablets. 2014.

5. European Medicine Agency. Guideline on the investigation on the bioequivalence. 2010.

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