RISK ANALYSIS OF THE PHOTOPROTECTION PROCESS OF CIPROFLOXACIN

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ABSTRACT

To ensure the integrity of the experiments in obtaining photoprotection of the API (Active Pharmaceutical Ingredient) ciprofloxacin, a Risk Analysis was conducted to identify the possible risks associated with the mixture of ciprofloxacin with the excipient curcumin in the respective proportions of 1/1, 1/0.5, and 2/1. Within this evaluation, it was possible to define the critical and non-critical attributes of the API that could interfere with the experiments. The methodology adopted to obtain the results followed the guidelines of the ICHQ9 Guide from January 2023, and the risk assessment of each attribute within the experiment was based on the information provided by the IFA manufacturer, Sigma-Aldrich, and data evidenced in the literature. According to the risk analysis, the only attribute considered critical for the experiment was the active ingredient content, which has a potency different from 100%, and its mass was adjusted so that the proportion between the mixtures of raw materials could be corrected.

Keywords: Ciprofloxacin, Photostability, Risk Analysis.

INTRODUCTION

The drug ciprofloxacin (Figure 1) belongs to the class of quinolone-based antimicrobials and has therapeutic action for the treatment of infections caused by susceptible bacteria: urinary tract infections, prostatitis, lower respiratory tract infections, acute sinusitis, otitis media, skin and skin structure infections, bone and joint infections, uncomplicated intra-abdominal infections, typhoid fever caused by Salmonella typhi, nosocomial pneumonia, empirical therapy for patients with febrile neutropenia. Ciprofloxacin has in vitro activity against a wide range of gram-negative and gram-positive microorganisms. The bactericidal action of ciprofloxacin results from the inhibition of bacterial type II topoisomerase (DNA gyrase) and topoisomerase IV, necessary for the replication, transcription, repair, and recombination of bacterial DNA. Furthermore, the pharmacokinetic properties of ciprofloxacin were evaluated in different human populations (TORNIAINEN; TAMMILEHTO; ULVI, 1996). The average maximum serum concentration at steady state obtained in adult humans treated with

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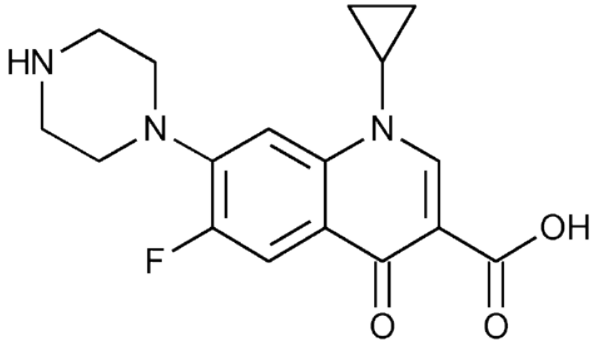
500 mg orally every 12 hours is 2.97 mcg/mL, while it is 4.56 mcg/mL after intravenous administration of 400 mg every 12 hours.

This drug exhibits photoinstability under certain conditions, such as concentration and pH of the medium, with the highest stability achieved at pH 3.0 - 4.0. The mechanism of possible photodegradation involves the piperazine ring, in which the nitrogen can be completely protonated, and the carboxyl group, which undergoes complete ionization (TORNIAINEN; TAMMILEHTO; ULVI, 1996).

Figure 1. Molecular structure of ciprofloxacin.



Source: Own elaboration.

Based on this characteristic of ciprofloxacin, the work focused on obtaining precise ratios between the API and curcumin (photoprotective agent), which result in the photoprotection of the drug. Thus, in order for the experiments to be conducted with high predictability, a risk analysis was proposed to define the critical and non-critical attributes of the API that could interfere with the experimental results. In addition to understanding the IFA attributes, the risk analysis provides accurate data for decision-making during the experiments.

According to the ICHQ9 Guide of January 2023, Risk Assessment is an approach that compares the estimated risk with specific risk criteria using a quantitative or qualitative scale to determine the significance of the risk associated with a change in scenario.

METHODOLOGY

The methodology adopted to obtain the results followed the guidelines of the ICHQ9 Guide from January 2023, a qualitative approach. The risk assessment of the present work will be based on the information provided by the IFA manufacturer, Sigma-Aldrich, and data evidenced in the literature.

To define the critical attributes of ciprofloxacin, it was necessary to establish the IFA quality profile, in which the main objective of this study (photoprotection of the active ingredient through the mixture with the excipient curcumin) was considered a fundamental criterion, where the biological and physicochemical characteristics of the IFA that could directly impact the results of the proposed tests were taken into account.

RESULTS

According to the risk analysis, the only attribute considered critical for the experiment was the active ingredient content, which has a potency different from 100%, and its mass was adjusted so that the proportion between the mixtures of raw materials could be corrected and this variable would not impact the results of the experiments.

CONCLUSION

Given the risk analysis approach aimed at evaluating potential problems during the execution of photoprotection experiments, it was possible to understand the characteristics of the IFA, identify an associated risk, and address it before the execution of the experiments.

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