Measurement uncertainty arising from sampling and analytical steps of dissolution test

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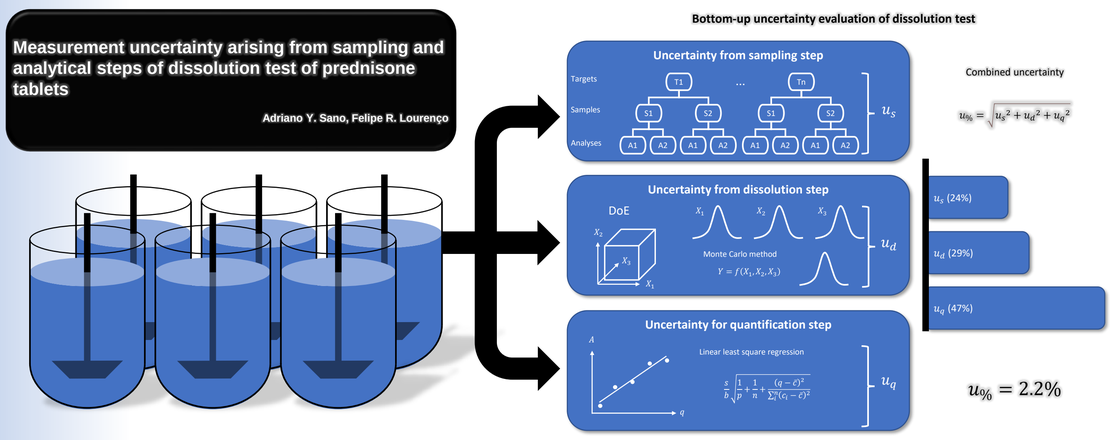
GRAPHICAL ABSTRACT



INTRODUCTION

Dissolution is used to determine the rate and extent of drug release from the dosage form into a dissolution medium, which allow to assess the batch-to-batch variability. Considering that the dissolution test is used predict the in vivo performance of the drug as well, it is important to guarantee the quality and reliability of dissolution test results. The aim of this work was to evaluate the measurement uncertainty arising from sampling and analytical steps of dissolution test of prednisone tablets.

MATERIALS AND METHODS

Dissolution test was performed using 900 mL of purified water as dissolution medium and a dissolution apparatus equipped with paddles rotating at 50 rpm for 30 minutes. Quantification was performed by UV spectrophotometer.

Uncertainty arising from sampling was estimated using the duplicate method (empirical approach), using 17-sampling target, two samples for each sampling target, and three replicas for each sample, totalizing 102 analyses.

Uncertainty arising from analytical steps considered the uncertainty from dissolution step (estimated using Monte Carlo method and regression equation obtained using DoE) and uncertainty from quantification step [1].

RESULTS AND DISCUSSION

Overall uncertainty value was found to be 2.2%, which is below the target uncertainty value (u^t=2.5%). The contribution of uncertainty sources were uncertainty from sampling (24%), uncertainty from dissolution step (29%), and uncertainty from quantification step (47%).

The results of dissolution test should be compared to the specification limits (Q). According to the pharmacopeia requirements, the batch of the medicine should be declared compliant if the dissolved amount of prednisone for six tablets are above the specification limits +5% (Q+5%=85%).

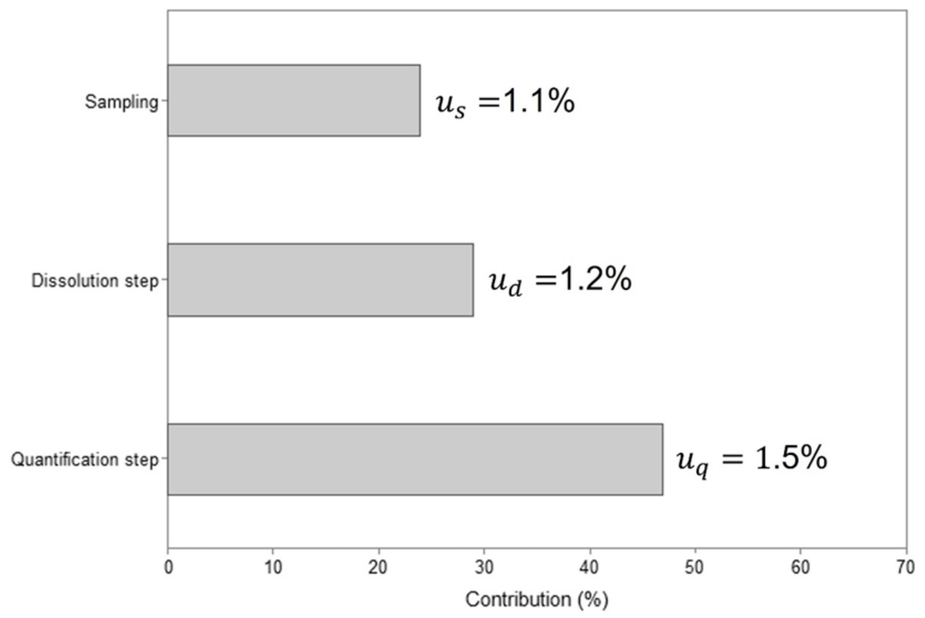


Figure 1. Pareto chart of the contributions of uncertainty arising from sampling (u_s), dissolution (u_d), and quantification (u_q) steps for the dissolution test of prednisone tablets.

Since the measured values for all six tablets (96.5%, 94.0%, 96,4%, 95.3%, 96.0%, and 96.9%) were above the multivariate acceptance limit (89.4%, calculate as the standard uncertainty multiplied by multivariate coverage factor) [2], the batch of the prednisone tablets was declared complaint, with a reduced total risk of false decision (total risk value below 5%).

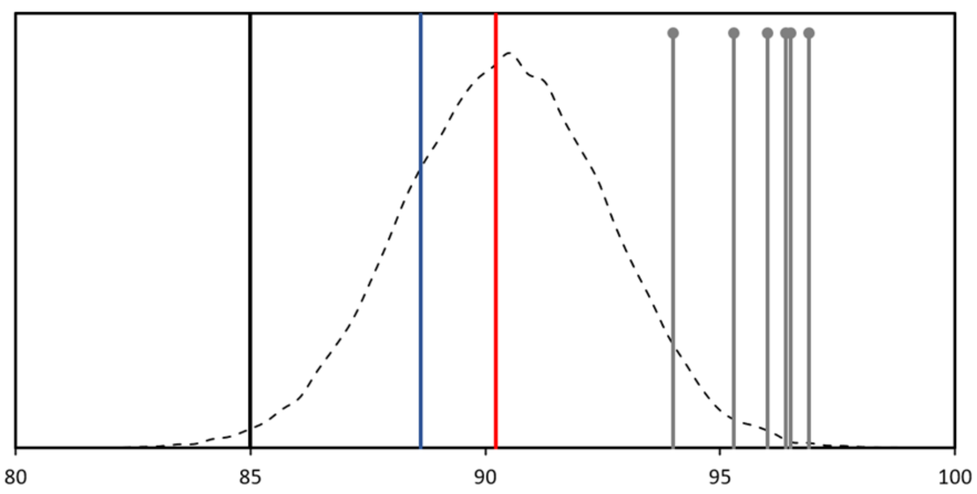


Figure 2. Measured values ( ), specification limits ( ), univariate ( ) and multivariate ( ) acceptance limits for the dissolution test of prednisone tablets.

References

[1] D.C. Romero, F.R. Lourenço, *Brazilian Journal of Pharmaceutical Sciences*, **2017**, *53(3)*, e00163.

[2] C.M. da Silva, F.R. Lourenço, *Journal of Pharmaceutical and Biomedical Analysis*, **2023**, *222*, 115080.

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