NON-DESTRUCTIVE QUALITATIVE AND QUANTITATIVE ANALYSIS OF A PIPERACILLIN-TAZOBACTAM FORMULATION USING SPECTROSCOPIC TECHNIQUES

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ABSTRACT

Many formulations are in form of powder and they should be reconstituted by adding either water or sodium chloride 0.9% before their administration. The qualitative as well as the quantitative analysis of the initial and final product is usually achieved by chromatography but this procedure is of high cost, time consuming and destructive for the sample. There is need for the development of a quick, non-destructive methodology for fulfilling two purposes. The first one is to identify the initial dry powder of the formulation without removing it out of the glass bottle, whereas the second one is to determine the mass ratio of the separate active substances as well as their concentration in liquid formulation after reconstitution. Although UV spectroscopy has been used for the simultaneous quantitative analysis of piperacillin and tazobactam, the method was proved to be complex and destructive for the sample.[1]

In the present study, two of the most widely used spectroscopic techniques, Raman and ATR spectroscopy, were utilized in combination, for the analysis of formulation powders before or after reconstitution. In particular, the generic drug of piperacillin and tazobactam was used, in which the mass ratio of the active substances is 8:1 respectively. This formulation is a combination of a beta-lactam antibiotic (piperacillin) and a beta-lactamase inhibitor (tazobactam). The commercial product is powder for injection and its active substances are in form of sodium salts.

Raman spectrum of the dry powder before reconstitution was acquired through the glass bottle, using the optical fiber of a portable micro-Raman instrument. This spectrum was then compared with that of the pure active substances and the characteristic peaks of piperacillin at 1003 cm^{-1} and tazobactam at 625 cm^{-1} (as shoulder) were detected. Afterwards, the reconstitution of the lyophilized powder was performed, by funneling NaCl 0.9% through the rubbery top of the bottle, using a syringe. Only 5 uL of the liquid formulation were put on ATR crystal and as soon as the solvent had been evaporated, the spectrum of the sample film was acquired. The infrared characteristic peaks of both piperacillin at 1713 cm^{-1} and tazobactam at 873 cm^{-1} were detected and the peak ratio confirmed the mass ratio of the active substances in the generic product. For this, a calibration curve was used which was based on the ratios of the characteristic peaks of standard mixtures. The linearity of the calibration curve found to be R^2 = 0.999 and the LOD of tazobactam in this method was in the range of 2% to 3% w/w. Finally, Raman spectra of liquid product through the glass bottle were recorded. That was done by appropriate focusing of the laser beam on the bottle. Standard solutions were then prepared by consecutive dilution of the initial solution and were measured in the same way. A Raman calibration curve was constructed, based on the characteristic Raman peak of piperacillin (1003 cm^{-1}). The linearity of the calibration curve was found to be R^2 = 0.997 and the LOD of piperacillin in this method was determined 0.22 mg/mL.

REFERENCES

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