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MEETING ABSTRACT

A7.1

Development of flow methods for the determination of *N*-acetyl-L-cysteine in pharmaceutical formulations

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Background: *N*-acetyl-L-cysteine (NAC) is a synthetic aminothiol antioxidant that has been in clinical use for more than 40 years, primarily as a mucolytic agent and in the management of paracetamol (acetaminophen) poisoning. There is a need for a new, robust, inexpensive, and rapid method of determination of NAC in pharmaceutical formulations, in order to assure proper quality control (QC). Patient safety during therapy, on the other hand, is indirectly linked to proper QC of the medication. Novel flow methods for the determination of NAC, such as the flow-injection method (FIA) or the sequential-injection method (SIA), have been developed and validated. Both methods are kinetic methods, which means that the measurement of the analytical signal is made under dynamic conditions in which the concentrations of reactants and products are changing as a function of time. The proposed flow methods of analysis (FIA and SIA) are interesting alternatives in NAC determinations instead of conventional batch methods and chromatography with different detectors. The advantages afforded by the flow methods of analysis are high sample frequency, low consumption of sample and reagents, low contamination risks, and significant reproducibility that provides high precision and enhanced selectivity as a result of the kinetic nature of the recorded analytical signal. Furthermore, the proposed flow methods of analysis require very limited laboratory bench space and necessary instrumentation.
Methods: The proposed methods are based on the reduction of Cu(II)-neocuproine reagent to Cu(I)-neocuproine with the analyte, in a Britton-Robinson buffer solution (pH 3.0). The non-steady-state absorbance of the formed yellow Cu(I)-neocuproine complex is measured at 458 nm. For the flow-injection method the three-line manifold with one reaction coil was used. Optimization of manifold parameters and experimental conditions were carried out by means of univariate method. The sequential-injection manifold consisted of a Cheminert® M50 pump (VICI Valco), a syringe-free stepper motor-driven pump, a 10-port selection valve model (C25-3180D) with a multiposition actuator control module (EMHCA-CE; VICI Valco). Both flow systems use a spectrophotometric detector.
Results: Using a flow-injection method of analysis, a linear calibration curve is established in a concentration range of 6×10^{-7} to 4×10^{-5} mol/l NAC with a detection limit of 9.4×10^{-8}. On the other hand, using the sequential-injection method of analysis, linearity was obtained in the concentration range of 4×10^{-6} to 3×10^{-4} mol/l. The detection limit was found to be 1.2×10^{-6} mol/l. The proposed methods are simple, rapid, sensitive and reproducible (FIA: RSD 0.9%, $n = 100$; SIA: RSD 1.9%, $n = 100$). In addition, the proposed methods are sensitive enough to enable determination of near-nanomole amounts of NAC without expensive instruments with an analytical frequency of 120/h (FIA) and 60/h (SIA).
Discussion: The proposed methods can be applied for the determination of NAC in pharmaceutical preparations. Therefore, they could be useful for QC of NAC-containing medications, indirectly improving patient safety during therapy (*e.g.* by reducing the risk of under- or over-dosage).

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