DEVELOPMENT OF ASSAY METHOD FOR SIMULTANEOUS DETERMINATION OF SALBUTAMOL SULFATE AND POTASSIUM SORBATE IN DOSAGE FORM

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Salbutamol sulfate is well known as a short acting-acting β_2-adregenic receptor agonist used for the relief of bronchospasm in treatment illnesses such as asthma and COPD. It is widely used in pediatric practice as a component of syrups. Also for inhibit yeasts, molds and bacterial growth in the dosage form, potassium sorbate was used as preservative. It is recognized as a safe additive and has limited adverse reactions (promotion of pseudo-allergic reactions).

There are many publications for analysis of salbutamol sulfate and potassium sorbate by HPLC, LC-MS, spectrophotometry and etc. But to best of our knowledge there is no method for simultaneous determination of these compounds. Such method may be practical tool for routine analysis of dosage forms that contain salbutamol and potassium sorbate.

A novel HPLC method for determination of salbutamol sulfate and potassium sorbate was described in this study. Effects of different conditions such as gradient modes, solvents for samples, pH and composition of mobile phase were investigated. Analytical method was validated according to the State Pharmacopoeia of Ukraine.

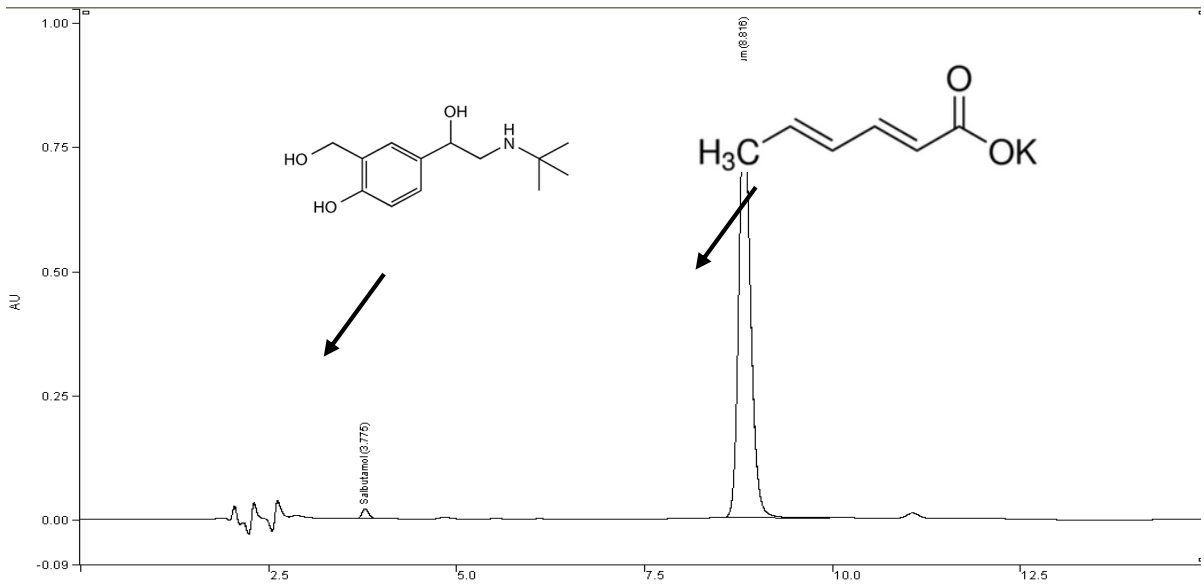
Analyses were performed using a Varian “ProStar” chromatograph. Separation of compounds was done with Supelcosil C8 column (150*4.6 mm, particle size 3μm). The two elution solvents were exchange the solvent A (mixture phosphate buffer with pH 3.0/acetonitrile/methanol) and solvent B (acetonitrile). The following linear gradient elution profile was used: 87% A/13% B–0 min, 87% A/13% B–4 min, 80% A/20% B–7 min, 80% A/20% B–10 min, 87% A/13% B–11 min, and 87% A/13% B–15 min. The flow rate was 1 mL/min. The effluent was determined at a wavelength of 277 nm. In proposed conditions retentions times of salbutamol sulfate and potassium sorbate were about 3.8 min and 8.6 min, respectively (Pic. 1).

All studies of different mobile phase’s compositions effect were performed with salbutamol sulfate standard. During method development different pH of phosphate buffer solutions were investigated. According to the literature source, salbutamol sulfate has less retention time in the acidic conditions and it save time of analysis that is advantage during routine control of dosage forms. For such studies the following pH in buffer were adjusted to 3.0, 3.5 and 4.0. According to obtained data, buffer with pH 3.0 had higher column efficiency and peak symmetry (6851; 1.42) than 3.5 (6661; 1.53) and 4.0 (6760; 1.51).

Also compositions of mobile phase A were investigated, column efficiency and peak symmetry were used as criterions of system suitability performance. Different compositions such as phosphate buffer, methanol, and acetonitrile in different rations were used. The most suitable conditions for salbutamol sulfate standard were found with mobile phase phosphate buffer pH 3.0/methanol/acetonitrile in ratio (900/80/20 v/v/v).

Among solutions such as methanol, water, buffer and mobile phase A, mobile phase A showed results. Therefore, weights of standards and dosage form (syrup) dissolved into mobile phase A.

Retentions times of potassium sorbate with usage only mobile phase A was too long, that’s why acetonitrile, as mobile phase B, was added. For optimization of retention time the different gradient modes were investigated.



Pic. 1. Typical chromatogram of standard solution of salbutamol sulfate and potassium

Developed method was validated according to the State Pharmacopeia of Ukraine in terms of linearity, precision, specificity, stability, and accuracy.

The specificity was studied with usage solution of salbutamol sulfate and potassium sorbate standards, test solutions, placebo and blank.

The obtained results showed that there was no interaction from syrup matrix to peaks of analyzed substances.

The linearity investigation was done with preparation 9 model solutions in the range of concentrations from 80% to 120% (differences 5%).

The linear curves were made and expressed by the following quadratic equation: for salbutamol sulfate R^2=0.9997 (y=1.0117x-1.3073) and potassium sorbate R^2=0.9997 (y=1.0079x-0.6512).

For study accuracy 9 model solutions, also in the same range as for linearity studies, were prepared.

The solutions were analyzed thrice at each level, the percentage of recovery and RSD were calculated for each concentration.

The obtained results suggested that accuracy of the method was acceptable. RSD of each level of concentrations was lower 0.512% for both substances.

The precision of the method was evaluated in 2 different days by 2 different analysts. The RSD deviation of assay values for salbutamol sulfate and potassium sorbate were 0.61; 0.52, respectively for intra-day and 1.15; 0.98 for inter-day.

The stability test of solution was carried out within 24 hours for solutions. It was established that stored solutions were stable for up 24 hours, because peaks deviations of salbutamol sulfate and potassium sorbate were 0.44 and 0.26 respectively.

The most suitable conditions of simultaneous analysis of salbutamol sulfate and potassium sorbate were found.

The method was validated and may be used for routine analysis different dosage forms that contain salbutamol sulfate and potassium sorbate.