Titrimetric micro-determination of (+)-6-aminopenicillanic acid using caroate

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6-APA is an abbreviation used for the name of the chemical compound (+)-6-aminopenicillanic acid (Fig.1) and is the key intermediate through which new penicillins and (6S,7S)-cephalosporins may be synthesized.

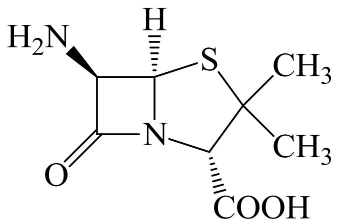

Fig. 1 Chemical formula 6-APA

Therefore, the development of new analytical methods for its quantification is very important. Several methods for quantifying 6-APA have been reported, including the iodimetry method. The present investigation was under taken with the aim of developing new, simple, rapid and accurate method free from many short comings that are usually encountered in other titrimetric methods. In this work, the oxidation of 6-APA with potassium caroate has been investigated and used to develop titrimetric procedure. In the proposed method, the potassium caroate left after the reaction with 6-APA was determined by reaction with an excess of iodide at acidic medium and the liberated iodine was titrated with thiosulfate. The kinetic curves of the oxidation reaction of 6-APA $KHSO_5$ are shown in Fig.2. In the present investigation, potassium caroate was found to react quantitatively with 6-APA in acidic medium to form the sulfoxide. A stoichiometry of the reaction between potassium caroate and 6-APA showed that for oxidation of 1 mol 5-APA 1 mol of potassium caroate were required. The probable explanation for the difference in the number of moles of oxidant reacting with each mole of 6-APA is that in method, wich the oxidation of the 6-APA occur in alkali condition is formed the sulfone (Fig. 3). The relationship between the titration end-points obtained by the proposed method and the 6-APA amounts was examined. The linearity between the amount of 6-APA and titration end-point is apparent from the correlation coefficient. The correlation coefficient of 0.999 show that the reaction between potassium caroate and the studied 6-APA proceeds stoichiometrically in a molar ratio of 1 : 1 (Fig. 3). To prove the validity and applicability of the proposed method, four replicate determinations at different concentration levels of 6-APA was carried out. The within-day RSD values were within 2%. The proposed method was applied to the analysis of samples 6-APAwith results comparable to those given by the official methods. The method is indirect visual titration method, and is simpler than, and superior to, many existing methods for the assay of 6-APA.

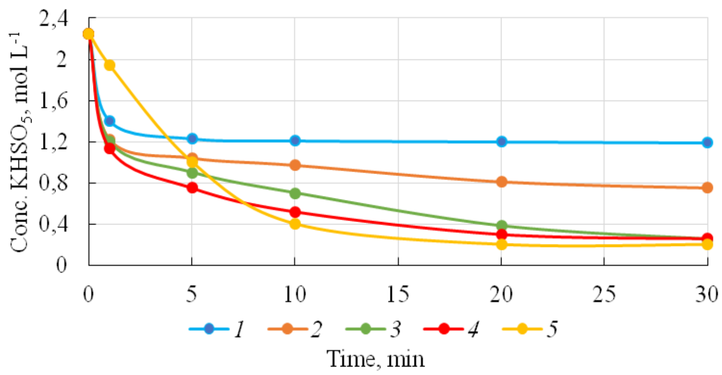

Fig. 2 Kinetic curves of the 6-APA oxidation reaction by $KHSO_5$. c(6-APA) $=1\cdot10^{-3}$ mol L^{-1}; $c(KHSO_5) = 2.25\cdot10^{-3}$ mol L^{-1}. pH: *1* - 3,0; *2* - 7,0; *3* - 8,4; *4* – 8,7; *5* – 12,0.

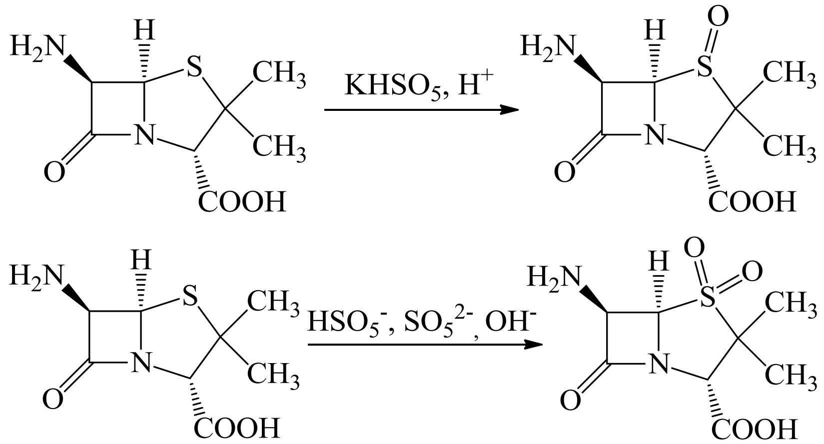

Fig. 3 Scheme of oxidation of 6-APA potassium caroate

The developed analytical methods are time saving, simple, accurate, economic, sensitive and reproducible and can be used in quality control laboratories.