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IODOMETRIC METHOD FOR THE DETERMINATION OF MEZLOCILLIN IN SOLUTIONS

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By the chemical structure penicillins are medicinal substances that belong to derivates of 6-aminopenicillanic acid (6-APA). It is a condensed system of tiazolidin and foursection azetedin (*β*-lactam) heterocycles, that differs in radical R connected with 6-APA aminogroup. Their characteristic feature is a rapid bactericide effect on the stage of microorganisms growth and insignificant side effects on human organism. Decomposition of one of the heterocycles leads to complete loss of activity meaning allergic action [1].

Mezlocillin is a 4^{th} generation penicillin antibiotic which kills certain bacteria that cause infection, or stops their growth. It treats many kinds of infections including those of the skin, blood, CNS, respiratory tract, sinuses. It also treats gynecological infections in women. This drug is discontinued in the US [2].

Mezl sodium monohydrate substance (CAS Number 51481-65-3) was used in the experiment. Its chemical structure is following (2*S*,5*R*,6*R*)-3,3-dimethyl-6-[(2*R*)-2-[(3-methylsulfonyl-2-oxoimidazolidine-1-carbonyl) amino]-2-phenylacetyl] amino]-7-oxo-4-thia-1-azabicyclo[3.2.0] heptan-2- carboxylate ($C_{21}H_{24}N_5NaO_8S_2$) [3].

Mezl has in vitro activity against gram-positiv and gram-negative aerobic and anaerobic bacteria. The bactericidal activity of mezlocillin results from the inhibition of cell wall synthesis and is mediated through mezlocillin binding to penicillin binding proteins (PBPs). Mezl is stable against hydrolysis by a variety of beta-lactamases, including penicillinases, and cephalosporinases and extended spectrum beta-

lactamases. Mezl can be used to treat susceptible stains of H. influenzae, Klebsiella species, Pseudomonas species, Proteus mirabilis, E. coli, Enterobacter species, Streptococcus faecelis, Peptococcus species, Peptostreptococcusspecies, Bacteriodes species, Serratia species, P. vulgaris and Providencia rettgeri [4].

Classical iodometry of hydrolysis products is determined to be a basic method of penicillin summary quantitative determination. It's disadvantage is duration at least 40 min, and the necessity in standard samples and in rigid conditions standardization, as iodine interaction with hydrolysis products of penicillin reaction doesn't proceed strictly stoichiometrically: iodine expense, and also the quantity of substance that is equivalent to 1.00 ml 0.005 mol/l (f=1/2, I_2) of iodine, depend on the reaction medium temperature [5].

By the method of back iodometric titration of $KHSO_5$ residue was determined that 1 mol of $KHSO_5$ is used per 1 mol of penicillin. The reaction finishes during 1 min and stays for 30 min (observation time at pH 1-4). The transformation scheme of analytical determination of Mezl is given on Fig. 1.

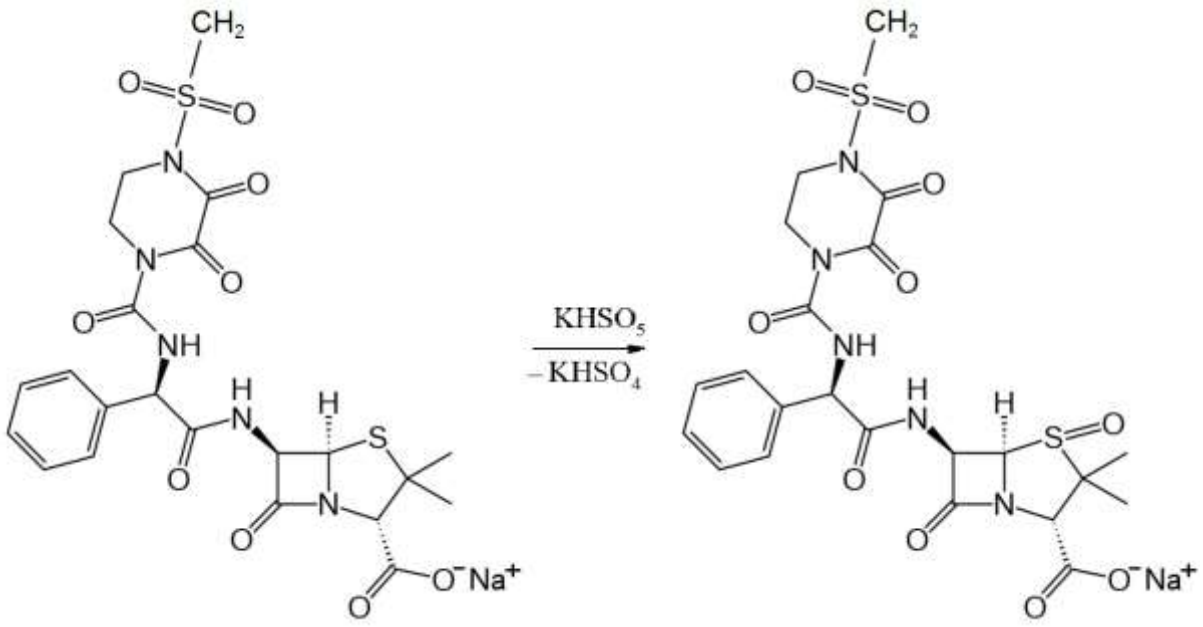

Figure 1. The scheme of Mezl S-oxidation by means of potassium hydroperoxymonosulfate ($KHSO_5$).

The following quantitative procedures of penicillin determination are described: using potentiometry titration and ionometry, spectrophotometry, extraction photometry, voltammetry and polarography, micelle electrokinetic capillary and paper chromatography, chemiluminescense and kinetic analysis methods [6-14].

Kinetics and stoichiometry S-oxidation reaction of sodium monohydrate Mezl by means of potassium hydrogenperoxomonosulfate in aqueous solutions using iodometric titration were studied.

Baypen® – powder Mezl sodium monohydrate in flacons for preparation of solution for injections (Mezl 1,0 g). A new iodometric method for quantitative determination of sodium monohydrate Mezl in Baypen® preparation using potassium hydrogenperoxomonosulfate ($KHSO_5$) as analytical reagent was proposed. Peroxomonosulfate acid as triple potassium salt $2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$ (Oxone®) of "extra pure" qualification was used as oxidant. At pH 1-4 for 1 mole of penicillin, 1 mole of $KHSO_5$ is consumed, the quantitative interaction is achieved within a time of more than 1 minute (observation time).

The results were obtained by the recommended procedure for seven replicate titrations of mixtures containing the three species at various concentrations. RSD = 2.01 %, δ = + 0.51 %. It can be seen that piperacillin can be determined successively with good accuracy and reproducibility. The new procedure was developed and ability of quantitative determination of penicillin in pharmaceutical preparation Baypen® by iodometric method using potassium hydrogenperoxomonosulfate ($KHSO_5$) as analytical reagent was shown [15].

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