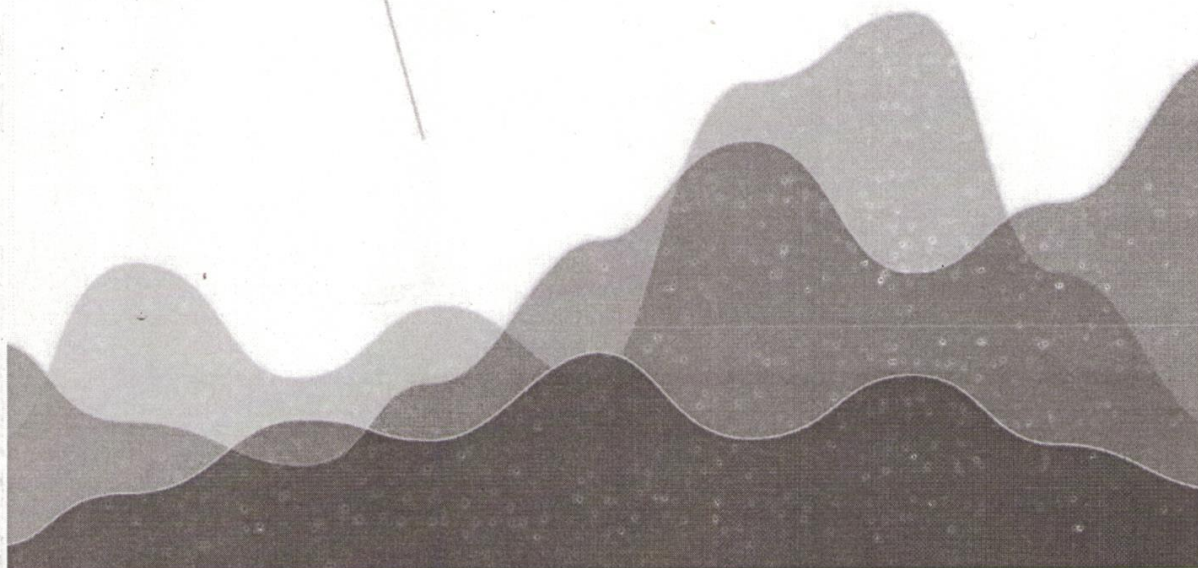


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DEVELOPMENT AND VALIDATION OF UV SPECTROPHOTOMETRIC AREA UNDER CURVE METHOD QUANTITATIVE ESTIMATION OF PIPERACILLIN

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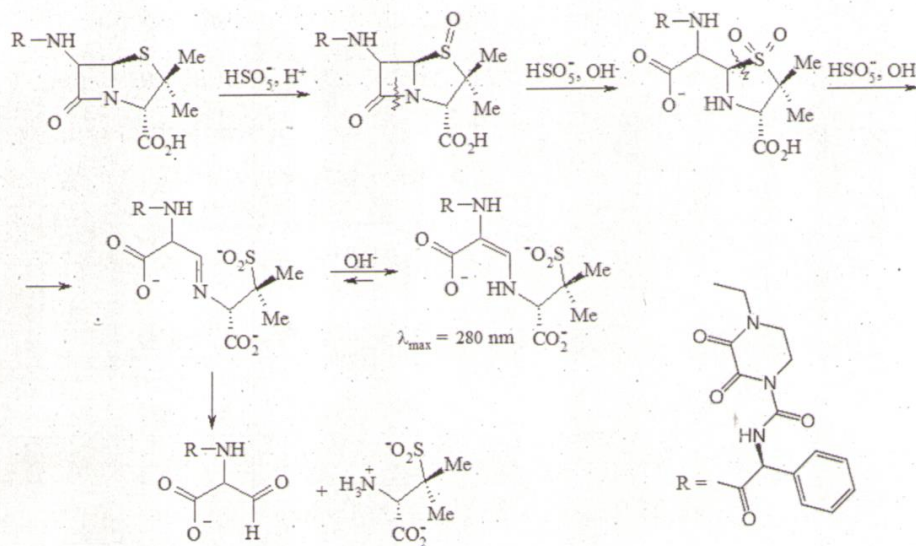
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Piperacillin/tazobactam is a combination antibiotic containing the extended-spectrum penicillin antibiotic piperacillin and the β -lactamase inhibitor Tazobactam (Taz) and is used to reduce the development of drug-resistant bacteria. [2S-[2a,5a,6b(S)]]-6-[[[(4-ethyl-2,3-dioxo-1-piperazinyl)carbonyl]amino]phenyl-acetyl]amino-3,3dimethyl-7-oxo-4-thia-1-azabicyclo-[3.2.0]heptanes-carboxylicacid (Pip) belongs to the ureidopenicillin class and it is used for the treatment of serious infections caused by susceptible strains of microorganisms. (2S,3S,5R)-3-methyl-7-oxo-3-(1H-1,2,3-triazolylmethyl)-4-thia-1-azabicyclo-[3.2.0]heptanes-2-carboxylic acid-4,4-dioxide (Taz) is used in combination with beta-lactamase antibiotic as antibacterial. Preparations of penicillin family are derivates of 6-aminopenicillanic acid (6-APA), a condensed system of thiazolidine and β -lactam tetramine cycles that differ by the radical R connected with 6-APA aminogroup [1].

Different methods, such as biological, chemical and physicochemical are recommended for its quantitative determination. Biological methods are based on the direct antibiotic biological action on a test-microorganism sensitive to the given

antibiotic. Disadvantages of the biological methods are the long-lasting procedure and the dependence of the results precision on the external factors [2].

The theoretical scheme of transformation of the reaction product is given on Figure:



The extensive literature survey reveals various methods of quantitative determination of penicillin family preparations, such as HPLC, spectrophotometry, iodometry, extraction photometry, different variants of voltametry, polarography and kinetic analysis are proposed.

The spectrophotometric methods that are based on the application of phenol Folin-Ciocalteu reagent, reactions with Mn(II), Co(II) and Ni(II) salts and etc. are also known. These methods give the possibility to determine penicillin in medical preparations in presence of different excipients [3-7].

Thus, the improvement of the known and development of new methods of quantitative determination of penicillin is rather important. The existing pharmacopoeial methods of penicillin preparations determination are quite complex, long-lasting and require the application of complex and expensive devices. The disadvantage of the known simple enough in performance methods of spectrophotometric determination of penicillin, which are based on the determination

of the final products of their hydrolytic cleavage, is the requirement of prolonged heating.

The developed method of Piperacillin (Pip) kinetic determination has several advantages: makes it possible to identify the preparation in much smaller quantities than the pharmacopoeial iodometric method, it is applicable to the same range of concentrations, as in photometric determination of hydrolysis products, but it doesn't require prolonged heating of the reaction mixture, it is simpler and faster than the method of chromatographic analysis.

It is based on the preliminary oxidation of Piperacillin (Pip) with potassium hydrogenperoxomonosulfate excess to the corresponding S-oxide, followed by determination of the hydrolytic conversion of its product in an alkaline medium by the kinetic spectrophotometric method (Initial rate (tangent) method).

The reaction kinetics of the peroxyacidic oxidation and perhydrolysis of ampicillin and oxacillin with potassium peroxomonosulfate in the alkaline medium is studied. As an oxidizing agent, the potassium triple salt of peroxymonosulfuric acid, $2\text{KHSO}_5 \cdot \text{KHSO}_4 \cdot \text{K}_2\text{SO}_4$, syn. "Oxone", was applied. The procedure was developed and the possibility of the quantitative determination of piperacillin in the Zopercin[®] preparation based on the results of the kinetic-spectrophotometric method with potassium peroxomonosulfate as reagent was shown. $\text{RSD} = 1.4\%$, $\delta = 1.0\%$.

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