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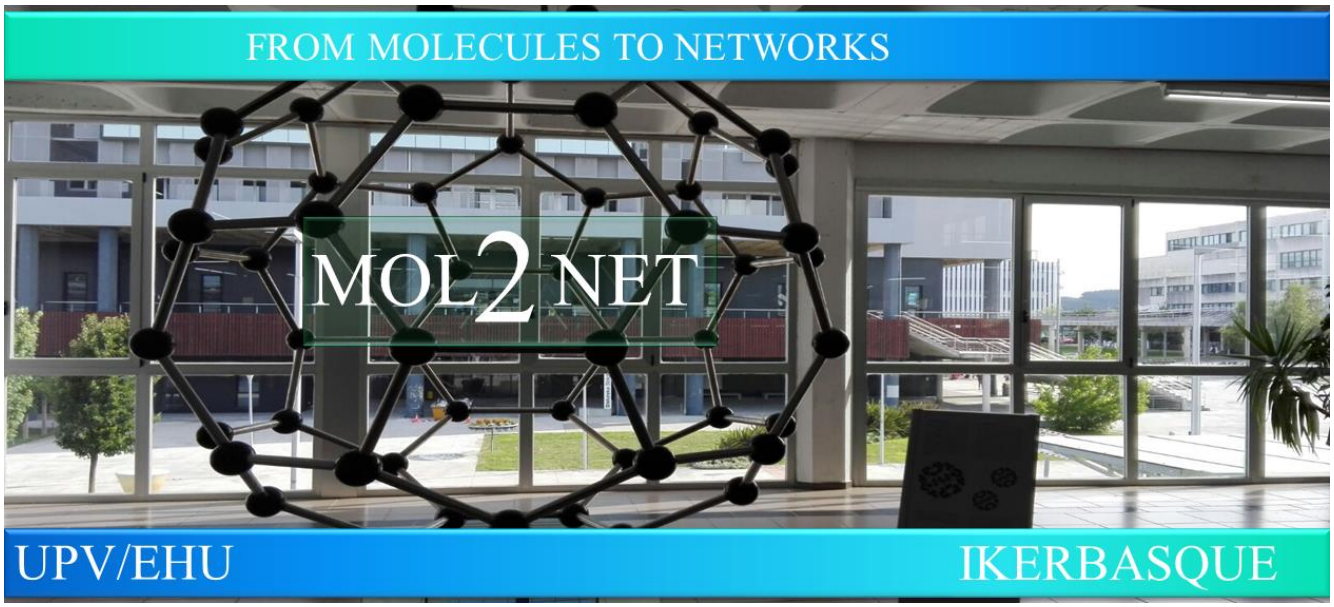

Development of the HPLC method for the determination of related substances in ramipril tablets

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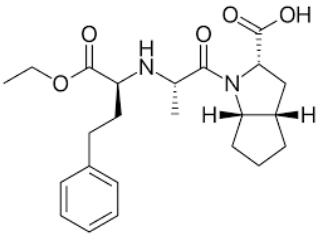
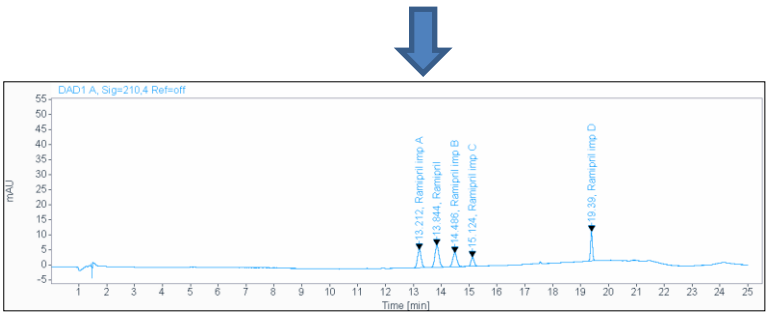
Graphical Abstract





Abstract.

The quality indicators of medicinal products, which ensure their effectiveness and safety, are established in the registration documentation and Pharmacopoeia. At the same time, the quality of medicinal products is established at the stage of pharmaceutical development, for which a general methodological approach and special approaches are defined in relation to different dosage forms, generic drugs, original drugs, etc. Considering the fact that there is no monograph on ramipril tablets in the European Pharmacopoeia of the 11th edition, but only on the ramipril substance, we drew attention to the need to develop an analytical method for determining related substances in ramipril tablets. It is clear that the approaches described in the development of the technique in the substance are unsuitable for the analysis of tablets. Therefore, the aim of our work was the development of HPLC method for the determination of related substances in ramipril tablets.

Material and methods. Analytical equipment: Agilent 1200 liquid chromatograph, 4.6x150 mm chromatographic column filled with octadecylsilyl silica gel for chromatography with a particle size of 3 µm (for example, Inertsil ODS-3). Chromatography was carried out in the mode of gradient elution. Mobile phase A - solution of 0.2 g/L of sodium hexanesulfonate R, the pH of which is adjusted to 2.7 with phosphoric acid; Mobile phase B - Acetonitrile.

Results and discussion. To separate the components of the model mixture, sodium hexanesulfonate was used, the pH of which was adjusted to 2.7 with phosphoric acid, and an organic modifier - acetonitrile in a gradient elution mode, a flow rate of 1.5 mL/min, and a detection wavelength at 210 nm. The retention time of impurity A, ramipril, impurity B,

	impurity C, impurity D was 13.2, 13.8, 14.5, 15.1, 19.4 min, respectively. Rationing at the time of release: impurities A, B, C: no more than 0.5% of each; amount of impurities D and E: no more than 0.5%; any impurity: no more than 0.2%; amount of impurities: no more than 1.0%. Rationing during the shelf life: impurities A, B, C: no more than 0.5% of each; amount of impurities D and E: no more than 5.0%; any impurity: no more than 0.5%; amount of impurities: no more than 5.0%. To confirm the efficiency of the method, the following parameters were studied specificity, linearity, accuracy and precision, limit of detection and limit of quantification. Conclusions. *Data on the influence of components interfering with the analysis were not found. The method is linear in the range of application. The accuracy and precision of the method are sufficient. The method provides the necessary level of detection of related substances. The limit of detection of unidentified impurities is 0.03%. To calculate the content of impurity C, a conversion factor of 2.5 must be used. The modified technique meets the established requirements and can be used for quality control of the drugs "Ramipril, tablets 2.5 mg", "Ramipril, tablets 5 mg", "Ramipril, tablets 10 mg" according to the quality indicator "Related substances".*