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ART DE LA PENSÉE SCIENTIFIQUE

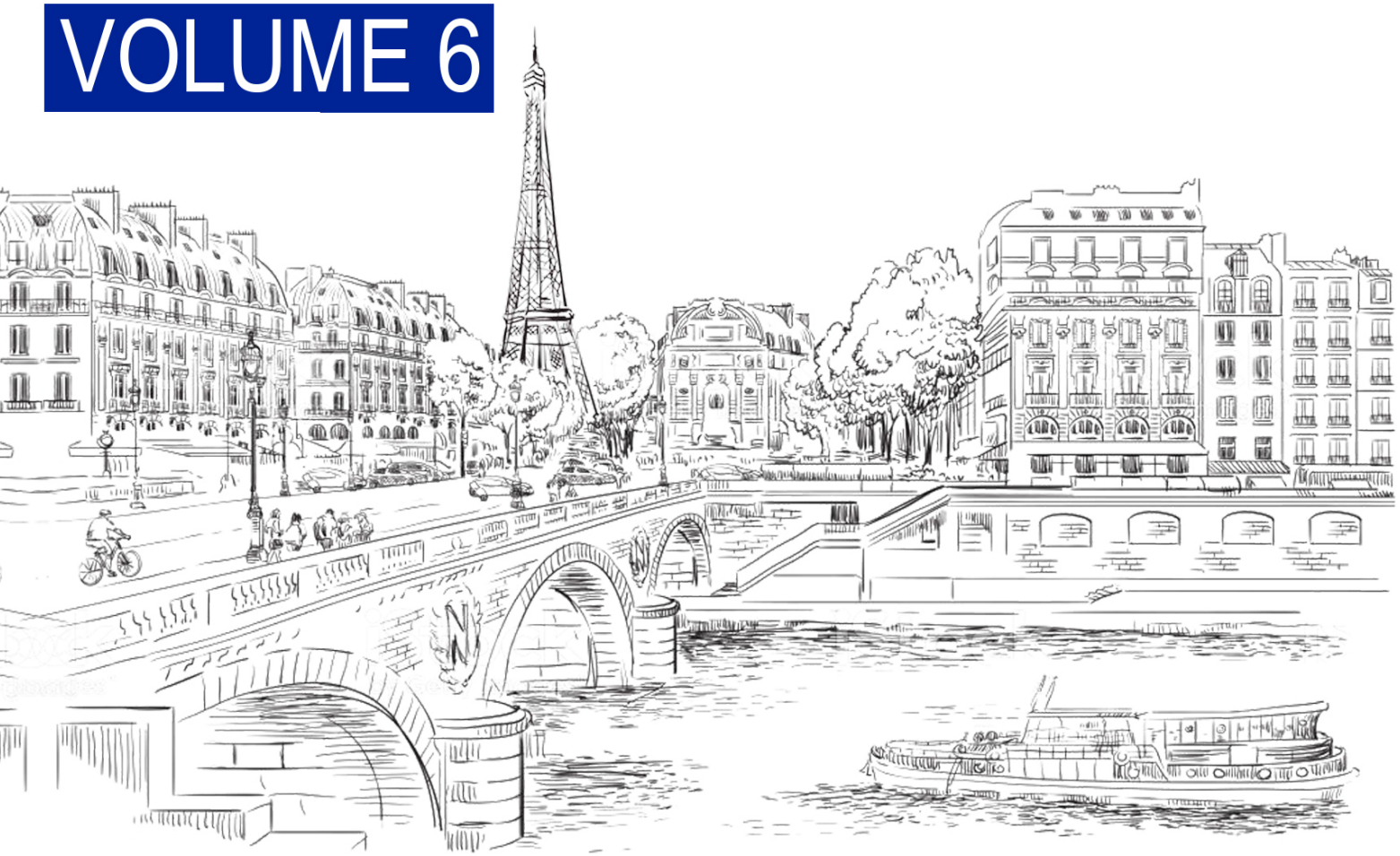
COLLECTION DE PAPIERS SCIENTIFIQUES

SUR LES MATÉRIAUX DE LA I CONFÉRENCE SCIENTIFIQUE ET PRATIQUE INTERNATIONALE

DÉBATS SCIENTIFIQUES ET ORIENTATIONS PROSPECTIVES DU DÉVELOPPEMENT SCIENTIFIQUE

5 FÉVRIER 2021 • PARIS, RÉPUBLIQUE FRANÇAISE

VOLUME 6



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SECTION XXXV.
PHARMACIE ET PHARMACOTHÉRAPIE

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ANALYSIS OF ALFUZOSIN BY HPLC METHOD

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Introduction. Alfuzosin hydrochloride - (*RS*)-*N*-[3-[(4-Amino-6,7-dimethoxy-quinazolin-2-yl)- methyl-amino]propyl] tetrahydrofuran- 2-carboxamide hydrochloride - belongs to the group of α_1-adrenoblockers and is used in medical practice for the treatment of arterial hypertension and prostatic hypertrophy [1,2]. When applying alfuzosin, there are possible side effects: dry mouth, nausea, headache, dizziness, weakness, drowsiness, tachycardia, angina symptoms, allergic reactions. In case of overdose or self-medicate with alfuzosin the cardiovascular system is affected, the activity of the central nervous system is suppressed, respiratory system is broken.

The previously developed methods of HPLC analysis of alfuzosin hydrochloride are distinguished by the use of different chromatographic conditions, which are based on the individual properties of investigated substance. Method of identification and quantification of alfuzosin by HPLC method in the application of various detection options in various matrices was carried out using different sorbents, composition of moving phases, buffer solutions in isocratic and gradient elution modes [3,4].

An important stage for further research of alfuzosin and other antihypertensive drugs is the development of a unified HPLC method and the creation of databases by the parameters of identification and quantitative determination of analytes. The results of research on a unified HPLC method can be recommended for the introduction into the practice of the bureau of forensic examination, toxicological centers, clinical laboratories regarding the study of medicinal substances in biological objects.

Aim. The identification and quantification of alfuzosin, when using unified conditions HPLC, suitable for studies of pharmaceuticals and biological objects.

Materials and method. Investigations of alfuzosin by HPLC-method were performed on the basis of scientific-production association "Analytics" (Kharkov).

Chromatography of alfuzosin was performed on microcolumn liquid chromatograph "Milichrome A-02" ("EcoNova", Russia) using standardized HPLC conditions: reversed-phase variant with using of metallic column with non-polar absorbent Prontosil 120-5C 18 AQ, 5 μm; mobile phase in the mode of linear gradient – from eluent A (5 % acetonitrile and 95% buffer solution – 0.2 M solution of lithium perchlorate in 0,005 M solution perchloric acid) to eluent B (100% acetonitrile) as during 40 min. Regeneration of column has been conducted during 2 min with mixture of solvents; the flow rate of the mobile phase has been formed 100 μl/min, injection volume – 4 μl. The detection of alfuzosin has been conducted by UV-detector at 8 wavelengths: 210, 220, 230, 240, 250, 260, 280, 300 nm; the optimal value of column temperature – 40◦C and pressure of pump – 4.2 MPa. The results of the identification and quantitative determination of the HPLC method were calculated using the computer program "MultiChrom" (Ampersend, Closed Joint-Stock Company, Russia), which was part of the chromatograph.

Results and discussion. The identification of alfuzosin conducted with using absolute parameters of retention time (t_R = 15.51 ± 0.02 min) and retention volume (V_R = 1551.1 ± 0.2 μl). To verify the choice chromatography conditions determined coefficients of peak symmetry and coefficients of capacity. Established that the values of coefficients peak symmetry - from 0.96 to 1.06 (less than 2.0) and the coefficients of capacity – 9.33 ± 0.03 (more than 0.5) showed the suitability of HPLC chromatographic analysis system. To ensure reliable detection of alfuzosin used spectral ratio values absorbance at wavelengths - from 220 to 300 nm - the values of absorbance at 210 nm, which are equal: 0.743; 0.951; 1.921; 2.007; 1.049; 0.269; 0.097. The detection limit of alfuzosin HPLC method was 2.0 μg / ml or 8.0 ng of sample.

For quantitative HPLC determination of alfuzosin by absolute calibration method was used the calibration curve constructed in the coordinates: S, mm^2 (peak area) – C, μg / ml (concentration of solution of the substance). In applying the method of least squares regression coefficients were calculated corresponding equation S = вC + a. The proposal the calibration curve meets equation of the line that has the form: S = $3{,}25 \cdot 10^{-3}$ C - $1{,}5 \cdot 10^{-3}$, where S - area of peak drug, mm^2; C - concentration of solution of the substance, μg / ml. Established that the linearity of the calibration curve in coordinates (S, mm^2) - (C, μg / ml) was observed in the concentration range 2,0 – 200,0 μg / ml, which corresponds to alfuzosin content in the sample (4 μl) of 8,0 ng to 800,0 ng respectively. In conducting HPLC analysis of alfuzosin in sample solutions using the proposed method relative uncertainty of the average results did not exceed ± 2,05 %. As a result of the metrological characteristics found no significant systematic errors HPLC analysis.

In a comparative assessment of the reproducibility of alfuzosin analysis by HPLC, it was found that the values of the relative standard deviation of the results of alfuzosin analysis during one day (intra-day) and during the second day (inter-day) in the region of low (20,0 μg / ml), medium (100,0 μg / ml) and high concentrations (200,0 μg / ml) did not exceed 0,86.

Conclusions. Identification and quantification of alfuzosin by unified HPLC-conditions were conducted. The main parameters of retention, spectral relations and detection limit of the drug (8,0 ng of sample) were established. The HPLC method of determination of alfuzosin was validated by parameters: linearity range, quantification limit, accuracy and precision in the regions of low, medium and high concentrations of the substances. As a result of the quantitative determination of alfuzosin by HPLC method defined linearity range depending on the peak area and concentration - 2,0 -

200,0 μg / ml of the drug and the limit of detection - 2,0 μg / ml. In carrying out HPLC-analysis of alfuzosin in model solutions relative uncertainty of the average result equal ± 2,05 %.

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