

CHROMATOGRAPHIC INVESTIGATION OF CLEMASTINE FUMARATE

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Nowadays more than 10 million people in Ukraine are affected by allergic diseases, that leads to the increase in the use of antihistamines in modern medical practice and relevance of their research using highly sensitive and selective chromatographic analysis methods. The most widely applied methods High Pressure Liquid Chromatography (HPLC) and Thin Layer Chromatography (TLC). Clemastine Fumarate (Tavegil) - (2R)-[2-1-(4-chlorophenyl)-1-phenyl ethoxy]ethyl]-1-methyl-pyrrolidine fumarate - belongs to a group of antihistamines I generation is characterized by multi-vector pharmacological effects, but causes heavy toxicity at exceeding of doses, affects the nervous and respiratory systems. For research of tavegil were used unifical conditions of HPLC analysis of drugs. The chromatographic process of clemastine was conducted on microcolumn liquid chromatograph «Milichrom A-02» on base research union «Analitlka» in reversed-phase variant with using of metallic column with non-polar absorbent Prontosil 120-5C 18 AQ, 5 μm . The preparation was eluated with lineal gradient – from eluent A (5% acetonitrile and 95% buffer solution – 0.2 M solution of lithium perchlorate in 0,005 M solution of perchloric acid) to eluent B (100% acetonitrile) during 40 min. The flow rate of the mobile phase 100 $\mu\text{l}/\text{min}$, the optimal values of column temperature – 37-40 $^{\circ}\text{C}$ and pressure of pump – 2.8 – 3.2 MPa, injection volum – 4 μl were selected. The detection of clemastine was conducted by UV- detector at 8 wavelengths: 210, 220, 230, 240, 250, 260, 280 and 300 nm.

The identification of clemastine was conducted with using absolute parameters of retention time ($t_{R \text{ Clemastine}} = 26,00 \pm 0,03 \text{ min}$), retention volum ($V_{R \text{ Clemastine}} = 2600 \mu\text{l}$) and spectral ratios, which were defined as ratio of values of absorbance at wavelengths – 220-300 nm – to values of absorbance at 210 nm. The symmetry factor of peak of clemastine ($K_s = 1,03$) and the value of distribution coefficients ($k' = 16,33$) were determined.

For selecting optimal chromatographic conditions of clemastine by TLC-method as thin layers of adsorbents were used chromatographic plates: Sorbfil PSTH-AF-A (silica STH-1A, 5-17 microns, thickness - 110 μm , a binding agent – silicasol, type bases - aluminum foil, plates size - 10x10 cm), Glass plates by "Merck" (Germany) (silica gel 60 F254, 10-12 microns, glass, 10x20 cm). Chromatographic behavior of clemastine was investigated by TLC in 9 solvent systems, which are recognized standard by the International Committee for systematic toxicological analysis of the International Association of Forensic Toxicologists – chloroform-acetone (80:20), ethylacetate, chloroform-methanol (90:10), ethylacetate-methanol-25% ammonia solution (85:10:5), methanol, acetone, methanol-25% ammonia solution (100:1,5), methanol- n-butanol (60:40), cyclohexane-toluene-diethylamine (75:15:10). For selecting optimal chromatographic conditions of clemastine were studied 4 solvent systems, which are used in general organic TLC screening substances – chloroform-acetone-dioxane-25% ammonia solution (47,5:45:5:2,5), toluene-acetone-ethanol-25% ammonia solution (45:45:7,5:2,5), ethylacetate-methanol – 25% ammonia solution (85:10:2,5), chloroform-n-butanol-25% ammonia solution (70:40:5). As a result of TLC studies were established the most optimal conditions for the identification of clemastine in the presence of biogenic impurities: solvent systems – methanol or methanol-25% ammonia solution (100:1,5); chromatographic plates – Sorbfil PSTH-AF-A ($R_{f \text{ Clemastine}} = 0,58-0,60$).

The results of investigations by HPLC- and TLC-method may be recommended for pharmaceutical and chemical-toxicological analysis of clemastine fumarate.