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THE STUDY OF ANAPRILIN BY METHOD OF THIN LAYER CHROMATOGRAPHY

Introduction. Anaprilin (propranolol hydrochloride) - (±)1-isopropylamino-3-(1-naphthyloxy) -2-propanol hydrochloride – non-selective β-adrenoceptor blocker, which is characterized by antianginal, antihypertensive and antiarrhythmic effects and is used for treatment of coronary heart disease, heart rhythm disorders and some forms of hypertension [1].

Anaprilin is used for treatment of anxiety disorders [2] and for treatment of patients with cirrhosis and varicose veins of the esophagus [3]. Combinations of anaprilin with other drugs are used for treatment of hypertension, which is more effective than monotherapy with anaprilin [4].

When using anaprilin, side effects are possible in the form of nausea, vomiting, diarrhea, bradycardia, general weakness, dizziness; sometimes there are allergic reactions, bronchiolospasm. Depression is possible.

Toxic effects should be considered when using anaprilin in combination with other drugs. Thus, the antihypertensive effect of anaprilin is enhanced in combination with diuretics, other antihypertensive, antiarrhythmic drugs, and ethanol. Clinical manifestations of poisoning included coma, convulsions, respiratory failure, hypoglycemia, and vascular shock [5].

The analysis of anaprilin in dosage forms and biological objects during therapeutic monitoring is carried out using sensitive and selective chromatographic methods. The TLC-method is characterized by sensitivity, high speed chromatographic process, relative simplicity and availability of experimental technique [6]. The development of new, modification and improvement of existing chromatographic methods for studying anaprilin is an urgent task.

Purpose of work – the selection of optimal TLC conditions for the analysis of anaprilin in dosage forms and biological objects with using modern highly sensitive and selective chromatographic plates, organic solvent systems and universal developers.

Materials and methods of research. The choice of optimal conditions for TLC chromatography of anaprilin was carried out on several different chromatographic plates, which were widely used in modern chemical-toxicological studies: A - Sorbfil PTLC -AF-A (type of sorbent - silica TLC -1A, graining - 5-17 microns, thickness - 110 mm, a binding agent – silicasol, type bases - aluminum foil, plates size – 10 x10 cm); B - Sorbfil PTLC-P-B-UV (type of sorbent - silica TLC - 1B, graining - 8-12 microns, thickness - 100 mm, a binding agent – silicasol, type bases - PETF-E (Polyethylene and Teflon), plates size – 10 x10 cm); C - Glass plates by "Merck" (Germany) (type of sorbent - silica gel 60 F_{254}, graining - 10-12 microns, type basis - glass plates size – 10 x 20 cm).

Chromatographic behavior of anaprilin was investigated by TLC in 14 solvents systems. The research was conducted in application systems of solvents, which are recognized standard by

the International Committee for systematic toxicological analysis of the International Association of Forensic Toxicologists: chloroform - acetone (80:20) (1); ethylacetate (2); chloroform - methanol (90:10) (3); ethylacetate – methanol – 25% solution of ammonium hydroxide (85:10:5) (4); methanol (5); methanol - n-butanol (60:40) (6); methanol - 25% solution of ammonium hydroxide (100:1,5) (7); acetone (8).

The general systems of solvents for TLC - screening of organic substances are used: chloroform – dioxane – acetone - 25% solution of ammonium hydroxide (47,5:45:5:2,5)(9); toluene – acetone – ethanol - 25% solution of ammonium hydroxide (45:45:7,5:2,5) (10); chloroform – n-butanol – 25% solution of ammonium hydroxide (70:40:5) (11).

Studies of some antihypertensive drugs were carried out in solvent systems: ethylacetate - methanol - hexane (80:10:10) (12); ethylacetate - methanol - hexane - 25% solution of ammonium hydroxide (45:45:5:5) (13); acetone - toluene - 25% solution of ammonium hydroxide (6:4:1) (14).

Organic solvents corresponded to the qualification of "PFA": chloroform, acetone, ethylacetate, methanol, n-butanol, dioxane, toluene, benzene, hexane (Sigma-Aldrich, USA). Reagents corresponded to the qualification of "PFA": 25% solution of ammonium hydroxide (Chimmed, Moscow, Russia).

For the identification of anaprilin the preliminary and confirmatory stages of spots detection were used:

1) in the previous stage of identification of anaprilin on chromatographic plates, using UV light (λ = 254 nm), violet spots were observed;

2) at the confirmatory stage on chromatographic plates after processing with reagent Dragendorff in the modification of Mounier orange spots were observed.

Results and discussion. As a result of TLC investigation were established the most optimal conditions for the preliminary and confirmatory studies of anaprilin and for the identification and purification of the test substance in the presence of biogenic impurities.

For analysis of anaprilin the most effective conditions (system of mobile solvents - chromatographic plates) are recommended:

- Sorbfil PTLC-P-B-UV; chloroform - methanol (90:10) (R_f = 0,49±0,03); ethylacetate – methanol – 25% solution of ammonium hydroxide (85:10:5) (R_f = 0, 61±0,03); methanol (R_f = 0,49±0,03); methanol - n-butanol (60:40) (R_f = 0,59±0,03);
- Sorbfil PTLC-AF-A; toluene – acetone – ethanol - 25% solution of ammonium hydroxide (45:45:7,5:2,5) (R_f = 0,44±0,03);
- Glass plates by "Merck"; ethylacetate – methanol – 25% solution of ammonium hydroxide (85:10:5) (R_f = 0,45±0,03).

Table

The R_f value of anaprilin for the various types of chromatographic plates in systems of organic solvents (n = 5)

Systems	Types of chromatographic plates		
	A	B	C
1	0	0,31±0,03	0,38±0,03
2	0	0,06±0,02	0,25±0,03
3	0,25±0,03	0,49±0,03	0,31±0,03
4	0,28±0,03	0,61±0,03	0,45±0,03
5	0,28±0,03	0,49±0,03	0,23±0,03
6	0,33±0,03	0,59±0,03	0,20±0,02
7	0	0,80±0,04	0,30±0,03
8	0,18±0,02	0,25±0,02	0,14±0,02
9	0,33±0,03	0,30±0,03	0,21±0,02
10	0,44±0,03	0,34±0,03	0,12±0,02
11	0,28±0,02	0,06±0,02	0,20±0,02
12	0,25±0,02	0,28±0,02	0,16±0,02
13	0,78±0,04	0,73±0,04	0,73±0,04
14	0,36±0,03	0,34±0,03	0,20±0,02

Conclusions

1. For analysis of anaprilin the most effective conditions (system of mobile solvents - chromatographic plates) are recommended: Sorbfil PTLC-P-B-UV; chloroform - methanol (90:10) (R_f = 0,49±0,03); ethylacetate – methanol – 25% solution of ammonium hydroxide (85:10:5) (R_f = 0, 61±0,03); methanol (R_f = 0,49±0,03); methanol - n-butanol (60:40) (R_f = 0,59±0,03).

2. The results of TLC investigation of anaprilin are intended for employees of the Bureau of Forensic Medical Examination, toxicological and narcological centers, clinical laboratories for the study of medicinal substances in biological objects.

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