DEVELOPMENT OF A METHOD OF ISOLATING ALKALOIDS FROM THE ABOVE-GROUND PORTION OF Scopolia Tangutica

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The rootstocks of Scopolia carniolica and the belladonna leaf are used as the raw material for the industrial production of atropine and hyoscyamine. Scopalamine is obtained from the incompletely ripened seeds and pods of the Indian thornapple.

The greatest quantity of tropanic alkaloids is found in the above ground portion of Scopolia tangutica [1-3] which contains both hyoscyamine and scopalamine [4, 5]. According to the literature [1], the yield of the above ground portion of three-year old Scopolia (plants) from fertilized land amounts to 40.5 to 65.3 centner/hectare in the Leningrad region with an alkaloid content of 1.21 - 1.5%. Double mowing during the vegetation period makes it possible to obtain a yield of 85 centner/hectare. Scopolia tangutica has advantages with respect to yield and alkaloid content compared to belladonna, henbane, thornapple, Scopolia carniolica, and Scopolia.

We carried out investigations on choosing a method for extracting and isolating the alkaloids from the above ground portion of Scopolia tangutica. During the development of a method for isolating hyoscyamine and scopalamine, we decided on the sorption method for isolating and purifying the alkaloids, which has a number of advantages.

The above ground portion of Scopolia gathered in the blossoming stage in the Leningrad region was used for expression. The overall alkaloid content determined gravimetrically [6] and by volumetric methods amounted to 0.55% on the air dried raw material based on the hyoscyamine content. The qualitative composition was determined by ascending paper and thin layer chromatography [7] on an unbound layer of "basic" aluminum oxide with a IV degree of activity in a chloroform–methanol (20: 1) system. The quan-

TABLE 1. Dependence of the Alkaloid Yield on the Feed Rate of Raw Material and the Ratio of the Phases

Exp. No.	Quantity of plant raw material (kg)	Alkaloid content in raw material (%)	Amount of extract obtained (liter)	Extractant	Feed rate of raw material (kg/h)	Alkaloid conc. in extract (%)	Ratio of raw material to extract	Alkaloid yield (%)
1	0,1	0,55	1,0	Distilled water	0,050	0,045	1:10	82
2	0,5	0,55	5,0	The same	0,065	0,045	1:10	82
3	0,4	0,55	4,0	" "	0,090	0,043	1:10	78
4	0,8	0,55	8,0	" "	0,100	0,044	1:10	80
5	0,4	0,55	5,0	" "	0,085	0,037	1:12,5	84
6	0,3	0,55	5,0	" "	0,090	0,030	1:16,5	91
7	0,3	0,55	6,0	" "	0,080	0,026	1:20	95
8	1,1	0,41	12,1	" "	0,090	0,031	1:11	82
9	0,3	0,41	3,1	0.5% Hydrochloric acid	0,090	0,035	1:10,5	88
10	0,3	0,41	3,4	0.5% Sulfuric acid	0,090	0,039	1:11	92

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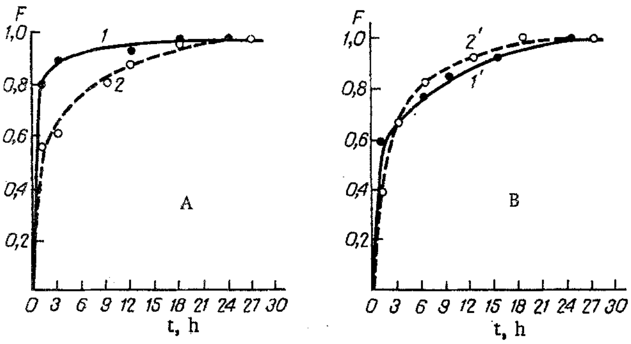

Fig. 1. Sorption rate of the tropanic alkaloids. A) From the solution of the mixture of pure alkaloids; B) from the extract; 1, 1') KU-5 cation exchange resin; 2, 2') SBS-3 cation exchange resin.

TABLE 2. Sorption of Tropanic Alkaloids by Various Cation Exchange Resins

Brand of cation exchange resin	Coefficient of swelling	Quantity of sorbed alkaloids (in mg-eq/g absolutely dry cation exchange resin)	
		from a solution of a mixture of the pure alkaloids	from the extract
KU-1	1,5	1,84	0,37
KU-2-8	1,6	1,68	0,39
KU-2, n-34	2,0	1,96	0,36
KU-5	1,9	2,28	0,47
KU-5	2,4	2,38	0,56
KU-5	2,7	2,30	0,49
KU-5	2,9	2,28	0,40
KU-25	2,6	1,25	0,30
SDV-3	4,1	2,20	0,19
SDV-3T	2,5	2,39	0,21
SBS-3	2,6	2,56	0,50
Dowex 50 WX-12	1,4	2,24	0,32
Dowex 50 WX-16	1,4	2,20	0,38
IR-120	1,8	1,88	0,16
IR-124	1,5	1,76	0,28

titative determination of the alkaloids was carried out by a thin layer chromatographic method on an unbound layer of sorbent by a known method [7]. The make up of the alkaloids obtained from the above ground portion of Scopolia consists of 54% hyoscyamine, 31% scopolamine, and 14% of an unidentified base.

The extraction of the alkaloids from the raw material which was ground to 3-5 mm was carried out with distilled water by a percolation method and constant countercurrent extraction in a spring-blade extractor [8]. The amount of alkaloids in the extract prepared by the percolation method came to 0.054% (98% yield); the content of the dry residue amounted to 3.23%. The yield in the spring-blade extractor depends on the rate of the raw material input and the ratio of the phase (Table 1); the dry residue amounts to 2.7% with an alkaloid content of 0.045% in the extract. The alkaloid yield is somewhat increased when they are extracted from the above ground portion of Scopolia with weak sulfuric and hydrochloric acid solutions (experiments 9, 10), but at the same time, the total dynamic capacity of the cation exchange resin decreases. An increase in the amount of extractant (distilled water) is the optimum solution. The total dynamic capacity of the KU-1 cation exchange resin decreases sharply [9] when the extract obtained by the percolation method is sorbed.

We studied the sorption properties of a series of strongly acidic cation exchange resins in order to choose one. Sorption was carried out under static conditions both from a 0.045% solution of the pure alkaloid mixture (0.034% hyoscyamine and 0.011% scopalamine) and from the extract obtained by the continuous countercurrent method with the same alkaloid content. The cation exchange resins were prepared by a well-known method [10] and used in the H^+ form. The dimensions of the particles came to 0.25 - 0.5 mm. As is evident from the data presented (Table 2), the highest selectivity of the sorption of the alkaloids from the solution and extract is observed on the KU-5 cation exchange resin with a coefficient of swelling of 2.4 and on the SBS-3 resin on which the kinetics of sorption was also investigated. It was established (Fig. 1) that the process proceeds more rapidly on the KU-5 ion exchange resin. A 90% surface coverage of this resin is approached within 3 h during the sorption of the pure alkaloid mixture from solution and within 12 h from the extract.

An investigation of the dependence of the capacity of the cation exchange resin on the magnitude of the pH of the extract and solution on KU-5 under static conditions showed that the greatest exchange capacity from the solution is observed at pH 4.0 and from the extract at pH 5.0 - 6.0 (Fig. 2). The highest exchange capacity under dynamic conditions from the extract obtained by the continuous countercurrent method takes place on the KU-5 cation exchange resin (up to 0.72 mg-eq/g) and on the SBS-3 resin (up to 0.44 mg-eq/g). The capacity for the KU-1 resin reached 0.21 mg-eq/g [11]. The elution curves at a passage rate of 0.25 liter/cm^2·h are given in Fig. 3.

In addition, we investigated the feasibility of isolating the tropanic alkaloids by ion exchange on the KU-5 cation exchange resin from the aqueous extract of the above ground portion of the common belladonna which was prepared in a spring-blade extractor with a raw material-to-extractant ratio of 1:10. The alkaloid content in the extract came to 0.024%; the pH was 5.1. The elution curves of the sorption from the Scopolia and belladonna extracts at a passage rate of 0.32 liter/cm^2·h are given in Fig. 4.

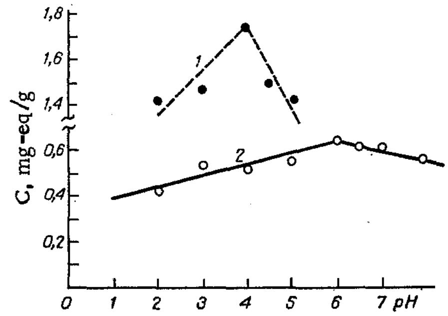

Fig. 2

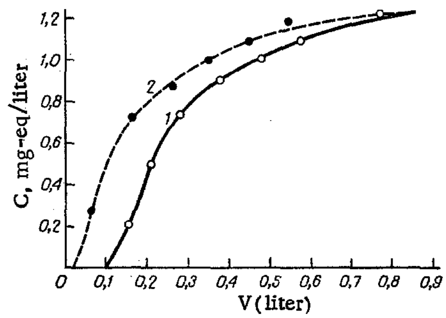

Fig. 3

Fig. 2. Dependence of the capacity of the KU-5 cation exchange resin with respect to tropanic alkaloids on the pH. 1) Sorption from a solution of the pure alkaloid mixture; 2) from the aqueous extract.

Fig. 3. Elution curves of the sorption of tropanic alkaloids from the aqueous extract. 1) KU-5 cation exchange resin; 2) SBS-3 cation exchange resin.

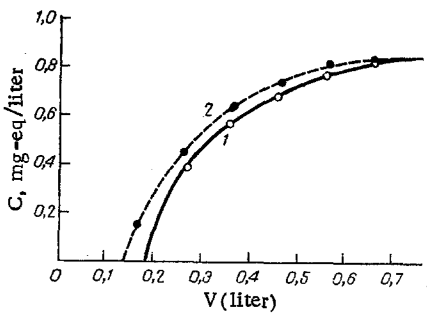

Fig. 4. Elution curves of the sorption of tropanic alkaloids on the KU-5 cation exchange resin in the H^+ form. 1) From the aqueous extract of Scopolia tangutica; 2) from the aqueous extract of the common belladonna.

The desorption of the alkaloids was carried out with a 1.5 - 4.5% solution of ammonia in acetone, methanol, ethanol, and isopropanol of various concentrations. A 3% solution of ammonia in 80-85% ethanol appeared to be the best; at this time, the alkaloid yield from the KU-5 cation exchange resin came to 94%, and from the SBS-3 cation exchange resin 85%. It should be mentioned that 12% less inert substances are desorbed from the KU-5 cation exchange resin than from the SBS-3 resin and at a higher desorption rate. The investigations we carried out showed that the use of KU-5 cation exchange resin for isolating tropanic alkaloids from aqueous extracts of Scopolia and belladonna is feasible. The ethanol eluate was brought to pH 5.0 - 5.5 with hydrochloric acid because the alkaloids decompose in an alkaline medium. The alcohol was distilled off at 55-60°C in vacuo at 620 mm. The aqueous solution was filtered through a layer of neutral aluminum oxide freeing it from resinous substances and pigments.

Separation of the alkaloids was carried out chromatographically on a column filled with aluminum oxide [12] and by a method of selective extraction at a specific pH [13]. The chromatographic method did not yield satisfactory results. As a result of the investigation of a selective extraction process, it was found that the best separation of scopalamine is observed by extracting it with chloroform and also with methylene chloride at pH 6.3-6.5 and with a ratio of phosphate buffer to alkaloid solution of 1:1. The feasibility of maintaining the necessary pH using an acidic and basic solution in order to employ a system of automatically regulating the pH in the production process and to exclude the use of buffer solutions was established. During the extraction process of scopalamine base, it was possible to regulate the pH by a single alkaline titrant aided by a single actuating mechanism.

The solvent was distilled from the dehydrated chloroform extract, an equal volume of absolute alcohol was added to the alkaloid mixture obtained, and a 65% hydrobromic acid solution was added at 3-5°C (to pH 4.0 - 4.3). The filtered and washed technical product was air dried; the scopalamine hydrobromide content was 82-85%. (The optical activity was controlled on a polarimeter.) The overall scopalamine yield from the raw material amounted to 61 - 62%.

The hyoscyamine was extracted at pH 10.0 - 11.0 with chloroform from the aqueous phase remaining after the isolation of the scopalamine, the extract was dehydrated, and the chloroform was distilled off; the hyoscyamine base was recrystallizaed from benzene. The overall hyoscyamine yield from the raw material amounted to 70 - 71%.

The investigations carried out demonstrated the feasibility and expediency of using the above ground portion of Scopolia tangutica as a raw material for obtaining tropanic alkaloids. The technology proposed can be recommended for isolating the alkaloids from the above ground portion of other kinds of plants containing the indicated tropanic alkaloids.

The isolation of the alkaloids by the technology developed was carried out in the Tashkent pharmaceutical plant from 70 kg of the above ground portion of Scopolia tangutica.

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