THE PRODUCTION OF CYTISINE FROM THE SEEDS OF Thermopsis lanceolata

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Cytisine is obtained from the seeds of Thermopsis lanceolata by extraction with dichloroethane [1] and from the epigeal parts of Th. alterniflora by aqueous extraction with subsequent sorption on ion-exchangers [2]. The isolation of cytisine and the alkaloids accompanying it from the seeds of Th. lanceolata with dichloroethane is associated with large losses of cytisine during the extraction of the alkaloids from its 10% solution with sulfuric acid and its regeneration. In addition, it has been shown that cytisine reacts with dichloroethane to form condensation products – ethylene-N,N'-dicytisine and N-β-chloroethylcytisine. This reduces the yield of final product to 25% [3]. Consequently, the development of a method for obtaining cytisine from the seeds which avoids the use of dichloroethane at all stages of production is of definite theoretical and practical interest. With this aim we have investigated the possibility of extracting the alkaloids from the seeds of Th. lanceolata with water and aqueous ethanol of various concentrations and the subsequent purification of the cytisine by means of ion-exchange resins. The content of cytisine in the extracts was determined gravimetrically [4].

Extract	Mean concentration of cytisine in the extract, %
Water	Mixture difficult to separate
Water (from steamed-out raw material)	"
0.5% solution of hydrochloric acid	"
Ethanol solution	
20%	0.05
45%	0.07
60%	0.07

From the information given above it can be seen that a 45% solution of ethanol (sp. gr. 0.93 g/cm^3) in water extracts cytisine from the seeds well and a further increase in the concentration of ethanol will apparently lead to the production of pure extracts, but the rate of extraction does not rise and the amount of extractant consumed for the complete extraction of the alkaloids from the raw material does not fall.

EXPERIMENTAL

Fifty kilograms of the seeds of Th. lanceolata was extracted with 45% ethanol, and the bulk of the ethanol was distilled off from the extract under vacuum. The residue was filtered and passed through a layer of KU-2 ion-exchanger in the H form, since we have previously shown the selective sorption of cytisine from an aqueous extract by this ion-exchanger and its effective desorption by means of ammoniacal ethanol in a preceding investigation [5].

The d : 1 ratio of the ion-exchanger was 1 : 4. The rate of flow of the extract was 750 liters/h · m^2.

A further increase in the rate of flow of the extract led to an excessive increase in the height of the layer of sorbent. This is due to the saturation of the extract with various protein substances and vegetable

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fats dissolved in the extract. Then the sorbent was washed with water and, after the last traces of water had been driven off in vacuum, the alkaloids were desorbed with a 4% solution of ammonia in ethanol.

The rate of flow of the eluent was 200 liters/h · m^2.

The extract obtained had a specific gravity of 0.870-0.890. The ratio of cytisine to extractive substances in it was 1 : 4. The solvent was distilled off from the eluate in a vacuum steam apparatus.

The still residue was brought to pH 10-12 with a 40% solution of caustic soda and carefully filtered. The alkaline solution of the alkaloids was saturated with sodium chloride and the alkaloids were extracted with small portions of chloroform until the reaction for cytisine was negative [6]. A total of seven extracts was obtained. The chloroform solution was dried with anhydrous sodium sulfate and distilled under vacuum to a pasty residue. The latter was quantitatively transferred to a porcelain dish and dried in a vacuum drying chest at a temperature of 80-85°C until the last traces of chloroform had been eliminated.

The dried mixture of alkaloids was transferred to a porcelain mortar, where it was covered with acetone to form a viscous pasty mass and was triturated for 1 h. Then the mixture was filtered on a suction filter and the technical cytisine remaining on the filter was washed with acetone and dried in the air.

The technical cytisine obtained was dissolved in acetone and the solution was filtered. Then it was cooled to 15-20°C, a small amount of ether was added, and the mixture was left in the refrigerator. After 24 h, the crystals that had deposited were filtered off from the mother liquor and dried in the air. The mother solution was distilled to small volume and cooled, and a small amount of ether was added and the mixture was left in the refrigerator for a day.

The crystals that had deposited were filtered off, dried, and combined with the first portion. The yield of cytisine, which satisfied the requirements of the State Pharmacopeia, Xth Edition, was 0.9% of the weight of the seeds.

SUMMARY

A method for obtaining cytisine from the seeds of Thermopsis lanceolata by extraction with aqueous solutions of ethanol and with the use of cation-exchangers has been developed. In this process the yield of cytisine is 0.9% of the weight of the seeds.

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