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ISOLATION OF A MIXTURE OF ALKALOIDS FROM THE LEAVES OF THE CULTURED VARIETY OF THE ZIZIPHUS JUJUBA MILL PLANT

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Abstract: This study focuses on the isolation and characterization of alkaloids from the leaves of the cultured variety of Ziziphus jujuba Mill. Using a combination of extraction methods and chromatographic techniques, the alkaloids present in the plant leaves were isolated, and their chemical properties were analyzed. The results demonstrate the potential pharmacological applications of the alkaloids obtained from this medicinal plant.

Keywords: Ziziphus jujuba, alkaloids, extraction, chromatography, pharmacological properties.

The majority of isoquinoline alkaloids found in the plant world include aporphines. So far, more than 450 alkaloids of this group have been found in plants belonging to *Berberidaceae, Magnoliaceae, Menispermaceae, Papaveraceae, Ranunculaceae, Rutaceae, Euphorbiaceae, Lauraceae, Monimiaceae, Annonaceae, Symplocaceae, Rham-naceae* families.

Ziziphus jujuba Mill is a plant belonging to the Rhamnaceae family and is widely cultivated as a medicinal fruit tree in Central Asia, including Uzbekistan.

Picture 1. Ziziphus jujuba Mill plant and its fruit

Previously, the alkaloids of this plant were not studied in our country, but the alkaloids of a number of plants belonging to the *Ziziphus genus* have been sufficiently studied abroad. For example, aporphine alkaloid-nutsiferin [1] was extracted from the leaves of the plant *Ziziphus amphibia A*. Chew, coclaurin, an alkaloid belonging to the benzylisoquinoline group, from the bark of Ziziphus jujuba, and N-methylcoclaurin and peptide alkaloids were extracted from the leaves of Z. mucronata Willd. Peptide alkaloids are the main part of alkaloids isolated from all types of plants belonging to the genus Ziziphus.

Alkaloids of cultivated and wild varieties of *Ziziphus jujube Mill* grown in Uzbekistan were the first to be studied in 1975. 9 alkaloids were isolated from the leaves of the cultured variety of Z. Jujuba chilon jiida collected during fruit ripening from the garden of Academician R.R. Schroeder Research Institute of Horticulture and Viticulture (Tashkent Region, Tashkent District) [13]. Among them, yuzifin (38), yuzirin (39), asimilobin (4), norisoboldin (34), isoboldin (35) are new alkaloids, and coclaurin (36) was discovered earlier from this plant.

The first representatives of aporphine alkaloids - apomorphine and morphothebains - the main alkaloids of the poppy plant (Papaver somniferum L) were synthesized in laboratory conditions during the study of the structure of morphine and thebains. -der was collected in the fruit ripening phase from the garden of the Horticulture and Viticulture Research Institute.

We moistened 25 kg of leaves of chilongjiida dried and crushed in a sunless place with 10% ammonia solution and extracted alkaloids with chloroform according to the usual method. The condensed chloroform extract was treated with 10% sulfuric acid solution. The acidic solution was washed with ether and made alkaline with 25% ammonia solution while cooling in ice water. Alkaloids were first extracted from the alkaline solution with ether and then with chloroform. Evaporating the solvents, we isolated 7.8 g of a mixture of bases with ether and 4.2 g of chloroform. The total yield is 12 g (or 0.048% of dry plant mass).

Coclaurin. As a result of treating 7.8 g of the mixture of ether bases with acetone, we isolated 3.2 g of colorless crystalline base. Alkaloid liquid recrystallized in alcohol. t. 218 – 220°C, [α]D23 + 13° (c 0.3; alcohol), Rf 0.34 system 1.

In the mixture of alkaloids isolated with a real sample of coclaurin, there is no depression of liquefaction temperatures. Their IR spectra are exactly the same.

Coclaurine hydrochloride. 0.38 g of coclaurin hydrochloride was obtained as a result of adding HCl to the crude solution from which coclaurin was extracted until a weakly acidic medium was formed. Recrystallized from methanol is the liquid chloride. t. 261 - 263°C.

Separation of the mixture of alkaloids into phenolic and non-phenolic parts. Evaporating the solvent from the stock solution of coclaurin hydrochloride, we dissolved the residue in water and made it alkaline with 10% ammonia solution, and extracted the alkaloids first in ether and then in chloroform (0.41 g). The ethereal extract was treated with 5% NaOH solution, then washed with water and dried with anhydrous potassium carbonate. After distilling the ether, we obtained 0.4 g of a mixture of non-phenolic alkaloids. The alkaline solution containing phenolic bases was acidified with HCl (1:1) solution, then alkalized with 25% ammonia solution and alkaloids were extracted into ether. After distilling the ether, we obtained 3.42 g of a mixture of phenolic alkaloids.

Separation of a mixture of phenolic bases in a silica gel column. 3.42 g of the mixture of alkaloids was chromatographed on a silica gel column and the column was filled with benzene-

ethanol (98:2); We washed with a mixture of (95 : 5) and (90 : 10) solvents. 0.25 g of isoboldin, 0.16 g of asimilobin and 0.05 g of yusifin from the benzene - ethanol (98 : 2) eluate, and 0.22 g of coclaurin and 1.35 g of the 3 bases from the benzene - ethanol (95 : 5) eluate. We isolated the mixture that we kept. 1.35 g of the mixture was again chromatographed on a silica gel column, and 0.12 g of yucine and 0.50 g of norisoboldin were isolated.

Isoboldin. Liquid base crystallized in benzene. t. 123 – 125°C, $[\alpha]_D^{22}$ +53° , R_f 0,52 the system 1.

UB – spektr , λ_{max} , nm: 220, 280, 304, 313 (lgε 4,50; 4,16; 4,20; 4,18);

IQ – spektr, ν_{max} , sm^{-1} : 845, 1080, 1110, 1250, 1280, 1315, 1335, 1415, 1585, 1605, 3300 – 3500.

Mass- spektr, m/z : 327 (M^+) ,326 (100%), 312, 296, 284, 269, 253, m^{++} 163,5.

Asimilobin. Liquid. t. 175 – 177°C (aseton), $[\alpha]_D^{23}$ – 210° (c 0,17; etanol), R_f 0,30 the system 1.

Norizoboldin. The alkaloid recrystallized in acetone is liquid. t. 192 – 194°C, $[\alpha]_D^{22}$ + 42° (c 0,20; spirt), R_f 0,22 the system 1.

UB – spektr , λ_{max} , nm: 221, 282, 305 (lgε 4,58; 4,22; 4,19);

IQ – spektr, ν_{max} , sm^{-1} : 770, 850, 885, 1010, 1095, 1300, 1335, 1405, 1480, 1510, 1600, 2840, 3280, 3300 – 3500.

Mass- spektr, m/z : 313 (M^+) ,312 (100%), 298, 296, 284, 283, 282, 269, 267, 165, 152, m^{++} 156,5.

0.05 g of norisoboldine is methylated according to the Hess method and is liquid. t, 122 - 124°C, we formed the most base. A mixture of this alkaloid and isoboldine does not cause depression of the liquefaction temperature.

Yuzifin. Liquid, t. 158 -159°C (methanol), $[\alpha]_D^{23}$ +18 (c 0,33; spirt).

It is liquid as a result of adding an alcoholic solution of HCl to an alcoholic solution of Yuzifin until it forms a weakly acidic medium. t. We formed yusifine hydrochloride with a temperature of 230-231°C (acetone). R_f 0.46 system 1.

UB – spektr , λ_{max} , nm: 227, 286 (lgε 4,33; 3,92);

IQ – spektr, ν_{max} , sm^{-1} : 1245, 1590, 1610, 2845, 3210 – 3330.

Mass- spektr, m/z : 192 (100 %) , 177, 148, 107.

Yuzirin. Liquid. t. 203 – 205° C (acetone), its hydrochloride liquid. t. 237 – 239°C (aseton), R_f 0,50 system 1, $[\alpha]_D^{23}$ ± 0° (c 0,20; methanol).

UB – spektr , λ_{max} , nm: 239, 273, 280, 331 (lgε 4,48; 3,63; 3,63; 3,32);

IQ – spektr, ν_{max} , sm^{-1} : 840, 925, 1140, 1450,1510, 1605, 2855, 3200 -3380.

Mass- spektr, m/z : 281(M^+), 280 (100 %) , 265, 264, 249, 236, 220, m^{++}140,5.

We heated a mixture of finely ground 0.1 g of coclaurin, 0.02 g of palladium black and 1.0 g of naphthalene at 205°C for 5 hours. Then we cooled the reaction mixture, treated with chloroform and filtered the catalyst. We took the reaction product from the chloroform filtrate into a 5% sulfuric acid solution. The acidic solution was washed with ether, made alkaline with 25% ammonia solution, and the alkaloid was extracted with chloroform. Evaporating the solvent, we dissolved the residue in 5 ml of acetone and added HCl dropwise from an alcoholic solution to the solution. As a result, liquid. t. We formed crystals with a temperature of 235-237°C. Directly comparing this chlorhydrate with yuzyrin chlorhydrate (liq. t., R_f and IR spectra), we found that they are exactly the same substance.

We extracted 12 kg of dried and crushed leaves of the wild chilon jiida collected in the fruit ripening phase from the banks of the Varzob River in the Republic of Tajikistan with chloroform according to the usual method. As a result, we isolated 4.8 g (2.85 g of ether and 1.95 g of chloroform) or 0.04% mixture of alkaloids based on dry plant mass. Then, the plant leaves were extracted with chloroform and ethanol. Ethanol was removed under low pressure created by a water suction, and the remaining residue was treated with 5% citric acid solution. The solution was washed with chloroform and made alkaline with 25% ammonia solution. Then we extracted alkaloids with chloroform. As a result, we isolated 0.95 g of the mixture of additional alkaloids.

We isolated 1.1 g of coclaurine by processing 2.85 g of ether alkaloids mixture with acetone. Passing the crude solution through a silica gel column, we isolated 0.085 g of N-methylcoclaurin, 0.06 g of thalymidine, 0.045 g of β-sitosterol and unidentified base 9, except for isoboldin and norisoboldin isolated from the cultured variety of this plant.

N – metilkoklaurin. Liquid. t. 177 – 178°C (aseton), $[\alpha]_D^{24}$ + 25° (c 0,18; spirt), R_f 0,40 system 1.

Talikmidin. Liquid. t. 192 – 194°C (aseton), $[\alpha]_D^{23}$ + 44° (c 0,15; spirt), R_f 0,63 system 1. Known alkaloids isolated: N - methylcoclaurine and

talikmidins were identified by direct comparison with their samples.

β – Sitosterin. Liquid. t. 136 – 138°C, $[\alpha]_D^{23}$ -37° (c 0,15; chloroform), R_f 0,66 system 1.

Asos № 1. Liquid. t. 256 – 258° (aseton), R_f 0,76 system 1.

Mass- spektr, m/z : M^+ 485, 471, 455, 443, 428, 414, 385, 344, 191, 160, 159, 146, 132.

Determination of the presence of peptide alkaloids. We took 0.025 g of the mixture of alkaloids with chloroform into a microtube and dissolved it in 2 ml of 6N HCl and heated the microtube at 110°C for 44 hours. Then we chromatographed the hydrolyzate on cellulose cellulose. Solvent system: acetone - isopropyl alcohol - 25% NH_3 (9 : 7 : 0.5). We observed the formation of 4 distinct spots with staining characteristic of free amino acids on the plate treated with ninhydrin solution.

By hydrolyzing the base No. 1 in 6 n HCl by the method mentioned above, we determined the presence of free amino acids in the hydrolyzate and that the base No. 1 belongs to the peptide alkaloid.

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