METHODS FOR EXTRACTING BETULIN EDUCATION

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Abstract. This article covers various methods of betulin extraction, whose biological activity is considered a high compound, which are listed in the literature.
Keywords. betulin, solvent, extraction, *Betula pendula* Roth, ethanol.

In the scientific literature, data on the structure of betulin, the synthesis of its derivatives, physico-chemical properties and biological activities are presented. However, the extraction of betulin with certain solvents, its spatial state, obtaining complex esters with certain carbonic acids and studying their properties, the synthesis of supramolecular complexes formed by the interaction of betulin with water-soluble compounds in different proportions, the structure, their physicochemical properties and biological activity have not been sufficiently studied.

Betulin is considered a triterpenoid with a natural five-ring Lupane structure and has antiviral, antibacterial, anti-various tumor and a number of other pharmacological activities. According to the results of research in recent years, these compounds are widely used in the treatment of metabolites, infections, cardiovascular and neurological diseases. Also, due to such properties as drug prolongation, increasing their biological suitability, interest in the study of betulin is increasing from year to year.

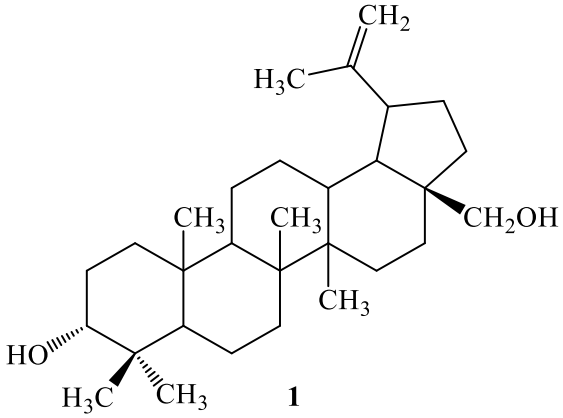


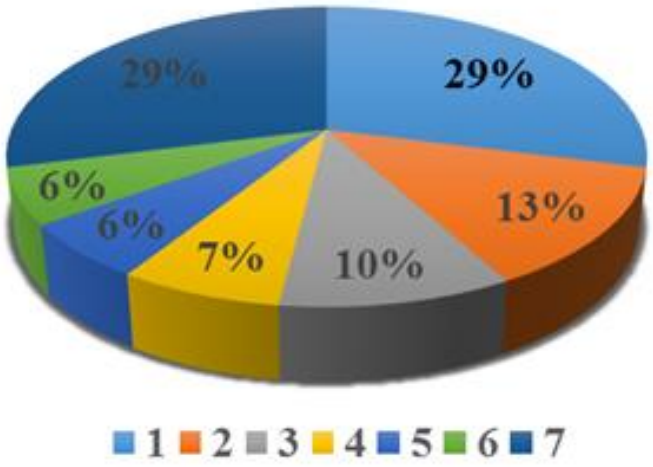
Figure 1. Betulin

Betulin-[3β,28-dihydroxy-20,(29)-lupen] or [lup-20(29)-en 3β,28-diol], betulinol, betulin alcohol, Birch camphor, lupendiol ($C_{30}H_{50}O_2$) is an alcohol that fills the cavity of bark tissue in the white birch tree and gives the bark a white tint, according to its chemical structure. Figure 1.

In the scientific literature, a number of methods for extracting betulin are presented, the study of which is considered important. Today, betulin and its derivatives are isolated from various plants (table 1). [1].

Table 1

Extraction of betulin from different sources

№	Source	Quantity
1	*Betulaceae*	
2	*Platanaceae*	
3	*Dilleniaceae*	
4	*Rhamnaceae*	
5	*Rosaceae*	
6	*Fagaceae*	
7	*Other sources*	

Betulin was first obtained by Lovis as early as 1788 using the sublimation technique from birch bark. Using the pyrolysis method, betulin was obtained through the vacuum sublimation method. At 2150s, 3G birch bark (Betula papyfera) under pressure of 0.5 kPa 75.1% recovered betulin was obtained when heated to obtain betulin for 90 minutes, purity level 87.9% [2]. But the betulin obtained by this method changes its structure when heated, and extraction methods have been used, with the assumption that the purity level is low. US scientists Eckerman and Ekman extracted betulin using organic solvents.

Betulin Rainbow Birch (*Betula verrucosa* Ehrh, *Betula pendula* Roth.) and extraction from soft Birch (*Betula pubescens* Ehrh) is common in Russia. In Europe, however, betulin has been isolated from white birch.

In the extraction of betulin from birch bark, the yield of the extract depends on the size of the initial homashion. If the size is 0.15–1.5 mm, the extraction will not depend on the type of extract. When the size is 0.8–4.0 mm, the yield and effect of the extraction depends on the type of extracting agent. Activation of birch bark with water vapor in an alkaline environment allows you to reduce extraction time and increase extraction productivity.

A great deal of research has been done on the extraction of betulin with various organic solvents, notably ethanol, benzene, diethyl ether, dichloromethane and acetone.

Solvents such as dichloromethane, methanol, or butanol-2, azeotropes of propanol-2, or ethanol, are very effective in isolating betulin and other triterpenoids from the outer bark with water. Extraction processes are observed in dichloromethane, methanol, isopropanol – water azeotropic mixture, ethanol, butanol-2 – water azeotropic mixture, in the order in which the results are put when carried in acetone: dichloromethane < isopropanol < butanol-2 = acetone< methanol < ethanol [3].

When betulin is excreted using organic solvents, Lupan dressing, a common phytosterol, β-sitosterol, is extracted. Also, depending on the species of Birch, the extract is found in low amounts, such as betulonic acid, betulonic aldehyde, allobetulin, oleanol aldehyde and betulinic acid. Betulin is present in large quantities in the white bark after it, rather than the outer bark of birch. Up to 97% betulin has been isolated in ethanol extraction if the bark is kept in NaOH solution for some time, boiling for 1-3 minutes at 240os.

Betula pendula Roth birch bark is dried up to 1% moisture with a ring of 105os da crushed up to 1-2 mm, an extract is carried out in a sachet apparatus and left for 36-40 hours. The hexane or ethanol solvent used in the extraction is launched in a rotor evaporator until a white powdery substance remains. In this case, a substance was isolated in hexane with 15-20%, in ethanol with up to 34% unum. The composition of the substance isolated in hexane extract was 60% betulin, 32% lupeol. 51% of the substances secreted in ethanol extract were found to be betulin, 34% lupeol.

The white birch bark was also extracted with betulin benzene. The extract is cooled and betulin filtered and dried. When separating betulin, it is also possible to extract the bark in petroleum ether, tetrachloromethane and chloroform. It has been proposed to extract betulin by directly acylating the extract in trichloroethylene and hydrolyzing diacetate betulin [4].

Bark in ethylacetate, isopropyl alcohol and water extraction

It is stored in a solvent for 10-12 hours, re-extracted 3 times to launch the solvent. The extract in hexane is stored in NaOH solution for 3 hours. Then it is filtered to rinse in water until it reaches a neutral state (pH =3-4) and extracted 3 times in diethylephyr, the reason is the loss of sulfate salts in the bark, in which the resulting substance is cleaned of up to 4-5% of essential products. The extract in ethylacetate, on the other hand, is boiled in a NaOH solution and kept in ethyl alcohol for 4 hours filtered and washed in water until neutral. The extract in isopropyl alcohol is processed in the same way. 10.5 in hexane using this method (90% betulin), 10.5% (60% betulin) in ethylacetate, 20.6% (46% betulin) in isopropyl alcohol with respect to the bark dry mass, the substance is isolated. When re-extracted, it was observed that 10.5% (90% betulin) ethylacetate in hexane secreted 5.2% (10% betulin) in 6.9% (1.4% betulin) isopropyl alcohol.

When extracted with benzene, the lupeol output is high and this results in extraction at high critical extraction system SO_2 and solvent 40–50os, 3-5 atmospheric pressures. With colon chromotography, the main component lupeol is isolated, by recrystallization the unum is increased by 1-1.5%, in which lupeol is separated at 90-95% purity.

Petroleum ether (70-100os) – toluene has a higher lupeol output even when it is extracted under the influence of temperature in a ratio of 1:1-7:3. Substances isolated from the extract are recrystallized and isolated by chromotographic method with betulin and lupeol colon.

Bark scraping is extracted in methyltretbutil ether (MTBE) for 2 hours. Then add MTBE again and boil for 40 minutes. This process is repeated 4 times and the extract is treated with NaOH solution, dried with Mdso4 and the solvent is launched. The extract is air-dried and recrystallized in hexane 1 hour to 4 times, secreting up to 95% betulin. Up to 95% of lupeol can be obtained at purity if the hexane extract solvent is re-crystallized in ethylacetate by launch, while solutions of n-propanol, n–butanol can also obtain 95% betulin, 5% lupeol by alkali–alcohol-water treatment, recrystallization [7].

In addition, the extracted substance is recrystallized with various solvents in order to increase the level of purity of betulin. In this case, betulin is obtained at a purity of up to 98%, depending on the use of a suitable solvent. Extraction on Propanol-2 or butanol-2 Increased betulin purity from 90% to 94%. The use of acetone with methanol and ethanol did not give such a high result.

When recrystallization is carried out using Butanol-2 – water azeotrope, 80% purity betulin, up to 95% purity, but up to 17% loss of betulin is observed. This loss is up to 15% for propanol 2. Acetone azeotropes with methanol and ethanol showed low product output and

were incompatible as a recrystallization solvent. Two alternative methods of extraction and crystallization of betulin from birch bark have been proposed, depending on the required purity of the Betulin product [8].

When cleaning betulin, it is not enough to use only crystallization and recrystallization techniques. Cleaning betulin by crystallization and subsequent use of Column Chromatography helps to obtain betulin with high purity. However, purification of untreated betulin using column chromatography is made partially difficult due to its low solubility in a variety of solvents. The rest of the research was carried out in two stages when obtaining pure betulin using column chromatography: initially untreated betulin extract is acetylated with acetic aldehyde. Untreated betulin diacetate is purified using silica gel column chromatography. Betulin diacetate is hydrolyzed in ethanol in the presence of excess mining, in the process a product with purity of 98% is obtained.

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