ENG

Betulin Lab | Latvijas Finieris Group

# From Nature to Your Success

# A wonder of nature

Birch bark extract is found in the outer layer of birch bark – a natural compound with antibacterial and cell regeneration properties. It has been extensively studied worldwide in recent decades, finding many unique application possibilities in healthcare, beauty, food and other industries.

# Sustainable product with low environmental impact

The birch bark used in the production of betulin, betulin acid and lupeol is obtained from controlled, traceable and certified sources with respect towards nature. It is an intelligent way to use by-products occurring in the production process of other birch wood products.

NATURAL & ORGANIC

SUSTAINABLE

VEGAN

SUITABLE FOR VEGAN PRODUCTS

Approved by ECOCERT RAW MATERIAL

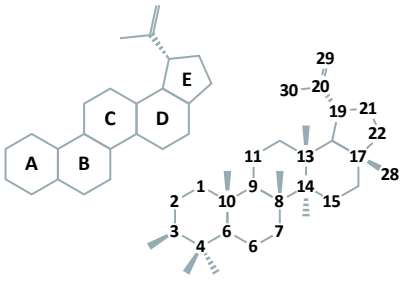
COSMOS APPROVED

# Let's look closer

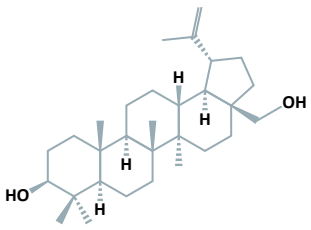
Birch bark extract is a light brown crystalline powder containing triterpenoids and phenol-containing components, including tannins, sugars, etc.
The most significant mass composes three lupane-type pentacyclic triterpenes: betulin, betulinic acid and lupeol. In the betulin molecule, there are three active reaction carbon atoms:

- C-3, secondary hydroxyl group
- C-28, primary hydroxyl group
- C-20, double bond

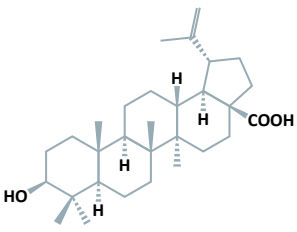
Birch bark extract containing triterpenes possess an extensive range of pharmacological activities such as anticancer, antioxidant, anti-inflammatory and antimicrobial activities. The range of birch bark extract application is extensive – skin conductive and wound healing component, food and cosmetic remedies, dental resin and textile fibre production, as well as perspective pharmaceutical wound healing agents.




*Structure and numbering of parent lupane [2].*

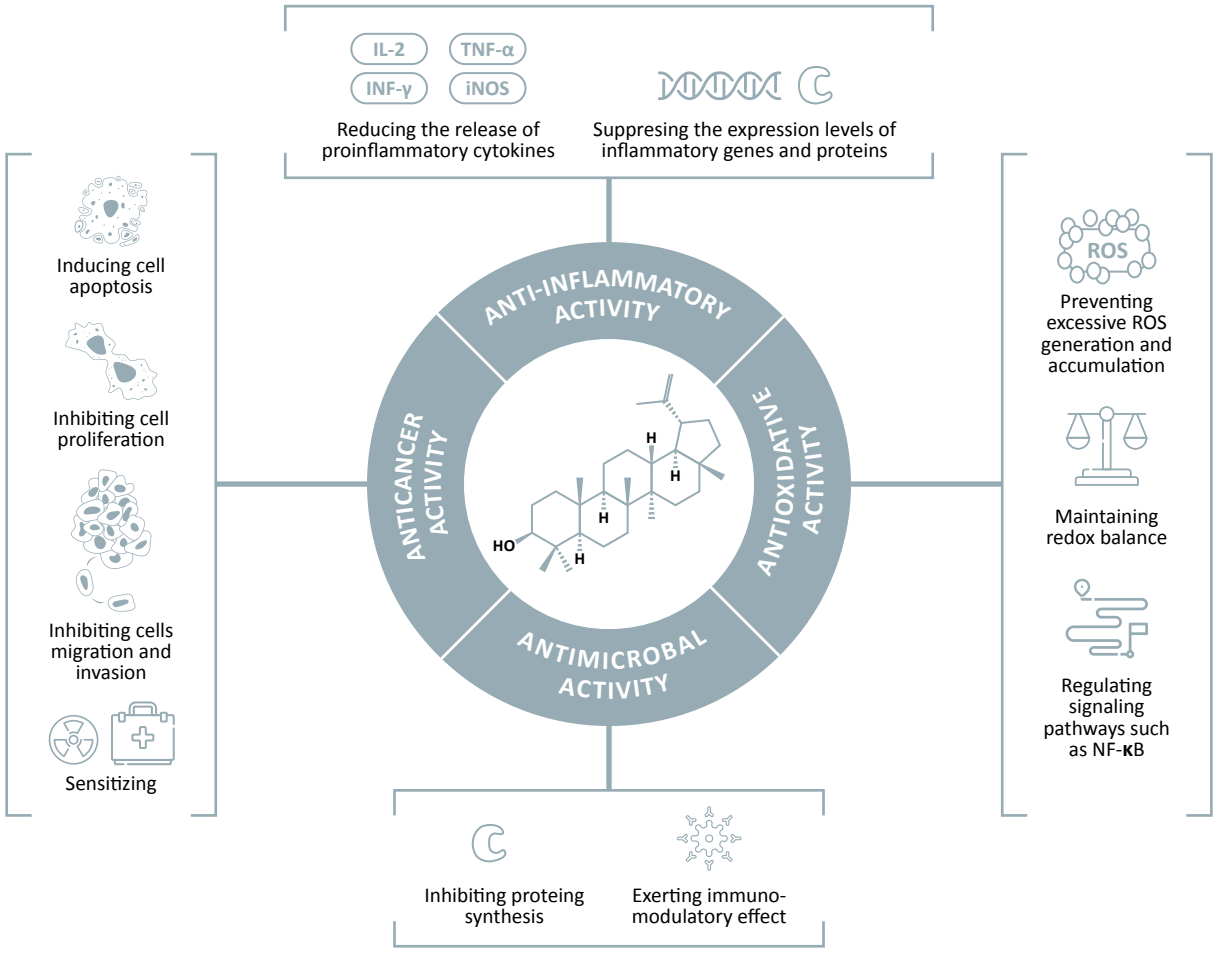



*Chemical structure of betulin [2].*




*Chemical structure of betulinic acid [2].*

## Birch bark extract – what does it do




*Birch bark extract triterpen's pharmacological activities [28].*

COSMETICS

# Beauty enhanced by nature

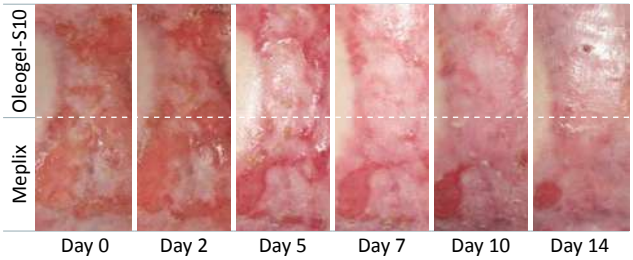
The unique properties of the birch bark extract serve as a natural skin conductive and wound healing component in cosmetics and have shown effective results in skin disease treatment. The extract meets the requirements of organic and natural cosmetic producers and consumers.

ANTIOXIDANT

WOUND HEALING

ANTIMICROBIAL

## Nature healing your skin

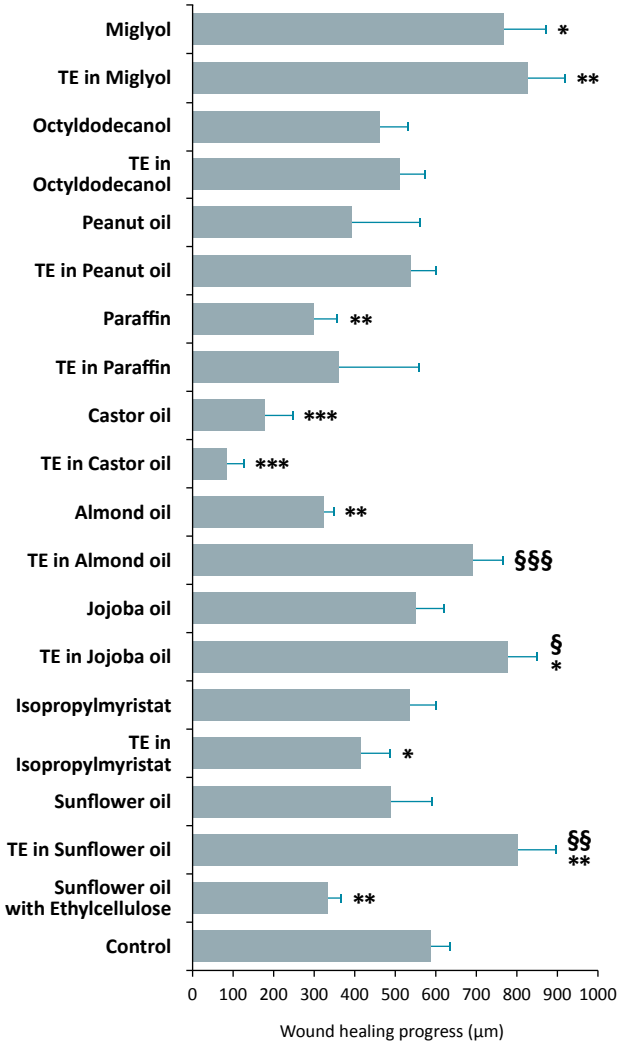


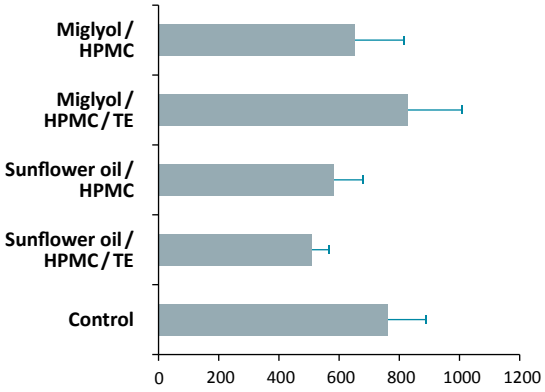

*Complete wound closure of the intervention wound at day 13 of treatment [7].*

Its natural antioxidant, anti-inflammatory, wound healing and antimicrobial properties assure effective and fast results in cosmetics where it is added. Due to big tannin content, birch bark extract is a potential natural source of antimicrobial and antifungal agents.
Its efficiency has been clinically proven.

# Effect of birch bark extract with various oils, oleogels and emulsions on wound healing

**TE – Birch Bark extract triterpenes**



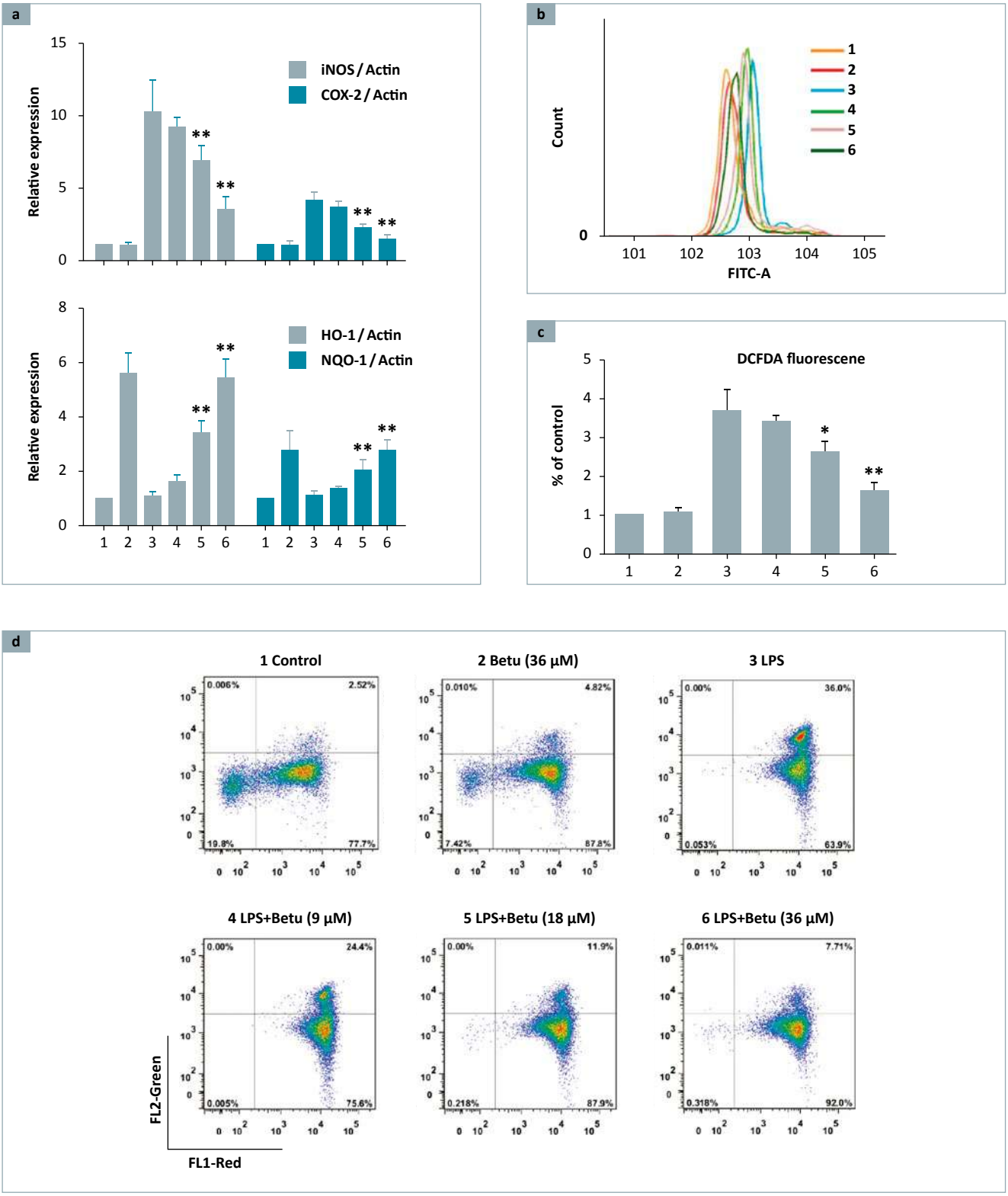




*Effect of various emulsions on wound healing progress in ex-vivo wound healing models after 48h of treatment [12]. Emulsions were prepared with method 1 ("suspension method") [12].*

*Effect of the various oils and oleogels on wound healing progress in ex-vivo wound healing models after 48 h of treatment.*

** compared to control, § comparison between oil and oleogel. */§. p<0.05, ***/§§§ p<0.001*
*Peanut oil, paraffin, TE in paraffin, castor oil, TE in castor oil, Miglyol, TE in Miglyol, octyldodecanol, TE in ocytldodecanol, almond oil, TE in almond oil, jojoba oil, TE in jojoba oil, isopropylmyristate, TE in isopropylmyristate, sunflower oil, TE in sunflower oil, sunflower oil with ethylcellulose [12].*

# Effects of betulin on anti-inflammatory and antioxidant reactions in LPS-stimulated macrophages




*RAW264.7 cells were plated in 12-well plates, preincubated with betulin (9, 18 and 36 µM) for 1 h, and then challenged with LPS (500 ng/ml) for 18 h [17].*

*(a) The expression of proinflammatory genes (iNOS and COX-2);*
*(b and c) Antioxidant enzymes (HO-1 and NQO1) were detected by quantitative real-time PCR;*
*(d) The cells were washed with PBS and incubated with JC-1.*

FOOD

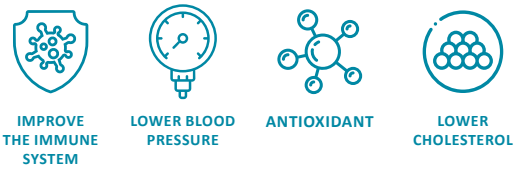
ORAL CARE

## Superfood properties

Birch bark extract is used as an antioxidant and conservator in food and cosmetic products. Its active components can improve health conditions by lowering cholesterol and blood pressure, improving the immune system and giving other benefits to overall well-being.

## Antibacterial properties for oral care products

Birch bark extract is an antibacterial dental resin that reduces the possibility of dental caries.

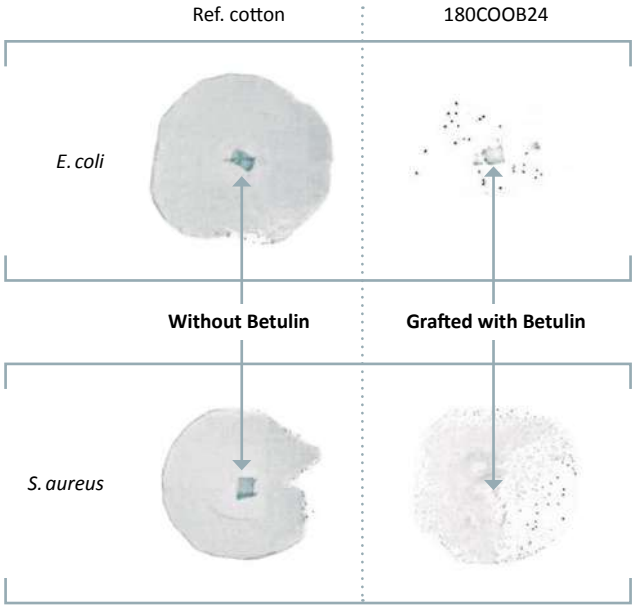




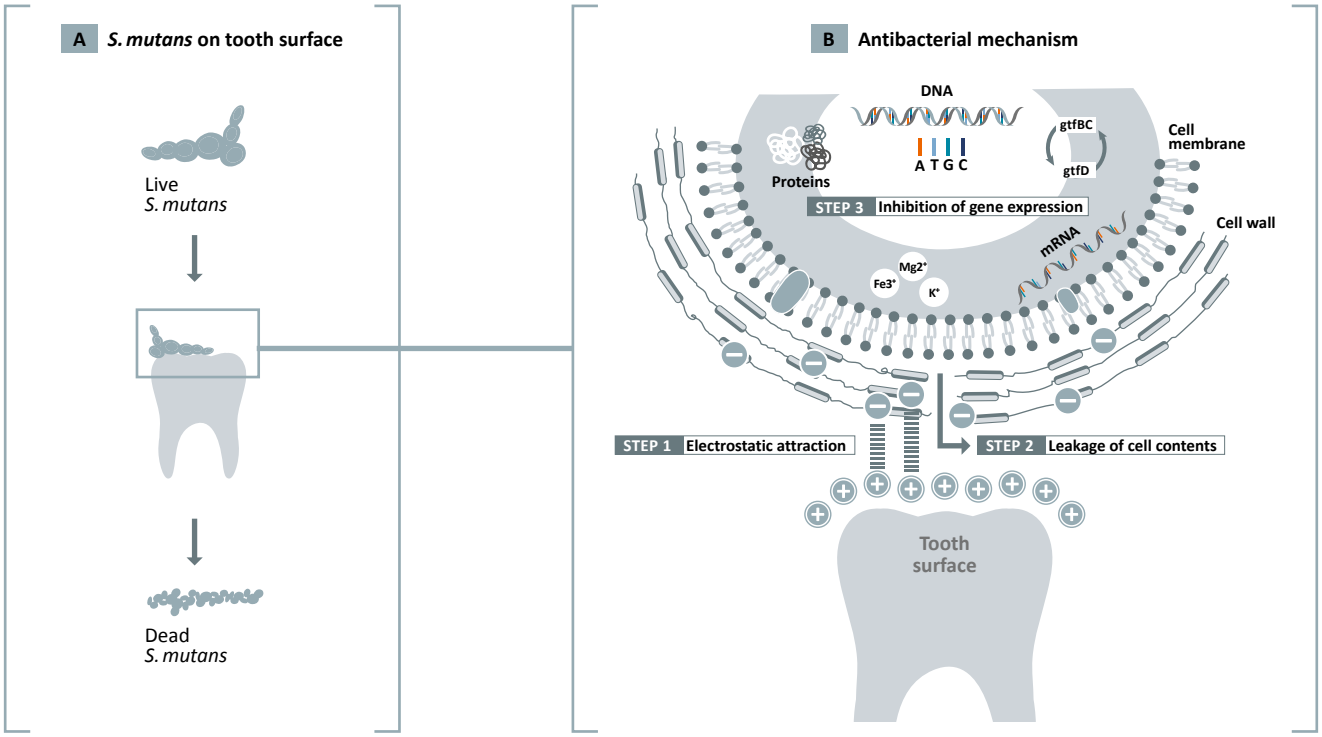
Birch bark extract and betulinic acid reveal cytotoxicity towards human gastric carcinoma and human pancreatic carcinoma drug-sensitive and drug-resistant cell lines. Furthermore, the conservation properties prevent food deterioration and prolong the food preserving period and birch bark extract triterpenes can be used as lamented agents for vegetable oils or other liquids.
The extract meets the requirements of natural, organic (e.g. as EcoCert requirements) and vegan products.

It is applicable in oral hygiene products, like toothpaste and mouth-washing liquids. The extract properties effectively fight against bacteria and, at the same time, are gentle for the oral cavity.

# The difference betulin makes




*Textile patterns "Ref. Cotton", without birch bark extract, and "180COOB24", grafted with extract, incubated on Petri films after 18 h immersion in Escherichia coli or Staphylococus aureus solutions [25].*




*Proposed antibacterial mechanism of dental resins containing "Bis-QADM-Bet" against Streptococcus mutans, which cause dental caries [24].*

All pictures shown are for illustration purposes only

# References


1. Berzins, R., Paze, A., Rizhikovs, J., Makars, R., Godiņa, D., Lauberts, M., Stankus, K., 2021. Influence of Solvents on the Antioxidant Properties of the Birch Outer Bark Extract in Cosmetic Emulsions. *In Key Engineering Materials* (Vol. 903, pp. 28–33). https://doi.org/10.4028/www.scientific.net/kem.903.28

2. Csuk, R., 2012. Targeting Cancer by Betulin and Betulinic Acid. Novel Apoptotic Regulators in Carcinogenesis (pp.267-287). (PDF) Targeting Cancer by Betulin and Betulinic Acid (researchgate.net)

3. Hordyjewska, A., Ostapiuk, A., Horecka, A., Kurzepa, J., 2019. Betulin and betulinic acid: triterpenoids derivatives with a powerful biological potential. *Phytochem Rev* (Vol. 18, pp. 929–951). Betulin and betulinic acid: triterpenoids derivatives with a powerful biological potential | SpringerLink

4. Herbal medicine: summary for the public Birch leaf, Betula pendula Roth and/or Betula pubescens Ehrh., folium (europa.eu)

5. Jäger, S., Laszczyk, M. N., Scheffler, A., 2008. A Preliminary Pharmacokinetic Study of Betulin, the Main Pentacyclic Triterpene from Extract of Outer Bark of Birch (*Betulae alba cortex*). *Molecules 13*, 3224-3235, doi: 10.3390. A Preliminary Pharmacokinetic Study of Betulin, the Main Pentacyclic Triterpene from Extract of Outer Bark of Birch (Betulae alba cortex) (nih.gov)

6. Günther, A., Makuch, E., Nowak, A., Duchnik, W., Kucharski, L., Pełech, R., Klimowicz, A., 2021. Enhancement of the Antioxidant and Skin Permeation Properties of Betulin and Its Derivatives. *Molecules 26*, 3435, doi: 10.3390. Enhancement of the Antioxidant and Skin Permeation Properties of Betulin and Its Derivatives (nih.gov)

7. Schwieger-Briel, A., Kiritsi, D., Schempp, C., Has, C., Schumann, H., 2017. Betulin-Based Oleogel to Improve Wound Healing in Dystrophic Epidermolysis Bullosa: A Prospective Controlled Proof-of-Concept Study. *Dermatology Research and Practice*, ID 5068969. 5068969.dvi (nih.gov)

8. https://www.resultsbykosmetikos.com/single-post/2017/05/15/the-top-5-benefits-of-birch-bark-extract

9. Herbal Essences Birch Bark Extract Sulfate-Free Shampoo ingredients (Explained) (incidecoder.com)

10. Herbal Essences Birch Bark Extract Sulfate-Free Hair Conditioner ingredients (Explained) (incidecoder.com)

11. Hoffmann, J., Gendrisch, F., Schempp, C. M., Wölfle, U., 2020. New Herbal Biomedicines for the Topical Treatment of Dermatological Disorders. Biomedicines, doi:10.3390 biomedicines-08-00027.pdf (nih.gov)

12. Steinbrenner, I., Houdek, P., Pollok, S., Brandner, J. M., Daniels, R., 2016. Influence of the Oil Phase and Topical Formulation on the Wound Healing Ability of a Birch Bark Dry Extract. *PLoS ONE* 11(5): e0155582. doi:10.1371 Influence of the Oil Phase and Topical Formulation on the Wound Healing Ability of a Birch Bark Dry Extract (nih.gov)

13. Ebeling, S., Naumann, K., Pollok, S., Wardecki, T., Vidal-y-Sy, S., Nascimento, J. M., ... & Merfort, I., 2014. From a traditional medicinal plant to a rational drug: understanding the clinically proven wound healing efficacy of birch bark extract. *PloS ONE*, 9(1), e86147. pone.0086147 1..18 (nih.gov)

14. Scheffler, A., 2019. The wound healing properties of betulin from birch bark from bench to bedside. *Planta medica*, 85(07), 524-527. https://doi.org/10.1055/a-0850-0224

15. Wardecki, T., Werner, P., Thomas, M., Templin, M. F., Schmidt, G., Brandner, J. M., Merfort, I., 2016. Influence of Birch Bark Triterpenes on Keratinocytes and Fibroblasts from Diabetic and Nondiabetic Donors. *J. Nat. Prod.,* 79, 4, 1112–1123. doi: 10.1021. Influence of Birch Bark Triterpenes on Keratinocytes and Fibroblasts from Diabetic and Nondiabetic Donors - PubMed (nih.gov)

16. Ueck, C., Volksdorf, T., Houdek, P., Vidal-y-Sy, S., Sehner, S., Ellinger, B., Lobmann, R., Larena-Avellaneda, A., Reinshagen, K., Ridderbusch, I., Kohrmeyer, K., Moll, I., Daniels, R., Werner, P., Merfort, I., Brandner, J. M., 2017. Comparison of *In-Vitro* and *Ex-Vivo* Wound Healing Assays for the Investigation of Diabetic Wound Healing and Demonstration of a Beneficial Effect of a Triterpene Extract. *PLoS ONE* 12(1): e0169028. doi:10.1371. Comparison of In-Vitro and Ex-Vivo Wound Healing Assays for the Investigation of Diabetic Wound Healing and Demonstration of a Beneficial Effect of a Triterpene Extract (nih.gov)

17. Ci, X., Zhou, J., Lv, H., Yu, Q., Peng, L., Hua, S., 2017. Betulin exhibits anti-inflammatory activity in LPS-stimulated macrophages and endotoxin-shocked mice through an AMPK/AKT/Nrf2-dependent mechanism. *Cell Death and Disease*, 8, e2798; doi:10.1038. Betulin exhibits anti-inflammatory activity in LPS-stimulated macrophages and endotoxin-shocked mice through an AMPK/AKT/Nrf2-dependent mechanism (nih.gov)

18. Ostapiuk, A., Kurach, L., Strzemski, M., Kurzepa, J., Hordyjewska, A., 2021. Evaluation of Antioxidative Mechanisms In Vitro and Triterpenes Composition of Extracts from Silver Birch (Betula pendula Roth) and Black Birch (Betula obscura Kotula) Barks by FT-IR and HPLC-PDA. *Molecules* 2021, 26, 4633. doi.org/10.3390. Evaluation of Antioxidative Mechanisms In Vitro and Triterpenes Composition of Extracts from Silver Birch (Betula pendula Roth) and Black Birch (Betula obscura Kotula) Barks by FT-IR and HPLC-PDA (nih.gov)

19. Blondeau, D., St-Pierre, A., Bourdeau, N., Bley, J., Lajeunesse A., Desgagne-Penix, I., 2019. Antimicrobial activity and chemical composition of white birch (*Betula papyrifera* Marshall) bark extracts. *Microbiology Open*, doi: 10.1002/mboi3.944 https://pubmed.ncbi.nlm.nih.gov/31580010/

20. Zavorokhina, N. V., at 2020 IOP Conf. Ser.: Earth Environ. Sci. 548 082017, doi:10.1088/1755-1315/548/8/082017 https://iopscience.iop.org/article/10.1088/1755-1315/548/8/082017/pdf

21. Grysko, M. K., Laszczyk, M. N., Jäger, S., Scheffler, A., & Daniels, R., 2009. A new emulsifier-free w/o system based on a triterpene extract from the outer bark of birch. *Planta Medica*, 75(09), PI17. https://doi.org/10.1055/s-0029-1234781

22. Ghaffar, K. A., & Daniels, R., 2020. Oleogels with birch bark dry extract: extract saving formulations through gelation enhancing additives. *Pharmaceutics*, 12(2), 184. https://doi.org/10.3390/pharmaceutics12020184

23. https://www.fitoterapija.lv/en/product-category/nutrition-supplements/

24. Zhang, L., Ma, Z., Wang, R., Zuo, W., & Zhu, M., 2023. Development of Antibacterial Dental Resins Containing Bis-Quaternary Ammonium Betulin-Based Dimethacrylate. *Mater. Adv*. doi.org/10.1039 d3ma00016h (rsc.org)

25. Huang, T., Chen, C., Li, D., 2019. et al. Hydrophobic and antibacterial textile fibres prepared by covalently attaching betulin to cellulose. *Cellulose* 26, 665–677. https://doi.org/10.1007/s10570-019-02265-8

26. Kruszniewska-Rajs, C., Strzałka-Mrozik, B., Kimsa-Dudek, M., Synowiec-Wojtarowicz, A., Chrobak, E., Bebenek, E., Boryczka, S., Głuszek, S., Gola, J. M., 2022. The Influence of Betulin and Its Derivatives EB5 and ECH147 on the Antioxidant Status of Human Renal Proximal Tubule Epithelial Cells. *J. Mol. Sci.*, 23, 2524. doi. org/10.3390. The Influence of Betulin and Its Derivatives EB5 and ECH147 on the Antioxidant Status of Human Renal Proximal Tubule Epithelial Cells (nih.gov)

27. Liu, K., Zhang, X., Xie, L., Deng, M., Chen, H., Song, J., ... & Luo, J., 2021. Lupeol and its derivatives as anticancer and anti-inflammatory agents: Molecular mechanisms and therapeutic efficacy. *Pharmacological research*, 164, 105373. https://doi.org/10.1016/j.phrs.2020.105373

28. Lou, H., Li, H., Zhang, S., Lu, H., & Chen, Q., 2021. A review on preparation of betulinic acid and its biological activities. *Molecules*, 26(18), 5583. https://doi.org/10.3390/molecules26185583

29. Aswathy, M., Vijayan, A., Daimary, U. D., Girisa, S., Radhakrishnan, K. V., & Kunnumakkara, A. B., 2022. Betulinic acid: A natural promising anticancer drug, current situation, and future perspectives. *Journal of Biochemical and Molecular Toxicology*, e23206. https://doi.org/10.1002/jbt.23206

30. Amiri, S., Dastghaib, S., Ahmadi, M., Mehrbod, P., Khadem, F., Behrouj, H., ... & Ghavami, S., 2020. Betulin and its derivatives as novel compounds with different pharmacological effects. *Biotechnology advances*, 38, 107409. https://doi.org/10.1016/j.biotechadv.2019.06.008

31. Tolstikov, G., Flekhter, O., Shul'ts, E., Baltina, L., Tolstikov, A., 2005. *Khim. Interesakh Ustoich. Razvit.*, 13, 1. https://www.sibran.ru/upload/iblock/4d9/betulin_and_its_derivatives_chemistry_and_biological_activity.pdf

32. Drag M., Surowiak P., Drag-Zalesinska M., Dietel M., Lage H. and Oleksyzyn J., 2009. Comparison of the Cytotoxic Effects of Birch Bark Extract, Betulin and Betulinic Acid Towards Human Gastric Carcinoma and Pancreatic Carcinoma Drug-sensitive and Drug-Resistant Cell Lines. *Molecules* 14, 1639-1651. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6254329/pdf/molecules-14-01639.pdf

33. A. Paže, J. Zandersons, J. Rižikovs, G. Dobele, V. Jurkjāne, B. Spince and A. Tadernaka, 2014. Apparatus and Selective Solvents for Extraction of Triterpenes from Silver Birch (*Betula pendula Roth.*) Outer Bark. *Baltic Forestry* 20(1): 88 – 97. https://www.researchgate.net/publication/264943259_Apparatus_and_Selective_Solvents_for_Extraction_of_Triterpenes_from_Silver_Birch_Betula_pendula_Roth_Outer_Bark

**www.betulin-lab.com**
**info@betulin-lab.com**

**Betulin Lab**
2 Finiera Street,
Riga, LV-1016, Latvia
+371 29230644

05/2023