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EPIDERMA, s.r.o.
Jankovcova 1595/14
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EPIDERMA® product review

EPIDERMA® brand products contain a unique patented composition of two ingredients - betulin and cannabidiol, the so-called Betuldiol®. This composition is used in dermocosmetics for the treatment of acne, eczema, psoriasis, and atopic dermatitis.

Betulin, which is mainly isolated from the bark of trees of the *Betula* genus, and cannabidiol (CBD), which is isolated from plants of the *Cannabis* genus, have undergone a research study developed on the basis of the latest scientific studies, mainly from recent years. The study is attached to this report.

The substance betulin is being intensively investigated in the treatment of inflammatory diseases due to its versatile effect in modulating the inflammatory response. Many studies support its use in dermatology not only for its modulation of pro-inflammatory mediators, but also for its ability to accelerate wound healing, protect against UVB damage and for its antibacterial effect against gram-positive bacteria, which are mainly involved in the development of acne or skin infections. Recent studies have also tested the use of betulin-containing triterpene extracts in burn therapy, in the treatment of lesions caused by laser skin resurfacing in combination with a facelift, in actinic keratoses and skin grafts, and as an option for the therapy or at least attenuation of the progression of atopic dermatitis. The registered drug Filsuvez® is also approved for use in adults and children aged 6 months and older with the rare hereditary disease epidermolysis bullosa. Betulin and extracts containing it are generally well tolerated, they can only have a slightly irritating effect. Its clinical use is severely limited by its very poor bioavailability and biodistribution directly related to its low water solubility. However, this disadvantage can be overcome by numerous nanoformulations that significantly improve the pharmacokinetic profile of this compound.

There is an overwhelming amount of scientific evidence for the therapeutic applications of CBD. CBD has an affinity for more than 65 molecular targets. Although it has a low binding

affinity for one of the two cannabinoid receptors (CB1 and CB2), it modulates several non-cannabinoid receptors and ion channels. CBD also acts via various non-receptor pathways, for example by delaying the "reuptake" of endogenous neurotransmitters (such as anandamide and adenosine) and by enhancing or inhibiting the coupling effect of certain G-protein-coupled receptors. Through these mechanisms, CBD may act on various multifactorial diseases such as atopic dermatitis, psoriasis, acne, epidermolysis bullosa, systemic sclerosis, seborrheic dermatitis, scalp psoriasis, androgenic alopecia, and melanoma. CBD has also been tested for its synergistic effect with antibiotics, in particular with bacitracin, which is a component of Framykoin®.

And it enhanced the anti-inflammatory effect of *Centella asiatica* extract and silymarin. Its biological activities thus lead to a demonstrable improvement in the diseases mentioned, and also in the quality of life of patients. The undeniable advantage of CBD is its excellent safety profile. However, the physicochemical properties of CBD, in particular its extremely hydrophobic nature, make it a difficult molecule for topical administration. To improve the penetration of CBD into the skin and maximize its biological properties, various technological strategies have been developed. These include improved conventional semi-solid formulations such as cryogels, hydrogels and ethanolic gels, as well as formulations with penetration enhancers such as transcutol, isopropyl myristate, oleic acid, lactic acid, dimethyl sulfoxide, or PEG-400. CBD has also been incorporated into various nanoformulations (e.g. ethosomes, polymeric micelles, nanometric emulsions, hybrid nanoparticles gelled in cross-linked chitosan, and others).

Nanoformulations offer high solubility, stability, and sustained release. Almost all developed nanoparticles have a simple architecture, are known and safe nanocarriers or are even simple nanosuspensions.

In my expert opinion, the combination of the substances betulin and cannabidiol is an innovative composition, which, with its anti-inflammatory, antibacterial and regenerative effect, rightfully takes its place in the therapy of many multifactorial dermatological diseases. I see its future in combination with other substances to enhance the anti-inflammatory or antimicrobial effect, and also in increasing the effect thanks to the best possible technological processing. I would also target regeneration products for plastic surgery and burn therapy.

PharmDr. Alice Sychrová, Ph.D.

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Expertise: Assistant Professor MUNI PHARM, Assistant Pharmacist

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Scientific activity	
Citations (WoS) H-index Publications	372 total 7 13 impacts
Grants	5x research IGA, 3x teaching IVA, 1x mobility IMA, 1x student GAMU, 2x research MUNI
Conferences	2010–2024: 27x research/postgradual education
Supervisor	31 successfully defended diploma theses (CR + SR), 4 successfully defended rigorous theses, 1 doctoral student studying an international doctorate as part of the MUNI Mendel Doctorandus program, 1 successfully defended student research activity
Foreign internships	November 2013 - National Center for Natural Products Research (NCNPR). Supervisor Prof. Samir Ross, School of Pharmacy, University of Mississippi, USA (4 weeks).

November–December 2014 – NCNPR. Supervisor Prof. Samir Ross, Dr. Mellissa Jacob, School of Pharmacy, University of Mississippi, USA (5 weeks).

Dr. Sychrová has been working at the Department of Natural Drugs since 2009 and has many years of experience in the field of phytochemical analysis and the study of the biological activities of natural substances. As part of her research, she specializes in both the isolation of natural substances and the testing of antimicrobial activity, with a focus on the eradication of methicillin-resistant staphylococci (MRSA) and the use of natural substances in the treatment of infected wounds. She also specializes in the use of natural substances, particularly in clinical practice. As part of postgraduate training, she gives lectures for doctors, pharmacists, and pharmaceutical assistants. She is a member of the editorial board of the cukrovka.cz website, which was created in cooperation with the Czech Diabetological Society ČLS JEP Z.S. She is an advisor in developing food supplements.