Effect of **c**ream paste containing pl**e**uran (β-glucan from *Pleurotus ostreatus*) on selected **sk**in **d**ermatoses.

ECESID study

Protocol of biomedical study

Basic Information about Research:

Title of Research:	Effect of cream paste containing pleuran (β-glucan from *Pleurotus ostreatus*) on selected skin dermatoses.
Acronym:	ECESID
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Study Design:	Multicentre, prospective, open-label study. with a novel cosmetic product.
Number of Patients:	cca. 100 patients aged from 3 weeks enrolled by investigators in 20 centres
Primary Endpoints:	To evaluate the clinical effect of Imunoglukan P4H® ACUTE! cream paste in selected skin dermatoses (diaper dermatitis, perioral dermatitis, neonatal pustulosis) on: • Clinical assessment of erythema using a 5-point severity scale (Clinician's Erythema Assessment - CEA) • Investigator's Global Assessment (IGA) using a 6-point scale
Secondary Endpoints:	To evaluate the tolerability of the cosmetic product Imunoglukan P4H® ACUTE! cream paste in selected skin dermatoses (diaper dermatitis, perioral dermatitis, neonatal pustulosis) using a 3-point tolerability scale.

Timeline of the biomedical research

Pre-screening of patients: march-april 2024
Date of first patient inclusion: april-may 2024
Study completion date: 31. 12. 2024
Patient follow-up duration: 2 weeks, with a total of 2 visits:

- V0 – initial visit **- day of enrolment**
- photodocumentation performed by the patient/legal representative after 7 days of application
- V1 – **control visit - after complete recovery from erythema or maximum 14 days from enrolment**

Introduction

Normalization of the skin barrier defence function can be supported by using products that promote the physiological process of keratinization and the immune functions of the skin. In patients with problematic skin, the use of alternative and complementary treatments also plays an important role, as they can be used as add-on to the standard of care treatment. A significant group among complementary medicine products includes preparations containing natural substances with a proven complex immunomodulatory effect – biologically active polysaccharides (BAP), such as beta-glucans.

Biologically active polysaccharides are glucose polymers commonly found in fungi, yeasts, bacteria, and cereals. They represent some of the most extensively studied natural immunomodulators with pluripotent biological effects (anti-infective, antiviral, immunomodulatory). Imunoglukan® is a

complex of biologically active polysaccharides with a predominant content of beta-1,3/1,6-D-glucan pleuran, obtained through a patented isolation technology from *Pleurotus ostreatus*.

In topical application, Imunoglukan® activates skin immune cells (Langerhans cells – skin macrophages) through Dectin-1 receptors on one hand, and on the other hand, it can also activate skin cells that are not part of the immune system (keratinocytes and fibroblasts).

In topical application, Imunoglukan® influences:

- function and viability of Langerhans cells
- proliferation and migration of keratinocytes
- stimulation of collagen production in fibroblasts
- tissue regeneration and remodelling
- rate of wound healing
- production of certain cytokines (e.g., IL-1, IL-8, TNF-α) and enzymes (MMP-9)
- enhancement of antioxidant effects
- slowing of cellular aging

The effectiveness and safety of Imunoglukan® for various types of skin problems have been confirmed by numerous laboratory experiments, clinical observations, and open-label studies. For instance, a multicenter open-label study conducted in ten dermatological centers in Slovakia and the Czech Republic demonstrated a positive effect on alleviating the symptoms of atopic dermatitis. At the sites of cream paste application, there was a significant reduction in the number of flare days, the intensity of disease exacerbation, and the sensation of itching. Clinical trials have also confirmed very good effects of Imunoglukan® cream paste in the treatment of leg ulcers, herpetic infections, and surgical wounds following extensive oncological procedures, as well as in healing crusts after chickenpox in pediatric patients. The skin condition of patients with seborrheic dermatitis, rosacea, or acne significantly improved after cream paste application, and even an anti-aging effect was observed.

The results of clinical studies and observations confirmed the complex immunomodulatory and regenerative effects of Imunoglukan® with no recorded adverse effects.

Study Design

It is a multicentre, prospective biomedical research conducted in outpatient healthcare facilities. In terms of the nature of the study, it is a biomedical research involving the novel cosmetic product Imunoglukan P4H® ACUTE! cream paste.

Investigators/physicians will enrol a total of 100 patients who meet the inclusion criteria.

Patients enrolled in the study will apply Imunoglukan P4H® ACUTE! cream paste at least 2–3 times daily (or as needed) in an appropriate layer to the affected area for a maximum duration of 2 weeks.

Ingredients (INCI): Aqua, Zinc Oxide, Neopentyl Glycol Dipelargonate, Cetyl PEG/PPG-10/1 Dimethicone, Triolein, Magnesium Stearate, Gluconolactone, Polyglyceryl-4 Isostearate, Glycerin, Sodium Hyaluronate, Beta-glucan, Zea Mays Starch, Tocopheryl Acetate, C10-18 Triglycerides, Glyceryl Dioleate, Polyvinyl Alcohol, Magnesium Sulfate, Sodium Benzoate, Calcium Gluconate.

The effect of the application of Imunoglukan P4H® ACUTE! cream paste on the clinical status of erythema in skin disease will be assessed by both the physician and the patient/legal representative using a 5-point severity scale (Clinician's Erythema Assessment – CEA) and through the Investigator's Global Assessment (IGA) on a 6-point scale. The tolerability of the cosmetic product Imunoglukan P4H®

ACUTE! cream paste in the selected indications will be assessed by the physician using a 3-point tolerability scale.

Discussion on the design

The multicentre, prospective design of the research provides a basis for obtaining clinically, scientifically, and statistically significant results with the aim of clarifying the impact of the investigated intervention on the primary and secondary objectives. For the clinical evaluation of erythema focused on reducing and alleviating the duration of selected skin problems, a 2-week follow-up period is justified. In addition to confirming the basic hypothesis, the pilot study should also provide data on the tolerability, safety, and potential adverse effects.

Subjects enrolled in the biomedical research will undergo anamnesis data collection during follow-up visits and will continuously complete the relevant questionnaire (Patient Diary).

Project endpoints:

Primary endpoints – to evaluate the clinical effect of the cosmetic product Imunoglukan P4H® ACUTE! cream paste in patients with selected skin dermatoses (diaper dermatitis, perioral dermatitis, neonatal pustulosis) on:

- Clinical assessment of erythema using a 5-point severity scale (Clinician's Erythema Assessment
- Investigator's Global Assessment (IGA) using a 6-point scale

Secondary endpoints – to evaluate the tolerability of the cosmetic product Imunoglukan P4H® ACUTE! cream paste in patients with selected skin dermatoses using a 3-point tolerability scale.

Inclusion criteria

- signed informed consent
- age ≥ 3 weeks
- diagnosis (at least one of the following):
    - perioral dermatitis
    - diaper dermatitis
    - neonatal pustulosis

Non-inclusion criteria

- refusal to provide informed consent
- ongoing application of topical corticosteroids, antihistamines or other immunomodulatory products
- ongoing use of oral corticosteroids or antihistamines
- known intolerance to any components of the investigational product

Exclusion criteria

- application of topical corticosteroids, antihistamines, or other immunomodulatory products
- use of oral corticosteroids or antihistamines
- intolerance to the investigational product

Patient Instruction

The attending physician will instruct the patient/legal representative on the **elimination of irritating factors** (such as soaps, shampoos, bath foams, perfumed wet wipes, sucking on hands/fingers/toys/food, etc.) and on **refraining from using any other products** for the topical treatment of the diagnosed skin condition during the course of the study.

List of data collected from subjects enrolled in the study

Basic Identification Data	○ Patient´s code ○ Patient´s initials ○ Date of birth ○ Date of the CRF / Visit date
Medical History and Demographic data	○ Age ○ Gender ○ Current comorbidities ○ Current treatment of the comorbidities
Diagnostic Procedures	○ Clinical assessment of erythema using a 5-point severity scale ○ Investigator's Global Assessment (IGA) using a 6-point scale ○ Assessment of cosmetic product tolerability using a 3-point scale
Primary Endpoints	○ Evaluation of the clinical status of erythema after treatment ○ Overall severity and improvementof selected dermatoses by the investigator
Secondary Endpoints	○ Evaluation of product tolerability

Visit schedule and assessment timeline

Number of the visit	**V0**	**V1**
Time of the visit	**Initial examination**	**After the disappearance of symptoms,** or **after14 days**
Informed consent	X	
Inclusion/Non-inclusion criteria	X	
Exclusion criteria	X	
Demographic data	X	
Medical history	X	
Comorbidities	X	
Dispensing of medication	X	
Clinical assessment of erythema (CEA)	X	X
Investigator's Global Assessment (IGA)		X
Assessment of tolerability		X
Number of papules in selected dermatoses	X	X
Adverse events		X
Photodocumentation of the affected area	X (**physician**)	X (**physician**)

Patient diary (completed continuously by the patient/parent)	X	X

Required diagnostic procedures

Clinical assessment of erythema (Clinician's Erythema Assessment **– CEA)**

At each visit, the physician will record in the CRF the value based on the Clinical Erythema Assessment (CEA) scale using a 5-point scale:

- 0 = no erythema
- 1 = very mild erythema: light pink
- 2 = mild erythema: pink
- 3 = moderate erythema: red
- 4 = severe erythema: intense red

Investigator's Global Assessment (IGA)

At visits V0 and V1, the physician will record in the CRF the value based on the Investigator's Global Assessment (IGA) using a 6-point scale:

- -1 = worsening
- 0 = no response
- 1 = mild response: 10–30% improvement
- 2 = moderate response: 31–60% improvement
- 3 = excellent response: 61–90% improvement
- 4 = complete response: 91–100% – clear improvement

Assessment of cosmetic product tolerability

At visit V1, the physician will record in the CRF the assessment of tolerability using the following scale:

- 0 = poor
- 1 = good
- 2 = excellent

Adverse event log

In the event of adverse events, the physician will complete the log and record the occurrence of adverse events in the CRF.

Patient diary

Throughout the study, the patient/parent will record selected parameters daily to assess the progress of the skin condition.

Amendments to the Protocol, Other changes in the Conduct of Biomedical Research

Any changes to the protocol will be implemented in the form of a Protocol Amendment. Changes in the conduct of the biomedical research are not permitted.

Personal Data Protection

All patients in this project will be identified using a unique ID. Patient identification using this ID will not be possible. Source data may only be verified by the monitor. The unique ID of a particular patient will be known only to the physician or monitor. Personal identification data included in this project will consist of: date of birth, gender, and patient initials. The nature of personal data identifiers complies with all relevant legislative requirements.