Safety and efficacy from nature

ICHTHYOL® PALE

Active substance for skin and hair

ICHTHYOL® PALE

ICHTHYOL-GESELLSCHAFT manufactures unique raw materials from highly sulfuric and organic matter-rich limestone in GMP compliant production under the umbrella term of Ichthyol substances. Fascinated by the numerous inclusions of prehistoric scale fish in the rock Greek “Ichthys” was combined with latin “Oleum” to the illustrious name of “ICHTHYOL®”.

Chemically regarded Ichthyol substances are sulfonated organic matter-rich limestone of highest purity. Their uniquely high content of organically combined sulphur is indispensable for their therapeutic efficacy.
The Ichthyol substances belong to the best documented active ingredients from nature today. Their versatile actions and their good tolerance are substantiated by clinical and toxicological studies, respectively.

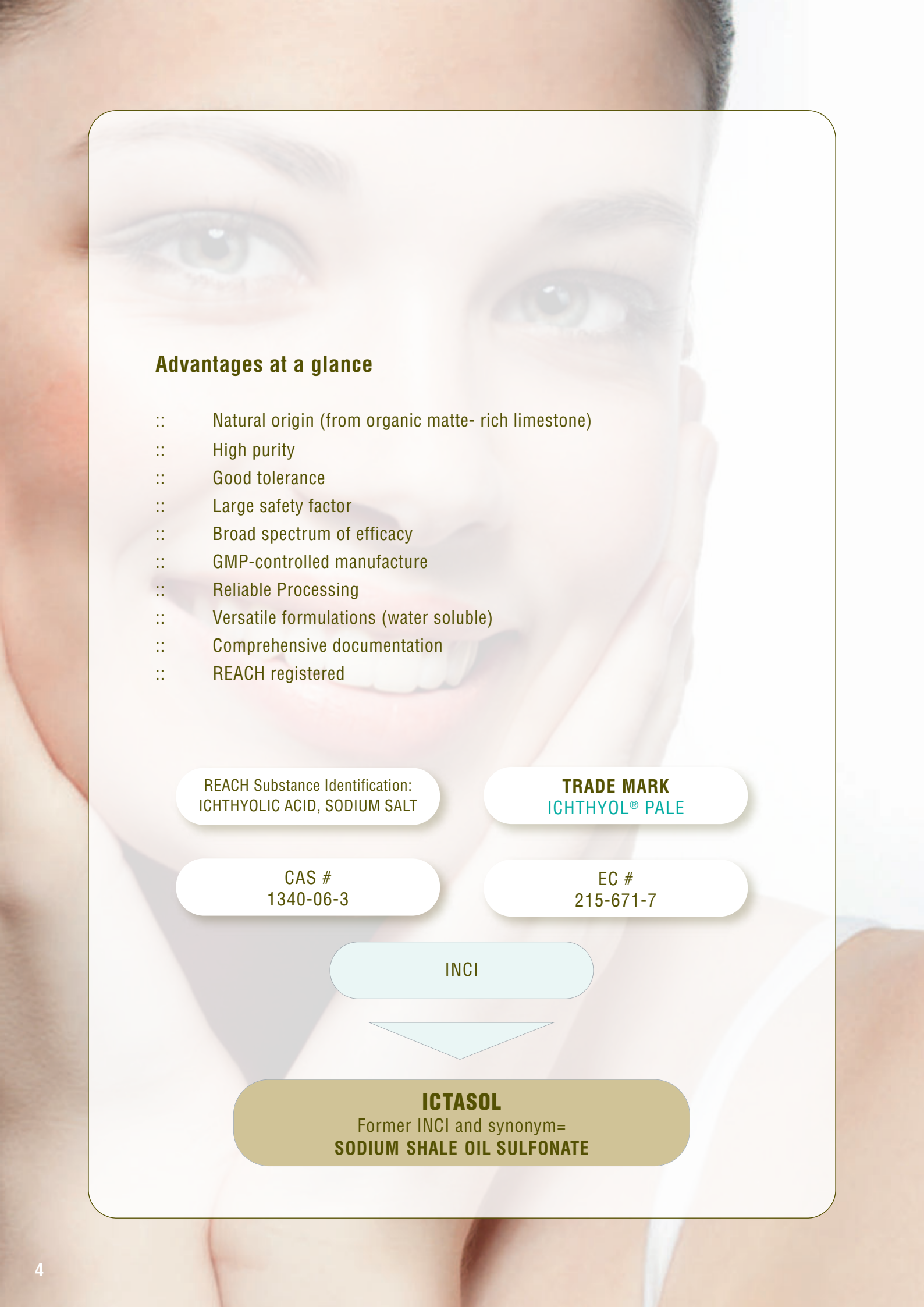
Under the name of ICHTHYOL® PALE a pale ICHTHYOL® substance specially developed for cosmetic application is offered. In hair and skin care the cosmetic agent with the official INCI-name “ictasol” has gained importance worldwide because of its broad action profile. Its benefits in control of severe dandruff and skin blemishes could be proven in a variety of clinical studies. ICHTHYOL® PALE is distinguished by versatile cosmetic formulation possibilities. Manufacture and quality are adapted to the evergrowing legal requirements in order to provide users of our raw material certainty for future utilization.

Convince yourself on the following pages about quality and action mechanisms of a unique raw material.

Thank you for your interest.

Sincerely yours,
ICHTHYOL GESELLSCHAFT

You can find more information under www.ichthyol.com



Advantages at a glance

:: Natural origin (from organic matte- rich limestone)
:: High purity
:: Good tolerance
:: Large safety factor
:: Broad spectrum of efficacy
:: GMP-controlled manufacture
:: Reliable Processing
:: Versatile formulations (water soluble)
:: Comprehensive documentation
:: REACH registered

REACH Substance Identification:
ICHTHYOLIC ACID, SODIUM SALT

TRADE MARK
ICHTHYOL® PALE

CAS #
1340-06-3

EC #
215-671-7

INCI

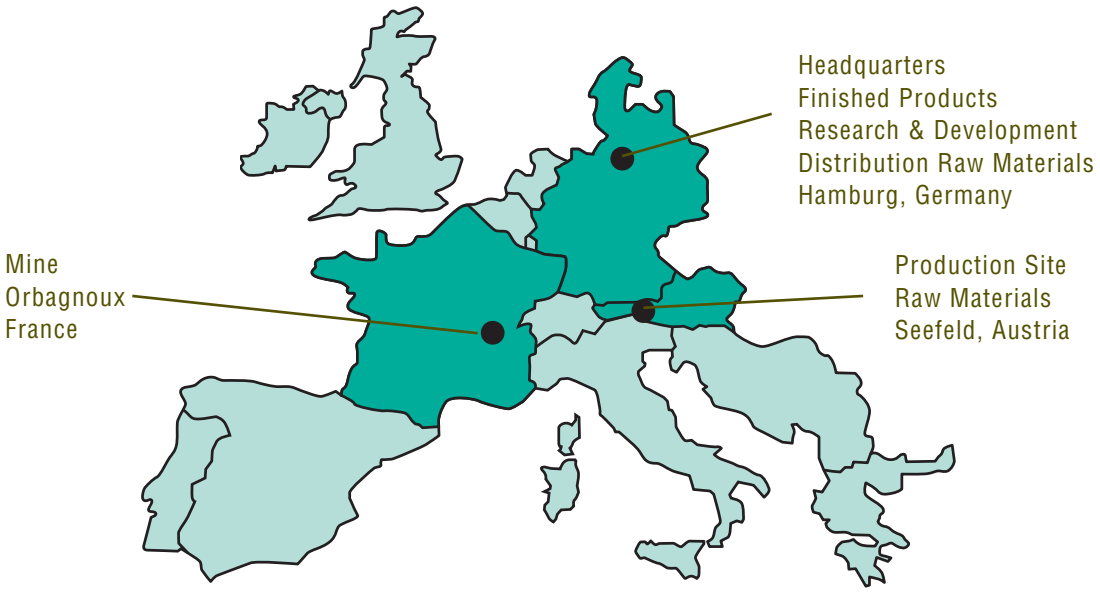
ICTASOL
Former INCI and synonym=
SODIUM SHALE OIL SULFONATE

ICHTHYOL-GESELLSCHAFT:
A story to tell

Founded back in 1884 ICHTHYOL-GESELLSCHAFT today is a renowned address in the dermatological field.
For more than 130 years the family-run company is based mainly on its unique active ingredient Ichthyol that gave the company its name.

Bringing together tradition and progress as well as science and service ICHTHYOL-GESELLSCHAFT offers comprehensive solutions for dermatological needs.

Laboratories and pilot plant capabilities give the company extensive possibilities for research and development.
From the river Rhone in France via the mountains of Austria to Hamburg the substance ICHTHYOL® PALE develops in a multinational cooperation.
The well-tolerated substance of natural origin can be used in hair care products (e.g. for treatment of dandruff) and for skin care as well (e.g. for treatment of blemishes) due to its broad spectrum of efficacy.



FORMULATONS:
Rinse-off: shampoo, rinses
Leave-on: hair lotion

ICHTHYOL® PALE Research - Hair Care/Dandruff

A complex condition requires an inspired answer

Characteristics of Dandruff	ICHTHYOL® PALE takes action[1]
Colonization with bacteria and fungi	Anti-bacterial and anti-fungal action
Skin redness, itching	Soothing, anti-inflammatory action
Greasy scalp and hair	Anti-seborrhoic action

ICHTHYOL® PALE

Take advantage of its broad spectrum of efficacy & compatibility with a variety of substances. **Exemplary shampoo formulation:**

64.1 %	Aqua
19.0 %	Sodium Laureth Sulfate
8.0 %	Potassium Cocoyl Hydrolyzed Collagen
5.0 %	PEG-7 Glyceryl Cocoate
1.0 %	ICTASOL
1.0 %	Sodium Chloride
0.8 %	Sodium Benzoate/Potassium Sorbate
0.5 %	Parfum
0.4 %	Sodium Citrate
0.2 %	Citric Acid

1 Gayko, G.: dealing with dandruff needs integrated approach, Personal Care Magazine, May (2009)
2 Gayko, G.: Sulfonate d'huile de schiste sodique contre les pellicules - Sodium Shale Oil Sulfonate against dandruff, Parfums Cosmétiques Actualités, No. 170, Avril/mai (2003)
3 Gayko, G. *et al.*: The use of a pale type of ICHTHYOL® in cosmetic dermatology, Clinical Dermatology 8 (4), (2006) 243-247

ICHTHYOL® PALE Research - Effect/Dandruff

Comparison with established anti-dandruff agents

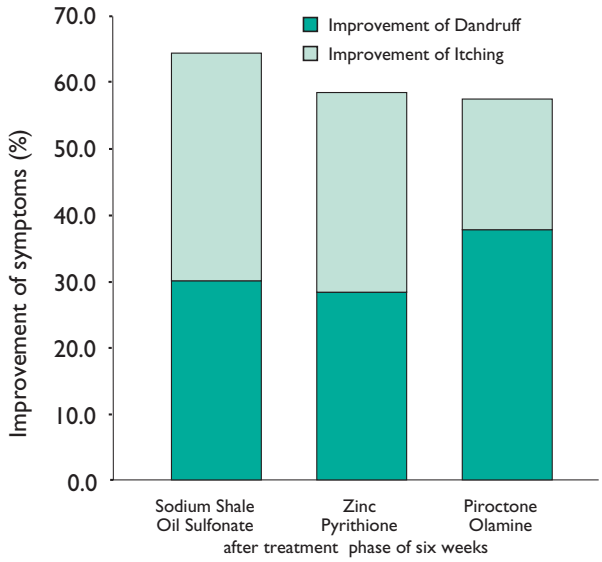


Fig. 1. Excerpt from studies of ICHTHYOL® PALE vs. Zinc Pyrithione and Piroctone Olamine. ICHTHYOL® PALE is superior in improving dandruff and itching due to its multifunctionality.

Dandruff most often comes along with unpleasant concomitant symptoms as skin redness, itching and greasy scalp and hair. ICHTHYOL® PALE is suitable for an all-embracing treatment.

This could be proved in studies in which it was compared with the well known synthetic anti-dandruff agents Zinc Pyrithione and Piroctone Olamine[2].

All findings reflect: ICHTHYOL® PALE is superior due to multifunctionality, good tolerance and long-term safety.

Combination with established anti-dandruff agents

In combination shampoos with potent anti-fungal agents ICHTHYOL® PALE provides valuable additional actions for an exceptional anti-dandruff performance. Faster and broader effects are observed and symptoms concomitant to dandruff are successfully countered[3].

ICHTHYOL® PALE Research - Effect/Dandruff

Comparison with coal tar

Coal Tar, clinically beneficial in the treatment of dandruff without doubt, is known to contain carcinogens.

On account of safety reasons, therefore, Coal Tar has already been banned from uncontrolled use in cosmetics in the European Union.

It could be proved that a safe, well-tolerated and, above all, similarly effective and 'broad spectrum' alternative of natural origin is available with ICHTHYOL® PALE to substitute Coal Tar in dandruff shampoos.[4]
In Europe, this exchange has already been done successfully.

ICHTHYOL® PALE -
well tolerated coal tar
substitute for reformulation

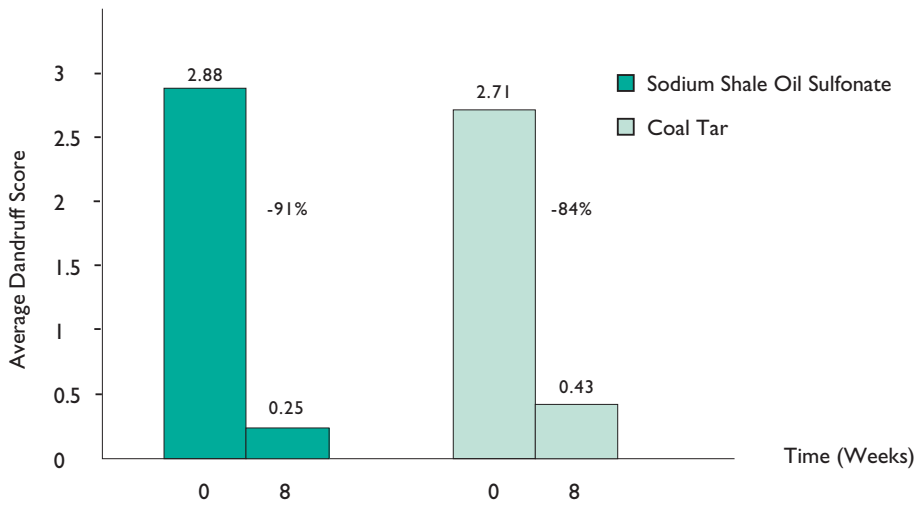


Fig. 2. Excerpt from the comparison study ICHTHYOL® PALE vs. Coal Tar: ICHTHYOL® PALE is as effective as Coal Tar in the reduction of dandruff, however, in contrast to Coal Tar it is safe in long-term treatment.

4 Gayko, G. *et al.*: Antidandruff Efficacy of Sodium Shale Oil Sulfonate versus Coal Tar, Cosmetics & Toiletries 120 (3), (2005) 83-92
5 Reinhard, S. and Warnecke, J., Helles sulfoniertes Schieferöl zur lokalen Behandlung der Acne vulgaris, Der Allgemeinarzt 17, (1995) 182 (engl. translation available)

FORMULATONS:
Clarifying creams, Cleansing milks, Alcoholic-aqueous solutions

ICHTHYOL® PALE Research - Skin Blemishes and pimples

When oil glands are out of control ...

ICHTHYOL® PALE makes no concessions: Threefold action in one ingredient for modern treatment of skin blemishes and pimples. In a study on 101 humans after a treatment period of 6 weeks great improvements in elimination of skin impurities could be observed in nearly 80 % of the cases using a cream containing 1 % of ICHTHYOL® PALE (see exemplary formulation below).

Characteristics of of impure skin	ICHTHYOL® PALE takes action [5]
Overproduction of oil glands	Anti-seborrhoic action
Microbial colonization of oil glands and hair follicles	Anti-microbial action
Inflammations	Anti-inflammatory action

Exemplary cream formulation:

68.3 %	Aqua	1.0 %	ICTASOL
13.0 %	Isopropyl Myristate	0.5 %	Parfum
8.0 %	Cetearyl Alcohol	0.2 %	Sorbic Acid
5.0 %	Propylene Glycol		
4.0 %	Tricetearet-4 Phosphate		

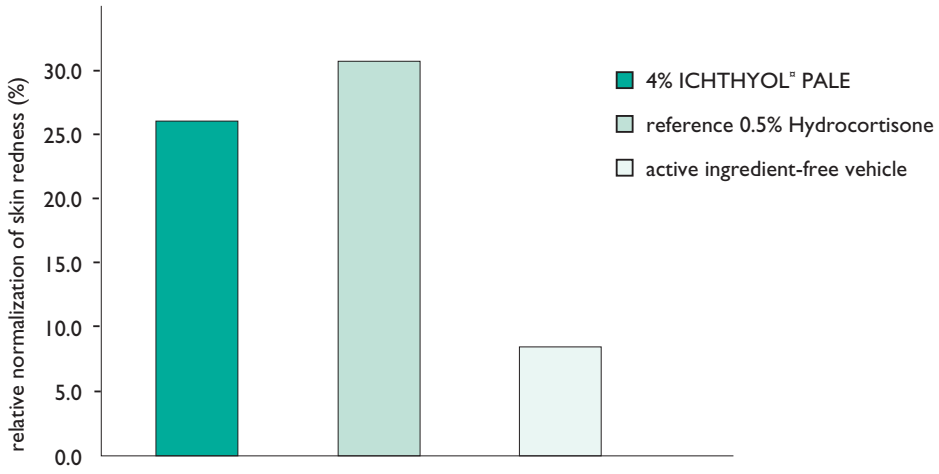
*ICHTHYOL® PALE is added to the water phase containing the hydrophilic compounds

ICHTHYOL® PALE Research – Skin irritations like redness and itching

Inflammatory processes like redness and itching of the skin can be countered excellently by ICHTHYOL® PALE.
The anti-inflammatory action was confirmed recently by means of the UVB erythema test.[6] In the study a cream with 4 % of ICHTHYOL® PALE was compared with the active ingredient-free vehicle and a reference product containing 0.5 % of hydrocortisone as active substance.

ICHTHYOL® PALE in a concentration of 4 % exerts an anti-inflammatory action equivalent to 0.5 % hydrocortisone:

COMPARISON OF SKIN COLOUR 24H AFTER UVB-IRRADIATION



6 Warnecke, J.: Teerersatzstoffe in der Dermatologe und Kosmetologie, Kosmetische Medizin 19(6), (1999) 332 (engl. translation available)
7 Leimbeck, R. and Sonnenschein, B.: Determination of the minimal inhibitory concentration (MIC) towards test strains of different species (1992), unpublished report.
8 Listemann, H. *et al.*: Anti-mycotic activity of sulfonated shale oil. Drug Researcj 43(II), 7 (1992), 784-788.

Strong
&
verified effect

ICHTHYOL® PALE Research - Effect: Bacteria and fungi

EFFECT OF ICHTHYOL® PALE

Micro-organism	MIC* (%)	Inhibiting zone Aqueous solution of 1 % ICHTHYOL® PALE	diameter (mm) Aqueous solution of 5 % ICHTHYOL® PALE	Growth reduction (log CFU)** Serial dilutions of ICHTHYOL® PALE in liquid broth
Staphylococcus aureus	0.039	1.0	2.5	6.5
Propionibacterium acnes	0.039	-	-	-
Malassezia spec.	-	2.0	11.0	-
Candida albicans	0.2-5.1	-	-	3.0-4.9
Dermatophytes *(e.g. Microsporum canis, Trichophyton spec.)*	0.05-0.1	-	-	4.9-5.1

* MIC / Minimum inhibitory concentration
** log CFU / logarithm of colony forming units (log CFU > 3 = strong growth reduction and anti-microbial efficacy)

ICHTHYOL® PALE exhibits anti-microbial actions in all micro-organisms relevant in cosmetically significant skin conditions.

The anti-bacterial and anti-mycetic actions of ICHTHYOL® PALE, expressed by the minimal inhibitory concentration (MIC), inhibiting zone diameters and logarithmic growth inhibition (log CFU), were determined in dilution and plate diffusion test as well as microplate-laser-nephelometry. [7, 8, 9, 10]

[9] Grimm, V. *et al.*: Investigations on the anti-microbial action of pale sodium bituminosulfonate, Biennial Meeting of the German Dermatological Society, Berlin, May 1st-5th. (2001), Poster No.: P201.
[10] Wiegand, C. *et al.*: Assessment of the antimicrobial activity of sodium bituminosulfonate against bacteria, yeast and dermatophytes in vitro, 52nd Scientific Conference of the German speaking Mycological Society (DMykG) e.V., Innsbruck, September 6th-8th (2018), Poster No.: 61 (S1).

ON THE SAFE SIDE
ICHTHYOL® PALE is well tolerated

ICHTHYOL® PALE Research - Safety evaluation

The good tolerance of ICHTHYOL® PALE has been verified in numerous toxicological studies.
ICHTHYOL® PALE showed itself to be well-tolerated both in short-term as well as long-term administration. There was no evidence of any teratogenic, mutagenic or cancerogenic properties.[11]

The safety of a raw material such as ICHTHYOL® PALE is best illustrated by calculating the „margin of safety".
With hair shampoo (rinse-off) and body lotion (leave-on) as formulation examples, safety factors clearly above the required minimum value of 100 result for ICHTHYOL® PALE.

Formulation	Safety Factor (required: ≥ 100)
Shampoo (rinse-off)	230769
Body Lotion (leave-on)	1730

ICHTHYOL® PALE can, therefore, be classified as a safe substance in accordance with the European Regulation on Cosmetic Products.

[11] Cholcha, W. *et al.*: Experimental Studies on the Tolerance of Pale Sulfonated Shale Oil Following Local and Systemic Application, Arzneim. - Forsch./Drug Res. 44(I), 2 (1994) 170

ICHTHYOL® PALE Research - Differentiation from tars

There are still some reports in the scientific literature in which organic matter-rich limestone, such as ICHTHYOL® PALE, are grouped with tars because of their related efficacy and characteristic odour. This classification, however, is wrong.
ICHTHYOL® PALE and tars differ in terms of:

ICHTHYOL® PALE	COAL TAR
From nature Raw material: limestone Processing temperature: <480 °C	From nature Raw material: coal Processing temperature: 1000 °C
Rich in sulphur (11-13.5 %)	Low in sulphur (<1 %)
Water-soluble	Non-water-soluble
Surface-active	Non-surface-active
High purity (<0.1 ppb BaP*)	Severely PAH-contaminated (>5,000,000 ppb BaP*)
Non-mutagenic, Non-cancerogenic	

The high purity of ICHTHYOL® PALE is also confirmed by PAH analyses.
It can be demonstrated with gas chromatography/mass spectrometry that ICHTHYOL® PALE contains only hardly detectable traces of polycyclic aromatic hydrocarbons (regulary less than 0.1 ppb benzo[a]pyrene). These findings coincide with the good tolerance of ICHTHYOL® PALE. In addition, if one considers the active ingredient concentration to be applied, i.e. 0.5 - 5 %, this means that the content of benzo[a]pyrene as leading substance is below the analytical detection limit in the finished cosmetic product.

ICHTHYOL® PALE Manufacture –
Origin and GMP-controlled manufacture

Organic matter-rich limestone

ICHTHYOL® PALE has an an extremely interesting history of development.

In geoscientific terms its origin goes back to deposits of microscopically small algae (phytoplankton) in a special lagoon milieu in the alpine region of the mesozoic era.

Under certain conditions large quantities of organically combined sulphur could be formed in the biomass during biological (anaerobic) degradation of the marine phytoplankton by sulphate reducing bacteria.
By diagenetic processes the periodic deposits developed into finely stratified sedimentary rocks (organic matter-rich limestone) that contain the marine biomass in a solidified form today.

The extraction of suitable organic matter-rich limestone from deposits inside the mountain and the further manufacture of ICHTHYOL® PALE are very complex and technically challenging. At the end of geological processes qualitatively appropriate, highly sulphuric deposits of limestone are hidden hardly accessible inside the mountains and have to be exploited in a complicated system of underground chambers.In the dry distillation process following underground mining the organic matter-rich limestone is gently heated under exclusion of air.

Thereby, biomass present in the rock is decomposed only to such an extent that it can be converted from a solid into a liquid form. The resulting oil is distinguished by a high content of organically combined sulphur (up to 15 %) which is unequalled world-wide.

Distillative refinement

The obtained oil is purified before undergoing further processing. A distillation treatment is carried out in order to remove finely distributed solid particles and high-molecular substances (e.g. polycyclic aromatic hydrocarbons, PAH). Thereby, one obtains a special, low-boiling oil fraction.

ICHTHYOL® PALE

The low-boiling oil fraction is allowed to react with concentrated sulphuric acid in a gentle sulfonation reaction

and is then neutralized with sodium hydroxide solution. The non-polar oil is thereby converted into the water-soluble and surface-active ICHTHYOL® PALE.

Quality Assurance

To constantly obtain a good quality of ICHTHYOL® PALE, it is absolutely necessary to carry out the manufacturing process under exactly defined and controlled conditions in accordance with the Guidelines for Good Manufacturing Practice, GMP.

Our manufacturing site is regularly inspected by health authorities. A corresponding GMP-Certificate is available.

Further information is available from
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