

# Pigmerise™

A safe and effective alternative to treat skin hypopigmentation disorders



## Pigmerise™

Pigmerise™ is a natural phytocomplex derived from black pepper (*Piper nigrum* L.) fruit extract in oleoresin, with high concentration of alkaloids and volatile oils.

Pigmerise™ promotes the melanogenesis and melanocytes proliferation leading to skin repigmentation. Pigmerise™ is indicated for treating different forms of hypomelanosis such as vitiligo, idiopathic guttate leukoderma, piebaldism, hypomelanosis of Ito and other disorders in which there is reduction in melanocytes.

Safety, stability and skin tolerance studies show that Pigmerise™ in Fitalite™ gel cream is a safe alternative for the treatment of hypopigmentation disorders of the skin, with significant results when compared to conventional treatments, sometimes considered controversial.

Pigmerise™ in Fitalite™ gel cream can be used in children and can be applied on sensitive skin and difficult to treat areas such as around the eyes, mouth and genitals.

## Benefits of Pigmerise™

- Pigmerise™ stimulates the melanocytes replication located deeply in the skin and it induces the formation of dendrites. It promotes skin repigmentation
- The liposomal formulation of Fitalite™ allows the Pigmerise™ phytocomplex to be deeply absorbed reaching the melanocytes for a more effective repigmentation process
- Pigmerise™ protects cellular DNA and does not trigger the development of melanoma
- Pigmerise™ is safe and effective with or without UV treatment
- Pigmerise™ is a great step forward to current treatment with psoralens and khellin in vitiligo

## Fagron Innovation in skin repigmentation: Pigmerise™ in Fitalite™

Piperine has been studied for several years and it reveals promising results in the treatment of skin repigmentation. However, it requires high concentrations to increase its effectiveness and requires a prior solubilization in alcohol that can cause skin irritation and reduced compliance to the topical treatment.

Based on new scientific evidence Fagron's R&D team developed Pigmerise™, a natural phytocomplex composed of black pepper (*Piper nigrum* L.) alkaloids and volatile oils for a synergistic effect.

Pigmerise™ is an oleoresin that can be easily compounded in Fitalite™ without the use of alcohol.

Pigmerise™ does not contain preservatives and antioxidants, and allows for fast and safe incorporation into topical formulations.

Pigmerise™ is available exclusively for individualized compounding formulations.

[fagron.gr](http://fagron.gr)



# Scientifically proven pigmentation

## A new approach for the treatment of hypopigmentation disorders

### Piperine + UV *in vitro*<sup>1</sup>

The first studies using piperine in vitiligo treatment investigated the effects of UVA / UVB radiation on the chemical stability of piperine, its melanocyte stimulatory effects and its ability to bind to protein and cellular DNA. It was found that piperine, an alkaloid of black pepper, stimulates replication of melanocytes and induces the formation of dendrites *in vitro*.

The study evaluated 4 groups: A) DMSO for 9 weeks B) Piperine + DMSO for 9 weeks C) Piperine + DMSO for 9 weeks + UV from the 5th week D) Isolated therapy with UV for 5 weeks.

In general, the treatment with piperine and UV enhanced a faster and more persistent color on the skin.

There was no evidence of piperine binding to cellular DNA before or after radiation. Therefore it showed no carcinogenic effects, unlike the results with psoralen + UV.

### Piperine + UV *in vivo*<sup>2</sup>

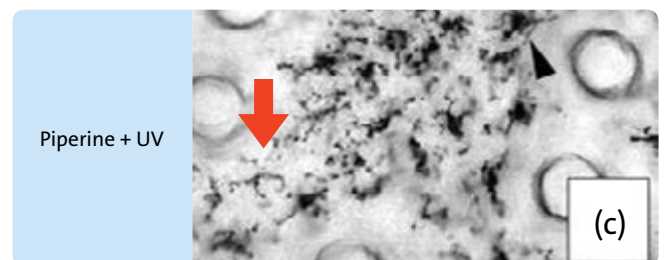
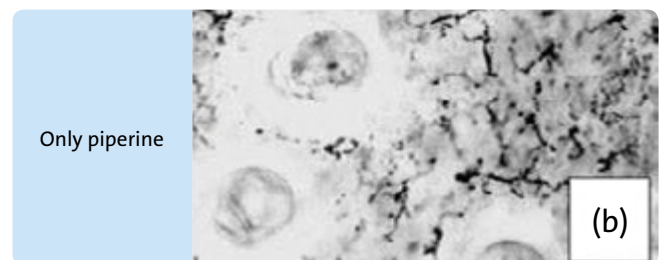
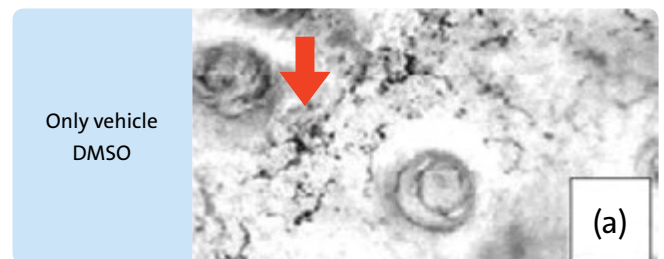
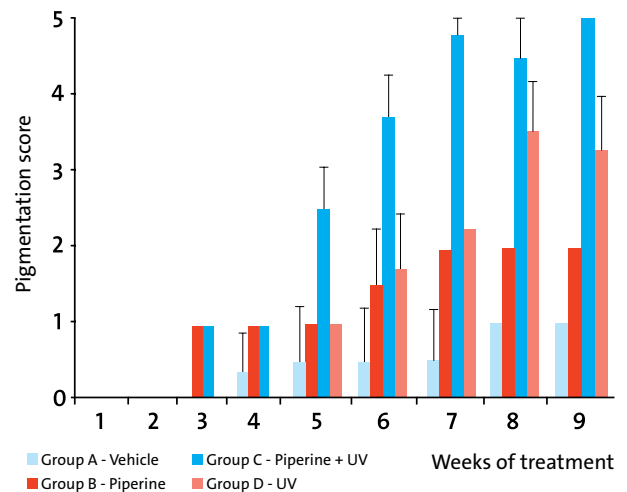
The *in vivo* study evaluated the efficacy of piperine with UV radiation to stimulate pigmentation in a strain of sparsely pigmented mice. The groups were treated with topical application of piperine and piperine derivatives (piperidine alkaloids) in different vehicles for 4 weeks without UV radiation. After, they received 8 UV radiation sessions (15% UVB, 85% UVA). The study evaluated 3 groups with: DMSO, piperine, UV radiation and piperine.

After 2 UV radiation sessions, there was evident pigmentation in mice treated with piperine and a degree of pigmentation in mice treated with DMSO. After 8 UV radiation sessions there was evident increase pigmentation in mice treated with piperine, light pigmentation in mice treated with DMSO and less uniform and intense pigmentation in mice treated with UV only. (Figure 1)

The study showed that piperine derivatives (piperidine alkaloids) from black pepper not only stimulates the formation of new melanocytes but also stimulates melanogenesis and thus the new melanin synthesis.

Topical treatment in combination with low dose UV significantly enhances the pigmentation response. The results were noticeably better when compared to conventional therapies for vitiligo, when applied in mice.

Evaluation of piperine use in radiation UVA/UVB



Histology in skin treated without piperine (a) with piperine (b) and piperine + UV (c). Magnification 200x. Melanocytes appear as dark irregular cells (see arrows). Treatment with piperine increases the number of melanocytes (versus b), while the addition of UV increases the number of melanocytes and the production of pigments, making them appear darker. (Arrow in c).Circular structures are hair follicles



## Efficacy and safety in the hypopigmentation disorders<sup>3</sup>

A study was conducted in Italy for 6 months, with 75 patients (18 to 53 years old), affected by vitiligo with varied extensions ranging from 5% to 35% of the total skin surface.

Evaluation 2 groups of patients:

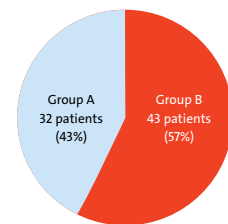
**Group A (32 patients)** - received treatment cream with piperine + 3 weekly 311 nm UVB phototherapy sessions.

**Group B (43 patients)** - received only cream with piperine.

### Results

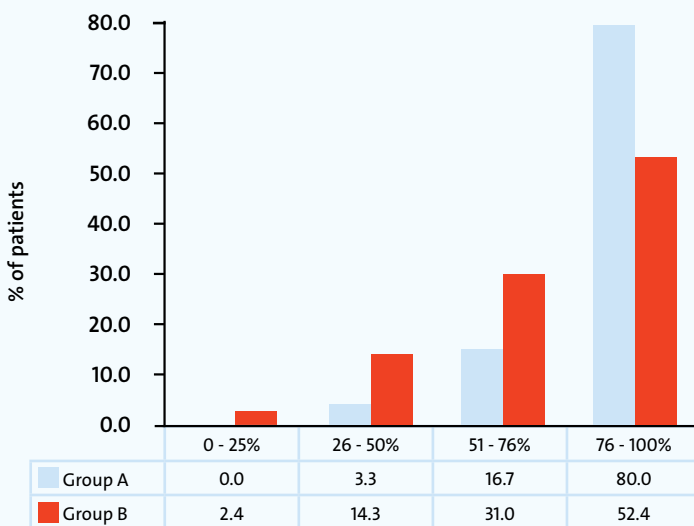
- In group A 80.0% of patients had 76-100% repigmentation
- In group B 52.4% of patients had 76-100% repigmentation
- More than half of patients in group A showed signs of repigmentation from the first month, while in group B this percentage was reached between the 2nd and 3rd month
- Only one patient belonging to the group B showed lower repigmentation than 25%
- The repigmentation rate obtained remained stable even after 3 and 6 months after the end of the protocol

### Evaluation of patients



- Cream with piperine + 3 weekly sessions of phototherapy
- Cream with piperine

### Repigmentation rate at the end of study



Repigmentation of halo nevus in 6 months of treatment

# Clinical evidence

## Results after 6 months of treatment

### Group A

80.0% of patients had from 76% to 100% repigmentation



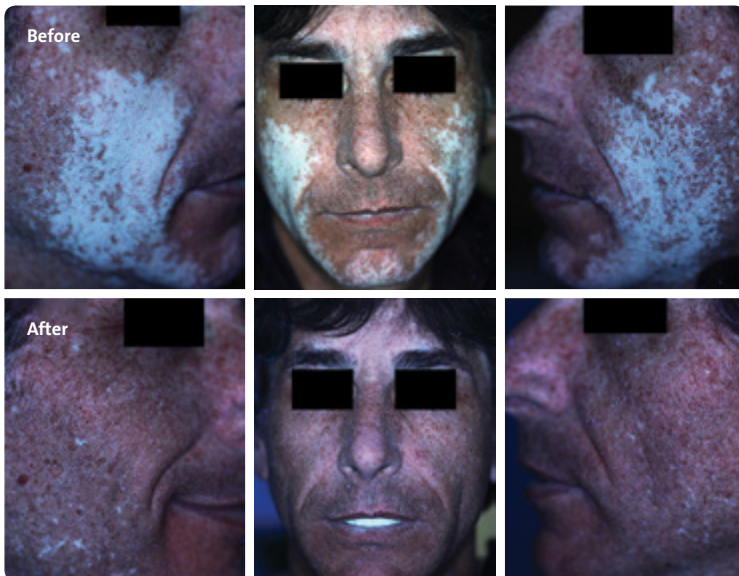
Patient with high level of repigmentation\*



Patient with pigmentation rate of 93%\*

### Group B

52.4% of patients had from 76% to 100% repigmentation



Patient with pigmentation rate at 95%\*



Patient with full repigmentation in the eyelids\*

\* Pictures were taken in WOOD lights

### Conclusion

The study carried out with 75 patients, demonstrated that the daily topical treatment with piperine cream has proved highly effective in inducing pigmentation in affected areas, with or without UV stimulation.

# Pigmerise™ in Fitalite™

## Rx/

Cream for skin pigmentation	
Pigmerise™	20%
Fitalite™	qsp 50 g

**Dosage:** Topical lesions once at night

The recommended dosage of Pigmerise™ is adequate to obtain the pigmentation result as referenced studies.

Dispense in airless packaging.

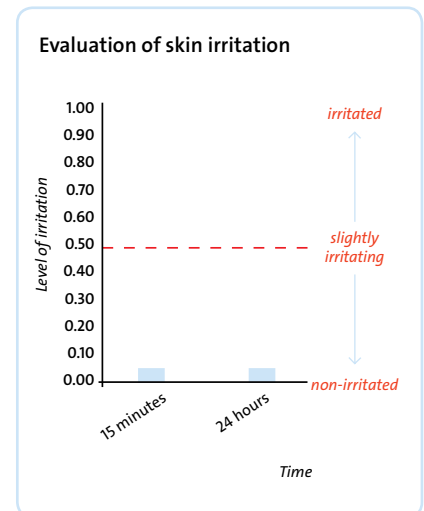
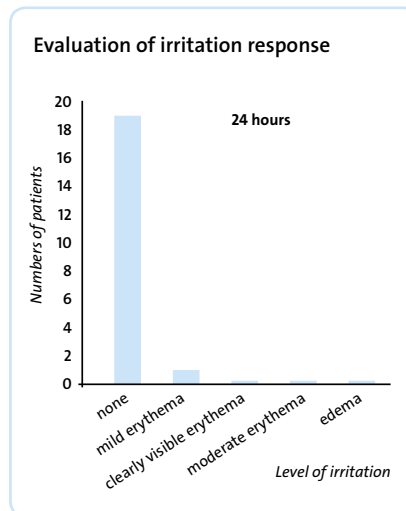
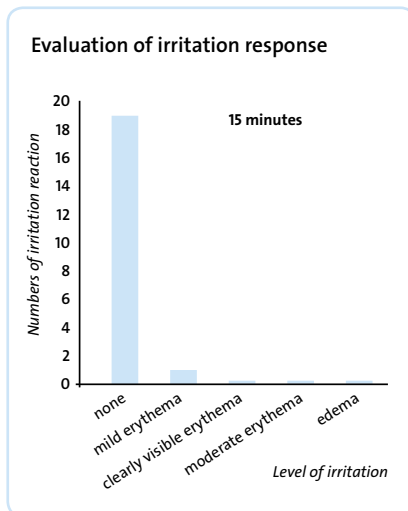
## Use recommendations

- The formulation can be used for the whole year
- Apply a thin layer enough to cover the total extent of the lesion
- Apply the formulation firstly in areas where the skin is thicker. Then, a thin layer on the most sensitive areas of skin such as the area around the eyes, mouth and genitals
- For application of other products or cosmetics, it is recommended to wait for 20 minutes after using the gel cream with Pigmerise™
- Before exposing to phototherapy (UV radiation), the treated area should be washed well because Pigmerise™ also acts as a UV inhibitor
- Attention: Pigmerise™ may stain fabrics

## Safety of Pigmerise™ in Fitalite™

The study<sup>4</sup> conducted by the Cosmetology Center at the University of Ferrara, Italy evaluated the formulation Pigmerise™ in Fitalite™. 20 healthy volunteers received Pigmerise™ in Fitalite™ under occlusive conditions.

The evaluation of the skin irritation reaction was classified according to the degree: mild, clearly visible, and from moderate to severe. The observations were after 15 minutes and 24 hours after the removal of the patch.



The study concluded that the formulation of Pigmerise™ and Fitalite™ showed no irritation response, such as erythema and/or skin edema in the healthy volunteers evaluated.

## Stability of Pigmerise™ in Fitalite™

The study<sup>5</sup> conducted by the Cosmetology Center at the University of Ferrara, Italy evaluated the formulation Pigmerise™ in Fitalite™ concluding that the formulation meets the intended physical and chemical quality standards as well as functionality and aesthetics when stored at room temperature for 6 months.

# Vitiligo treatment

## Vitiligo and compounding

### FAGRON ADVANCED DERMA CONVENIENCE PACK PF

Fagron Advanced Derma Convenience Pack PF offers a quick, safe and convenient solution for efficient compounding of a topical pharmaceutically stable extemporaneous preparation. Fagron Advanced Derma Convenience Pack PF contains pre-weighed Pigmerise™ 20%, pre-weighed Fitalite™, a dispensing container for the patient and compounding instructions.



## Natural gel cream base

### FITALITE™

- Natural, ultra-light, hydrophilic gel cream
- Contains natural emulsifying phytosomes: triglycerides from linoleic and oleic acids are at high concentrations in the phytosomes
- Elegant, light, non-greasy skin feel
- Gentle hydration effect
- Non-comedogenic
- Compatible with a broad range of APIs and DCIs
- Especially suitable for oily, balanced and affected skin



## Innovative alkaloid phytocomplex

### PIGMERISE™

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- 1 Soumyanath A, Venkatasamy R, Joshi M, Faas L, Adejuyigbe B, Drake AF, Hider RC, Young AR. Uv Irradiation affects melanocyte stimulatory activity and protein binding of piperine. *Photochem Photobiol*, 2006 Nov-Dec;82(6):1541-8.
- 2 Faas L, Venkatasamy R, Hider RC, Young AR, Soumyanath A. In vivo evaluation of piperine and synthetic analogues as potential treatments for vitiligo using a sparsely pigmented mouse model. *Br J Dermatol*. 2008 May;158(5):941-50.
- 3 G. Menchini, C. Comacchi. Testing a piperine cream with and without ultraviolet B phototherapy in 75 patients affected by bilateral vitiligo, GISV- Italian Group for the Study and Treatment of Vitiligo, 2009.
- 4 Prof. Simonato Michele. Patch test occlusivo Pigmerise™ in Fitalite™, Centro di cosmetologia Università di Ferrara, 2015.
- 5 Prof. Manfredini Stefano. Studio di stabilità di formulazioni cosmetiche Pigmerise™ in Fitalite™, AmbrosiaLab srl, Centro di cosmetologia Università di Ferrara, 2016.

Disclaimer: While a great deal of effort has been spent to ensure the accuracy of the dosages and formulations contained herein, no claims are made as to the uses, safety, efficacy or bioavailability of these recommendations. The content of this table cannot be construed as being a (medical) advice, recommendation or opinion. Medical professionals, doctors and compounding pharmacists using this information are advised to do so solely if appropriate in their own professional opinion and judgement. Fagron does not accept and cannot be held responsible or liable in any case for the formulation or information contained herein.