PIGMERISE™

Pimenta negra na pigmentação cutânea

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DESCRIÇÃO

O Pigmerise™ é um fitocomplexo obtido dos frutos da pimenta negra (*Piper nigrum L.*) padronizado, mínimo 20% de piperine e 10% de óleos voláteis.

MECANISMO DE AÇÃO

Pigmerise™ aumenta a dispersão da melanina levando ao escurecimento dos melanóforos (células contendo grânulos de melanina) que podem dispersar-se ou concentrar-se, determinando assim modificações na cor da pele. Além disso, estimula a proliferação de melanócitos e a formação de dendritos, responsáveis por injetar os grânulos de pigmento levando à pigmentação. Estas propriedades conferem à Pigmerise™ uma alternativa ao tratamento de vitiligo e a outros transtornos de despigmentação cutânea.

INDICAÇÕES

- Vitiligo;
- Hipopigmentação causada por luz pulsada intensa (IPL);
- Hipomelanose iatrogênica, gutata idiopática (sardas brancas);

DOSE USUAL

Recomendação tópica de 20% de Pigmerise™ ao dia.

SUGESTÕES DE FÓRMULAS

**Pigmerise™** (*Piper nigrum L.*) ............... 20%
Creme Adimax qsp ...................................... 15g

**Modo de uso:** aplicar sobre as regiões afetadas no período noturno ou conforme orientação do prescritor.

+ **Ginkgo biloba** (ext. seco - 24% ginkgolídeos) ...... 60mg

**Modo de uso:** 1 dose, 2 vezes ao dia.
**Indicação:** tratamento do vitiligo.

**Pigmerise™** (*Piper nigrum L.*) ............... 20%
Fitalite qsp ............................................. 15g

**Modo de uso:** aplicar sobre as regiões afetadas no período noturno ou conforme orientação do prescritor.

**Indicação:** estímulo da repigmentação cutânea.

PRINCIPAIS REFERÊNCIAS


Testing a piperine cream with and without ultraviolet B phototherapy in 75 patients affected by bilateral vitiligo.

The bilateral vitiligo vulgaris (VVB) is an autoimmune disease with clinical course somewhat unpredictable. It affects about 1% of the population without significant differences of race and sex. To date there is no universally accepted effective treatment. Based on more than 10 years of study and treatment of these patients and the observations on piperine in the international literature (1-4), we decided to use a cream with the active principle Piperine to evaluate their effectiveness. The proposed wording for vititan, the name of the cream has been developed around the piperine based on observing the team at King's College London who had tested on animal model the efficacy of the extract of Piper nigrum as a stimulator of melanocytes (1). In this work, mice were treated with piperine in health with and without ultraviolet irradiation, which is why we have decided to experiment with and without ultraviolet B irradiation 311nm, now the gold standard of treatment of vitiligo.

Patients: 75 patients affected by SV underwent topical treatment with piperine cream. Of the 75 patients 39 were males and 36 females aged between 18 and 53 years. The extension of vitiligo ranged between 5 and 35% of the total skin surface. 32 patients (group A) carry 311nm UVB phototherapy, but the other 43 patients not subjected to any form of phototherapy (group B). Patients enrolled in this open study should satisfy the following rules:

Inclusion criteria:
1. SV with an extension from 5 to 50% of the total skin surface;
2. Aged between 18 and 65;
3. Compilation of written informed consent.

Exclusion criteria:
1. SV with an area greater than 50% of the total skin surface and other forms of vitiligo (seborrheic, segmental, etc.);
2. Age outside the range between 18 and 65;
3. Serious local infection;
4. Specific therapies carried out continuously in the two months preceding the enrollment phase.
5. Pregnancy

During the first visit in addition to completing the clinical pictures were made (with a particular flash to fluorescent lighting and ambient lighting) for an objective proof of the initial clinical picture and provided all information relating to therapy. All patients had given informed consent prior to treatment also includes the possible alternative treatments and possible side effects and patients recruited for the written declaration that they were not pregnant. None of the patients had undergone in the two months prior to other drug continuous systemic treatment, topical and / or physical vitiligo. Some patients (3 men and 4 women and 5 men in Group A Group B) were used occasionally in the two months prior to topical corticosteroids. Similarly prohibited was any other medication and / or physically during and after a minimum of two months from the end of the protocol. The patient history is another important feature, it is essential to discuss the expectations of the patient, medication taken on, assessing the presence of scars, keloids, and local infection, the immune status of patients, patient's habits than the exposure the sun.

The protocol provided for a single daily application of the cream in the morning to piperine for six consecutive months. Patients were visited and photographed at the time of first visit and every month until the end of the treatment protocol. Patients were visited and photographed in each patch; Through a morphometric evaluation of the spots using a dedicated software (DDAX-MIPS) were then determined the percentage of repigmentation of each individual at intervals of photography. The percentage of repigmentation refers therefore to the extension of vitiligo as a percentage of taxable value. For ease of viewing and conformation studies in this field we divided the percentage of repigmentation in 4 values: 0 to 25% from 26 to 50% from 51 to 75% and finally 76 to 100%. With regard to phototherapy, all patients in group A performed the standard protocol for UVB phototherapy. The study lasted 10 months, from July 2008 to May 2009.

Of the initial 75 patients completed the study 3 did not accurately and were therefore eliminated from this report, two have performed occasionally (one in group A and one from group B) applying the cream for reasons other than itself, a patient but did not show the last two controls (group B).
No patient experienced acute or chronic side effects both locally and in general within six months of experimentation. Known only to report a burning sensation and transient erythema at the application without the skin around the lips and eyelids. The feeling lasted from 5 to 30 minutes and was quite bearable, nothing to see on other skin areas. Consequently, patients in the study of which 72 are: Group A is formed by 30 individuals, 12 males and 18 females while the group B 42 patients including 25 males and 17 females. The percentage of repigmentation obtained at the end of 6 months of treatment is shown in Figure 1. As you can see the results are very good with a repigmentation of between 76 and 100% in 80% (24 patients) in group A and 52.4% (22 patients) of group B. If we look at the trend over time of two groups, and relatively Figure 2 for group A and Figure 3 for group B, we see a fairly regular pattern of repigmentation in the two groups, with significant prevalence and speed improvements for group A. Only one patient showed repigmentation of 72 less than 25% belonged to group B. Over 50% of patients in group A began to show signs of repigmentation from the first month, while group B this percentage has been reached between the 2nd and 3rd month. The percentage of repigmentation obtained remained stable even after 3 and 6 months after the end of the protocol. The cream in Vittan monoapplicazione daily, has proved highly effective in inducing repigmentation of vitiligo affected skin areas with and without stimulation ultraviolet B 311 nm. The patient compliance was excellent and only transient burning sensations were complained by some patients especially during the implementation of the lips and eyelids. Repigmentation rates were extremely positive, although as always, the face and chest have responded faster and more complete patches of the limbs. We believe that both ultraviolet treatment without the cream vititan is the real novelty in the treatment of vitiligo.

Amides from *Piper nigrum L.* with dissimilar effects on melanocyte proliferation in-vitro.

Melanocyte proliferation stimulants are of interest as potential treatments for the depigmentary skin disorder, vitiligo. *Piper nigrum L.* (Piperaceae) fruit (black pepper) water extract and its main alkaloid, piperine (1), promote melanocyte proliferation in-vitro. A crude chloroform extract of *P. nigrum* containing piperine was more stimulatory than an equivalent concentration of the pure compound, suggesting the presence of other active components. Piperine (1), guineensine (2), pipericide (3), N-feruloyltyramine (4) and N-isobutyl-2E,4E-dodecadienamide (5) were isolated from the chloroform extract. Their activity was compared with piperine and with commercial piperlongumine (6) and safolie (7), and synthetically prepared piperettine (8), piperlonguminine (9) and 1-(3, 4-methylenedioxyphenyl)-decane (10). Compounds 6-10 either occur in *P. nigrum* or are structurally related. Compounds 1, 2, 3, 8 and 9 stimulated melanocyte proliferation, whereas 4, 5, 6, 7 and 10 did not. Comparison of structures suggests that the methylenedioxyphenyl function is essential for melanocyte stimulatory activity. Only those compounds also possessing an amide group were active, although the amino component of the amide group and chain linking it to the methylenedioxyphenyl group can vary. *P. nigrum*, therefore, contains several amides with the ability to stimulate melanocyte proliferation. This finding supports the traditional use of *P. nigrum* extracts in vitiligo and provides new lead compounds for drug development for this disease.

UV irradiation affects melanocyte stimulatory activity and protein binding of piperine.

Piperine, the major alkaloid of black pepper (*Piper nigrum L.*; Piperaceae), stimulates melanocyte proliferation and dendrite formation in vitro. This property renders it a potential treatment for the skin depigmentation disorder vitiligo. However, piperine does not stimulate melanin synthesis in vitro, and treatments based on this compound may therefore be more effective with concomitant exposure of the skin to ultraviolet (UV) radiation or sunlight. The present study investigated the effect of UVA and simulated solar radiation (SSR) on the chemical stability of piperine, its melanocyte stimulatory effects and its ability to bind protein and DNA. Chromatographic and spectroscopic analysis confirmed the anticipated photoisomerization of irradiated piperine and showed the absence of any hydrolysis to piperinic acid.
Isomerization resulted in the loss of ability to stimulate proliferation of a mouse melanocyte cell line, and to bind to human serum albumin. There was no evidence of DNA binding by piperine either before or after irradiation, showing the absence of photoadduct formation by either piperine or its geometric isomers. This is unlike the situation with psoralens, which form DNA adducts when administered with UVA in treating skin diseases. The present study suggests that exposure to bright sunlight should be avoided both during active application of piperine to the skin and in the storage of piperine products. If UVA radiation is used with piperine in the treatment of vitiligo, application of the compound and irradiation should be staggered to minimize photoisomerization. This approach is shown to effectively induce pigmentation in a sparsely pigmented mouse strain.

**Melanogenesis stimulation in murine B16 melanoma cells by Piper nigrum leaf extract and its lignan constituents.**

A methanolic extract from the leaves of *Piper nigrum* L. showed a significant stimulatory effect on melanogenesis in cultured murine B16 melanoma cells. Activity-guided fractionation of the methanolic extract led to the isolation of two known lignans, (-)-cubebin (1) and (-)-3,4-dimethoxy-3,4-desmethyleneoxycubebin (2), together with a new lignan, (-)-3-desmethoxycubebinin (3). Among these lignans, 1 and 2 showed a significant stimulatory activity of melanogenesis without any significant effects on cell proliferation.

**Mediation of cholinergic-piperine like receptors by extracts of Piper nigrum induces melanin dispersion in Rana tigerina tadpole melanophores.**

AIM: The present study was carried out to determine the effects of lyophilized dried fruit extracts of *Piper nigrum* and pure piperine on the tadpole melanophores of frog *Rana tigerina* which offer excellent in vitro opportunities for studying the effects of pharmacological and pharmaceutical agents. The nature of specific cellular receptors present on the neuromelanophore junction and their involvement in pigmentary responses has been explored. MATERIAL: Effects of lyophilized extracts of *P. nigrum* and pure piperine were studied on the isolated tail melanophores of tadpoles of the frog *R. tigerina* as per the modified method. RESULTS: The extract of *P. nigrum* and its active ingredient piperine caused significant melanin dispersal responses leading to darkening of the tail melanophores, which were completely antagonized by atropine and hyoscine. These per se melanin dispersal effects were also found to be markedly potentiated by neostigmine an anticholinesterase agent. CONCLUSION: It appears that the melanin dispersal effects of the extracts of *P. nigrum* and pure piperine leading to skin darkening are mediated by cholinergic muscarinic or piperine-like receptors having similar properties.
REFERÊNCIAS


