Clinical study on the efficacy and tolerability of a cream for local use in the treatment of psoriasis

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Introduction

Psoriasis is a widespread disease that affects 2-3% of the world population. Although it has been known for 2000 years, its pathogenetic mechanisms have not been clarified yet. Certainly, the pathogenesis is complex and multifactorial. First of all, genetic factors come into play: the incidence of the disease has increased in HLA-CW6 and / or HLA-DR7 positive individuals, even if the penetration of the genes appears to be quite low and their expression irregular.

In any case, 36% of patients show a predisposition to the disease, considering that in their family history there is at least one relative affected by psoriasis. The pathogenesis of the disease highlights both an altered immune response and a dysregulation of the proliferation of keratinocytes.

On the one hand there is overproduction of self-antigens, and production of pro-inflammatory cytokines, such as TNF-alpha and IL-beta (1,2), by helper T cells, and subsequently, of inflammatory cytokines, such as interferon-gamma, and IL -8 by effector T lymphocytes (3.4). IL-8 supports epidermal hyperproliferation and induces chemotaxis of mononuclear blood elements (neutrophils, lymphocytes and NK-T) - (5,6,7).

A vicious cycle is created that preserves the hyperproliferation of keratinocytes and inflammation. Together with the hyperproliferation of keratinocytes a local alteration of angiogenic balance occurs induced by over-production of angiogenic growth factors such as vascular VEGF and bFGF (8,9); other growth factors, such as EGF (10) and amphiregulin (11,12), as well as an inhibitor of apoptosis, such as IL-15 (13,14) are overexpressed.

Furthermore, a hypo-expression of certain molecular pathways, involved in neuro-ectodermal differentiation, such as the Delta/Notch pathway, involves abnormal hyperproliferation, due to de-regulation of the program of epidermal differentiation (15).

Taking into account the complexity of the pathogenetic mechanisms involved and the fact that current medical treatments of psoriasis show rather limited efficacy, a cosmeceutical product has been created aimed at restoring the physiological balance

of the skin altered in such a condition. Considering that in the pathogenesis of psoriasis some mediators play a significant role in promoting inflammation and protecting the immune system, a product has been developed that contains: Boswellia serrata, 18-beta glycyrrhetinic acid, extract of Zanthoxylum alatum, 7-dehydrocholesterol, vitamin E and an extract obtained from fertilized Zebrafish eggs taken at specific times and made up of about 99% proteins and 1% of nucleic acids.
The rationale of the above composition is based on the following considerations: a) the boswellic acids obtained from Boswelia serrata have shown to inhibit 5-lipoxygenase, which is capable of inhibiting the production of the usual mediators of both acute (leukotriene LTB4) and chronic (leukotrienes LTC4, LTD4, LTE4) inflammation with consequent reduction of the inflammatory response, typical of immune and allergic reactions (16). b) when administered locally, 18-beta-glycyrrhetinic acid has shown a significant anti-inflammatory activity due to inhibition of 11-beta-hydroxysteroid dehydrogenase inside tissues, which hampers the natural conversion of cortisol from inactive to active form: by this enzyme interaction, glycyrrhetinic acid prolongs the normal anti-inflammatory activity of cortisol normally released within tissues due to inflammation (17,18). c) The extract of Zanthoxylum alatum has been known for a long time for its properties against itching, due to its active moiety (alkylamides: hydroxy-alpha/beta/gamma-sanshools), reported by several authors (19, 20). d) 7-dehydro-cholesterol, the precursor of vitamin D3, which is converted to vitamin D3 with beneficial effect shown in patients affected by psoriasis (21, 22, 23) as a result of everyday exposure to sunlight. e) Vitamin E, has been known for a long time for its nourishing and protecting action on the skin; it is useful for keeping the skin hydrated and healthy. f) fertilized Zebrafish egg extract containing proteins conserved during phylogenesis (24) and collected at specific times: they have proven to be able to slow down an abnormal proliferation of pathological cell clones, inducing their differentiation or apoptosis, by regulating the basic molecules of the cell cycle, such as p53 or pRb (25,26,27,28,29,30,31,32).

The purpose of this study is to clinically verify if the above mentioned product is able to improve the skin imbalance, due to psoriasis, by reducing the symptoms and the skin lesions caused by this disease.

Materials and Methods

A clinical study has been carried out on the efficacy and tolerability of a product in the treatment of psoriasis. This product contains all the ingredients listed in the introduction in the following concentration: boswellic acids: 1.5%; 18 beta-glycyrrhetinic acid: 1%; extract of Zanthoxylum alatum: 1%, and 7-dehydro-cholesterol: 0.0002%; protein extract of zebrafish eggs: 0.02%.
20 patients affected by various forms of psoriasis have been enrolled:

psoriasis patches in a limited or widespread area,
psoriasis of the scalp,
inverse psoriasis affecting the perianal region,
pustular psoriasis.

20 patients were treated for one month with the product in question.
The treatment consisted in applying the cream twice daily (morning and evening) on the skin lesions. The treatment involved all the lesions appeared in each single patient, except for one case, where the most widespread lesion has been treated by comparing it with the untreated lesions after the treatment (besides the lesions before treatment).

The data on the tolerability and efficacy of the product were collected according to certain standards and considered the following characteristics of the lesions: size and number of lesions, erythema, and desquamation.

Every clinical feature has been evaluated in a four degree scale; this scale also collects the subjective judgment of patients on the intensity of itching as well as on the degree of tolerability and efficacy of the product. At the end of the monitoring visit the dermatologist has given his/her assessment on the tolerability and efficacy of the product based on his/her clinical judgment.
Each patient signed the informed consent form.
The examinations for each patient were three: one at the beginning, when s/he was explained the necessary methods of treatment, the recommendation to stop it in cases of adverse reactions and how to contact a doctor during the treatment, if necessary.

At the first examination a photo was taken to identify the condition of lesions before treatment.
The second examination was made 15 days after the first clinical evaluations on the efficacy and tolerability to treatment. Therefore, during this examination the data collection form was filled out and the doctor expressed his/her opinion on the clinical efficacy and tolerability of treatment.

The third examination took place after thirty days: the aim was to evaluate the efficacy and tolerability at the end of the study according to the methods already described for the second examination.
At the end of this examination a second photograph was taken to compare it with the first photograph taken before treatment in order to visually observe the results achieved.

Results

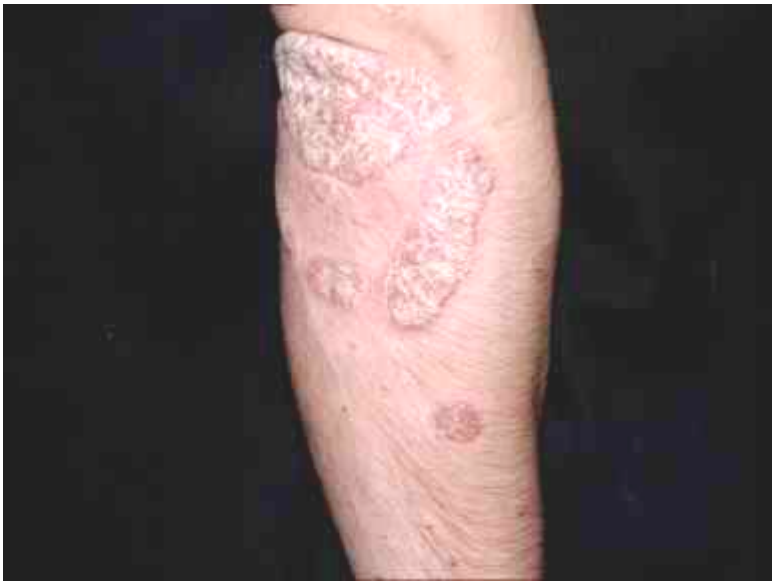
All 20 patients accepted the treatment and regularly underwent the 3 scheduled examinations: all the patients were monitored within this study, so the clinical evaluation included 100% of the treated population.

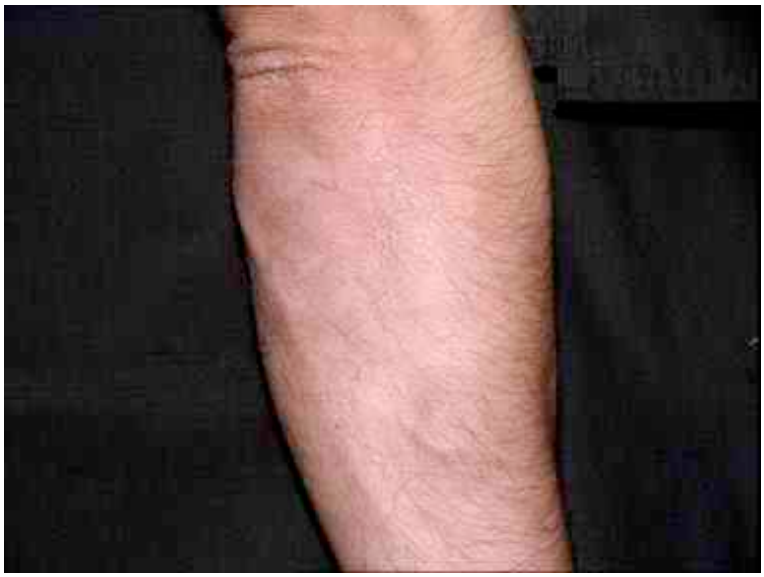
4 male patients and 6 female patients were treated: the average age was 52 years (S.D.: 19,7). Among these, 15 showed psoriasis patches in areas of the body more or less widespread; 2 of them showed a scalp psoriasis; another 2 showed an inverse psoriasis and 1 of them showed a pustular psoriasis.
The excellent efficacy of the product has usually been confirmed by both patients and physicians in 18 cases out of 20 (90%). Two cases (1 case of psoriasis patches on the elbows and 1 case of inverse psoriasis) showed complete disappearance of patches and disorders 30 days later.
In the remaining 16 patients the improvements concerned a reductions of hyperkeratosis, desquamation, erythema and itching (completely disappeared in 8 cases).
Moreover, in 7 cases of psoriasis patches, besides an improvement of symptoms related to individual lesions, there has been a reduction in their number. The clinical improvement of these parameters occurred in about ten days and was therefore already highlighted in the first medical examination.
In two cases the efficacy was considered too weak. However, in these two patients, affected by psoriasis patches, the emotional aspects (anxiety neurosis and personality disorders) were very evident. Tolerability was assessed as excellent in 18 patients (90%), whereas it was assessed as less satisfactory by the two patients showing evident emotional aspects.

There were no adverse reactions of any kind: in two patients there was a slight increase in itching and erythema in the first two days of treatment, which was followed, however, by a rapid reduction of symptoms. Therefore, the product analyzed in this study has shown an excellent tolerability and efficacy in the treatment of psoriasis in 90% of cases, even in patients affected by severe and widespread lesions, who had shown poor healing following other treatments on the market nowadays .

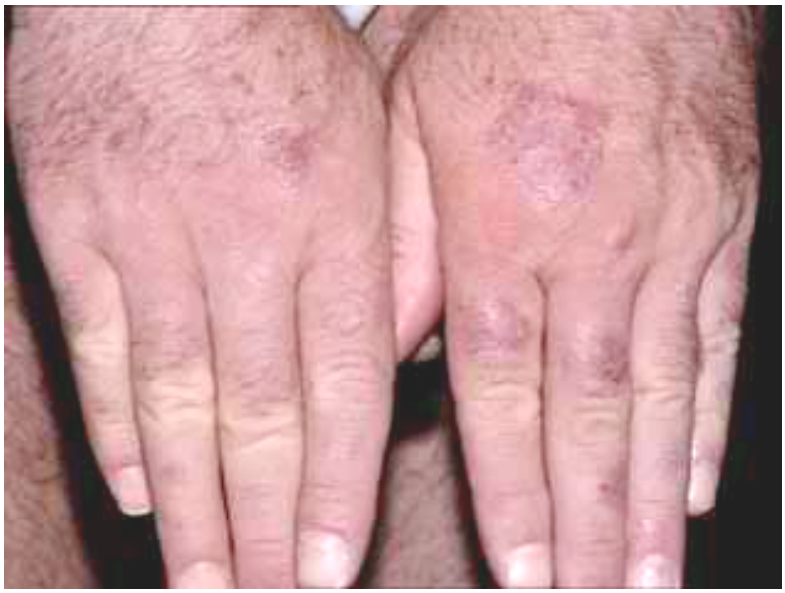
This product seems to give more modest results in patients in whom the emotional aspect that accompanies the disease is very strong. It should also be noted that in 10% of cases in the first two days of treatment, the product may cause a slight worsening of disorders, followed by a rapid improvement, however, already starting from day 3.

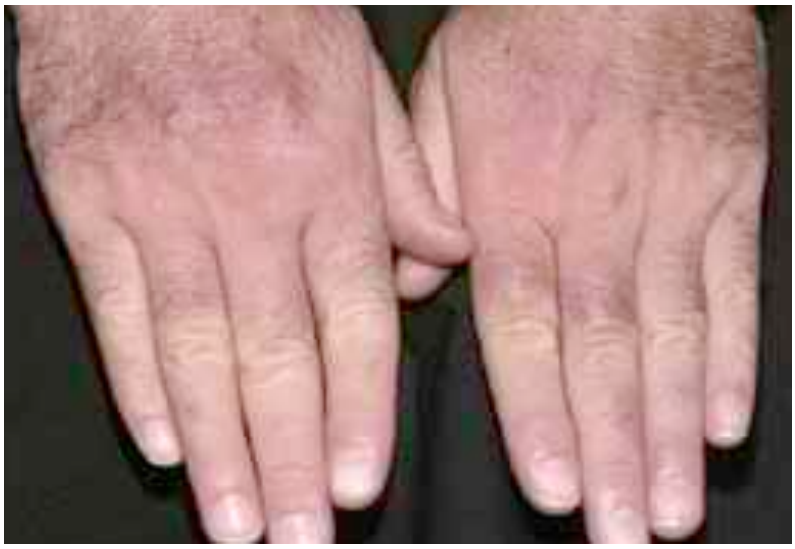
Photos before – after 30 days of treatment with Stamibio Derm





Photos before – after 30 days of treatment with Stamibio Derm





Discussion and Conclusions

The product, which is the subject of this study, aims at restoring the physiological balance of the skin, which is altered due to psoriasis, by normalizing autoimmune processes and reducing the proliferation of keratinocytes.
On the other hand, the factors contained in the extract of fertilized eggs of Zebrafish have been shown in vitro to reduce the proliferation of abnormal clones in cellular multiplication. A combined use of both active ingredients contained in the extracts of

zebrafish eggs, as well as in the extracts of the other ingredients of the formulation of the cream, helps counteract those specific and selective mechanisms that are responsible for the onset of this disease, thus restoring the altered physiological skin balance. It is worth noting that the action of the active ingredients mentioned above is performed through a biological mechanism, aimed at selectively counteracting pathological events, which undermine the skin balance. Therefore, physiological conditions are restored through a regulating and modulating action. This current clinical study seems to confirm that the action of the ingredients of the cream is evident not only in cells in vitro, but also in the clinical trial. It should be noted that 90% of patients affected by psoriasis have responded favorably to treatment, thus showing a reduction of the subjective symptoms such as itching, as well as a reduction in objective symptoms, such as erythema, desquamation and hyperkeratosis. Both patients and dermatologist agreed upon the assessment of efficacy in 90% of cases. Efficacy was assessed as low only by two patients (10%), but this assessment was not completely shared by the dermatologist. In both cases, however, the superstructural factors of disease were very evident.

Probably in these patients a local treatment only is not expected to be successful, as the etiopathogenesis of the disease in these cases involves general and, above all, psychological aspects. Finally, it should be recorded that the side effects of treatment were very mild, being an exacerbation of itching and erythema in 2 patients (10%) in the first two days followed by a rapid reduction of these symptoms, as early as Day 3 of treatment. Furthermore, it should be noted that in 2 patients, there was a complete disappearance of lesions and disorders. Finally, the treatment of psoriasis with a cream for local use, which has been the subject of this study, seems to show a good efficacy and tolerability, with minor side effects. Further randomized controlled studies are needed to validate the results suggested by this clinical trial.

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