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Psoriasis – Plant-based Approach to Strengthen the Skin's Immune System

S. Hettwer, E. Besic Gyenge, B. Suter, B. Obermayer

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abstract

No other issue has preoccupied the entire world in the last two years as much as the Corona pandemic. Accordingly, the topic of the immune system and how to keep it strengthened to avoid infection came into focus. And indeed, we can observe that the appearance of the skin suffers greatly when we have caught an infection. But there are also chronic skin conditions that are immunologically caused and where there is no infection. Psoriasis is such a condition. Six out of 2000 people asked in the UK suffer from psoriasis, independent from age or gender (Mintel). Psoriasis is currently not curable. We can only try to alleviate the symptoms. Here we show how a medicinal mushroom used for thousands of years can provide relief. It regulates the immune system and the skin microbiota, and can thus reduce psoriasis. This concept coincides with the consumer’s desire for a natural solution to their condition.

Introduction

Psoriasis is a multifactorial disease. It is the result of complex environmental influences and genetic predisposition of the skin [1]. The initial development of psoriasis is not exactly understood, but it seems to be caused by a certain over-reactivity of the skin’s immune system against own proteins, associated with over-activation of certain T-cells.

The immunological response to this condition is well studied. It is mediated by T cells and dendritic cells, releasing IL-23 and IL-12 to activate IL-17 producing T cells. These T cells (Th1 and Th22) produce IL-17, INF- γ , TNF and IL-22, which are abundant in psoriasis. Acting on keratinocytes, these cytokines amplify the psoriatic inflammation causing them to release cytokines as well. Besides general pro-inflammatory cytokines like IL-1, IL-8 plays a pivotal role in the phenotype of psoriasis. One characteristic of psoriatic skin is an increased turnover of keratinocytes, resulting in a thickened stratum corneum and scaling, promoted by IL-8 [2]. The purpose might be to accelerate loss of surface keratinocytes and eliminate pathogens [3]. In favour of this involvement of undesired microbes is the fact that anti-microbial peptides are upregulated in psoriatic skin conditions.

Psoriasis is characterised by very dry, red and scaly skin. It can be localised or spread over large areas of the body. It is particularly unpleasant on hairy parts of the body, as the itching is usually greatest here.

Treatment is very difficult because it is directed against the body’s own immune system and thus often only symptomatic treatment is possible. For example, salicylic acid is used to remove the scales or irradiation with UV light to inhibit the proliferation of keratinocytes. Hormone preparations with

cortisone or vitamin D preparations are also used, which are anti-inflammatory and also target the proliferation of keratinocytes, but which can have side effects. Urea is used to improve skin moisturisation.

Recent work has linked psoriasis to epigenetic aberrations. It has been reported that the commonly used drug in psoriasis, methotrexate, can interfere with methyl transfer function of folate, thereby reverting to normal methylation [4].

Psoriasis is a disease that can occur in episodes with outbreaks that require medical treatment. For fading or mild episodes, however, well-tailored cosmetic care that can alleviate the symptoms, and cosmetic care for the skin is sufficient. As the root cause may be a disarrangement of the DNA-methylation pattern, an active ingredient recalibrating the epigenetic landscape can be of help here. Modulating the immunological response of T cells and dendritic cells of the skin can help mitigate the subsequent factors involved in the expression of psoriasis.

The water-based extract of the medicinal mushroom *Ganoderma lucidum* is known to act positively on misdirected immune cells like T cells and dendritic cells due to its specific *Ganoderma lucidum* polysaccharides (GLPS) [5]. It has at the same time immune-stimulation activity. This fact has been exploited in Traditional Chinese Medicine since hundreds and thousands of years. *Ganoderma lucidum* or Ling Zhi, how it is called in Chinese (Reishi in Japanese), is prepared as a tea to rebalance the “Qi”, the inner spiritual energy. It is the number one of the traditional Chinese herb medicines and said to be the herb of longevity or immortality. We can take this as an analogy for a

proper functioning immune system and a perfectly balanced epigenetic landscape of our cells. As such, the use of *Ganoderma lucidum* extract as a remedy for psoriatic skin is worth to be tested.

Materials and Methods

Ganoderma lucidum extract (LIFTONIN®-QI, INCI: Propanediol, Water, Ganoderma lucidum (Mushroom) Stem Extract, Citric Acid) is produced by extracting the mushroom grown in the laboratory with water. The process is similar to that used by the Traditional Chinese Medicine. The energy consumption for the entire manufacturing process is calculated and the carbon dioxide equivalents are offset in sustainability projects to make this active ingredient climate neutral (for details visit <https://fpm.climatepartner.com/tracking/12934-2002-1001/en>).

The *in-vivo* study was performed in accordance with the Declaration of Helsinki of the World's Medical Association. All study participants signed a written informed consent at the beginning of the study.

20 subjects with psoriasis (male and female, average age 47.8 years, age range 20 - 82 years) participated on the study. 10 subjects applied an emulsion without cosmetic active ingredient (placebo, INCI: Water, Caprylic/Capric Triglyceride, Glycerol Stearate Citrate, Pentylene Glycol, Cetearyl Alcohol, Glycerin, Sodium Anisate, Sodium Levulinate, Xanthan Gum, Citric Acid) and 10 with the same emulsion containing 5% *Ganoderma lucidum* extract twice daily on affected skin areas for 56 days. The visible improvement was recorded by photography of the lesional sites. Skin hydration was assessed with a Corneometer CM825. Psoriatic skin condition parameters (scaling, redness) were assessed by a dermatologist. A subjective survey served as indication on consumer perceptions. Measurements were made at day 0 and 56, assessments were made at day 0, 28 and 56.

In-vitro study: bacterial growth was performed in liquid cultures. Growth of different strains of the skin microbiota in buffered chloride-peptone solution (NPP, Biolife 4013952) and transfer of 100 - 1000 cfu/ml into phosphate/citrate buffer (10 mM citrate, 20 mM disodium hydrogen phosphate, 1.09 g/l NaCl, 0.37 g/l KCl, 0.055 g/l

CaCl₂·2H₂O, 0.011 g/l MgCl₂·6H₂O). Growth of the strains was determined after 24 hours by plating and counting the colony forming units (cfu).

Results and Discussion

The epigenetic *in-vitro* study (published elsewhere) as well as literature data [6] made it obvious that the *Ganoderma lucidum* extract (LIFTONIN®-QI) could possibly reduce severe skin conditions appearing in psoriasis. As evident in our *in-vitro* experiment, large detachments of corneocytes from the skin barrier (big scales) are the predominant phenotype in psoriasis accompanied with skin redness and itching, as a result of an inflammatory state of the skin. We have also shown that the keratinocyte proliferation enhancing cytokine IL-8 can be reduced by 53% when 0.1% *Ganoderma lucidum* extract was present in the cell culture medium of keratinocytes stressed with hyper-methylation (published elsewhere). Psoriasis is largely determined by an immunological reaction of a subset of T-helper cells which makes the *Ganoderma lucidum* extract quite suitable for the accompanying cosmetic treatment as it contains immune regulating GL-polysaccharides.

The visible improvement of the condition is represented in **Figure 1**. Psoriatic skin lesions, resulting from sustained itching and scratching as well as scaly skin are improved substantially after application of 5% of the extract in the emulsion. This is especially visible on joints, like the elbow, which are typically stronger affected by scaling and inflammation.

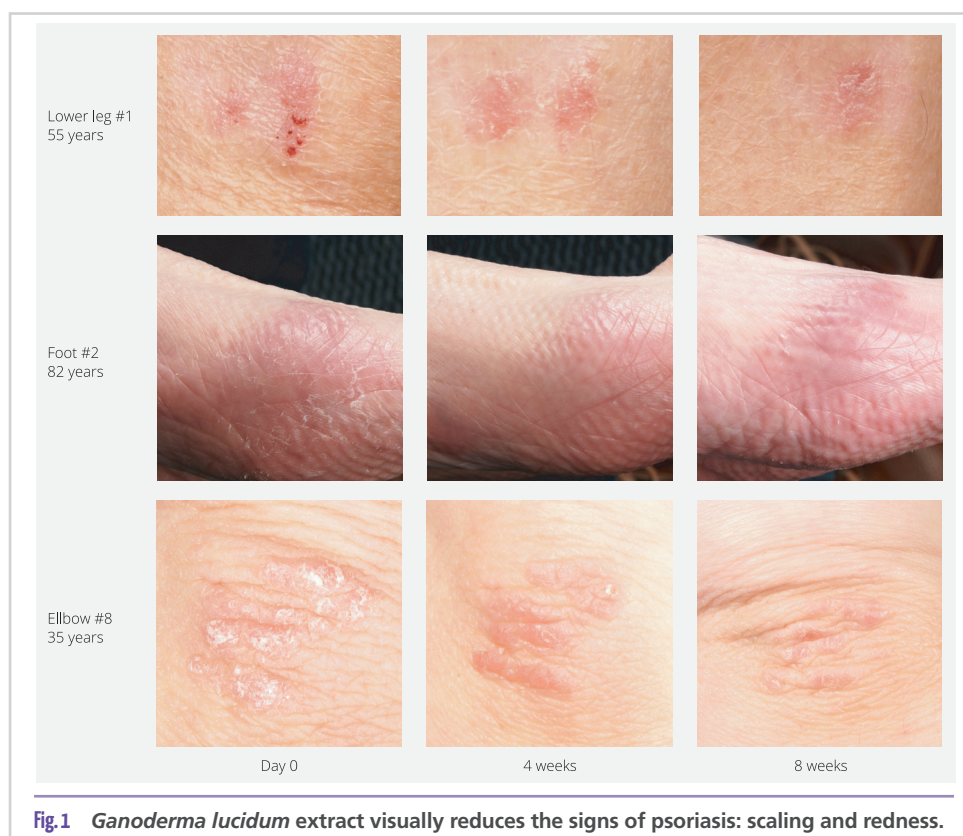


Fig.1 *Ganoderma lucidum* extract visually reduces the signs of psoriasis: scaling and redness.

The skin hydration in psoriatic skin was detected to be extremely dry. At D0, the average corneometer value was 9. After 56 days, the hydration increased by 85% compared to initial condition, double as much as for placebo (Figure 2).

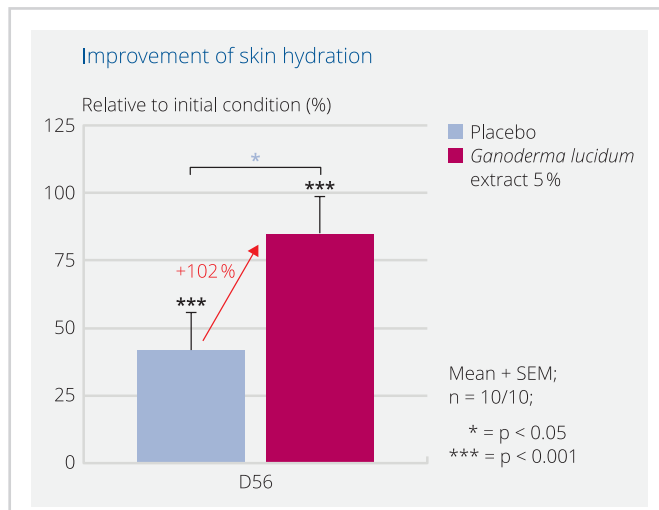


Fig.2 *Ganoderma lucidum* extract provides urgently needed moisture to the very dry psoriatic skin. After 56 days, the moisture content was 85% higher than at the beginning, significantly outperforming placebo by 102%. Student's t-test based on differences. Statistical values in black refer to comparison with baseline, values in blue refer to comparison with placebo.

The dermatological assessment for psoriatic skin parameters revealed an outperforming in reduction of scaling for 5% *Ganoderma lucidum* extract in comparison with placebo at day 28 and 56, both significant over baseline (-35.6% or -61.5%, respectively, Figure 3). Due to compliance reasons on the severe skin condition of psoriasis, the placebo was already formulated in a skin supporting way with 15% oil, the reason for not having significant results over placebo with the chosen number of participants.

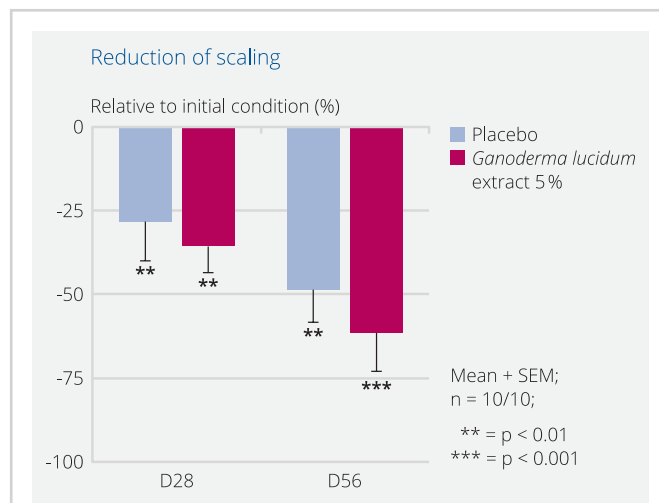


Fig.3 *Ganoderma lucidum* extract significantly and continuously reduces psoriatic scaling reaching a reduction by 61.5% after 56 days, outperforming placebo. Statistical values in black refer to comparison with baseline.

The same is true for skin redness as also evaluated by the dermatologist. *Ganoderma lucidum* extract at 5% rapidly and significantly reduced skin redness by 25.5% after 28 days while placebo showed only a non-significant tendency (not shown). After 56 days, both formulations reduced redness by 46-47%. As a conclusion, *Ganoderma lucidum* extract is the perfect care for psoriatic skin.

The findings are confirmed by the subjective survey (Figure 4): 90% of the study participants who used the verum formulation claimed it reduces skin redness. Surprisingly all verum users confessed that *Ganoderma lucidum* extract also reduces itching, soothes the skin, supports dry skin and leaves a pleasant skin feeling. This is very important because psoriasis creates a tense, tingling skin sensation that makes it difficult to forget about the condition. Thus, people are constantly preoccupied with the disease and cannot find a way to let go of it. If a pleasant skin feeling is created, this can help enormously in pushing psoriasis aside and living a more relaxed life. In all parameters, *Ganoderma lucidum* extract clearly outperformed the placebo.

The importance of a proper skin microbiota in psoriatic skin conditions has yet to be revealed in detail. However, it is known that psoriatic skin releases more anti-microbial peptides like psoriasins, defensins and others, than normal skin and this should have a purpose [3]. The physical and immunological skin condition of psoriasis offers feeding ground for undesired skin microbiota which can prevent the resolution of the condition. As in atopic dermatitis, an over-colonisation of *Staphylococcus aureus* can be seen in psoriatic skin conditions. Patients with psoriasis were 4.5 times more likely to be colonized by *S. aureus* than healthy controls [7].

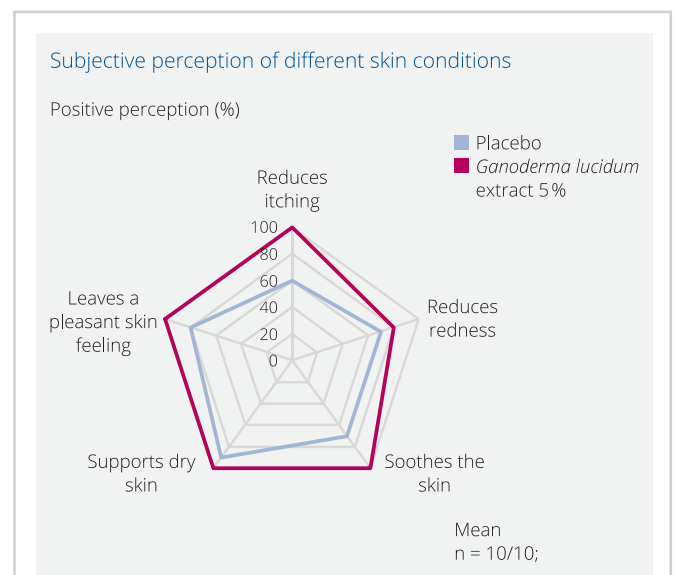


Fig.4 *Ganoderma lucidum* extract is a trustworthy ingredient in cosmetic formulations designed to help in psoriatic skin conditions. Although placebo already reached a high performance level, the acceptance of *Ganoderma lucidum* extract was at 100% in almost all assessed parameters.

We now know that *S. epidermidis* is capable to induce distinct innate immune signaling pathways in keratinocytes to augment antimicrobial peptide-killing of *S. aureus* [8]. The establishment of a “normal” skin microbiota can thus be an important contribution to mitigate effects of critical skin microbiota of psoriatic skin and give better prognosis for the course of the psoriatic break-out. In our *in-vitro* experiment, we opted on determining prebiotic properties of *Ganoderma lucidum* extract on beneficial skin microbiota as it contains specific polysaccharides. These polysaccharides can be a feeding ground for some skin germs. In our experiment, we grew bacterial stains of the skin microbiota under optimal conditions and transferred them into a nutrient poor environment resembling human sweat in terms of the salt composition. As such, most of the strains grew less under those conditions. Only when *Ganoderma lucidum* extract was present, *S. epidermidis* was promoted in its growth by the factor of roughly 20 when compared to the untreated control. Other less positive skin germs like *Bacillus subtilis*, *Corynebacterium variabile* and *Micrococcus luteus* were not motivated to grow further (Figure 5).

Ganoderma lucidum extract (LIFTONIN®-QI) can not only moisturise and soothe the skin but tackles multiple root causes of the problem - the epigenetic dissonance as well as an imbalanced skin microbiota - to alleviate the problem. It relieves from tingling and tensing skin feelings and reduces reddening and scaling. In this way, people suffering from psoriasis can regain a lot of self esteem. *Ganoderma lucidum* is natural and proven for thousands of years in Traditional Chinese Medicine. It is a prebiotic and immune-regulating active ingredient best suited for accompanying care of psoriasis or whenever a stronger skin microbiota is needed.

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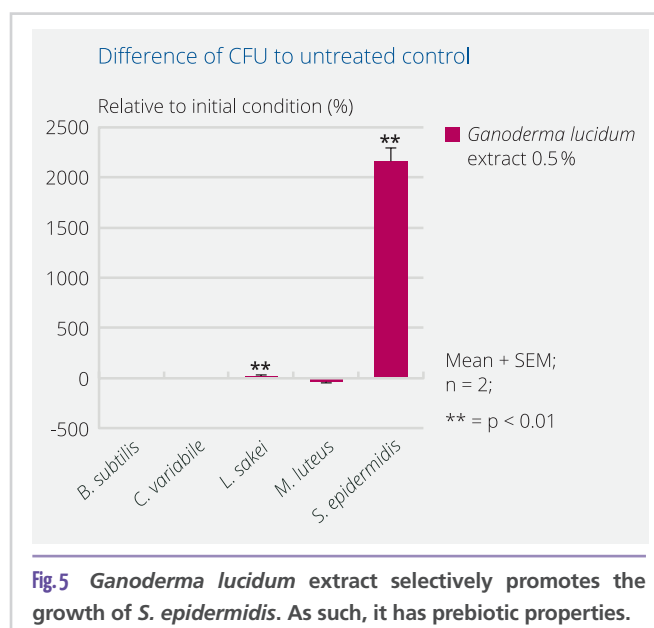


Fig.5 *Ganoderma lucidum* extract selectively promotes the growth of *S. epidermidis*. As such, it has prebiotic properties.

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authors

Stefan Hettwer, PhD,
Emina Besic Gyenge, PhD,
Brigit Suter,
Barbara Obermayer

RAHN AG | Dörflistrasse 120 | 8050 Zürich | Switzerland

Corresponding Author:
stefan.hettwer@rahn-group.com