

# Topical treatment of some dermatoses with molecularly activated formulations of zinc pyrithione

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## SUMMARY

### Background

Molecular activation is a new technology that is applied to the active principles of antioxidants making them more effective. Many factors can influence the activation of antioxidants. The most important chemical factors are molecular structure, active functional groups, specific antioxidant catalysts, molecular weight, pH, double carbon bonds, their coefficient of solubility, as well as the antioxidant capacity of each molecule. The duration and intensity of molecular activation are among the most influential physical factors. Not all antioxidants require the same activation time to reach their maximum antioxidant capacity; the most important parameter for the control of better performance is their optimisation. Once their highest antioxidant capacity is at its most favourable peak, activation must be suspended because, after that maximum peak, their antioxidant capacity starts to diminish. Blue Cap with its active principle, ACTIVATED zinc pyrithione, regulates the abnormal proliferation of keratinocytes, which is the common feature of the main illnesses which we have studied: psoriasis, atopic dermatitis and seborrhoeic dermatitis. It also has a strong antibacterial action against a series of pathogenic microorganisms.

### Patients and methods

BLUE CAP products for external use (cream, spray, shampoo, shower gel) were used in the treatment of 35 patients aged 14 to 73 years (22 males and 13 females). The diagnosis of skin disease was established by clinical examination. For each patient a questionnaire was filled out at the beginning and at the end of a three week therapy. According to symptoms, patients were divided into the following groups: psoriasis: 21 patients; atopic dermatitis: 5 patients; seborrhoeic dermatitis: 9 patients.

### Results

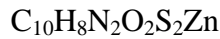
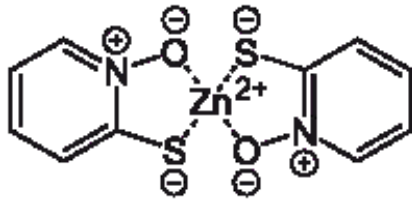
After the first week of treatment, improvement was evident. During the treatment, no local or systemic side effects were reported. RESULTS ANALYSIS after three weeks: There were 13 cases of complete remission, 16 cases of evident improvement, whereas partial response was observed in 6 patients. Results are presented in Table 3. The best results were achieved in patients with seborrhoeic dermatitis on the face.

### Conclusions

Blue Cap products are a safe and effective therapeutic option for early control of different skin diseases.

## INTRODUCTION

Zinc pyrithione is the [chelate](#) between the [zinc](#) atom and two [pyridine](#) rings which are bound to zinc through [oxygen](#) or [sulphur](#) atoms.



Pyrithione has long been known as an inhibitor of membrane transport processes in fungi. The degree of inhibition decreases with the increase of the pH of the inhibition medium. However, there is no reciprocal correlation between pyrithione concentration and exposure time. At low pyrithione concentrations, the fungi can detoxify the inhibitor. The relationship between the ability of pyrithione to inhibit membrane transport and the anti-dandruff activity remains unclear. The inhibition of the growth of scalp microflora might be involved in the efficacy of pyrithione. From this point of view it is understandable that a number of hair care products are weak, lipid-soluble acids.

New insights into human keratinocyte and melanocyte cell cultures demonstrated that even nanomolar concentrations of zinc pyrithione induce enzymes responsible for heat shock which leads to genomic instability. Furthermore, the substance itself causes depletion of ATP levels in the cell which also leads to a transport blockade. Along with the evidence on penetration of the substance into the skin of mammals, these insights provide strong evidence for the influence of zinc pyrithione on proliferation of keratinocytes or melanocytes.

Blue Cap products for topical use are based on the specific properties of the new formulation of molecularly activated zinc pyrithione which exerts a high antibacterial action against a series of pathogenic microorganisms (streptococcus, staphylococcus), and antifungal action against *Pityrosporum ovale* and *Pityrosporum orbiculare*. Due to its *citostatic (citotoxic) action*, Blue Cap products inhibit the abnormal proliferation of keratinocytes and inflammatory cells, and prolong cell division cycles. In this way they exert anti-inflammatory activity. Through an unclear mechanism of action they reduce within 24–48 hours the production of cytokines by inducing apoptosis – cell death in keratinocytes – and in this way exert immunosuppressive activity.

**How does zinc pyrithione work?** The zinc pyrithione molecule is activated (has higher antioxidant capacity) through the presence of excess electrons on the outer orbits. Upon contact with free radical molecules, the excess electrons are used to neutralise these molecules; the zinc pyrithione molecule therefore retains a greater antioxidant power. It stabilizes enzymes, considerably improving the stability of cellular membranes. The exact mechanism of action of activated electrons on free radicals and oxide molecules is not known. The advantages of Blue Cap products are their effectiveness and quick action, total absence of corticosteroids and cytostatics, high moisturizing power, ability to penetrate into the deepest layers of the dermis and absence of any side effects.

## Patients and methods

The study was carried out in May and June 2010 in the Novo mesto hospital dermatology clinic. 35 patients with clinical diagnosis of psoriasis, atopic or seborrhoeic skin inflammation were enrolled. There were 22 males and 13 females in the study group. All participants filled out a questionnaire that comprised general information, information on type and duration of the disease, previous therapies, the type of the Blue Cap product they were using and the method of use. After three weeks, the questionnaire was additionally supplemented with the information about the results of the product use.

## Results

A total of 35 patients participated in the study, 22 males and 13 females.

Table 1: Structure of participants by gender

|         | Number of participants | Percentage |
|---------|------------------------|------------|
| Males   | 22                     | 62.9       |
| Females | 13                     | 37.1       |
| Total   | 35                     | 100.0      |

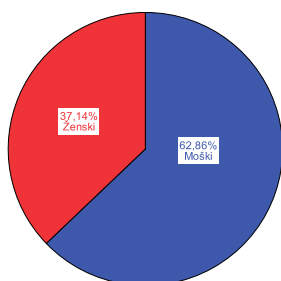
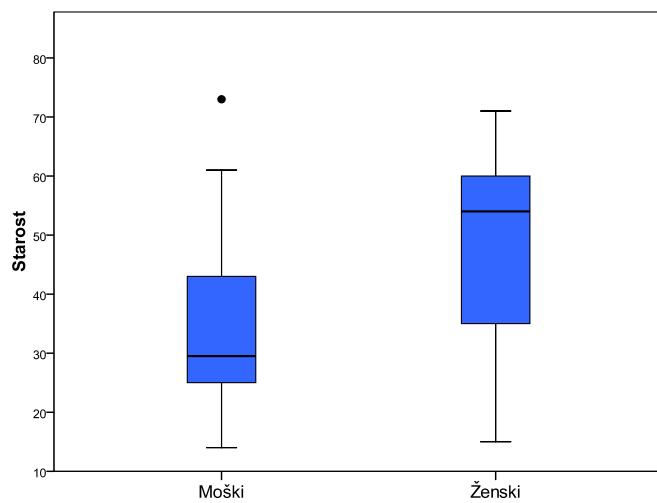


Table 2: Structure of participants by age

|          | Number of participants | Percentage | Average age | Standard deviation of age | Median age | Min age | Max age |
|----------|------------------------|------------|-------------|---------------------------|------------|---------|---------|
| Males    | 22                     | 62.9       | 34.41       | 15.146                    | 29.50      | 14      | 73      |
| Females  | 13                     | 37.1       | 47.31       | 17.816                    | 54.00      | 15      | 71      |
| Together | 35                     | 100.0      | 39.20       | 17.138                    | 36.00      | 14      | 73      |

The average age was slightly higher in female participants, i.e. 47.31 years; the average age of male participants was 34.41 years.

Graph 1: Structure of participants by age

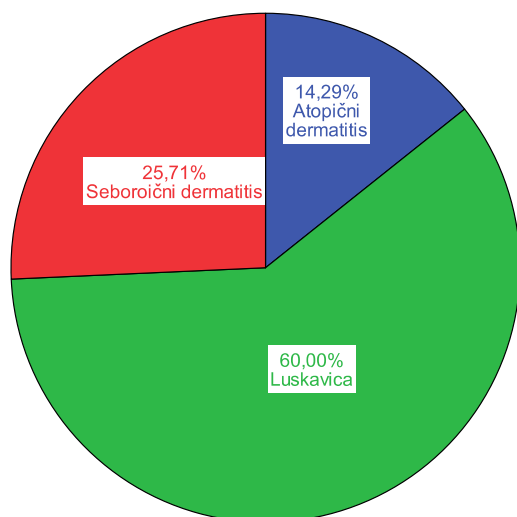


Age  
Males  
Females

Table 3: Structure of participants by diagnosis

|                        | Number | Percentage |
|------------------------|--------|------------|
| Atopic dermatitis      | 5      | 14.3       |
| Psoriasis              | 21     | 60.0       |
| Seborrhoeic dermatitis | 9      | 25.7       |
| Total                  | 35     | 100.0      |

Most patients (60%) had psoriasis, only 14.3% of patients had atopic dermatitis. This can be attributed to the fact that during the summer months the proportion of patients with atopic dermatitis is in general smaller.

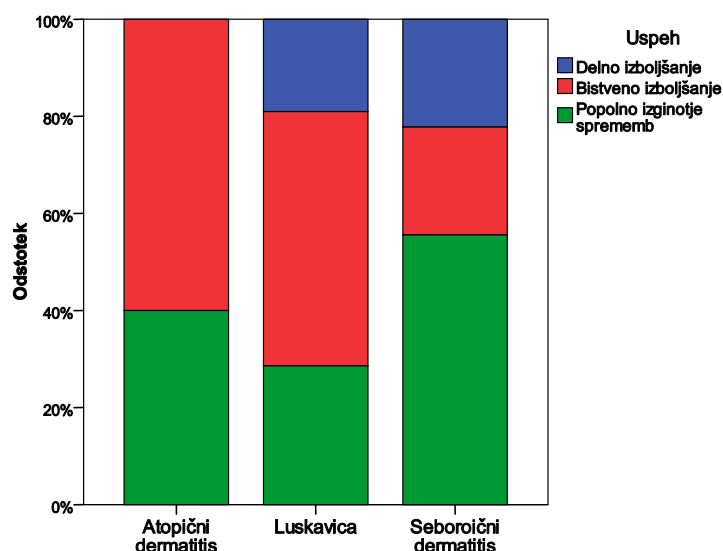


14.29% Atopic dermatitis  
 25.71% Seborrhoeic dermatitis  
 60.00% Psoriasis

**Table 4: Treatment results with regard to diagnosis**

| Diagnosis              | Result                         |                     |                     | Overall      |
|------------------------|--------------------------------|---------------------|---------------------|--------------|
|                        | Complete remission of symptoms | Evident improvement | Partial improvement |              |
| Atopic dermatitis      | 2<br>40.0%                     | 3<br>60.0%          | 0<br>0.0%           | 5<br>100.0%  |
| Psoriasis              | 6<br>28.6%                     | 11<br>52.4%         | 4<br>19.0%          | 21<br>100.0% |
| Seborrhoeic dermatitis | 5<br>55.6%                     | 2<br>22.2%          | 2<br>22.2%          | 9<br>100.0%  |
| <b>Total</b>           | 13<br>37.1%                    | 16<br>45.7%         | 6<br>17.1%          | 35<br>100.0% |

**Graph 5: Treatment results with regard to diagnosis**



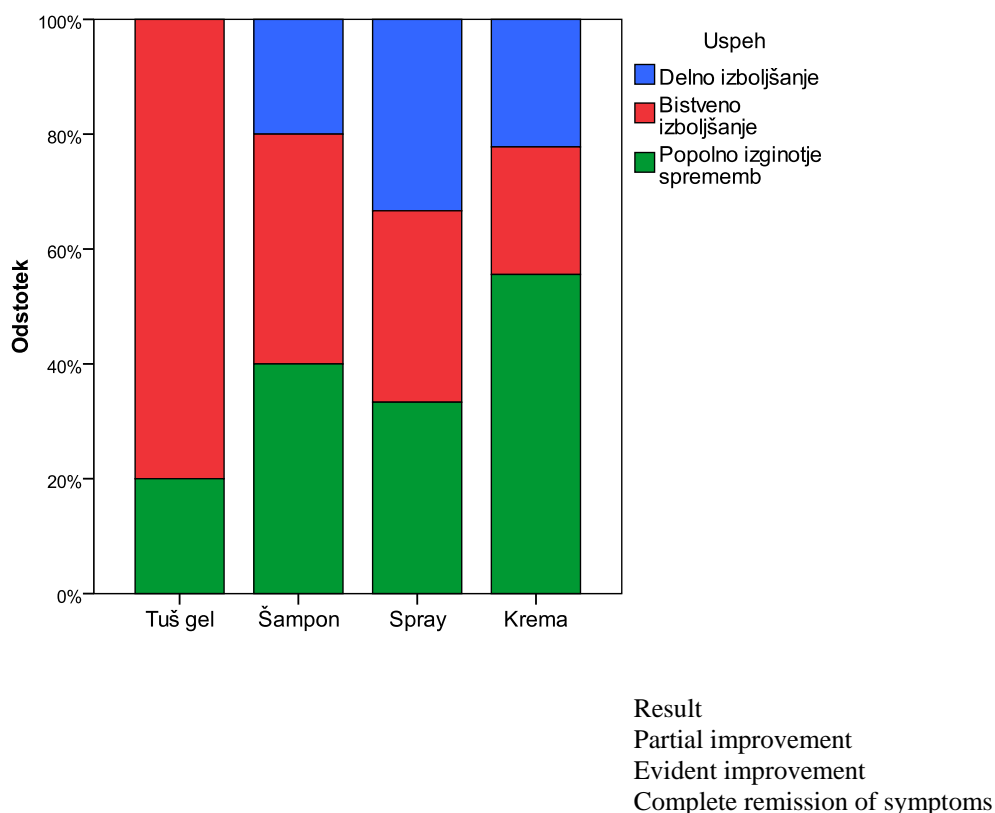
Result  
 Partial improvement  
 Evident improvement  
 Complete remission of symptoms

Best treatment results were obtained in patients with seborrhoeic dermatitis. As many as 55.6% of these patients demonstrated a complete remission of symptoms. This reflects most likely the influence of the product on microorganisms and consequently the improvement of the skin symptomatics.

**Table 5: Treatment results with regard to product type**

| Product    | Result                         |                     |                     | Overall |
|------------|--------------------------------|---------------------|---------------------|---------|
|            | Complete remission of symptoms | Evident improvement | Partial improvement |         |
| Cream      | 5                              | 2                   | 2                   | 9       |
|            | 55.6%                          | 22.2%               | 22.2%               | 100.0%  |
| Spray      | 2                              | 2                   | 2                   | 6       |
|            | 33.3%                          | 33.3%               | 33.3%               | 100.0%  |
| Shampoo    | 4                              | 4                   | 2                   | 10      |
|            | 40.0%                          | 40.0%               | 20.0%               | 100.0%  |
| Shower gel | 2                              | 8                   | 0                   | 10      |
|            | 20.0%                          | 80.0%               | 0.0%                | 100.0%  |
| Total      | 13                             | 16                  | 6                   | 35      |
|            | 37.1%                          | 45.7%               | 17.1%               | 100.0%  |

Graf 5: Treatment results with regard to product type



Best treatment results were obtained with shower gel. The patients reported predominantly the relief from itching and burning, skin lesions faded considerably.

## CONCLUSION

Blue Cap products have been established as a good supplementary therapy or monotherapy in treatment of certain skin diseases, especially seborrhoeic dermatitis. Their use reduces the need for topical corticosteroids in the short-term. Physical properties of the products are patient-friendly. In order to confirm long-term efficacy, further studies are necessary.

Literature:

1. Chandler CJ, Segel IH (1978). ["Mechanism of the antimicrobial action of pyrithione: effects on membrane transport, ATP levels, and protein synthesis"](#). *Antimicrob. Agents Chemother.* **14** (1): 60–8
2. Maria PP. Antioxidants: New applications in dermatology. *Dermatološki dnevi* (6; 2009; Maribor)

3. Sarah D. L, Christopher M. Cabello TW, Georg TW. The topical antimicrobial zinc pyrithione is a heat shock response inducer that causes DNA damage and PARP-dependent energy crisis in human skin cells. *Cell Stress Chaperones*. 2010 May; 15(3): 309–322.