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CLINICAL REPORT

Title of the study

**Use of Soritex sjampo in psoriasis capitis and
seborrhoea capitis**

Study site

**Semmelweis University, Clinic of Dermatological and
Sexually Transmitted Diseases**

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Chapter 1

Summary

Soritex cream sjampo is a new remedy for the treatment of seborrhoea capitis (seborrhoea of the scalp) and psoriasis capitis (psoriasis of the scalp).

Soritex cream sjampo contains four different groups of active ingredients in a lipophilic vehicle. These groups include: 1./ Propolis; 2./ Natural (sea) salt; 3./ Extracts from 13 medicinal plants widely used in dermatology and cosmetology; 4./ Vitamins (d-panthenol and vitamin-A). The active ingredients of Soritex have been applied in the past and present for the treatment of psoriasis separately in many different preparations of different manufacturers. These groups of ingredients are unified in Soritex in order to benefit from their synergistic effects.

Soritex is from technological point of view not an usual shampoo but as above indicated a cream shampoo. It contains active ingredients exclusively of natural origin in an unique composition and in high concentration achieved by specific pharmaceutical technological manufacturing procedures. It has highly concentrated active ingredients and small water content. When used, the skin of the scalp does not become dry and at the same time the sebaceous (fatty) secretion of the scalp gets reduced. The pH of the cream shampoo is 5,5 which is in the same range with the skin's natural pH value.

In order to verify Soritex sjampo's effect and safety in the clinical practice, IN VITRO Ltd. performed an open clinical study with 40 patients, 20 of them having seborrhoea capitis and 20 having psoriasis capitis.

During the study there was a 2 week long wash-out period what was followed by a 3 week long administration of the shampoo. The total time of the study was 5 weeks. During the study 4 medical examinations (rounds) took place (1st round: 2 weeks (wash out period); 2nd round: 0. week (starting point); 3rd round: 1st week; 4th round: 3rd week). Patients used Soritex sjampo for their daily hairwash for 1 week, then as needed.

The evaluation was performed according to a 4-score (0, 1, 2, 3) scale representing the severity of symptoms. The studied parameters in psoriasis capitis included parakeratosis, infiltration, erythema and itching, while in seborrhoea capitis desquamation, inflammation, fatty hair and itching.

There was a subjective evaluation of Soritex sjampo, too, made by the patients and their doctors using 3 categories: excellent effect, good effect, no effect.

The results support the previous observations that Soritex sjampo can be successfully applied in seborrhoea capitis to reduce desquamation, inflammation, fatty hair and itching and in psoriasis capitis to decrease parakeratosis, infiltration, erythema and to a smaller extent itching which are four key symptoms of psoriasis capitis. The beneficial effects appear quickly, after one week of treatment.

Results of the subjective evaluation of patients on efficacy of the treatment showed that the majority of the patients considered the efficacy of the treatment to be either good or excellent. The doctor's evaluation showed the same results.

Chapter 2

Introduction

Seborrhoea is a very frequent dermatological disease with an inherited element, characterized basically by hypersteatosis (increased production of sebum). Seborrhoea usually begins in the teenage years and is more frequent in men than in women. Characteristic for this disease the fatty skin of the face, the desquamation, pityriasis and the inflammation, the infiltration and the fatty hair. In the treatment of seborrhoea hair-cleaning preparations with the capacity to normalize sebum production provide benefit.

Psoriasis is a chronic, inflammatory skin disorder that affects millions of people all over the world, although its incidence depends on geographical and ethnic factors. Its incidence in the developed countries is about 2% of the population. No one knows exactly what causes this disease, although recent medical thinking holds that it is an immune-mediated disorder.

There are various forms of psoriasis. Psoriasis can be limited to a few plaques or can involve moderate to extensive areas of skin. Psoriasis can range from mild to moderate to very severe and disabling. However, for most people, psoriasis tends to be mild. Some people experience spontaneous, transitory remissions, but no one knows why this happens and they are unpredictable.

Most commonly the scalp, knees, elbows, hands and feet are affected by the disease. It rarely affects the face. However, no area of the skin is exempt, including the genital area. Infiltration and parakeratosis are characteristic. In psoriasis of the scalp (psoriasis capitis) seborrhoea is the most important provoking factor.

Both males and females get psoriasis in equal numbers. It can strike at any age, but most often between 15 and 35 years.

There is no medical test for psoriasis. The doctor makes the diagnosis after observing the skin, and studying the psoriatic plaque cells under a microscope. There is no cure at the moment, but there are many different treatments, both topical and systemic, that can clear psoriasis for periods of time. Experimentation is often required to find a treatment that works for a particular person. Every treatment improving seborrhoea as provoking factor, has the potential to improve psoriasis as well. Successful treatment of the scalp lesions can be very difficult.

Against psoriasis there are active agents of strong pharmacological effect like steroids, retinoids, psoralen, calcipotriol. These agents, especially steroids can be very effective, but at a cost of disturbing, sometimes very serious side effects. Therefore, there is a great need for effective but mild and safe remedies.

Soritex sjampo is a new remedy against seborrhoea and psoriasis of the scalp which to a large extent fulfills the above requirements.

Soritex sjampo contains a combination of different active ingredients of natural origin as follows:

1. Propolis: complex composition: volatile oils, balsams, flavones, mineral substances, etc. Originates from saps of different plant's buds, twigs and leaf-stalks collected by bees.

Propolis used in the manufacturing of DERMIPSOR cream shampoo is produced by a special technological procedure eliminating the possible allergenic components.

2. Sea-salt: sodium, potassium, selenium, chloride, fluoride, iodide, etc.)

3. Medicinal plants:

- Thyme (*Thymus vulgaris* L.)
- Lemon (*Citrus medica* L. var. Limonum)
- Tea tree (*Melaleuca alternifolia*):
- Chamomile (*Matricaria chamomilla* L.)
- Yarrow (*Achillea millefolium* L.)
- Dill (*Anethum graveolens* L.)
- Parsley (*Petroselinum crispus*)
- Great nettle (*Urtica dioica* L.)
- Calendine (*Chelidonium majus* L.)
- Oak (*Quercus robur* L.)
- Willow (*Salix alba* L.)
- Marigold (*Calendula officinalis* L.)
- Dandelion (*Taraxacum officinale* Web.)

4. Vitamins: d-panthenol, vitamin A

As demonstrated by the above data, Soritex sjampo contains 21 active ingredients in a lipophilic vehicle. The special composition of Soritex (via its surface-active compounds) ensures that the loss of fat from the hair during hairwash is substituted, preventing the dehydration of the scalp and the hair. Soritex sjampo contains exclusively ingredients of natural origin. Synthetic odorants are excluded. The pH of the preparation is 5.5 which is in the same range with the skin's natural pH value.

All the above substance-groups and their representatives have been separately applied in different preparations against psoriasis, seborrhea and other skin problems or simply in many cosmetics. They contain compounds of antiseptic and anti-inflammatory effect.

The idea behind Soritex sjampo is to combine these ingredients in one preparation in order to help each other's effect in the symptomatic treatment of psoriasis and seborrhea capitis (seborrhea of the scalp)

The complex composition was a challenge from pharmaceutical technological/manufacturing point of view, too, which has been successfully solved.

The cream shampoo has the unique characteristic of carrying anti-inflammatory and antiseptic ingredients, and at the same time supplying lipids (fats) to the skin.

After the development of Soritex sjampo, this preparation has been used by thousands of seborrhoeic and psoriatic patients (in seborrhea capitis and/or psoriasis capitis) in different countries, usually with very positive results. However, these are case reports and the developer company, IN VITRO Ltd. decided to perform clinical studies in order to scientifically support the efficacy and safety of Soritex sjampo.

Chapter 3

Aim of the study

Scientific examination of effects, side effects and safety of Soritex sjampo in symptoms of psoriasis capitis and seborrhoea in an open clinical study.

Chapter 4

Study protocol

Title of the study

Use of Soritex sjampo in psoriasis capitis and seborrhoea capitis

Study site

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Participants to be involved

- Patients with psoriasis capitis or seborrhoea capitis

- Age: patients of both sexes above 18 years
- Patients not receiving systemic antipsoriasis or antiseborrhoea treatment, or hormonal contraceptives within 3 months before the start of the study.
- Patient who signed the declaration on voluntary participation

Participants excluded from the study

Excluded were from the study those, who

- received internal treatment (Neotigason, corticosteroids, cytostatic drugs) within 3 months before the start of the study
- women taking hormonal contraceptives
- known hypersensitivity to any of the components of the shampoo
- receiving other local antipsoriasis or antiseborrhoea treatment
- has not signed the declaration on voluntary participation
- demonstrated poor compliance

Number of enrolled patients:

Patients with seborrhoea capitis:

N = 20 (11 women, 9 men)

Patients with psoriasis capitis:

N = 20 (15 women, 5 men)

Study design

Time span of the study:

Wash out period: 2 weeks

Administration of the shampoo: 3 weeks

Total time: 5 weeks

Date of rounds (medical examinations):

1st round: 2 weeks (wash out period)

2nd round: 0. week (starting point)

3rd round: 1st week

4th round: 3rd week

Total number of rounds: 4.

Patients used during the wash-out period a neutral shampoo supplied by the sponsor of the study. They did not received any other concomitant antiseborrhoeic and/or antipsoriasis treatment neither during the wash-out period nor during the active treatment period.

Frequency of use of Soritex sjampo: daily hairwash for 1 week, then as needed.

Study medicine (batch number):

- 07012003
- 12012003

Packaging and labeling: Packaging (plastic tube as primary and carton box as secondary (outer) packaging material) and labeling of the study medicine was identical to that of the commercial batches.

Evaluation of efficacy

The evaluation is performed according to a 4-score (0, 1, 2, 3) scale

Studied parameters

A. Seborrhoea capitis

Desquamation	0= not	1 = mild	2 = medium-level	3 = serious
Inflammation	0= not	1 = mild	2 = medium-level	3 = serious
Fatty hair	0= not	1 = mild	2 = medium-level	3 = serious
Itching	0= not	1 = mild	2 = medium-level	3 = serious

Registration of possible side effects

B. Psoriasis capitis

Parakeratosis	0= not	1 = mild	2 = medium-level	3 = serious
Infiltration	0= not	1 = mild	2 = medium-level	3 = serious
Erythema	0= not	1 = mild	2 = medium-level	3 = serious
Itching	0= not	1 = mild	2 = medium-level	3 = serious

Registration of possible side effects

Symptoms are evaluated based on individual patient data sheets.

Evaluation of side effects

Cosmetic effect/tolerability

A. Evaluation of the patients on the efficacy of the treatment:

- no effect
- good
- excellent

B. Evaluation of the doctors on the efficacy of the treatment:

- no effect
- good
- excellent

Would the patient later intend to use the study preparation?

- yes
- not

Chapter 5.

Results

A. Seborrhoea capitis

Patient description

20 patients were enrolled in the study at visit 1 (11 woman, 9 men).

Data of 18 patients are included in the evaluation, because two patients dropped out:

1 patient (male) no reason

1 patient (male): contact dermatitis-like symptoms. In the epicutan allergy test he had hypersensitivity to fragrance mix and balsam of Peru.

The mean age of patients was 42,8 years (range 23 to 69 years)

No statistically significant difference was observed between age in the gender comparison.

Evaluation of efficacy

In the evaluation data of screening (visit 1) and data of baseline (visit 2) were compared.

No statistically significant difference was observed in visit 1 and visit 2 comparison of symptoms.

The evaluation of the therapy was performed between visit 2 and visit 4, while the patients used the cream shampoo.

	Visits (medical examinations)/average score of symptoms (1-3)	
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Studied parameters	1 st	2 nd	3 rd	4 th	Process of changing
Desquamation score	1,94	2,11	0,83	0,5	(p < 0,001)
Inflammation score	1,33	1,33	0,39	0,28	(p < 0,001)
Fatty hair score	1,94	1,94	0,83	0,56	(p < 0,001)
Itching score	2,33	2,28	0,78	0,72	(p < 0,001)
Summary score*	7,56	7,67	2,85	2,06	(p < 0,001)

*Summary score: summary of symptoms' score by patients

Table 1.: Evaluation of Soritex sjampo's efficacy in seborrhoea capitis patients (n = 18 without the 2 drop-outs)

Statistically significant difference was observed in visit 2 and visit 4 comparison of symptoms (see Attachment, Figure a, b, c, d).

Cosmetic effect/tolerability

A/ The patient's (subjective) evaluation on the efficacy of treatment

No effect	5,6% (1)
Good	50% (9)
Excellent	44,4% (8)

B./ The doctor's evaluation on the efficacy of treatment

No effect	5,6% (1)
Good	44,4% (8)
Excellent	50% (9)

C./ Would the patient later intend to use the study preparation?

Yes	94,4% (17)
Not	5,6% (1)

Possible side effects

One male patient dropped out because of contact dermatitis-like symptoms. In the epicutan allergy test he had hypersensitivity to fragrance mix and balsam of Peru.

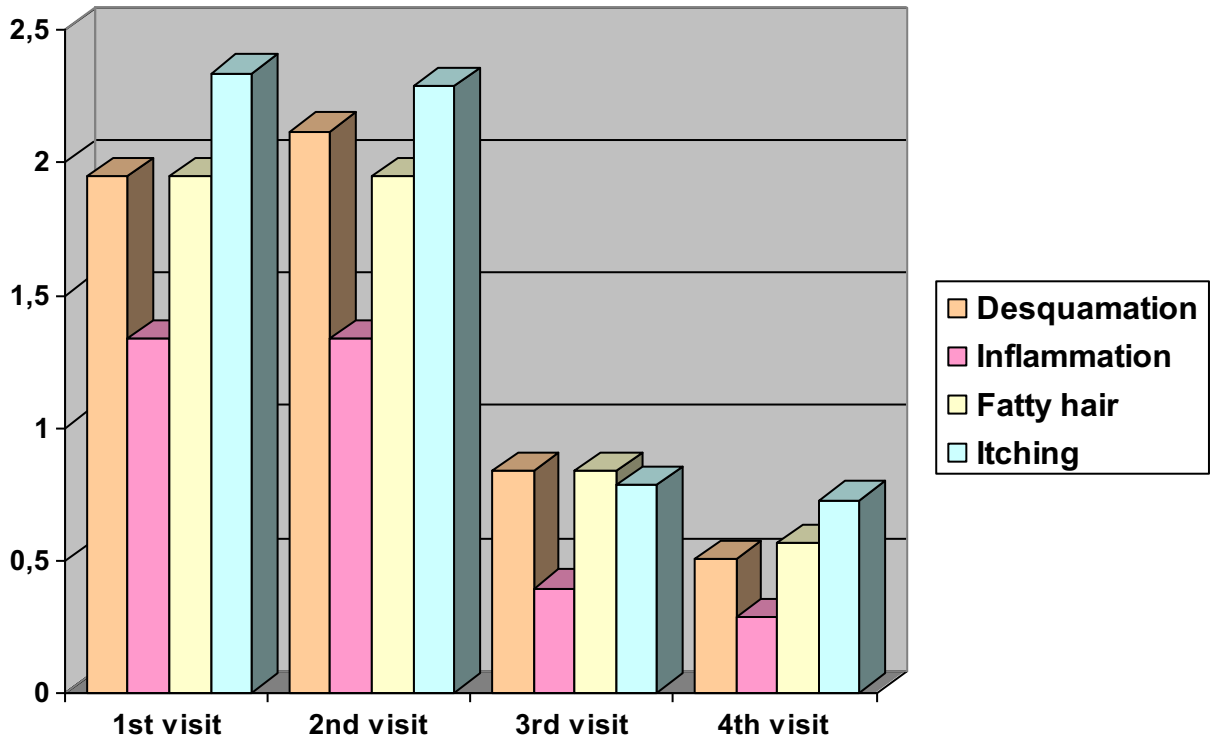


Figure 1.: Visits (medical examinations)/average score of symptoms (1-3)

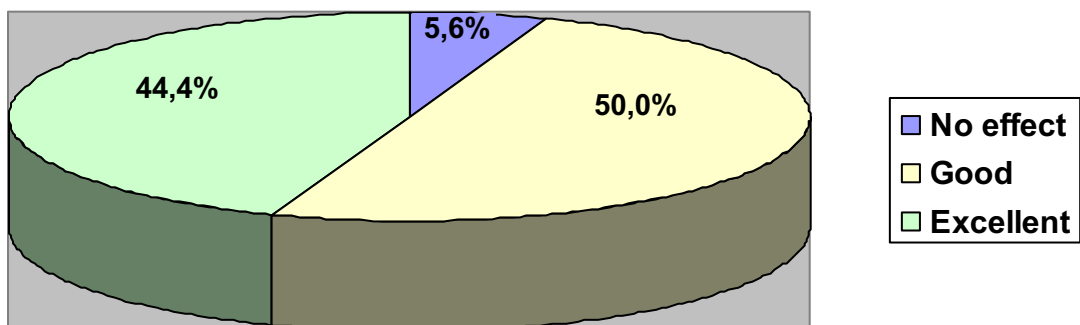


Figure 2.: The patient's (subjective) evaluation on the efficacy of treatment

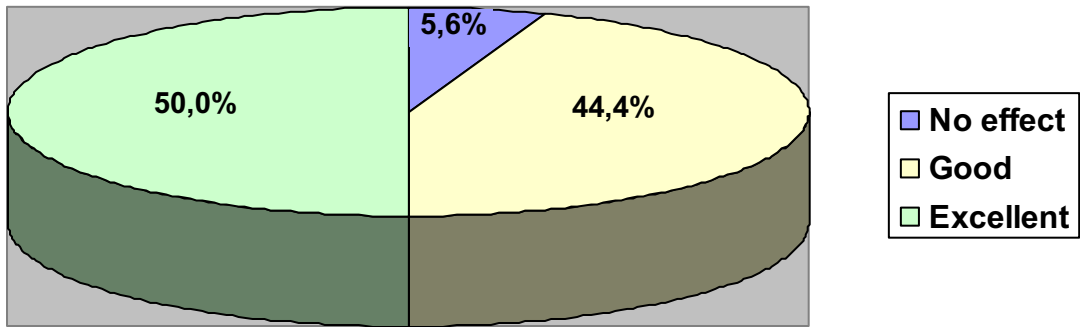


Figure 3.: The doctor's evaluation on the efficacy of treatment

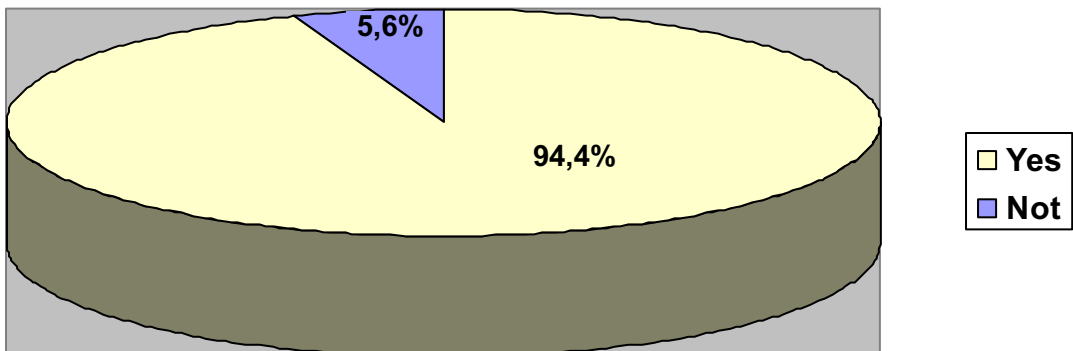


Figure 4.: Would the patient later intend to use the study preparation?

B. Psoriasis capitis

Patient description

20 patients were enrolled in the study at visit 1 (15 woman, 5 men).

Data of 19 patients are included in the evaluation, because one patient dropped out because of lack of time to take part in the study

The mean age of the patients was 46,5 years (range 19 to 75 years).

The mean age of the male patients was 65,4 years, whereas the mean age of the female patients was 39,8 years

Evaluation of efficacy

In the evaluation data of screening (visit 1) and data of baseline (visit 2) were compared.

No statistically significant difference was observed in visit 1 and visit 2 comparison of symptoms.

The evaluation of therapy was performed between visit 2 and visit 4, while the patients used the shampoo.

Studied parameters	Visits (medical examinations)/average score of symptoms (1-3)				Process of changing (p < 0,001) (p < 0,001) (p < 0,001) NS (p < 0,001)
	1 st	2 nd	3 rd	4 th	
Parakeratosis score	2,37	2,42	1,16	1,11	
Infiltration score	2,16	2,21	1,37	1,26	
Erythema score	2	2,1	1,32	1,26	
Itching score	1,11	1,0	0,68	0,74	
Summary score*	7,63	7,74	4,53	4,37	

***Summary score:** summary of symptoms' score by patients

Table 2.: Evaluation of Soritex sjampo's efficacy in psoriasis capitis patients (n = 19 without the 1 drop-out)

Statistically significant difference was observed in visit 2 and visit 4 comparison of symptoms, with the exception of itching (see Attachment, Figure e, f, g, h).

There was no statistically significant difference in visit 1 and visit 2 comparison of symptoms.

Cosmetic effect/tolerability

A./ The patient's (subjective) evaluation on the efficacy of treatment

No effect	26,3%
Good	63,2%
Excellent	10,5%

B./ The doctor's evaluation on the efficacy of treatment

No effect	26,3%
Good	63,2%
Excellent	10,5%

C./ Would the patient later intend to use the study preparation?

Yes	78,9%
Not	21,1%

Possible side effects

In one female patient itching developed (4th visit). Intensity: 2 (moderate); Connected to the use of shampoo: 3 (possibly); symptomatic treatment: 2 (not needed).

In one male patient 5 minutes after the use of the shampoo itching developed (3rd visit). Intensity: 1 (mild); Connected to the use of shampoo: 3 (possibly); symptomatic treatment: 2 (not needed).

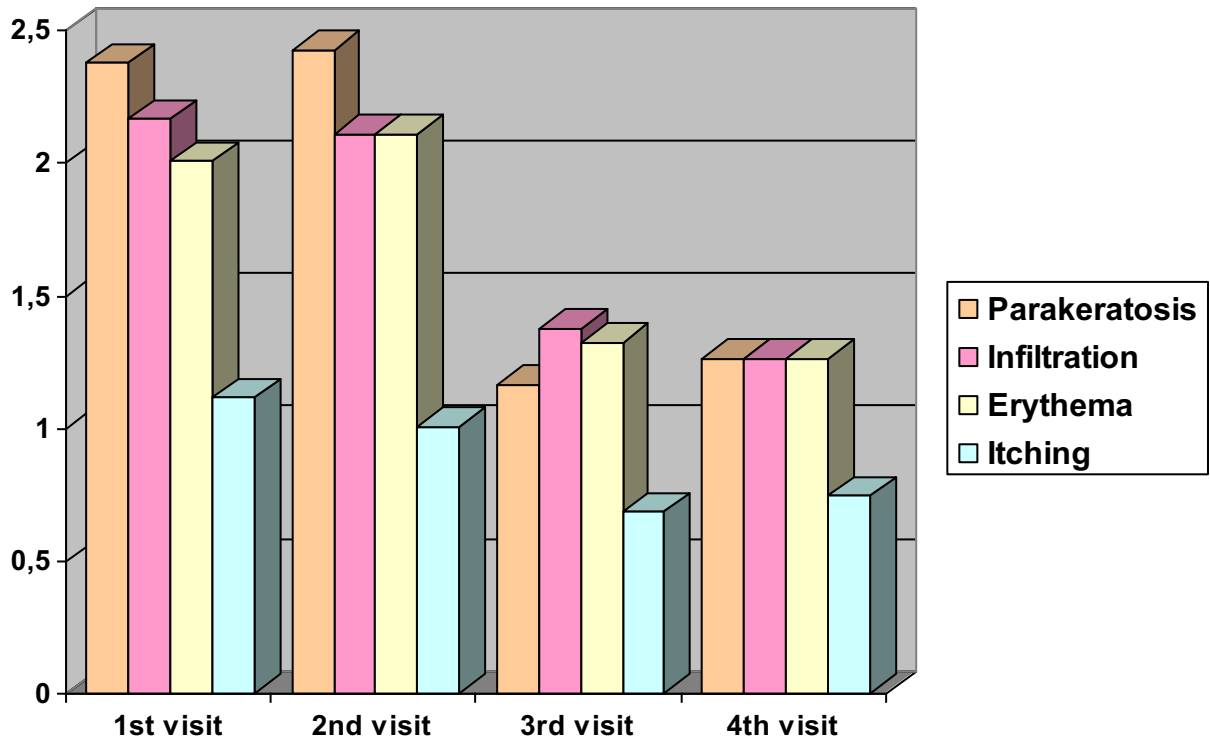


Figure 5.: Visits (medical examinations)/average score of symptoms (1-3)

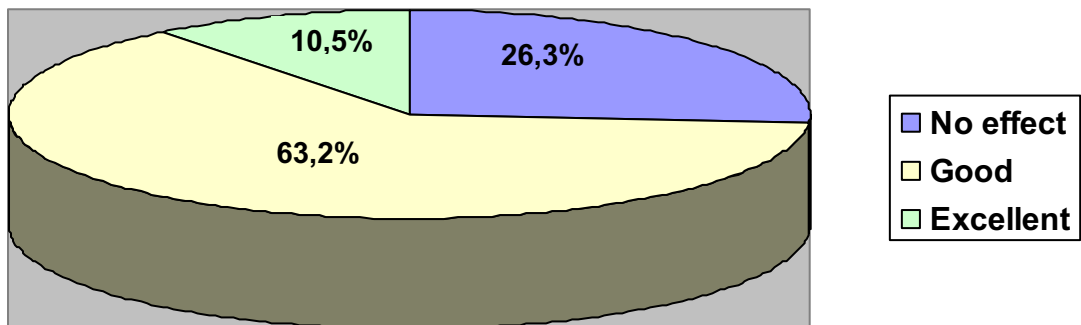


Figure 6.: The patient's (subjective) evaluation on the efficacy of treatment

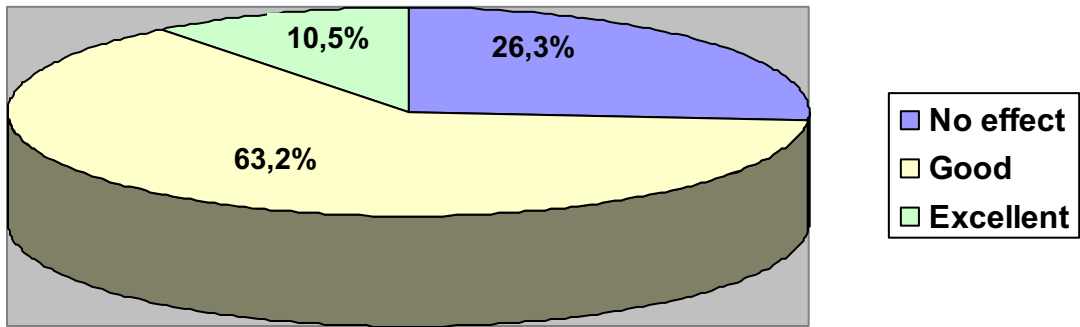


Figure 7.: The doctor's evaluation on the efficacy of treatment

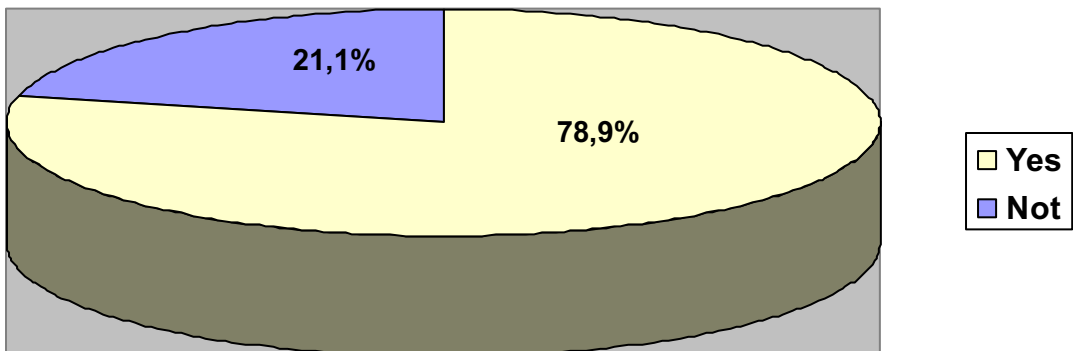


Figure 8.: Would the patient later intend to use the study preparation?

Chapter 6.

Discussion

Prior to the above described open clinical study, experiences on the efficacy and safety of Soritex sjampo has been limited to case reports from many thousands of patients who used the preparation. Their feed-back was generally very positive.

However, until now there was no *lege artis* clinical data and IN VITRO Ltd. decided to perform the above open, prospective clinical trial to prove Soritex sjampo's efficacy and safety in seborrhoea capitis and psoriasis capitis in a dermatological clinical setting.

This trial will be continued and extended to accumulate additional long-term data.

According to the results **in seborrhoea capitis** Soritex sjampo **significantly** reduced the severity of desquamation, inflammation, fattiness of the hair and itching which are the leading symptoms of seborrhoea disturbing very much the quality of life of the patients.

99,4% of the seborrhoea patients and the doctors found Soritex sjampo to have excellent or good efficacy and 99,4% of the patients intended to continue the use of the preparation.

In psoriasis capitis parakeratosis, infiltration and erythema have been **significantly** reduced. Itching had a tendency to alleviation but the result did not reached the level of significance.

73,7% of the psoriatic patients and the doctors found Soritex sjampo to have excellent or good efficacy and 78,9% of the patients intended to continue the use of the preparation.

As to the safety, in the seborrhoea capitis arm of the study one patient dropped out because of contact dermatitis-like symptoms. In the epicutan allergy test he had hypersensitivity to fragrance mix and balsam of Peru. (Soritex sjampo contains neither added fragrances nor balsam of Peru. Allergology testing for these substances is part of the routine medical test procedure.).

In the psoriasis capitis arm in two patients itching developed at various times during the study with possible connection to the use of the cream shampoo. No special treatment was needed.

The exact mechanism of action of Soritex sjampo is unknown. The active ingredients (propolis, sea salt, medicinal plant extracts and vitamins) of the cream shampoo contain compounds of antiinflammatory and antimicrobial effects and are well known and used in the treatment of inflammatory skin conditions, among others in seborrhoea and psoriasis. The original idea behind Soritex was their combination in one preparation hypothesizing that they could have synergistic effects.

The clinical results support this hypothesis but the exact role of the individual components remain unknown. The highly lipophilic vehicle plays an additional, important role in the effect, partly by supplementing lipids to the scalp.

Chapter 7.

Conclusions

Soritex sjampo can be successfully used

- **in seborrhoea capitis** to significantly reduce the severity of desquamation, inflammation, fattiness of the hair and itching, and
- **in psoriasis capitis** to significantly decrease parakeratosis, infiltration, and erythema. Itching can be influenced positively, too, but the cream shampoo's effect regarding this parameter does not reached the level of significance in the above open clinical trial.

The beneficial effects appear quickly, usually after one week of daily treatment.

The safety of Soritex sjampo is good. In some cases hypersensitivity or itching can develop.

Based on the earlier case report from thousands of patients and on the results of the above open clinical trial **Soritex sjampo can be successfully used in mild to medium level seborrhoea capitis and psoriasis capitis as a first-line therapy before other medicines of stronger effects and with a risk of serious side effects are tried.**

Attachments:

To the seborrhoea capitis arm: Figure a, b, c, d

To the psoriasis capitis arm: Figure e, f, g, h