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DIAGNOSTIC PROCESS AND TREATMENT MONITORING OF SEBORRHOEIC DANDRUFF BY MEANS OF A IMAGEANALYTICAL PROCEDURE

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Summary

After briefly going into the clinical picture of (seborrhoeic) dandruff, its pathogenesis and therapy, the clinical proof procedure on the scalp is pointed out.
A new imageanalytical method, based on past examinations is described. Here, the number of scales (SZ) and the measuring area covered with scales (SF) are measured. From this, a relative scale size (SG) can be calculated
Additionally the scale sizes are shown in per cent in 9 categories.
In three exemplarily presented comparative tests, the suitability of the method for the evaluation of an antidandruff formula against a standard product, the influence of the basis and different effects of individual active antidandruff ingredients could be demonstrated.
Score-determinations on the scalp which were carried out in comparison had the same result, but overall were less selective.

Riassunto

Dopo aver descritto brevemente la patogenesi e la terapia della forfora seborroica, viene descritta una procedura di controllo da eseguire sul cuoio capelluto basata su un metodo di analisi di immagine. Viene misurato il numero di squame (SZ) e l'area che esse ricoprono (SF). Viene quindi calcolata la loro relativa grandezza media (SG).
La grandezza percentuale delle squame è suddivisa in 9 categorie. Con tre test comparativi viene verificata l'esattezza del metodo, controllando anche una formula antiforfora, paragonata ad una formulazione standard, verificandone anche l'influenza della sua base e di diversi principi attivi.
Con la metodica a punteggio si sono ottenuti gli stessi risultati, ma con minore selettività.

INTRODUCTION

Increased scaling off of the stratum corneum of the scalp, which oversteps the normal mark, leads to the clinical image of "dandruff".

Keratinization disturbances (e.g. a parakeratosis in case of psoriasis capitis) or a xerosis (e.g. in case of dermatitis atopica in the sense of an etat craquelé) can be pathogenetic causes. In the latter case, irritative factors (e.g. tensides) can additionally lead to an inflammatory hyperkeratosis.

The most common form is, however, the so-called seborrhoeic dandruff (pityriasis capitis), which affects around 5% of the population (1). Men are more often affected than women and the main age group are the 20 to 40-year olds, so there is reason to believe that there are hormonal influences.

The question whether pityriasis capitis as a primarily non-inflammatory variation - in English it is often called "dandruff" - can be delimited from seborrhoeic dermatitis or whether there is a fluid transition, is being controversially discussed in the respective literature (2).

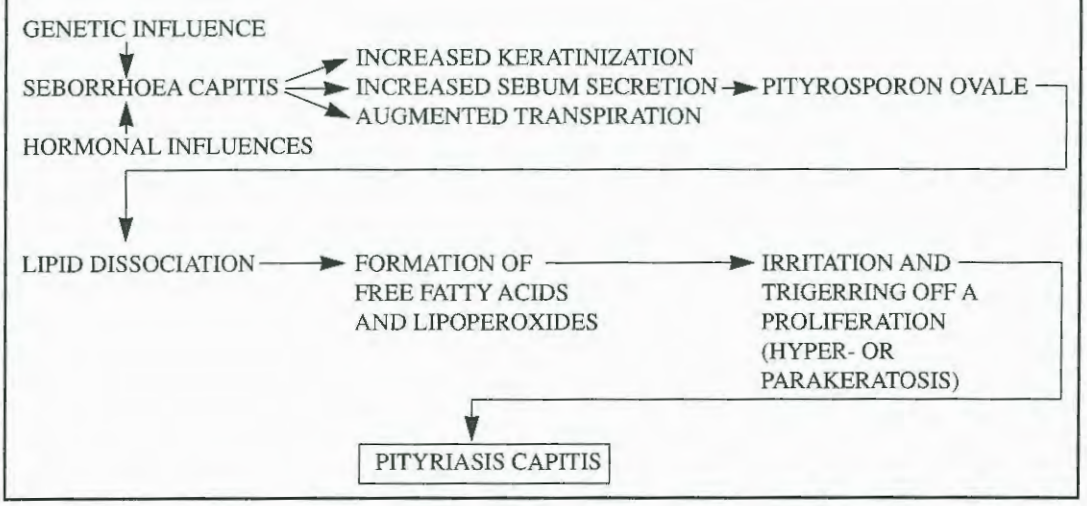
Considering of the clinical impression as well as the therapeutical approaches, the following developmental pattern can be assumed for pityriasis capitis (Table I).

The genetically predetermined and hormonally activated seborrhoea leads sui generis to an increased proliferation of the keratinous layer (example: intra-follicular hyperkeratosis in case of acne) and to an increased secretion of sebum and sweat. These, in turn, represent an ideal culture medium for the lipophile yeasts of the type pityrosporon ovale, which are present everywhere on the skin. They cause a lipid dissociation with formation of free fatty acids and lipoxides, which have an irritant effect on the skin. This leads to an inflammatory proliferation of the epidermal cells up to a hyper- or parakeratosis, respectively. The result is a changed scaling on the skin surface, i.e. in larger scales, which is found to be cosmetically disturbing. A minimal variation of seborrhoeic dermatitis develops, which includes an increased sensitivity of the scalp and is sometimes combined with itching and erythema.

In the case of an especially intensive secretion of sebum these changes, also called seborrhoea

Table I

DIAGRAM OF PITYRIASIS SIMPLEX



sicca, turn into a seborrhoea oleosa by adhesion of the dandruff with sebaceous residues, which can then lead to firmly adhering dandruff caps and needs to be treated dermatologically.
The validity of these pathogenetic conclusions is confirmed by the frequent clinical observation that after a successful (antimicrobial) treatment of pityriasis capitis there is at first an increase of the amount of sebum on the scalp with corresponding influence on the hair style.
In the past, mainly keratolytics like salicylic acid and resorcin, as well as sulphur, selenium disulphide, zinc-pyrithion and tar were used for the treatment of the cosmetically disturbing dandruff. If there is a heavily inflammatory component, topical glucocorticoids were also used.
The new substances which have a good in vitro effect against p. ovale (3) are for instance piroctон-olamin as well as some different azoles, also used as antimycotics.
For the treatment of cosmetic dandruff, i.e. a moderate seborrhoeic pityriasis capitis of the type seborrhoea sicca, antidandruff shampoos with tensides as formulas which are free of active ingredients are being offered (4).
The determination of the degree of a pityriasis capitis and a therapy control can be done by means of an evaluation of the dandruff according to scores on the head with hair. If necessary, this can also be done in individual areas of the scalp.
In order to objectively detect cosmetically disturbing dandruff, one can use a test procedure which was developed more than 20 years ago. Its imageanalytical updating is described methodologically in the following.
During the development of the early method it was already found out that compared to the determination of the amount of combed-out scales (number or weight), the differentiation of the sizes in predetermined categories e.g. by diameter or the surface of the scales, also represents a sensitive parameter.
It was therefore advisable to not only record the number of combed-out scales but also the categorisation into different sizes and the measuring area covered by scales in the imageanalytical process. The ratio of number of scales and covered measuring area can be used as an additional measure for a relative average scale size.
Thus, the evaluation of the dandruff status is similar to the photoanalysis applied in the evaluation of cellular cohesion on the hairless skin by use of adhesive films (6, 7).

METHOD FOR IMAGEANALYTICAL DETERMINATION OF DANDRUFF

Under defined conditions (combing procedure and closeness of the comb's teeth) the test

Fig. 1 - Combing out of the dandruff under defined conditions.

Fig. 2 - Measuring device for measuring scales.

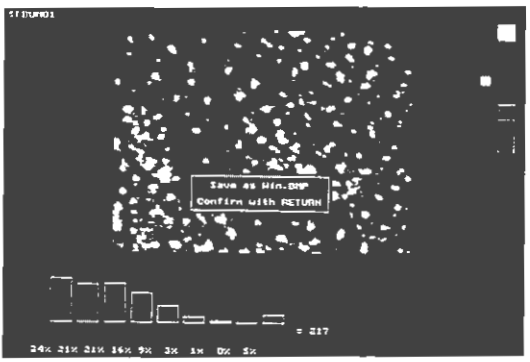


Fig. 3 - Dandruff image with analysis by means of special software.

subject's dandruff is combed onto a black film (Fig. 1), then put into a Petri dish and distributed evenly in a 25×25 mm measuring field with a fine brush. This measuring field is then completely measured in the stationary measuring device, consisting of a high-resolution CCD camera and a fluorescent UV -lamp , installed for even illumination (Fig. 2). The picture, transmitted onto a PC monitor (Fig. 3) is then analysed according to the following parameters by means of a special software:

Number of scales in the measuring field (SZ)

Measuring area covered with scales (SF) in %

Relative scale size (SG)

$$SG = \frac{SF \times 100}{SZ}$$

Distribution of scale sizes in % into 9 categories (Table II)

A mistake in the method, which is negligible in practice, is that scales which are lying on top of each other by chance are not measured separately. In case of very high scale density, it is therefore advisable to evaluate the scales in two measurings.

When carrying out effectiveness studies of, for example, antidandruff shampoos, one has to take care that not only the procedure of combing out is done in a defined way, but also that the test subjects do not change their hairstyle or use different additional hair care products during the study.

Table II
CLASSIFICATION FOR SCALE SIZE

Category I	<	0.05	mm	∅
II	to	0,08	mm	∅
III	to	0,10	mm	∅
IV	to	0,13	mm	∅
V	to	0,15	mm	∅
VI	to	0,18	mm	∅
VII	to	0,20	mm	∅
VIII	to	0,23	mm	∅
IX	>	0,25	mm	∅

STUDY DESIGN OF EFFECTIVENESS TEST OF ANTIDANDRUFF PRODUCTS

For a comparative test of antidandruff products, the test subjects with cosmetically disturbing seborrhoeic dandruff to be included in the test, should be chosen after a preliminary dermatological examination. The group should comprise a minimum of 20 test subjects. In the first examination, an initial imageanalytical condition is additionally determined. This is complemented by a dermatological dandruff score of the scalp (Table III). These parameters are complemented by an additional evaluation of the degree of dandruff by the test person according to the same scores.

Table III
SUBJECTIVE EVALUATION KEY FOR THE OBJECTIVE AND SUBJECTIVE DANDRUFF INVASION

Score	
0 =	No scales visually perceptible
1 =	Single scales
2 =	Several scales
3 =	Dense dandruff invasion
4 =	Extensive dandruff invasion

Following this, there is a conditioning phase with a neutral shampoo. This shampoo should be applied at least twice a week over a period of 14 days.
After that, the dandruff situation is once again examined by means of imageanalysis and scores (measuring time 0). After that, there is a treatment phase of 4 to 6 weeks with weekly examinations of the dandruff status. Afterwards, a rinsing phase of 2 to 4 weeks with fortnightly further examinations is advisable.
If several products are to be tested comparatively, i.e. different groups of test subjects are needed, an assignment of the test products to the different groups at measuring time 0 is advisable in order to achieve comparable initial values. This does not apply, if a double blind randomisation is intended.

EXAMPLES OF RESULTS FROM COMPARATIVE DANDRUFF STUDIES

In order to show the practical relevance of the results to be achieved as well as the usability of the presented test procedure, which we have been using for several years, three comparative tests are shown exemplarily in the following.

Evaluation of a test product in comparison to an introduced reference product

In order to test the effectiveness of a newly-developed antidandruff formula, one can carry out a comparison with a standard product, i.e. a product which is already on the market.
Table IV shows the result of such a test for photo-analytical evaluation. Here there is a clear increase of dandruff formation in all three measuring parameters for the test product after a conditioning phase of two weeks with a neutral shampoo. In the treatment phase over a period of 4 weeks, the measuring parameters decrease depending on time, i.e. formation of dandruff decreases. Here, the values for measuring time 0 compared to measuring time 4 are highly significant statistically. After putting the test subjects onto a neutral shampoo in the following 6 weeks, the dandruff increases again gradually up to the value of measuring time 0.
A striking fact in the reference group is that there is no significant increase of the dandruff values after the conditioning. This leads to differences of the initial values of the two groups at the beginning of the treatment phase. To avoid this, a randomisation is only advisable at this point in time.
In this test subject group B, the dandruff values also decrease during the 4-week treatment and even after withdrawing the verum in the following weeks, a further decrease of the dandruff values can be established.
In the evaluation of the score values of the scalp a similar picture presents itself, including the presented specific differences in the development in the two groups (Table V).

Evaluation of the influence of the basic formula which is free of active ingredients

The basic formula which is free of active ingredients is especially important for the effect of antidandruff products, especially shampoos, because the possibly irritant effect of these ingredients on the scalp, which is highly sensitive anyway (in the sense of a seborrhoeic dermatitis), could weaken the antidandruff effect of a substance, or as has been shown in some of our own examinations, even neutralise it.
In a comparison of two formulas with 0,1% pi-

Table IV
IMAGEANALYTICAL COMPARISON OF A TEST SUBSTANCE (A) AND A STANDARD SUBSTANCE (B)

A Shampoo with 2% Climbazol (n=23)
B Shampoo with 2% Ketoconazol (n=19)

MZ	AN	A			B		
		SZ	SF	SG	SZ	SF	SG
–2	P	218	9,5	4,4	179	7,6	4,2
0	P	246	18,2	7,4	161	7,9	4,9
1	V	182	15,0	8,2	143	5,6	3,9
2	V	224	9,8	4,4	161	5,5	3,4
3	V	180	6,4	3,6	159	4,3	2,7
4	V	149	5,1	3,4	157	4,5	2,9
6	P	198	6,8	3,4	132	4,3	3,3
8	P	236	9,4	4,0	119	4,3	3,6
10	P	277	10,3	3,3		–	
12	P	284	12,3	4,3		–	

MZ - Measuring Time (Weeks)
AN - Applied Product; V - Verum; P - Placebo
SZ - Number of Scales
SF - Area of Scales %
SG - Rel. Size of Scales

$$SG = \frac{SF \times 100}{SZ}$$

rocton-olamin in different basic ingredients, formula B is clearly superior to formula A in all relevant parameters of imageanalytical evaluation (Table VI).
The dermatological score comparison also shows the superiority of formula B (Table VII).

Evaluation of the influence of the active ingredients

As a last example, a comparative test with two different active ingredients (azoles) in the same shampoo basis is presented.
As is shown in Table VIII, the formula with Azol B proves to be more efficient in the imageanalytical evaluation. The differences between the two formulas become especially clear during the last two weeks of treatment.
It is possible that the differences in efficiency are due to the different solubility of the applied components.
In the score evaluation (Table IX), these differences are less pronounced, above all when the different initial values are not taken into account.

DISCUSSION

The determination of dandruff occurring with pityriasis simplex by analysis of scales that could be combed out and not in scores on the scalp was already described more than 20 years

Table V
DERMATOLOGICAL SCORE-COMPARISON OF A TEST SUBSTANCE (A) WITH A STANDARD SUBSTANCE (B)

A Shampoo with 2% Climbazol (n=23)
B Shampoo with 2% Ketoconazol (n=19)

MZ	AN	Score	
		A	B
–2	P	1,2	1,2
0	P	1,5	1,2
1	V	1,2	1,2
2	V	1,2	1,0
3	V	1,2	0,7
4	V	0,9	0,8
6	P	0,7	0,6
8	P	0,8	0,6
10	P	0,7	–
12	P	0,9	–

MZ - Measuring Time
AN - Applied Product

ago. By use of imageanalytical evaluation processes its quality can be improved and, at the same time, it can be simplified methodologically. The results achieved with this method correspond in principle to those of the in vivo evaluation of dandruff. It has to be said, however, that the latter evaluation is less selective.

Apart from the number of scales (SZ) and the measuring area covered with dandruff by which the relative scale size can be calculated, the classification of the different scale sizes gives some information about the pathogenesis. An increase of many small scales (e.g. in therapy) indicates an exsiccation of the stratum corneum. If, however, there is an increase of larger scales, or are they already present, an inflammatory epidermal proliferation can be inferred.

A shift in the classification from larger to smaller scales during treatment (Table X) is a very reliable indicator for the evaluation of a successful therapy.

Table VI
IMAGEANALYTICAL COMPARISON OF TWO FORMULAS WITH DIFFERENT BASIC FORMULA

A Basic Formula A with 0,1% Pirocton-Olamin (n=23)
B Basic Formula B with 0,1% Pirocton-Olamin (n=23)

MZ	AN	A			B		
		SZ	SF	SG	SZ	SF	SG
–2	P	172	1,4	8,4	217	17,4	8,0
0	P	245	26,4	10,8	297	21,9	7,4
1	V	186	19,1	10,3	191	13,6	7,1
2	V	196	15,8	8,1	151	7,4	4,9
3	V	183	13,7	7,5	150	7,0	4,7
4	V	152	11,4	7,5	113	4,4	3,9
6	P	294	18,1	6,2	241	10,7	4,4
8	P	370	25,3	6,8	305	12,6	4,1

MZ - Measuring Time (Weeks)
AN - Applied Product; V - Verum; P - Placebo
SZ - Number of Scales
SF - Area of Scales %
SG - Rel. Size of Scales

$$SG = \frac{SF \times 100}{SZ}$$

Table VII

DERMATOLOGICAL SCORE-COMPARISON OF TWO BASIC FORMULAS

A Basic Formula A with 0,1% Pirocton-Olamin (n=23)

B Basic Formula B with 0,1% Pirocton-Olamin (n=23)

MZ	AN	Score	
		A	B
–2	P	1,5	1,4
0	P	1,5	1,4
1	V	1,3	1,1
2	V	1,1	0,8
3	V	1,0	0,7
4	V	0,9	0,7
6	P	0,9	1,0
8	P	1,4	1,3

MZ - Measuring Time
AN - Applied Product

The imageanalytical method is not only suitable for the evaluation of a current state, but, as is to be shown in examples, for the evaluation of treatment types.

It is advisable to have a group of test subjects comprising about 20 people or more, and in case of comparative studies to use randomisation after a 2-week conditioning with a neutral shampoo, for example. For the evaluation of efficiency, a treatment cycle of 4 weeks is usually sufficient. The reaction time of applied substances can be evaluated in a neutral after-care phase.

In the studies made up to now, it has become clear that the basic formulas without active ingredients used for the effect of antidandruff shampoos have a special significance. A drying-out of the scalp and, even more, an irritation of the sensitive scalp lead to an intensification of dandruff.

Table VIII

IMAGEANALYTICAL COMPARISON OF TWO FORMULAS WITH DIFFERENT ACTIVE INGREDIENTS IN THE SAME BASIC FORMULA

A 1% Azol A (n=24)
B 1% Azol B (n=27)

MZ	AN	A			B		
		SZ	SF	SG	SZ	SF	SG
–2	P	–	–	–	–	–	–
0	P	199	12,4	6,2	184	10,8	5,9
1	V	180	10,8	6,0	141	11,5	8,2
2	V	148	7,7	5,2	132	7,9	6,0
3	V	144	8,7	6,0	112	8,1	7,2
4	V	140	8,1	5,8	103	6,3	6,1

MZ - Measuring Time (Weeks)
AN - Applied Product; V - Verum; P - Placebo
SZ - Number of Scales
SF - Area of Scales %
SG - Rel. Size of Scales

$$SG = \frac{SF \times 100}{SZ}$$

Table IX

DERMATOLOGICAL SCORE-COMPARISON OF TWO FORMULAS WITH DIFFERENT ACTIVE INGREDIENTS AND THE SAME BASIC FORMULA

A 1% Azol A (n=24)
B 1% Azol B (n=27)

MZ	AN	Score	
		A	B
–2	P	–	–
0	P	1,2	1,5
1	V	1,4	1,5
2	V	1,0	1,2
3	V	0,7	0,9
4	V	0,8	0,8

MZ - Measuring Time
AN - Applied Product

Table X

EXAMPLE OF A FREQUENCY DISTRIBUTION OF SCALE SIZES

Substance A with 0,1% Pirocton-Olamin (n=23)

MZ	Freqnency distribution (%)								
	I	II	III	IV	V	VI	VII	VIII	IX
0	44,7	22,0	11,4	7,1	4,4	2,4	1,9	1,2	4,3
2	58,1	20,3	7,9	5,0	3,0	1,4	1,3	0,7	2,4
4	57,8	19,9	8,8	5,4	3,5	1,7	0,6	0,7	1,5

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