Phytomedicine 10 (2003) · Supplement IV; pp. 31–37

http://www.urbanfischer.de/journals/phytomed

Phytomedicine

Topical treatment of atopic dermatitis with St. John's wort cream – a randomized, placebo controlled, double blind half-side comparison

Christoph M. Schempp[1], Timo Windeck[2], Svea Hezel[1], and Jan C. Simon[1]

[1] Freiburg University Clinic, Department of Dermatology, Freiburg, Germany
[2] Lichtwer Pharma AG, Berlin, Germany

Summary

Background: Recent investigations suggest an anti-inflammatory and antibacterial effect of hyperforin, which is a major constituent of *Hypericum perforatum* L. (Saint John's wort).
Objective: In the present half-side comparison study we assessed the efficacy of a cream containing Hypericum: extract standardised to 1.5% hyperforin (verum) in comparison to the corresponding vehicle (placebo) for the treatment of subacute Atopic Dermatitis. The study design was a prospective randomised placebo-controlled double-blind monocentric study.
Methods: In twenty one patients suffering from mild to moderate Atopic Dermatitis (mean SCORAD 44.5) the treatment with verum or placebo was randomly allocated to the left or right site of the body, respectively. The patients were treated twice daily over a period of four weeks. Eighteen patients completed the study. The severity of the skin lesions on the left and right site was determined by means of a modified SCORAD-index (primary endpoint).
Results: The intensity of the eczematous lesions improved on both sites of treatment. However, the hypericum-cream was significantly superior to the vehicle at all clinical visits (days 7, 14, 28) ($p < 0.05$). Skin colonisation with *Staphylococcus aureus* was reduced by both verum and placebo, showing a trend to better antibacterial activity of the hypericum-cream ($p = 0{,}064$). Skin tolerance and cosmetic acceptability was good or excellent with both the hypericum-cream and the vehicle (secondary endpoints).
Conclusion: Taken together, the present study shows a significant superiority of the hypericum-cream compared to the vehicle in the topical treatment of mild to moderate Atopic Dermatitis. The therapeutic efficacy of the hypericum-cream, however, has to be evaluated in further studies with larger patient cohorts, in comparison to therapeutic standards (i.e. glucocorticoids).

Key words: Hyperforin, St. John's wort, Severity Scoring of Atopic Dermatitis, randomised clinical trial, Half-side comparison

Introduction

St. John's wort oil is traditionally used for the topical treatment of wounds, burns and nerve lesions (Roth, 1990; Maisenbacher and Kovar, 1992). St. John's wort (*Hypericum perforatum* L.) is also used as a homeopathic remedy for eczematous skin conditions (Metzger, 1991), although to date there have been no controlled studies to substantiate such efficacy. Hypericin, which fluoresces red and possesses photodynamic activity, has been identified as one principal constituent of St. John's wort. Hypericin is a naphthodianthrone

Translation from "Der Hautarzt" 54(2003): 248–253; english translation and reproduction with kind permission of Springer Verlag, Berlin/Heidelberg

1433-187X/03/10/Suppl. IV-031 $ 15.00/0

that displays typical fluorescence in the red wavelength range (588 nm). The substance exhibits dose-dependent photosensitising activity (for review, see Schempp et al. 2002a). In our own research we have studied the photosensitising effect of topically applied St. John's wort extracts. Mild photosensitisation to solar simulated radiation was detected with St. John's wort oil but not with St. John's wort cream containing hypericin (Schempp et al. 2000a). Another characteristic constituent of St. John's wort is the phloroglucin derivative hyperforin, which has long been known to possess antibacterial activity (Gurevich et al. 1971). We have shown that hyperforin also inhibits the growth of multiresistant strains of *Staphylococcus aureus* (Schempp et al. 1999). St. John's wort also contains tannins and flavonoids (Roth, 1990; Kaul, 2000; Schempp et al. 2002a). In further studies we have found that a hyperforin-containing St. John's wort cream and pure hyperforin exert an inhibitory effect on epidermal Langerhans cells comparable to the immunosuppressant effect of UVB irradiation (Schempp et al. 2000b). These actions of hyperforin may possibly prove beneficial in the treatment and aftercare of subacute eczema. The present randomised, double-blind, placebo-controlled Phase II study was therefore conducted to compare the effects of a St. John's wort cream with a standardised hyperforin content (referred to below as hyperforin cream) and of placebo (a colour-matched vehicle) in patients with subacute atopic dermatitis treated over a 4-week period. The study was designed as a half-side (within-patient left/right) comparison.

Methods

Study design

The study was conducted using a prospective, randomised, placebo-controlled, double-blind, single-centre design incorporating a half-side comparison. Twenty-one patients with symmetrical subacute atopic dermatitis of limited extent were included in the study. The patients were treated for 4 weeks with the hypericum-cream and placebo on the left or right body side, and the active treatment (hyperforin cream) was randomly allocated to the left or right body side. The study medications were applied twice daily to the skin of the appropriate body side. At the end of the study the tubes containing the study medications were collected and counting (tube weighing) was performed to verify equal application to left and right body sides. The primary endpoint was the effect on skin condition, calculated separately for each body side using a modified version of the SCORAD Index. The secondary endpoints were skin colonisation with *Staphylococcus aureus*, cosmetic acceptability, and skin tolerance of the creams. The study was approved by the Ethics Committee of the Freiburg Medical Faculty (favourable opinion 264/2000).

Inclusion criteria

Male and female patients between the ages of 12 and 59 years. Diagnosis of subacute atopic dermatitis of limited extent (SCORAD Index score <80). The Scoring of Atopic Dermatitis (SCORAD) Index is an established instrument for assessing the severity of atopic dermatitis (Sears et al. 1997). It is based on the extent of affected skin areas, on the severity of erythema, papulation, crust, excoriation, lichenification and scaling, as well as on the subjective parameters pruritus and sleep loss. The SCORAD Index score was calculated using the algorithm recommended by the European Task Force on Atopic Dermatitis (1993). As additional inclusion criteria, patients were to have signed an informed consent form, were to be willing to comply with the study conditions, and were to apply the study medications in line with the stipulated dosage instructions. The patients also had to be willing and able to complete self-assessment scales as part of the follow-up assessment visits.

Exclusion criteria

Infectious diseases, severe underlying clinical disease, underlying malignant disease, markedly reduced general level of health, known dependence on alcohol or drugs (social or medicinal). Women of childbearing age without adequate contraception. Pregnant and breast-feeding women. Participation in another clinical study during the previous 4 weeks. Simultaneous participation in another clinical study. Concurrent use of topical agents or medicinal products containing corticosteroids. Systemic administration of corticosteroids and antihistamines during the previous 2 weeks. Topical therapy with corticosteroids during the previous week. Known hypersensitivity to hypericum preparations or to any of the cream ingredients. Current treatment with psychotropic medicines, and medical requirement for concurrent medication with substances that possess anti-inflammatory, immunomodulatory or antibiotic activity.

Study medication

The preparations were manufactured, quality controlled, packaged and dispensed in accordance with the current version of the guidelines for the manufacture and quality control of clinical trial materials (Good Manufacturing Practice and Good Laboratory Practice). The composition of the vehicle for the two creams was identical: water, white soft paraffin, propylene glycol, neutral oil, Tagat, Lanette, Eusolex T,

Tegin M, phenoxyethanol, and butylated hydroxytoluene. In addition to the vehicle, the active cream contained 5% of an apolar extract of St. John's wort (*Hypericum perforatum* L.) according to *DAC 86*. The extraction process was performed with overcritical carbon-dioxide as eluting agent. The drug-extract-ratio amounted to 20 to 25:1. The extract contained 9.9% of total hyperforin (8.5% hyperforin and 1.4% adyhyperforin). Levels of flavonoids and hypericin were below the limit of detection. The final concentration of hyperforin was thus appr. 1.5%. The placebo consisted of an identical vehicle with added chromogenic substances (to colour the vehicle for purposes of treatment blinding).

Primary endpoint

The primary endpoint of the study was the clinical intensity of the skin lesions on the right or left body side. Skin condition was calculated for each body side using a modified SCORAD Index based on the extent and intensity of erythema, papulation, crust, excoriation, lichenification and scaling. Intensity was classified for each variable using a 4-point scale (0 – none, 1 – mild, 2 – moderate, 3 – severe).

The point score on the modified SCORAD Index was calculated using the following algorithm: (% skin area affected: 5) + (intensity score × 3.5). This is the same algorithm as for the SCORAD Index but excluding the subjective variables pruritus and sleep loss (European Task Force on Atopic Dermatitis, 1993).

Secondary endpoints

The following scales and indices were analysed as secondary endpoints: bacterial colonisation of skin lesions (colony-forming units [CFUs]) at Day 0 and Day 28, skin tolerance and cosmetic acceptability of the study medications. At the start and end of the study a contact agar plate (Columbia agar plates with counting grid, diameter 6 cm, Becton & Dickinson, Heidelberg) was applied to one defined treatment area each on the right and left body side. The contact plates were incubated at 37 °C for 24 hours, and the CFUs were then counted along a diagonal axis. The colonies of *Staphylococcus aureus* were identified macroscopically without further subtyping. The CFU count was assessed using the following scale: – (0 CFUs), + (1–10 CFUs), ++ (11–20 CFUs), +++ (> 20 CFUs). The skin tolerance and cosmetic acceptability of the study medications were scored by the patients themselves at Visits 2–4 using the following scale: excellent – good – moderate – poor.

Laboratory investigations

Laboratory investigations were performed before the start of the study and again at Visit 4. The following serum variables were determined: haemoglobin, haematocrit, red blood cells, white blood cells, creatinine, SGOT, SGPT, γ-GT, alkaline phosphatase, and bilirubin. Urine status (blood, protein, bacteria) was determined in addition. Women of childbearing age also underwent a pregnancy test (urine sample) before the start of the study.

Statistical methods

In line with the pilot nature of the study, the sample size was fixed at 20 patients based on pragmatic considerations. A sample size calculation was not performed because no reference data were available for this purpose. The populations for analysis were identified before database closure. All statistical analyses were performed using the SAS system.

Initially, three analysis populations were considered. The per-protocol (PP) analysis was performed using all patients who completed the study according to protocol with the scheduled treatment period and with (at most) minor protocol violations. Patients who were treated for a period of at least 10 days formed the intention-to-treat (ITT) population. Efficacy was analysed in the ITT/PP population. The data relating to demographics and medical history were analysed using the safety population and the ITT/PP population.

The efficacy of the hypericum-cream and placebo was assessed in terms of changes in the modified SCORAD Index score. For this purpose the data collected at Visits 1, 2, 3 and 4 were analysed descriptively. In addition to descriptive statistics, the change in the modified SCORAD Index score from baseline to end of treatment was calculated for the hypericum-cream and placebo. To compare the hypericum-cream and placebo, these changes were analysed using Wilcoxon's rank sum test for dependent samples at the 5% level, and 95% confidence intervals were calculated for the medians of the changes.

Similarly, for bacterial colonisation, the change from baseline (reduced, unchanged, increased) was calculated and Wilcoxon's rank sum test was performed.

Results

Populations analysed

Twenty-one patients took part in the study. Eighteen patients satisfied the predefined criteria for the analysis of efficacy variables (see above) and were included in the ITT population. Because the protocol violations in this group of patients were only ever classed as minor, the ITT population and the PP population were identical. The safety population comprised all 21 patients. Patients were excluded from the ITT/PP population be-

cause of missing efficacy data after 10 days of treatment (1 patient) and because treatment lasted for less than 10 days (2 patients). The demographic data for the ITT/PP population are presented in Table 1.

Efficacy (half-side comparison)

The primary endpoint was a modified SCORAD Index score, which is based on the assessment of skin lesion intensities. In order to determine these intensities, the presence and severity of erythema, crust, lichenification, papulation, excoriation and scaling were scored. The individual scores were then totalled to calculate a sub-score for each treatment side (see Methods).

In the half-side comparison of skin lesion intensities between the hypericum-cream and placebo, there was a reduction of 5.4 points with the hypericum-cream compared with 2.3 points with placebo after 28 days of treatment (Table 2). The superior efficacy of the hypericum-cream compared with placebo was demonstrated at all clinical visits (Days 7, 14 and 28) and was statistically significant ($p < 0.05$, see Fig. 1).

In terms of the total SCORAD Index, the score for treatment with the hypericum-cream fell from 44.9 (± 16.9) points at baseline to 23.9 (± 17.2) points after 28 days. The score for treatment with placebo (drug-free vehicle) showed a reduction of 10.3 points (from 43.9 (17.9 points at baseline to 33.6 ± 16.5 points after 28 days).

Table 1. Demographic data for the ITT/PP population (n = 18).

Total SCORAD	44.5 ± 17.5; min. 16.5; max. 66.5
Age (years)	30.4 ± 12.9
Height (cm)	171.6 ± 10.2
Body weight (kg)	71.6 ± 16.7
Sex (male/female)	10/8

Bacterial colonisation

The antibacterial efficacy of therapy was determined at the beginning and end of the study by counting the number of CFUs of bacteria in general and of *Staphylococcus aureus* in particular. The number of CFUs of *Staphylococcus aureus* was more markedly reduced in response to treatment with the hypericum-cream than with placebo ($p = 0.064$, see Table 3). Bacterial colonisation of the skin by other organisms was not affected by treatment with either hypericum-cream or placebo.

Skin tolerance and cosmetic acceptability

The investigator made a global assessment of the skin tolerance of the hypericum-cream and placebo at each clinical visit. Both study medications were classified as good or excellent by more than 80% of patients at all clinical visits. No differences were detected between the groups in terms of skin tolerance.

The cosmetic acceptability of both study medications was described as good or excellent by more than

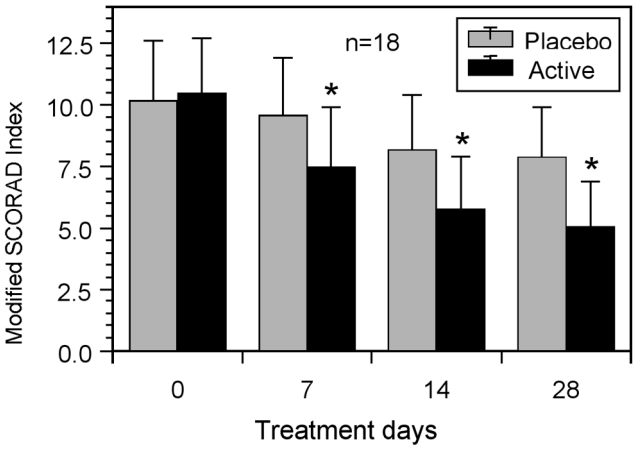

Fig.1. Modified SCORAD Index score over time during treatment with hypericum-cream (verum) and vehicle (placebo). * $p < 0.05$.

Table 2. Modified SCORAD Index score in half-side comparison: change from baseline.

Visit	Treatment	Mean ± SD	Median [min.; max.]	95% CI	p-value*
Day 7	hypericum-cream*	–3.0 ± 3.1	–3.0 [–10.0; 5.0]	[–5.0; –2.0]	0.002
	Placebo	–0.6 ± 1.2	–0.5 [–2.0; 2.0]	[–2.0; 0.0]	
Day 14	hypericum-cream*	–4.7 ± 3.3	–6.0 [–10.0; 2.0]	[–7.0; 3.0]	0.016
	Placebo	–2.1 ± 3.0	–2.0 [–10.0; 4.0]	[–4.0; 0.0]	
Day 28	hypericum-cream*	–5.4 ± 4.9	–6.5 [–12.0; 5.0]	[–9.0; –4.0]	0.022
	Placebo	–2.3 ± 3.3	–2.5 [–8.0; 5.0]	[–4.0; –1.0]	

*Wilcoxon's rank sum test. 95% CI = 95% confidence intervals for the medians

65% of patients at all clinical visits. With 5 patients (27.8%) reporting moderate acceptability (at Visits 2, 3 and 4) and 1 patient (5.6%) reporting poor acceptability (at Visit 4), the hypericum-cream was found to be less cosmetically acceptable than the placebo (2 patients (11.1%) rated acceptability as moderate at each clinical visit).

Laboratory variables

To provide an assessment of the safety of the study medications standard haematological variables were recorded and analysed before and after treatment. No clinically relevant changes in laboratory variables were detected in any patient at any time.

Adverse events

In total, 4 adverse events (AEs) were recorded in 3 patients. None of the AEs was classified as serious. In all cases there was acute episode of atopic dermatitis leading to withdrawal from the study. One patient additionally developed contact eczema; in this instance a relationship with the study medication (hypericum-free vehicle) was considered probable.

Discussion

In the present study a St. John's wort cream with a standardised hyperforin content of 1.5% was found to be more effective than placebo in the treatment of subacute atopic dermatitis. Despite the relatively small sample size (n = 18), the half-side design permits a within-patient comparison in which psychological effects can be virtually ruled out. Compared with placebo, the significantly better performance of the hypericum-cream described in the present study is noteworthy because in dermatological topical therapy there are no placebos in the true sense, only bland vehicles. In eczematous conditions in particular it is known that considerable therapeutic effects can be achieved with the correct choice of vehicle (Patzelt-Wenczler et al. 2000; Thumm et al. 2000), a phenomenon that was also confirmed in the present study. We were also able to confirm the finding that in a half-side comparison the untreated or placebo-treated body side gains on the active-treated body side during the course of treatment: there was a steady reduction in the difference between the hypericum-cream and placebo during the course of treatment, as reflected in the pattern of diminishing statistical significance over time on Days 7, 14 and 28. The advantages conferred by the hypericum-cream tested here are the absence of any photosensitisation thanks to the use of a hypericin-free St. John's wort extract, and the probably very minimal risk of sensitisation because typical plant allergens such as sesquiterpene lactones, terpenes and polyacetylenes are not present in the extract (for review, see Schempp et al. 2002b). Cases of sensitisation to traditionally used St. John's wort oil are also unknown.

Table 3. Effect on bacterial colonisation with *Staphylococcus aureus.*

No. of CFUs	hypericum-cream*		Placebo*	
	N	%	N	%
Assessment 1 (Day 0)				
0	1	5.6	1	5.6
1–10	4	22.2	7	38.9
11–20	4	22.2	1	5.6
>20	9	50	9	5.0
Assessment 4 (Day 28)				
0	2	11.1	1	5.6
1–10	8	44.4	5	27.8
11–20	4	22.2	1	5.6
>20	4	22.2	11	61.1

N, number of patients per treatment group
%, percentage of patients per treatment group
* Comparison hypericum-cream – placebo: p = 0.064 (Wilcoxon's rank sum test)

The efficacy of herbal medicines in eczematous diseases has been investigated in a relatively small number of other studies; to our knowledge, however, the present study is the only one to demonstrate an unequivocal advantage for a herbal medicine over placebo.

In a triple-arm randomised, double-blind study, groups each comprising 36 patients with atopic dermatitis were treated for 14 days with hamamelis distillate cream, 0.5% hydrocortisone cream or drug-free vehicle. The hamamelis distillate cream was clearly less effective than the hydrocortisone cream and did not differ significantly from the drug-free vehicle (Korting et al. 1995). In another randomised, double-blind study 22 patients with atopic dermatitis were treated with hamamelis ointment in a half-side comparison with the anti-inflammatory agent bufexamac. No drug-free vehicle was used as a control. The treatment period was not of standard duration and ranged from 5 to 22 days. The improvement in eczema score achieved with the hamamelis ointment was comparable with that produced by bufexamac (Swoboda and Meurer, 1991).

Other herbal medicines used in the treatment of eczema include chamomile, calendula flowers and bittersweet. In one four-arm study (half-side comparison) in the maintenance therapy of eczematous diseases, chamomile cream was as effective as a 0.25% hydrocortisone cream and more effective than a 0.75% fluo-

cortin butyl ester cream and a 5% bufexamac cream. In this study, however, all patients had been pre-treated with a 0.1% diflucortolone valerate cream, the periods of pre-treatment (3 to 14 days) and follow-up treatment (3 to 4 weeks) were of differing duration and the sizes of the comparator populations were different (72, 58, and 31 patients respectively) (Aertgeerts, 1985).

The same chamomile cream was applied in a single-centre, four-arm, partially double-blind Phase III study in a half-side comparison with the drug-free vehicle cream (placebo) and a 0.5% hydrocortisone cream in patients with atopic dermatitis. A total of 72 patients were included and treated over a 2-week period. The chamomile cream was slightly superior to the hydrocortisone cream, but was only marginally superior to the drug-free vehicle. The publication provided no details about the statistical significance of the differences (Patzelt-Wenczler et al. 2000).

Calendula flower ointment is used traditionally in the treatment of eczema, wounds that are suppurating or difficult to heal, as well as burns and varicose veins. However, there are no clinical trials to date to substantiate efficacy in these indications.

Bittersweet (*Solanum dulcamara* L.) cream is also used for the treatment of atopic dermatitis. However, the anti-inflammatory activity of the steroid alkaloids and saponins in bittersweet has not yet been confirmed by controlled clinical trials and the postulated mechanism of corticosteroid-like activity remains controversial (Niederer, 1996).

Previous studies with herbal medicines in the treatment of eczema are therefore flawed in terms of methodology or have failed to demonstrate superior efficacy for the herbal medicine than for the drug-free vehicle. In contrast, the hyperforin-rich St. John's wort cream studied here displays efficacy superior to that achieved with the drug-free vehicle. One advantage of the product used in this study is that the St. John's wort extract contains no constituents known to possess sensitising activity; it is also hypericin-free, thus avoiding the risk of photosensitisation that normally exists with St. John's wort preparations. It is not yet possible to assess the clinical relevance of the trend towards a better reduction in *Staphylococcus aureus* colonisation with the hypericum-cream compared with the drug-free vehicle.

In our estimation, in the treatment of childhood atopic dermatitis, there exists a particular need for a topically administered herbal medicine, such as the hypericum-cream described here, firstly because parental corticosteroid phobia (justifiable to some degree) is on the increase, and secondly because bufexamac, the alternative commonly prescribed by paediatricians, displays a relatively high risk of sensitisation coupled with minimal efficacy (Gniazdowska et al. 1999).

In summary, the present half-side comparison shows significantly better efficacy for the hyperforin-rich St. John's wort cream compared with placebo. This hypericum-cream may be an effective herbal remedy for the treatment of mild to moderate atopic dermatitis. However, further studies with larger patient cohorts and a comparison with a standard (glucocorticoid) therapy are required to confirm the potency of a cream of this type.

Acknowledgement

This study was conducted with the support of Lichtwer Pharma AG, Berlin.

References

Aertgeerts P, Albring M, Klaschka F, Nasemann T, Patzelt-Wenczler, Rauhhut K, Weigl B (1985) Vergleichende Prüfung von Kamillosan-Creme gegenüber steroidalen (0,25% Hydrocortison, 0,75% Fluocortinbutylester) und nichtsteroidalen (5% Bufexamac) Externa in der Erhaltungstherapie von Ekzemerkrankungen. Z Hautkr 60: 270–277

European Task force on Atopic Dermatitis (1993) Severity Scoring of Atopic Dermatitis: The SCORAD Index. Consensus Report of the European Task force on Atopic Dermatitis. Dermatology 186: 23–31

Gniazdowska B, Rueff F, Przybilla B (1999) Delayed contact hypersensitivity to non-steroidal anti-inflammatory drugs. Contact Dermatitis 40: 63–65

Gurevich AI, Dobrynin VN, Kolosov MN, Popravko SA, Riabova ID (1971) Hyperforin, an antibiotic from Hypericum perforatum L. Antibiotiki 16: 510–513

Kaul R (2000) Johanniskraut. Botanik, Inhaltsstoffe, Qualitätskontrolle, Pharmakologie, Toxikologie und Klinik. Wiss. Verlagsges. Stuttgart

Korting HC, Schafer-Korting M, Klovekorn W, Klovekorn G, Martin C, Laux P (1995) Comparative efficacy of hamamelis distillate and hydrocortisone cream in atopic eczema. Eur J Clin Pharm 48: 461–465

Maisenbacher P, Kovar KA (1992) Analysis and stability of Hyperici oleum. Planta Med 58: 351–354

Mezger J (1991) Gesichtete homöopathische Arzneimittellehre: Hypericum perforatum. Haug Verlag, Heidelberg, pp 761–765

Niedner R (1996) Solanum dulcamara L. – a "plant cortisone"? Med Monatsschr Pharm 19: 339–340

Patzelt-Wenczler R, Ponce-Poschl E (2000) Proof of efficacy of Kamillosan(R) cream in atopic eczema. Eur J Med Res 19: 171–175

Roth L (1990) Hypericum – Hypericin. Botanik, Inhaltsstoffe, Wirkungen. Ecomed Arzneipflanzen-Monographie. Ecomed, Landsberg/Lech

Schempp CM, Pelz K, Wittmer A, Schöpf E, Simon JC (1999) Antibacterial activity of hyperforin from St John's wort, against multiresistant Staphylokokkus aureus and gram-positive bacteria. Lancet 353: 2129

Schempp CM, Winghofer B, Lüdtke R, Simon-Haarhaus, Schöpf E, Simon JC (2000a) Effect of topical application of Hypericum perforatum extract (St. John's wort) on skin sensitivity to solar simulated radiation. Photodermatol Photoimmunol Photomed 16: 125–128

Schempp CM, Winghofer B, Lüdtke R, Simon-Haarhaus, Schöpf E, Simon JC (2000b) Topical application of St. John's wort (Hypericum perforatum L.) and of its metabolite hyperforin inhibits the allostimulatory capacity of epidermal cells. Br J Dermatol 142: 979–984

Schempp CM, Müller KA, Winghofer B, Schöpf E, Simon JC (2002a) Johanniskraut (Hypericum perforatum L.) – eine Pflanze mit Relevanz für die Dermatologie. Hautarzt 53: 316–321

Schempp CM, Schöpf E, Simon JC (2002b) Durch Pflanzen ausgelöste toxische und allergische Dermatitis (Phytodermatitis). Hautarzt 53: 93–97

Sears HW, Bailer JW, Yeadon A (1997) Efficacy and Safety of Hydrocortisone Buteprate 0,1% Cream in Patients with Atopic Dermatitis. Clin Ther 19: 710–719

Swoboda M, Meurer J (1991) Therapie von Neurodermitis durch Hamamelis virginiana-Extrakt in Salbenform. Z Phytother 12: 114–117

Thumm EJ, Stoss M, Bayerl C, Schürholz T (2000) Überprüfung der Wirksamkeit einer 20%igen und 10%igen Sanddornkernölcreme bei Patienten mit leichter bis mittelgradiger atopischer Dermatitis. Akt Dermatol 26: 285–290

Adress

C. M. Schempp, University Dermatology Clinic, Hauptstr. 7, D-79104 Freiburg
Tel.: ++49-761-270-6701; Fax: ++49-761-270-6829;
e-mail: schempp@ haut.ukl.uni-freiburg.de