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ORIGINAL RESEARCH

Evaluation of Biophysical Parameters of the Skin of Patients With Atopic Dermatitis After Application of an Ointment Containing 30% Cannabidiol and 5% Cannabigerol

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Introduction: A growing number of publications are devoted to topical cannabinoid therapies in present-day cosmetology, as they appear to be safe and effective treatment modalities aimed at improving the comfort and quality of life of patients with atopic dermatitis (AD). A thorough patient interview, physical examination, clinical picture, and aetiopathogenesis of AD allow for a correct diagnosis and enable the choice of the least invasive pharmacological treatment.

Purpose: In our medical experiment, we found a correlation between the findings of studies by other authors and the validation of our hypothesis that topical cannabinoid therapy is effective in the prevention and management of AD flares. A thorough analysis of the obtained results provided insights into the extent to which the applied ointment influenced the improvement of the skin's biophysical parameters (hydration, lipid content, transepidermal water loss, and erythema).

Patients and Methods: This medical experimental study was conducted from May to July 2022 and included a group of nine patients (five men and four women) aged 20- to 67-years-old were diagnosed with AD. The study involved transdermal delivery of an ointment compounded with cholesterol ointment, 30% cannabidiol (CBD), 5% cannabigerol (CBG), and hemp seed oil, and assessment of biophysical skin parameters, including corneometry (skin hydration), TEWL, sebumetry, and pH (acidity).

Results: A preliminary analysis of our pilot study points to the potential of employing ointments and creams containing 30% CBD and 5% CBG as alternatives to conventional auxiliary therapies during both flare-ups and remission. The results we achieved included improved skin hydration, sebum level, and TEWL as well as reduced erythema in the studied areas (forearms).

Conclusion: Our results demonstrate that topical cannabinoid therapy is effective in reducing itching and improving the quality of life of patients with AD, leading to symptom remission in some cases.

Keywords: atopic dermatitis, xerosis, cannabigerol, cannabidiol, Cannabis sativa L. var sativa seed oil, CBD, CBG, AD

Introduction

Atopic dermatitis (AD) is the most common, chronic, and relapsing non-contagious inflammatory skin condition, frequently involving the entire integument, including the epidermis and dermis. The characteristic clinical picture includes coexisting pruritus and the resulting excoriations. In severe cases, inflammation may involve 90% or more of the skin (erythroderma).[1–3]

The main risk factors for severe AD include genetic, immunological, and microbiological disorders, external factors such as socioeconomic status, living conditions, smoking, excessive alcohol intake, psychological factors, epidermal barrier dysfunction, as well as food, atmospheric and bacterial allergens.[1,4–11]

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The presentation and location of lesions vary depending primarily on the patient's age. Cutaneous manifestations develop as early as infancy and persist into adulthood. It is chronic and involves severe itching. In infancy and early childhood, lesions typically appear on protuberant body areas, such as the forehead, chin, and cheeks, and later progress to convex areas, such as the skin folds, ulnar fossa, forearms, popliteal fossa, palms, and dorsal part of the hands, neck, and chest. The clinical picture includes skin xerosis, papules and blisters, erythema, skin erosions, and excoriations formed because of scratching and lichenization.[3,7]

Based on various criteria, such as aetiopathogenesis, clinical picture, and severity of the symptoms, various pharmacological treatment modalities have been adopted, ranging from systemic to topical to biological. In mild cases, corresponding to a (SCORAD) index <25, topical corticosteroids, calcineurin inhibitors, crisaboroles, and antiseptics are used, with the mainstay of AD treatment being the emollient regime and prophylaxis. For moderate AD with SCORAD = 25–50, proactive therapy, climate therapy, psychological and psychiatric counseling, and phototherapies (in adults) with UVB 311, UVA 1, and PUVA are recommended. Severe AD, in turn, with a SCORAD of more than 50, may warrant hospitalisation, oral corticosteroid therapy (no longer than 7 days), immunosuppressive treatment (methotrexate, mycophenolate mofetil), or the use of biologics, such as dupilumab or cyclosporine (CsA).[6,8,9,12]

Both advantages and disadvantages of either the systemic or topical approach are linked to the improvement and/or deterioration of the comfort and quality of life of patients with AD. Based on a comprehensive literature review and our experience, transdermal therapy with an emulsion composed of cholesterol ointment, Cannabis sativa L. var sativa oil, and selected cannabinoids (cannabidiol [CBD] and cannabigerol [CBG]) at different concentrations (from 5% to 50%) shows great promise.

Cannabinoids

Cannabinoids comprise a group of approximately 60 chemical compounds with 21 carbon atoms that occur naturally in hemp plants such as Cannabis sativa and Cannabis indica. They affect the human and animal endocannabinoid systems. The principal cannabinoids present in hemp are tetrahydrocannabinol (THC) and CBD. CBD, as opposed to THC, has no psychoactive effect.[13–15]

Cannabinoids may be divided into:

a. Phytocannabinoids, occurring in the form of plant alkaloids, eg, THC, CBD.[13,16]
b. Endocannabinoids are present in the human body and in animals, for example, 2-arachidonoylglycerol (2-AG) and anandamide (AEA) are released during sleep and relaxation.[13,17–19]
c. Synthetic cannabinoids, lab-made substances such as CP-55940, HU-210 or parahexyl.[13,16]
d. Neutral cannabinoids, lacking a side-chain and a psychoactive effect, such as CBG.[13,16]
e. Acid cannabinoids, naturally occurring in raw hemp plants, are transformed into active substances during the process of drying or heating, such as cannabidiolic acid (CBDA) or tetrahydrocannabinolic acid (THCA).[13,16]
f. Cannabis derivatives, such as nabiximols marketed as Sativex are chemically modified to achieve the desired properties or reduce side effects.[13,16]

The substances most valuable in dermatology (for both topical and systemic therapies) are CBG and CBD, used as active constituents in compounded medications as well as in ready-made solutions, gels, ointments, creams, pastes, and suspensions (see Table 1).[20]

The Endocannabinoid System

The endocannabinoid system (ECS) is a neuromodulatory system that controls various critical physiological processes such as blood pressure, body temperature, appetite, mood, sleep, and pain.[26] Its first mention dates back to 1988 when Howlett and Derone discovered cannabinoid receptors,[25] among which CB1R and CB2R play principal roles. According to a study by Kaniewski et al,[27,28] CB1 receptors are abundant throughout the central and peripheral nervous systems (eg, the cortex, hippocampus, cerebellum tonsils, basal ganglia, substantia nigra, spinal cortex, and cortical interneurons), but are also found in the cells of other anatomical structures, including the lungs, kidneys, bladder, adipocytes, cardiomyocytes, hepatocytes, and

Table 1 The Characteristics of the Selected Cannabinoids, Used for the Formulation of the Ointment Tested in Our Study.[21–23]

Cannabidiol (CBD)	a. One of the several dozen naturally occurring cannabinoids.[21] b. Obtained in different concentrations from hemp (Cannabis sativa L. var sativa).[23] c. Manifests anti-inflammatory, antiemetic, anxiolytic, neuroprotective, antipsychotic, antipruritic, antibacterial and, antifungal qualities.[19,24,25] d. As opposed to Δ^9 –THC, does not have psychoactive effect, including intoxication.[21] e. Used in dermatology to relieve skin xerosis and pruritus, especially in management of AD, acne and psoriasis.[23] f. CBD inhibits the activation of mast cells resulting in histamine release inducing severe itching.[23] g. Delivered topically is absorbed within 20–45 min and remains active for 6–8 hours.[23] h. In AD, CBD is delivered in the form of an ointment or cream 1 or 2 times a day, at the dosage of 10–20 mg, increasing it after 4–5 days to twice at a dosage if tolerance is good.[23]
Cannabigerol (CBG)	a. Manifests anti-inflammatory, antineoplastic, and immunomodulating potential.[22] b. Reduces skin inflammation by suppressing the release of proinflammatory cytokines.[22] c. Has an antibacterial effect, inhibiting Staphylococcus bacteria growth which contributes to skin infection.[22] d. Acts as an anti-inflammatory and antifungal agent in the treatment of AD; inhibits the activity of enzymes responsible for the synthesis of fatty acids (eg, arachidonic acid which is an important mediator of inflammation in AD, hence the inhibition of its production may help limit inflammation in AD patients).[22]

cells of the gastrointestinal tract. CB2 receptors are expressed in immune cells (keratocytes, leukocytes, T and B lymphocytes, macrophages, astrocytes in the central nervous system, osteoclasts in the bone marrow, haematopoietic stem cells, peripheral nerve endings,or microglia).[15,27–30]Additionally, CB1R and CB2R are found in integument cells (hair follicles, sebocytes in sebaceous glands, and skin nerve fibers).[26]

Materials and Methods

This experimental (interventional) study was conducted on a group of patients with AD from May to June 2022. This study was approved by the relevant Bioethics Committee of the Medical University of Silesia in Katowice (Decision no. 18.05.2021, ID no. PCN/022/KB1/40/2). The study was conducted in accordance with the Declaration of Helsinki. All study participants (patients) provided written informed consent before participating in the medical research experiment. It was financed with funds designated for the maintenance and development of research potential, subsidies for teaching and research purposes in 2022, a contract for the execution of a research task by a Young Researcher of the Medical University of Silesia in Katowice (ID No. PCN-2-023/N/2/F).

The study included nine patients (five men and four women), aged 20- to 67-years-old, diagnosed with AD based on clinical criteria, who were included following initial examinations (ie, patient interview and physical examination including skin assessment by a dermatologist) and a diagnostic survey (see Table 2).

The patients were over 18-years-old and reported no oversensitivity to the active agents found in the emulsion (CBD and CBG), and no excessive use of medications, psychoactive and psychotropic substances, alcohol, or smoking. Based on the patients' histories, no personality disorders were identified, including mental conditions or other mental health problems that could interfere with collaboration with overseeing physicians or with the course and reliability of the study.

The patients underwent allergy tests which were performed to rule out allergic reactions to the compounds in the emulsion (ie, CBD, CBG, hemp seed oil). Before the beginning of the study and directly upon its completion, clinical parameters were evaluated using SCORAD (SCORing Atopic Dermatitis) and EASI (Eczema Area and Severity Index) tools.

The study involved the at-home transdermal delivery of a specially formulated ointment (see Table 3). The patients were instructed to apply a generous layer of the ointment to the same site (the forearms) once daily before sleep and to cover the area with a wet wrap dressing to enhance its effectiveness and protect bedsheets.

Results

Capillaroscopy and evaluation of biophysical skin parameters in nine patients with AD after a course of therapy involving transdermal delivery of an ointment compounded with 30% CBD, 5% CBG, Cannabis sativa L. sativa oil,

Table 2 Group Characteristics

The Studied Group	ICD-10	Age	Sex
Patient 1	AD (ICD-10: L.20.0)	41-years-old	Male
Patient 2		39-years-old	Male
Patient 3		25-years-old	Male
Patient 4		34 years old	Male
Patient 5		30-years-old	Male
Patient 6		31-years-old	Female
Patient 7		25-years-old	Female
Patient 8		67-years-old	Female
Patient 9		20-years-old	Female

Table 3 The Content, Weight, and Purpose of the Formulation

	Substance	(g)
Content and weight (100.0 g):	30% CBD 5% CBG Cannabis Sativa L. Oleum Unguentum cholesteroli	10.0 10.0 10.0 70.0
Purpose:	To treat skin following long-term therapy with corticosteroid ointments, itching, thermal and chemical skin damage, AD, psoriasis and xerosis.	

and cholesterol ointment were performed in the Department of Practical Cosmetology and Skin Diagnostics of the Faculty of Pharmaceutical Medicine in Sosnowiec of the Medical University of Silesia in Katowice.

The findings of capillaroscopy performed before starting therapy versus at 8 weeks are shown in the photographs below (see Figures 1–9).

Measurements of the biophysical parameters of the skin were performed with a Courage + Khazaka electronic GmbH device using the following probes: Sebumeter® SM815, Skin-pH-Meter® PH 905, Mexameter® MX 18, Corneometer® CM 825, and Tewameter® TM 300. The BECHTOLD and CO guidelines and MPA CTplus software were used to interpret the reference ranges. To ensure the reliability of the measurements (to obtain comparable measurements), examinations were performed at the

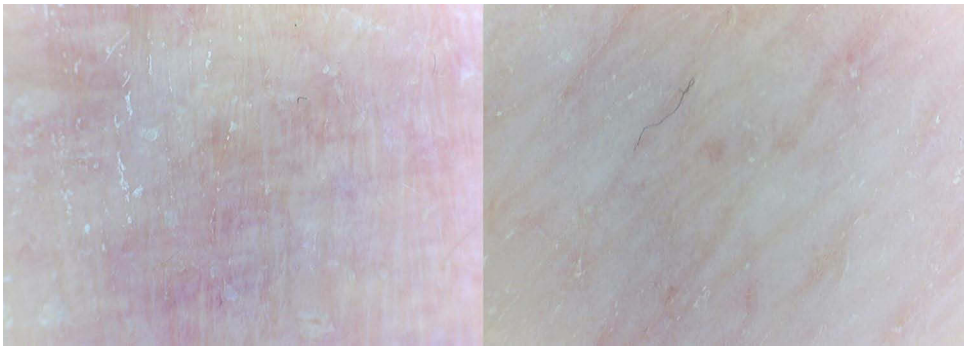

Figure 1 A capillaroscopy image showing the skin of a 41-year-old male with AD (photo on the left – right forearm, skin beforethe start of the therapy; photo on the right – the skin of the right forearm at eight weeks into the transdermal cannabinoid therapy).

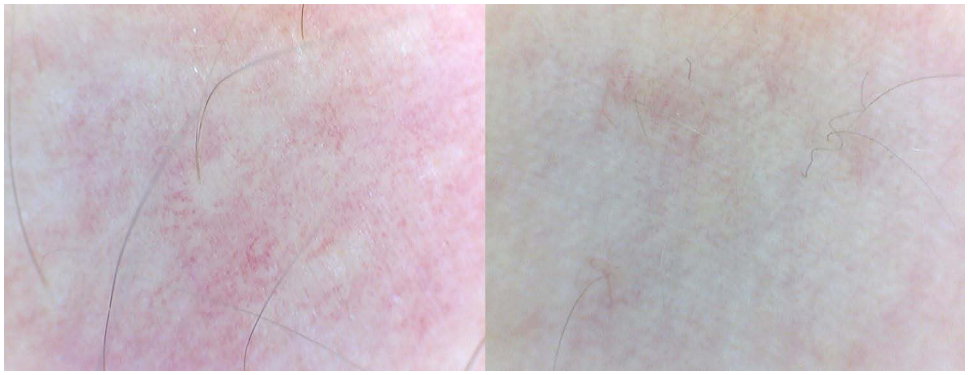

Figure 2 A capillaroscopy image showing the skin of a 39-year-old male with AD (photo on the left – the skin right forearm, skin before the start of the therapy; photo on the right – the skin of the right forearm at eight weeks into the transdermal cannabinoid therapy).

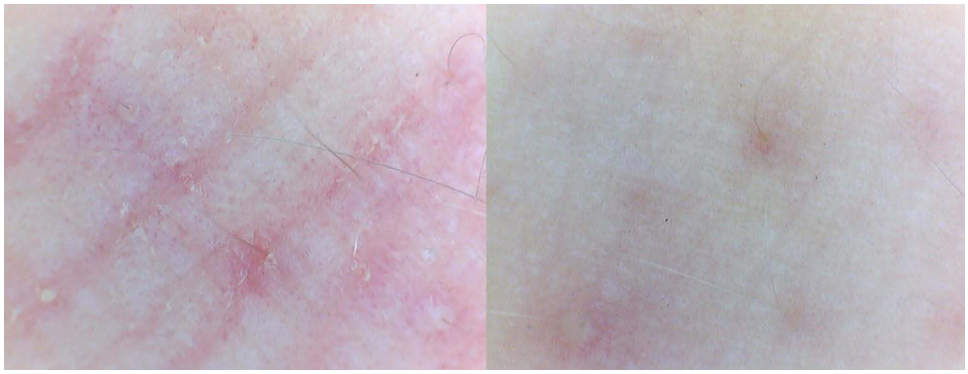

Figure 3 A capillaroscopy image showing the skin of a 25-year-old male with AD (photo on the left – right forearm, skin beforethe start of the therapy; photo on the right – the skin of the right forearm at eight weeks into the transdermal cannabinoid therapy).

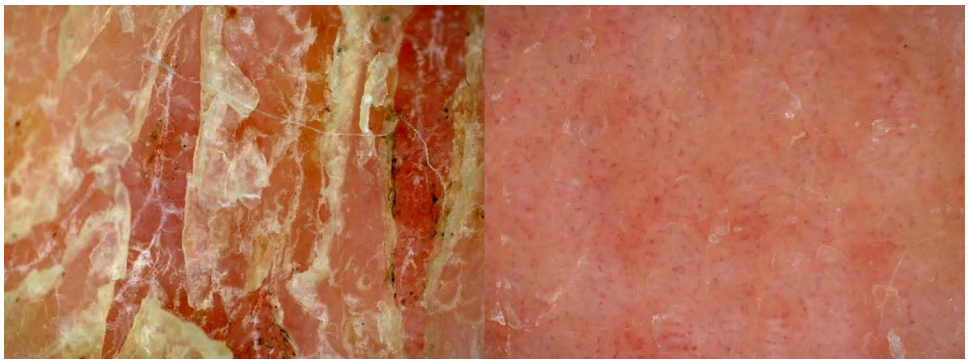

Figure 4 A capillaroscopy image showing the skin of a 34-year-old male with AD (photo on the left – right forearm, skin before the start of the therapy; photo on the right – the skin of the right forearm at eight weeks into the transdermal cannabinoid therapy).

same time of the day, ie, between 8.30 a.m. and 1 p.m., under the same environmental conditions, ie, 20–24°C and 40–60% humidity. Measurements were taken for the same duration of time for each participant in the study, ie, for 15–25 minutes. Baseline measurements were performed directly before starting therapy, followed by measurements at four and eight weeks into the therapy on different skin areas (the left ulnar fossa, left forearm, and right forearm). After signing an informed consent form, the participants were presented for the examination without having washed the skin or applied any cosmetics or medications for the 5 hours preceding the evaluation. Before the measurements, the participants were acclimatized for 20 min and rested upon arrival at the facility. They were instructed to stop using for the duration of the study any cosmetic and medical products

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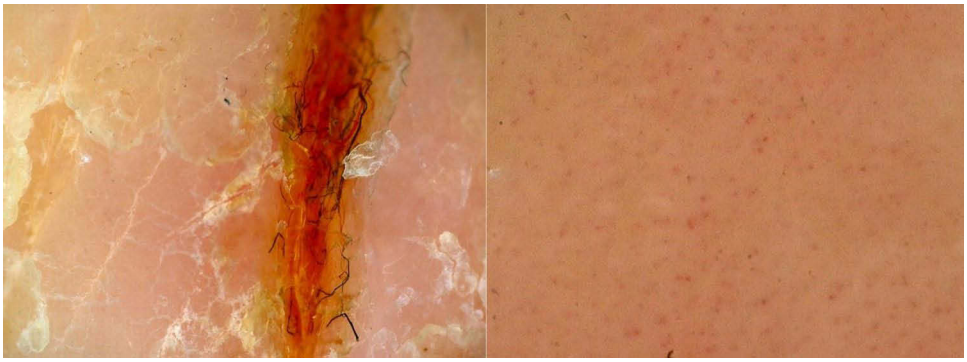

Figure 5 A capillaroscopy image showing the skin of a 30-year-old male with AD (photo on the left – right forearm, skin before the start of the therapy; photo on the right – the skin of the right forearm at eight weeks into the transdermal cannabinoid therapy).

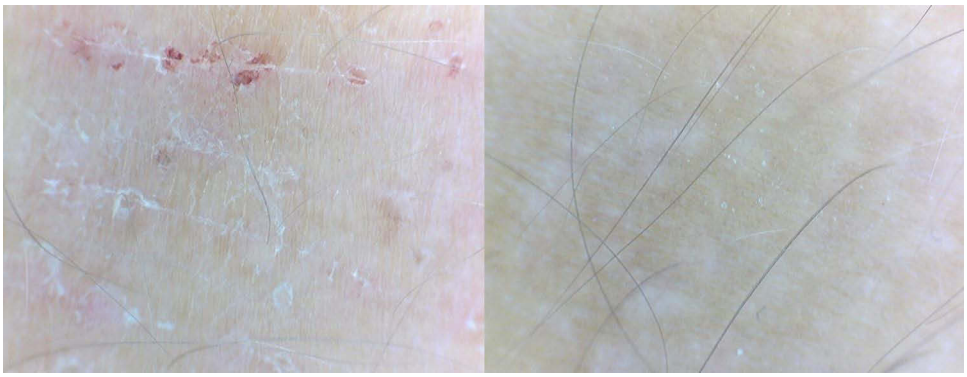

Figure 6 A capillaroscopy image showing the skin of a 31-year-old female with AD (photo on the left – right forearm, skin before the start of the therapy; photo on the right – the skin of the right forearm at eight weeks into the transdermal cannabinoid therapy).

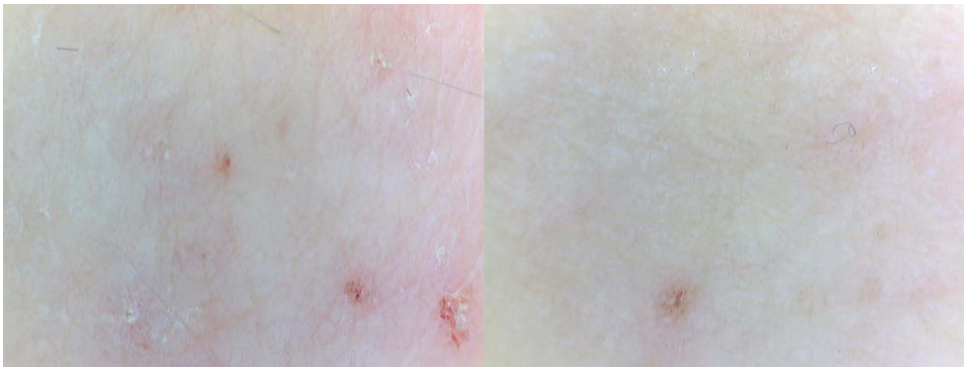

Figure 7 A capillaroscopy image showing the skin of a 25-year-old female with AD (photo on the left – right forearm, skin before the start of the therapy; photo on the right – the skin of the right forearm at eight weeks into the transdermal cannabinoid therapy).

(detergents, emollients) that could affect the skin's parameters, ie, hydration of the stratum corneum, pH, TEWL, and sebum level. The results are presented in Tables 4–8.

Statistical Analysis

The distribution of variables was evaluated using the Shapiro–Wilk test and the quantile-quantile plot, and data for normally distributed variables were expressed as mean values and standard deviations (M p-values).

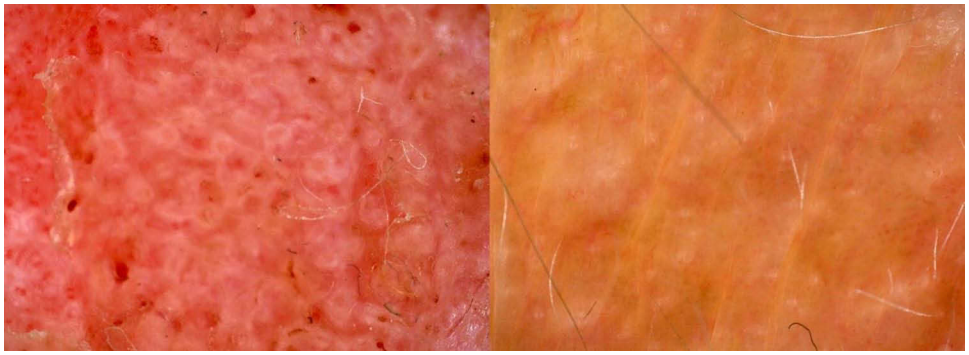

Figure 8 A capillaroscopy image showing the skin of a 67-year-old female with AD (photo on the left – right forearm, skin before the start of the therapy; photo on the right – the skin of the right forearm at eight weeks into the transdermal cannabinoid therapy).

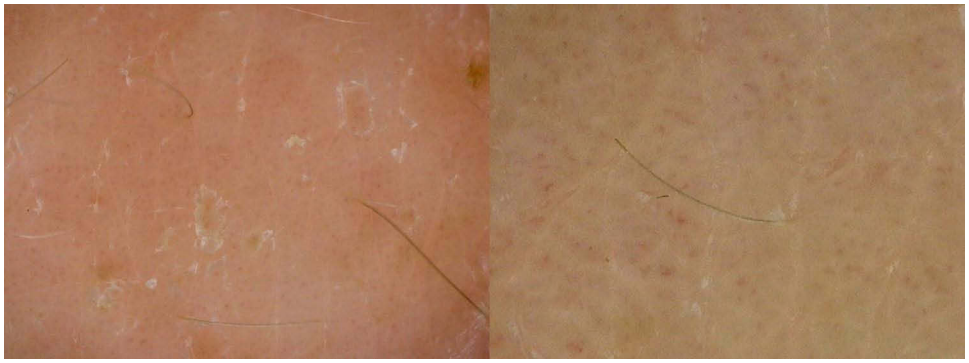

Figure 9 A capillaroscopy image showing the skin of a 20-year-old female with AD (photo on the left – right forearm, skin beforethe start of the therapy; photo on the right – theskin of the right forearm at eight weeks into the transdermal cannabinoid therapy).

For the comparison of variables by sex, Student's *t*-test for independent variables was used, and the homogeneity of variance was assessed using Levene's test. ANOVA test for Repeated measures analysis of variance was used to assess the effectiveness of the therapy, and sphericity was verified using the Mauchly test. Detailed comparisons at given time

Table 4 Mean Hydration Values in the Studied AD Patients Prior to and Following the Therapy With the Cannabinoid-Based Ointment

AD patients	**Mean hydration values expressed in [CU] measured with Corneometer® CM 825 prior to and after transdermal cannabinoid therapy.**		
	early	**late**	
Evaluation	**Baseline**	**At 4 weeks**	**At 8 weeks**
Patient 1 (41-year-old male)	17.77	11.80	21.36
Patient 2 (39-year-old male)	35.00	30.07	46.50
Patient 3 (25-year-old male)	16.08	24.08	38.60
Patient 4 (34-year-old male)	6.50	10.50	22.43
Patient 5 (30-year-old male)	12.40	4.98	13.20
Patient 6 (31-year-old female)	15.33	28.40	25.17
Patient 7 (25-year-old female)	21.13	25.60	29.14
Patient 8 (67-year-old female)	24.67	27.17	36.93
Patient 9 (20-year-old female)	24.10	17.90	45.33

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Table 5 Mean TEWL Findings in the Studied AD Patients Prior to and Following the Application of the Cannabinoid-Based Ointment

AD patients	**Mean TEWL value expressed in g/m^2/h, measured with Tewameter® TM300 prior to and after transdermal cannabinoid therapy.**		
	Early	**Late**	
Evaluation	**Baseline**	**At 4 weeks**	**At 8 weeks**
Patient 1 (41-year-old male)	27.86	22.76	16.14
Patient 2 (39-year-old male)	44.96	39.57	17.94
Patient 3 (25-year-old male)	17.42	15.26	12.90
Patient 4 (34-year-old male)	48.89	29.49	20.18
Patient 5 (30-year-old male)	64.13	40.77	35.96
Patient 6 (31-year-old female)	31.43	27.90	17.75
Patient 7 (25-year-old female)	47.15	41.87	35.53
Patient 8 (67-year-old female)	17.81	21.76	15.32
Patient 9 (20-year-old female)	18.91	17.94	13.94

Table 6 Mean Sebum Level Measurements in the Studied AD Patients Prior to and Following the Application of the Cannabinoid-Based Ointment. The Result Is Expressed in mg/cm^2

AD patients	**Mean sebum level result expressed in mg/cm^2 prior to and after transdermal cannabinoid therapy.**		
	Early	**Late**	
Evaluation	**Baseline**	**At 4 weeks**	**At 8 weeks**
Patient 1 (41-year-old male)	5.00	39.00	47.00
Patient 2 (39-year-old male)	0.00	11.00	76.00
Patient 3 (25-year-old male)	5.00	8.00	6.00
Patient 4 (34-year-old male)	1.00	25.00	13.00
Patient 5 (30-year-old female)	4.00	13.00	18.00
Patient 6 (31-year-old female)	0.00	1.00	1.00
Patient 7 (25-year-old female)	1.00	20.00	34.00
Patient 8 (67-year-old female)	4.00	13.00	8.00
Patient 9 (20-year-old female)	3.00	4.00	7.00

points were performed using Tukey's post hoc test. The figures represent mean values with 95% confidence intervals (95% CI).

Statistical significance was set at a value <0.05, and all tests were two-tailed. Statistical analysis was performed using the STATISTICA 13 PL software (TIBCO Software Inc. (2017). Statistical software (Data Analysis Software System) version 13. http://statistica.io).

Table 7 Mean Melanin and Erythema Measurements in the Studied AD Patients Prior to and Following the Application of the Cannabinoid-Based Ointment

Patients with AD		**Mean erythema and melanin values, measured with Mexameter® MX18 in AD patients prior to and after transdermal cannabinoid therapy.**		
		Early	**Late**	
Evaluation		**Baseline**	**At 4 weeks**	**At 8 weeks**
Patient 1 (41-year-old male)	Melanin	186.33	130.00	146.25
	Erythema	476.33	397.67	365.86
Patient 2 (39-year-old male)	Melanin	118.33	62.67	96.00
	Erythema	485.33	479.00	381.67
Patient 3 (25-year-old male)	Melanin	79.67	96.00	83.20
	Erythema	450.58	373.33	324.00
Patient 4 (34-year-old male)	Melanin	80.67	12.00	23.00
	Erythema	425.33	306.67	387.67
Patient 5 (30-year-old male)	Melanin	23.00	38.67	21.67
	Erythema	338.67	281.00	362.00
Patient 6 (31-year-old female)	Melanin	60.55	121.00	125.46
	Erythema	368.67	303.67	287.36
Patient 7 (25-year-old female)	Melanin	177.33	160.33	145.43
	Erythema	353.00	300.73	258.86
Patient 8 (67-year-old female)	Melanin	211.00	247.00	199.00
	Erythema	431.33	332.00	390.00
Patient 9 (20-year-old female)	Melanin	46.67	33.33	45.33
	Erythema	218.67	289.00	159.33

Table 8 The Mean pH Value in the Studied AD Patients Prior to and Following the Application of the Cannabinoid-Based Ointment

Patients with AD	**Mean skin pH measured with Skin-pH-meter® PH 905 prior to and after transdermal cannabinoid therapy.**		
	Early	**Late**	
Evaluation	**Baseline**	**At 4 weeks**	**At 8 weeks**
Patient 1 (41-year-old male)	5.67	5.83	5.25
Patient 2 (39-year-old male)	6.10	5.70	5.81
Patient 3 (25-year-old male)	5.52	6.34	5.45
Patient 4 (34-year-old male)	6.63	6.35	6.43

(*Continued*)

Table 8 (Continued).

Patients with AD	Mean skin pH measured with Skin-pH-meter® PH 905 prior to and after transdermal cannabinoid therapy.		
	Early	Late	
Evaluation	**Baseline**	**At 4 weeks**	**At 8 weeks**
Patient 5 (30-year-old male)	4.88	6.42	6.29
Patient 6 (31-year-old female)	5.78	5.15	5.81
Patient 7 (25-year-old female)	4.97	6.19	5.15
Patient 8 (67-year-old female)	5.81	6.20	6.20
Patient 9 (20-year-old female)	6.16	6.00	6.24

Analyses

The study involved nine participants, with the majority being male (five individuals, 56%). The average age in the study group was 34.7 ± 13.9 years. There were no statistically significant differences in age ($p = 0.623$), initial hydration concentration ($p = 0.391$), TEWL ($p = 0.540$), sebum ($p = 0.455$), melanin ($p = 0.903$), erythema ($p = 0.178$), and pH ($p = 0.903$). In further analyses, patients were considered collectively.

Statistically significant differences were observed in the duration of cannabinoid-based hydration therapy ($p<0.001$) (Table 9). Therapy led to an increase in hydration, and the results after four weeks of treatment did not differ from those before treatment ($p = 0.943$). However, an increase in hydration was observed in the 8th week compared to both the pre-treatment data ($p<0.001$) and the 4th week of therapy ($p<0.01$) (see Figure 10a).

A similar effect was observed for TEWL therapy ($p<0.001$). The therapy resulted in a reduction in TEWL values only in the eighth week compared to the pre-treatment values ($p<0.001$) and the fourth week ($p<0.05$) (see Figure 10b).

Sebum level had an impact on treatment duration ($p<0.05$). A significant increase was observed only in the eighth week of treatment ($p<0.05$) (see Figure 11a).

Statistically significant differences were observed in erythema parameters during treatment ($p<0.01$). A decrease in concentration was observed as early as the fourth week ($p<0.05$) and a further decrease was observed in the eighth week of treatment ($p<0.01$) (see Figure 11b).

No differences were observed in melanin concentration ($p = 0.624$) or pH ($p = 0.389$) during treatment.

Table 9 Statistical Analysis of Obtained Results Assessing Biophysical Skin Parameters Before (0 Before Therapy), During Therapy (After Four Weeks), and After Completion of Therapy (After Eight Weeks) Following the Application of an Ointment Containing 30% CBD, 5% CBG in Topical Treatment

Variables	Time of Therapy (at weeks)			p	$p_{0 \text{ vs } 4 \text{ weeks}}$	$p_{0 \text{ vs } 8 \text{ weeks}}$	$p_{4 \text{ vs } 8 \text{ weeks}}$
	0 Before Therapy	4	8				
Hydratation [CU]	19.22±8.23	20.06±9.08	30.99±11.50	<0.001	0.943	<0.001	<0.01
TEWL [g/m^2/h]	35.40±16.63	28.59±10.11	20.62±8.84	<0.001	0.074	<0.001	<0.05
Sebum [mg/cm^2]	2.56±2.07	14.89±11.68	23.33±24.71	<0.05	0.203	<0.05	0.453
Melanin	109.28±67.48	100.11±74.12	98.37±61.22	0.624	–	–	–
Erythema	394.21±84.28	340.34±65.08	324.08±77.16	<0.01	<0.05	<0.01	0.706
pH	5.72±0.56	6.02±0.41	5.85±0.48	0.389	–	–	–

Abbreviations: TEWL, transepidermal water loss; Me(Q_1-Q_3) – median (lower-upper quartile); p, statistical significance.

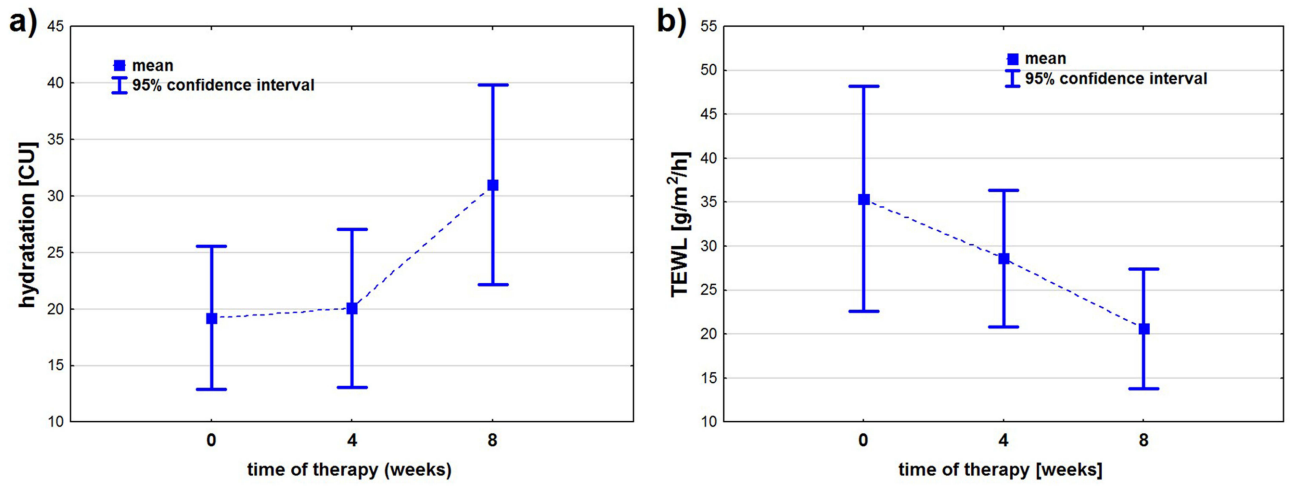

Figure 10 Hydratation level [CU] (**a**) and TEWL; [g/m2/h] (**b**) during therapy.

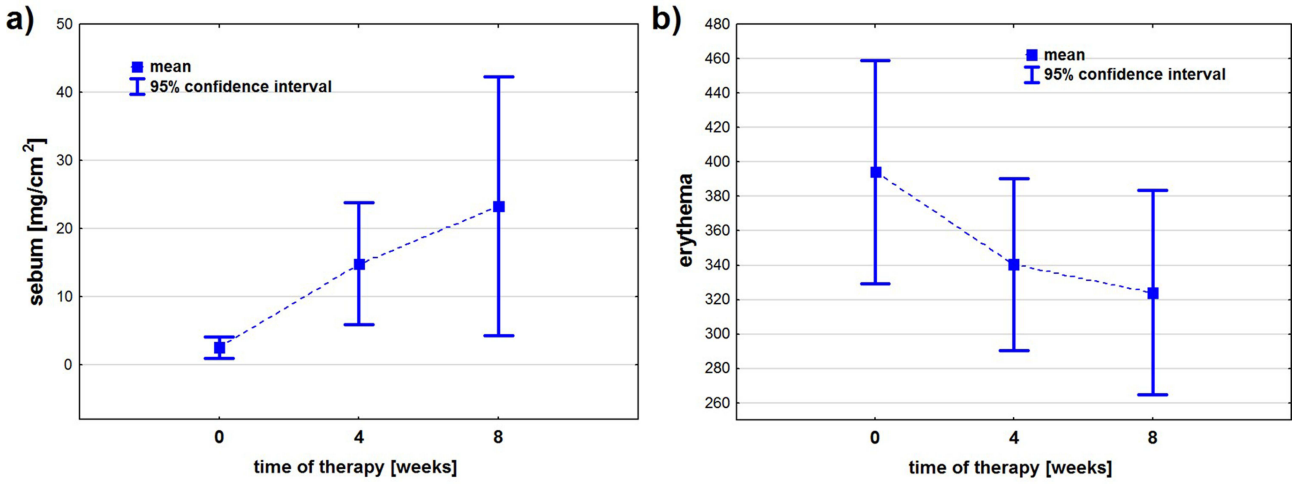

Figure 11 Sebum concentration [mg/cm2] (**a**) and erythema level (**b**) during therapy.

Discussion

Throughout the ages, the medicinal properties of hemp have been recognized, and the plants have been used to treat all types of skin inflammation. The current state of knowledge based on a review of the literature complying with evidence-based medicine guidelines facilitates not only the use of hemp seed oil, but also high-quality plant-derived cannabinoids for the formulation of safe, effective, and innovative ready-made medical products, as well as compounded liquid and semi-solid medications (emulsions vs ointments and creams, respectively) for application in modern-day dermatology. Topical delivery of cannabinoids to the skin is a safe alternative treatment modality that may improve the quality of life of patients with certain types of dermatitis including AD, psoriasis and, acne.[31] Considering the therapeutic potency of cannabinoids and their beneficial effects on the stratum corneum (ie, hydration, sebum level, limiting TEWL), patients will be able to choose between onerous topical steroid therapy and the cannabinoid-based skincare regimen not associated with adverse effects, including the rapid development of drug tolerance, which is typical for corticosteroid therapy.

A comparison of the results of our study with the findings of other studies has shown a common correlation between the application of creams and ointments containing selected cannabinoids and the improvement of the skin parameters in the studied patients, including hydration, sebum level, TEWL, erythema, and skin pH level.

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The use of hemp seed oil and cannabinoids aids in the treatment of chronic relapsing and inflammatory skin conditions.[32] Palmieri et al reported 20 patients (14 female, six male) aged 20- to 80-years-old who had AD (five patients), psoriasis (five patients), and the resulting scars (10 patients). According to their report, the studied patients, who regularly, twice a day, for a period of three months, applied an ointment compounded with hemp seed oil containing CBD, Indian mango (Mangifera Indica), calendula (Calendula officinalis), lavender (Lavendula officinalis), chamomile, Amyris oil (Amyris Balsamifera), and shea butter to the affected areas, that is, the forehead, neck, and cheeks, showed improvement in hydration of the skin (5.5–6.9%), TEWL (17.6–28.1%) and TEWL (17.1–27.1%). This improvement was presumably due to the essential unsaturated fatty acids (α-linolenic acid, γ-linolenic acid, linoleic acid, oleic acid, and phytosterols (β-sitosterol]) present in the cream, which can inhibit 5-α-reductase. In addition, a decrease in the number of papules (by 20%) and pustules (by 35%) was observed pursuant to therapy.[33]

Sivesind et al also reported that topical application of 1% CBD infusion gel and ointment for three months in a group of 21 female patients with AD significantly improved TEWL.[25]

A study conducted at the Department of Dermatology of the University of Wrocław in 2005 demonstrated that significant relief was achieved with the use of a cream containing endogenous cannabinoids in 21 patients with uraemia. The findings of the study were promising, as the application of the cream led to the complete elimination of uraemic pruritus in 38% of the patients and a significant reduction in itching as well as a complete reduction of xerosis in as many as 81% of the participants. Although the preliminary results seem to have been encouraging regarding skin cornification in haemodialysis patients, further studies are required to clarify the usefulness of cannabinoid therapy for dermatological conditions.[34] Unfortunately, 14 days after the completion of therapy, pruritus and xerosis had increased compared to day 21 (end of therapy). Nonetheless, only two participants (9.5%) considered the outcome to be poorly satisfactory. The therapy was well tolerated by all patients (100%), and no adverse effects were observed in this group.[35]

Rogowska-Szadkowska, referring to a study by Grinspoon et al, reported the case of a 60-year-old male, who had AD for 41 years. He had a history of military service from the age of 19 to 39. Due to his aggravated AD symptoms, he was released from the military in 1956 after 20 years of service. His skin lesions were primarily located on his hands and arms. The patient was pharmacologically managed with antibiotic and cortisone therapy according to the medical constraints of time and received tranquillizers to manage his severe itching. He had to discontinue cortisone therapy because of intolerance despite symptom improvement. After recreational use of hemp (vaping) for three years, he noticed remission of pruritus and skin inflammation.[36]

Filipiuc et al cited the results of another study in which the administration of a cannabinoid emulsion to the skin led to clinical resolution and prevented relapse of AD in 80% of the studied patients. In another study, the participants reported improved quality of sleep and diminished itching by an average of 60% following the application of a cream containing PEA, an endocannabinoid. Because of their antipruritic and anti-inflammatory effects, the emulsions tested in both studies were reported as excellent alternatives to conventional AD therapies, including corticosteroid and antihistamine therapies as well as calcineurin inhibitors.[8] According to Filipiuc et al, inhibition of CB2 receptors results in suppressed basal lipid production, suggesting that CB2 antagonists may be effective in the management of dermal conditions characterised by sebaceous gland dysfunction. Topical delivery of a cream containing 3% hemp seed extract in a group of 11 patients twice daily for a period of 12 weeks showed that CBD inhibited the proliferation of sebocytes, resulting in improved sebum production.[37]

However, the growing interest in this treatment paradigm has fuelled a multitude of conflicting scientific reports and publications that are not compliant with the principles of EBM, seemingly suggesting cannabinoids to be a panacea for all dermatological conditions. An example may be the case of a patient with basal cell carcinoma (BCC) involving the face and neck who, following the application of high-concentration THC, allegedly experienced full resolution of his oncological condition, as reported in a book by Singal.[23] Another common problem is the use of misleading terminology, referring to "oil" products, without clearly distinguishing between essential and fixed oils, which may result in patients attempting self-medication at home. An oil (fixed oil) due to the extraction and production processes of fixed oils differs substantially from those of essential oils. Oils are lipid-based fatty substances that are usually fragrance-free and nonvolatile. Essential oils, on the other hand, are mixtures of terpenes, aldehydes, esters, ketones, and alcohols that are used in aromatherapy and are not suitable for direct application to the skin because they can cause irritation. In some languages, like Polish, the word "oil" in the popular idiom is synonymous with "essential oil". Hence, it is crucial that all

review and pilot studies, as well as popular reports, accurately specify the tested products and their concentrations to prevent any degree of misinterpretation.

Conclusion

We have compared the findings of our experimental study exploring the potential of selected cannabinoids (30% CBD and 5% CBG) for the adjunctive topical management of AD flare-ups with the findings of other authors who have over the past 18 years (2005–2023) studied the biophysical parameters of the skin following the application of liquid (emulsions) and semi-solid (creams, ointments, pastes) cannabinoid-based formulations.

The preliminary analysis of the findings of the pilot study based on a review of recent EBM-compliant studies and the results of our experimental study conducted over a period of three months showed that the topical delivery of the ointment compounded with Cannabis Sativa L. var. sativa oil, cholesterol ointment, 30% CBD, and 5% CBG led to the remission of skin lesions on the forearms of the included patients. Furthermore, in the course of the therapy, patients adhering to the topical cannabinoid regimen achieved satisfactory skin parameters, including normal hydration and sebum levels, as well as improved TEWL and erythema, as opposed to patients who reported failure to comply with the regimen owing to the fatty texture of the formulation, despite the instructions they received.

Nevertheless, it should be noted that our experimental study was performed from May to July 2022, when AD frequently enters remission. Thus, a repeat study is required to further test the effect of the formulation during the autumn-to-winter months, when AD symptoms are typically exacerbated in many patients.

Disclosure

The authors report no conflicts of interest in this work.

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