Influence of oxidative injury and monitoring of blood plasma by Differential Scanning Calorimetry on patients with psoriasis

Doctoral (Ph. D) thesis

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I. Introduction

Clinical characteristics

Psoriasis is a long-lasting skin disorder, which is appearing in different severity form. It has a predilection for presenting on the scalp, extensor surfaces of the limbs, hands and feet, sacral and genital regions, and sometimes accompanied with nail changes, but the total body surface area affected can vary. According to dermal symptoms there are five types of psoriasis: plaque, guttate, inverse, pustular, and erythrodermic. The lesions characterized mainly by red, scaly, and raised plaques. In about 80% of cases, plaque psoriasis presents as symmetrical, sharply demarcated, erythematous, dry, scaling, pruritic plaques affecting the top first layer of the epidermis. Psoriasis should be a systemic disorder; in 10-30% of the cases can also cause inflammation of the joints (psoriatic arthritis, PsA) and often involves extra-articular sites, such as the gastrointestinal tract and the eye. Recently, mounting evidence for an association between severe psoriasis and systemic metabolic disorders, such as obesity, insulin resistance, hypertension, dyslipidaemia, cardiovascular disease, periodontitis, and depression were found. Along with local (skin look, itching, pain) and general physical symptoms patients have negative body image due to social stigmatization and decreased quality of life, which explains that psoriasis recently has been in the focus of experimental and clinical research.

Etiology, epidemiology, and prevalence

Psoriasis involves hyperproliferation of the keratinocytes in the epidermal layer, increased vasodilation, and skin infiltration by leukocytes. Abnormal growth and differentiation of keratinocytes cause a significant increase in the epidermal cell turnover rate. The cause of the loss of control of keratinocyte turnover is unknown yet exactly. According to current knowledge, psoriasis is a multifactorial disease, namely genetic, environmental, and immunologic factors appear to play a role in its development.

Many environmental factors beside stress, have also been observed to trigger proliferations and exacerbations, including trauma. Certain medications are associated with triggering psoriasis, including iodide derivatives, steroid withdrawal, aspirin, lithium, some beta-blockers (e.g. propranolol), non-steroidal anti-inflammatory drugs (e.g. indomethacin). Moreover, the following factors (cold, addictions, infections) provoke the disease. In contrast, hot weather, sunlight and pregnancy (not universally) may be beneficial to the progression.

Disease worldwide prevalence is about 2% but varies according to regions. It is affecting 2–3 % of the general population in Europe. It shows a lower prevalence in Asian and some African populations, and up to 11% in Caucasian and Scandinavian populations.

Psoriasis can begin at any age, yet there is a biphasic peak between age 15-35 years and

50-60 years. Approximately 10 to 15 % of new cases begin in children before 10 years. It appears to be slightly more prevalent among women than in men, a male preponderance is with sex ratio of 1.5:1. Exact epidemiology data like in Eastern Europe it's not known in Hungary either. The estimated prevalence is to be about 2% of the total population (200,000 people) and approximately 20% of patients (40,000 persone) has PsA in Hungary.

Pathophysiology and the role of oxidative stress

The last 30 years of research and clinical practice have revolutionized our understanding of the pathogenesis of psoriasis as the dysregulation of immunity triggered by environmental and genetic stimuli. Beforehand, psoriasis was originally regarded as a primary disorder of epidermal hyperproliferation. In normal epidermis there is a tight coordination between vertical migration and differentiation state, with characteristic molecules expressed and morphology manifested at each level. This pattern includes a markedly thickened skin or acanthosis, elongated downward extensions of the epidermis into the dermis or rete pegs and aberrant keratinocyte differentiation. Extreme mitotic activity is visible at the basal layer of keratinocytes demonstrating rapid proliferation and maturation responsible for incomplete terminal differentiation.

Despite more and more research and increasing clinical experience the process of disease developing remains extremely complex, and all details of its pathogenesis is still not completely understood. Multiple theories exist regarding triggers of it process including an infectious episode, traumatic insult, and stressful life event. No doubt, one of the important environmental insult that have a postulated role in the pathogenesis is oxidative stress.

Oxidative stress is defined as an imbalance between oxygen free radical (OFRs) production and the antioxidant defence mechanisms in favour of OFRs. The skin is constantly exposed by OFRs, such as superoxide radical ($^{\bullet}O_2^-$) and hydroxyl radical ($OH^{\bullet-}$) generated from both endogenous sources and external pro-oxidant stimuli. As endogenous sources, OFRs are produced during a variety of biochemical reactions within all cells in organelles such as in mitochondria, in peroxisomes, and in endoplasmic reticulum. Increased infiltration of polymorphonuclear (PMN) leukocytes in psoriatic lesions leads to direct release of OFRs. Moreover, they produce and store the lysosomal enzyme myeloperoxidase (MPO) in their granules, which produce the cytotoxic hypochlorous acid from H_2O_2 and chloride to kill bacteria and other pathogens. External pro-oxidant stimuli are pollutants, heavy metals, tobacco, smoke, drugs, xenobiotics, or ionizing radiation. OFRs degrade polyunsaturated lipids, forming malondialdehyde (MDA). This compound is a reactive aldehyde and is one of the many reactive electrophile species that cause toxic stress in cells and form covalent protein adducts. The production of this aldehyde is used as a biomarker to measure the level of oxidative stress in an organism. The overproduction of pro-oxidant cellular processes can cause lipid peroxidation, contribute to protein degradation, induce the inflammatory processes and

DNA and/or RNA damage to the cells, and finally lead to cell dysfunctions and consequently cell death.

Under normal conditions, the organism is equipped with efficient defence mechanisms against oxidative stress, mainly based on the antioxidants. This system is composed of two major groups: the group of antioxidant enzymes among the others superoxide dismutase (SOD) and catalase (CAT), and the group of the low molecular weight antioxidants such as reduced glutathione (GSH) and sulfhydryl (-SH) groups. Although endogenous antioxidants attenuate the harmful effects of OFRs, increased or prolonged presence of OFRs can override defence mechanisms and mediate numerous cellular responses that contribute to the development of psoriasis. Production of OFRs from PMNs, keratinocytes, and fibroblasts can contribute to neutrophil and keratinocyte proliferation, prominent alteration in dermal vasculature, and overall a chronical and recurrent inflammatory state in the skin. Recent studies showed that cellular signalling pathways such as mitogen-activated protein kinase (MAPK), activator protein 1, nuclear factor-kappa B (NF-kB), and Janus kinase (JAK) signal transducers and activators of transcription are known to be redox-sensitive and proven to be involved in the progress of psoriasis. Increase of oxygen radicals lead to the activation of T helper lymphocytes (Th1, Th17) and keratinocyte cells through MAPK, NF-κB and JAK-STAT3 pathways, resulting in overproduction of interleukins, TNF-alfa, interferon gamma, and vascular endothelial growth factor. These inflammatory factors activate T cells and keratinocytes, causing further a self-amplifying process leading to psoriatic skin phenomenon with keratinocyte overproliferation, hypervascular hyperplasia, and tissue inflammation appearance.

Clinical diagnosis and monitoring

Clinical picture of psoriatic lesions are very characteristic, the localization and appearance of the skin lesions for a specialized dermatologist is a diagnostic means, therefore the diagnosis of psoriasis primarily based on the clinical picture of the disease, but of course there are cases in which, there is a need for histologic examinations as well .

There are also signs, which are also diagnostic for psoriasis. The Auspitz sign, the appearance of punctate bleeding spots when psoriasis scales are scraped off, named after *Heinrich Auspitz* (1835-1886), the Austrian dermatologist who first identified the clinical symptom. The Koebner phenomenon, also called the Koebner response or the isomorphic response, attributed to the renowned German dermatologist *Heinrich Koebner*, who worked in the second part of the XIX. Century. Vaccinations, sunburns, and tattoo can all trigger a Koebner response, which is the appearance of skin lesions on lines of trauma.

Clinical types of psoriasis

Chronic plaque psoriasis. The most common type, it is affecting more than 80% of patients

with psoriasis. Plaques are typically located on the extensor surface of the extremities, sacral and gluteal regions, as well as on the trunk.

Scalp psoriasis. In most cases there is also involvement of scalp. On the scalp, behind the ears there are hyperkeratotic erythematosus base plaques.

Inverse psoriasis. Lesions are on the big skin folds (intertriginous areas) and genital regions. The plaques are thin, well demarcated with slight scaling and difficult to treat.

Guttate psoriasis. Acutely appearing numerous small pinkish-reddish papules with fine scaling over the trunk and limbs. Usually appears when an inflammation is present.

Erythrodermic psoriasis. Acutely appearing, generalized erythema, over more than 80-90% of the whole body, accompanied with loss of electrolyte and albumin, hypothermia.

Pustular psoriasis. Presence of pustules (sterile pustules) on the surface of skin surrounded by erythematosus skin, it can be life-threatening if it becomes generalized.

Localized pustular psoriasis (palmo-plantar pustulosa). Hyperkeratotic erythematosus scaling plaques on palms and soles accompanied with pustules.

Psoriasis arthritis (arthropahtic psoriasis). Psoriatic skin lesions accompanied with arthritis, mostly DIP and PIP joints are involved, but other joints could be involved as well.

Nail psoriasis. The nail lesions are very typical and diagnostic for psoriasis. It may be present without concomitant skin plaques. Nail involvement is often present in PsA patients.

Measurement of the severity of psoriasis

Fredriksson and co-worker in 1978 developed the Psoriasis Area Severity Index (PASI). The most widely used tool for the measurement of severity of psoriasis is PASI score, it combines the assessment of the severity of erythema, induration and desquamation of the lesions and the area affected, into a single score in the range 0 to 72.

From the beginning of XXI. Century online calculator is available compiled by Corti yet. PASI is better validated and more detailed, it remains the score of choice for clinical trials, but the simpler PGA may be well suited for community-based outcomes projects.

Basis of the calculation method is the following: the body is divided into four sections (head (H) (10% of a person's skin); arms (A) (20%); trunk (T) (30%); legs (L) (40%). Each of these areas is scored by itself, and then the four scores are combined into the final PASI. Within each area, the severity is estimated by three clinical signs: *induration* (thickness), *erythema* (redness), and *desquamation* (scaling). Severity parameters are measured on a scale of 0 to 4, from none to maximum. The sum of all three severity parameters is then calculated for each section of skin, multiplied by the area score for that area and multiplied by weight of respective section. For calculating the affected areas of the skin, we can use the Body Surface Area (BSA) measurement.

Classic comorbidities of psoriasis

Psoriasis is a chronic inflammatory systemic disease. Evidence shows an association of psoriasis with arthritis, depression, metabolic syndrome, inflammatory bowel disease, Non-Alcoholic Fat Liver Disease, and cardiovascular diseases. Recently, several other comorbid conditions have been proposed as related to the chronic inflammatory status of psoriasis. The understanding of these conditions and their treatments will certainly lead to better management of the disease. The present article aims to synthesize the knowledge in the literature about the classical and emerging comorbidities related to psoriasis.

The physical, emotional, and social impact of psoriasis on quality of life is similar and sometimes even worse than that observed in patients with ischemic heart disease, cancer, arthritis, and diabetes mellitus. Psoriasis is associated with low self-esteem and prevalence of anxiety and depressive disorders (30% and 60%, respectively).

Metabolic syndrome comprises a group of risk factors, including central obesity, dyslipidaemia, hypertension, and insulin resistance. Associations with obesity, hypertriglyceridemia and hyperglycaemia also increase with the severity of psoriasis.

Definition of treatment goals for moderate to severe psoriasis

Definition of plaque psoriasis severity. It is defined in two main categories: mild versus moderate-to-severe. There was intense discussion among all experts on how to define “mild” and “moderate to severe” plaque psoriasis by using BSA, PASI, and DLQI. There was agreement, however, that a single unifying definition could not include all clinical situations which may be present in a psoriasis patient. *Definition of mild plaque psoriasis.* If BSA ≤ 10 and PASI ≤ 10 indicates mild disease but DLQI > 10 indicates significant impact on quality of life psoriasis can be considered moderate to severe and systemic therapy may be initiated when the patient’s disease cannot be controlled by topical treatment. *Definition of “moderate to severe” plaque psoriasis.* If BSA > 10 or PASI > 10 indicates moderate to severe disease but DLQI ≤ 10 indicates no significant impact on quality of life psoriasis can be considered mild disease.

Treatment and prognosis

According to clinical guideline approximately 90% of psoriasis sufferers will be managed using topical therapy. Therefore, topical therapy (moisturiser, coal tar, salicylic acid, corticosteroid, retinoids, phototherapy, etc) is an appropriate first-line treatment along with practical advice and support in the application and use of the topical treatment. However, topical therapy alone may not provide satisfactory disease control systemic treatment should be chosen.

European S3-Guidelines on the systemic treatment of psoriasis vulgaris summarizing the evidence of the systemic treatment as monotherapies. Conventional systemic therapeutic agents as

second-line drugs are retinoids (acitretin), ciclosporin-A (CsA), and methotrexate (MTX).

Introduction of biological drugs implied the greatest advance in the management of moderate to severe psoriasis of the past decade. In 2004, *etanercept* was the first biological drug registered by the European Medicines Agency, followed by infliximab, adalimumab, ustekinumab, secukinumab, ixekizumab, guselkumab, risankizumab, and apremilast.

Thermal analysis by Differential Scanning Calorimetry (DSC)

In Nature, changes in the internal structure of matter take place in accordance with certain laws. The state parameters of a given biological system (pressure, temperature, volume, concentration) are related to each other, which are described by state equations, which inform about the energy state, internal order, and stability of the system. A complete understanding of biochemical reactions/life processes involves studying the energy transitions in the system. Under certain conditions, specific macromolecules (e.g. proteins), and many life-stages, can be characterized energetically by many sub-states with nearly the same energy. One conformation can be assigned to each sub-state; the biological system, even in a state of thermodynamic equilibrium, can pass from one state to another.

In this view, the positions of the atoms that make up the biomolecule in the macromolecule are not constant, and relatively significant internal motion is to be expected. Among the movements, those which determine the biochemical/ physiological processes are of primary importance to the researchers. It is currently understood that coordinated collective movements within the biological system are responsible for different biological functions. Collective motion refers to the process of moving a well-defined region/domain of a protein as a unit, relative to the rest of the protein. Interactions between ions and small molecules generate fluctuations in the structure of the protein; water molecules, ions can bind to or dissociate from the protein. Binding and dissociation can alter the electrical charge distribution of the protein, thereby attracting or repulsive forces are generated that modulate the movement of the protein or its individual functional domain and can ultimately facilitate or inhibit transitions from one conformational state to another. The dynamic state of the protein or its domains in some way influences biological function.

Under given environmental conditions (pressure, temperature, ion concentration, pH, etc.), the structure of the native protein is a kinetically preferable structure, one of the possible many metastable structures of the polypeptide chain. Intermolecular interactions influence the equilibrium space structure and its dynamic properties. The stability of the spatial structure can be well studied by thermodynamic methods. Of importance are the methods which are capable continuously measure small thermal effects by continuous heating or cooling the system. Such a device is a constant pressure differential scanning calorimeter for continuous measurement of the heat flux (heat capacity). The temperature dependence of the heat flux provides information on the nature of the

thermally induced macromolecular melting process, whether it is a simple or complex process. The cooperativity of the thermal transformation informs about the extent of the reversibility of thermal transformation and how affect the change in environmental conditions the temperature of the transition and the enthalpy of the transformation. Thermodynamic analysis describes many properties, e.g. helps determine heat capacity, melting points, structural stability, transformations, conformational changes etc.

Principles of DSC structure and function

The Micro DSC-II is an extremely sensitive instrument for measuring structural and conformational changes in biological and biochemical processes, which can be used in the range of -20 °C to 100 °C.

The device operates on the principle of measuring the heat flow. The measuring and reference cell is deposited in a heat sink unit which can be heated/cooled according to an adjusted temperature program.

Measured output parameter is the heat flow in the function of temperature or time. The temperature difference between the heat sink and the sample holder as well as between the sample and reference cell provides the control signals for program execution. The sample and reference are filled and weighed so that the heat capacity of the two cells is nearly the same, because the mass difference is ± 0.1 mg.

Thus, during programmed heating, the temperature of the two vessels changes in the same way, and this way the temperature difference between them is zero (the reference is the sample buffer) until some process (endo/exothermic) takes place in the measuring cell containing the investigated macromolecular system. Depending on the sign of the temperature difference and its magnitude, power must be supplied to either the sample or reference cell to maintain thermal balance between the original heating program and the cells. In these cases, the supplied energy during the programmed heating cannot increase the internal energy (that is the temperature) of the sample, because the energy is used to evoke structural changes (breaking H-bonds, unfolding of protein etc.). The output of the measuring/controlling system is this energy (heat flow) as a function of time or current temperature. Information directly obtained from the process under investigation is the integral of the output signal, which is the so-called calorimetric enthalpy (ΔH_{cal}, cells are under constant pressure due to hermetic sealing).

From this, by graphical processing, one can easily obtain the heat capacity of the sample at constant pressure (because the system is inhomogeneous), as well as the change in free enthalpy and entropy calculated for T_m.

In the case of biological/medical samples, a so-called instrument baseline is first required. In this case, both the reference cell and the sample cell contain a buffer appropriate to the nature of the

experiment. The resulting baseline is the feature of the device; this is the so-called "gait" of the instrument. In practice, the real heat flux - temperature curve of a sample is determined by applying a second heating on the irreversibly denatured sample. In this case we also get an instrument baseline. Subtracting this curve from the first heat - flow we get the denaturation curve of our sample.

From the DSC curves different thermal parameters can be derived, which characterize the processes carried out in the studied system. The most frequently used thermodynamic data are:

- T_m maximum or melting temperature, where the heat flow reaches a maximum value, and the 50% of the macromolecule denatured (unfolded). In a complex system we can detect pretransitions, independent from the main one. The higher the T_m, the more bound the macromolecule or its thermally separable domain is.
- ΔH_{cal} area of the heat flow temperature curve below the temperature interval T_1 and T_2. Greater calorimetric enthalpy means strongly bound structure, because to destroy the chemical bonds more energy is required.
- $T_{1/2}$ is the so called „half width" of the denaturation. That temperature range is, where the heat flow is the half of maximum heat flow. Greater $T_{1/2}$ is the sign of loosening of the structure after some intervention (smaller cooperativity between the thermal domains of macromolecule), while smaller one reports about the more rigid system (it behaves as a single structural unit).
- ΔC_P refers to the consequence of denaturation. The structural change during the thermal process can change the heat capacity. Its magnitude is proportional to the measure of final structural change.

A DSC detects the change in heat capacity extremely sensitive manner, but it cannot give information about the definite segment of the system that undergone these structural changes. It means, that additional information is wanted, e.g. histological, biochemical, electron microscopic, or in case of a composed system the thermal characteristic of the individuals.

Our denaturation experiments on human blood plasma were performed in the Department of Biophysics, Medical School University of Pécs (MS UP), by a Micro DSC-II micro calorimeter (produced by SETARAM, France, Caluire-et-Cuire). Hastelloy cells were used for the measurements. The total mass of the tested samples was 950 mg on average. As a control, physiological salt solution was added into the reference cell. The system baseline stability in the isothermal mode was less than ± 0.2 μW and the heating/cooling rate was 0.3 K/min. In case of used it pre-calibration did not require.

Statistical analysis

The results were evaluated using mean and standard error (SE). Significance level was $p < 0.05$ in case when at least 5 samples were in a group. MicroCal Origin 6.0 (Microcal Software, USA) was used for graphic presentation.

II. Aims and hypothesis

Extensive research over the years in the field of psoriasis has greatly extended our understanding of the underlying mechanism of this chronic, immunological mainly skin disorder and manifestation of general symptoms in any organs. Because of, many questions are yet to be elucidated, especially regarding the monitoring severity and its treatment, all studies were performed on patients with psoriasis by DSC analysis of their blood plasma samples.

In our first series of psoriasis investigations, we aimed to detect blood plasma thermal changes with DSC technique in 18 adult psoriasis patients with different clinical stages. Taking in consideration the severity of symptoms, we stratified them in 3 groups (symptomless, minimal symptoms, symptoms) based on PASI scoring system. Furthermore, according to medical treatment human plasma samples were divided into 3 groups: healthy controls, patients without or with medication therapy.

In second series of study, we set upon examining blood plasma with DSC technique in untreated patients and following different therapies in 72 patients with psoriasis, namely after conventional systemic drug treatment, and following application of biologic response modifier agents.

In the third series of project, our purpose was to detect oxidative stress parameters and to determine the calorimetric enthalpy changes under constant pressure by DSC on previously mentioned 72 patients.

In the fourth part of investigation, our aim was to clarify the summarized blood plasma thermal curves content elements by deconvolution process of DSC curves. Furthermore, we were also curious how these sub-curves are related to psoriatic patient severity and their treatment.

III. Manuscripts offprints

Research results and the PhD thesis based on manuscripts have been seen below:

III.1. Differential scanning calorimetry (DSC) analysis of human plasma in different psoriasis stages.
J Therm Anal Calorim 2013;111:1801-4.
DOI 10.1007/s10973-012-2468-2

III.2. Evaluation of blood plasma changes by differential scanning calorimetry in psoriatic patients treated with drugs.
J Therm Anal Calorim 2014;116:557-62.
DOI 10.1007/s10973-013-3585-2

III.3. Influence of oxidative injury and monitoring of blood plasma by DSC on patients with psoriasis.
J Therm Anal Calorim 2016;123:2037-43.
DOI 10.1007/s10973-015-4674-1

III.4. Deconvoluted plasma DSC curves on patients with psoriasis.
J Therm Anal Calorim 2020;142:789-96.
https://doi.org/10.1007/s10973-020-09443-y

IV. Results and discussion

In 2014, the World Health Organization adopted a resolution characterizing psoriasis as “a chronic, non-communicable, painful, disfiguring and disabling disease for which there is no cure”. Although, at first sight this is “just a skin disease”, but related to its systemic inflammatory nature psoriasis is also associated with an increased incidence of chronic comorbid conditions, like cardiovascular disease (e.g. high blood pressure), metabolic syndrome (e.g. obesity, diabetes, hyperlipidaemia), or musculoskeletal lesions (e.g. psoriatic arthritis) resulting an increased overall mortality risk in patients.

Few methods are used to assess the severity of psoriasis as a measure of treatment response in clinical trials and in day-to-day clinical practice. Current guidelines recommend that clinicians should consider the patient holistically, objective evaluations, including body surface area involvement, the location and thickness of lesions, symptoms and comorbidities (with physical and psychosocial manifestations), and the presence or absence of psoriatic arthritis, with a subjective assessment of the physical, emotional, concomitant medication and patient preference. Generally accepted the Psoriasis Area and Severity Index which we use also, the Physician’s Global Assessment, and the Dermatology Life Quality Index, which determine quantitatively the severity of disease.

Even though recently psoriasis is not only considered a skin disease, but a complex disease, its clinical monitoring is still based on skin symptoms and their changes using that scores mentioned above. Thus, the diagnosis is almost exclusively clinical. There are no generally accepted methods, or objective and specific laboratory parameters to assess effectiveness of treatment or to follow the disease in any stage. Laboratory examinations are useful only if starting systemic therapies such as immunological inhibitors, consider obtaining baseline laboratory studies (full blood cell count, blood urea nitrogen/creat, liver function tests, hepatitis panel, tuberculosis screening, pregnancy test).

As mentioned earlier, the cause of psoriasis remains unknown, and there is no cure. Several hypotheses have been advanced, and models proposed over the years concerning its pathogenesis. “Oxidative stress” as a concept in redox biology and medicine has been generally formulated in 1985. Regarding, skin is the largest organ in body that is subjected to oxidative injury, and this stress is known to influence numerous cutaneous diseases.

Well known, that OFRs are highly reactive species generated by biochemical redox reactions as part of normal cell metabolism. In view of the generation of OFR, certain adverse effects also occur. Practically, all the essential biomolecules can undergo oxidative reactions mediated by OFR, so for example (1) damage of DNA or RNA, (2) oxidations of polyunsaturated fatty acids in lipids (lipidperoxidation), (3) oxidations of amino acids in proteins, and (4) oxidative

deactivation of specific enzymes by oxidation of co-factors. In normal steady state, cells have different antioxidant systems and various antioxidant enzymes to defend themselves against free radical attacks. Superoxide dismutase, the first line of defence against OFR, catalyses the dismutation of hydrogen peroxide, which the catalase will further decomposes into water and radical nature nascent oxygen. Glutathione-dependent antioxidant system consisting of reduced GSH and an array of functionally related enzymes plays a fundamental role in cellular defence against OFRs and other oxidant species. A similar function is performed by -SH group with its radicals detoxifying effect.

These preliminary literature data encourage us to investigate the presence of oxidative stress markers from both the pro-oxidant and antioxidant sides among our various severity psoriatic patients. Our results with peripheral blood measurements showed that lipid peroxidation, and total production of OFRs and MPO activity of the PMNs were significantly greater in the untreated patients with moderate and severe symptoms and in all drug-treated groups compared with healthy control group. Regarding of values, the highest level was found in untreated patients with severe symptoms comparing all examined cases. Several investigators confirmed significant correlation between elevation of pro-oxidant status and PASI score. From these, it can be highlighted for example that Kural et al showed increased MDA and lipid peroxide levels in patients when compared to healthy volunteers as control group. Similarly, Kökçam et al., Wozniak and co-workers also found that MDA levels were increased in patients with psoriasis. Another study showed that total oxidant status (TOS) levels of patient were significantly increased. Moreover, increasing evidence suggests that acceleration of pro-oxidant status is not the only reason, but a consequence of the skin inflammatory diseases, which is also true for psoriatic patients. Although, it should be noted that direct measurement of radical production by PMN leukocytes has been published very few studies.

At the same time, we demonstrated that from antioxidants the concentrations of GSH and -SH groups and the activities of SOD and CAT in blood plasma were significantly decreased in untreated patients with severe symptoms compared with those in healthy control individuals. Current data also confirmed that depletion of antioxidant and scavenger capacity in blood is related to the severity of psoriasis. Other researcher confirms our result, for example Kural and co-workers found that activity of CAT, SOD, and glutathione peroxidase enzymes, and total antioxidant status (TAS) levels were decreased. Similar results received Emre and colleagues when measured low level TAS in patients with psoriasis. Changes of redox status in blood during psoriasis are also confirmed by the fact that one of the first drug treatments was different antioxidants (e.g. Vitamin E, beta carotene, selenium).

After these results, the question arises whether it is recommended to give antioxidants to the psoriatic patients. Our current research did not examine this separately, but several

publications confirmed that all fruits and vegetables naturally contain a range of antioxidants, such as carotenoids, flavonoids and vitamin C that are known to reduce oxidative stress in the body. Numerous foods that are especially rich in antioxidants include berries, grapes, nuts, dark green vegetables, whole grains, orange-coloured fruits and vegetables, and green tea. Increasing dietary antioxidants may help reduced oxidative stress associated with psoriasis. Currently there are specific studies solely on the effects of fruit and vegetable consumption on psoriasis, it should be overlooked as an adjunctive therapy in the treatment of disease. Publications in leading nutritional scientific journal recommend that before adding antioxidant supplements into your psoriasis treatment regime consult with a dermatologist.

The aims of anti-psoriasis drug therapies to control clinical manifestations of the disease, contributing to improve the patient's quality of life. The choice of treatment by dermatologist depends on following factors, such as the PASI score, the skin type, the response to previous treatments, the patient's age, and clinical history. Usually, monotherapy or combination of systemic agents (MTX, retinoids, and biological therapy) is used for moderate and severe psoriasis. As a second-generation retinoid, it binds to gene transcription, regulating nuclear receptors and reducing epidermal hyperplasia and cell reproduction. This part of our study showed firstly that from anti-psoriatic agents, acitretin significantly increased the total OFR level and MPO activity compared with healthy controls, but decreased these oxidative stress parameters and better preserved scavengers and antioxidants in blood compared to untreated individuals with severe symptoms. The exact mechanism of these effects in this study is not yet known. But other investigators confirmed that administration of acitretin induced mitochondrial permeability transition and apoptosis in liver cells, which was not prevented by thiol-group protecting and antioxidant agents, excluding the involvement of oxidative stress mechanisms.

One of the first-generation anti-psoriatic drugs is methotrexate, despite its many side effects as antimetabolic agent is commonly used systemic therapies for moderate to severe psoriasis. Of the used anti-psoriatic systemic drugs, the most severe changes in the patients' oxidative stress status were observed after MTX therapy. This drug dramatically increased the total OFR level and MPO activity compared with healthy controls, but values were significantly lower than in patients without medication. Moreover, it caused a significant decrease in levels of GSH and -SH groups and in activity of SOD. Similar observations have been made by Elango and co-workers in a study, where psoriatic patients were treated with methotrexate monotherapy.

Recently, the effect of biologic response modifier agents was detected to measure oxidative stress markers of the blood on psoriatic patients. These chimeric monoclonal anti-TNF-alpha antibodies caused the lowest oxidative damages to the patients, because of their specific binding to the cells' specific receptors did not impair the cell membranes causing lipid peroxidation and did not accelerate the general inflammatory processes.

One of the newest study in the theme declared that high levels of plasma and red blood cell MDA resulting from decreased activity of CAT and glutathione peroxidase should be as markers of plaque psoriasis exacerbation, and offer the measurement of these markers from saliva. While our blood oxidative stress tests can be determined after a simple, routine blood sampling from peripheral vein. At present, even easier, non-invasive techniques have emerged. Fact, the collection of saliva as a diagnostic material has numerous advantages over peripheral blood, the most important being non-invasive collection, lower anxiety of patients, and greater willingness to monitor one's health. Unfortunately, the deficiency of this study is that studied patients did not take anti-psoriatic drugs, so we could not compare with our drug treated patient's lab data.

DSC is a thermoanalytical method which is used firstly during the research of the physical properties of mineralogical and inorganic materials since the 1960s years. The technique was first described by Watson and O'Neill in the Perkin-Elmer Corporation in USA. Later, this validated and efficient method used for the demonstration of structural changes not only in the physical sciences, but also at behaviour of numerous biological macromolecules (carbohydrate, proteins, nucleic acids, etc.), in different experimental animal models, and in clinical researches.

In the beginning of the 2000s years, Garbett and co-workers have shown in their early works, that DSC thermogram is an unique signature for biomolecules reflecting the normal or pathomorphological changes under different conditions.

More than a decade since DSC measurements of patients has been focused in the researches more and more authors confirmed importance and advantages of DSC data. Summary, these are the follows:

1. Thermal results (heat absorption, transition temperature, and calorimetric enthalpy) of blood plasma or serum are significantly different in healthy individuals and in patients with various disease, namely in systematic inflammatory disorders or in tumorous diseases.
2. Changes of DSC data show a strong correlation with clinical stages of each diseases.
3. DSC curves completely reflect the protein composition of the plasma or serum sample.
4. Significant changes in thermograms follow not only from quantitative changes of major plasma proteins, but from interactions of small molecules or peptides also.
5. Additionally, the shape of DSC curves is very sensitive to conformation changes of proteins, to protein-protein or to ligand-protein interactions, to appearance of new proteins (e.g. paraproteins in cancerous diseases), or to influence of different medications to plasma proteins.

According to our knowledge, we were the first who published several DSC data and results received from psoriatic patients in the literature. Regarding there were no preliminary results for psoriasis at all, we had to perform several preliminary DSC measurements from blood samples. Moreover, in several cases lack of other researcher results for comparison caused problem, which made more difficult evaluation works for us. One of the first task was blood sampling and plasma

measurements from healthy volunteers. Here 3 main denaturation melting points (T_{ms} ~ 56, 62 and 65 °C) were appeared. These results were consistently in line with results of all researchers.

Our goal was to check the applicability of DSC technique in this dermatological disease. In untreated and symptomless patients, the average melting temperature was around 63 ºC, while the calorimetric enthalpy was in the range which is usual in case of this kind of biological materials (ΔH ~ 1.25 J/g). The DSC scans in case of patients without medicinal treatment clearly demonstrated the thermodynamic consequence of the severity of the skin disease: decreasing melting temperatures, decrease of the mean value of calorimetric enthalpies compared with healthy controls. In contrast, in case of treated patients a definite heat capacity changes have been seen between the native and denaturized states (the shift of base line indicates it), which could be the sign of different water binding of serum proteins. Groups of patients who undergone medicinal treatment with oral retinoid or with cytostatic (MTX) showed a thermodynamic tendency of the deterioration of the skin disease.

This significant decrease of the melting temperatures, and the increased calorimetric enthalpy are signs of less thermal stability of the macromolecular structure. The pronounced heat capacity change between denatured and native states is also an indicator of the structural change in disease compared with the healthy controls. Unfortunately, this pilot study involved low number of patients in medical treatment group, so we could not draw any statistically based conclusion. Investigations performed on increased sample number could check the validity of our observations, but some trends were visible. Results showed that DSC should be a useable method to not only during medical treatment cases, but DSC curves make a distinction between patients with psoriasis and healthy controls. However, there were no data in the literature indicating the possible diagnostic and staging method of human blood plasma by DSC in psoriasis patients, but similar findings have been described in another report, where applied the DSC method to investigate its utility for other systemic immunological syndromes. DSC curves for rheumatoid arthritis, systemic lupus erythematosus and Lyme disease showed unique signature for blood plasma that could provide the basis of the use of the DSC method as a clinical diagnosis. First application of the DSC method has provided a potential new tool for diagnosis and monitoring of psoriasis patients.

In the second study, has been investigated the thermal changes of human blood plasma in an increased number of untreated patients, and in patients following systematic drug treatment. Each group was subdivided into symptoms-free, mild, and seriously affected parts. In drug treatment the data was separated into cytostatic intervention (MTX), retinoid treatment (acitretin), and biologic response modifier (adalimumab, infliximab, and ustekinumab) agents' group. During the denaturation of samples -independently from their classification- in most cases three melting temperatures (T_{m1} in the range of 55.50–59.50 °C, T_{m2} in the range of 63–69.5 °C as well as T_{m3} between 67.3 and 89.5 °C) could be observed. The calorimetric enthalpy values were in the usual

range of this kind of biologic materials (ΔH ~ 1.3–2.0 J g^{-1}). The DSC scans of patients without any medication clearly demonstrate the thermodynamic consequence of the severity of the skin disease: significant increase in T_{m1}, decreasing T_{m2} melting temperatures, absence of T_{m3}, and increase of calorimetric enthalpies, while in serious symptoms only the first melting and the calorimetric enthalpy changed compared with symptoms-free controls.

Firstly, the effect of traditional anti-psoriatic agents (methotrexate and acitretin) is defined by DSC analysis of human blood plasma changes. Our results showed that DSC scans of patients with symptoms exhibited significant differences ($p<0.05$) in melting temperatures, and in calorimetric enthalpy, showing thermal stability of plasma compared with the untreated symptoms free patients. Detection of blood plasma changes by thermoanalytical method is novel and similar data are not found in the literature either. The background of our experiments is not known exactly, but behind the results should be those blood plasma changes caused by these oral drugs. First, oral-administrated methotrexate is reversibly bound to serum protein, mainly to albumin, and then it is easily diffused into cells, where the drug is actively transported across the cell membranes. The other important and well-known change of blood components that causes long-term methotrexate therapy is leukopenia. Due to known side effects of methotrexate justified to check laboratory tests (such as hemogram and serum creatinine) periodically in the clinical practice. The other administrated drug was acitretin, which is highly lipophilic and penetrates readily into cells. After oral intake and gastrointestinal adsorption its protein binding to the main plasma protein albumin exceeds 99%. Due to its lipophilic nature, serum cholesterol and triglycerides must be monitored, especially in high-risk patients and during long-term treatment. Use of acitretin rarely associated with elevated white blood cell count. Presumably, DSC results associated with changes in blood plasma may be caused by these side-effects of drug administration.

The first approach of different diseases by DSC method was published by Garbett et al. This important paper published that diseases revealed significant changes in the plasma curve with a shift of the curve toward higher denaturation temperatures. Whereas studies have indicated that these changes are resulted from interactions of small molecules or peptides with these proteins.

The extraordinary success of biologic drugs targeting TNF-alfa as well as IL-12 and IL-23 have dramatically changed psoriatic patient care. These new classes of treatments consist in the fusion of proteins and mAb that specifically target the activity of T cells or inflammatory cytokines by inhibiting or modulating specific immune system actors. These biologic drugs can save other organs and minimize side effects. For treatment biologic agents, such as TNF-alfa blockers (infliximab and adalimumab) and IL-12, 23 blocker (ustekinumab) are indicated for moderate to serious lesions in adults who fail to respond to, have a contraindication to, or are intolerant to other systemic therapies. Despite knowing their specific effects, unfortunately at least 20% of patients do not respond to biologic therapy, meaning that key pathogenic mechanisms are still understood, and

the known mechanisms may not always apply to every individual. Recently, from biologic response modifier agents the effect of infliximab, adalimumab, and ustekinumab were detected, defined by thermoanalytical method of blood plasma components. Our results may show that these modern drugs improved thermal stability of plasma in all measurable thermodynamic parameters and promising more effective therapy than the traditional drug interventions even in severe cases. The currently used chimeric (human–murine) monoclonal anti-TNF-alfa antibodies are given by multiple intravenous or subcutaneous injections subsequently in intervals of 4-8 weeks. The biologic agents have Fc regions of the human immunoglobulin IgG1 subtype, which is advantageous in terms of *in vivo* half-life. These large glycoprotein macromolecules stream without carrier plasma components and primarily distributed within the blood. These pharmacokinetic properties should explain our DSC results. Monthly given, low drug doses are sufficient to achieve the biologic treatment in the patients, so these large molecules do not disturb the structure of blood plasma compared to daily taken, transport by plasma proteins non-specific conventional anti-psoriatic treatments.

More and more things are known about the pathogenesis of the process, and parallel to this new and better treatment options are already available today. According to our knowledge, proinflammatory cyto- and chemokines, adhesion and growth factors, different T cells (CD4+, DCs, CD8+), and their receptors act in that inflammatory and proliferative processes which finally appear as psoriatic skin signs and symptoms. Despite all this, psoriasis is a chronic relapsing disease, which often necessitates a long-term therapy. The choice of treatment for it is determined by disease severity, comorbidities, and access to health care. Mild to moderate psoriasis can be treated locally (topical therapy with corticosteroids, vitamin D analogues, retinoids, and phototherapies). In some moderate cases and in every severe case, systemic treatment (drug administration in monotherapy or in combination) should be required. The task is not easy, because to the intervention of the pathogenesis today only few molecular attack points are known, meaning that key pathogenic mechanisms are still not understood, and the known mechanisms may not always apply to every individual. Unfortunately, at least 15–20% of patients do not respond to the newest, targeted anti-psoriatic agents; thus, in such cases or during exacerbation we must return to the conventional and conservative steroid drug therapy. Biologic therapies in psoriasis are highly effective and can be classified according to their mechanism of action. The two main classes of biological agents are targeted at T cells or at cytokines. Moreover, the second-generation retinoids have been well useful drugs, and they have relatively few, local side effects.

In the last part of current research our group was looking for an answer to the question that how the different medications and the variable symptoms affect the human blood plasma composition on patients with psoriasis. For this purpose, DSC thermal curves were deconvoluted. Briefly, blood plasma is a complex protein mixture. Therefore, it contains from a thermal point of view different “thermal domains” which can be assigned to the different compounds. It means that

a DSC scan can be decomposed into a sum of Gaussian curves; that way, their total area is nearly the same as of the experimental curve one, within a reasonable error (<1%). To have the best fitting, we applied more than five curves, but some contribution was less than the error of enthalpy determination, so they cannot influence our final interpretation of data.

Convoluted curves of the average DSC scans of persons with psoriasis after steroid, retinoid, and biological treatment in symptomless, in moderate, and in severe stages were used. To find individual components, we have chosen the critical plasma protein melting points to perform the deconvolution of the curves on the basis of papers published by Garbett et al., Michnik et al., Todinova et al., Monaselidze et al., Kikalishvili et al. as well as Tenchov et al. According to these studies, today the next melting points are well accepted for the identification of plasma protein compounds: at ~ 50 °C fibrinogen, ~ 62 °C albumin, ~ 70 °C Ig and the transition of the tail of albumin, ~ 76 °C C3 protein, IgA, IgG, and albumin, and ~ 82 °C IgG and transferrin. Characteristic thermal parameters (T_m and ΔH_{cal}) have been collected on the one hand from healthy volunteers and on the other hand from patients who were differently treated for their various symptoms. Our aim with the deconvolution of average experimental curves was to get particularly good fitting (R was better than 0.99) between the deconvoluted and the experimental curves, using the above-accepted melting points. The control samples exhibited only four separable plasma compounds: fibrinogen at 56 °C which is higher than the widely accepted 50 °C. This deviation could be explained by our different DSC equipment (heat flow SETARAM Micro DSC-II with a sample holder of 1 mL), and we used -because of the big volume- the original plasma concentration without any dilution. (In most papers, the samples are 20-fold diluted, to avoid the unpleasant consequential of irreversible denaturation of proteins during the cleaning of the sample holders.) The very characteristic albumin contribution appeared at 62.5 °C (in the literature for healthy plasma is 62 °C), while the denaturation of C3, IgA and IgG as well as albumin parts was at 74.8 °C (in the literature 76 °C). The transition at 65.3 °C was identified as the contribution of Ig and the tail of albumin (in the literature 70 °C).

The thermal data of DSC scans measured in the case of psoriatic patients treated with different interventions showed practically partly identical results in T_{ms} and ΔH_{cal} for the symptomless cases. (We have throughout those decomposition values where the enthalpy contribution was in the range of ~ 3% of total enthalpy.) In terms of detail, the following observations can be made in the symptomless samples: (1) T_{m1} decreased slightly during steroid therapy (56.0 °C vs. 54.5 °C), while the decrease was the same following the retinoid and biological drug treatment and less than next to steroids therapy (56.0 °C vs. 55.5 °C). (2) At T_{m2}, T_{m3}, and T_{m4}, the melting temperatures generally increased in every symptomless patient, and after steroid drug administration this elevation was notable. (3) Only retinoid administration caused a well measurable fifth thermal transition (T_{m5} at 85.5 °C) in plasma samples.

Comparing the melting temperatures on deconvoluted curves of patients with moderate or severe symptoms, different drug treatments show changes as follows: (1) a significant decrease in plasma in moderate-symptom patients treated with steroids compared to symptomless cases (51.0 °C vs. 54.5 °C). (2) But in terms of temperature, retinoid and biological drugs did not cause any difference in T_{m1}. The second transitions (T_{m2}) have been identified between 61 and 64.8 °C to the albumin contribution being the dominant constituent of plasma. Most values were higher than in control and compared with the symptomless state in all treatment, and its value decreased in moderate and severe stadium. As it can be assumed from the results that the denaturation in 68-72 °C range is coming from Ig and the transition of the albumin tail, the control and the moderate stages in biological and steroid treatments exhibited smaller T_{ms}, but based on calorimetric enthalpy we put them into this contribution. The enthalpy of T_{m2} transitions increases significantly in almost all treated cases, while T_{m3} transition enthalpies decreased in the function of the severity of disease in each case of biological, retinoid, or steroid treatments.

In the case of healthy plasma, the denaturation around 76 °C is assigned to C3 protein, IgA and IgG fragments, and albumin. In the treated cases, the same compounds in the 72-80 °C temperature range (the biologic moderate state was put here because of its high enthalpy contribution) could be identified. Following retinoid and biological therapy, the calorimetric enthalpy slightly fluctuates, but in steroid-treated moderate stage an extra enthalpy jump has been observed. The widely accepted fifth denaturation temperature is around ~ 82 °C, which involves the contributions of IgG and transferrin. According to our data, we can set them into the 70.6-90 °C range. These changes could not be found in cases of healthy controls, neither after steroid nor after biological treatment in symptomless patients, as well as following retinoid therapy in a moderate stage. Surprisingly, the enthalpy of this transition was high in biologically treated moderate state, while in other cases it was lower value.

These results can be considered as novel because no other results describing such blood plasma changes with a deconvoluted thermoanalytical method on patients with psoriasis have ever been reported, but the present observations are in accordance with our previous results also, in which we have demonstrated similar results on patients with chronic pancreatitis, as in other systematic inflammatory diseases. An indisputable fact that results are in line with other previous findings observed during inflammatory processes.

Several research groups have investigated blood plasma changes in patients who were treated for cancer, inflammatory disease, or other causes, but this is the first research that shows the changes in plasma protein components through the “glasses” of DSC. No doubt, the importance and role of DSC analysis is incontestable for understanding the stability of biological systems in the human body in the future.

V. Novel findings

1. Our initial research described firstly in the literature that there are thermoanalytically detectable differences (transition temperature, calorimetric enthalpy) in blood plasma of patients with psoriasis of different severity based on PASI scoring system. In this preliminary study, an association between plasma DSC abnormalities (decreased transition temperature and increased calorimetric enthalpy) and different type of treatment was already suspected.

2. The second series of dissertation confirmed us that conventional systemic agents (retinoids, MTX) are useful in the treatment of psoriasis, but the new generation of specific monoclonal therapy is more effective in severe or therapy-resistant cases. Blood plasma structural changes measured by DSC method showed that biologic response modifiers caused an improved thermal stability of plasma in all measurable thermodynamic parameters.

3. In the third series of project, our purpose was to detect oxidative stress parameters and to determine the calorimetric enthalpy changes under constant pressure by DSC on previously mentioned 72 patients. Results with peripheral blood measurements showed that balance was loosen between pro- and antioxidants, and state of oxidative stress has been formed on our patient with psoriasis. These changes were significantly greater in systematically treated compare to untreated patients with moderate and severe symptoms. From anti-psoriatic drugs, biologic response modifier agents (adalimumab, infliximab, ustekinumab) caused significantly lesser oxidative stress, than conventional therapy (retinoids, methotrexate).

4. After general knowledge of blood plasma changes, complex DSC curves were deconvoluted in several individual transitions (T_{m1}-T_{m5}), modelling each individual transition. In the examined psoriasis stages, the thermodynamic parameters excess heat capacity and enthalpy of the transitions in proportion corresponded to the targeted treatment and the degree of disease severity, as well as the numbers of transitions were determined from the calorimetric profiles. This examination has shown that drug therapy affects the composition of plasma proteins, which should be always considered for the evaluation of DSC results in similar studies.

Publications

Thesis is based on the following publications

1. **Moezzi Mehdi**, Tamás Fekecs, István Zapf, Andrea Ferencz, Dénes Lőrinczy. Differential scanning calorimetry (DSC) analysis of human plasma in different psoriasis stages.
   J Therm Anal Calorim 2013;111:1801-4. DOI 10.1007/s10973-012-2468-2
   IF**: 2.206**
   Citing papers: **41**; Independent citation count: **30**; Self citation count: **11**
2. **Moezzi Mehdi**, Andrea Ferencz, Dénes Lőrinczy. Evaluation of blood plasma changes by differential scanning calorimetry in psoriatic patients treated with drugs.
   J Therm Anal Calorim 2014;116:557-62. DOI 10.1007/s10973-013-3585-2
   IF: **2.042**
   Citing papers: **27**; Independent citation count: **17**; Self citation count: **10**
3. **Moezzi Mehdi**, István Zapf, Tamás Fekecs, Klára Nedvig, Dénes Lőrinczy, Andrea Ferencz. Influence of oxidative injury and monitoring of blood plasma by DSC on patients with psoriasis.
   J Therm Anal Calorim 2016;123:2037-43. DOI 10.1007/s10973-015-4674-1
   IF: **1.953**
   Citing papers: **26**; Independent citation count: **19** Self citation count: **7**
4. Dénes Lőrinczy, **Moezzi Mehdi**, Andrea Ferencz. Deconvoluted plasma DSC curves on patients with psoriasis.
   J Therm Anal Calorim 2020;142:789-96. https://doi.org/10.1007/s10973-020-09443-y
   IF: **2.731** (2019)

Impact factor of publication the Thesis based on: 8.942
Citing papers of publication the Thesis based on: 94 (independent: 66, self: 28)

Other publications:

1. Csete B, **Moezzi M**, Lengyel Zs, Hódosi B, Zombai E, Battyáni Z. Florid cutaneous papillomatosis leading to social exclusion.
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Psoriasis.
In: Lambert, W (eds.) Psoriasis: Epidemiology, Diagnosis and Management Strategies. Hauppauge (NY), United States of America: Nova Science Publishers, 2016, pp. 45-64.

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J Therm Anal Calorim 2016;123:2029-35.
IF: 1.982
Citing papers: 18; Independent citation count: 12; Self citation count: 6

List of quoted abstracts related to the topic

1. Ferencz A, Fekecs T, Zapf I, **Moezzi M**, Lőrinczy D. DSC analysis of blood plasma on patients with skin and breast cancer, and psoriasis. 4th Joint Czech-Hungarian-Polish-Slovak Thermoanalytical Conference, 2013, Book of Abstracts pp. 19.
2. **Moezzi M**, Ferencz A, Lőrinczy D. Differential Scanning Calorimetry (DSC) analysis of human blood plasma following different therapy in patients with psoriasis. 4th Joint Czech-Hungarian-Polish-Slovak Thermoanalytical Conference, 2013, Book of Abstracts pp. 25.
3. Andrea Ferencz, Tamás Fekecs, **Mehdi Moezzi**, Dénes Lőrinczy. DSC analysis of blood plasma on patients with skin cancer, and psoriasis. Regional Biophysics Conference Smolenice Castle, 2014, Book of Abstracts pp. 106.

4. Dénes Lőrinczy, **Mehdi Moezzi**, Andrea Ferencz. Telling signs of plasma DSC thermograms on patients with psoriasis. 2nd Journal of Thermal Analysis and Calorimetry Conference, 2019, Book of abstracts, pp. 529.

List of presentations:

1. Ferencz A, Fekecs T, Zapf I, **Moezzi M**, Lőrinczy D. DSC analysis of blood plasma on patients with skin and breast cancer, and psoriasis. (oral)
4th Joint Czech-Hungarian-Polish-Slovak Thermoanalytical Conference, 24-27 June 2013, Pardubice, Czech Republik.
2. **Moezzi M**, Ferencz A, Lőrinczy D. Differential Scanning Calorimetry (DSC) analysis of human blood plasma following different therapy in patients with psoriasis. (poster)
4th Joint Czech-Hungarian-Polish-Slovak Thermoanalytical Conference, 24-27 June 2013, Pardubice, Czech Republik.
3. Andrea Ferencz, Tamás Fekecs, **Mehdi Moezzi**, Dénes Lőrinczy. DSC analysis of blood plasma on patients with skin cancer, and psoriasis. (poster) Regional Biophysics Conference, 15-20 May 2014, Smolenice Castle, Slovakia.
4. Ferencz A, Fekecs T, **Mehdi M**, Zapf I, Lőrinczy D. DSC as a diagnostic tool in the medical applications. (poster) Thermal Analysis and Calorimetry in Industry and Research - 40 Years of GEFTA Annual congress with participation of GEFTA's European partner associations, 16-19 September 2014, Berlin, Germany.
5. Dénes Lőrinczy, **Mehdi Moezzi**, Andrea Ferencz. Telling signs of plasma DSC thermograms on patients with psoriasis. (poster) 2nd Journal of Thermal Analysis and Calorimetry Conference, 18-21 June 2019, Budapest, Hungary.

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