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Summary of 2018 highlights

In this Highlights Newsletter edition we cover the 21st European Congress of Physical and Rehabilitation Medicine (PRM) held in Vilnius, 1-5 May 2018. There was a scientific workshop supported by Heel on *Injection Techniques in the Management of Musculoskeletal Disorders*.

Other posters and abstracts at international congresses comprised: additional bioinformatic data of the Traumeel genomics project presented at EULAR, held in Amsterdam, 13–16 June 2018 and findings on the promotion of inflammation resolution at the Frontiers of Science conference, New York, 25–26 June 2018.

Literature on a selection of abstracts, posters and guidelines summaries are provided for interest and further reading.

ESPRM 2018

The 21st European Congress of Physical and Rehabilitation Medicine (PRM) was held in Vilnius, Lithuania, 1–6 May, 2018. Over 1,200 delegates attended the event.

The aim of the European Society of Physical and Rehabilitation Medicine (ESPRM) is to facilitate international exchange of knowledge, skills and attitudes between experts, researchers, clinicians and trainees.

The White Book

The White Book (WB) of PRM in Europe is produced by the four European PRM Bodies and constitutes the reference book for PRM physicians in Europe. The official launch of the third edition was held at the ESPRM 2018.

The WB has multiple purposes, including: providing a unifying framework for European countries, to inform decision-makers on European and national level, to offer educational material for PRM trainees and physicians and information about PRM to the medical community, other rehabilitation professionals and the public.

Heel at ESPRM

Heel was the Gold Sponsor of this important scientific congress organized by the ESPRM and the Lithuanian Society of Physical and Rehabilitation Medicine. Several events were held, including plenary sessions, consensus conferences, workshops and opportunities to meet the experts.

Heel's exhibition booth provided an opportunity to engage with healthcare professionals. On show at the booth was the video of Traumeel mode of action and a quiz on clinical benefits of Traumeel and Zeel.

Traumeel and Zeel materials comprise product monographs, clinical summaries, the knee osteoarthritis pocket guide, Traumeel peer-reviewed publications (the MOZArT study, and Traumeel – an option for acute musculoskeletal injuries) and entry forms for the Hans-Heinrich Reckeweg Clinical Case Award 2018.

Heel supported a scientific workshop at the congress on *Injection Techniques in the Management of Musculoskeletal Disorders*. A summary of the workshop is on pages 4–5.



Selection of abstracts and posters from ESPRM 2018

Low-back pain

Better knowledge about low back pain (LBP) improves patients' positive understanding of disease prognoses and perceived benefits of following treatment guidelines.

A study in 102 patients with non-specific LBP found significant correlations between overall knowledge of the condition and the estimate of disease outcomes, perceived severity, and perceived benefits.¹

Good physical fitness plays a major protective role in preventing pain chronicity according to a study in 202 female nurses. Healthcare personnel with recurrent LBP, working daily in higher relative physical workload are less fit, experience more anxiety, less energy, and higher pain-related fear towards work and physical activity.²



Multiple surgeries could be an important biological factor contributing to allostatic load according to an analysis of 107 consecutive cases.

Patients with chronic pain syndromes undergoing mainly orthopedic surgeries (spine surgery being the most common) to alleviate musculoskeletal symptoms report aggravation of their chronic pain following multiple surgeries. It is concluded that patients with existing chronic pain should be carefully evaluated before considering further surgery.³

1. Tamuliene D, et al. Relation between patients' beliefs and knowledge about low back pain (page 437).
2. Kaistila T, et al. Objectively assessed relative daily energy expenditure is associated with physical fitness, depressive symptoms, fear avoidance beliefs and energy but not intensity of pain in female health care personnel with recurrent low back pain (LBP) (page 397).
3. Jamnik H. Managing chronic pain: to do another surgery or not to do? (page 427).

Traumeel – recent literature review

Traumeel is a multi-component, multi-targeted preparation for the treatment of inflammatory pathologies and is available in oral, topical and injection formulations. The authors, Grech et al, developed an inclusion criteria model for selecting manuscripts published between 1980 and December 2015 reporting on efficacy, adverse events and mode of action. The relevant publications are critiqued.¹ Additionally, this review attempts to determine if the literature supports substituting Traumeel for non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids, or if the use of Traumeel, in conjunction with these treatment protocols, benefits patients with inflammation. NSAIDs and corticosteroids are highly effective but are known to have side effects that limit both their short and long term use in many patients.²

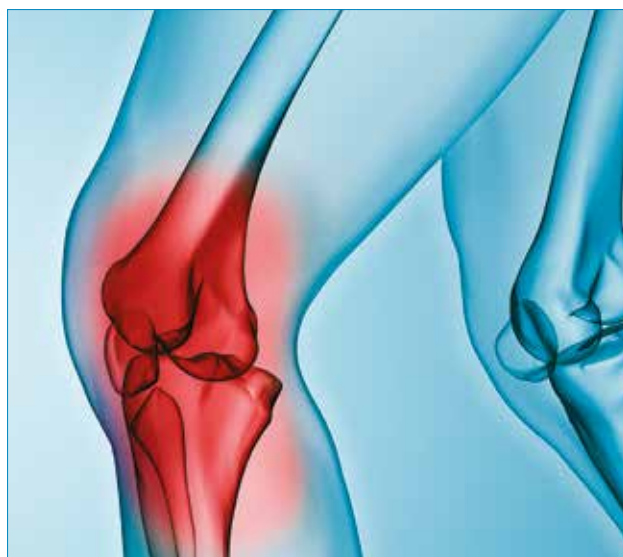
Several studies demonstrate that Traumeel can decrease the incidence or severity of certain disease states associated with inflammation. In terms of musculoskeletal injuries and sports injuries, the following studies were identified. In a multi-center, randomized, controlled trial with 449 physically active adults, the investigators examined pain relief following ankle sprains and demonstrated that there was no significant difference between diclofenac and Traumeel treatment groups.³ In a multi-center, observational, non-randomized study with 184 patients, it was found that Traumeel could replace NSAIDs for the short-term treatment of epicondylitis, describing improvement in pain relief as either “very good” or “good”.⁴ In a controlled, double blind study with 102 patients the authors stated that Traumeel reduced swelling, had a lower pain index, and an earlier return to physical activity.⁵ An observational cohort study consisting of 133 patients, divided its cohorts into exclusively Traumeel and Traumeel as an adjunct to conventional therapy. Primary outcomes were reported as resolution of pain symptoms. This study concluded that Traumeel was as effective as conventional therapy in the treatment of mild-moderate injuries and trauma as well as safer and better tolerated.⁶



Porozov et al. assessed secretion of inflammatory mediators such as IL-1 β , TNF- α and IL-8 by T-cells, monocytes, endothelial cells and gut epithelial cells, finding that patients had decreased levels of all three mediators. Additionally, Traumeel was shown to decrease the potentially damaging effects of an inflammatory response while preserving those cells required to combat infection.⁷

This literature review identifies Traumeel as a compound that does not have the side effect profile of NSAIDs and corticosteroids and appears to provide better pain-free outcomes following musculoskeletal and tissue injuries.

1. Grech D et al. Critical literature review of the homeopathic compound Traumeel for treatment of inflammation. *Pharmacology & Pharmacy*. 2018;9:67–83.
2. Jin J. JAMA patient page. Nonsteroidal anti-inflammatory drugs. *JAMA*. 2015 Sep.
3. González de Vega C et al. Traumeel vs. diclofenac for reducing pain and improving ankle mobility after acute ankle sprain: a multicentre, randomised, blinded, controlled and non-inferiority trial. *Int J Clin Pract*. 2013;67(10):979–89.
4. Birnesser H et al. The homeopathic preparation Traumeel S compared with NSAIDs for symptomatic treatment of epicondylitis. *Journal of Musculoskeletal Research*. 2004;8:119–128.
5. Böhmer D, Ambrus P. Treatment of sports injuries with Traumeel ointment: A controlled double-blind study. *Biological Therapy*. 1992;4:290–300.
6. Schneider C et al. The role of a homeopathic preparation compared with conventional therapy in the treatment of injuries: an observational cohort study. *Complement Ther Med*. 2008;16:22–7.
7. Porozov S et al. Inhibition of IL-1 β and TNF- α secretion from resting and activated human immunocytes by the homeopathic medication Traumeel S. *Clin Dev Immunol*. 2004;2:143–9.



In the electronic version, click onto the icon to link onto publications and websites

Traumeel and Zeel: the MOZArT study

A recent narrative review of advances in intra-articular (IA) drug delivery systems for osteoarthritis therapy, refers to the MOZArT study, where IA injections present advantages, such as the delivery of the drug to the active site with limited adverse side effects.¹ The authors define Traumeel and Zeel in the API (active pharmaceutical ingredient) class, relieving pain – anti-inflammatory, antiedematous, antiexudative combination formulation.

1. Maudens P et al. Recent advances in intra-articular drug delivery systems for osteoarthritis therapy. *Drug Discov Today*. 2018 Oct;23(10):1761–1775.

Workshop at the European Congress of PRM, Vilnius



Injection techniques in the management of musculoskeletal disorders

Dr Dalius Barkauskas, Sports Medicine Specialist and Chief Medical Officer of the Lithuanian Olympic team, led an interactive medical education workshop for rehabilitation specialists describing diagnostic assessment and the importance of appropriate injection technique when treating musculoskeletal disorders. The session moderator was Dr John Macfarlane, Consultant Rehabilitation Medicine Physician, Mercy University Hospital, Cork, Ireland.

Workshop topics

- » Overview of musculoskeletal disorders
- » Fundamentals of human lifestyle & movement
 - The importance of posture
- » Injection therapy
 - Technique
 - Safety
 - Contraindications
 - Referred pain
- » Clinical decision making
- » Shoulder
 - Diagnostic assessment
 - Scapula and humerus
 - Subdeltoid
 - Impingement syndrome
- » Knee joint
 - Diagnostic assessment
 - Coronary ligament
 - Patellar tendon-jumpers knee
 - Quadriceps tendon-runners knee

Dr Barkauskas provided the workshop with an insight into his treatment philosophy: for him the key word is 'balance' including balance of routine, nutrition and movement. An abundance of food and relative physical inactivity means that we are now living very different lives to those that drove human evolution, providing

challenges to the musculoskeletal system. He described techniques to incorporate more activity into everyday life, as well as stressing that not all calories are equal; calories from different sources can have various effects on weight management.

Encouraging audience participation throughout the workshop, Dr Barkauskas demonstrated diagnostic assessment, carried out on several volunteer physicians. Examples of injection techniques were discussed, including how to safely inject proximal to the knee, around the shoulder, neck and upper arm. Importantly, also discussed were details of how to avoid injurious effects of inaccurate needle placement and needlestick injuries. When injecting, it is important to 'anchor' the needle to the patient to ensure you have complete control over the injection. This can be done by having one hand on the patient, which supports the other hand holding the needle. He also stated the importance of ensuring that when examining using palpation, only gentle pressure is used: if you use too much pressure, you will only feel your own fingers and not the patient.

The workshop was extremely well received, incredibly popular and was oversubscribed. Feedback forms rated the workshop as 'Excellent', with a 'Very good tutor'. 74% of attendees stated they felt confident they would implement what they had learnt. The session was recorded, and highlights will be available in Q1 2019.



Profile: Dr Dalius Barkauskas

Since 1996, Dr Dalius Barkauskas has worked as a senior member of the medical team for the Lithuanian Olympic Committee. He was an Olympic team physician in Atlanta 1996, Sydney 2000, Salt Lake City 2002, Athens 2004, Torino 2006, Beijing 2008, Vancouver 2010, London 2012, Sochi 2014 and Rio 2016. Since the year 2000, he has been Chief Medical Officer for the Lithuanian Olympic Team. He describes working with athletes as rewarding, saying “their bodies are their tool; they have to keep themselves at optimal operational performance.”

In addition to his Olympic responsibilities, Dr Barkauskas also runs clinics seeing a wide range of patients from children to octogenarians. These patients have often received multiple treatments from previous interventions, which have not achieved the desired outcome.

When assessing patients, Dr Barkauskas takes a holistic view of the patient, looking at all aspects of their life, including nutrition, posture, activity levels and routine. When treating musculoskeletal injury, he believes in assisting the natural healing processes and uses Traumeel daily in his practice.



Dr Dalius Barkauskas (DB) on his background and Olympic support career:

I am a sports medicine physician working for the Lithuanian Olympic Committee for a number of years. My passion is functional medicine, as well as human movement, and that is what brings me closer to biological medicine as well. My career as Olympic team physician started in Atlanta summer Olympics 1996 and from that time I have been in six summer Olympics and three winter Olympics, working as a team physician and after the Sydney 2000 Olympics as Chief Medical Officer for the Lithuanian Olympic team.

DB on functional medicine: Functional medicine is a very interesting field and less and less understood by doctors, because we usually depend on high technology and we forget what it is to be a human being. Functional medicine as a medical field lies between neurology, orthopaedic medicine and gerontology and it takes the best of them, and those fields depend on functional evaluation and functional medicine.

DB on inflammation resolution and the healing process: If we have a totally resolved inflammatory reaction, we have good regeneration of our tissue in the proper way.

The problem is that because of our diet and our sedentary lifestyle, we often have patients with so-called low-grade chronic inflammatory conditions and because low-grade inflammation is non-productive, it will not go into the regeneration of a tissue. And in the sedentary population, we have a lot of problems. You have to change the daily routine of your patient, starting from sleeping, going into their diet, managing the exercise routines and things like that. It is not only treatments such as injections, it will be about lifestyle changes.

DB on chronic conditions and resolution: It will take a lot of willpower from the patient because usually when we manage the chronic conditions that is not about the skillful doctor. That's about the willingness of the patient to resolve the problem. I will say that I will not treat chronic conditions, but I will help the patient's body in the healing process.

DB on side effects: I will try to avoid, as much as possible, side effects of chemical drugs and be on the side of safety. Patients come to me after having seen their general practitioner, and they have a lot of pills in their pocket.

They are facing the side effects and they want another way of being treated. That is how I am challenged to think in a different way and to practice more gentle medicine.

More and more patients want to know about the side effects, they want to know the drug interactions and that is good. Because patients are more informed about what they will use on a daily basis, and that opens up options to change the whole management process.

DB on Traumeel and explaining its effects to a first-time patient: I will explain that inflammation is the natural process of how we recover after injury. Traumeel will not stop the inflammation, but will support the inflammatory action and keep it in the safe limit. Usually that is totally understood by most patients.

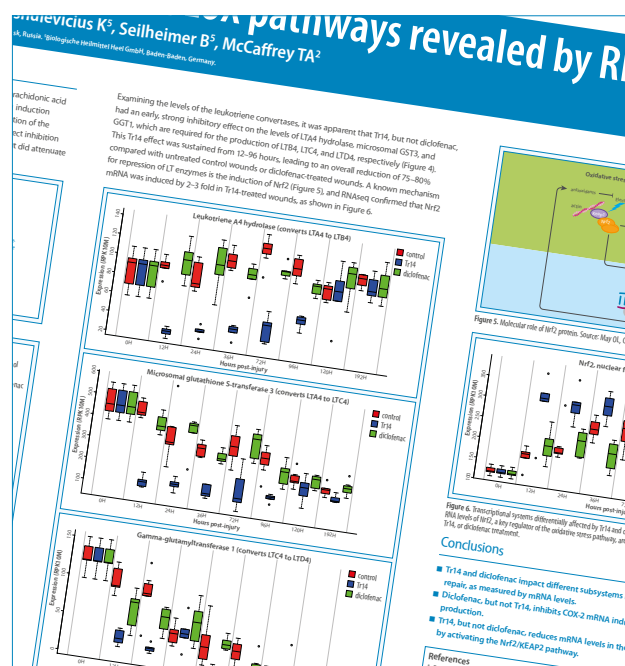
I use Traumeel every day in a broad spectrum of conditions and the main logic will be immunomodulation, because nowadays we have a lot of conditions that have unproductive chronic inflammation.

Traumeel genomics data at EULAR 2018

The European League Against Rheumatism (EULAR) 2018 was held in Amsterdam from 13 June to 16 June – 14,700 delegates attended from 130 countries. Heel is delighted to announce that two abstracts (one abstract also as a poster presentation) on additional bioinformatic data of the Traumeel Genomics project were accepted by this prestigious scientific congress.

Key findings from these submissions were:

- » Traumeel and diclofenac impact different subsystems in the COX/LOX pathways during wound repair, as measured by mRNA levels.
- » Diclofenac, but not Traumeel, inhibits COX-2 mRNA feedback induction by blocking downstream PGE2 production.
- » Traumeel, but not diclofenac, reduces mRNA levels in the leukotriene synthetic pathway, likely by activating the Nrf2/KEAP2 pathway.¹
- » Traumeel and diclofenac had very different effects on the specialized pro-resolving mediators (SPM) synthetic pathway after cutaneous wounding.
- » Traumeel stimulated mRNA levels of several key regulators of SPM synthesis, and had a marked effect on the mRNA levels of the SPM receptors.
- » Traumeel, not diclofenac, suppressed mRNA levels for NFκB subunit p65/RelA, which may explain some of the anti-inflammatory and proresolving properties of Traumeel.²



Section from the Differential effects of Traumeel vs diclofenac¹ poster, presented by Dr Bernd Seilheimer

1. St. Laurent G, Toma I, Seilheimer B et al. Differential effects of tr14 versus diclofenac on cox/lox pathways revealed by rnaseq. *Ann Rheum Dis.* 2018;77:238–239. THU0021.
2. St. Laurent G, Toma I, Tackett M, et al. Differential effects of tr14 versus diclofenac on pro-resolving lipid mediators revealed by RNAseq. *Ann Rheum Dis.* 2018;77:1237–1238. AB0080.

EULAR recommend physical activity in osteoarthritis

EULAR has published guidance on the promotion of physical activity in inflammatory arthritis and osteoarthritis (OA). The overarching principles are:

1. Physical activity is part of a general concept to optimize health-related quality of life.
2. Physical activity has health benefits for people with rheumatoid arthritis, spondyloarthritis, hip and knee OA.
3. General physical activity recommendations, including the four domains (cardiorespiratory fitness, muscle strength, flexibility and neuromotor performance) are applicable (feasible and safe) to people with rheumatoid arthritis, OA and spondyloarthritis.
4. The planning of physical activity requires a shared decision between healthcare providers and people with rheumatoid arthritis, spondyloarthritis, hip and knee OA, which takes people's preferences, capabilities and resources into account.

The recommendations are informed by evidence and expert opinion to provide guidance in the development, conduct and evaluation of physical activity interventions and promotion in people with inflammatory arthritis and OA. It is advised that these recommendations should be implemented considering individual needs and national health systems.

Rausch Osthoff A-K, et al. 2018 EULAR recommendations for physical activity in people with inflammatory arthritis and osteoarthritis. *Ann Rheum Dis.* 2018;77:1251–60.



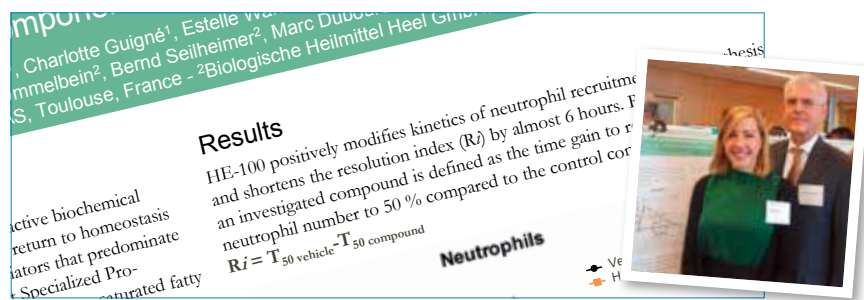
The New York Academy of Sciences – 2018

Dr Bernd Seilheimer and Dr Natascha Krömmelbein, Heel HQ, Baden-Baden, Germany, attended the New York Academy of Sciences conference on *Resolution of Inflammation, Infection and Tissue Regeneration* in New York, 25–26 June 2018.

Pre-eminent researchers at the cutting edge of the field convened at this conference to discuss mechanisms of inflammation, tissue repair, regeneration, and explored the existing hurdles to clinical approaches.

There were four key congress sessions:

- » Inflammatory Mediators and Cellular Mechanisms
- » Resolution of Cardiovascular and Systemic Inflammation
- » Tissue Repair and Infection
- » Clinical Development and Therapeutic Potential for Inflammatory Disease



Section from the Multicomponent medication poster¹ presented by Dr Bernd Seilheimer [photo: Dr Natascha Krömmelbein and Dr Bernd Seilheimer]

Dr Bernd Seilheimer presented the findings of the accepted poster on inflammation resolution.¹

Key findings

Recently it was shown that Specialized Proresolving Mediators (SPMs), derivatives of polyunsaturated fatty acids (PUFAs), are essential in the resolution in inflammation.

The effects of Traumeel were investigated in inflammation resolution, using a self-

limited zymosan-induced peritonitis model in mice. The preliminary results support the hypothesis that Traumeel may promote inflammation resolution:

- » Traumeel improved neutrophil resolution index by almost 6 hours
- » Traumeel favored recruitment of macrophages
- » Traumeel stimulated synthesis of pro-resolving mediators

1. Baillif V, Guigné C, Wanecq E et al. A multicomponent medication (HE-100) promotes inflammation resolution. Poster at New York Academy of Sciences conference 25–26 June.

Literature of interest

A meta-analysis of 15 observational studies involving a total of 358,944 participants, including 80,911 osteoarthritis (OA) patients and 29,213 cardiovascular disease (CVD) patients, found that OA is a significant risk factor for CVD. Pooled estimates calculated by a random effects model showed that the risk of CVD was significantly increased by 24% in patients with OA compared with the general population.¹

A group from Canada investigated this link further to try to establish the role that NSAIDs might play in this increased CVD risk. Using population-based health administrative data from 720,055 patients in British Columbia, they found a 23% higher risk of developing CVD in OA patients compared with people without OA after adjusting for common influencing factors. Approximately 67.51% of the total effect of OA on the increased risk of CVD was mediated through current NSAID use.

They conclude that OA is an independent risk factor for CVD and that the mediating role of NSAID use substantially contributes to the OA-CVD association.²

1. Wang H, Bai J, He B et al. Osteoarthritis and the risk of cardiovascular disease: a meta-analysis of observational studies. *Sci Rep*. [Internet] 2016;6(1). [🔗](#)
2. Atiquzzaman M, Kopec J, Karim ME et al. The role of nsoids in the association between osteoarthritis and cardiovascular diseases: a population-based cohort study. *Ann Rheum Dis*. 2018;77(Suppl):A144. [🔗](#)

A set of recommendations, designed to help health professionals implement approaches to pain management in inflammatory arthritis and osteoarthritis patients has been published by EULAR.¹

Health professionals should have full knowledge of patients' needs, preferences and priorities, pain characteristics and history to provide comprehensive patient-centred care which should include patient education and considerations for multidisciplinary intervention.

1. Geenen R et al. EULAR recommendations for the health professional's approach to pain management in inflammatory arthritis and osteoarthritis. *Ann Rheum Dis* 2018;77:797–807. [🔗](#)

Further reading

New insights into the role of sleep in chronic pain

Aili K, Andersson M, Bremander A, et al. Sleep problems and fatigue as a predictor for the onset of chronic widespread pain over a 5- and 18-year perspective. A 20-year prospective study. EULAR 2018; Amsterdam: Abstract OP0072. [🔗](#)

Hypermobility and sports injury

Nathan J, Davies K. To assess whether there is an association between hypermobility and sports injury. *Ann Rheum Dis*. 2018;77:470. Abstract THU0532. [🔗](#)

Depressive symptoms associated with disease severity in patients with knee osteoarthritis

Rathbun AM et al. Association between disease severity and onset of depression in knee osteoarthritis. EULAR 2018; Amsterdam: Abstract OP0003. [🔗](#)

Knee osteoarthritis pocket guide

A pocket guide for GPs and specialists on the Diagnosis and Management of Knee Osteoarthritis has been developed by international experts, supported by an educational grant from Heel.

It features a concise algorithm for treatment and recommendations for initial, advanced, and severe case management.

The knee osteoarthritis pocket guide has been translated into Italian, Portuguese, Russian and Spanish and will be available at Heel educational events.



Date for your diary

» European League Against Rheumatism (EULAR), Madrid, June 12–15, 2019

Publications on Traumeel studies are available

Differential effects of Tr14 versus diclofenac on COX/LOX pathways revealed by RNAseq

St. Laurent G¹, Toma F², Tackett MR³, Zhou J⁴, Ri M^{1,3}, Vyatkin Y^{1,3}, Shtokalo D^{1,3,4}, Jepson T⁵, Cesnulevicius K⁶, Seilheimer B⁷, McCaffrey TA²

¹The St. Laurent Institute LLC, Vancouver, WA, USA; ²The George Washington University Medical Center, Washington, DC, USA; ³StudentGate LLC, Novosibirsk, Russia; ⁴U.S. Fish and Wildlife Service, Novosibirsk, Russia; ⁵Biological Institute of Heel GmbH, Baden-Baden, Germany

Introduction

Tr14 is a combination of diluted plant and mineral extracts that has been used widely for the treatment of acute musculoskeletal conditions, like sprains and traumatic injuries, for over 60 years. Previously published *in vitro* and *in vivo* studies have demonstrated its anti-inflammatory effects, which may result from a decrease in secretion of interleukin 1 beta (IL1β), tumor necrosis factor alpha (TNF-α), and interleukin 8 (IL8).

In this study, we examined the effects of Tr14 and diclofenac in a mouse model of wound healing, collecting samples at multiple time points and using RNA sequencing to examine gene expression changes in response to treatment.

Methods

Female 8–10 week old C57BL/6 mice were anesthetized and a full-thickness skin wound (1.5 cm x 1.5 cm) was created on the back of the mice. Mice were treated with Tr14 topical diclofenac (2 mg/kg) daily (Figure 1). Mice were sacrificed at 4, 8, 12, 24, 48, 72, 96, 120, 144, 168, 192, 216, 240, 264, 288, 312, 336, 360, 384, 408, 432, 456, 480, 504, 528, 552, 576, 600, 624, 648, 672, 696, 720, 744, 768, 792, 816, 840, 864, 888, 912, 936, 960, 984, 1008, 1032, 1056, 1080, 1104, 1128, 1152, 1176, 1200, 1224, 1248, 1272, 1296, 1320, 1344, 1368, 1392, 1416, 1440, 1464, 1488, 1512, 1536, 1560, 1584, 1608, 1632, 1656, 1680, 1704, 1728, 1752, 1776, 1800, 1824, 1848, 1872, 1896, 1920, 1944, 1968, 1992, 2016, 2040, 2064, 2088, 2112, 2136, 2160, 2184, 2208, 2232, 2256, 2280, 2304, 2328, 2352, 2376, 2400, 2424, 2448, 2472, 2496, 2520, 2544, 2568, 2592, 2616, 2640, 2664, 2688, 2712, 2736, 2760, 2784, 2808, 2832, 2856, 2880, 2904, 2928, 2952, 2976, 3000, 3024, 3048, 3072, 3096, 3120, 3144, 3168, 3192, 3216, 3240, 3264, 3288, 3312, 3336, 3360, 3384, 3408, 3432, 3456, 3480, 3504, 3528, 3552, 3576, 3600, 3624, 3648, 3672, 3696, 3720, 3744, 3768, 3792, 3816, 3840, 3864, 3888, 3912, 3936, 3960, 3984, 4008, 4032, 4056, 4080, 4104, 4128, 4152, 4176, 4200, 4224, 4248, 4272, 4296, 4320, 4344, 4368, 4392, 4416, 4440, 4464, 4488, 4512, 4536, 4560, 4584, 4608, 4632, 4656, 4680, 4704, 4728, 4752, 4776, 4800, 4824, 4848, 4872, 4896, 4920, 4944, 4968, 4992, 5016, 5040, 5064, 5088, 5112, 5136, 5160, 5184, 5208, 5232, 5256, 5280, 5304, 5328, 5352, 5376, 5400, 5424, 5448, 5472, 5496, 5520, 5544, 5568, 5592, 5616, 5640, 5664, 5688, 5712, 5736, 5760, 5784, 5808, 5832, 5856, 5880, 5904, 5928, 5952, 5976, 6000, 6024, 6048, 6072, 6096, 6120, 6144, 6168, 6192, 6216, 6240, 6264, 6288, 6312, 6336, 6360, 6384, 6408, 6432, 6456, 6480, 6504, 6528, 6552, 6576, 6600, 6624, 6648, 6672, 6696, 6720, 6744, 6768, 6792, 6816, 6840, 6864, 6888, 6912, 6936, 6960, 6984, 7008, 7032, 7056, 7080, 7104, 7128, 7152, 7176, 7200, 7224, 7248, 7272, 7296, 7320, 7344, 7368, 7392, 7416, 7440, 7464, 7488, 7512, 7536, 7560, 7584, 7608, 7632, 7656, 7680, 7704, 7728, 7752, 7776, 7800, 7824, 7848, 7872, 7896, 7920, 7944, 7968, 7992, 8016, 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