



Traumeel[®]


Product Monograph

-Heel



Foreword

Sportsmen and women are increasingly requesting complementary alternative medicines (CAMs), used alongside traditional medicines. CAMs, such as Traumeel® reviewed in this monograph, are now an important part of sportspeople's armamentarium against the effects of injury. This has occurred for several reasons. It is partly due to increasing opportunities for scientific evaluation and investigation of alternative medicines leading to their increasingly positive evidence base. It is also partly due to the desire of sportspeople to avoid the recognized side effects of some traditional medicines, such as non-steroidal anti-inflammatory drugs (NSAIDs). Individual people suffer from the well-known side effects of NSAIDs to varying degrees and, with injuries so prevalent in sports, this has led to ever-increasing interest in CAMs. Finally, there are significantly less worries about anti-doping issues, with many CAMs from renowned companies working with high quality control standards, such as Traumeel® from Heel.

Outside of sports medicine, many patients are buying CAMs over the counter after having been made aware of their positive effects in a variety of rheumatic and traumatic inflammatory-based injuries. For example, surgeons, physiotherapists, orthopedic surgeons and general practitioners are often recommending their use.

The extensive and growing evidence base for Traumeel® is presented in this monograph. However, as with many traditional medicines, we still need more evidence in the form of well-controlled clinical studies. We also need to study the effect of Traumeel® under varying inflammatory conditions.

I now have over 12 years experience of using Traumeel®. In my clinical practice and sports medicine experience, it has proven extremely useful to many professional sports teams, Olympic teams and amateur athletes. Having the confidence of the anti-inflammatory action of Traumeel® with no relevant side effects means that people enjoy its benefits and continue to request it.

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1. Overview

Traumeel® is an effective treatment for acute musculoskeletal injury and inflammation that improves/promotes healing.

Traumeel® is indicated for

1. Injuries

- The relief of repetitive or overuse injuries (such as tendonitis, bursitis, epicondylitis) and of mild to moderate pain associated with such conditions

2. Inflammation of the musculoskeletal system

- The relief of symptoms associated with inflammatory, exudative and degenerative processes due to acute trauma (such as contusions, lacerations, fractures, sprains, post-operative wounds, etc.)
- The relief of mild to moderate backache and myalgia
- The relief of minor to moderate pain from post-traumatic arthritis, osteoarthritis and gouty arthritis.

The clinical effectiveness of Traumeel® is supported by scientific evidence and over 60 years of worldwide usage.

Traumeel® is not a non-steroidal anti-inflammatory drug (NSAID); however, it is as effective at reducing symptoms of inflammation as NSAIDs, such as diclofenac. As with many other commonly used therapeutic agents, the exact mechanism of action of Traumeel® is not fully understood. However, it is known that Traumeel® can have an inhibitory effect on various pro-inflammatory mediators¹ (see '4.2. Mechanism of action of Traumeel®' section). Traumeel® is not known to interact with other medications and is very well tolerated with minimal side effects (see '6. Safety and toxicology' section).

Traumeel® is not listed on the World Anti-Doping Agency (WADA) list of banned products. In fact, in Germany, Traumeel® is listed as "to be used" on the National Anti-Doping Agency (NADA) list. For this reason, and its effectiveness in sports medicine (see '5.1. Traumeel® in acute injuries and inflammation of the musculoskeletal system' section), Traumeel® is widely used in the treatment of acute musculoskeletal injury and inflammation in athletes and sports professionals.

Traumeel® is available in a variety of formulations (galenic forms) for flexibility of use and to maximize patient convenience and compliance. Traumeel® can be used in all age groups, including children 2 years and older and the elderly.

Today, Traumeel® is available in more than 60 countries worldwide, with millions of patients treated each year, most frequently using the ointment formulation.

Reference

1. Porozov S, Cahalon L, Weiser M, Branski D, Lider O, Oberbaum M. 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;11(2):143-149.

2. Introduction to Traumeel®

2.1 What is Traumeel®?

Traumeel® is an effective treatment for acute musculoskeletal injury and inflammation. It rapidly reduces inflammation, relieves pain and bruising and promotes healing after an accident, injury or surgery. Traumeel® has been used to aid recovery from sprained joints, strained/pulled muscles, bruises, nerve pain, swelling, post-surgical pain and to promote wound healing. It is widely used in sports medicine.

The beneficial effects of Traumeel® have been demonstrated in clinical trials, as well as in *in vitro* experimental models, including the carrageenan-induced edema test and the adjuvant arthritis test.¹

Traumeel® has been shown to have both local² and systemic³ efficacy in reducing pain and inflammation (see '5. Evidence base for Traumeel®' section) and is as effective at reducing symptoms of inflammation as NSAIDs, such as diclofenac.

Research into the mechanism of action of Traumeel® suggests that it has an inhibitory effect on various pro-inflammatory mediators⁴ (see '4.2. Mechanism of action of Traumeel®' section).

Traumeel® has no known interactions with other medications and is very well tolerated with minimal side effects. Traumeel® can be used in all age groups, including children 2 years and older and the elderly.

When more than one formulation of Traumeel® is used concomitantly, a more rapid relief of symptoms can be observed.

The effects of Traumeel® are supported by scientific research and over 60 years of worldwide use as a first-line treatment for patients with acute musculoskeletal injury and inflammation.

2.2 In which patients might Traumeel® be useful?

Traumeel® is a first-line treatment for patients with acute musculoskeletal injury and inflammation that delivers the efficacy of NSAIDs but with fewer side effects, irrespective of age. The use of Traumeel® should be considered in patients who require relief of

symptoms associated with ankle, knee, neck and back sprains (see '3.2. Indications and dosages' section).

Unlike NSAIDs, Traumeel® has hardly any known side effects and contraindications (see '6. Safety and toxicology' section). For this reason, Traumeel® can be used in a variety of patient groups. For example, elderly patients with inflammatory diseases and injuries who cannot tolerate the gastrointestinal side effects associated with NSAIDs, and for patients with blood clotting disorders. It can also be used in children 2 years and older (see '6. Safety and toxicology' section).

Traumeel® is included on page 1,725 of the 2009 Physicians Desk Reference (PDR), the 'German Red List' (equivalent to the PDR) and the 'Russian Red List', as well as recommended in several other reference books. Reference books particularly recommend its use for musculoskeletal system injuries, post-traumatic arthritis and other arthritic conditions.⁵⁻¹⁰

2.3 To whom this monograph is addressed

You may be most interested in using Traumeel® in your patients if you are a:

- General practitioner/family practitioner
- Physician of any specialty, with an interest in complementary medicine
- Orthopedic surgeon (orthopedist)
- Rheumatologist
- Physician with sports medicine training
- Complementary alternative medicine (CAM) practitioner (e.g. homeopath, naturopath, chiropractor)
- Physiotherapist
- Pharmacist
- Physician with patients unable to take NSAIDs
- Any of the above, whose patients are interested in using Traumeel®.

2.4 The different formulations of Traumeel®

Traumeel® is available in a variety of formulations (galenic forms) for flexibility of use and to maximize patient convenience and compliance. It can be obtained in:

- Ointment/gel for topical application
- Oral tablets
- Ampoules of solution for injection
- Oral drops

Key point: Traumeel® is a first-line treatment for patients with musculoskeletal injury and inflammation that delivers the efficacy of common NSAIDs with fewer side effects, irrespective of age.

References

1. Conforti A, Bertani S, Metelmann H, Chirumbolo S, Lussignoli S, Bellavite P. Experimental Studies on the Anti-Inflammatory Activity of a Homeopathic Preparation. *Biomed Ther.* 1997;XV(1):28-31.
2. Böhmer D, Ambrus P. Behandlung von Sportverletzungen mit Traumeel-Salbe – Kontrollierte Doppelblindstudie [Treatment of Sports Injuries with Traumeel Ointment: A Controlled Double-Blind Study]. *Biologische Medizin* 1992;XXI(4):260-8. (English translation available in: *Biol Ther.* 1992; X(4):290-300)
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4. Porozov S, Cahalon L, Weiser M, Branski D, Lider O, Oberbaum M. 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;11(2):143-149.
5. Hess H. *Biological Medicine in Orthopedics, Traumatology, and Rheumatology.* 1st edition Baden-Baden: Aurelia Verlag, 2001.
6. Fügen I, Heine H, Frase W. *Biological Medicine in Geriatrics.* 1st edition. Baden-Baden: Aurelia Verlag, 2003.
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9. Ricken K-H. *Homotoxikologie für die Praxis – Therapieschemata chronischer Erkrankungen.* 1st edition. Baden-Baden: Aurelia Verlag, 1995.
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3. The components of Traumeel®

All of the formulations of Traumeel® contain 14 components. These are listed in Table 1, including the characteristics** of each ingredient as well as the declaratory potency* of each of the dosage forms.

Table 1.
Traumeel® product declaratory potencies* and characteristics**

Constituent	Characteristics	Ointment/gel		Tablets		Injection solution		Oral drops	
		Decl. Potency	Quantity per 100 g	Decl. Potency	Quantity per tablet = 300 mg	Decl. Potency	Quantity per 2.2 ml	Decl. Potency	Quantity per 100 g
Achillea millefolium <i>Milfoil</i>	Hemorrhages, especially precapillary arteriovenous (anastomosis), oozing hemorrhages.	Ø	0.09 g	D3	15 mg	D3	2.2 µl	D3	5 g
Aconitum napellus <i>Monkshood</i>	Fever with hot, dry skin, neuralgia, inflammatory rheumatism; improvement of the vasotonia; analgesic, hemostatic.	D1	0.05 g	D3	30 mg	D2	1.32 µl	D3	10 g
Arnica montana <i>Mountain arnica</i>	To stimulate the healing of wounds, fractures, dislocations, contusions, hematomas, myocardial weakness, neuralgia, myalgia, analgesic, hemostatic.	D3	1.5 g	D2	15 mg	D2	2.2 µl	D2	5 g
Atropa belladonna <i>Deadly nightshade</i>	Localized reaction phases, cerebral sensitivity with cramp and delirium.	D1	0.05 g	D4	75 mg	D2	2.2 µl	D4	25 g
Bellis perennis <i>Daisy</i>	Dislocations, contusions, sensation of soreness in the abdominal wall/cavity, exudative processes, resorption of edema.	Ø	0.1 g	D2	6 mg	D2	1.1 µl	D2	2 g
Calendula officinalis <i>Calendula</i>	Slowly healing wounds, promotes granulation, analgesic.	Ø	0.45 g	D2	15 mg	D2	2.2 µl	D2	5 g
Chamomilla (Matricaria) recutita <i>Chamomile</i>	Anti-inflammatory; stimulates granulation, promotes healing in difficulty healing wounds and ulcers; fistulae, hemorrhoids, mastitis, intertrigo, aphthous stomatitis, conditions of restlessness and excitation, disorders of dentition, otitis media, glandular swellings.	Ø	0.15 g	D3	24 mg	D3	2.2 µl	D3	8 g
Echinacea angustifolia <i>Narrow-leaved cone flower</i>	Increase in the mesenchymal defenses; inflammation of all kinds and locations, septic processes; hyaluronidase inhibiting, anti-inflammatory action.	Ø	0.15 g	D2	6 mg	D2	0.55 µl	D2	2 g
Echinacea purpurea <i>Purple cone flower</i>	Increase in the mesenchymal defenses; inflammation of all kinds and locations, septic processes; hyaluronidase inhibiting, anti-inflammatory action.	Ø	0.15 g	D2	6 mg	D2	0.55 µl	D2	2 g
Hamamelis virginiana <i>Witch-hazel</i>	Venous stasis, varicose veins, (thrombo-) phlebitis, crural ulcers, hemorrhoids, venous hemorrhages, anti-inflammatory, analgesic.	Ø	0.45 g	D2	15 mg	D1	0.22 µl	D2	5 g

Constituent	Characteristics	Ointment/gel		Tablets		Injection solution		Oral drops	
		Decl. Potency	Quantity per 100 g	Decl. Potency	Quantity per tablet = 300 mg	Decl. Potency	Quantity per 2.2 ml	Decl. Potency	Quantity per 100 g
Hepar sulfuris <i>Calcium sulphide</i>	Tendency to suppuration, especially on the skin and lymph glands (furuncles, pyoderma, panaris, phlegmons), tonsillar abscesses, chalazions, hordeolums, hemicrania, urinary disorders, hypersensitivity to cold and draughts.	D6	0.025 g	D8	30 mg	D6	2.2 µl	D8	10 g
Hypericum perforatum <i>St. John's wort</i>	Neural and cerebral injuries, e.g. commotio cerebri neural pains upon or after injuries hemostatic.	D6	0.09 g	D2	3 mg	D2	0.66 µl	D2	1 g
Mercurius solubilis Hahnemanni <i>Mixture containing essentially mercurio-amidonitrate</i>	Suppurations, abscesses, gingivitis, stomatitis, nasopharyngeal catarrh, catarrh of the sinuses, cholangitis, shrinking action on edematous conditions.	D6	0.04 g	D8	30 mg	D6	1.1 µl	D8	10 g
Symphytum officinale <i>Comfrey</i>	To accelerate callus formation in fractures periostitis, causalgia, disorders arising from amputation stumps contusions.	D4	0.1 g	D8	24 mg	D6	2.2 µl	D8	8 g

	Ointment/gel	Tablets	Injection solution	Oral drops
Carrier substances	Ointment: cetostearyl alcohol, paraffin, 13.8% alcohol Gel: carbomers, sodium hydroxide, 25% alcohol	6 mg lactose, 1.5 mg Mg-stearate	0.9% saline solution	35% alcohol

In some countries the number of ingredients and their concentration may vary slightly. For country-specific product information, please contact your local Heel partner.

Notes:

Ø= undiluted, i.e. the so called 'mother tincture'.

D= 'dilution of 1 in 10'; the figure after the letter 'D' refers to how many times the mother tincture has been diluted.

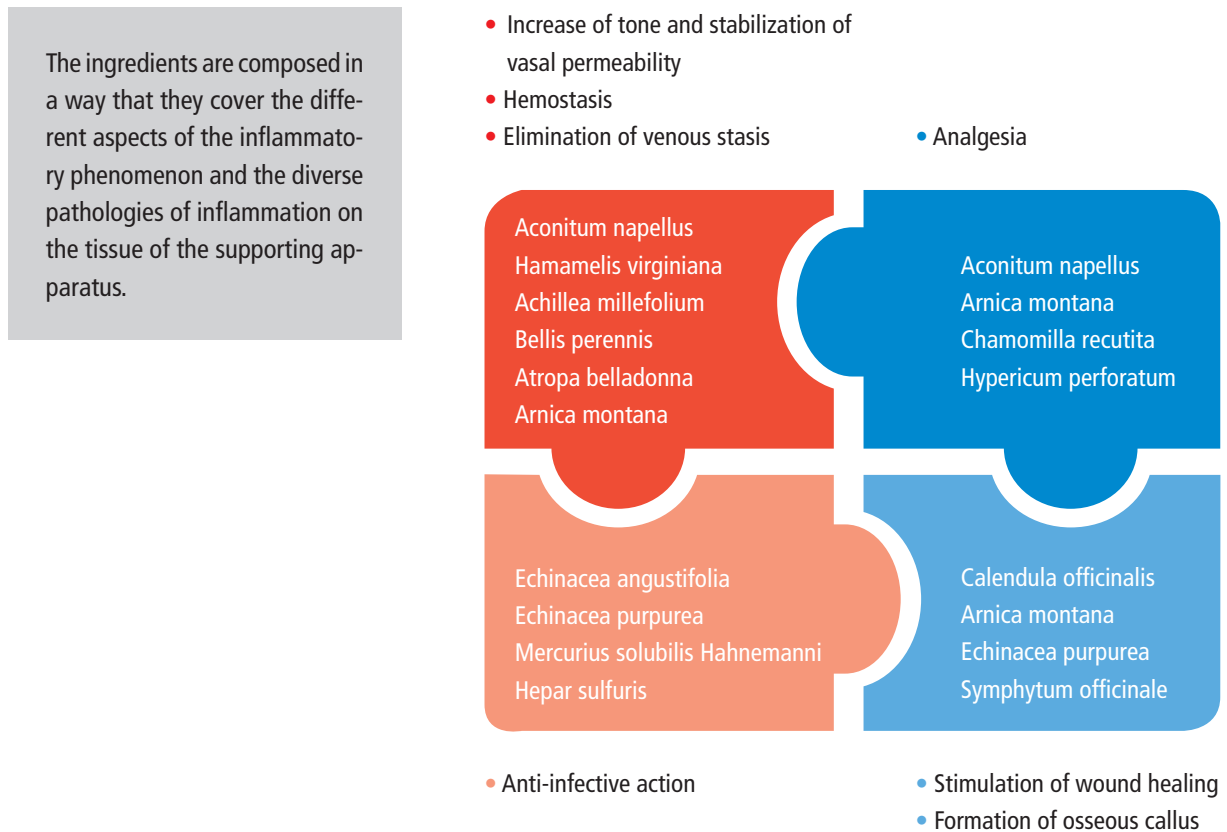
* 'Declaratory potency'=the number of 10X dilutions applied to the 'mother tincture' of the ingredient, e.g. for Belladonna D4, that means 4 times 1 in 10 dilutions before it is mixed with the other ingredients; for Symphytum D8 or Mercurius D8, that means 8 times 1 in 10 dilutions.

** Characteristics with reference to: Reckeweg H-H. *Materia Medica – Homoeopathia Antihomotoxica*. 4th edition. Baden-Baden: Aurelia Verlag, 2007.

3.1 Completeness of action

Together, the components of Traumeel® ensure a completeness of action (see Figure 1).

Figure 1. Completeness of action of Traumeel®.



Key point: The various formulations of Traumeel® contain 14 components in differing potencies, with each component having different characteristics.

3.2 Indications and dosages

A broad indication for Traumeel® formulations is given in Box 1 (see '10. Appendix' section for list of standard doses for the various formulations of Traumeel®). However, the exact indication and dosage for each formulation varies slightly in each country in which it is available. Please refer to country-specific package instructions for exact indication and dosage recommendations.

Contraindications and adverse events of Traumeel® can be found in the '6. Safety and toxicology' section of this monograph.

Box 1. Broad indication and usage for Traumeel®.

Improvement in conditions, such as sprains and other traumatic injuries, and as supportive therapy in pain and inflammation, such as that caused by conditions of the musculoskeletal system.

Although Traumeel® is suitable to treat a broad spectrum of primary and secondary inflammation, research and experience have shown it to be particularly effective in the treatment of inflammation and trauma in the musculoskeletal system.¹⁻⁶ For example:

- **Trauma**
Contusions, distortions, sprains, dislocations, hematomas and fractures
- **Inflammation of the musculoskeletal system**
Arthritis, polyarthritis, reactivated arthrosis, bursitis, synovitis, scapulohumeral periarthritis, tendonitis and tendovaginitis.

Key point: Traumeel® is suitable to help manage a broad spectrum of disorders, such as sprains and other traumatic injuries, and as supportive therapy in pain and inflammation, such as that caused by conditions of the musculoskeletal system. The exact indication and dosage of the various Traumeel® formulations can be found on the country-specific package inserts.

References

1. Füsgen I, Heine H, Frase W. *Biological Medicine in Geriatrics*. 1st edition. Baden-Baden: Aurelia Verlag, 2003.
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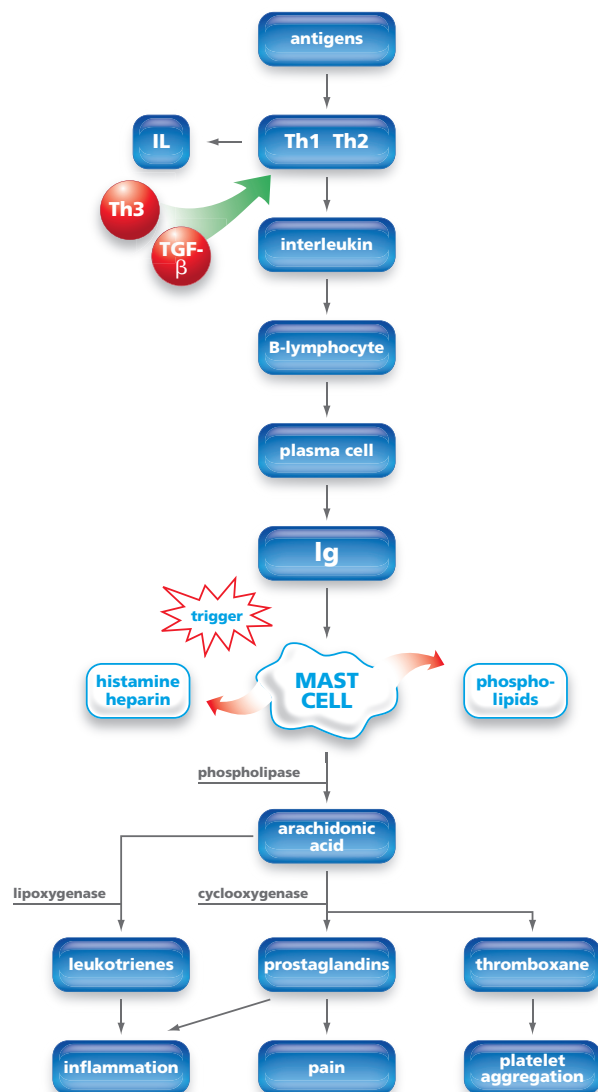
4. Conventional anti-inflammatory approach versus Traumeel®

Non-steroidal anti-inflammatory drugs (NSAIDs) are commonly used as analgesics, anti-inflammatories and anti-pyretics. They are either used alone or in combination with paracetamol and/or weak/strong opioids.

4.1 Mechanism of action of NSAIDs

NSAIDs produce a range of effects in the body by inhibiting the cyclooxygenase (COX) enzyme systems. COX is the main enzyme system which converts arachidonic acid to prostaglandins, thromboxane and prostacyclins (Figure 2). It is found in many central and peripheral tissues in the body, which explains why NSAIDs have such a wide range of effects.

Figure 2. The inflammation cascade.



The known effects of NSAIDs are:

- Analgesic – acting on peripheral tissues, the dorsal horn of the spinal cord and the brain
- Anti-inflammatory – via a prostaglandin synthesis-inhibiting effect
- Anti-pyretic – via effect on cortical temperature control.

Although NSAIDs are widely used and effective in suppressing the end phase of the inflammatory process, their mechanism of action means that they may result in well-recognized side effects that can limit their use in certain patients. These are most commonly:

- Gastric ulceration – impaired gastric lining protection
- Anti-platelet, anti-thromboxane effect. Prevents platelet aggregation which increases the risks of bleeding
- Renal impairment – altered renal blood flow control, occasionally leading to sodium and water retention
- Increased wheezing in susceptible asthmatics by increasing muscle tone in the bronchi of the lungs via the leukotrienes.

For this reason, the cautions and contraindications shown in Box 2 apply.

Box 2. Cautions and contraindications for NSAIDs.

NSAIDs should be used with caution in the elderly, in allergic disorders (they are contraindicated in patients with a history of hypersensitivity to aspirin or any other NSAID – which includes those in whom attacks of asthma, angioedema, urticaria or rhinitis have been precipitated by aspirin or any other NSAID), during pregnancy and breast feeding, and in coagulation defects. Long-term use of some NSAIDs is associated with reduced female fertility, which is reversible on stopping treatment. In patients with renal, cardiac, or hepatic impairment, caution is required since NSAIDs may impair renal function; the dose should be kept as low as possible and renal function should be monitored.

All NSAIDs are contraindicated in severe heart failure. The selective inhibitors of COX-2 are contraindicated in ischemic heart disease, cerebrovascular disease, peripheral arterial disease, and moderate or severe heart failure. The selective inhibitors of COX-2 should be used with caution in patients with a history of cardiac failure, left ventricular dysfunction, hypertension, in patients with edema for any other reason, and in patients with risk factors for developing heart disease.

The UK Committee on Safety of Medicines (CSM) has advised that non-selective NSAIDs are contraindicated in patients with previous or active peptic ulceration and that selective inhibitors of COX-2 are contraindicated in active peptic ulceration. While it is preferable to avoid NSAIDs in patients with active or previous gastrointestinal ulceration or bleeding, and to withdraw them if gastrointestinal lesions develop, nevertheless patients with serious rheumatic diseases (e.g. rheumatoid arthritis) are usually dependent on NSAIDs for effective relief of pain and stiffness.

There are two forms of the COX enzyme – COX-1 and COX-2. Older NSAIDs inhibit both enzyme types, whereas newer NSAIDs have high specificity for the COX-2 enzyme. COX-2 specific NSAIDs produce comparable analgesic and anti-inflammatory effects whilst helping to reduce gastric ulceration and anti-platelet effects. However, in August 2005 the CSM in the UK advised that patients who have ischemic heart disease or cerebrovascular disease should not receive COX-2 selective inhibitors due to emerging concerns about cardiovascular safety. The Federal Drug Agency (FDA) had already expressed concerns in 2004 which, in late 2004, resulted in the worldwide withdrawal of the COX-2 inhibitor, Vioxx®, from the market, followed in 2005 by the second product from this class, Bextra®.

Traumeel® appears to be as effective at reducing symptoms of inflammation as NSAIDs, such as diclofenac (see '5. Evidence base for Traumeel®' section). However, due to its different mechanism of action and constituents, none of the side effects commonly observed with NSAIDs or COX-2 inhibitors are observed with Traumeel® (Table 2).

Traumeel® is well tolerated and, apart from a rare hypersensitivity against certain components of the formula, few side effects have been reported (see '6. Safety and toxicology' section).

Table 2. Comparison of Traumeel® vs. NSAIDs.

	Traumeel®	NSAIDs
Anti-inflammatory	Yes	Yes
Analgesic	Yes	Yes
Evidence base	Yes	Yes
Gastrointestinal toxicity	No	Yes
Interactions with other medications	No	Yes
Deterioration of wound healing	No	Yes
Sodium/Water retention	No	Yes

Key point: The mechanism of action of NSAIDs and COX-2 inhibitors means that they are effective anti-inflammatory and analgesic agents but are associated with side effects that can limit their use in certain patients. Traumeel® appears as effective at reducing symptoms of inflammation as NSAIDs, such as diclofenac (see '5. Evidence base for Traumeel®' section), but differs in its mechanism of action from NSAIDs and COX-2 inhibitors, and, consequently, is very well tolerated with minimal side effects.

4.2 Mechanism of action of Traumeel®

4.2.1 Effective treatment for acute musculoskeletal injury and inflammation

Traumeel® is a first-line treatment for patients with acute musculoskeletal injury and inflammation (e.g. ankle, knee, neck and back sprains) that delivers the efficacy of NSAIDs but with fewer side effects, irrespective of age.

As with many other commonly used therapeutic agents, the exact mechanism of action of Traumeel® is not fully understood. However, various cellular and biochemical pathways appear to be affected by the products' ingredients.

Placebo-controlled studies, drug monitoring studies and *in vitro* experimental models, including the carrageenan-induced edema test and the adjuvant arthritis test, have all demonstrated the effectiveness of Traumeel® at reducing symptoms of inflammation.¹⁻⁷

Evidence for the action of Traumeel® on symptoms of inflammation comes from Porozov et al⁸ who conducted a study to evaluate the effect of Traumeel® on human leukocyte function. Specifically, the action of Traumeel® was studied on activated human T-cells, monocytes and gut epithelial cells in terms of its effect on the pro-inflammatory mediators IL-1 β (interleukin-1beta), TNF- α (tumor necrosis factor alpha) and IL-8 (interleukin-8) *in vitro*.

The researchers found that Traumeel® modulates the secretion of IL-1 β , TNF- α and IL-8 in resting as well as activated immune cells. The reduction in secretion was:

- IL-1 β by up to 70% in both resting and activated cells
- TNF- α by up to 65% in resting cells and 54% in activated cells
- IL-8 by 50% in both resting and activated cells ($p < 0.01$ for all cells).

It was observed that T-cell and monocyte proliferation was not affected.

The researchers concluded that Traumeel® reduces pro-inflammatory cytokines in resting and activated immunocytes *in vitro*, as well as in resting and activated colon epithelial cells, suggesting that the first-line and mobile arm of immune defense is activated by Traumeel®.

Key point: Traumeel® has an inhibitory effect on pro-inflammatory mediators, such as IL-1 β , TNF- α and IL-8, in resting as well as activated immune cells.⁸

Furthermore, *in vivo* and *in vitro* studies have shown that Traumeel® does not act in the same way as conventional anti-inflammatory drugs. Conforti et al² assessed the effects of Traumeel® on recognized and accepted models of chronic (using adjuvant arthritis as the recognized model) and acute (using carrageenan-induced edema as the recognized model) inflammation.

Administration of Traumeel® led to a significant reduction in acute local inflammation (first phase of adjuvant arthritis) compared with the control group. Since this occurred during the first 2-7 days, it suggests an action on local inflammation rather than a capacity to modulate the entire arthritic process. In the acute model, systemic administration of Traumeel® reduced edema volume by up to 15% ($p = 0.05$). The study's authors noted "This inhibition by Traumeel® is similar to the effect exerted by aspirin at a dose of 30 mg/kg in the same experimental model."

Furthermore, *in vitro* studies² showed that the ingredients of Traumeel® are non-cytotoxic to granulocytes, lymphocytes, platelets and endothelial cells, indicating that the normal defensive and homeostatic functions of these cells are preserved during treatment with Traumeel®.

Overall, this study showed that Traumeel® appears to exert its therapeutic effects by interacting with fine and complex regulation of acute local inflammation where neuropeptides and cytokines play a critical role, as opposed to interacting with a specific cell type or biochemical mechanism (see Figure 3, page 13).

Figure 3. Traumeel® activity on experimental models *in vitro* and *in vivo*².

Experimental model	Action of Traumeel®
Neutrophil adhesion and superoxide anion production	↔
Platelet adhesion	↔
Carrageenan-induced edema	↓
Adjuvant arthritis	↓ First acute phase
	↔ Second chronic phase
↓ =inhibition ↔ =no significant effect	

Key point: The ingredients of Traumeel® are non-cytotoxic to granulocytes, lymphocytes, platelets and endothelial cells indicating that the defensive functions of these cells are preserved during treatment with Traumeel®.²

Additional data alluding to the mechanism of action of Traumeel® come from basic research⁹ which has shown that the organic components of Traumeel® stimulate lymphocytes to synthesize and secrete the cytokine TGF-β (transforming growth factor beta) in whole blood cultures. TGF-β reduces pro-inflammatory substances such as TNF-α, inhibits the activity of pro-inflammatory CD4+ T-lymphocytes and stimulates the activity of fibroblasts. From this, inflammation is down-regulated and tissue repair is favored at the level of the extracellular matrix. This effect on the inflammatory processes indicates that the immunological 'bystander reaction' may play a role in the action of Traumeel®.

Key point: Components in Traumeel® elevate the levels of anti-inflammatory cytokine, TGF-β, indicating that the immunological 'bystander reaction' may play a role in the action of Traumeel®.⁹

4.2.2 The relationship between the mechanism of action of Traumeel® and its effects on injuries/trauma

Although additional studies are needed to clarify the causal relationship between the inhibition of cytokine/chemokine secretion in cell culture and the reported clinical effects of Traumeel®, the various *in vitro* and *in vivo* results presented in this section do offer a mechanism for the effectiveness of Traumeel® at reducing symptoms of inflammation which is observed in clinical practice.^{2,8,9}

Furthermore, by the secretion of TGF-β,⁹ numerous pro-inflammatory markers are inhibited, including

cytokines released by TH-1 and TH-2 CD4+ lymphocytes. However, conversely, the activity of fibroblasts is stimulated and this will result in the production of proteoglycans, glucosaminoglycans and the basic fibers of the connective tissue. In this way, the extracellular matrix is regenerated and wound healing is supported.

However, since Traumeel® is a mixture of several plant extracts and minerals, the contribution of each ingredient, as well as possible synergistic effects of the composition, needs further study.⁸

Key point: The various *in vitro* and *in vivo* studies offer a mechanism for the effectiveness of Traumeel® in reducing symptoms of inflammation observed in clinical practice.

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5. The evidence base for Traumeel®

The following pages present the extensive evidence base supporting the use of Traumeel® in various indications.

5.1 Traumeel® in acute injuries and inflammation of the musculoskeletal system

5.1.1 The efficacy of Traumeel® vs. diclofenac and placebo ointment in tendinous pain in elite athletes; a randomized controlled trial

Reference: Orizola AJ, Vargas F. The Efficacy of Traumeel® Versus Diclofenac and Placebo Ointment in Tendinous Pain in Elite Athletes. A Randomized Controlled Trial. *Med Sci Sports Med Exerc.* 2007;39(5,Suppl.): S79, abstract 858.

Study design randomized, double-blind, three-armed, parallel-group study.

Formulation Traumeel® ointment.

Indication(s) various non-traumatic tendinopathies.

Objective

To investigate the efficacy of Traumeel® vs. diclofenac vs. placebo ointment in non-traumatic tendinous pain in Chilean elite athletes.

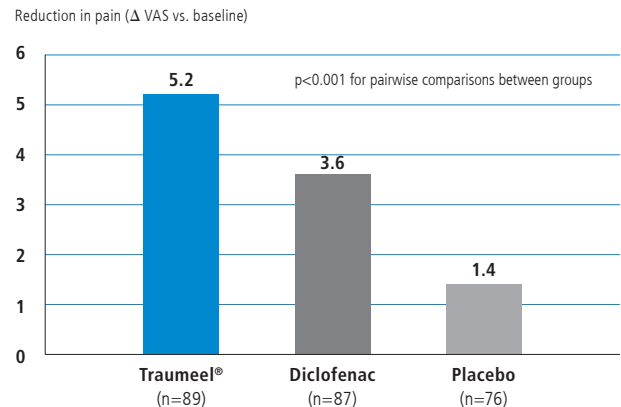
Study design

- Basic data of participants:
 - n=252 elite athletes (169 male, 83 female)
 - Traumeel® group: 89 athletes (59 m, 30 f)
 - diclofenac group: 87 athletes (60 m, 27 f)
 - placebo group: 76 athletes (50 m, 26 f)
 - Mean age of all participants: 23.5 years.
- Elite athletes with various tendinopathies randomized to receive Traumeel® ointment, diclofenac ointment or placebo ointment four times daily for at least 21 days.
- Echographic assessment was then undertaken, based on measurement of peritendinous diameter and edema.
- Assessment was made on a ten-point visual analog scale (VAS) of mean pain reduction (VAS-P), return to sports (number of days) and tolerability.

Results

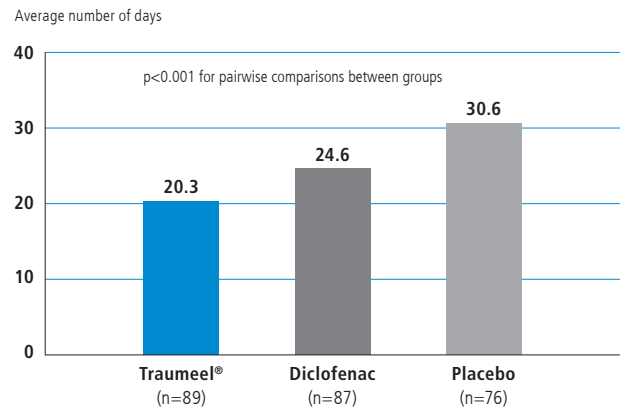
- Both medications enhanced pain reduction compared to the placebo treatment (see Figure 4). But Traumeel® (VAS-P=5.2) alleviated pain better than diclofenac (VAS-P=3.6).

Figure 4. Change of VAS-P (mean pain reduction) recorded in elite athletes.



- The use of Traumeel® allowed the athletes to resume training on average after 20.3 days whereas the athletes in the diclofenac group could return to sport only after 24.6 days on average (see Figure 5).

Figure 5. Average number of days to return to sports.



- All treatments were generally well-tolerated. Only 4 patients dropped out; all in the diclofenac group due to allergic skin reactions).

Conclusion

Traumeel® ointment is an effective and safe alternative to diclofenac ointment in the treatment of non-traumatic tendinopathies in elite athletes.

5.1.2 Treatment of acute musculoskeletal injuries with Traumeel® ointment: A controlled double blind study

Reference: Böhmer D, Ambrus P. Behandlung von Sportverletzungen mit Traumeel-Salbe – Kontrollierte Doppelblindstudie [Treatment of Sports Injuries with Traumeel Ointment: A Controlled Double-Blind Study]. *Biologische Medizin*. 1992;XXI(4):260-268. (English translation available in: *Biol Ther*. 1992;X(4):290-300)

Study design	randomized, placebo-controlled double-blind study.
Formulation	Traumeel® ointment.
Indication(s)	musculoskeletal injuries.

Objective

To compare the effectiveness of Traumeel® ointment with placebo in out-patients with sports injuries.

Study design

- Basic data of participants:
 - n=68 patients (44 male, 24 female)
 - Traumeel® group: 34 patients (21 m, 13 f)
 - placebo group: 34 patients (23 m, 11 f)
 - age: 18-50 years (mean age in Traumeel® group: 31.1, in placebo group: 29.5).
- Patients received their first medication no later than on the fourth day after the injury (no other medication was given between injury and beginning of treatment).
- Following initial treatment, the patients applied 6-10 g of either Traumeel® or placebo ointment twice daily themselves, until day 15. They added an occlusive bandage over the ointment for 1/2 hour and covered the dressing with a cold compress. During this 1/2 hour period the injured extremity had to be rested.
- The primary criteria employed for effectiveness were regression of swelling and reduction in skin temperature (evaluated by means of difference of circumference and temperature, respectively, between injured and contralateral noninjured side).
- Secondary criteria for effectiveness were:
 - the increase in maximum muscle force (measured as decreasing difference of maximum muscle force between the injured body part and the contralateral uninjured side)

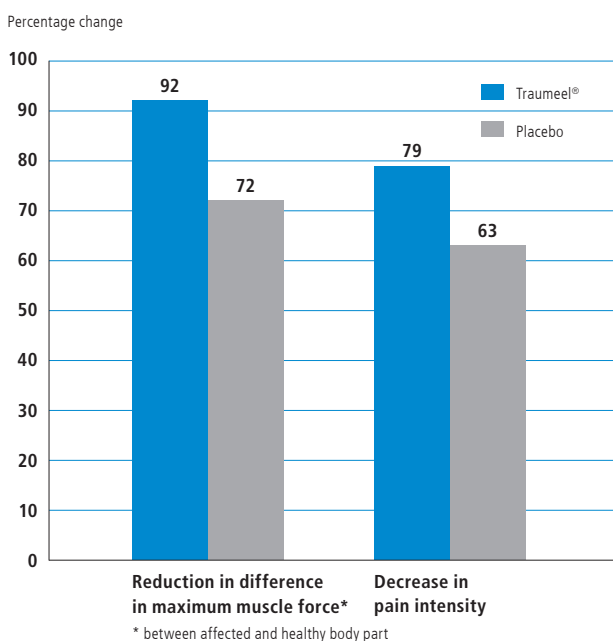
- reduction in pain intensity (pain index measured as cumulative index of pain at rest, upon movement and under pressure, 0=no pain, 1=slight pain, 2=severe pain)
- time until resumption of training
- overall evaluation of effectiveness by patient and physician (very good, good, moderate, poor).

- Data were evaluated for all patients.

Results

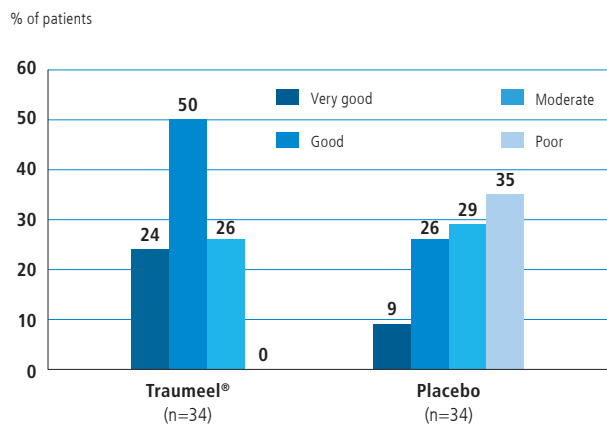
- Swelling decreased more in the Traumeel® group than in the placebo group.
- Although skin temperature dropped more considerably in the Traumeel® than in the placebo group, there were no statistical differences between the treatment groups according to the Mann-Whitney test. It was therefore considered being ineffective as an indicator for therapeutic success.
- All secondary criteria proved to be suitable indicators of therapeutic effectiveness being confirmed by a significant difference between Traumeel® and placebo ($p < 0.001$ for the pain index and the overall evaluation, day 15); the Mann-Whitney characteristic $P(X < Y)$ reveals that these differences are of considerable clinical significance.
 - After 15 days the difference of maximum muscle force had dropped over 90% in the Traumeel® group in comparison to only 72% in the placebo group (see Figure 6).

Figure 6. Changes in maximum muscle force and decrease in pain after 15 days of treatment in %.



- The pain index had decreased in the Traumeel® group by nearly 80%, in the placebo group only by 63% (see Figure 6).
- Regarding the Traumeel® group therapists assessed the overall effectiveness as 'very good' or 'good' in nearly three-quarter of patients. By contrast only 35% of therapists evaluated it accordingly in the placebo group. Assessment as 'poor' only occurred in the placebo group (see Figure 7).

Figure 7. Overall efficacy rated by therapists after 15 days of treatment (in % of patients).



- At the end of the study, patients and physicians evaluated the tolerance of both Traumeel® and placebo either as 'good' or 'very good'.
- No undesired side effects were observed in the treatment groups.

Conclusion

Traumeel® is significantly more effective than placebo in the treatment of sports injuries.

5.1.3 The treatment of recent traumatic blood effusions of the knee joint

Reference: Thiel W, Borho B. Posttraumatische Kniegelenksergüsse und intraartikuläre Traumeel-N-Injektion [The Treatment of Recent Traumatic Blood Effusions of the Knee Joint]. *Orthopädische Praxis*. 1991;11:721-725. (English translation available in: *Biol Ther*. 1994;XII(4): 242-248.)

Study design randomized, placebo-controlled double-blind trial.

Formulation Traumeel® N injection.

Indication(s) hemarthrosis of the knee.

Objective

To determine whether application of Traumeel® N (+ Aristolochia D11) solution and, where necessary, subsequent puncture of the joint, has a favorable influence on the course of post-traumatic, acute irritation of the knee joint with hemarthrosis, in comparison with a placebo (physiological saline solution).

Study design

- Basic data of participants:
 - n=73 out-patients (>60% male):
 - Traumeel® group: 37 out-patients
 - placebo group: 36 out-patients
 - mean age: 36 years.
- Observation period for each patient: 36 days (study period: 2 years).
- Patients with traumatic hemarthrosis of the knee joint were treated by puncture of the knee (only if necessary because of severe swelling) and by intra-articular administration of either 2 ml of Traumeel® N or physiological saline solution (= placebo) on the 1st, 4th and 8th treatment day. Afterwards a support dressing was applied. Patients were allowed to apply cold compresses at home but had to abstain from exercises.
- All patients were initially incapable of work; none of the injuries required surgical intervention.
- Main target criteria:
 - a decrease in the differences in joint mobility between the healthy joint and the injured joint
 - a decrease in joint circumference between the healthy joint and the injured joint by the eighth day of treatment.

- The extent to which full mobility was restored to the knee joint was determined as the difference in the total of angles of flexion and extension between the injured joint and the unaffected joint.
- Treatment was evaluated as successful if the total angle difference returned to 10 degrees at the same time as the difference in the circumference returned to 0.5 cm.
- Secondary criteria included:
 - hemostasis (decrease in red coloration of the punctate) by the 8th day
 - level of repeated joint effusion observed
 - total pain score for pain at rest, upon movement and under pressure by the 8th day.

Results

- After a single injection, only 13.5% of the patients in the Traumeel® N group required further punctures, compared with 25% in the placebo group.
- On the 8th day after the start of treatment, the punctate was still bloody in 5.4% of the Traumeel® N group vs. 19.4% of the placebo group.
- Degree of movement was improved on day 8: 82.8% with Traumeel® N group vs. 56% with placebo.
- Reduction in the circumference of the joint (decrease in mean values from 2.02 to 0.54, Traumeel® N; 2.18 to 1.06, placebo) and the total pain scores.
- There were no drug-related adverse effects.

Figure 8. Success of treatment by the 8th day (maximum difference in circumference of joint 0.5 cm and maximum difference in mobility 10 degrees between injured and healthy joints).

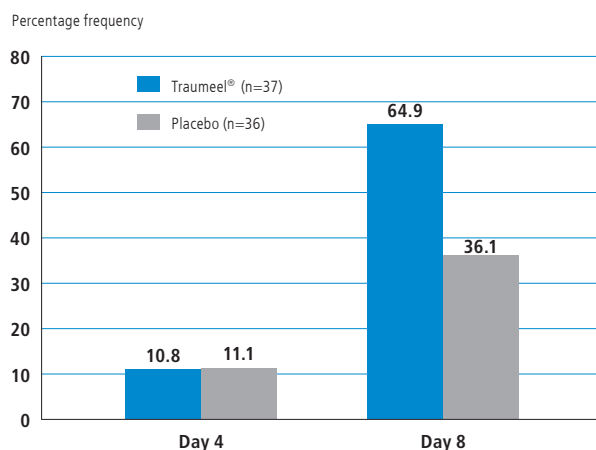
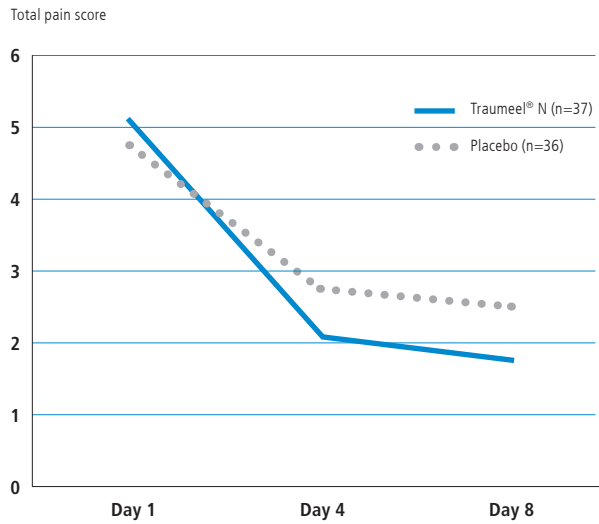


Figure 9. Mean values for total pain score on day 1, 4, and 8.



Conclusion

This study shows that intra-articular injection therapy with Traumeel® N produces fast regression of blood effusions of the knee.

Note: The therapeutic process for treating recent traumatic blood effusions of the knee joint not involving any ligament or cartilage bone structures involves effusion (the escape of fluid) punctures in the area under sterile conditions to drain the hemarthrosis. During the puncture process, the joint may also be flushed using a neutral liquid, such as physiological saline solution, and this is usually followed by an intra-articular injection of an anti-inflammatory agent.

5.1.4 Treatment of acute sprains of the ankle

Reference: Zell J, Connert WD, Mau J, Feuerstake G. Behandlung von akuten Sprunggelenksdistorsionen: Doppelblindstudie zum Wirksamkeitsnachweis eines homöopathischen Salbenpräparats [Treatment of Acute Sprains of the Ankle: A Controlled Double-Blind Trial Test the Effectiveness of a Homeopathic Preparation]. *Fortschr Med.* 1988; 106(5): 96-100. (English translation available in: *Biol Ther.* 1989;VII(1):1-6)

Study design	randomized, placebo-controlled double-blind study.
Formulation	Traumeel® ointment.
Indication(s)	sports-related ankle sprains.

Objective

To determine how Traumeel® ointment influences the progress of disorders among patients with distortion of the articular-capsule ligaments (sprain) and of the tendons of the ankle.

Study design

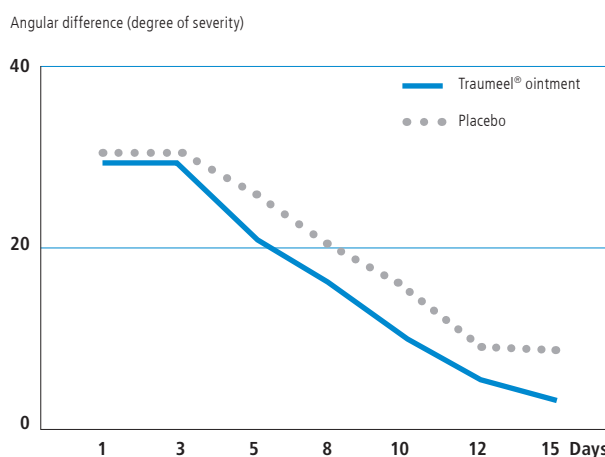
- Basic data of participants:
 - n=69 patients (50 m, 19 f)
 - Traumeel® group: 33 patients (25 m, 8 f)
 - placebo group: 36 patients (25 m, 11 f)
 - mean age: 23 (Traumeel®) and 22 years (placebo).
- Treatment was administered on an out-patient basis for 2 weeks – patients visited clinic on days 1, 3, 5, 8, 10, 12 and 15.
- Both therapist and patients were blinded to medication.
- All patients received electrotherapy as basic treatment.
- Approximately 10-12 g of either Traumeel® or placebo ointment was administered in the form of applying a compression ointment bandage in accordance with the lesion concerned, together with a basic therapy consisting of interference-current treatment. [The placebo was the ointment base of Traumeel®, i.e. ointment without active constituents].
- As a quantifiable objective measure for the degree of improvement in ankle mobility, the difference in total angulation of the joint – measured in extension and flexion between affected and non-affected joints – was taken as ‘target criterion’ (due to the pilot study conducted in advance).
- Secondary comparison criteria included:

- the inversion angle (supination); and
- the degree of pain suffered upon movement.
- Pain at rest, pain upon movement and pain under pressure were reported on a three-point scale with the score values of:
 - 0=no pain
 - 1=mild pain
 - 2=severe pain.

Results

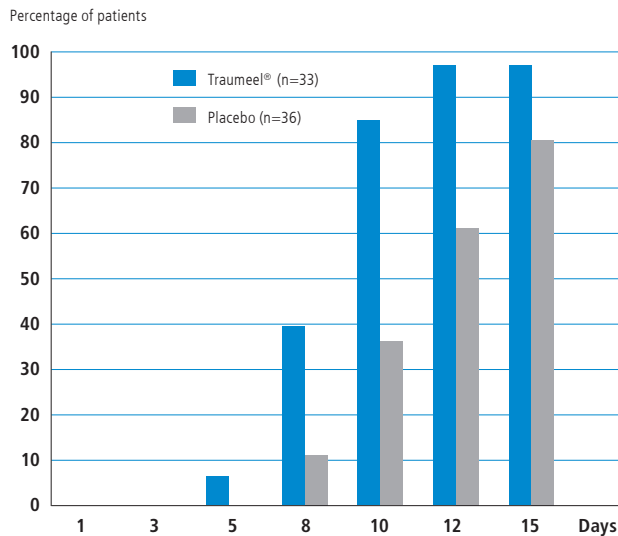
- In both groups, the basic treatment produced an improvement in joint mobility. In the test group, improvement (as established on the reference day stipulated prior to the start of the trial, i.e. the tenth day after injury) was considerably more frequent in the Traumeel® group (p=0.03) compared with the placebo group (see Figure 10).

Figure 10. Median changes in the difference of angular sums (flexion + extension) between injured and non-injured ankles through increase in mobility of the upper ankle for therapy with Traumeel® ointment and for treatment with a placebo.



- Regarding pain upon movement there was significant difference between the two groups on the tenth day (p≤0.0001; adjusted after Bonferroni method*: p≤0.0003): after 10 days 28 (85% of the) patients in the Traumeel® group did not feel pain anymore upon movement in comparison to only 13 (about one third of the) patients in the placebo group (see Figure 11).

Figure 11. Patients with no pain upon movement within two weeks after beginning of therapy with Traumeel® ointment (in %).



- For the inversion angle (supination), a difference between the groups on the tenth day was observed, too. However, this was not significant ($p=0.13$).

Conclusions

- Traumeel® is effective in the treatment of sports-related sprains of the ankle.
- Traumeel® improved ankle mobility and pain.

Confirmation of the methodological quality of the study

The methodological quality of the Zell study¹ was verified in a meta-analysis in the *British Medical Journal*.² Of 107 homeopathic studies reviewed, the Zell study¹ ranked within the top 5% for methodological quality. More recently, in a meta-analysis with homeopathic products from three different controlled studies demonstrated the effectiveness of Traumeel® over placebo.³ Furthermore, Traumeel® was included in a recent Cochrane analysis after the quality of studies with this product were considered sufficiently high to be included in the entry criteria.⁴

- * Bonferroni method – a statistical method that adjusts the significance level when multiple comparisons are made.

References

1. Zell J, Connert WD, Mau J, Feuerstake G. Behandlung von akuten Sprunggelenksdistorsionen: Doppelblindstudie zum Wirksamkeitsnachweis eines homöopathischen Salbenpräparats. [Treatment of Acute Sprains of the Ankle: A Controlled Double-Blind Trial to Test the Effectiveness of a Homeopathic Preparation.] *Fortschr Med.* 1988;106(5):96-100 (English translation available in: *Biol Ther.* 1989;VII(1):1-6)
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3. Reilly D, Taylor MA, Beattie NGM, et al. Is evidence for homoeopathy reproducible? *Lancet.* 1994;334(10):1601-1606.
4. Worthington HV et al. *The Cochrane Database of Systematic Reviews.* 2006, Issue 2. Art. No.: CD000978. DOI: 10.1002/14651858.CD000978.

5.1.5 The role of Traumeel® compared with conventional therapy in the treatment of injuries

Reference: Schneider C, Schneider B, Hanisch J, van Haselen R. The role of a homeopathic preparation compared to conventional therapy in the treatment of injuries: an observational cohort study. *Complement Ther Med.* 2008,16(1): 22-27. DOI:10.1016/j.ctim.2007.04.004 (Epub 12 Jul 2007)

Study design Multi-centre, prospective, parallel-group, observational (maximum 3 months), pharmaco-epidemiological cohort study.

Formulation Traumeel® in various forms, e.g. tablets, ointment and injections.

Indication(s) trauma and minor acute injuries, e.g. sprains, strains, contusions, etc. of the ankles, knees and hands.

Objective

To assess the daily use, effectiveness and safety of Traumeel® compared with conventional therapies (e.g. analgesics/antirheumatics, anticoagulants, anti-inflammatory drugs) in the treatment of trauma and injuries.

Study design

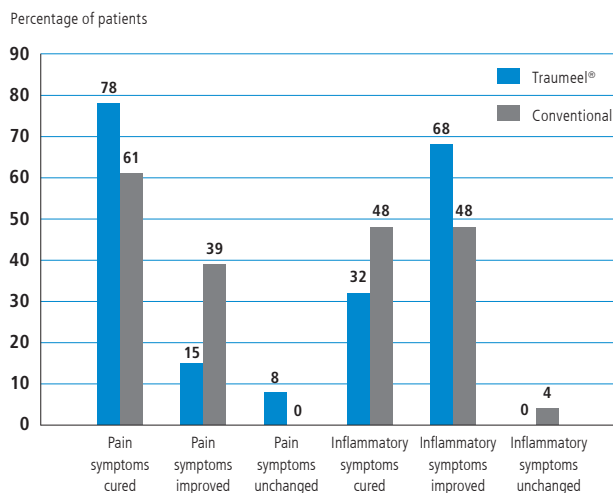
- Patients with various musculoskeletal injuries being treated by German physicians using homeopathy.
- Basic data of participants:
 - n=133 patients
 - Traumeel® group: 69 patients (39 m, 30 f)
 - conventional treatment group: 64 (31 m, 33 f)
 - mean age: 33 (Traumeel® group) and 32 years (conventional treatment group).
- In the Traumeel® group Traumeel® was used as only one application form (e.g. tablets or ointment) in 67% of the patients treated with Traumeel®, in 33% with more than one application form. The conventional treatment (e.g. analgesics, antirheumatics) was applied as monotherapy in 69% of patients and as combination of various medications in 31%, respectively.
- Additional measures (e.g. functional treatment, compression) and the use of co-medication were permitted and recorded.

- Outcome measures
 - Primary: rate of resolution of the principal and second symptoms at the end of therapy
 - Secondary: time until symptomatic improvement and treatment outcome as assessed by the physician.
- The physician recorded the principal and second symptom, and graded both for severity/intensity on scale of mild, moderate or severe.
- Both treatment groups were well-matched at baseline.

Results

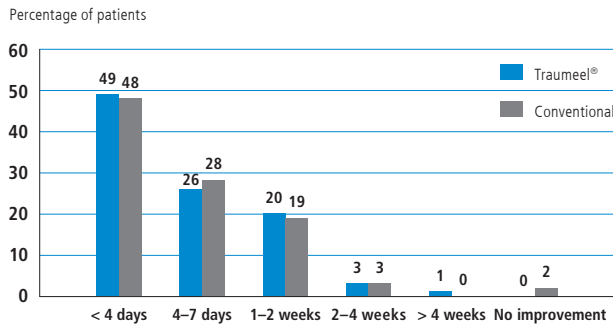
- The principal symptom (most commonly pain, then inflammation) had resolved completely at the end of therapy in 41 patients (59.4%) in the Traumeel® group vs. 37 patients (57.8%) in the conventional group (p=NS). Figure 12 shows detailed information on the respective outcomes for pain and inflammation.

Figure 12. Changes in the principal symptoms of pain and inflammation at the end of the treatment period.



- The rates of improvement were comparable in both treatment groups with nearly 50% of the patients improving within four days of treatment (34 patients = 49% in Traumeel® group vs. 31 patients = 48% in conventional group; see Figure 13). However, Cox's Proportional Hazard test indicated faster healing and improvement times with Traumeel®: both the unadjusted and adjusted Hazard ratio showed similar values smaller than 1: 0.95 (95% confidence interval 0.67-1.37) and 0.94 (95% confidence interval 0.65-1.37), respectively.

Figure 13. Time until improvement of all principal symptoms.



- No adverse events were reported in the Traumeel® group compared to 6 mild-to-moderate adverse events (9.3%) in the conventional group.
- Physician-assessed tolerability was significantly greater in the Traumeel® group vs. the conventional therapy group (90% judged tolerability to be “very good” with Traumeel® vs. 50% in conventional group; p (Wilcoxon-Mann-Whitney test)=0.001).

Conclusions

- Traumeel® is as effective as conventional medicines in the management of mild to moderate injuries/trauma.
- Traumeel® was safe and judged by physicians to be better tolerated than conventional medicines.
- This study contributes to the evidence for the broad clinical effectiveness of Traumeel® in the treatment of acute injuries and trauma.

5.1.6 Traumeel® compared with 1% diclofenac gel for acute symptomatic treatment of tendinopathy

Reference: Schneider C, Klein P, Stolt P, Oberbaum M. A homeopathic ointment preparation compared with 1% diclofenac gel for acute symptomatic treatment of tendinopathy. *Explore*. 2005;1(6):446-452.

Study design	non-randomized, observational study.
Formulation	Traumeel® ointment.
Indication(s)	tendinopathies of varying etiologies.

Objective

To assess the non-inferiority of Traumeel® ointment with diclofenac 1% gel in patients with tendinopathies of varying etiology.

Study design

- Study carried out in 95 medical practices in Germany, from September 2003 to March 2004.
- Basic data of participants:
 - n=457/357 patients (safety/efficacy population)
 - Traumeel® group: 160/122 patients
 - diclofenac group: 297/235 patients
 - range of age (efficacy population): 18-93 (Traumeel® group) and 19-91 years (diclofenac), average in both 48 years.
- Ailments: tendinopathy of varying etiology based on excessive tendon load rather than inflammation.
- Treatment was executed for a maximum of 28 days.
- Application frequency of ointment and other therapy information:

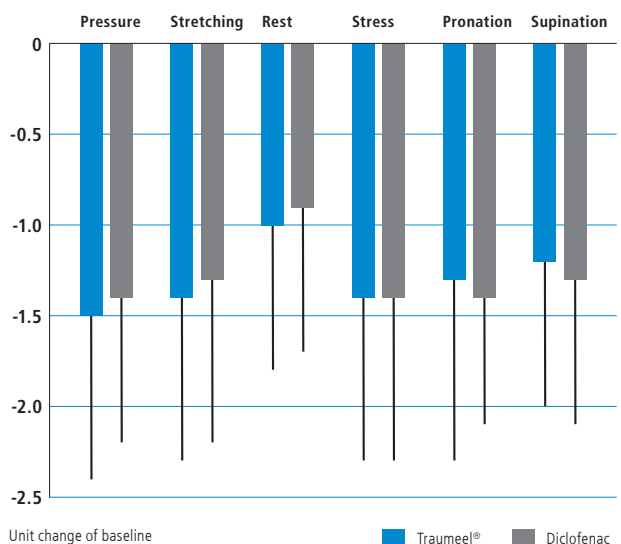
	Traumeel® in %	Diclofenac 1% in %
2x daily	15.6	18.3
3x daily	57.4	60.9
4x daily	26.2	18.3
Other dosage	0.8	2.6
Additional bandages	46.7	28.5
Adjuvant therapies	69.7	73.2

- In both groups the number of daily applications was reduced in some patients (Traumeel®: 19.7%; diclofenac: 10.6%) during treatment.
- Main outcome measures:
 - efficacy – measured on a four-degree scale on pain-related variables (0=no pain, 1=mild, 2=moderate, 3=severe) related to mobility and overall treatment outcome
 - tolerability – monitored as adverse events
 - compliance – assessed by practitioner and patient on a four-degree scale.

Results

- 38 patients of the Traumeel® group and 62 patients of the diclofenac group had to be excluded for the efficacy analysis due to protocol violation. The remaining groups were comparable at baseline.
- The changes in summary score of all pain-related variables were -5.3 ± 2.7 in the Traumeel® group and -5.0 ± 2.7 in the diclofenac group (all values: means \pm SD). Figure 14 shows the change of scores for each variable separately.

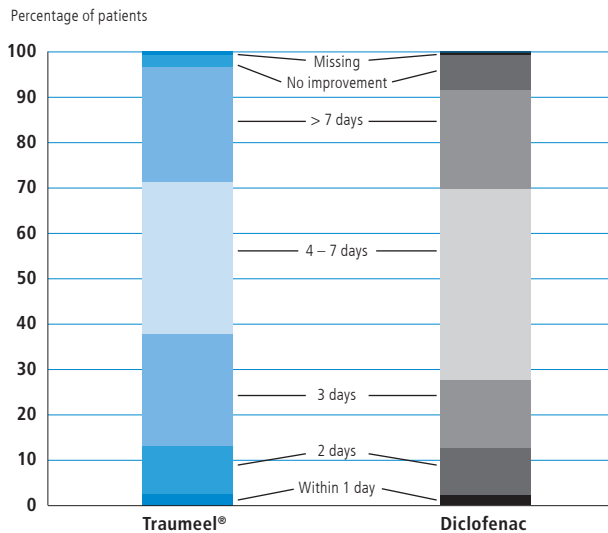
Figure 14. Change of pain-related variables at the end of the treatment phase in comparison to the initial value.



- Changes for all mobility-related variables were -4.2 ± 3.8 with Traumeel® and -3.7 ± 3.4 with control therapy. There was a trend towards superiority of Traumeel®.
- The summary scores for all clinical variables were reduced by -9.5 ± 5.7 with Traumeel® therapy and by -8.7 ± 5.4 with diclofenac-based treatment.

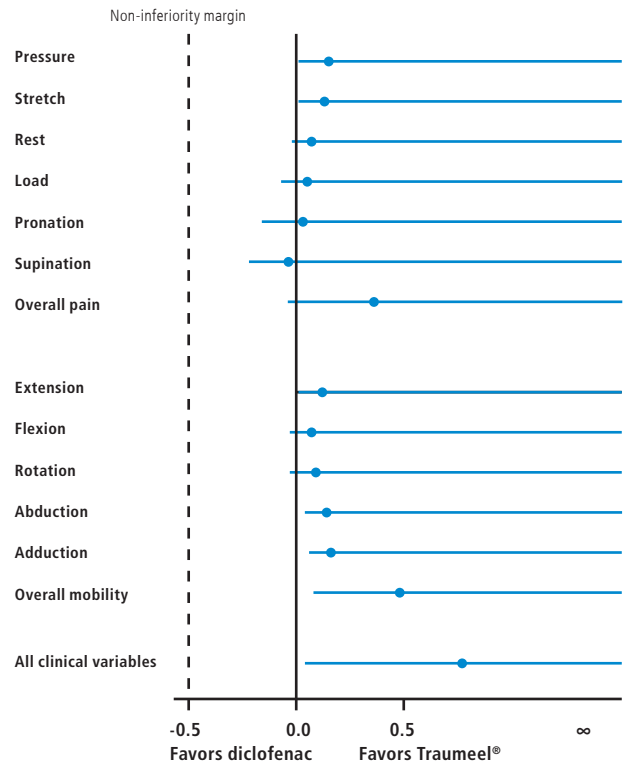
- In most cases symptoms started to improve after 3 to 7 days (patients' own recordings). Only 2.5% of the patients in the Traumeel group (7.7% in the diclofenac group) reported a lack of symptomatic improvement within the treatment period of 28 days (see Figure 15).

Figure 15. Time to first symptomatic improvement with Traumeel® treatment (left-hand column) and diclofenac treatment (right-hand column), respectively.



- Traumeel® was non-inferior to diclofenac therapy for all variables (see Figure 16).
- The positive verdicts 'good' (=symptoms have improved noticeably) and 'very good' (= symptom-free) were given in about 88% of Traumeel® cases and 82% of diclofenac cases (p=0.09).
- Treatments were well tolerated ('very good' was reported in 92.5% and 87.9% of Traumeel® and control patients, respectively), with no treatment-related adverse events.

Figure 16. Point estimate and one-sided 95% confidence interval for the difference between scores for Traumeel® and control for all variables.



(Positive values indicate a favorable effect of Traumeel®; negative values favor the diclofenac group. The border of non-inferiority is shown as a dotted line. The zero line indicates no differences between therapeutic effects.)

Conclusions

- Traumeel® ointment is an effective and well tolerated alternative to diclofenac 1% gel for the acute symptomatic treatment of patients with tendinopathy of varying etiology.
- With respect to mobility, Traumeel® appears to be superior to diclofenac 1% gel.

5.1.7 Traumeel® compared with NSAIDs for symptomatic treatment of epicondylitis

Reference: Birnesser H, Oberbaum M, Klein P, Weiser M. The Homeopathic Preparation Traumeel S Compared with NSAIDs for Symptomatic Treatment of Epicondylitis. *J Musculoskeletal Research*. 2004;8(2-3):119-128.

Study design	non-randomized, observational study.
Formulation	Traumeel® injection.
Indication(s)	epicondylitis.

Objective

To compare the effects of Traumeel® with standard NSAID therapy on symptomatic relief in patients with diagnosed epicondylitis.

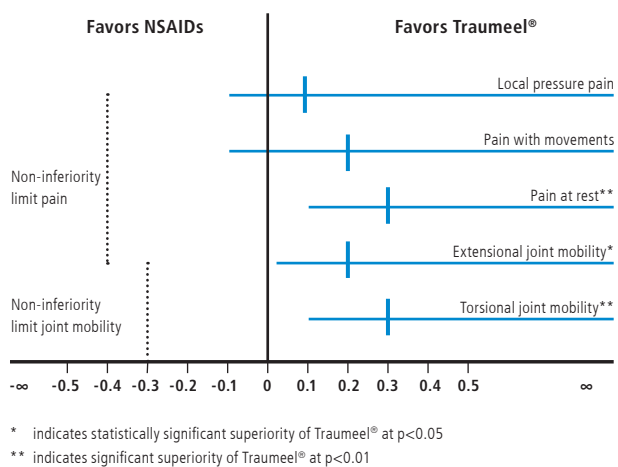
Study design

- Study conducted in 38 primary care centers in Germany.
- Basic data of participants:
 - n=184 patients with diagnosed epicondylitis (efficacy population: n=163)
 - Traumeel® group: 106 patients (efficacy population: n=86)
 - NSAIDs group: 78 patients (efficacy population: n=77)
 - mean age: 49 (Traumeel®) and 46 years (NSAIDs).
- Duration of study=2 weeks.
- At the start of the study, patients were given initial injections of either Traumeel® or NSAID (52% received diclofenac of unspecified dose).
- In some patients receiving Traumeel®, further injections were necessary. Other treatments were allowed in both groups, e.g. oral analgesics (in the NSAID group only) or physiotherapy.
- Treatments were evaluated on clinically relevant variables:
 - three pain variables (local pain pressure, pain with movements, pain at rest) evaluated on a five-point scale; and
 - two mobility variables (extensional joint mobility, torsional joint mobility) evaluated on a four-point scale.

Results

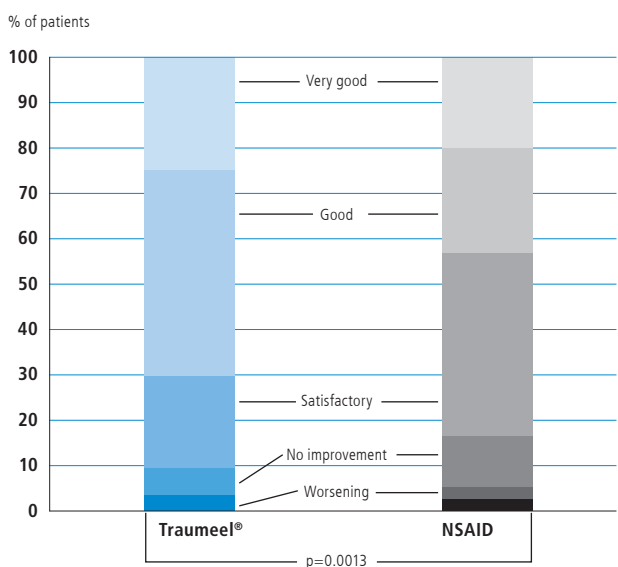
- Both treatments significantly improved scores on all five variables with no significant differences in time to onset of action.
- Traumeel® was equivalent to NSAIDs on all variables and was significantly superior to NSAID therapy on the variables 'pain at rest', 'torsional joint mobility' (both $p < 0.01$), and 'extensional joint mobility' ($p < 0.05$) (see Figure 17).

Figure 17. Mean difference between symptom scores after two weeks for patients treated with NSAIDs (n=77) and Traumeel® (n=86).



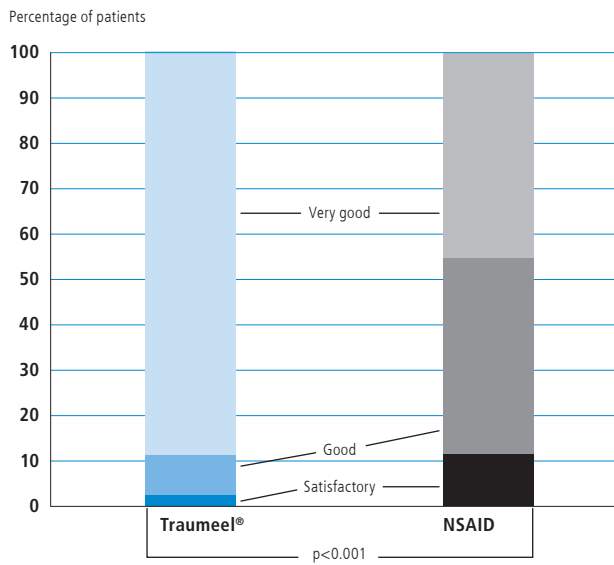
- The global assessment of therapies also favored Traumeel® over NSAIDs (see Figure 18).

Figure 18. Global evaluation of the outcomes of therapy in the Traumeel® and NSAID treatment groups, respectively.



- Treatment was assessed as 'good' or 'very good' by 71.0% of patients in the Traumeel® group compared with 44.2% of patients receiving NSAIDs (p=0.013).
- Both treatments were well tolerated, but there were significant differences in favor of Traumeel®. 87.7% receiving Traumeel® reported 'very good' tolerability compared with 44.9% in the NSAID group (see Figure 19). Only three adverse events were reported during the study, all in the NSAID group.

Figure 19. Global evaluation of tolerability in the Traumeel® and NSAID treatment groups, respectively.



Conclusions

- Traumeel® is a well tolerated alternative to NSAIDs for providing symptomatic relief in the early treatment of epicondylitis.
- Traumeel® was equivalent or superior to NSAID therapy in reducing pain and improving mobility.

5.1.8 Therapy experience with Traumeel®: Results of drug surveillance conducted in 3,422 patients

Reference: Zenner S, Metelmann H. Therapieerfahrungen mit Traumeel S Salbe: Ergebnisse einer multizentrischen Anwendungsbeobachtung an 3,422 Patienten [Therapy Experience with a Homeopathic Ointment: Results of Drug Surveillance Conducted on 3,422 Patients]. *Biologische Medizin*. 1992;XXI(5):341-9. (English translation available in: *Biol Ther*. 1994; XII(3):204-211)

Study design	multi-centric, post-marketing drug surveillance.
Formulation	Traumeel® ointment.
Indication(s)	various, e.g. sprains, hematomas, myogelosis, contusion, tendosynovitis and arthrosis.

Objective

To investigate the effectiveness, patient tolerability and most-frequently employed routes of administration of Traumeel®.

Study design

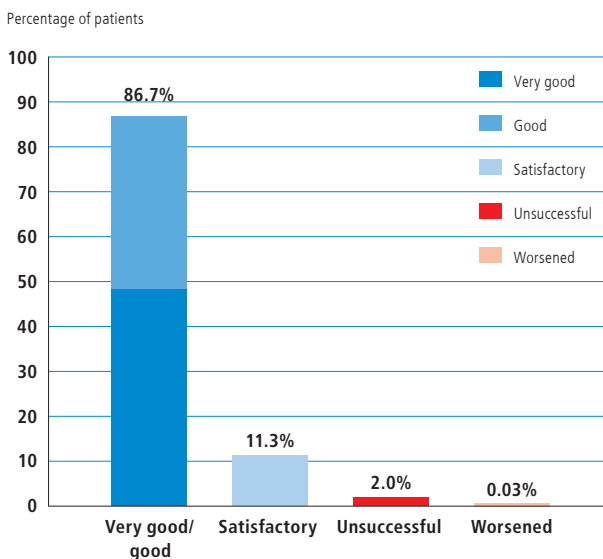
- Basic data of participants:
 - n=3,422 documented cases of therapy
 - mean age: 39.9 years.
- 378 physicians took part in the survey.
- The most frequent application of Traumeel® was for sprains. Further principal areas of application were: hematomas, myogelosis, contusion, tendosynovitis and arthrosis.
- 37.7% of the cases were treated exclusively with Traumeel® ointment. The remaining patients received additional medical (in half of these cases other Traumeel® formulations) and/or non-medical therapies: 9.8% were medical, 31.3% were non-medical adjuvant therapies and 20.3 % a combination of both.
- The frequency of application was twice daily for 47.5% of patients; three times a day for 34.3% of patients; once daily for 14.9% and 1.9% received only one application every other day.

- In 48% of the patients Traumeel® ointment was applied without dressings whereas, in 45% of patients, ointment dressings were used. In 4.3% of patients, ointment was applied in conjunction with iontophoresis.
- 22.4% were treated with Traumeel® ointment for less than one week; 63.6% one week to one month; 9.8% 1-3 months; 1.6% 3-6 months; and 1.4% longer than 6 months.
- For purposes of assessment of the results, five grading categories were used:
 - 1='very good'
 - 2='good'
 - 3='satisfactory'
 - 4='unsuccessful'
 - 5='worsening'.

Results

- The overall therapeutic results were graded mostly as 'very good' (48.3%) or 'good' (38.4%) (see Figure 20). Only one case was reported as 'worsening'.

Figure 20. Results of therapy for patients with the biological preparation Traumeel® ointment (n=3,422).



- Exclusive Traumeel® therapy was superior to Traumeel® therapy combined with adjuvant therapies. 92.2% of patients judged the former as 'good' or 'very good' whereas the same result was achieved in only 76.9% of the patients treated additionally with a combination of medical and non-medical therapies; 86.8% of the patients with non-medical and 86.6% with medical adjuvant therapies.

- As only in 13 cases undesired side effects were reported, patient tolerability to the medication can be judged as very good. The side effects involved local skin irritation and allergic reactions to the medication, as evidenced by redness of the skin and/or itching.
 - Most serious allergic reactions were observed among only 3 patients, for whom the therapy had to be terminated.
 - In one of these cases, the patient reacted in the form of a generalized allergy with hydroblepharon and moderately severe erythema.

Conclusion

This surveillance verifies the high tolerability of Traumeel® ointment and demonstrates the predominantly 'good' to 'very good' therapeutic results achieved. Traumeel® satisfies all pre-requisites for low-risk therapy of trauma and its sequelae of soft tissue swelling, as well as inflammatory degenerative processes.

5.1.9 Application possibilities of Traumeel® injection solution: Results of a multi-centric drug monitoring trial conducted in 3,241 patients

Reference: Zenner S, Metelmann H. Einsatzmöglichkeiten von Traumeel S Injektionslösung: Ergebnisse einer multizentrischen Anwendungsbeobachtung an 3241 Patienten [Application Possibilities of Traumeel S Injection Solution: Results of a Multicentric Drug Monitoring Trial Conducted on 3,241 Patients]. *Biologische Medizin*. 1992;XXI(3):207-219. (English translation available in: *Biol Ther*. 1992;X(4):301-310)

Study design	multi-centric, drug monitoring trial.
Formulation	Traumeel® injection.
Indication(s)	various, e.g. arthrosis, myogelosis, sprains, periarthropathia humeroscapularis, epicondylitis and tendovaginitis.

Objective

- To document the effectiveness and tolerance of Traumeel® injection solution under conditions of daily medical practice.

Study design

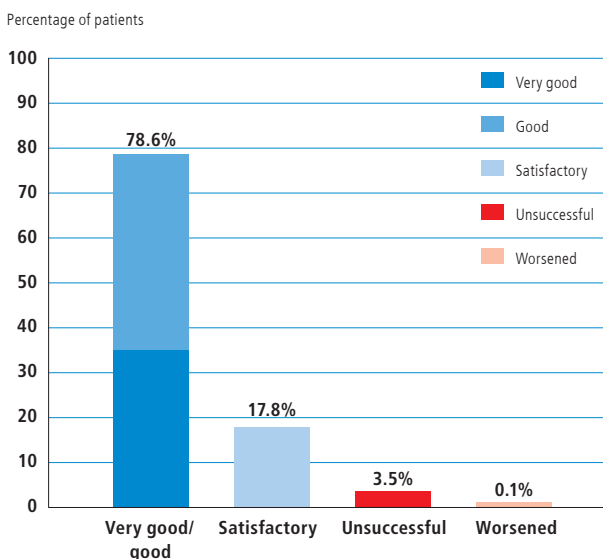
- Basic data of participants:
 - n=3,241 documented cases of therapy
 - mean age: 47.5 years.
- A total of 348 physicians took part in this post-marketing drug surveillance – doctors recorded all relevant data on a standardized data collection form for each treated and documented case.
- Arthrosis – especially cases of gonarthrosis and coxarthrosis – was the main area of application. Within this indication, the study included analyses of the mode and frequency of application of the preparation. In addition, patients suffering from myogelosis, sprains, periarthropathia humeroscapularis, epicondylitis and tendovaginitis were also frequently among those treated with Traumeel® injection solution.
- Traumeel® injection solution was administered three times a week in 27.7% of patients; twice weekly in 40.1%; weekly in 13.6%; daily in 15.2%.
- 19.7% of the cases were treated exclusively with Traumeel® injection solution. The remaining patients received additional medical (in half of these cases other Traumeel® formulations) and/or non-medical therapies: 14.9% were medical, 33.3% were non-medical adjuvant therapies and 32.1% a combination of both.

- Of the various methods of administration, intramuscular injection was the most frequent (24%) followed by subcutaneous (17.8%), periarticular (14.6%), and intra-articular (10.6%).
- Term of therapy was between one week and one month for the majority of patients (62.7%); for 15.9%, the therapy lasted less than one week; in 15.2%, between 1-3 months; in 3.2%, up to 6 months and, in 2.1%, more than 6 months.
- Of all the patients, 47% received adjuvant medical therapy (analgesics, antirheumatics as well as other forms of Traumeel®, e.g. drops, tablets or ointment) and 65% obtained non-medical therapy which included massage, applications of heat and cold, and electrotherapy.
- For purposes of assessment of results, five grading categories were available:
 - 1='very good'
 - 2='good'
 - 3='satisfactory'
 - 4='unsuccessful'
 - 5='worsening'.

Results

- In 78.6% of all treated cases, the results were formally assessed as 'good' or 'very good'; 17.8% of patients demonstrated 'satisfactory' results; 3.5% were deemed 'unsuccessful'; 5 patients (0.1%) reported worsening of complaints during the period in which the preparation was administered (see Figure 21). However, tolerance to the medication was good.

Figure 21. Results of therapy among patients treated with Traumeel® injection solution (n=3,421).



- Exclusive Traumeel® therapy was superior (85.2%) in receiving 'good' or 'very good' assessments, compared with those receiving additional treatments (combination of additional medical and non-medical therapies: 71.1%; non-medical adjuvant therapies: 79.6%; medical adjuvant therapies: 82.8%).
- The fraction of 'good' or 'very good' results was greater with shorter administration intervals between injections than for applications with longer time periods between injections; e.g. daily application resulted as 'good' and 'very good' comments in 90.1%, weekly application only in 68.2%.

Conclusion

Traumeel® injection solution is effective for therapy of post-traumatic conditions (sprains), as well as inflammatory and degenerative processes affecting the musculoskeletal system.

5.1.10 Oral treatment of traumatic, inflammatory and degenerative conditions with Traumeel®

Reference: Weiser M, Zenner S. Orale Therapie traumatischer, entzündlicher und degenerativer Affektionen mit einem Homöopathikum [Oral Treatment of Traumatic Inflammatory and Degenerative Conditions with a Homeopathic Remedy]. *Biologische Medizin*. 1996;25(5):211-216. (English translation available in: *Biol Ther*. 1997;XV(1):22-26)

Study design multi-center, prospective study.

Formulation Traumeel® tablets and drops.

Indication(s) injuries, e.g. bruises, sprains and hematomas, inflammatory and degenerative conditions, e.g. arthrosis, frozen shoulder and carpal tunnel syndrome.

Objective

To document the usage indications, therapeutic efficacy and tolerability of Traumeel® tablets and drops in a large group of patients.

Study design

- Basic data of participants:
 - n=1,359 patients
 - mean age: 47.5 years, aged 21-80 years.
- A total of 138 practicing physicians took part.
- 69% of subjects were treated with Traumeel® tablets, 29% with Traumeel® drops, and 2% were treated with both forms of the medication.
- The medication was used primarily for injuries such as bruises, sprains and hematomas, as well as degenerative and inflammatory conditions, such as arthrosis, frozen shoulder and carpal tunnel syndrome.
- Additional drug or non-drug therapies were prescribed for approximately two thirds of patients.

- In 94% of patients treated with the drops, the dosages prescribed fell between a minimum dosage of 5 drops, 5 times daily and a maximum of 30 drops, 6 times daily (standard dosage: 10 drops 3 times daily). For tablets, the recommended standard dosage (1 tablet 3 times a day) was followed in 74% of cases treated with tablets; other frequently prescribed dosages were 1-2 tablets 6 times daily, 2 tablets 3 times daily and 1 tablet 2 times daily. The initially prescribed dosages were maintained in approximately 95%; they were lowered only in 5% of the patients.

- 23% of the patients received Traumeel® over a period of 1-7 days; 27% for 1-2 weeks; 22% for 2-3 weeks; 14% for 4-5 weeks; 6% for 6-8 weeks and 8% for more than 8 weeks.

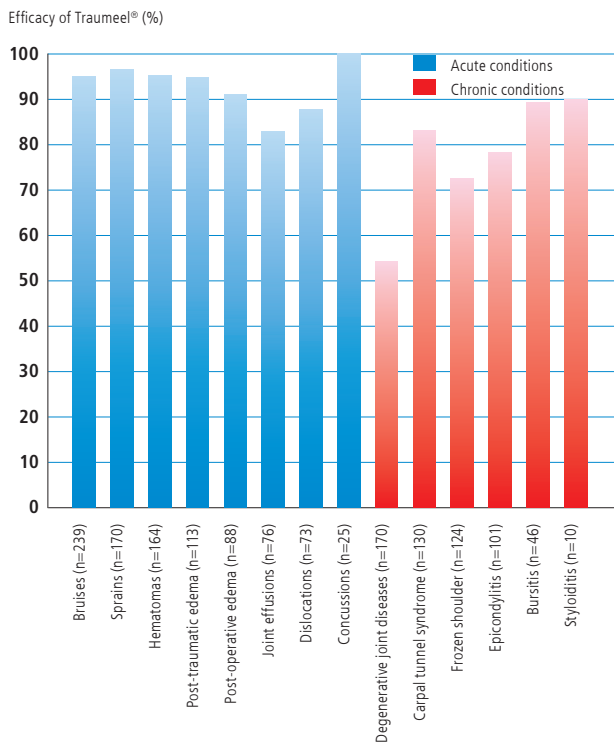
- Adjuvant therapies (medical and non-medical) were allowed and administered in two thirds of the cases.

- The 5 point scale utilized target criteria:
 - 'very good' (complete freedom from symptoms)
 - 'good' (noticeable improvement)
 - 'satisfactory' (slight improvement)
 - 'unsuccessful' (symptoms remained the same) or 'worsened'.

Results

- In 83% of all cases, therapeutic results were rated as 'good' or 'very good'. In 13%, treatment was rated as 'satisfactory', while in 4% it was 'unsuccessful'. Figure 22 shows the results as sums of "good" or "very good" for each disorder separately. The success rate in patients with symptoms of arthrosis and frozen shoulder were lower although, even in these instances, positive therapeutic results were achieved in the majority of cases.
- Improvement of symptoms could be observed in about 50% of all patients already within the first week of treatment, especially in cases of injuries; for another 34% it could be stated between 1 and 3 weeks.

Figure 22. Good to very good efficacy of Traumeel® , in % (as rated by therapists)



- There was no difference in the results of treatment with the two different oral forms of the medication.
- No cases of adverse drug reactions were reported.

Conclusions

- Both orally administered forms of Traumeel® are suitable for treating acute post-traumatic conditions, inflammatory and inflammation-related symptoms, and degenerative joint diseases.
- Both forms of Traumeel® are well tolerated.
- There are no restrictions in combining Traumeel® with other medications.

5.2 Traumeel® in asthma

5.2.1 Treatment of corticosteroid-dependent asthma with Traumeel®

Reference: Matusiewicz R. Traumeel S in der Behandlung von kortikoid-abhängigem Bronchialasthma. [The Homeopathic Treatment of Corticosteroid-Dependent Asthma. A double-blind, placebo-controlled study]. *Biologische Medizin*. 1996;XXV(3):107-112. (English translation available in: *Biol Ther*. 1997; XV(4):117-122)

Study design	placebo-controlled, double-blind study.
Formulation	Traumeel® injection.
Indication(s)	corticosteroid-dependent bronchial asthma.

Objective

To analyze the effects of Traumeel® on the clinical condition and certain spirometric and immunological indices in patients with corticosteroid-dependent asthma.

Study design

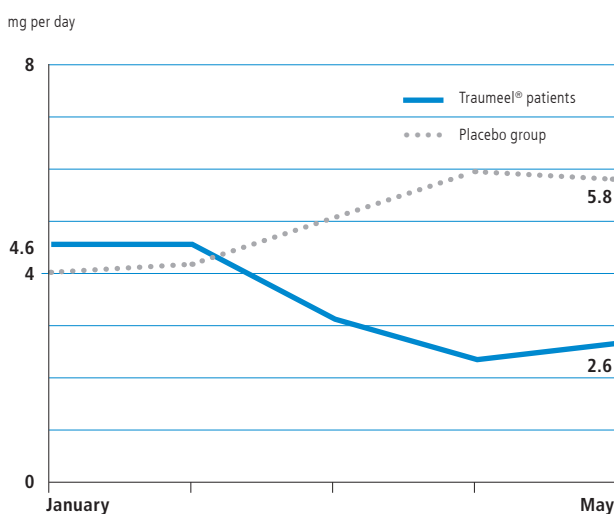
- Basic data of participants:
 - n=103 patients (n=62 females, n=41 males) with corticosteroid-dependent asthma
 - Traumeel® group: 71 patients
 - diclofenac group: 32 patients
 - mean age: 48 years, aged 20-74 years.
- Patients had been taking the corticosteroid triamcinolone (≥ 5 years), at a dosage of 4-8 mg/day. They already experienced numerous adverse events such as osteoporosis, spontaneous bruising or weakness.
- For gaining reference values a control group of 20 healthy subjects, aged 24-60 years (mean age 38 years), was chosen.
- Patients received either Traumeel® injections, one ampoule of 2.2 ml subcutaneously at intervals of 5-7 days, or placebo.
- Methylxanthine preparations were given for liquefaction of mucus. Patients were allowed to take tetracycline in cases of exacerbation of infection.

- Before and after 20 weeks of treatment, spirometric tests were conducted and levels of the serum immunoglobulins IgE, IgG, IgA and IgM were measured. Other tests performed included: granulocyte migration; quantitative assessment of superoxide radical O_2 generation; eosinophilic cationic protein (ECP) in serum; and morphotic elements of blood and urine.
- Patients recorded daily forced vital capacity (FVC), forced expiratory volume (FEV_1) and peak expiratory flow rate (PEFR) values as well as the daily intake of corticosteroids.

Results

- Corticosteroid dosage in patients treated with Traumeel® was reduced from 4.6 to 2.6 mg/day; in contrast, the placebo group changed from 4.0 to 5.8 mg/day (see Figure 23).

Figure 23. Mean daily doses of corticosteroids for Traumeel® patients and for placebo group.



- Patients treated with Traumeel® demonstrated significant improvement in their general clinical condition.
- Complications of corticosteroid therapy were less evident in the group treated with Traumeel®, muscle power increased.

- Infections reappeared at max. once after starting treatment with Traumeel® while this had happened 3-4 times before treatment with Traumeel®.
- Significant improvements were found in serum IgE levels in patients who were treated with Traumeel® – before treatment mean serum IgE level was 132 µg/l ± 67.0 and following treatment it fell to 40.1 µg/l ± 32.0 (control group: 38.4 µg/l ± 12.0). In the placebo group, the IgE value did not change significantly (84.0 µg/l ± 67.0 before treatment; 79.2 µg/l ± 58.0 after treatment).
- The migration ability of granulocytes was equal in both treatment groups before treatment (about 27 mm²). It increased to 34.25 mm² ± 10.07 with Traumeel®, which might be a reason why recurrent infections were less frequent, whereas it even dropped slightly in the placebo group (value in control group: 42.13 mm² ± 10.03).
- Free radical production (superoxide O₂) and serum ECP decreased significantly in the Traumeel® group. In the placebo group the values remained unchanged.
- Significant differences were not found in PEFr, FVC and FEV₁: before treatment 289 ml, 2.66 ml and 1.95 ml, respectively; after treatment: 302 ml, 2.72 ml and 1.92 ml, respectively.

Conclusion

Traumeel® appears to be useful in the treatment of corticosteroid-dependent bronchial asthma reducing the likelihood of serious side effects.

5.3 Traumeel® in dentistry

5.3.1 Biological management of endodontics:

Use of Traumeel® on Root Canal Treatment

Reference: Osorio Díaz J, Fajardo Marino F. Biologische Versorgung von Endodontien: Verwendung von Traumeel bei der Behandlung des Wurzelkanals [Biological Management of Endodontics: Use of Homeopathic Medication on Root Canal Treatment]. *Biologische Medizin*. 1998;XXVII(6):243-246. (English translation available in: *Biomed Ther*. 1999;XVII(1):41-44)

Study design randomized, controlled study.

Formulation Traumeel® ointment and injection.

Indication(s) root canal treatments.

Objective

To investigate a therapeutic alternative, Traumeel® mixed with different zinc oxide based fillings, as a replacement for conventional substances in root canal fillings in order to avoid interference fields.

Study design

- Basic data of participants:
 - n=28 patients with required root canal treatment: 14 patients with and 14 patients without previous root canal infections
 - n=50 participants in the control group who had already undergone root canal treatment and thus providing reference values (constitutes active interference fields*)
 - aged between 19 and 55 years.
- In the 28 patients a total of 52 root canal procedures were performed.
- Prior to the root filling and during the biomedical medication Traumeel® injection solution was used on all patients to irrigate the canals.
- Traumeel® ointment was added to different zinc oxide-based root canal filling material and used to prevent inflammation and the development of granulomas.
 - For treatment of non-infected root canals Traumeel® ointment was mixed with either zinc oxide in combination with zinc acetate (hardening agent) or conventional Coltosol®**:

- For treatment of previously infected root canals the filling material consisted of a mixture of Traumeel® ointment, zinc oxide and calcium hydroxide which has an antibacterial effect due to its high pH.
- For sealing the root canals gutta percha cones were used.

Results

- Use of Traumeel® resulted in the absence of painful symptoms during the procedure and in the few days following treatment.
- Interference fields appeared only in four (11.2%) of the patients treated with any of the methods compared, all of them showing chronic periapical damage, compared with 46 (92%) in the control group. In the latter, interference fields were noted not only in root canal patients with chronic periapical damage but also in patients whose periodontia was normal.
- The absence of symptoms and lack of x-ray evidence of periapical changes suggests that patients benefited from root canal treatment using one of the combinations in the treatment group, unless pre-existing damage was evident.
- The Traumeel®/Coltosol® mixture was not superior to the Traumeel®/zinc oxide or zinc acetate mixture.

Conclusions

- This study may serve as basis for further research to establish the use of Traumeel® ointment as a standard component of the ideal filling material for root canal treatment.
- Use of Traumeel® makes it possible to avoid the negative effects of conventional root canal procedures.

** An interference field is any element which alters the normal flow of information through an organism to a zone that does not properly conduct the energetic impulse, or to a depolarized zone. It is brought about by the presence of materials in the tissues which cannot be broken down. Interference fields in the oral cavity remain problematic and can seriously jeopardize a patient's well-being. Caused by the teeth, interference fields can make their presence felt anywhere throughout the body through a great variety of symptoms. These disturbances are primarily caused by root canal treatments and especially certain types of root canal filling materials. Therefore, a search for more biocompatible dental materials is on-going.*

*** Composition of Coltisol: zinc oxide, zinc-1-hydrate sulphate, hemi-hydrated calcium sulfate, diatom soil, dibutyl phtalate, polyvinyl chloride, acetate copolymer, mint fragrance.*

5.4 Traumeel® after surgery

5.4.1 Efficacy of a Traumeel® in control of post-operative pain: a pilot clinical trial

Reference: Singer SR, Amit-Kohn M, Weiss W, et al. Efficacy of a homeopathic preparation in control of post-operative pain – A pilot clinical study. *Acute Pain.* 2007;9(1):7-12.

Study design Open, prospective, quasi-randomized triple-arm clinical trial.

Formulation Traumeel® injection and tablets.

Indication(s) post-operative pain after Hallux valgus surgery.

Objective

Pilot trial to assess two regimens of Traumeel® in minimizing post-operative pain and analgesic consumption following elective Hallux valgus surgery.

Study design

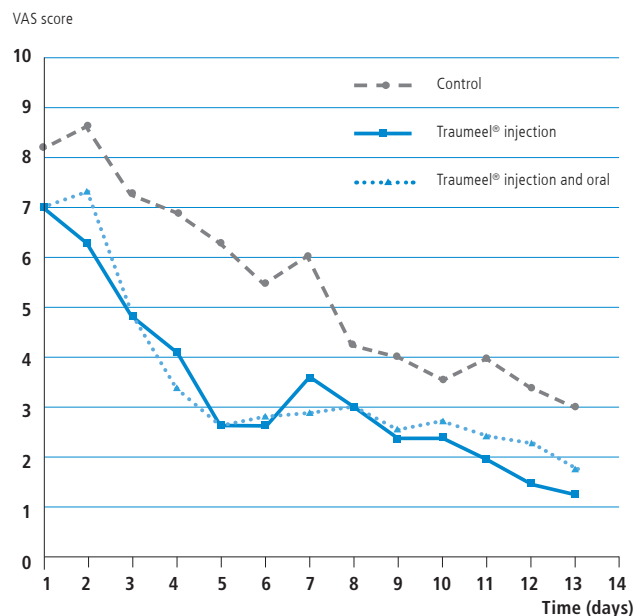
- Basic data of participants:
 - n=30 consecutive patients scheduled for elective Hallux valgus surgery were assigned by week of operation to receive treatment as follows:
 - n=9 in the injection only group: injection of Traumeel® (2.2 ml) into the operative incision upon conclusion of surgery
 - n=10 in the injection + PO group: injection of Traumeel® (2.2 ml) into the operative incision upon conclusion of surgery and oral Traumeel® tablets post-operatively three times daily for 13 days or until pain was "negligible or non-existent" (VAS* < 3)
 - n=11 in the control group: received only conventional care.
 - age: 18-80 years.
- Operations were performed under local anesthesia using Bupivacaine 0.5% and lidocaine 1%.
- In case of pain after the operation patients were asked to take only paracetamol 325 mg with codeine 15 mg (primary oral analgesic). As "rescue" analgesic tramadol hydrochloride 100 mg was prescribed.

- Outcome measures were:
 - daily VAS score – repeated measures of maximal pain at rest during 13 days post-operatively using a linear mixed effects model
 - total consumption of analgesics between the groups.
- Follow-up visits were to take place on day 6 and 13.

Results

- Both the Traumeel® single injection group and the injection + PO group experienced from day 1 on lower mean VAS scores (lower mean pain) compared with the control group ($p=0.02$ and $p=0.05$, respectively) (see Figure 24).
 - The interaction between time and group was significant ($p<0.0001$) indicating that the magnitude of the differences between groups was not constant over time.

Figure 24. Mean pain repeated measures according to study group.



- The means for the Traumeel® single injection group and the injection + PO groups did not differ significantly during the entire study period.
- Mean total consumption of analgesics (number of tablets) was lower in both Traumeel® treatment groups compared with the control group (not statistically significant). The largest magnitude of dif-

ference between the Traumeel® treatment groups and the control group was in the first week after surgery. In contrast to the study design the patients took a large variety of analgesics.

Conclusions

- In this pilot study post-operative pain following Hallux valgus surgery was significantly reduced in patients given either a single intra-operative injection of Traumeel® or a single intra-operative injection of Traumeel® followed by daily oral Traumeel® treatment compared with no active treatment.
- This pilot study has provided preliminary data on which to base a larger, randomized double-blind, placebo-controlled study examining the reduction in post-operative pain and use of analgesics with Traumeel®.

**A Visual Analog Scale (VAS) is a measurement instrument to gauge a characteristic or attitude that is believed to range across a continuum of values and cannot easily be directly measured. For example, in this case, the amount of pain that a patient feels ranges across a continuum from none to an extreme amount of pain.*

5.5 Traumeel® in pediatrics

5.5.1 A randomized controlled clinical trial of Traumeel® in the treatment of chemotherapy-induced stomatitis in children undergoing stem cell transplantation

Reference: Oberbaum M, Yaniv I, Ben-Gael Y, et al. A Randomized, Controlled Clinical Trial of the Homeopathic Medication TRAUMEEL® in the Treatment of Chemotherapy-Induced Stomatitis in Children Undergoing Stem Cell Transplantation. *Cancer*. 2001;923:684-690.

Study design randomized, placebo-controlled, double-blind clinical trial.

Formulation Traumeel® injection.

Indication(s) chemotherapy-induced stomatitis.

Objective

To assess the efficacy of Traumeel® in the management of chemotherapy-induced stomatitis in children undergoing bone marrow transplantation.

Study design

- Basic data of participants:
 - n=32 patients years who had undergone allogeneic (n=16) or autologous (n=16) stem cell transplantation
 - aged 3-25 years.
- In addition to twice-daily mouth washes with chlorheximide, amphotericin B as well as gentle tooth brushing patients used sterile placebo (n=16) or Traumeel® (n=16) ampoules (2.2 ml) as a mouth rinse, administered five times daily from 2 days after transplantation for a minimum of 14 days, or until at least 2 days after all signs of stomatitis were absent. As in each group 1 patient complained about nausea after a single dose and thus treatment was stopped, only 15 in each group could be taken into account for the evaluation.
- Patients were instructed to rinse their mouth with Traumeel® or placebo for at least 30 seconds before swallowing; keeping the liquid as long as possible on particularly troublesome lesions in the mouth.
- Stomatitis scores were evaluated according to the World Health Organization 5-scale grading system for mucositis.

- In addition, a subjective scoring system was used in which the patient or parents judged the degree of oral pain, discomfort, dryness of the mouth and tongue, dysphagia and ability to swallow. A five-grade system was used (0=no complaints to 4=very severe complaints, unable to even swallow liquids).

Results

- Five patients (33%) in the Traumeel® group did not develop stomatitis compared with only one patient (7%) in the placebo group. Mean AUC (area under curve) scores were: Traumeel® 10.4 vs. placebo 24.3 (p<0.01) (see Table 3).

Table 3: Stomatitis area under the curve scores and time to worsening of symptoms by allocated treatment.

Traumeel®			Placebo		
Patient	AUC ^a	Time to worsening (days) ^b	Patient	AUC ^a	Time to worsening (days) ^b
1	9	>8	2	27.5	4
3	0	>18	4	16	4
6	4	>9	5	16	2-3
7	20	4-5	8	36	1-2
9	11	3-5	10 ^c	4	6-7
12 ^d	38	20.0	11	56	4
13	0	>13	14	14	2-3
15	0	>13	16	20	2-3
17	0	>5	18	31	10-11
19	17	5.0	20	21	3
22	0	>10	21	0	>6
23	17	4-7	24	26.5	5
25	3	>8	26	45	4
28	5	7.0	27	35	10
30	26.5	2-3	29	16	4
Mean	10.4	6.9 ^e	Mean	24.3	4.3 ^e
Median	5.0	4.7 ^e	Median	21.0	4.3 ^e

AUC: area under the curve.

a Test for difference in AUC: Wilcoxon rank sum score, 167.5; expected score, 232.5 (p<0.01).

b Test for difference in time to worsening: chi-square test, 13.4 with 1 degree of freedom (p<0.001).

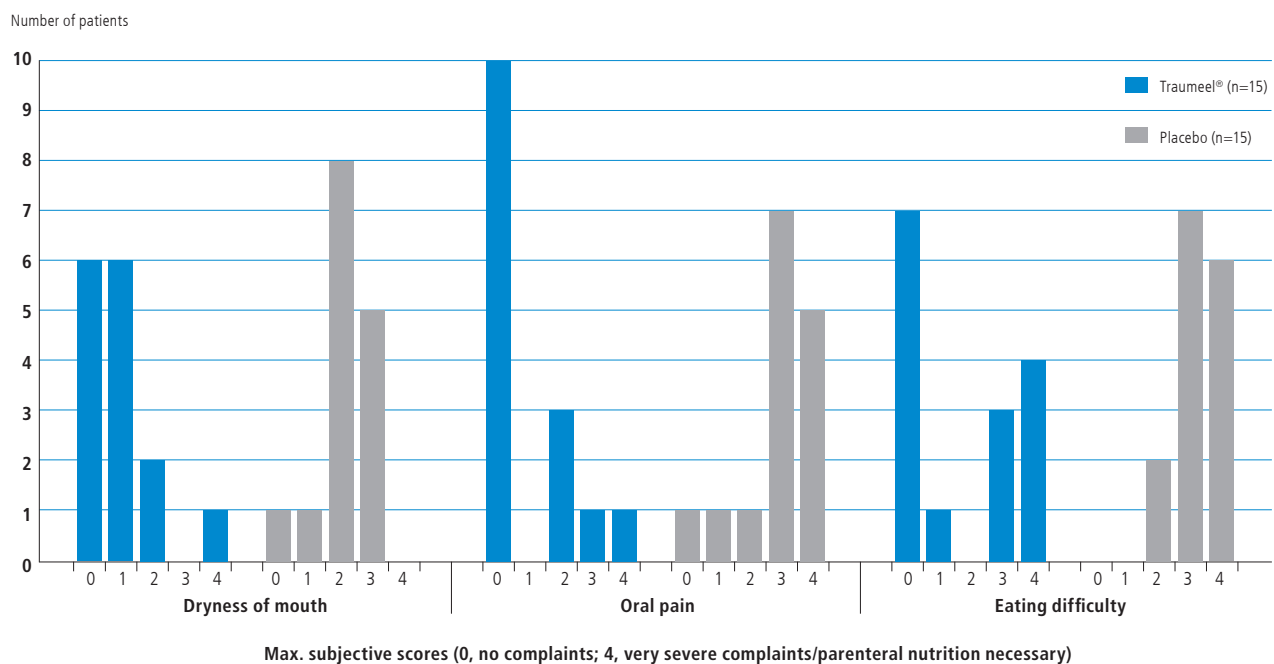
c The patient received TRAUMEEL® accidentally.

d There was doubt regarding the AUC score and time to worsening. An alternative interpretation would be AUC, 0; time>19 days.

e Means and medians of uncensored times only are shown.

- Stomatitis worsened in 7 patients (47%) in the Traumeel® group; 14 (93%) in the placebo group. Median time to worsening of symptoms was; Traumeel® 4.7 days; placebo 4.0 days (see Table 3).
- The maximum symptom scores for dryness of the mouth, oral pain and eating difficulty over the first 7 days of Traumeel® and placebo treatment showed that patients in the Traumeel® group demonstrated a clear reduction in severity of symptoms in all three categories compared with placebo (see Figure 25).
- There was a high incidence of serious complications but no significant difference between the groups.

Figure 25. The maximum subjective score during the first 7 days of study treatment with Traumeel® for dryness of mouth, oral pain, and eating difficulty.



Conclusion

Traumeel® significantly reduces the severity and duration of chemotherapy-induced stomatitis in children undergoing bone marrow transplantation.

5.5.2 Treating pediatric trauma with Traumeel®

Reference: Ludwig J, Weiser M. Treating Pediatric Trauma with a Homeopathic Ointment. *J Biomed Ther.* 2001; Summer: 8-11.

Study design	observational study.
Formulation	Traumeel® ointment.
Indication(s)	traumatic, inflammatory and degenerative disorders, primarily contusions, sprains, hematomas and dislocations.

Objective

- To examine usage indications, efficacy and tolerance of Traumeel® in pediatric patients.

Study design

- Basic data of participants:
 - n=157 children, 70 (45%) girls and 87 (55%) boys
 - aged 0-12 years, majority 10 years of age (24%).
- 32 pediatricians took part.
- Traumeel® was prescribed for a broad range of traumatic, inflammatory and degenerative disorders, primarily contusions, sprains, hematomas and dislocations.
- The majority of patients (80%) sought treatment for acute symptoms that had persisted for less than a week.
- 11% of patients had received prior medical treatment (e.g. analgesics, antirheumatics or anti-inflammatories) for their condition.
- Duration of treatment: one week in two thirds of patients.
- In 84% of the patients, Traumeel® was applied 1-3 times daily, sometimes in combination with bandaging.

- 62% of the patients were treated exclusively with Traumeel®. The remaining 38 % received adjuvant non-medical therapies (e.g. hot and cold packs, immobilization, massage, chiropractic) or medical adjuvant therapies (e.g. analgesics, antirheumatics or anti-inflammatories).

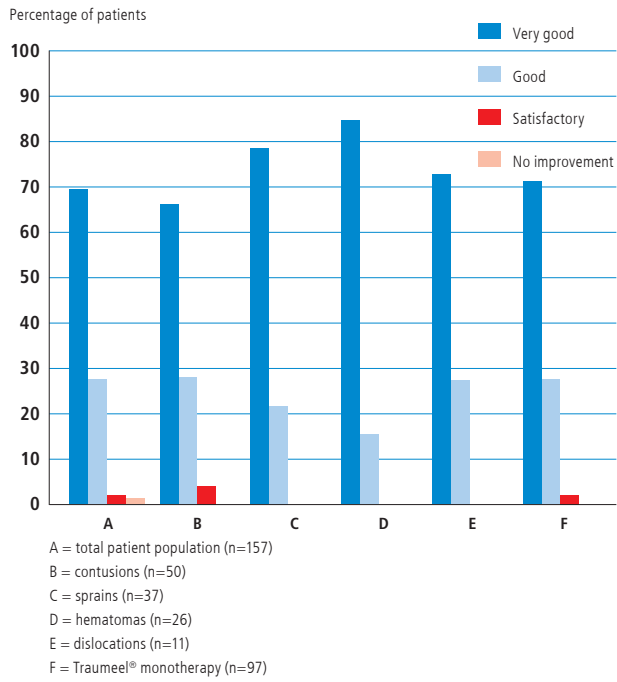
Outcome results:

- Efficacy was rated by the pediatrician on a five-point scale (very good, good, satisfactory, no improvement, worse).
- Patient tolerance was rated by the pediatrician on a four-point scale (excellent, good, moderate, poor).
- Further, time of first improvement was recorded.

Results

- No adverse effects were reported from the use of Traumeel®.
- In all patients, tolerance to the medication was rated 'excellent' or 'good,' regardless of whether Traumeel® was prescribed as monotherapy or in combination with additional medical or non-medical therapies.
- Overall analysis of the therapeutic results indicated that the treatment was rated (regardless of age or type of symptoms) as 'very good' in 70% of patients and 'good' in 27% of patients (see Figure 26).
- Monotherapy with Traumeel® was rated as 'very good' or 'good' in 98% of patients (see Figure 26).
- Symptoms improved in two thirds of the patients within the first 3 days of treatment.

Figure 26. Results of therapy with Traumeel®.



Conclusions

- Traumeel® is effective in treating blunt trauma and muscle, joint and soft-tissue disorders of varying etiologies in pediatric patients.
- Traumeel® is well tolerated in pediatric patients.

5.5.3 Traumeel® in the treatment of intramuscular hematomas in children with hemophilia: Pilot study

Reference: Tsymbal IN, Plahuta TG, Vdovin VV, Svirin PV, Shiller EE, Ivanova IV. Traumeel S in treatment of intramuscular hematomas in children with haemophilia: Pilot study. *Thromb Homeost.* 1997;246: abstract PS-1007.

Study design	pilot study.
Formulation	Traumeel® tablets.
Indication(s)	intramuscular hematomas.

Objective

A pilot study to determine the effectiveness of Traumeel® as an alternative treatment for intramuscular hematomas (IH) in children with hemophilia.

Study design

- Basic data of participants:
 - n=5 patients with severe hemophilia A (extra-peritoneal IHs (n=3), IH of the shin (n=1) and IH of the hip (n=1))
 - aged 12-15 years, majority 10 years of age.
- All patients recovered on infusion of factor VIII concentrate or cryoprecipitate, Traumeel® (one oral tablet, three times/day, 14-28 days) and phonophoresis [the use of ultrasound to increase the percutaneous adsorption of drugs] of hydrocortisone and dioxidine.

Results

- The duration and expression of pain was less with Traumeel® treatment compared with the control group.
- There was a decrease of sonographic dimensions; the density of IHs was clearer compared with the control group.
- The total amount of substitute therapy decreased by 30% with Traumeel® treatment, and by 30-50% of in-patient treatment.
- Traumeel® decreased period to recovery of movement in joints and walking.
- Aggregation of platelets with collagen was higher in patients treated with Traumeel® compared with the control group.

- The therapeutic level of factor VIII during Traumeel® treatment was maintained for longer (8-10% during 24 hours after infusion) compared with the control group.

Conclusion

Further research may be warranted to study Traumeel® as an alternative treatment for intramuscular hematomas (IH) in children with hemophilia.

5.6 Traumeel® in arthritis

Experience and evidence suggests that Traumeel® may have a place in the treatment of osteoarthritis and rheumatoid arthritis, in combination with glucosamine sulfate and chondroitin sulfate.¹

Reference:

1. Ross G. The use of glucosamine sulphate and chondroitin sulphate and homeopathic remedies in arthritic patients. *Biomed Ther.* 1999;XVII(3): 107-109.

Key point: Numerous clinical studies show the evidence base for Traumeel® in sports medicine, and also in asthma, dentistry and pediatrics.

6. Safety and toxicology

Traumeel® is very well tolerated with minimal side effects.

In a four-week study conducted according to FDA standards,¹ 20 healthy volunteers (aged 18-75 years) received Traumeel® oral tablets sublingually, three times a day. Laboratory tests were performed once a week to assess the effect of Traumeel® on complete blood count, liver profile, serum chemistry, bleeding time, coagulation time and the gastrointestinal system.

The results showed that there was no significant effect from baseline to study completion on any measured laboratory parameter, including gastrointestinal toxicity.

A total of 11 subjects reported 36 adverse events after taking Traumeel®:

- Headache was the most commonly reported adverse event (n=15)
- Other common events included diarrhea and stomach discomfort/bloating (n=6), feelings of nausea (n=2)
- All events were considered to be mild (n=30; 83.3%) or moderate (n=6; 16.7%)
- No events required Traumeel® to be stopped, all were transient and resolved despite continuation of the study drug and the majority (n=22; 61%) were considered to be unrelated to the study medication
- No severe toxic events were observed and there was no evidence of gastrointestinal bleeding.

It should be noted that this was not a placebo-controlled study. It was concluded that Traumeel® is safe and well tolerated in healthy subjects. The authors felt that Traumeel® should be considered as a safer alternative to NSAIDs, particularly considering its apparent lack of gastrointestinal toxicity.

“Traumeel® has anti-inflammatory and analgesic effects and does not inhibit the arachidonic acid pathway of prostaglandin synthesis. Traumeel® deserves consideration as a safer alternative for patients at high risk of gastrointestinal bleeding with conventional NSAIDs.”¹

In vitro studies

An *in vitro* study² has shown that neither the ingredients of Traumeel®, nor Traumeel® itself, are cytotoxic to granulocytes, lymphocytes, platelets and endothelia. This indicates that the defensive functions of these cells are preserved during treatment with Traumeel®.

Adverse effects

Adverse effects with Traumeel® are extremely rare. Traumeel® exhibits no known adverse renal, hepatic, cardiovascular, gastrointestinal or central nervous system effects.

Hypersensitivity reactions can occur in individual cases. Skin rash and pruritus and, in rare cases, facial swelling, dyspnea, dizziness and a fall in blood pressure have been observed after treatment with products containing Echinacea extracts.

In rare cases, patients with hypersensitivity to botanicals of the Compositae family may experience an allergic reaction after the administration of Traumeel®, including an anaphylactic reaction. Traumeel® ingredients of the Compositae family are: Arnica montana (mountain arnica), Calendula officinalis (marigold), Achillea millefolium (milfoil), Chamomilla (Matricaria) recutita (chamomile), Bellis perennis (daisy), Echinacea angustifolia (narrow-leaved cone flower) and Echinacea purpurea (purple cone flower).

The following paragraph applies only to systemic formulations: As a general principle, based on possible immunological reactions after the intake of Echinacea, Traumeel® should be avoided in cases of progressive systemic disorders, such as tuberculosis, leukemia, collagen vascular diseases, multiple sclerosis, HIV infection, AIDS and other autoimmune disorders.

Drug interactions

There are no known drug interactions with Traumeel® and other medications or molecules, and Traumeel® is not known to interact with any laboratory tests. Furthermore, the administration of an oral or injectable dosage form of Traumeel® can be safely augmented by the application of a topical dosage of Traumeel®.

Carcinogenesis

No studies have been performed to evaluate the carcinogenicity of Traumeel®. However, in worldwide post-marketing surveillance studies, no evidence of carcinogenicity has been found.³

Pharmacokinetics and pharmacodynamics

As previously mentioned, the exact pharmacokinetics and pharmacodynamics of Traumeel® have not been established. However, the activity of Traumeel® as an effective treatment for musculoskeletal injury and inflammation can be worked into a plausible hypothesis.

The effects of Traumeel® cytokines involved in the inflammatory cascade have been seen *in vitro*, notably in the reduction of concentrations of pro-inflammatory cytokines, as well as in the secretion of the regulating cytokine, TGF-β.

Due to the low concentration of antigen present in Traumeel®, it is, therefore, postulated that regulatory T-cells, and notably Th3 cells, may be introduced. In a preliminary study, plant materials (*Atropa belladonna* and *Bellis perennis*, ingredients of Traumeel®) were shown to increase TGF-β, which is secreted apart from regulatory Th3 cells, as well as others.⁴ The induction of regulatory T-cells by small concentrations of antigens has previously been well described.⁵⁻⁷

Of special interest in the inflammatory cascade is the role of the transcription factor, NF kappa beta (NF-κB). NF-κB is a family name for a complex of transcription factors that play a crucial role in the regulation of genes that steer the induction of inflammation, apoptosis and cell proliferation. At rest, NF-κB is a complex in the cytoplasm; once activated by a variation of mediating stimuli, it breaks down into substances that will move to the cell nucleus where it will bind to DNA sites and activate the release of cytokines and other mediators.

The NF-κB family of transcription factors is involved mainly in stress-induced, immune and inflammatory responses. In acute inflammation, NF-κB is activated and increases the expression of several pro-inflammatory cytokines and chemokine genes. Conversely, the most potent NF-κB activators are the pro-inflammatory cytokines, IL-1 and TNF.⁸

By inhibiting the release of pro-inflammatory cytokines, Traumeel® will, in fact, indirectly inhibit the activation of NF-κB upstream, as well as directly inhibiting the inflammatory events downstream.

More interesting, however, is the effect that Traumeel® might exert directly on NF-κB. Helenalin, which is a sesquiterpene lactone found in the asteracea family of plants (of which several are included in Traumeel®, e.g. *Arnica montana* and *Bellis perennis*) has been shown to selectively inhibit NF-κB.⁹

From the above, it is clear that Traumeel® may have several potential actions on the inflammatory cascade, from modulating pro-inflammatory cytokines to influencing transcription factors, as well as inducing regulatory T-cells to restore the balance between Th1 and Th2 CD4 cells. Furthermore, TGF-β plays a role in wound healing and matrix remodeling which concludes the final phase of inflammation, namely reconstitution.

Due to the low concentration of the ingredients, no pharmacokinetics exist for Traumeel®. It is thought that the nanogram concentrations, such as are found in Traumeel®, may have a regulatory effect on the organism by stimulating the innate adaptive response, probably in a paracrine fashion, or via the immune system as seen in the immunological bystander reaction.

The concept of hormesis, where substances show a biphasic effect on dose response curves (U- or J-shaped dose response curves are seen) has now been well established in the literature.¹⁰ Small amounts of often toxic substances show a stimulatory effect at levels below the 'no adverse effect level' (NOAEL).

In this case, one sees a biphasic response, where high dilutions will have no effect, then an effect is seen but as the concentration of the substances increases, the effect seen is the opposite.

This was seen in the studies by Porozov on IL-1, TNF-α and IL-8. Porozov² mentions that between dilutions of 10⁻¹ to 10⁻⁷, Traumeel® has a selective effect on the pro-inflammatory cytokines. This constitutes a working hypothesis for the action of the low concentration of ingredients in Traumeel®.

Contraindications

None, except for hypersensitivity to Traumeel® or any of its ingredients (see above under Adverse Effects).

Long-term use

If required, Traumeel® can be used for long-term use. There is no risk of tachyphylaxis or addiction, and tolerance to all formulations of Traumeel® is high.

Lack of age limitation

There is no age limitation for the use of Traumeel®. Traumeel® has been used to manage inflammation and trauma in children 2 years and older with no adverse events, and has been used extensively in the elderly.

Pregnancy

In general, medications such as Traumeel® that are classified as homeopathic, are not known to cause direct or indirect harm to the fetus. However, animal reproduction studies have not been performed and there are no well-controlled studies in pregnant women. In pregnancy or suspected pregnancy, Traumeel® should only be used if the potential benefits justify the potential risks to the fetus.

Nursing mothers

It is not known whether any of the ingredients in Traumeel® are excreted in human milk. However, because many drugs are excreted in human milk, Traumeel® should be administered with caution to nursing mothers.

Storage

See packaging instructions for specific storage recommendations of each Traumeel® formulation. Products should not be frozen or exposed to excessive heat.

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7. Doping

An important point, particularly for users, recommenders and prescribers of Traumeel® to athletes and sports professionals, is that none of the components of Traumeel®, in the micro-doses they are present in the products, are considered doping. Consequently, Traumeel® is not listed on the WADA (World Anti-Doping Agency) list of banned products. In fact, in Germany, Traumeel® is listed as “to be used” on the National Anti-Doping Agency (NADA) list. For this reason, in sports medicine, Traumeel® is widely used in the treatment of trauma and inflammation of joints and soft tissues.

Heel doping statement

Heel, the manufacturer of Traumeel®, has issued the following doping statement:

Doping

Medications manufactured by Heel are successfully used for the treatment of amateur and professional sportsmen worldwide. Sometimes the question arises whether administration of the Heel medications could result in positive doping effects, especially since some of these medications contain substances in highly diluted form that are generally listed in international doping lists, such as testosterone and cortisone.

However, an independent toxicological institute now clarified this question and the results are undisputable: Dilutions with a final concentration (i.e. concentration in our finished products) of 10^{-6} (D6) or higher (D7, D8, etc.) cannot lead to any effect of doping. The amounts or concentrations of the dilutions of Heel medications given in therapy do not lead to a substitutional effect that is equated with an effect of doping.

Conclusion

In spite of their documented therapeutic efficacy, no positive doping effects are to be expected for the medications of Heel.

'Statement to the question of dosage and doping by hormone-containing homeopathics' by Dr Wolfgang Strösser*

For further reading on this topic, the document (Figure 27) 'Statement to the question of dosage and doping by hormone containing homeopathics' is recommended.

Figure 27. Contents of 'Statement to the question of dosage and doping by hormone-containing homeopathics' by Dr Wolfgang Strösser*

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Doping letter from Dr Hans-Wilhelm Müller-Wohlfahrt**

Additional reassurance on the lack of effect of Traumeel® on doping tests can be obtained from a letter from Dr Müller-Wohlfahrt in which he states that “Doping with Traumeel® can be excluded with 100% certainty” and “Traumeel® does not appear on WADA’s List of Prohibited Substances and Methods.”

In fact, on some national lists (for example, the German NADA), Traumeel® is listed as a medication to be used without concerns.

Key point: Traumeel® is very well tolerated with minimal side effects. It is not considered doping.

*Dr Wolfgang Strösser has a PhD in Pharmacology and is an MD; he works as an independent consultant in the field of pharmaceuticals.

** Dr Hans-Wilhelm Müller-Wohlfahrt is an orthopedist, has a practice in Munich for Sports Medicine, and since 1977 he has been team physician of Bayern Munich, one of the top five teams worldwide in football/soccer; in addition he has been a member of the medical team of the German National Football/Soccer Team since 1996. Furthermore, he is the treating physician of the top Kenyan and Ethiopian long distance runners.

8. Testimonials, articles of praise, and worldwide experience and availability

Traumeel® has been used in 60 countries around the world for over 60 years, during which time over 9 million units have been used each year, of which 2.3 million units are tubes of ointment.

Traumeel® has been, and continues to be, used successfully by a variety of professional and amateur athletes, sporting organizations and teams.

The following teams regularly use Traumeel®:

- The German Olympic Team, Athens 2004
- The German Olympic Team, Turin 2006
- The German Olympic Team, Beijing 2008
- The team physicians of the following soccer teams:
Chelsea, London, UK
Real Madrid & Atletico Madrid, Spain
Bayern Munich, Germany

Traumeel® has won the following accolades:

- Homeopathic Product of the Year in Canada: 2003, 2004, 2005, 2006, 2007, 2008, 2009
- Product of the Year for Pharmacists in Germany: 2001, 2002, 2003

Traumeel® is included on page 1,725 of the 2009 Physicians Desk Reference (PDR) the 'German Red List' (equivalent of the PDR) and the 'Russian Red List', as well as being recommended in several other textbooks.¹⁻⁶

Furthermore, the use of Traumeel® has been endorsed in a popular and widely circulated book entitled '*Injured – what now?*' by Dr H-W Müller-Wohlfahrt and HJ Montag. This book, last published in 2005 (first published in 1996), advises sports coaches, physical education instructors, parents, adolescents and adults undertaking a variety of sports on how best to manage injuries. The book even suggests that Traumeel® ointment should be included in first aid kits.

Traumeel® is available in over 60 countries worldwide. Please refer to the Heel homepage at www.heel.com for a full list of Heel's marketing and sales partners.

Key point: Traumeel® has been used in more than 60 countries around the world for over 60 years. Traumeel® has been, and continues to be, used successfully by a variety of professional and amateur athletes, sporting organizations and teams.

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9. Summary

Traumeel®:

- Provides effective treatment for musculoskeletal injury and inflammation
- Is as effective at reducing symptoms of inflammation as NSAIDs, such as diclofenac
- Is very well tolerated with minimal side effects
- Is available in tablets, drops, ointment/gel and ampoules for injection, thereby enabling flexibility of administration
- Is a valuable alternative to NSAIDs in inflammation and trauma
- Acts quickly and reliably with few known side effects, contraindications and interactions
- Has a variety of uses which are continuing to expand with increasing research and experience
- Can be used by the whole family
- Is used extensively by professional and amateur athletes and sports people
- Is expressly recommended by the German NADA (national anti-doping agency) list and not prohibited by the WADA list, i.e. it is not considered doping
- Has been used worldwide for over 60 years.

10. Appendix*

Traumeel®

Drops • Tablets • Injection solution • Ointment/Gel

• Compositions

Drops: 100 g containing: Arnica montana D2, Calendula officinalis D2, Hamamelis virginiana D2, Achillea millefolium D3 5 g each; Atropa bella-donna D4 25 g; Aconitum napellus D3, Mercurius solubilis Hahnemanni D8, Hepar sulfuris D8 10 g each; Matricaria recutita D3, Symphytum officinale D8 8 g each; Bellis perennis D2, Echinacea D2, Echinacea purpurea D2 2 g each; Hypericum perforatum D2 1 g. Contains 35 vol.-% alcohol.

Tablets: 1 tablet containing: Arnica montana D2, Calendula officinalis D2, Hamamelis virginiana D2, Achillea millefolium D3 15 mg each; Atropa bella-donna D4 75 mg; Aconitum napellus D3, Mercurius solubilis Hahnemanni D8, Hepar sulfuris D8 30 mg each; Matricaria recutita D3, Symphytum officinale D8 24 mg each; Bellis perennis D2, Echinacea D2, Echinacea purpurea D2 6 mg each; Hypericum perforatum D2 3 mg.

Injection solution: 2.2 ml containing: Arnica montana D2, Calendula officinalis D2, Chamomilla recutita D3, Symphytum officinale D6, Achillea millefolium D3, Atropa bella-donna D2 2.2 mg each; Aconitum napellus D2 1.32 mg; Bellis perennis D2 1.1 mg; Hypericum perforatum D2 0.66 mg; Echinacea D2, Echinacea purpurea D2 0.55 mg each; Hamamelis virginiana D1 0.22 mg; Mercurius solubilis Hahnemanni D6 1.1 mg, Hepar sulfuris D6 2.2 mg.

Ointment: 100 g containing: Arnica montana D3 1.5 g; Calendula officinalis Ø, Hamamelis virginiana Ø 0.45 g each; Echinacea Ø, Echinacea purpurea Ø, Matricaria recutita Ø 0.15 g each; Symphytum officinale D4, Bellis perennis Ø 0.1 g each; Hypericum perforatum D6, Achillea millefolium Ø 0.09 g each; Aconitum napellus D1, Atropa belladonna D1 0.05 g each; Mercurius solubilis Hahnemanni D6 0.04 g; Hepar sulfuris D6 0.025 g. Excipients: Paraffinum liquidum, cetostearyl alcohol (type A), emulsifying, white soft paraffin, purified water, ethanol, preserved with 13.8 vol.-% ethanol.

Gel: 10 g containing: Arnica montana D3 0.15 g; Calendula officinalis Ø, Hamamelis virginiana Ø 0.045 g each; Echinacea angustifolia Ø, Echinacea purpurea Ø, Chamomilla recutita Ø 0.015 g each; Symphytum officinale D4, Bellis perennis Ø 0.01 g each; Hypericum perforatum D6, Achillea millefolium Ø 0.009 g each; Aconitum napellus D1, Atropa belladonna D1 0.005 g each; Mercurius solubilis Hahnemanni D6 0.004 g; Hepar sulfuris D6 0.0025 g. Excipients: Carbomers, purified water, sodium hydroxide solution, ethanol. Contains 25 vol.-% alcohol.

Ø = undiluted i.e. the so called 'mother tincture'.

• Indications

Drops, tablets, injection solution: Blunt injuries, such as sprains, dislocations, contusions, hemarthrosis and effusions into a joint. Fractures; post-operative and post-traumatic edema and swelling of the soft tissues; inflammatory processes and degenerative processes associated with inflammation on the various organs and tissues, including, in particular, the musculoskeletal system (tendovaginitis, styloiditis, epicondylitis, bursitis, scapulohumeral periarthritis, etc.); arthrosis of the hip, knee and small joints; acute cerebral contusion.

Ointment: Injuries of all kinds (sports injuries and accidents) including blunt injuries, such as sprains, dislocations, contusions, hemarthrosis and effusions into a joint. Closed fractures, etc; inflammatory processes and degenerative processes associated with inflammation on the various organs and tissues, including, in particular, on the support and mobility apparatus (tendovaginitis, bursitis, scapulohumeral periarthritis), arthrosis of the hip, knee and small joints.

Gel: Blunt injuries, such as sprains, dislocations, contusions, effusions of blood and effusions into a joint. Closed fractures, inflammatory and degenerative processes associated with inflammation of various organs and tissues, including, in particular, the support and mobility apparatus (tenosynovitis, styloiditis, epicondylitis, bursitis); arthrosis of the hip, knee and small joints.

- **Contraindications**

Drops, tablets, injection solution: Hypersensitivity to one of the active ingredients or excipients, to Arnica, Chamomilla, Achillea millefolium or to other plants of the daisy (composite) family. As a matter of principle, Echinacea should not be used in progressive, systemic diseases such as tuberculosis, leukemia or leukemia-like diseases, inflammatory diseases of the connective tissue (collagen disease), autoimmune diseases, multiple sclerosis, AIDS, HIV infections or other chronic viral diseases.

Ointment, gel: Hypersensitivity to one of the active ingredients or excipients, to Arnica, Chamomilla, Achillea millefolium or to other plants of the daisy (composite) family.

- **Side effects**

Drops, tablets, injection solution: In rare cases hypersensitivity reactions or allergic skin reactions (redness, swelling and pruritus) can occur in people with known hypersensitivity to composites (e.g. Arnica, Chamomilla, Achillea millefolium), in which case use of the product should be discontinued. Skin rash and itching (pruritus), and in rare cases facial swelling, shortness of breath (dyspnea), dizziness and a fall in blood pressure, have been observed after treatment with products containing Echinacea extracts. Hypersalivation may occur after administration, in which case use of the product should be discontinued, too. Allergic reactions may occasionally occur on account of the homeopathic active substance Mercurius solubilis, too.

Injection solution: In individual cases, hypersensitivity reactions (up to the anaphylactic reaction) are possible in persons with hypersensitivity to composites (e.g. Arnica, Chamomilla, Achillea millefolium). Temporarily, reddening, tumefaction and pain may occur on the puncture site.

Ointment, gel: Hypersensitivity reactions or local allergic reactions (cutaneous inflammation, redness, swelling and pruritus) may occur in rare cases, in which case use of the product should be discontinued.

- **Interactions with other medication:** None known.

- **Dosage**

Drops: In general, 10 drops 3 times daily; for swelling of the soft tissues 30 drops 3 times daily.

Tablets: In general, 1 tablet to be dissolved in the mouth 3 times daily.

Injection solution: In acute disorders daily, otherwise 3-1 times weekly 1-2 ampoules i.m., s.c., i.d., i.v., per-articular.

Ointment: Apply to the affected parts and rub in, morning and evening, or if necessary, more often, possibly also applying an ointment dressing.

Note: Do not apply the ointment to large areas for a longer time or directly into open wounds.

Gel: Apply to the affected parts 1-2 times daily, or if necessary, more often.

- **Package sizes**

Drops: Drop bottles containing 30 and 100 ml.


Tablets: Packs containing 50 and 250 tablets.

Injection solution: Packs containing 10 and 100 ampoules of 2.2 ml each.

Ointment: Tubes containing 50 and 100 g of ointment.

Gel: Tubes containing 50 and 100 g of gel.

* Medication names, indications, and formulas may vary from country to country; package inserts provide country-specific information.



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