Clinical Safety of a Homeopathic Preparation
Sanjeev Arora, MD; Tanya Harris, RN, BSN; Claudia Scherer, RN, BSN

Abstract

Background: Traumeel® is a homeopathic medication containing 12 botanical substances and 2 mineral substances. It has been sold in the United States since 1986 and in Germany since 1937, and it is available worldwide for use as an anti-inflammatory, analgesic, antiinflammatory, and antiinflammatory drug. The indications for its use include temporary relief of symptoms associated with inflammatory, exudative, and degenerative processes due to acute trauma, repetitive or overuse injuries, and minor pain from osteoarthritis, rheumatoid arthritis, gouty arthritis, and ankylosing spondylitis.

Objective: To evaluate the clinical safety of Traumeel® tablets by measuring changes from baseline to post-treatment in the following: complete blood count cell, liver profile, serum chemistry, bleeding time, coagulation time, and the gastrointestinal system (presence of occult blood in the stool).

Methods: The four-week study was performed with one group of 20 volunteers. Baseline measures included case history, physical examination, vital signs, hematology, urinalysis, and a clinical chemistry. Volunteers received the study drug, two Traumeel® tablets sublingually three times per day. Selected laboratory tests were performed once a week. Each subject was required to keep a daily log of study drug intake and report any adverse symptoms following drug ingestion. A final examination of each study participant was performed during the fourth week of the study.

Results: Statistical evaluation of the laboratory data revealed no significant (P>0.05) differences from baseline to post-treatment in this study. All adverse events experienced by the subjects were mild to moderate in severity, transient, and subsequently resolved without intervention despite continued use of Traumeel®. Some examples reported by subjects were stomach discomfort, headache, diarrhea, dizziness, nausea, insomnia, and arm/leg pain.

Conclusion: Traumeel® is well tolerated and safe in healthy subjects. There was no significant gastrointestinal toxicity in the form of symptoms or gastrointestinal blood loss. Conventional nonsteroidal anti-inflammatory drugs cause gastrointestinal ulceration and bleeding in some patients and are especially hazardous for patients with diseases or taking medications that interfere with normal coagulation. Traumeel® has anti-inflammatory and analgesic effects and does not inhibit the arachidonic acid pathway of prostaglandin synthesis. It deserves consideration as a safer alternative for patients at high risk for gastrointestinal bleeding with conventional NSAIDs.

Traumeel® is a broad-spectrum, antiinflammatory, antiinflammatory and analgesic composed of biological and mineral substances, and it is a homeopathic combination medication. It has been used to treat inflammation and a variety of injuries, mainly to stimulate wound healing, provide pain relief, stop bleeding, improve muscle tone, and for a potential antiviral effect. It is a safe alternative to nonsteroidal anti-inflammatory medication. Traumeel® has 12 biological ingredients and 2 mineral substances: Arnica montana, radix (mountain arnica), Calendula officinalis (calendula), Hamamelis virginiana (witch hazel), Millefolium (milfoil), Belladonna (deadly nightshade), Aconitum napellus (monkshood), Chamomilla (chamomile), Symphytum officinale (comfrey), Bellis perennis (daisy), Echinacea angustifolia (narrow-leaved coneflower), Echinacea purpurea (purple coneflower), Hypericum perforatum (St John's wort), Hepar sulphuris calcarea (calcium sulfide), and Mercurius solubilis (no common name).

The objectives of this study were to explore the nature of adverse events caused by Traumeel® and to research the possible interaction of Traumeel® with biological function and/or gastrointestinal tract occult bleeding. Our primary objective was to document any adverse reactions to the study medication, and the secondary objective was to document any significant variation in physiological parameters.

This study was designed to evaluate the clinical safety of Traumeel® by instructing healthy subjects to ingest the medication on a daily basis. Adverse effects and physiological parameters were evaluated throughout the study. The Human Research Review Committee of the University of New Mexico School of Medicine approved this study on the basis of the final protocol in April 1998.

METHODS

Subject Population

Twenty healthy volunteers from the University of New Mexico Hospital who met the inclusion criteria were enrolled in the study. The volunteers received detailed written information on the trial medication and study procedures. In addition, the participants were informed about the possible risks of the study medication by a physician in the study and subjects provide written informed consent. The subjects informed that they could withdraw from the study at any time by their own discretion. The confidentiality of any medical data collected in the study was maintained respective to applicable federal and state laws and regulations.

Healthy men and women aged 18 to 75 years were eligible to participate. Children, pregnant or lactating women, patients with known allergies to the study drug, and subjects taking any investigational drug within 4 weeks of the start of the study were excluded.
Other exclusion criteria included inability to comply with the trial protocol, concomitant diseases, adverse events due to use of a birth control pill, and use of illegal substances. Subjects taking drugs or other therapies with comparable/interactive effects to the study drug or synthetic medications or herbal substances were asked to stop the regimens at least four weeks before participation in the study.

Medication

The study medication was first dispensed during the baseline visit. The subjects were instructed to take two Traumeel® tablets (300 mg each) sublingually at 8:00 AM, noon, and 5:00 PM every day, for a total of 28 days. A research coordinator reminded each subject to take the medication at the designated times. Subjects were instructed to take the medication at least 10 minutes before eating or drinking. The usual therapeutic dose of Traumeel® is one tablet three times per day. The number of tablets given to the subject was compared with the remaining tablets to assess compliance. Each subject's daily log was inspected to evaluate compliance. No concomitant medications were allowed.

Assessments

The first visit to the study center was the baseline screening visit, during which each subject's medical history was taken, including history of cardiovascular; head, eyes, ears, nose, and throat; pulmonary; gastrointestinal; endocrine; musculoskeletal; neurologic; renal; hepatic; and psychiatric diseases. A history was also taken of allergic reactions, past alcohol and drug abuse, and current medications. A physical examination with vital signs was performed at baseline and post-treatment. A serum sample to determine prothrombin time (PT), partial thromboplastin time (PTT), complete blood cell count, liver and kidney profile, and clinical chemistry, and a stool sample to test for occult blood were collected during this visit. A urine pregnancy test was also administered to all female subjects. At this first visit, informed consent was discussed and signed.

Participants were required to fast for eight hours prior to each visit after 7, 14, 21, and 28 days had passed for individual weekly follow-up. During the subsequent follow-up visits, serum and stool samples were collected to evaluate any physiological changes due to ingestion of the study medication. The following measurements were performed: blood pressure (systolic and diastolic), heart rate measurements in sitting position, respiratory frequency, oral body temperature. Laboratory analyses were performed at the University of New Mexico Hospital Laboratory, 2211 Lomas Boulevard NE, Albuquerque, NM 87131. Hemoglobin, hematocrit, red blood cells, white blood cells with differential count, neutrophils and platelet counts were measured at baseline and each follow-up visit. Creatinine, fasting glucose, sodium, potassium, albumin, γ-glutamyltransferase, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, total bilirubin, and direct bilirubin measurements were also performed at baseline and each follow-up visit. Analyses of PT and PTT were performed at baseline, week 2, and the final visit.

Each subject's daily log was evaluated for occurrence of adverse events and study drug compliance. During the final visit, a physical examination recheck was performed on each subject. There were no dropouts or premature terminations of subject participation in the study.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>Post-treatment</th>
<th>t Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hematocrit, %</td>
<td>42.8±3.3</td>
<td>42.7±3.2</td>
<td>0.19</td>
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<tr>
<td>Hemoglobin, g/dL</td>
<td>13.9±2.6</td>
<td>14.3±1.3</td>
<td>0.92</td>
</tr>
<tr>
<td>Neutrophils, x109/L</td>
<td>3.56±1.1</td>
<td>3.68±1.4</td>
<td>0.52</td>
</tr>
<tr>
<td>Platelets, x109/L</td>
<td>259.9±50.2</td>
<td>255.4±44.7</td>
<td>0.99</td>
</tr>
<tr>
<td>Red blood cells, x1012/L</td>
<td>4.98±0.44</td>
<td>4.92±0.47</td>
<td>1.83</td>
</tr>
<tr>
<td>White blood cells, x109/L</td>
<td>5.9±1.3</td>
<td>5.0±1.5</td>
<td>0.94</td>
</tr>
</tbody>
</table>

*All data are presented as mean ± SD.

Table 1: Hematological Laboratory Measurements at Baseline and Post-treatment

Adverse Events

Adverse events included all disturbances of general health status, subjective and objective disease symptoms (including relevant changes of laboratory values), intercurrent diseases, observed in the context of the trial irrespective of a possible causal relationship with administration of the study drug. Each subject reported adverse events in the daily diary provided by the investigator. Interim analysis was made at 7, 14, and 21 days by examination of the patient diary.

Regardless of causal relationship, all adverse events reported by subjects or observed by the investigator were recorded on the Adverse Events Data Sheet. Severity of the adverse event was ranked on a scale from 1 to 4: 1=mild; 2=moderate; 3=severe; and 4=life-threatening. Relationship of each adverse event to the ingestion of the study drug was ranked on a scale from 1 to 5: 1=unrelated; 2=remote; 3=possible; 4=probable; and 5=related. Action taken to relieve the adverse event was categorized from 1 to 4: 1=no action taken; 2=discontinued drug; 3=treatment required; and 4=hospitalization required. Finally, the outcome of the adverse event was ranked as 1=event resolved or 2=event or reaction continues. Had any serious adverse events occurred they would have been reported immediately by the primary investigator to the Scientific Department of HEEL Inc., the manufacturer of the drug.

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The purpose of this research was to evaluate the clinical safety of Traumeel®, measured in conjunction with vital signs. All subjects' vital signs remained stable throughout the study.

### Laboratory Values

The hematological laboratory values measured at baseline and post-treatment are compared in Table 1. The clinical chemistry laboratory values measured at baseline and post-treatment are compared in Table 2. Analysis of PT and PTT revealed no significant differences from baseline to post-treatment in all subjects (t19=1.18; P>0.05). Stool samples were negative for occult blood throughout the study for all subjects.

### Adverse Events

A total of 11 subjects of 20 reported 36 adverse events after ingestion of the study medication. Headache was the most commonly reported adverse event (n=15). Other common events included diarrhea, stomach discomfort/bloating (n=6), feelings of nausea and perceptions of "feeling buzzed" (n=2). The least frequently reported adverse events (n=1) were right arm pain, puffy eyelids, insomnia, thigh pain, and dizziness.

All these events were considered to be mild (n=30; 83.3%) or moderate (n=6; 16.7%) in severity. No action was taken to relieve these symptoms. Also, every adverse event experienced by the 11 study participants was transient and resolved despite continuation of the study drug. The majority (n=22; 61%) of adverse events were considered to be remotely related to the study medication, while 33% of the events (n=2) were considered to be possibly related to the study medication. Only 2 cases (6%) were completely unrelated to the study drug. No adverse event was considered probably or definitely related to ingestion of the study medication.

### Comment

The purpose of this research was to evaluate the clinical safety of Traumeel®,

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**Table 2: Clinical Chemistry Results at Baseline and Post-treatment**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>Post-treatment</th>
<th>t Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin, g/dL</td>
<td>4.05±0.22</td>
<td>4.06±0.25</td>
<td>0.18</td>
</tr>
<tr>
<td>Alkaline Phosphatase, U/L</td>
<td>61.8±15.2</td>
<td>64.0±14.6</td>
<td>0.79</td>
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<tr>
<td>Aspartate transaminase, U/L</td>
<td>29.7±8.4</td>
<td>31.4±9.6</td>
<td>0.94</td>
</tr>
<tr>
<td>Alanine transaminase, U/L</td>
<td>21.3±8.3</td>
<td>24.6±11.9</td>
<td>1.68</td>
</tr>
<tr>
<td>Calcium, mg/dL</td>
<td>9.04±0.24</td>
<td>9.12±0.27</td>
<td>1.22</td>
</tr>
<tr>
<td>Creatinine, mg/dL</td>
<td>0.895±0.16</td>
<td>0.910±0.14</td>
<td>0.77</td>
</tr>
<tr>
<td>Direct bilirubin, mg/dL</td>
<td>0.20±0.0</td>
<td>0.20±0.0</td>
<td></td>
</tr>
<tr>
<td>Total bilirubin, mg/dL</td>
<td>0.96±0.41</td>
<td>0.88±0.30</td>
<td>1.36</td>
</tr>
<tr>
<td>Gastrin, pg/mL</td>
<td>50.2±22.4</td>
<td>67.5±45.7</td>
<td>1.81</td>
</tr>
<tr>
<td>Uric acid, mg/dL</td>
<td>32.2±18.1</td>
<td>34.7±27.4</td>
<td>0.98</td>
</tr>
<tr>
<td>Glucose, mg/dL</td>
<td>88.2±12.6</td>
<td>87.2±8.6</td>
<td>0.33</td>
</tr>
<tr>
<td>Potassium, mmol/L</td>
<td>4.05±0.25</td>
<td>4.00±0.20</td>
<td>0.71</td>
</tr>
<tr>
<td>Magnesium, mg/dL</td>
<td>2.0±0.14</td>
<td>2.9±3.9</td>
<td>1.02</td>
</tr>
<tr>
<td>Sodium, mmol/L</td>
<td>140.4±1.8</td>
<td>140.3±1.5</td>
<td>0.48</td>
</tr>
<tr>
<td>Phosphorus, mg/dL</td>
<td>4.6±6.3</td>
<td>3.2±0.58</td>
<td>0.89</td>
</tr>
<tr>
<td>Uric acid, mg/dL</td>
<td>4.8±1.1</td>
<td>5.0±1.5</td>
<td>1.28</td>
</tr>
</tbody>
</table>

*All values are presented as mean ± SD. Ellipses indicate t test was not conducted to evaluate changes.*

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**Statistical Analysis**

The independent variable was treatment by the study drug taken over the course of 28 days. The dependent variables were the laboratory test variables, adverse events, severity of adverse events, relationship of adverse events to administration of the study drug, action taken to resolve the event, and outcome of the adverse events. The study conditions were standardized throughout the group. The sample size (n=20) was decided by the sponsor, Heel Inc., 11600 Cochiti Road SE, Albuquerque, NM 87123. The study was a within-subjects design and was not blinded.

All adverse events were listed together with information on onset, duration, severity, relationship to drug, and outcome. Frequency statistics were run to evaluate the frequency of adverse events, their severity, their relationship to study medication, any action taken to resolve them, and the outcomes of the events. A paired samples t test was used to evaluate changes that occurred in the physiological variables from baseline to post-treatment. The biometrical evaluation was performed using a personal computer with the SPSS statistical software package (SPSS Inc, Chicago, IL). The study conformed to the principles of the Declaration of Helsinki as well as with German drug law and the requirements thereof.

**RESULTS**

According to the trial protocol, all subjects were placed into the treatment group and received Traumeel® tablets sublingually three times per day for 28 days. Vital signs were monitored weekly throughout the study. Blood pressure, respiratory rate, heart rate, body temperature, weight, and height were also...
an investigational homeopathic anti-inflammatory analgesic. All the events experienced by the subjects were reported as being mild to moderate in severity, unrelated to possibly related to ingestion of the study medication, and subsequently resolved without intervention despite continuation of the drug.

In conclusion, with respect to the data, the use of Traumeel® was very well tolerated by participants in this study. No severe toxic effects were observed and there was no evidence of gastrointestinal bleeding. Conventional non-steroidal anti-inflammatory drugs cause gastrointestinal ulceration and bleeding in some patients and are especially hazardous for patients with diseases or taking medications that interfere with normal coagulation. Traumeel® has anti-inflammatory and analgesic effects and does not inhibit the arachidonic acid pathway of prostaglandin synthesis. It deserves consideration as a safer alternative for these patients.

Reference


[Acknowledgements. This study was sponsored by Heel GmbH and Heel Inc. with the assistance of Dr. M. Weiser and Dr. R.T. Clément and monitored by Dr. David Riley.]

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Press Release

Centennial Celebration Honors Complementary Medicine

The American Institute of Homeopathy is planning a gala rededication celebration of the Hahnemann Memorial, one of Washington, D.C.'s most unique monuments. Originally dedicated in 1900, the Hahnemann Memorial commemorates Dr. Samuel Hahnemann, the physician founder of homeopathic medicine. It is the only monument in the nation's capital dedicated to a medical doctor. The centennial rededication by the American Institute of Homeopathy (AIH) is the public highlight of a 4-day scientific celebration of homeopathy as a contemporary cornerstone of complementary health care in the U.S.

The AIH is the oldest national medical association in the United States. Founded in 1844, the AIH membership is comprised of medical doctors, dentists, osteopathic physicians, and other medical professionals practicing homeopathy. The AIH originally dedicated the Hahnemann Memorial on June 21st 1900, presenting the monument as a gift to the citizens of the United States. President McKinley, cabinet members, prominent homeopathic physicians, and thousands of members of Washington society attended the dedication of this impressive memorial to Dr. Hahnemann and his work.

"Homeopathy is reemerging in the United States as an important component in alternative and complementary health care. Growing public knowledge and interest and an increase in homeopathic medical research is driving physicians' interest in rediscovering homeopathy as a specialty field of practice," says Dr. Sandra Chase, president of the AIH. "This wonderful event emphasizes the important role that homeopathy, alternative and complementary medicine have played in American history and the continued evolution of medical practice in the United States."

The rededication ceremony will be on the 100th anniversary of the unveiling of the monument, June 21st 2000 at 3:00 p.m., at the Hahnemann Memorial, located at Scott Circle, Washington, D.C. Prominent members of the homeopathic medical community, international leaders in homeopathy and alternative medicine, personnel of the National Institutes of Health, as well as members of the press and public have been invited to participate in this milestone event. Member companies of the American Association of Homeopathic Pharmacists who have been helping to support the rededication celebration will also be represented.

In conjunction with the rededication, a Medical and Research Conference will be sponsored by the AIH. The conference will include reports on clinical studies, research, the role of homeopathy in all areas of health care, homeopathic pharmacy, education, and political issues surrounding complementary health care topics. The Wyndham Hotel, the site of the conference, is located across the street from the Hahnemann Memorial at 1400 N. St. NW, Washington, D.C. The conference will conclude with a gala dinner and dance celebration Saturday, June 22nd. For more information on this event, the Journal of the American Institute of Homeopathy, or their educational programs, contact the American Institute of Homeopathy at 703-246-9501, or visit their website at www.homeopathyusa.org.