

# Dietary supplement based on six plant extracts in osteoarthritis treatment

Clinic for Rheumatology and Rehabilitation, Poznan University of Medical Sciences

## Study background

The authors investigated a dietary supplement specially designed for people with joint problems. It has a unique formula of specially selected plant extracts received by way of a patented extraction technology that ensures high potency of active ingredients and their targeted effect. This dietary supplement provides in a capsule a unique complex of six plant extracts - Angelica root, Astragalus root, Broccoli sprout, German chamomile, Lemon fruit and Pineapple fruit - that have a beneficial effect on synoviocytes (cells of the synovial membrane<sup>1</sup>) and chondrocytes (cells that produce and maintain the cartilaginous matrix). Average dosage two capsules a day. People with a high body weight (BMI<sup>2</sup> ≥30) double the dose. The aim of the study was the evaluation of the efficacy and tolerance of these six plant extracts by osteoarthritis<sup>3</sup> (OA) patients.

## Group and method

Sixty patients with osteoarthritis stage II/III according to Kellgren-Lawrence<sup>4</sup> OA criteria were qualified for the study. The study was conducted as a double blind test. All subjects were divided into two parallel and randomized<sup>5</sup> groups. After a one week wash-out period<sup>6</sup>, one group received the preparation being investigated - the *verum* group and the other a *placebo*<sup>7</sup> for 6 weeks. The patients were investigated before the study and after 3 and 6 weeks. The following parameters were evaluated: general well-being by Likert scale<sup>8</sup>, quality of life by SF-12 questionnaire<sup>9</sup>, pain intensity experienced within last 24 hours before examination and pain intensity after a 15 meters walk was evaluated by visual

<sup>1</sup> Synovial membrane (or *synovium*) is the soft tissue lining the inside of joint capsule. This membrane also provides the synovial fluid that lubricates joint surfaces and nourishes cartilages.

<sup>2</sup> Body Mass Index = body mass in kg divided by the square of body height in meters. One of the most common criteria used to assess how much an individual's body weight departs from what is a normal or desirable value.

<sup>3</sup> Osteoarthritis (OA) also known as degenerative joint disease, is a group of mechanical abnormalities involving degradation of joints, including articular cartilage and subchondral bone. Symptoms may include joint pain, tenderness, stiffness, locking, and sometimes an effusion.

<sup>4</sup> Kellgren-Lawrence criteria is radiological grading of osteoarthritis. Stage II – small changes: distinct osteophytes, joint space not changed or slightly narrowed; stage III – medium changes: moderate osteophytes, distinct joint space narrowing, possible joint deformation.

<sup>5</sup> Randomization - selecting or dividing a random sample of a population (important in statistical sampling).

<sup>6</sup> Wash-out period - a run-in period when treatments that participants were using before entering the clinical trial are discontinued in order not to influence investigation.

<sup>7</sup> Placebo - in medical research, a placebo is given as control treatments and depends on the use of measured deception. The Placebo looks exactly the same as the medicine tested however, it is inactive. Sometimes patients given a placebo treatment will have a perceived or actual improvement in a medical condition, a phenomenon commonly called the placebo effect.

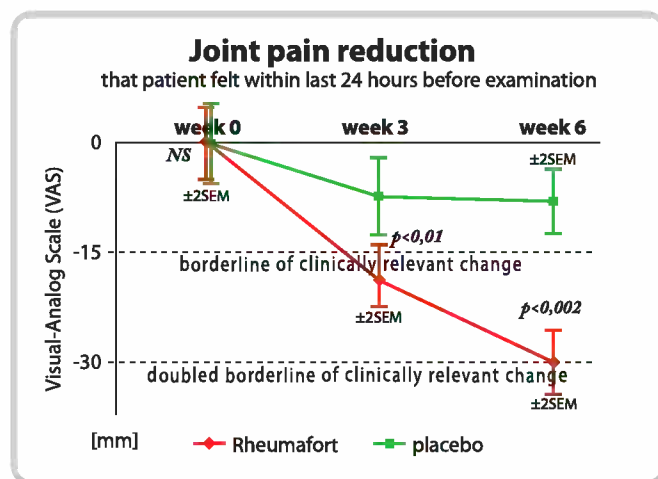
<sup>8</sup> Likert scale, named after Dr. Rensis Likert, a sociologist at the University of Michigan, five grade psychometric scale: 0 = None, 1 = Slight, 2 = Moderate, 3 = Very, 4 = Extremely. Patient chose this option that corresponds with his well-being most.

<sup>9</sup> SF-12 questionnaire is selected part of SF-36 questionnaire used for quality of life survey related to the physical activity.

analog scale<sup>10</sup> (VAS). Intensity of pain, stiffness and joint function was evaluated by integrated WOMAC index<sup>11</sup>. Patients that interrupted (dropped) the study were investigated to the moment they interrupted. All side and adverse effects reported by patients were registered. Lab tests evaluated liver and kidney function and basic biochemical blood parameters. The statistical analysis was carried out by use of nonparametric Mann-Whitney U-test<sup>12</sup>.

## Results

In the group receiving the placebo the reduction of pain intensity<sup>13</sup> that the patient experienced within the last 24 hours before examination was 7 mm and 8 mm on average after 3 and 6 weeks respectively. And pain intensity reduction in the group receiving the investigated preparation containing plant extracts (Rheumafort) was 18 and 30 mm after 3 and 6 weeks respectively. The reduction of pain intensity was statistically highly significant in the Rheumafort group; confidence level  $p < 0.05$  after 3 weeks and  $p < 0.002$  after 6 weeks. It is accepted that the change of 15 mm and more in VAS has a clinical importance. The pain intensity reduction by 30 mm and more (so twice as much as taken as clinically relevant) was found in up to 79% of patients in the Rheumafort group after 6 weeks.



The reduction in pain intensity after a 15 meters walk in the Rheumafort group as compared to the placebo group has also been found to be statistically highly significant. The mean value of pain intensity in the Rheumafort group decreased by 40 mm and in the control group by 6 mm only. A reduction of pain intensity by 30 mm or more (so twice as much as taken as clinically relevant) has been

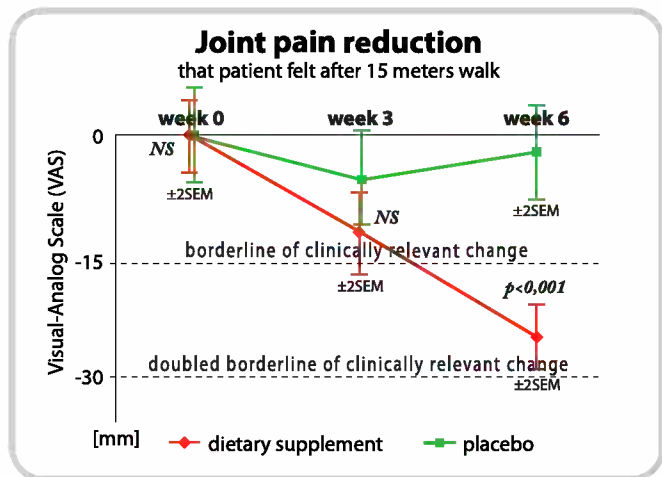
<sup>10</sup> There are many tools to assess pain intensity. The most popular is Visual Analogue Score (VAS). Using ruler 100 mm define once pain intensity where 0 means no pain and 100 the most intense pain one can image.

<sup>11</sup> WOMAC index (Western Ontario and McMaster Osteoarthritis Index) is a widely used measure of symptoms and physical disability in osteoarthritis. The WOMAC evaluates 3 dimensions: pain, stiffness, and physical function with 5, 2, and 17 questions, respectively.

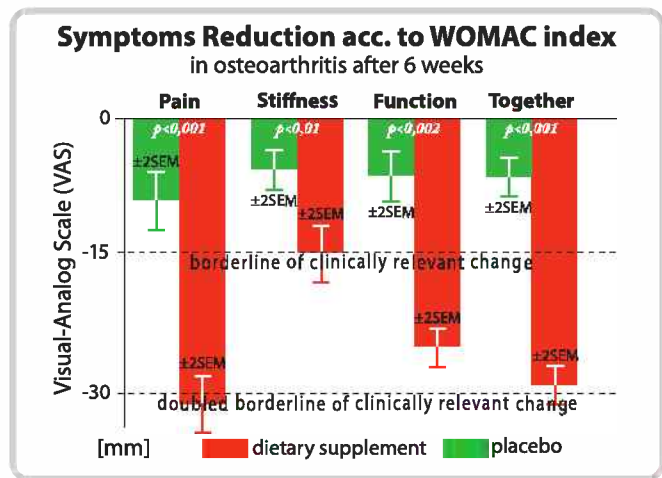
<sup>12</sup> The Mann-Whitney U test (also called the Mann-Whitney-Wilcoxon (MWW) or Wilcoxon rank-sum test) is a non-parametric statistical hypothesis test for assessing whether one of two samples of independent observations tends to have larger values than the other. It is one of the most well-known non-parametric significance tests used for small groups of variables or/and not normal distribution of variables, particularly.

<sup>13</sup> In a properly performed study evaluating a subjective factor like pain sensation it is almost always seen a certain improvement effect after placebo administration. It is called "placebo effect". The lack of this "placebo effect" suggests methodological error of a study.

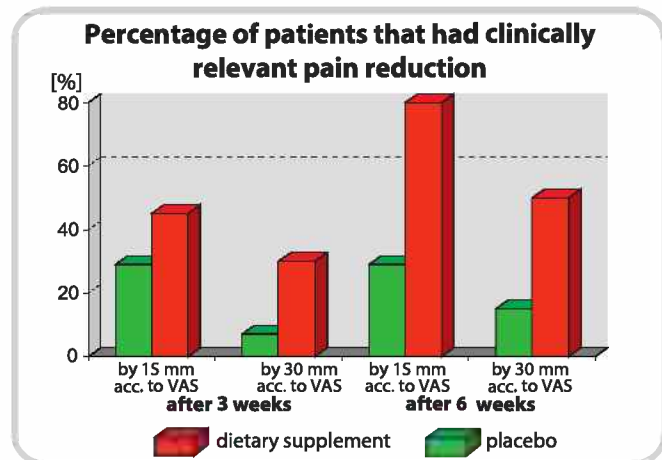
observed in 86 % of patients in the *verum* group. The pain intensity reduction was statistically highly significant in the group receiving plant extracts; confidence level  $p < 0.02$  after 3 weeks and  $p < 0.001$  after 6 weeks. The results are presented graphically on hereinafter presented graph.



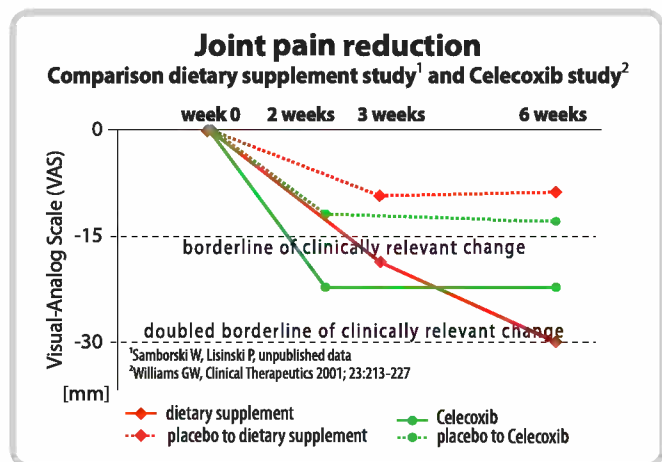
Changes in the integrated WOMAC index (including pain, stiffness, function) showed a statistically highly significant reduction of osteoarthritis symptoms in the group receiving plant extracts after 6 weeks of treatment as compared to the control group receiving the placebo ( $p < 0.001$ ). The average reduction of the three symptoms (pain, stiffness, function) together in the *verum* group (receiving investigated dietary supplement) was 23 mm and in the placebo group only 5 mm. Pain reduction in the group receiving plant extracts was 28 mm, stiffness reduction was 14 mm, joint function improvement was 22 mm. In comparison, in the placebo group these symptoms decreased by 9 mm, 4 mm and 5 mm, respectively.



Over eighty percent of patients had experienced clinically important pain reduction (15 mm and more on VAS scale) after 6 weeks of investigated dietary supplement treatment. And the double clinically relevant pain reduction (30 mm and more in VAS scale) was found in 55% of patients. These findings have been presented in graphically hereinafter.



We have compared Rheumafort to selective cyclooxygenase 2 inhibitor (COX-II) Rx<sup>14</sup> medicine Celecoxib. Both preparations have been evaluated in a similar way, however Celecoxib was evaluated<sup>15</sup> after 2 and 6 weeks and Rheumafort after 3 and 6 weeks. This comparison (presented graphically below) has shown a similar effect of Rheumafort and Celecoxib on pain reduction in osteoarthritis patients - see the graph below.



#### Conclusions

1. Supplementing the daily diet with the investigated dietary supplement shows a clinically significant beneficial effect in osteoarthritis patients.
2. Administration of investigated dietary supplement, containing complex of six plant extracts, leads to joint functional improvement in osteoarthritis (assessed by WOMAC index) and a reduction in disease related symptoms (pain and stiffness).
3. Treatment of investigated dietary supplement improves the quality of life of patients with osteoarthritis.
4. There were no side nor adverse effects related to investigated dietary supplement treatment observed within the 6 weeks of the study course.

<sup>14</sup> Rx is a symbol meaning prescription. This symbol originated in medieval manuscripts as an abbreviation of the Late Latin verb *recipe*, the imperative form of *recipere* or "to take".

<sup>15</sup> Williams GW, Hubbard RC, Yu, SS, et al. Comparison of once-daily and twice-daily administration of Celecoxib for the treatment of osteoarthritis of the Knee. Clinical Therapeutics 2001; 23: 213-227