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# The Effects of a Standardized Herbal Remedy Made from a Subtype of *Rosa canina* in Patients with Osteoarthritis: A Double-Blind, Randomized, Placebo-Controlled Clinical Trial

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## ABSTRACT

***Background:*** A standardized rose-hip powder produced from the seeds and husks of fruit from a subtype of *Rosa canina* has been reported to inhibit leukocyte functions that cause cell injury in osteoarthritis.

***Objective:*** The aim of this study was to assess the impact of standardized rose-hip powder on mobility of the hip and knee joints, activities of daily living, quality of life, and pain in patients with osteoarthritis.

***Methods:*** Patients with a diagnosis of osteoarthritis of either the hip or knee, verified on radiography, participated in this randomized, placebo-controlled, double-blind study. Half of the patients were given five 0.5-g capsules of standardized rose-hip powder twice daily for 4 months, and the other half received identical placebo capsules twice daily for the same period. Mobility of the hip or knee was measured in both groups after the initial screening and again after 4 months of therapy.

***Results:*** One hundred patients (65 women, 35 men; mean [SD] age, 65.2 [11.1] years) were divided into 2 treatment groups of 50 patients each. Hip joint mobility improved significantly in the treatment group compared with the placebo group ($P = 0.033$). Similarly, pain decreased significantly in the treatment group compared with the placebo group ($P = 0.035$). Two patients (4%) from each group withdrew during the early stages of the trial for reasons not related to treatment.

***Conclusions:*** In this study population, standardized rose-hip powder reduced symptoms of osteoarthritis, as 64.6% of patients reported at least some reduction of pain while receiving treatment. Standardized rose-hip powder may improve hip flexion and reduce pain in patients with osteoarthritis. (*Curr Ther Res Clin Exp.* 2003;64:21–31) Copyright © 2003 Excerpta Medica, Inc.

***Key words:*** osteoarthritis, stiffness, pain, rose-hip powder, *Rosa canina*.

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## INTRODUCTION

During the past decade, the commonly used drugs for osteoarthritic pain were aspirin, other nonsteroidal anti-inflammatory drugs (NSAIDs), and corticosteroids.[1] However, side effects have been associated with prolonged use of these drugs. During the past 5 years, selective inhibitors of cyclooxygenase-2 (an enzyme involved in the synthesis of proinflammatory cytokines) have shown promising analgesic and anti-inflammatory actions without serious adverse effects.[2] However, these drugs are expensive, and the need remains for a low-cost, safe remedy for long-term treatment of osteoarthritis.

As a possible alternative, a standardized rose-hip powder* made from the seeds and husks of fruit from a subtype of *Rosa canina* is available. This powder inhibits leukocyte functions that cause cell injury in osteoarthritis. The plants are grown according to good agricultural practice in standardized fields in Denmark and Sweden. When the fruits are mature, they are harvested and frozen immediately. Selection of optimal fruits for later production of powder is made by a laser technique, and the computerized drying process does not exceed 40°C. The vitamin and mineral content of the powder is controlled.

Uncontrolled exploratory trials[3,4] of this standardized dry rose-hip powder showed analgesic action in patients with osteoarthritis. This finding was evidenced by a mean (SD) decrease in the serum concentration of C-reactive protein from 8.25 (4.9) mg/L before treatment to 6.67 (2.6) mg/L after treatment, and inhibition of polymorphonuclear chemotaxis. These findings were sufficient to encourage the present trial.

The aim of this study was to assess the impact of the standardized rose-hip powder on mobility of the hip and knee joints, activities of daily living (ADLs), quality of life, and pain in patients with osteoarthritis.

## PATIENTS AND METHODS

This was a single-center, double-blind, randomized, placebo-controlled study. All patients had a diagnosis of osteoarthritis of the hip or knee, verified on radiography, within 12 months before the study. Patients with pain for >6 months and who were on a waiting list for either hip or knee surgery, or on a list for final evaluation for surgery, were included. Patients who reported allergy to plant products or who had severe asthma or liver disease were excluded. All patients provided written informed consent to participate, and approval from the ethics committee of the study site (an outpatient clinic in Norway) was obtained.

Patients were randomized in groups of 10 using an independent computerized system. One group was randomized to treatment with five 0.5-g capsules of standardized rose-hip powder twice daily for 4 months. The other group received the same quantity of placebo capsules (identical in appearance, taste, and

*Trademark: Hyben-Vital® (Hyben-Vital International, Tulleboelle, Langeland, Denmark).

smell to the rose-hip powder capsules) for the same time period as the active treatment group.

### Primary Outcome Measures

Mobility of the hip or knee was measured in both groups after the initial screening and again after 4 months of therapy. Mobility measurements included the full range of external and internal rotation of the hip; maximum flexion and extension of the hip and knee measured using a goniometer (Gallus Plesner, Oslo, Norway) during passive movement; and active voluntary rotation, flexion, and extension by the patient. Goniometry can result in some variation if the test is not conducted by the same researcher at each visit. For that reason, all measurements were taken by the same investigator and data given are expressed as the mean of 3 test episodes. The measurements of joint movement are presented in 2 ways: as the numeric measurements taken and also as a *degree of restriction*, calculated by subtracting these measurements from a standard value of 125° for hip flexion, 140° for knee flexion, and 45° for external and internal hip rotation.[5]

### Secondary Outcome Measures

At the start of the trial and again after 1, 2, and 4 months of treatment, patients recorded any difficulties in performing ADLs, such as walking, getting into and out of a car, shopping, and getting up and down from the lavatory. The difficulty was estimated on a visual analog scale ranging from 0 (no difficulty) to 10 (great difficulty).

After 4 months of therapy, patients gave their overall assessment of the effectiveness of the study medication on relief of joint pain using a categoric scale of 0 (no improvement) to 4 (almost total relief of pain). The patients also were asked about relief of pain on a simple yes-or-no questionnaire after 1, 2, and 4 months of treatment.

During the trial, patients were asked to maintain their daily dosage of NSAIDs. Any changes that did occur were to be recorded in a diary. Compliance was estimated by counting the number of capsules returned by patients. Adverse events were recorded on the case-report forms completed at each visit.

### Statistical Analysis

Statistical analysis was performed on an intent-to-treat basis. Results in the 2 groups were compared using the Mann-Whitney test for parallel data. The Wilcoxon signed rank test for matched pairs was used to compare baseline findings with those after 1, 2, and 4 months of treatment in each group separately. The chi-square test was used for the questionnaires. All data are presented as mean (SD). Statistical significance was set at $P < 0.05$.

## RESULTS

One hundred patients (65 women, 35 men; mean [SD] age, 65.2 [11.1] years) were enrolled. The treatment group comprised 34 women and 16 men (mean [SD] age, 65.1 [12.2] years). The placebo group comprised 31 women and 19 men (mean [SD] age, 65.3 [9.9] years). The demographic and osteoarthritic characteristics of the 100 patients entering the study (intent-to-treat population) and of the 96 patients who completed the study (per-protocol population) are shown in Table I. The demographic characteristics and consumption of medicine were similar in the intent-to-treat and per-protocol populations. At baseline, active flexion of the hip, however, was significantly different in the active-treatment group versus the placebo group in both the intent-to-treat and the per-protocol populations. Active external rotation of the hip was significantly different in the active-treatment group compared with the placebo group only in the intent-to-treat population. All passive movements were comparable between groups.

Among the 100 patients, there were 44 hip joints (25 in the treatment group, 19 in the placebo group) and 56 knee joints (25 in the treatment group, 31 in the placebo group) involved in the trial. All patients had experienced osteoarthritic pain for 2 to 12 years.

Four patients (4%) withdrew during the early stages of the trial: 1 woman and 1 man in the placebo group because of cardiac problems and a sore throat, respectively, and 1 woman and 1 man in the treatment group due to the possibility of hip surgery earlier than expected and because of the desire not to continue, respectively. These 4 patients comprised 3 hip joints (1 in the treatment group and 2 in the placebo group) and 1 knee joint (in the treatment group). The baseline demographic characteristics, medication, and osteoarthritic characteristics of the 2 groups were similar, except for range of motion for active hip flexion and active external hip rotation ($P = 0.041$ for treatment group vs placebo group).

### Effects of 4 Months' Treatment on Joint Movement

Patients receiving standardized rose-hip powder showed significant improvements at 4 months in passive hip flexion ($P = 0.003$), external rotation ($P = 0.006$), and internal rotation ($P < 0.001$) (Table II). The placebo group showed a significant improvement in passive hip internal rotation ($P = 0.031$), but not in flexion or external rotation. The between-group comparison at 4 months showed a significant difference in improvement in passive hip flexion ($P = 0.033$), but not in internal or external rotation.

The same patterns of change in joint movement (and in $P$ values) were found when hip flexion and rotation were actively performed by the patients (Table III). However, it should be noted that the baseline values for active hip flexion and active external hip rotation were not identical in the 2 groups (Table I), which makes the interpretation of these results difficult.

**Table I.** Baseline demographic and osteoarthritic characteristics of the study population.

| | Intent-to-Treat Population | | Per-Protocol Population | |
|---|---|---|---|---|
| | Placebo (n = 50) | SRHP (n = 50) | Placebo (n = 48) | SRHP (n = 48) |
| Age, y* | 65.3 (9.9) | 65.1 (12.2) | 65.8 (14.7) | 65.5 (14.2) |
| Sex, no. (%) | | | | |
| Women | 31 (62.0) | 34 (68.0) | 29 (60.4) | 33 (68.8) |
| Men | 19 (38.0) | 16 (32.0) | 19 (39.6) | 15 (31.3) |
| No. (%) of patients with OA of the hip | 19 (38.0) | 25 (50.0) | 17 (35.4) | 24 (50.0) |
| No. (%) of patients with OA of the knee | 31 (62.0) | 25 (50.0) | 31 (64.6) | 24 (50.0) |
| Hip joint movement, deg* | | | | |
| Passive flexion | 111.05 (12.76) | 116.00 (13.92) | 111.47 (13.20) | 115.62 (14.09) |
| Active flexion | 97.63 (15.49) | 105.60 (13.10)† | 97.94 (16.01) | 105.42 (13.34)‡ |
| Passive external rotation | 19.72 (11.56) | 26.40 (9.74) | 20.00 (16.01) | 25.62 (9.13) |
| Active external rotation | 13.06 (10.17) | 20.00 (9.79)§ | 13.44 (10.76) | 19.17 (9.05) |
| Passive internal rotation | 28.61 (11.61) | 28.80 (13.17) | 29.37 (12.09) | 28.75 (13.45) |
| Active internal rotation | 21.39 (10.68) | 21.20 (12.61) | 22.19 (11.10) | 21.04 (12.85) |
| Knee joint movement, deg* | | | | |
| Passive flexion | 128.71 (14.37) | 132.40 (9.14) | 128.71 (14.37) | 132.08 (9.20) |
| Active flexion | 123.55 (14.73) | 124.80 (11.77) | 120.35 (24.95) | 124.58 (11.97) |
| No. (%) of patients taking concomitant medication | | | | |
| None | 15 (30.0) | 11 (22.0) | 14 (29.2) | 10 (20.8) |
| NSAIDs | 20 (40.0) | 24 (48.0) | 19 (39.6) | 23 (47.9) |
| Paracetamol | 12 (24.0) | 14 (28.0) | 12 (25.0) | 14 (29.2) |
| Opioids | 2 (4.0) | 0 (0.0) | 2 (4.2) | 0 (0.0) |
| Asthma medication | 2 (4.0) | 0 (0.0) | 2 (4.2) | 0 (0.0) |
| Antihypertensive | 2 (4.0) | 2 (4.0) | 2 (4.2) | 2 (4.2) |
| Heart disease medication | 5 (10.0) | 3 (6.0) | 5 (10.4) | 3 (6.3) |

SRHP = standardized rose-hip powder; OA = osteoarthritis; NSAIDs = nonsteroidal anti-inflammatory drugs.
*Values are expressed as mean (SD).
†$P = 0.020$ versus placebo.
‡$P = 0.039$ versus placebo.
§$P = 0.041$ versus placebo.

**Table II.** Passive hip joint movements before therapy and after 4 months of treatment with standardized rose-hip powder (SRHP) and placebo.

| Type of Movement | Baseline, deg* | Restriction of Movement, deg | At 4 Months of Therapy, deg* | Improvement, % |
|---|---|---|---|---|
| Flexion | | | | |
| SRHP | 116.00 (13.92) | 9.0 | 119.37 (14.09)†‡ | 40.0 |
| Placebo | 111.05 (12.76) | 13.9 | 112.38 (14.27) | 6.7 |
| External rotation | | | | |
| SRHP | 26.40 (9.74) | 18.6 | 28.96 (8.84)§ | 17.1 |
| Placebo | 19.72 (11.56) | 25.3 | 22.50 (11.40) | 10.0 |
| Internal rotation | | | | |
| SRHP | 28.80 (13.17) | 16.2 | 34.38 (13.41)‖ | 35.0 |
| Placebo | 28.68 (11.61) | 16.4 | 33.13 (12.09)¶ | 24.0 |

*Values are expressed as mean (SD).
†$P = 0.003$ versus pretreatment.
‡$P = 0.033$ versus placebo.
§$P = 0.006$ versus pretreatment.
‖$P < 0.001$ versus pretreatment.
¶$P = 0.031$ versus pretreatment.

Changes in passive flexion of the knee did not differ significantly between the 2 groups (data not shown). Active treatment resulted in a mean (SD) improvement of 2.71° (4.42°) ($P = 0.012$); this value improvement was 3.75° (5.32°) in the placebo group ($P = 0.005$). A similar pattern occurred when flexion was performed actively by the patients at the request of the researcher.

### Activities of Daily Living

Changes in difficulty performing ADLs did not differ significantly between the 2 groups. Significant improvement was observed in the following ADLs in the placebo group after 1 month of treatment: walking down the street ($P < 0.05$), getting into and out of a car ($P = 0.258$), shopping ($P < 0.001$), putting on/taking off stockings ($P = 0.251$), and getting up and down from the lavatory ($P = 0.154$). After 2 months of treatment, the following improvements were observed in the placebo group: walking down the street ($P < 0.05$), getting into and out of a car ($P < 0.001$), putting on/taking off stockings ($P < 0.001$), and getting up and down from the lavatory ($P = 0.274$). These improvements were not found at 4 months of treatment in the placebo group. In contrast, the group treated with the standardized rose-hip powder showed significant changes in the majority of ADL functions after 1 month of treatment, as follows: walking down the street ($P < 0.001$), getting into and out of a car ($P < 0.05$), shopping ($P < 0.001$), putting on/taking off stockings ($P < 0.001$), and getting up and down from the lavatory ($P < 0.05$). After 2 months of treatment, improvement was found in all of these ADLs ($P < 0.001$ for all), and this group continued to show significant

**Table III.** Active hip joint movements made voluntarily by patients before treatment and after 4 months of treatment with standardized rose-hip powder (SRHP) and placebo.

| Type of Movement | Baseline, deg* | Restriction of Movement, deg | At 4 Months of Therapy, deg* | Improvement, % |
|---|---|---|---|---|
| Flexion | | | | |
| SRHP | 105.60 (13.10) | 19.4 | 109.79 (14.71)[†‡] | 22.3 |
| Placebo | 97.63 (15.49) | 27.3 | 102.06 (15.11) | 15.2 |
| External rotation | | | | |
| SRHP | 20.00 (9.79) | 25.0 | 21.87 (9.19)[§] | 10.5 |
| Placebo | 13.06 (10.17) | 31.9 | 15.94 (9.70) | 7.9 |
| Internal rotation | | | | |
| SRHP | 21.20 (12.61) | 23.8 | 24.58 (14.52)[‖] | 14.8 |
| Placebo | 21.39 (10.68) | 23.6 | 25.94 (11.58)[¶] | 16.4 |

*Values are expressed as mean (SD).
[†]$P = 0.002$ versus pretreatment.
[‡]$P = 0.026$ versus placebo.
[§]$P = 0.023$ versus pretreatment.
[‖]$P = 0.010$ versus pretreatment.
[¶]$P = 0.023$ versus pretreatment.

improvement in the majority of ADL performances at month 4 compared with baseline, as follows: walking down the street ($P = 0.038$), getting into and out of a car ($P = 0.054$, borderline significant), shopping ($P = 0.024$), putting on/taking off stockings ($P = 0.019$), and getting up and down from the lavatory ($P = 0.016$).

## Joint Pain

Significantly greater relief of joint pain was found in the group receiving standardized rose-hip powder than in the placebo group after 4 months of treatment ($P = 0.035$; Figure). At month 4, 31 of 48 (64.6%) patients in the active-treatment group reported some effect, ranging up to almost total relief of pain, whereas 17 of 48 (35.4%) patients reported no effect. In the placebo group, 27 (56.3%) patients reported no effect of treatment, whereas 21 (43.8%) patients reported various degrees of improvement. When pain relief was assessed on a yes-or-no basis, significantly more patients in the treatment group compared with the placebo group indicated that they had pain relief at both 1 month ($P = 0.014$) and 4 months ($P = 0.046$) of treatment, but not at 2 months of treatment.

## Compliance, Concomitant Medication, and Tolerability

Compliance was 98% in the treatment group and 97% in the placebo group. Although patients were asked to maintain their daily doses of analgesic therapy throughout the study, in the group receiving the standardized rose-hip powder, 7 (14.6%) patients reduced their consumption of NSAIDs, and none

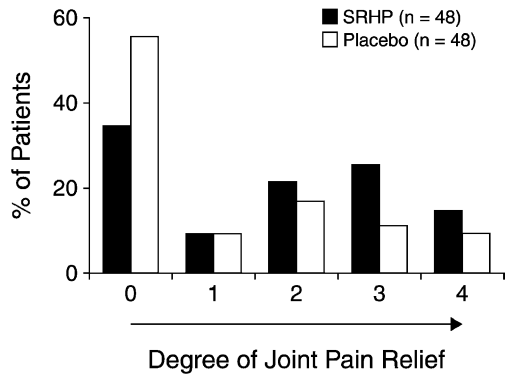


**Figure.** Degree of joint pain relief on a scale from 0 (no impact) to 4 (almost total relief of pain) after 4 months of treatment with standardized rose-hip powder (SRHP) or placebo. $P = 0.035$ for SRHP versus placebo (Mann-Whitney test).

increased it. In contrast, 4 (8.3%) patients in the placebo group decreased their consumption of NSAIDs, and 4 (8.3%) patients increased it. The decrease in NSAID use in the treatment group was statistically significant ($P < 0.016$); however, the between-group difference was not. Three (6.3%) patients in the treatment group and 2 (4.2%) in the placebo group decreased their consumption of paracetamol. In the placebo group, 1 of the 2 (50%) patients taking an opioid drug (tramadol) reduced their consumption of that drug.

The only adverse event reported was mild gastrointestinal discomfort (2 [4.2%] patients in each group).

## DISCUSSION

The aim of this controlled study was to answer the following questions: Does the standardized rose-hip powder improve mobility of the hip and knee joints? Does it reduce the functional disability in performing ADLs that goes with the restricted hip and knee joint movements? Does it relieve pain?

We found that, in the group treated with standardized rose-hip powder, (1) functional capacity of the hip, as assessed by an objective method, was improved; (2) the impact on functional capacity and ADLs, when measured subjectively, was less pronounced; and (3) pain was reduced in approximately two thirds of these patients. This response rate was comparable to that reported for ginger,[6,7] another natural remedy often used by patients with osteoarthritis.

The difference between the effects on objective measures of hip and knee flexion is difficult to explain. The large-scale, controlled trial[8] of avocado/soybean unsaponifiables in 101 instances of osteoarthritis of the hip and 62 of the knee showed a similar, sharp difference between the therapeutic response of the 2 joints. The fact that the hip joint is a ball and socket, whereas the knee joint is more like a modified hinge, does not seem to adequately explain the

difference, and the possibility that the pain is differently mediated in the 2 joints is based on unsupported conjecture.

Pain is the cardinal symptom of osteoarthritis. Due to degeneration of the cartilage and lack of joint stability, small intra-articular traumas do occur. Injuries of this kind are reflected in biochemical responses, some of which involve cytokines.[9] Cytokines have proinflammatory effects that are manifested as episodes of pain, joint swelling, and redness. Our interest in these mechanisms lies in the fact that the standardized rose-hip powder used here inhibits the polymorphonuclear chemotaxis that is a step in the proinflammatory action of various cytokines. This could be the basis of the effects of the standardized rose-hip powder on joint pain.[4] Further support for an anti-inflammatory action of this compound is that the serum concentration of C-reactive protein, a marker for inflammation, decreases significantly during treatment with the compound, as shown by a mean (SD) decrease from 8.25 (4.9) mg/L to 6.67 (2.6) mg/L.[3,4] The basic mechanism of the anti-inflammatory action of standardized rose-hip powder does not reside in a blockade of the cyclooxygenase pathway, as is known to be the case for the anti-inflammatory drugs (aspirin and other NSAIDs) and the herbal remedy ginger.[10,11] This was shown in a study[12] measuring platelet aggregation during treatment with the same standardized rose-hip powder in doses far higher than that used in the present study. In contrast to drugs inhibiting the cyclooxygenase pathway, platelet aggregation was not affected by these high doses. In fact, the powder seems to stabilize cell membranes, as shown by the finding that erythrocytes from individuals treated with the powder, when routinely stored in a blood bank, leak less hemoglobin than expected.[13]

Natural vitamins C and E are present in standardized rose-hip powder. However, it does not seem likely that these vitamins can explain the present findings because vitamin C was not involved in the anti-inflammatory action reported for rose-hip powder,[4] and vitamin E has been reported to be ineffective for symptomatic relief of osteoarthritis.[14] Also, the prevalence of gastrointestinal adverse events was low in the present trial and similar to that of placebo. Moreover, several years of use of the powder in the Scandinavian countries has not disclosed significant data on any adverse events.

Although a significant increase was found in mobility of the hip joint and a significant decrease in pain was found in the majority of patients who received the standardized rose-hip powder, the clinical benefit of 4 months of treatment should not be overestimated. Future research should include long-term studies to evaluate joint mobility, clinical improvements, and consumption of NSAIDs and other types of concomitant pain-reducing medicine. It is also important to find the active ingredient(s) in rose-hip and clarify whether the content of such active ingredient(s) (as well as the content of vitamins and minerals) differ among subtypes, as species of rose-hip can be very different from each other regarding biological activity.[15]

## CONCLUSIONS

In this study population, standardized rose-hip powder reduced symptoms of osteoarthritis, as 64.6% of patients reported at least some reduction of pain while receiving treatment. Standardized rose-hip powder may improve hip flexion and reduce pain in patients with osteoarthritis.

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