Brief Reports are generally shorter than full-length articles and are meant to communicate new data. For consideration in this section, pilot studies, brief evaluations, and reviews should present authoritative information on the integration of complementary and alternative therapies with conventional medical practices.

THE EFFECTIVENESS OF COMMIPHORA MUKUL FOR OSTEOARTHRITIS OF THE KNEE: AN OUTCOMES STUDY

Betsy B. Singh, PhD, Lakshmi C. Mishra, BIMS, PhD, Sivarama Prasad Vinjamury, MD (Ayurveda), Nanette Aquilina, DC, Vijay J. Singh, BA, Neil Shepard, BA

Betsy B. Singh is a professor and dean of research at Southern California University of Health Sciences. Lakshmi C. Mishra is a professor and Ayurvedic practitioner at Southern California University of Health Sciences. Sivarama Prasad Vinjamury is an associate professor and projects coordinator at Southern California University of Health Sciences. Nanette Aquilina was the projects coordinator at the Research Division at the Southern California University of Health Sciences and is now in private practice in New York City. Vijay J. Singh is a research assistant at Southern California University of Health Sciences and a graduate student at Argosy University. Neil Shepard is a program manager at Southern California University of Health Sciences and a graduate student at California State University, Fullerton.

Context • Ayurveda, the traditional system of healthcare in India, has many remedies for Osteoarthritis (OA). One of the ingredients most commonly found in Ayurvedic arthritis formulas is guggul, an oleanolic acid of the herb Commiphora mukul (CM). The authors have conducted both preclinical and clinical investigations of guggul for reduction of pain, stiffness, and improved function, and to determine tolerability in older patients with a diagnosis of OA of the knee.

Methods • The study was conducted using an outcome, quasi-experimental, model. Thirty male and female participants meeting the inclusion/exclusion criteria, with a score of 2 or more on the Kellgren-Lawrence scale for at least 1 knee, were admitted in the study. CM was administered in capsule form (500 mg concentrated exact delivered TID) along with food. The WOMAC Total Score was used as a primary outcome measure. VAS scales, 6-minute walk-test, and WOMAC subscales were used as outcome measures.

Results • At the end of treatment, there was a significant difference in the scores of the primary and secondary outcome measures. On the primary measure, WOMAC total score, participants were significant-by improved (P<0.0001) after taking the supplement for 1 month and continued to improve at the 2-month marker and follow-up. Secondary measures of pain in the VAS format demonstrated participant improvement; however, mood state, and current pain were not significantly different (P<0.05) than baseline until the 2 month assessment (P<0.001).

Conclusions • Overall data indicate significant improvement for participants during the trial in both scales and objective measures used for assessment purposes. There were no side effects reported during the trial. CM appears to be a relatively safe and effective supplement to reduce symptoms of OA.

Osteoarthritis (OA) is a debilitating, slowly progressive and degenerative disease of diarthroial joints affecting men and women as they age. It is the most common form of arthritis affecting approximately 70-80% of the aged population worldwide, and is the second most-common form of disability in the United States. Although it affects both men and women, women are more likely to be symptomatic. In the Western world, OA ranks fourth in health impact among women and eighth among men.

Osteoarthritis of the knee and hip is the most common cause of musculo-skeletal disability in the elderly. Classic symptoms of osteoarthritis, such as joint stiffness and pain, instability, and loss of function affect day-to-day activities such as rising from a chair, climbing stairs, kneeling, standing, walking and maintaining stability. Conventional treatment of OA includes pharmacological, non-pharmacological, and intra-articular methods. While NSAIDS constitute a substantial proportion of pharmacological therapy, non-pharmacological methods generally include physical therapy, muscle-strength exercises, and patient education. Intraarticular injections of hyaluronan or glucocorticoids are given mostly as palliatives. However, all these methods and NSAIDS are potentially toxic with unpleasant and often dangerous side effects. Data from epidemiological studies show that 20-30% of all hospitalizations and deaths...
Among persons age ≥ 65 years due to a peptic ulcer diagnosis were attributable to therapy with NSAIDs. In severe cases of OA, joint replacement surgery is recommended. However this poses risks, particularly in elderly patients, who often have other medical conditions.

Although many advances have been made in understanding the pathophysiology and treatment of this disease, there is no definitive treatment that will stop the progression of the disease, as well as cure it. Hence there appears to be a general need for remedies with good efficacy and a low toxicity in the treatment of OA. In a survey conducted by Eisenberg et al in 1997, 27% of people in the USA who described themselves as suffering from "arthritis" had used some form of complementary and alternative medicine (CAM) in the previous 12 months, and one third of them were seeing a therapist.

Ayurveda, the traditional system of healthcare in India, has been practiced for thousands of years and has many remedies for OA. One of the ingredients most commonly found in Ayurvedic arthritis formulas is guggul, an oleoresin of the herb Commiphora mukul. Several earlier animal studies in India have demonstrated the effectiveness of guggul extract in standard OA models. The authors have conducted both animal and clinical investigations of guggul for OA prior to this study. The goal of this study was to determine the effectiveness of guggul for reduction of pain, stiffness, function, and other symptoms that arise from osteoarthritis. The research design used American College of Rheumatology (ACR) criteria to establish the OA diagnosis, and standardized outcome measures to provide greater rigor in design over earlier clinical trials of guggul.

AYURVEDA

Ayurveda, a combination of the two Sanskrit words ayu (longevity) and ved (knowledge), is the traditional medical system that has been practiced in India for more than 5000 years. It adopts a holistic and systematic approach to treating ailments. Health, according to Ayurveda, is the balance of the physical, mental, social and spiritual well-being of a person, and any break or imbalance in the communication between these components results in disease. Diagnosis of illness in Ayurveda is complex and is based on history, physical examination, pulse, and assessment of the state of the three doshas (humors)—vata, pitta and kapha. The treatment for any disease is focused upon bringing the doshas back to constitutional equilibrium for the patient. These changes are accomplished through lifestyle interventions, spiritual nurturing, and treatment with herbo-mineral formulas.

Osteoarthritis is known as Sandhivata in Ayurveda. It is due to the blockage of the freely moving vata in the joints, which causes pain and swelling. The treatment involves elimination of the blocked vata from the joints through cleansing methods (panchakarma) and then herbs such as Guggul, which are given orally to reduce the pain and swelling. Guggul, an Ayurvedic rasayan (a rejuvenating tonic, which checks degenerative processes in the body), is one of many components of most herbal formulas that have been used in Ayurvedic medicine for the treatment of arthritis, obesity, skin diseases, serious wounds, and inflammation for several thousand years. Forty-two studies of the usefulness of guggul, including works from India, were reviewed by this team, and published in 2000. The anti-inflammatory activity of guggul has been studied in several animal models and by this team in a structured case study of a person with severe OA. These studies support the use of guggul as part of a holistic treatment in inflammatory ailments and arthritis. As guggul is readily available as a single agent in many health food stores and through other venues in the US, it is being investigated as a 'single agent' in this study to evaluate the effectiveness of the product. The purpose of the study was not to evaluate holistic Ayurvedic therapy for OA of the knee. Other studies are being undertaken by this research team to address the issue of pragmatic Ayurvedic care.

METHODS

The analyses presented here were derived from an outcomes, quasi-experimental model implemented to determine if CM concentrated extract (3.5% guggulsterones) 500mg delivered 3 times a day with meals would relieve symptoms of OA of the knee. The trial was also conducted to determine the tolerability of this Ayurvedic rasayan in older patients with a diagnosis of OA of the knee. The study n=30.

Sample Generation

Participants meeting the inclusion/exclusion criteria, which included demographic, health status, and specific OA status, were serially admitted into the study. Community recruitment methods were used, which included announcements at professional meetings, local civic centers, and local newspaper advertisements. Patients who received treatment in the University Clinic system were eligible for screening.

Patients meeting the following inclusion criteria after phone and clinical screening and who signed a University-approved informed consent form were eligible for the study: 1) 50 years or older, 2) knee pain greater than 6 months, 3) knee pain most days of exacerbation; that cause unrelenting pain; that interfere with patient’s ability to perform a walk test, 2) obvious medical or psychological disorders, 3) involvement in litigation, 4) intra-articular corticosteroid injection into the knee(s) within 4 weeks immediately preceding entry to study, 5) Kellgren/Lawrence grade 2 or greater.

Patients who were determined to have one or more of the following during the phone or clinical screen were excluded from the study: 1) serious medical problems (eg, advanced cancer, heart failure, etc; any medical condition in advanced stage/state of exacerbation; that cause unrelenting pain; that interfere with patient’s ability to perform a walk test), 2) obvious medical or psychological disorders, 3) involvement in litigation, 4) intra-articular corticosteroid injection into the knee(s) within 4 weeks immediately preceding entry to study, 5) history or clinical indications of bleeding diathesis (eg, hemophilia, thrombocytopenia, etc), including current use of anti-coagulants (eg Heparin, Warfarin, Coumadin, Miradon), 6) current use of hypertensive and/or cardiac regulatory medication (Diltiazem, Cardizem), or 7) current use of narcotic analgesics.
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Administration of Supplement

The herb Commiphora Mukul, commonly known as guggul, was administered in the form of a capsule (500mg delivered three times daily). Participants were advised to take it along with food to avoid any palatability or reflux problems. Concurrent treatments or medications for problems other than OA were continued throughout the period of study without change.

Data Collection Points

Patient data were collected at baseline, one month, and two months during the treatment period for each participant. Patients were followed for an additional one-month period after treatment was terminated. Baseline data included demographic information, orthopedic exam parameters including a bilateral standing knee x-ray, WOMAC Index, visual analog scale (VAS), total symptom count (TSC), body mass index (BMI), and 6 minute walk. The WOMAC, VAS, TSC, and 6-minute walk data were collected at one- and two-month treatment periods, and at the one-month follow-up.

Results

Data indicate significant improvement for participants during the trial in both scales and objective measures used for assessment purposes. Participants reported a significant improvement by month one, and continued to improve during the second month of treatment. Patients regressed in their improvement slightly during the one-month follow-up, during which time they were not being treated. However, even after not taking the supplement for a month, participants still showed significant improvement over their baseline scores and over their one-month scores while on the supplement for many outcome measures.

All participants were monitored for side effects, including gastrointestinal (GI)-related effects, but none were reported (GI related or other) during the trial. Participants had been asked at the baseline visit to maintain their current level of analgesia support during the two-month trial. However, most participants interpreted the instruction to mean that they were not to increase the dosage. Over-the-counter (OTC) analgesia was not proposed as an outcome measure; however, oral reports by most participants indicated a decrease or complete cessation of OTC support during the treatment period. This result was consistent with other published work in which participants decreased their dosage of analgesic support after beginning guggul therapy. Thus, no secondary adverse events were reported for guggul consumption, nor for the amount of analgesic support participants consumed.

Participant Demographics and Baseline Health Parameters

The sample consisted of 36.7% males and 63.3% females. The age range for females was between 52 and 81, and the male age range was 55 to 85. The mean age of the total sample was 65.24. The minimum duration of OA pain experienced by the participants was one year, and the maximum duration of the ailment was 30 years. The mean duration of the disease for participants was 7.57 years.

The majority of the participants reported some neuro-musculoskeletal symptoms such as tingling in arms, leg pain, or low back pain as a comorbid condition. Interestingly, almost 27 out of 30 had been treated earlier for some GI problem such as heartburn, colitis, or stomach pain. Most females in the sample had undergone treatment for some gynecological problem prior to participation in the study. All participants reported at least one comorbidity upon history and systems...
review, and many of the participants suffered from other conditions that include a pain component. Thus, the test of Commiphora mukul (guggul) was rigorous.

**Clinical Exam Factors: Baseline**

Of the trial participants, 40% ranked a 2, 33.3% ranked a 3, and 20% ranked a 4 for the left knee on the Kellgren-Lawrence scale. For the right knee, 48.3% received a 2, 34.5% received a 3, and 10.3% received a 4. For this scoring system, the higher the number, the more severe the OA rating from radiographic screening. Most participants reported onset type to be traumatic (48.3%), an additional 34.5% reported insidious onset, and the balance attributed their condition to a variety of causes. The knee with the highest Kellgren-Lawrence score was identified as the target knee for study purposes.

**Pain Characteristics: Baseline (Table 1)**

Just over half of patients reported severe stiffness (56.7%), 80% reported bilateral pain, and 40% reported constant pain, with the remaining participants reporting frequent pain episodes. Over 13% were found to have inflammation upon exam, with over 73% demonstrating tenderness on exam. A wide variety of factors were noted to both ameliorate and exacerbate pain (see Table 2). Participants were able to identify more than one type of pain quality; thus, the percentage sum is greater than 100. Ninety percent reported aching, with 50% also reporting sharp pains; and 100% were found to demonstrate crepitus. Twenty percent were found to have varicosities, over 13% had bony enlargements, and 100% were found to have Erythema.

**Effectiveness Data: During Treatment Period and Follow Up (Table 2)**

**WOMAC**

At the end of treatment, there was a significant difference in the scores of the primary outcome measure and the WOMAC total score, as well as the secondary outcome measures (WOMAC subscales, VAS scale, and 6-minute walk test).
Participant change scores across a variety of pain, affective, and functional measures all showed improvement.

The WOMAC total score was significant (p<0.0001) at the end of one month, with continued improvement noted at two months. Similarly, all the WOMAC subscale scores, which include pain, stiffness and function, were significant at the end of one month and at the end of treatment (p<0.0001), except stiffness, which was significant at p<0.001 at the end of two months. At the end of the one-month follow-up, scores for the WOMAC total score remained better than baseline (p<0.005).

**VAS**
A visual analog scale (VAS) assessment was made for current, least, and worst pain, function, and mood state. Current pain was significant at the two-month treatment period (p<0.05), but was not significant at one month. Measures of least and worst pain were significantly improved at both one month (p<0.0001 & 0.005) and two months (p<0.001 & 0.005) during the treatment period. However, these items were not significantly different than baseline scores when compared to scores collected at the one-month follow-up period.

Participant scores for the VAS function question showed significant differences for one-month (p< 0.0001) and two-month (p< 0.0001) measures during treatment. These scores remained significantly different than baseline after one month off the product (p< 0.0001).

**TSC**
In addition, a total symptom count (TSC) was collected. The symptom count was significantly improved after one month (p< 0.0001), and continued to improve through the two-month measurement period during treatment (p< 0.0001). The scores remained significantly better than baseline at the one-month follow-up period (p<0.005).

**6-Minute Walk**
Six-minute walk distance values were recorded in feet and inches. The walk distance was not significantly improved at one month, but was significant at the two-month treatment period.

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### TABLE 2 Outcome Measures: Baseline Through 1st Month In-Person Followup

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>1 Month Exam</th>
<th>2 Month Exam</th>
<th>1 Month Exam</th>
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<td>68.07</td>
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<tr>
<td>Pain</td>
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<td>69.5</td>
<td>66.55</td>
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<td>63.1</td>
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<tr>
<td>Function</td>
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<td>68.47</td>
<td>70.83</td>
<td>67.03</td>
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<td>VAS Current</td>
<td>3.57</td>
<td>3.3</td>
<td>2.4*</td>
<td>3.07</td>
</tr>
<tr>
<td>Least</td>
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<td>2</td>
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<tr>
<td>Worst</td>
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<td>5.2*</td>
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<td>5.45</td>
</tr>
<tr>
<td>Function</td>
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<td>2.9</td>
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<tr>
<td>Mood</td>
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<td>3.37</td>
<td>2.3*</td>
<td>2.34</td>
</tr>
<tr>
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<td>3.3</td>
<td>3.79</td>
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<tr>
<td>Six Minute Walk</td>
<td>1418'3''</td>
<td>1435'6''</td>
<td>1481'9''</td>
<td>1416'6''</td>
</tr>
</tbody>
</table>

**Key**
- *=P ≤ 0.05
- †=P ≤ 0.01
- ‡=P ≤ 0.0005
- §=P ≤ 0.0001
- ||=P ≤ 0.0001
- ¶=Not Significant
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Summary

This outcomes study followed publication of literature reviews, basic science work, and a published, structured case study of a severely impaired patient with OA of the knee treated with CM. These steps were taken to develop a clear picture of the potential safety issues as well as effectiveness of CM.

Participants in this trial scored at least “moderate” on the Kellgren-Lawrence scale, with some participants scoring a 4. Additional information about these participants is given in tables 1 and 2. On the primary measure, WOMAC total score, participants were significantly improved after taking the supplement for one month, and continued to improve at the two-month mark. After supplementation was stopped for a month, participants remained improved over their baseline scores for this measure. WOMAC stiffness and function sub-scores were significantly improved after one month on the supplement, continued to be significant at two months, and remained significantly improved over baseline at follow-up (one month after treatment was completed). The symptom count demonstrated the same pattern of improvement as the WOMAC scores.

Secondary measures of pain in the VAS format demonstrated participant improvement. However, mood state and current pain were not significantly different than baseline until the two-month assessment. Least and worst pain were significant at one-month measurement points and continued to be significant at two months, but had decayed to baseline levels after participants had not taken the supplement for a month. Participant data showed improvement in walk distances by the second month, but patients had decayed to a level slightly less than baseline for the follow-up measure.

Conclusions

All WOMAC scores, total scores and subscores, improved and remained improved during follow-up. Other measures showed a progressive benefit for participants; however, other scales reported decay, which placed the participants in the baseline range one month after ceasing to take the supplement. As there were no side effects reported during the trial or the case study, along with data from case series which are ongoing, the investigators believe that CM is a relatively safe and effective supplement for patients suffering with moderate to severe OA of the knee.

These data encourage the research team to pursue the usefulness of CM for treatment of OA patients in additional clinical studies, including a subsequent double-blind randomized clinical trial (RCT) to remove bias that may not have been eliminated in this intermediate design, which does not call for a control group. However, the team expects to learn much from this trial and to be better able to execute a rigorous RCT as a result.

Additionally, clinical investigations of pragmatic, holistic Ayurvedic therapy are planned. The team has recently completed and published the results of basic science studies of CM and other Ayurvedic rasayans that were conducted in collaboration with investigators at USC.

References