

# Effects of a reduced iso-alpha-acids (RIAA), rosemary extract, and oleanolic acid supplement on pain in subjects with osteoarthritis (OA)

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## ABSTRACT

*Osteoarthritis (OA) is a common affliction that compromises physical function and results in joint pain and defective articular cartilage. Data indicate inflammatory mediators that lead to production of PGE<sub>2</sub> are involved in OA. We have previously shown that a combination of reduced iso-alpha-acids (RIAA), rosemary extract, and oleanolic acid inhibits PGE<sub>2</sub> production in vitro and in ex vivo clinical studies. In the present study, we report our clinical observations of an 8-week, open-label pilot trial using this supplement in OA subjects. A significant 50% decrease in pain by Visual Analog Scale (VAS;  $p < 0.0001$ ) was observed after supplementation with RIAA, rosemary extract, and oleanolic acid. Arthritis symptoms assessed by the Arthritis Impact Measurement Scale (AIMS2) also showed a significant 40% decrease ( $p < 0.0001$ ). These data suggest the RIAA, rosemary extract, and oleanolic acid combination may be beneficial for symptoms control in OA subjects.*

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## INTRODUCTION

Osteoarthritis (OA), the most common form of arthritis in the world, affects 10% to 20% of people over age 60 worldwide, and over 20 million Americans annually.<sup>1,2</sup> OA is characterized by joint pain with defective articular cartilage and joint margin bone structure. Data indicate it involves inflammatory cytokines such as IL-1 $\beta$  and TNF- $\alpha$ , which initiate a vicious cycle of catabolic and degradative events in cartilage.<sup>3,4</sup> These cytokines are also known to induce production of PGE<sub>2</sub> as part of OA inflammation.

We have shown that a combination of reduced iso-alpha acids (RIAA), rosemary extract, and oleanolic

acid inhibits COX-2-specific PGE<sub>2</sub> production in vitro.<sup>5</sup> In previous studies conducted at the Functional Medicine Research Center (FMRC), we have observed corroborating ex vivo data on inhibition of PGE<sub>2</sub> production from serum of subjects after consuming the RIAA, rosemary extract, and oleanolic acid.<sup>6</sup> Since PGE<sub>2</sub> production has been implicated in OA, we performed an 8-week pilot trial to monitor clinical observations with this combination of RIAA, rosemary extract, and oleanolic acid.

## METHODS

The open-label, 8-week observational trial was performed at the FMRC in subjects with diagnosed OA. This study was conducted under IRB and in accordance with the ethical principles of the Declaration of Helsinki. Candidates who agreed to participate signed Informed Consents.

Subjects were initially assessed at screening by questionnaires, physical exam, and laboratories (general chemistry and CBC) for inclusion criteria. Subjects selected for the trial were reassessed at Visit 1 and the combination RIAA, rosemary extract, and oleanolic acid (440 mg per tablet) was begun at a dose of 1 tablet tid. Visit 2 occurred after 4 weeks and subjects were reassessed. If clinically suggested, the dose was changed to 2 tablets bid. Final assessment was performed after a subsequent 4 weeks at Visit 3. During the trial, subjects continued taking their usual medications and supplements.

Pain was monitored using the Visual Analog Scale (VAS), a commonly used research measure in which subjects rate pain on a 10-cm scale at each visit,<sup>7</sup> and the condition-specific, validated Abridged Arthritis Impact Measurement Scale (AIMS2). The AIMS2 has been shown to have test-retest reliability over time in arthritis subjects.<sup>8,9</sup> The MOS Short-Form 36 (SF-36)

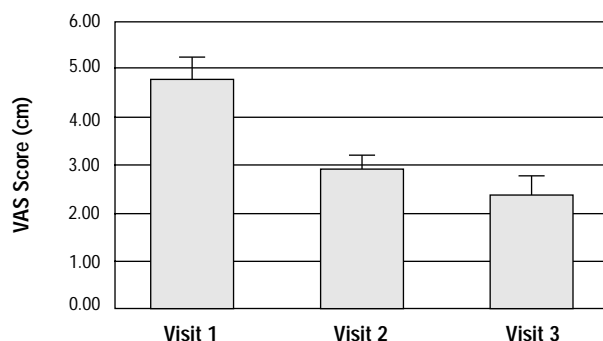
was also used as a general quality-of-life assessment, and has been reported with arthritis subjects.<sup>10</sup>

Data were analyzed by a one-way analysis of variance (ANOVA) on log-transformed data or by standard non-parametric analyses using the JMP Statistical Package (SAS Institute, Cary, NC). Laboratory variance was assessed with multiple split samples. Averages are presented mean  $\pm$  standard error of the mean (sem) unless otherwise noted. Significance was predetermined as  $p < 0.05$ .

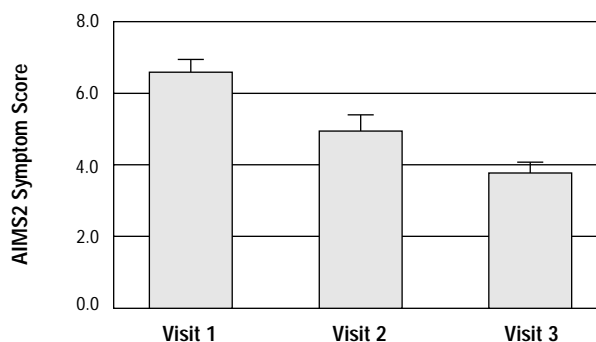
## RESULTS

Thirty-seven OA subjects entered the trial, and 32 OA subjects completed the trial (9 males, 23 females; average age  $55 \pm 8$  years). Subjects were on a dose of 1 tid for the first 4 weeks of the trial, at which time 80% of the subjects were instructed to increase the dose to 2 bid.

A significant 50% decrease in pain was observed by VAS ( $p < 0.0001$ ; Wilcoxon-ranked sums). The majority of decrease occurred between Visit 1 and Visit 2 (Fig. 1), when the dose of all the subjects was 1 tid. The magnitude of change is similar to that reported in a recent efficacy trial with OA subjects, and is greater than the reported placebo group, which showed a decrease of 26% in VAS score after 8 weeks.<sup>7</sup> In the present trial, VAS scores were nearly the same at the screening visit and Visit 1, which occurred a few weeks later (only varying from 4.6 cm to 4.8 cm) indicating stability in the baseline VAS value.



*Figure 1.* Visual Analog Scale (VAS) Score for the 28 OA subjects completing the trial and providing complete questionnaire data. A significant decrease of 50% was observed from before ( $4.8 \pm 0.4$  cm) to 8 weeks after ( $2.4 \pm 0.4$  cm;  $p < 0.0001$ ) supplementation. The trend in pain decrease from Visit 1 to Visit 3 was also significant when assessed by regression analysis ( $p < 0.0001$ ).



*Figure 2.* The abridged Arthritis Impact Measurement Scales (AIMS2) Score for the 28 OA subjects completing the trial and providing complete questionnaires. The AIMS2 Symptoms Scale rates arthritis pain. A significant decrease of 40% was observed from before ( $6.6 \pm 0.3$ ) to 8 weeks after ( $3.8 \pm 0.4$ ;  $p < 0.0001$ ) supplementation. The trend in pain decrease from Visit 1 to Visit 3 was also significant when assessed by regression analysis ( $p < 0.0001$ ).

## CONCLUSION

These data suggest the proprietary RIAA, rosemary extract, and oleanolic supplement promotes decreased pain in subjects with OA.

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## NOTE

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