Journal of Nutrition & Food Sciences
ISSN: 2155-9600

Bloomer et al., J Nutr Food Sci 2019, 9:1
DOI: 10.4172/2155-9600.1000748

Research Article Open Access

Blood MSM Concentrations Following Escalating Dosages of Oral MSM in Men and Women

Richard J Bloomer[1]*, Matthew Butawan[1], Ling Lin[2,3], Dejian Ma[3] and Charles R Yates[3]

[1]*Center for Nutraceutical and Dietary Supplement Research, School of Health Studies, University of Memphis, USA*
[2]*Regenerative Medicine Research Center, West China Hospital, Sichuan University, China*
[3]*Department of Pharmaceutical Sciences, University of Tennessee College of Pharmacy, USA*

Abstract

Background: Methylsulfonylmethane (MSM) is an organosulfur compound used as a dietary supplement. We determined the plasma MSM concentration following four months of oral MSM supplementation at escalating dosages.

Methods: 45 men and women (25 ± 5 years) participated in this study. Subjects were assigned to ingest either 1, 2, or 3 grams of MSM daily for 16 weeks. Blood was collected at baseline and following weeks 4, 8, 12, and 16 and analyzed for plasma MSM concentration using a LC-MS/MS method.

Results: A group ($p<0.0001$), time ($p<0.0001$), and group x time ($p=0.0005$) interaction was noted. Values were higher for the 2 and 3 grams/day group as compared to the 1 gram/day group and were also higher for the 3 grams/day group as compared to the 2 grams/day group ($p<0.05$). Values at weeks 4, 8, 12, and 16 were higher as compared to baseline ($p<0.05$) but no differences were noted between weeks 4-16 ($p>0.05$). With regards to the interaction, at weeks 4, 8, 12, and 16, values were higher for the 3 grams/day group as compared to the 1 gram/day group ($p<0.05$). Although a gender effect was noted ($p=0.01$), with higher overall plasma MSM values in women (1082 ± 1006 μM) as compared to men (845 ± 805 μM), no gender interactions were noted ($p>0.05$).

Conclusion: Both men and women respond to MSM supplementation in a similar manner as related to plasma MSM concentration. A higher dose of supplement results in a greater plasma MSM concentration. Values reach peak concentration within the initial 4 weeks of supplementation and do not increase further during subsequent weeks of treatment.

Keywords: MSM; Plasma; Dosing; Concentration; Dietary supplement

Introduction

Methylsulfonylmethane (MSM) is a commonly used dietary supplement for those seeking relief from joint pain and muscle soreness. One brand, OptiMSM®, manufactured by Bergstrom Nutrition, is a Generally Recognized as Safe (GRAS) dietary ingredient and typically consumed orally at a dosage between 1 and 6 grams daily [1-3]. It has documented success in reducing inflammation associated with knee osteoarthritis [2-5] and in improving aspects of exercise recovery [6-8]. Furthermore, MSM is a recognized treatment for interstitial cystitis [9] and is used as a permeability enhancer for a number of dermatologic agents [10-12]. These broad applications may be partly attributed to its antioxidant properties [13-18] and effects [19,20].

Our recent work has noted that a daily dosage of 3 grams of MSM results in a significant increase in blood MSM after just two weeks of treatment, with a continued rise in blood MSM after four weeks of treatment. Specifically, in a sample of 20 men, all baseline MSM samples but one (0.028 mM) were below the limit of quantification for the assay and serum MSM values increased across time to a mean (± SD) of 1.68 ± 0.60 mM at week 2 and 1.91 ± 0.81 mM at week 4 [21].

What is presently unknown is whether or not a longer time course of treatment with MSM will result in continued elevation in serum MSM and/or if a lower dosage of MSM (e.g., 1 or 2 grams daily) could yield a similar blood MSM concentrations if ingested over a longer period of time (2, 3, or 4 months versus only 1 month as in our prior work). Knowing this information will allow for more specific recommendations to be made concerning MSM dosing. Therefore, the primary purpose of this study was to investigate the impact of different dosages of MSM (1, 2, or 3 grams daily) over a four month period in relation to blood MSM concentrations in men and women. A secondary purpose of this work was to determine if gender differences exist with regards to blood MSM concentration following oral administration.

Materials and Methods

Subjects

Healthy, nonsmokers between the ages 18 and 41 years were recruited by word-of-mouth conversations, formal presentations discussing participation, and recruitment flyers posted on and off campus. A total of 31 men and 16 women initially enrolled in this study. Two subjects (1 male and 1 female) elected to drop out after the first month of supplementation: one due to an unpredictable future work schedule and the other due to a reoccurring illness. All subjects were required to: have a body mass less than 102 kg (225 pounds), not use any sulfur-containing supplement or medication, and not be allergic to sulfur-containing supplements or medications. While our

***Corresponding author:** Richard J. Bloomer, PhD, Center for Nutraceutical and Dietary Supplement Research, School of Health Studies, The University of Memphis, Memphis, TN 38152, USA, Tel: 901-678-5638; Fax: 901-678-3591; E-mail: rbloomer@memphis.edu

Received December 12, 2018; **Accepted** January 28, 2019; **Published** February 09, 2019

Citation: Bloomer RJ, Butawan M, Lin L, Ma D, Yates CR (2019) Blood MSM Concentrations Following Escalating Dosages of Oral MSM in Men and Women. J Nutr Food Sci 9: 748. doi: 10.4172/2155-9600.1000748

prior work included only males, females were included in the present study due to a lack of previous data related to female absorption of MSM and because sulfur metabolism varies across the menstrual cycle [22]. Female subjects were not pregnant, not using oral contraceptives, and reported regular menstrual cycles (27-33 days) over the prior six months.

Health history, medication and dietary supplement usage, and physical activity questionnaires were completed by all subjects and reviewed in detail by an investigator to determine eligibility. Before participation, each subject was informed of all procedures, potential risks, and benefits associated with the study through both verbal and written form. The study procedures were approved by the University of Memphis Institutional Review Board for Human Subjects Research (# PRO-FY2018-26).

Subjects were randomly assigned into one of three groups with equal numbers per group (n=15) with 10 men and 5 women per group. Specifically, subjects were assigned to ingest either 1 gram, 2 grams, or 3 grams of MSM daily for 16 weeks. The MSM was administered as OptiMSM® and was provided by Bergstrom Nutrition (Vancouver, WA). Capsules were provided to subjects in unlabeled bottles every four weeks and subjects were instructed to ingest the capsules in the morning hours each day. Subjects returned their capsule bottles to investigators at the end of each four week period and the remaining capsules were counted to determine compliance to intake. Compliance was calculated as 91% for the 1 gram and 2 gram groups, and 90% for the 3 gram group.

Subjects reported to the lab following an overnight fast and provided a blood sample for analysis of plasma MSM on five occasions: baseline (prior to beginning supplementation) and following weeks 4, 8, 12, and 16 of supplementation. No MSM was ingested on the morning of each lab visit/blood draw. All subjects were instructed to maintain their normal diet and physical activity patterns throughout the 16 week study period. Subjects were asked to record food and drink consumption five days prior to each test visit and refrain from strenuous exercise 24 hours prior to each test visit. Diet logs were analyzed using nutritional software (Food Processor Pro, Esha Research, Salem, OR).

Prior to obtaining the blood sample, subjects voided and then rested quietly while seated in a chair for a period of 10 minutes. Diet logs and capsule bottles were collected. Duplicate measurements of resting heart rate and blood pressure were measured using an automated unit (HEM-907XL; Omron Healthcare, Hoofddorp, Netherlands). Venous blood samples were collected from an antecubital vein into a Vacutainer®. Blood samples were processed in a refrigerated centrifuge (4˚C) in order to obtain plasma. Samples were removed and stored at -70˚C until analyzed using a LC-MS/MS method, as described elsewhere [23].

Data analysis

Values for all variables were calculated using a repeated measures Analysis of Variance. Tukey post-hoc testing was performed as appropriate. Gender was included in the model initially to determine the potential differences between men and women. Gender was subsequently removed from the model for further analysis. Analyses were performed using JMP software (SAS, Cary, NC). Data are presented as mean ± SD. Statistical significance was considered at $p<0.05$.

Results

A total of 45 subjects completed this 16 week intervention study. Data were obtained from all subjects, with the following missing blood samples (subject number-week number): 2-12, 8-4, 9-12, 11-0, 11-4, 11-8, 15-4, 21-8, 21-12, 23-4, 23-12, 25-4, 28-0, 28-4, 28-8, 29-16, 30-12, 36-12, 37-12. This accounts for 10 male and 9 female samples of which 7, 9, and 3 were ingesting either 1, 2, or 3 grams per day, respectively. Moreover, this includes 2, 6, 3, 7, and 1 samples missing from weeks 0, 4, 8, 12, and 16 weeks, respectively. Subject characteristics are presented in Table 1. No differences of statistical significance were noted between groups for any variable ($p>0.05$).

Diet records indicated several group differences ($p<0.05$); however, there were no differences across time and no group x time interactions ($p>0.05$). Table 2 presents dietary data and the respective statistical differences.

A group effect was noted for heart rate ($p=0.002$), with values higher for the 3 grams/day group as compared to the 1 gram and 2 gram groups ($p<0.05$). No differences of statistical significance were noted for systolic or diastolic blood pressure ($p>0.05$). Data for heart rate and blood pressure are presented in Table 3.

With regards to plasma MSM, a group ($p<0.0001$), time ($p<0.0001$), and group x time ($p=0.0005$) interaction was noted. Specifically, values were higher for the 2 and 3 grams/day group as compared to the 1 gram/day group and were also higher for the 3 grams/day group as compared to the 2 grams/day group ($p<0.05$). Values at weeks 4, 8, 12, and 16 were higher as compared to baseline ($p<0.05$) but no differences were noted between weeks 4-16 ($p>0.05$). With regards to the interaction, at weeks 4, 8, 12, and 16, values were higher for the 3 grams/day group as compared to the 1 gram/day group ($p<0.05$). At week 4, values were also higher for the 3 grams/day group as compared to the 2 grams/day group ($p<0.05$). Data for plasma MSM for all subjects are presented in Figure 1. Since values for week 4 for the respective dosages were near identical to weeks 8, 12, and 16, data for week 4 are not shown and are included in our methodology paper [23]. It should be noted that the response curve when including week 4 data is essentialy the same as that shown in Figure 1, with the exception of the additional week 4 time prior to week 8.

When including gender in the model, we noted a gender effect ($p=0.01$). Specifically, higher overall plasma MSM values were observed in women (1082 ± 1006 μM) as compared to men (845 ± 805 μM). The greatest difference between genders occurred with the 2 gram per day

Variable	1 Gram (n=15)	2 Grams (n=15)	3 Grams (n=15)
Age (years)	24.9 ± 5.7	23.3 ± 2.7	25.5 ± 6.0
Height (cm)	175.0 ± 9.1	172.4 ± 11.8	169.1 ± 7.3
Weight (kg)	78.6 ± 12.4	75.8 ± 12.4	71.8 ± 11.1
BMI ($kg \cdot m^{-2}$)	25.6 ± 3.3	25.4 ± 2.6	25.1 ± 3.9
Waist (cm)	83.4 ± 7.5	80.7 ± 6.6	79.3 ± 9.5
Hip (cm)	101.8 ± 4.8	101.5 ± 4.7	98.1 ± 8.1
Waist:Hip Ratio	0.82 ± 1.57	0.80 ± 1.39	0.81 ± 1.17
Heart Rate (bpm)	64.5 ± 9.3	65.9 ± 10.5	71.5 ± 9.9
Systolic Blood Pressure (mm Hg)	122.5 ± 8.4	122.6 ± 12.4	127.0 ± 4.8
Diastolic Blood Pressure (mm Hg)	76.9 ± 9.4	74 ± 9.1	77.9 ± 6.3
Anaerobic Exercise (years)	7.2 ± 7.1	3.9 ± 3.0	4.6 ± 5.4
Anaerobic Exercise ($hr \cdot wk^{-1}$)	3.3 ± 2.3	3.3 ± 2.5	2.9 ± 2.7
Aerobic Exercise (years)	7.0 ± 7.8	8.1 ± 5.9	4.9 ± 5.6
Aerobic Exercise ($hr \cdot wk^{-1}$)	2.6 ± 2.0	3.3 ± 4.8	2.6 ± 2.0

Table 1: Subject characteristics of 45 men and women assigned to MSM for 16 weeks.

No differences of statistical significance noted for any measured variable ($p>0.05$).

Variable	1 Gram	2 Grams	3 Grams
Kilocalories			
Week 0	2321 ± 725	2189 ± 958	1888 ± 442
Week 4	2348 ± 813	2047 ± 717	1837 ± 587
Week 8	2262 ± 751	2032 ± 847	1827 ± 546
Week 12	2337 ± 771	2061 ± 809	1897 ± 493
Week 16	2318 ± 812	2142 ± 866	1884 ± 446
Mean	2317 ± 752	2094 ± 822	1871 ± 495*
Protein (g)			
Week 0	140 ± 87	109 ± 74	88 ± 28
Week 4	134 ± 95	98 ± 55	84 ± 45
Week 8	134 ± 92	110 ± 62	95 ± 58
Week 12	130 ± 93	105 ± 65	95 ± 47
Week 16	138 ± 91	115 ± 74	87 ± 40
Mean	135 ± 89*	107 ± 65	90 ± 44
Carbohydrate (g)			
Week 0	240 ± 64	251 ± 101	217 ± 57
Week 4	247 ± 81	240 ± 78	205 ± 69
Week 8	231 ± 54	222 ± 99	197 ± 60
Week 12	240 ± 80	232 ± 89	210 ± 55
Week 16	240 ± 86	244 ± 83	223 ± 63
Mean	240 ± 72	238 ± 88	211 ± 60*
Fiber (g)			
Week 0	25 ± 9	21 ± 15	20 ± 9
Week 4	26 ± 14	19 ± 12	16 ± 7
Week 8	25 ± 10	18 ± 14	17 ± 7
Week 12	23 ± 10	21 ± 15	19 ± 10
Week 16	25 ± 13	20 ± 14	19 ± 7
Mean	25 ± 11*	20 ± 14	18 ± 8
Sugar (g)			
Week 0	82 ± 40	77 ± 50	67 ± 35
Week 4	80 ± 44	74 ± 49	55 ± 23
Week 8	74 ± 28	64 ± 55	63 ± 29
Week 12	73 ± 44	66 ± 50	73 ± 27
Week 16	82 ± 52	71 ± 48	68 ± 27
Mean	78 ± 41	70 ± 49	66 ± 28
Fat (g)			
Week 0	91 ± 34	79 ± 41	77 ± 20
Week 4	94 ± 39	76 ± 36	74 ± 33
Week 8	92 ± 34	73 ± 34	73 ± 29
Week 12	96 ± 35	75 ± 36	73 ± 29
Week 16	91 ± 37	73 ± 37	73 ± 23
Mean	93 ± 35*	75 ± 36	74 ± 26
Vitamin C (mg)			
Week 0	72 ± 36	67 ± 52	67 ± 65
Week 4	97 ± 63	54 ± 39	56 ± 52
Week 8	83 ± 37	63 ± 49	52 ± 25
Week 12	55 ± 39	77 ± 59	84 ± 112
Week 16	106 ± 117	77 ± 77	51 ± 28
Mean	83 ± 67	67 ± 56	62 ± 63
Vitamin E (mg)			
Week 0	9 ± 5	8 ± 14	5 ± 6
Week 4	8 ± 6	4 ± 5	3 ± 2
Week 8	9 ± 8	6 ± 9	4 ± 2
Week 12	6 ± 5	4 ± 3	4 ± 2
Week 16	8 ± 9	7 ± 9	3 ± 2
Mean	8 ± 7*	6 ± 9	4 ± 3
Vitamin A (RE)			
Week 0	578 ± 427	652 ± 743	362 ± 369
Week 4	792 ± 531	726 ± 689	431 ± 583
Week 8	700 ± 336	576 ± 512	405 ± 233
Week 12	596 ± 446	727 ± 836	572 ± 537
Week 16	654 ± 476	858 ± 1338	492 ± 368
Mean	663 ± 442	708 ± 850*	456 ± 430

Table 2: Dietary data of men and women assigned to MSM for 16 weeks.

Data are mean ± SD.

*Group effects: kilocalories: 3 Grams > 1 Gram (p=0.0011); protein: 1 Gram > 2&3 Grams (p=0.0006); carbohydrates: 3 Grams < 1&2 Grams (p=0.035); fiber: 1 Gram > 2&3 Grams (p=0.002); fat: 1 Gram > 2&3 Grams (p=0.0004); vitamin E: 1 Gram > 3 Grams (p=0.0007); vitamin A: 2 Grams > 3 Grams (p=0.029).

No other statistically significant differences noted (p>0.05).

Variable	1 Gram	2 Grams	3 Grams
Heart rate (bpm)			
Week 0	64.8 ± 11.6[a]	64.9 ± 13.8[b]	70.3 ± 11.9[a, b]
Week 4	69.6 ± 12.3	65.1 ± 15.2[b]	72.1 ± 14.0[b]
Week 8	67.6 ± 13.6	68.3 ± 12.5[b]	74.7 ± 11.7[b]
Week 12	72.0 ± 14.9	66.9 ± 12.6[b]	75.7 ± 15.1[b]
Week 16	69.4 ± 12.8	66.9 ± 13.3[b]	78.3 ± 12.2[b]
Mean	68.6 ± 15.1	66.5 ± 15.2	74.2 ± 15.5
Systolic blood pressure (mm Hg)			
Week 0	123.3 ± 10.8	124.6 ± 11.9	127.3 ± 12.8
Week 4	125.3 ± 10.3	123.7 ± 10.5	125.1 ± 10.9
Week 8	124.9 ± 8.8	126.8 ± 10.6	125.9 ± 10.4
Week 12	127.1 ± 10.1	127.8 ± 12.5	126.3 ± 7.8
Week 16	126.4 ± 12.5	124.5 ± 9.9	124.6 ± 10.9
Mean	125.4 ± 17.8	125.5 ± 10.9	125.8 ± 17.9
Diastolic blood pressure (mm Hg)			
Week 0	72.9 ± 10.6	74.2 ± 9.1	76.5 ± 8.4
Week 4	76.4 ± 10.3	74.3 ± 9.6	75.6 ± 7.0
Week 8	74.3 ± 7.4	75.5 ± 9.2	77.7 ± 8.7
Week 12	76.3 ± 10.6	75.7 ± 8.2	76.6 ±7.4
Week 16	73.7 ± 6.6	73.7 ± 6.8	75.9 ± 6.8
Mean	74.7 ± 12.5	74.7 ± 8.4	76.4 ± 11.6

Table 3: Heart rate and blood pressure data of men and women assigned to MSM for 16 weeks.

Data are mean ± SD.

*Group effect for heart rate (p=0.002); values higher for the 3 grams/day group as compared to the 1 gram and 2 gram groups (p<0.05); values sharing the same superscript letters are different from one another when compared at the respective time (i.e., week #)

No other statistically significant differences noted (p>0.05).

dosage. No gender interactions were noted: gender x group (p=0.32), gender x time (p=0.71), and gender x group x time (p=0.99). Data for plasma MSM, separated by gender, are presented in Figure 2.

Discussion

We evaluated plasma MSM concentrations in men and women following 16 weeks of oral MSM supplementation at dosages of 1, 2, or 3 grams daily. Our main findings are as follows: 1) baseline plasma MSM concentrations are in the very low micromolar range as measured via LC-MS/MS; 2) plasma MSM concentrations reach a dose-dependent steady-state by week 4 and are maintained through week 16 with continuous supplementation; 3) the steady-state plasma MSM concentrations increased linearly with increasing dosages; 4) women had higher overall plasma MSM concentrations than men but values

displayed a very similar pattern across time and dependent upon dose. The results presented here are near identical to previously reported pharmacokinetic data, in that baseline MSM values were in the low micromolar range [21,24,25] and blood MSM concentrations after 4 weeks of daily supplementation with 3 grams/day were approximately 1900 µM [21].

Acute MSM pharmacokinetic data indicate that MSM is rapidly absorbed in the upper gastrointestinal tract and slowly removed from the serum [25]. Previous animal studies have reported similar findings, in that MSM is likely absorbed via passive diffusion into enterocytes of the upper gastrointestinal tract followed by homogenous tissue distribution throughout the body [26]. Considering the unique membrane penetrability properties and homogenous tissue distribution of MSM, it stands to reason that body weight may impact blood MSM concentrations as suggested previously [21,25]. Furthermore, difference in blood volume may also influence blood MSM concentrations, as this can be affected by weight, height, and even gender (i.e., women lower than men). Taken together, these factors may contribute to the higher MSM concentrations we observed in women (Figure 2), as body weight was significantly lower ($p<0.0001$) in women (65 kg) as compared to men (80 kg). Moreover, these discrepancies may have contributed to the observed greater values in the 3 grams/day group compared to the 2 grams/day, though the body weight of our 3 grams/day group was not significantly lower from a statistical point of view.

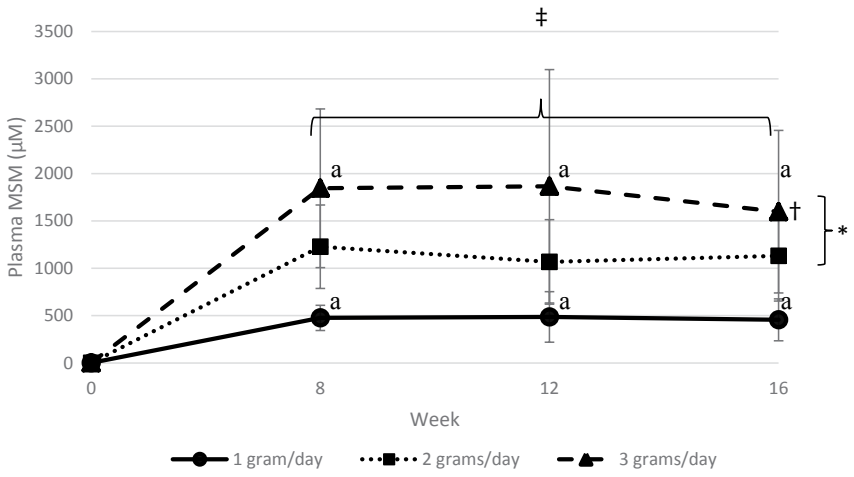

Figure 1: Plasma MSM concentrations of men and women assigned to MSM for 16 weeks.
Data are mean ± SD.
Group: * - 2 and 3 grams/day > 1 gram/day; † - 3 grams/day > 2 grams/day. Time: ‡ - Weeks 8, 12, and 16 > Week 0. Group x time interaction: a – 3 grams/day > 1 gram/day at weeks 8, 12, and 16.
No other statistically significant differences noted ($p>0.05$).

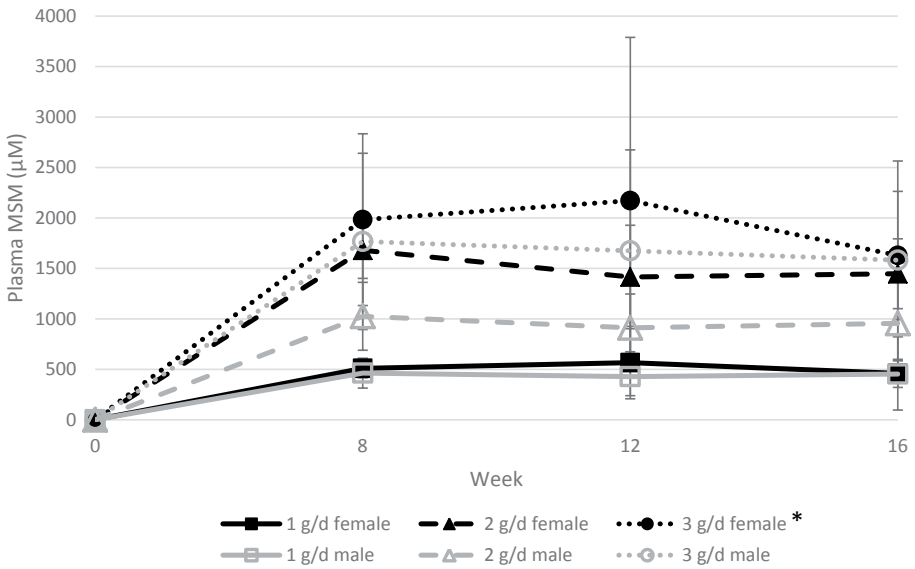

Figure 2: Plasma MSM, separated by gender, through 16 weeks of MSM supplementation.
* Gender effect ($p=0.01$); higher plasma MSM in women.

In our previous study evaluating oral supplementation at 3 grams/day, serum MSM concentrations appear to have risen non-linearly over the 4-week period, though only 3 measurements were taken [21]. This may suggest values could reach a steady-state as early as 3-4 weeks. Previous clinical trials have demonstrated MSM to be an effective osteoarthritis treatment at dosages of 6 grams/day for 12 weeks [3], 3.375 grams/day for 12 weeks [2,27], and 6 grams/day for 26 weeks [28]. In fact, aggregated locomotor function which includes three functional movement timed tests was significantly improved after only 6 weeks of supplementation with 3.375 grams/day [2]. Unfortunately, these studies, nor any other clinical trials, have correlated blood MSM concentrations with clinical effectiveness. Future studies should focus on eliciting this information in order to develop best dosing practices for MSM and its variety of uses. Moreover, a better determination of elimination half-life and turnover rates for different steady-state concentrations would greatly aid in the development of suggested dosing. These variables may help better understand how quickly MSM levels return to baseline, as prior acute pharmacokinetic data utilizing a cross-over design and dosing of one, two, and three grams demonstrated a significant "order effect" and "carry-over" of MSM between visits following a seven day washout period [25].

In summary, the response to MSM supplementation at escalating dosages was similar between men and women such that low micromolar baseline values rose to dose-dependent steady-states after only 4 weeks of supplementation. With continued daily supplementation, levels were maintained throughout the 16-week trial. If higher plasma MSM values are desired, longer use of lower dosages do not seem to be effective, as bioaccumulation is minimal.

Acknowledgement

Funding for this work was provided by Bergstrom Nutrition and The University of Memphis.

Author Contributions

RJB and CRY were responsible for the conception and design of the study, as well as manuscript preparation. RJB was responsible for data analysis. MB was responsible for subject recruitment, screening, data collection, and manuscript preparation. LL, DM, and CRY were responsible for assay development and analysis of blood samples. All authors contributed to and approved of the final manuscript.

Conflicts of Interest

RJB and CRY have received research funding from Bergstrom Nutrition, including this study. Bergstrom Nutrition was consulted in the design of this study. All other authors have no competing interests.

References

1. Barrager E, Veltmann JRJ, Schauss AG, Schiller RNA (2002) Multicentered, open-label trial on the safety and efficacy of methylsulfonylmethane in the treatment of seasonal allergic rhinitis. J Altern Complement Med 8: 167-173.
2. Debbi EM, Agar G, Fichman G, Ziv YB, Kardosh R, et al. (2011) Efficacy of methylsulfonylmethane supplementation on osteoarthritis of the knee: a randomized controlled study. BMC Complement Altern Med 11: 50.
3. Kim LS, Axelrod LJ, Howard P, Buratovich N, Waters RF (2006) Efficacy of methylsulfonylmethane (msm) in osteoarthritis pain of the knee: a pilot clinical trial. Osteoarthritis Cartilage 14: 286-294.
4. Notarnicola A, Maccagnano G, Moretti L, Pesce V, Tafuri S, et al. (2015) Methylsulfonylmethane and boswellic acids versus glucosamine sulfate in the treatment of knee arthritis: randomized trial. Int J Immunopathol Pharmacol 29: 140-146.
5. Notarnicola A, Tafuri S, Fusaro L, Moretti L, Pesce V, et al. (2011) The "mesaca" study: methylsulfonylmethane and boswellic acids in the treatment of gonarthrosis. Adv Ther 28: 894-906.
6. Kalman DS, Feldman S, Samson A, Krieger DR (2013) A randomized double blind placebo controlled evaluation of msm for exercise induced discomfort/pain. FASEB J 27: 1076-77.
7. Kalman DS, Feldman S, Scheinberg AR, Krieger DR, Bloomer RJ (2012) Influence of methylsulfonylmethane on markers of exercise recovery and performance in healthy men: a pilot study. J Int Soc Sports Nutr 9: 46.
8. Melcher DA, Lee SR, Peel SA, Paquette MR, Bloomer RJ (2016) Effects of methylsulfonylmethane supplementation on oxidative stress, muscle soreness, and performance variables following eccentric exercise. Gazz Med Ital-Arch Sci Med (in press) 175: 1-13.
9. Childs SJ (1994) Dimethyl sulfone (dmso2) in the treatment of interstitial cystitis. Urol Clin North Am 21: 85-88.
10. Berardesca E, Cameli N, Cavallotti C, Levy JL, Piérard GE, et al. (2008) Combined effects of silymarin and methylsulfonylmethane in the management of rosacea: clinical and instrumental evaluation. J Cosmet Dermatol 7: 8-14.
11. Berardesca E, Cameli N, Primavera G, Carrera M (2006) Clinical and instrumental evaluation of skin improvement after treatment with a new 50% pyruvic acid peel. Dermatol Surg 32: 526-531.
12. Fleck CA (2006) Managing ichthyosis: a case study. Ostomy Wound Manage 52: 82-86.
13. Amirshahrokhi K, Bohlooli S (2013) Effect of methylsulfonylmethane on paraquat-induced acute lung and liver injury in mice. Inflammation 36: 1111-1121.
14. Amirshahrokhi K, Bohlooli S, Chinifroush M (2011) The effect of methylsulfonylmethane on the experimental colitis in the rat. Toxicol Appl Pharmacol 253: 197-202.
15. Bohlooli S, Mohammadi S, Amirshahrokhi K, Mirzanejad-asl H, Yosefi M, et al. (2013) Effect of methylsulfonylmethane pretreatment on aceta-minophen induced hepatotoxicity in rats. Iran J Basic Med Sci 16: 896-900.
16. DiSilvestro RA, DiSilvestro DJ, DiSilvestro DJ (2008) Methylsulfonylmethane (msm) intake in mice produces elevated liver glutathione and partially protects against carbon tetrachloride-induced liver injury. FASEB J (in press) 22.
17. Kamel R, El Morsy EM (2013) Hepatoprotective effect of methylsulfonylmethane against carbon tetrachloride-induced acute liver injury in rats. Arch Pharm Res 36: 1140-1148.
18. Mohammadi S, Najafi M, Hamzeiy H, Maleki-Dizaji N, Pezeshkian M, et al. (2012) Protective effects of methylsulfonylmethane on hemodynamics and oxidative stress in monocrotaline-induced pulmonary hypertensive rats. Adv Pharmacol Sci 2012: 507278.
19. Ahn H, Kim J, Lee MJ, Kim YJ, Cho YW, et al. (2015) Methylsulfonylmethane inhibits nlrp3 inflammasome activation. Cytokine 71: 223-231.
20. van der Merwe M, Bloomer RJ (2016) The influence of methylsulfonylmethane on inflammation-associated cytokine release before and following strenuous exercise. J Sports Med (Hindawi Publ Corp) 2016: 7498359.
21. Bloomer R, Melcher D, Benjamin R (2015) Serum msm concentrations following one month of msm treatment in healthy men. Clin Pharmacol Biopharm 4: 1.
22. Calil C, Lima P, Bernardes C, Groppo F, Bado F, et al. (2008) Influence of gender and menstrual cycle on volatile sulphur compounds production. Arch Oral Biol 53: 1107-1112.
23. Ling L, Ma D, Bloomer RJ, Butawan M, Yates CR (2018) Development of an lc-ms/ms method for determining methylsulfonylmethane (msm) pharmacokinetics in humans J Chromatogr B (Submitted).
24. Engelke UF, Tangerman A, Willemsen MA, Moskau D, Loss S, et al. (2005) Dimethyl sulfone in human cerebrospinal fluid and blood plasma confirmed by one-dimensional 1h and two-dimensional 1h-13c nmr. NMR Biomed 18: 331-336.
25. Krieger DR, Schwartz HI, Feldman R, Pino I, Vanzant A, et al. (2009) A pharmacokinetic dose-escalating evaluation of MSM in healthy male volunteers; Miami research associates: Miami, FL, Pp: 1-83.
26. Wong T, Bloomer RJ, Benjamin RL, Buddington RK (2017) Small intestinal absorption of methylsulfonylmethane (msm) and accumulation of the sulfur moiety in selected tissues of mice. Nutrients 10: 19.
27. Debi R, Fichman G, Ziv YB, Kardosh R, Debbi E, et al. (2007) The role of MSM in knee osteoarthritis: a double blind, randomized, prospective study. Osteoarthritis Cartilage 15: C231.
28. Pagonis TA, Givissis PA, Kritis AC, Christodoulou AC (2014) The effect of methylsulfonylmethane on osteoarthritic large joints and mobility. Int J Orthop (Hong Kong. Online) 1: 19-24.