Skin Studies

Skin Studies-Human **Study Title Study Summary** Anthonavage, M. et al. 2015 Effects of Oral Two-part study. Part one was a pre-clinical evaluation of gene **Supplementation With** expression in a 3D skin model. Results supported the design of Natural Medicine Journal clinical portion. Part two was a double-blind placebo controlled Methylsulfonylmethane on Skin Health design. 20 healthy females randomized to take 3g MSM per day Study using OptMSM[®] and Wrinkle Reduction or placebo for 16 weeks. Significant improvements in skin appearance and condition were found in the treatment group when evaluated by expert grading, instrumental analysis, and participant self-assessment.

Exercise Recovery Studies

Exercise Recovery Studies				
Exercise Recovery Studies-Human	Study Title	Study Summary		
Melcher et al. 2017	Effects of Methylsulfo-	A double-blind placebo controlled study evaluating 3g of		
Gazzetta Medica Italiana - Arch per le Sci Mediche 2017, May; 176(5): 271-283 OptMSM Study using	nylmethane supplementation on oxidative stress, muscle soreness, and perfor- mance variables following eccentric exercise	MSM/day for 28 days in healthy exercise-trained males. MSM supplementation provides some degree of muscle protection following exercise by reducing muscle soreness by approx 15-20% over placebo and providing faster recovery of isometric quadriceps force. Oxidative stress did not increase following exercise in this model.		
Withee E et al. 2017	Effects of MSM on	Double blind, placebo controlled study design. 22 healthy adults		
Journal of International Society of Sports Nutrition (2017) 14:24 doi 10.1186/ s12970-017-0181-z	exercise induced oxidative stress, muscle damage, and pain following a halfmarathon: a double blind, randomized,	randomly assigned to take either 3g of MSM per day or placebo for 21 days before running a half marathon. MSM group saw clinically significant reductions in both muscle and joint pain.		
OptiMSM® Study using	placebo controlled trial			
van der Merwe, M. et al. 2016	The Influence of Methylsulfonylmethane on Inflammation-	Double-blind, placebo controlled study. 40 healthy, resistance trained males received 3g MSM or placebo for 28 days before eccentric knee exercise. In-vivo cytokine analysis was performed		
Journal of Sports Medicine, vol 2016, Article ID 7498359	Associated Cytokine Release before and following Streneous Exercise."	before and through 72 hours post-exercise. Additional cytokine analysis was performed in-vitro and ex-vivo on whole blood and isolated single blood cells from a subset of subjects, with and without LPS stimulation. Results indicate MSM dampens		
OptiMSM* Study using		inflammatory expression following exercise and reduces post-exercise immunosuppression.		
Peel S. et al. 2015	The Effects of MSM Supplementation on	Double-blind, placebo controlled study. 40 healthy resistance-trained men; 3 g/day for 28 days before eccentric		
Presented at American Society for Biomechanics Conference Aug, 2015 At Columbus, OH	Knee Kinetics during Running, Muscle Strength, and Muscle Soreness following	knee exercise. Testing occurred before exercise (Baseline) then at 0hr, 24hrs, 48hrs and 72 hrs post exercise. @ 72 hrs Maximum Isometric Force (MIF) normal in MSM group but still 8% below BL for Placebo. Absolute change in muscle soreness		
Published abstract and poster presentation	Eccentric Exercise- Induced Quadriceps Damage	during passive knee flexion was smaller in MSM group. Some findings of this study suggest individuals may be able to return to regular training more quickly following knee extensor damage with MSM supplementation.		
OptiMSM® Study using		damage with MisiM supplementation.		



Kalman D. et al. 2013

FASEB J, 2013, 27:1076.7

Published abstract and poster presentation



A Randomized Double Blind Placebo Controlled Evaluation of MSM for Exercise Induced Discomfort/Pain

Double-blind, placebo controlled study. 24 healthy adult males randomly assigned to receive either treatment or placebo for 14 days. Intervention of 3 grams of MSM per day for the 14 day period resulted in significantly lower (1.55 + 0.82 vs. 3.75 + 2.58 p=0.012) pain/discomfort 2 hours following a leg extension exercise to muscle failure when compared to the placebo group.

Nakhostin-Roohi B. 2013

Iranian J of Pharma Research 2013, 12(4): 845-853 Effect of Single Dose Administration of Methylsulfonylmethane on Oxidative Stress Following Acute Exhaustive Exercise 16 subjects randomly assigned to receive either 100mg/kg BW (6g for a 60kg person) MSM in water or placebo (just water) were subjected to treadmill running until exhaustion. Protein Carbonyls were lower at 2, and 24 hrs post exercise. Plasma TAC was higher at 24 hrs after exercise. Serum levels of bilirubin and uric acid were significantly lower immediately after exercise in the MSM group. Results suggest a single oral dose of MSM lowers exercise induced oxidative stress in healthy untrained men, but is not adequate to significantly affect reduced glutathione levels.

Barmaki, S. et al. 2012

J. Sports Med Phys Fitness 2012;52:170-4

Effect of MSM Supplementation on Exerciseinduced Muscle Damage and Total Antioxidant Capacity Double-blind, placebo controlled study. 18 subjects; treatment = 50mg/kg BW/day MSM for 10 days before a 14 km run. CK and Bilirubin was significantly reduced in MSM group vs. placebo. TAC significantly increased. MSM decreased muscle damage via antioxidant capacity.

Kalman D. et al. 2012

J. of Int. Society of Sports Nut. 2012, 9:46



Influence of MSM on Markers of Exercise Recovery and Performance and Total Antioxidant Capacity 8 subjects were randomly assigned either 1.5 or 3.0g of MSM per day for 30 days. Leg extension exercise to exhaustion. TEAC increased in a dose-dependant manner. Fatigue and homocysteine decreased in dose dependant manner. MSM may favorably influence selected markers of exercise recovery, especially at 3g/day.

Nakhostin-Roohi et al.2011

Journal of Pharmacy and Pharmacology 2011, 63:1290-1294 Effect of Chronic Supplementation with MSM on Oxidative Stress Following Acute Exercise in Untrained Healthy Men Double-blind, placebo controlled study. 18 subjects; treatment = 50mg/kg BW/day MSM for 10 days before a 14 km run. Serum MDA, PC, GSSG, GSH, and GSH/GSSG ratio were evaluated. MDA, PC, GSSG were significantly reduced in treatment group vs. placebo and GSH and ratio were increased. MSM decreased oxidative stress following acute exercise.

Exercise Studies-Animal

Study Title

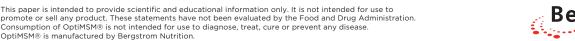
Study Summary

Marañón et al. 2006

Acta Veterinaria Scandinavica 2008; 50:45 doi:10.1186/1751-0147-50



The Effect of MSM Supplementation on Biomarkers of Oxidative Stress in Sport Horses Following Jumping Exercise 24 jumping horses divided into 3 groups; control, MSM@ 8mg/kg BW and combo of 8mg/kg MSM and Vit C 5mg/kg. Blood samples collected before and after exercise. NO, CO, Lipid Hydroperoxides, and Antioxidant enzymes, glutathione peroxidase, glutathione transferase and glutathione reductase measured. Exercise induced significant increase in lipid peroxidation, NO, and CO. Reduced glutathione, and antioxidant enzyme activity was decreased. MSM significantly ameliorated all of these exercise-related changes and the combo of MSM/Vit C potentiated this effect with some of the parameters close to pre-exercise levels.





Joint Support Studies- Human	Study Title	Study Summary
Lubis AMT et al. 2017	Comparison of Glucos- amine-Chondroitin Sulfate	Double blind, placebo controlled study evaluated 147 patients with grade I-II knee OA. treated with either 1500mg Gluc
Acta Med Indones – Indones J Intern Med. Vol 49 Number 2 April 2017	with and without MSM in Grade I-II knee osteoarthri- tis: A double blind random- ized controlled trial	1200mg Chond (n=49), or 1500mg Gluc, 1200mg Chon, 500mg MSM (n=50), or placebo (n=48). GCM showed significant clinical improvement compared with GC and placebo, especially in pain.
Pagonis et al. 2014 Int Journal of Orthopae-	The Effect of Methylsul- fonylmethane on Osteoarthritic Large	Double-blind, placebo controlled study. 100 subjects took MSM 3g twice daily for 26 wks. Statistically significant improvement for MSM group in all WOMAC and SF-36 quality of life scores. No
dics 2014 June 23 1(1): 19-24 ISSN2311-5106	Joints and Mobility	adverse effects reported.
Debbi et al. 2011	Efficacy of Methylsulfo- nylmethane Supplemen-	Double-blind, 49 subjects, 12 week treatment with 1.125 g of MSM 3X daily. Significant improvement seen in pain and
BMC Comp and Alt Med 2011, 11:50	tation on Osteoarthritis of the Knee: A Random- ized Controlled Study	physical function. WOMAC, VAS, KSKS, ALF scales utilized.
Kim et al. 2006	Efficacy of MSM in Osteoarthritis Pain of	Double-blind, placebo controlled study. 50 subjects MSM 3g twice daily for 12 wks. Significant reduction for MSM group in
OsteoArthritis and Cartilage 2006, 14:286-294	the Knee: A Pilot Clinical Trial	WOMAC pain, Urine MDA and Plasma Homocysteine. SF-36 scores indicated improvement in basic performing activities in the treatment group.
Usha and Naidu. 2004	Randomized, Double- Blind, Parallel, Placebo-	118 patients randomized to receive placebo, 500mg Glu, 500mg MSM, or combo of 500mg Glu + 500mg MSM for 12 wks. Glu,
Clin Drug Invest 2004, 24:6 353-363	Controlled Study of Oral Glucosamine, Methylsulfonylmethane and their Combination in Osteoarthritis	MSM and their combination produced analgesic and anti-inflammatory effect. VAS, Lesquene index and consumption of rescue meds measured.

Joint Support Studies

Joint Support Studies- Animal	Study Title	Study Summary
Akramas et all. 2017 Turkish J Vet Anim Sci, 2017, 41:748-756	Anti-inflammatory and anti-oxidative effects of herbal preparation EM 1201 in adjuvant arthritic rats	This study investigated effects of 2 herbal formulas in rats with adjuvant arthritis (an RA model) Turmeric, Devils Claw, Milk Thistle with and without MSM were compared with the NSAID Dilcofenac. Results show these formulations are promising agents comparable to DF and may provide a safer alternative for the treatment and prevention of arthritis.
Ezaki et al. 2012 J Bone Miner Metab. 2013 Jan;31(1):16-25. doi: 10.1007/s00774-012-0378-9. Epub 2012 Aug 10.	Assessment of Safety and Efficacy of MSM on Bone and Knee Joints in OA Animal Model	This study evaluated cartilage formation in growing rats and cartilage degradation in mice, both are acceptable Human OA models at recommended human dosage of 0.6g/kg BW/day and at 10x & 100X. Intake of MSM for 4 wks did not affect cartilage formation in rat's knee joints. MSM Intake for 13 weeks decreased degeneration of the cartilage on knee joint surface of the mice. 100X dosage significantly decreased organ wt. compared to control.



Hasegawa T, Ueno S, Kumamoto S, Yoshikai Y 2004

Jpn Pharmacol Ther 2004;32(7):421-7.

Suppressive effect of methylsulfonylmethane (MSM) on type II collagen-induced arthritis in DBA/1J mice Oral administration of OptiMSM® modified immune responses in DBA/1J mice. Arthritic deformation and swelling induced by type II collagen injections (an animal model of rheumatoid arthritis) were significantly diminished in mice drinking MSM compared to controls. Abnormal white blood cell proliferation in lymph nodes was also reduced in mice drinking MSM.

Murav'ev et al. 1991

Patol Fiziol Eksp Ter 1991, 2:37–39

Effect of DMSO and MSM on a Destructive Process in the Joints of Mice with Spontaneous Arthritis Oral administration of DMSO or its main metabolite MSM lessened the destructive changes in joints of 36 Mrl/Mn/lnr female mice.

Moore et al. 1985

Proceedings of Fed of American Soc. Of Exp Bio 1985, 530: Abstract 692 Diminished Inflammatory Joint Disease in MRL/lpr Mice Ingesting DMSO or MSM A 3% solution of either DMSO or MSM was administered in drinking water, ad libitum for 3 months. Inflammatory reaction of synovial tissue was found in 95% of control, 82% of DMSO and 71% of MSM. Pannus formation was significantly reduced in MSM vs. placebo.

Oxidative Damage Protection Studies

Additional Oxidative				
Damage Protection				
Studies-Animal				

Study Title

Study Summary

Amirshahrokhi, K et al. 2017

European J of Pharmacology, 2017, http://dx.doi.org/10.1016/j.ejphar.2017.06.034

Methylsulfonylmethane is effective against gastric mucosal injury

This study evaluated Oral MSM's effect on ethanol/HCL induced gastric injury. Pre-treatment with MSM significantly increased GSH, CAT, and PGE2 and significantly decreased gastric inflammation (NF $k\beta$, TNF- α , IL-1 β , IL-6, MCP-1) and oxidative damage (MDA, MPO, PC, and NO).

Radwan et al. 2016

J of Biomed and Pharma Res, 2016, 5(3):10-17



Actions of Taurine, Methylsulfonylmethane and Silymarin Against Acetaminophen-Induced Neuro- and Hepato-Toxicity in Rat

This study evaluated the effects of pretreatment (14 days) with either MSM (400mg/kg/day), taurine, or silymarin on acetaminophen (APAP)-induced liver and brain injury in rats. MSM pretreatment resulted in significant amelioration, over control, of APAP-induced changes in liver enzymes AST and ALT; brain and liver markers of oxidative stress - MDA, GSH, GSSG, NO, and 8-OHdG; and 2 brain monoamines - norepinephrine, and serotonin. MSM significantly outperformed taurine and silymarin pretreatment in liver NO levels and brain 8-OHdG.

Amirshahrokhi, K. et al. 2013

Inflammation. 2013 Oct;36(5):1111-21. doi: 10.1007/s10753-013-9645-8. Effect of MSM on Paraquat-Induced Acute Lung and Liver Injury in Mice Mice treated with 500mg/kg/day i.p. for 5 days histological and biochemical examination of lung and liver tissue. Results showed a significant reduction in liver and lung tissue damage and a significant reduction in tissue levels of MDA, MPO and TNF-a. MSM significantly increased level of SOD, CAT and GSH. Findings suggest MSM attenuates PQ-induced pulmonary and hepatic oxidative injury.



Bohlooli et al. 2013

Iran J. of Basic Med Sci, 2013, 16:896-900



Effect of Methylsulfonylmethane Pretreatment on Acetaminophen Induced Hepatotoxicity in Rats The study evaluated effect of pretreatment of MSM on acetaminophen-induced liver injury in rats. Dosage of MSM pre-treatment = 100 mg/kg BW for one week. On day 7 rats received acetaminophen @ 850mg/kg to induce liver injury. Blood serum levels of AST and ALT measured 24 hrs post dose. Tissue samples of liver were evaluated for MDA, GSH, SOD and MPO activity. Results show acetaminophen caused a negative impact on all measured biological indices and pre-treatment with MSM significantly attenuated this negative impact.

Kamel et al. 2013

Arch. Pharm. Reas. 2013, doi:10.1007/s12272-013-01 10-x Hepatoprotective Effect of MSM Against Carbon Tetrachloride-Induced Liver Injury in Rats Pre-treatment with MSM (400mg/kg) before a single dose of CCl4 (2ml/kg, i.p.) inhibited serum ALT and AST activities, decreased liver MDA, TNF-α, IL-6 and Bax/Bcl2 ratio compare to CCl4 group. MSM raised SOD and CAT activity as well as CYP2E1 level in liver tissues. MSM protects liver from CCl4 injury possibly through its antioxidant, anti-inflammatory and anti-apoptotic properties.

Mohammadi et al. 2012

Adv in Pharma Sci 2012, doi:10.1155/2012/507278



Protective Effects of MSM on Hemodynamics and Oxidative Stress in Monocrotaline-Induced Pulmonary Hypertensive Rats MSM administered to rats at 100, 200, and 400 mg/kg/day for 10 days before a single dose of 60 mg/kg, IP, MCT. Blood samples analyzed for CAT, SOD, GPx, GSH and MDA. MSM treatment showed potential protective antioxidant effects by a significant increase in antioxidant enzyme activity and associated reducing agents.

Amirshahrokhi, K. et al. 2011

Tox and App Pharm 2011, doi 10.1016/j.ta-ap.2011.03.017

Effect of MSM on Experimental Colitis in the Rat Colitis induced by intra-colonic instillation of 1 ml of 5% acetic acid. Rats treated with MSM at 400mg/kg/day orally for 4 days. Colon evaluated histologically and biochemically. Micro and macroscopic colonic damage was decreased. MDA, MPO, and IL-1 were significantly decreased while GSH levels increased. MSM may have a protective effect in experimental ulcerative colitis.

DeSilvestro et al. 2008

FASEB J, 2008, 22:445.8

Published abstract and poster presentation



MSM intake in Mice Produces Elevated Liver Glutathione and Partially Protects against CCl4 -Induced Liver Damage MSM administration (5 weeks, 80 mg/100 ml drinking water) produced a statistically significant increase in liver GSH (mean increase of 78%). A similar effect was not seen in lung or skeletal muscle. Also, MSM partially inhibited liver injury after injection of CCl4, which induces liver oxidative stress.



Allergy/Immune Studies

Allergy/Immune Studies **Study Title Study Summary** Godwin, S. et al. 2015 MSM enhances LPS-Supplementation of MSM blunted the increase in systemic Journal of the International induced inflammatory levels of inflammatory cytokines (IL-6 & IL-1ß) immediately after Society of Sports Nutrition response after exercise. However, Ex vivo incubation of blood from various exercise. time points with LPS caused a dramatic increase in inflammato-Published abstract and ry cytokines after exercise only in the group treated with MSM. poster presentation Also, a 2-3 fold increase in IL-10 was seen only in the MSM group after LPS stimulation despite lower IL-10 levels before exercise. Study using OptMSM[®] Hasegawa T, Ueno S, Anti-Inflammatory Effect of 3 aspects of anti-inflammatory effects of OptiMSM evaluated: 1) Kumamoto S 2005 Methylsulfonylmethane Skin damage by UV, 2) Skin inflammation by ovalbumin injection and 3) Itching from histamine. Results: 1) OptiMSM suppressed (MSM) in Mice Jpn Pharmacol Ther skin inflammation from UV light. 2) Mice that consumed 2.5% 2005;33(12):1217-1223 OptiMSM in solution suppressed immediate-phase swelling reaction. 3) Scratching behavior was considerably less in mice following ingestion of 2.5% MSM solution for 1 week before histamine injections. Conclusion: Study confirms MSM is an Study using **OptMSM** anti-inflammatory agent, and it mitigates abnormal immune reactions that trigger inflammation. A Multi-Centered, 50 person study consumed 2600mg/day MSM orally for 30 days. Barrager E, Veltmann JR, Schauss AG, Schiller RN Open Label Trial on the Clinical respiratory symptoms and energy levels evaluated by 2002 Safety and Efficacy of questionnaire at the beginning and @ days 7, 14, 21, and 30. Methylsulfonylmethane in Immune and inflammatory reactions were also determined by lab tests. After 1 week, frequency of upper respiratory symp-J Altern Complement Med the Treatment of 2002; 8:167-73. Seasonal Allergic Rhinitis toms were significantly improved. At 3 weeks, participants also had significant improvements in lower respiratory symptoms. Study using All respiratory improvements were maintained through day 30. **OptMSM** Energy levels improved significantly by day 14, and were maintained through day 30. Minimal side effects reported during trial.

Sulfur Donation Studies- Animal	Study Title	Study Summary
Wong et al. 2018	Small Intestinal Absorption of	This study used radiolabeled S(35) to evaluate the absorption and metabolism of MSM using mice. The study found that MSM
Nutrients, 2018, 10(19):1-9	Methylsulfonylmethane (MSM) and Accumulation	is easily and readily absorbed in the small intestine, creating a pool of sulfur available to the body, relieving the bioburden on
OptiMSM* Study using	of the Sulfur Moiety in Selected Tissues of Mice	SAAs. It found that MSM sulfur in incorporated into proteins, likely though post-translational sulfation.

