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Abstract: With the increasing demand for feed additives that are green, safe, and free of drug residues, methylsulfonylmethane (MSM) has received extensive attention in animal production, and the research has been deepening. MSM is a sulfur-containing organic substance that is widely distributed in nature, with many biological functions, including antioxidant, anti-inflammatory, immune regulation, improvement of intestinal health, joint protection, and skin and hair nourishment, etc. It plays an important role in maintaining normal metabolism in the body and has considerable potential for application in the healthy rearing of animals. This paper reviews the biological functions and regulatory mechanisms of MSM, as well as its applications in animal production, including improving growth performance, reducing lipid peroxidation, improving meat quality, increasing disease resistance, and enhancing anti-stress ability. This is done in order to provide a reference for subsequent scientific research.

Key words: Methylsulfonylmethane, biological functions, mechanism of action, animal production

1. INTRODUCTION

With the increasing emphasis on animal health and livestock product safety, the development of non-toxic, residue-free, and multifunctional "green" feed additives has become an inevitable trend in the development of the livestock industry [1]. Methylsulfonylmethane (MSM) is a stable metabolite of dimethyl sulfoxide (DMSO), which has the characteristics of low toxicity, low residue, and low susceptibility to pathogen resistance [2–4]. Research indicates that MSM has biological functions, including antioxidant, anti-inflammatory, immune regulation, and improvement of intestinal health [5,6]. At the same time, when used as an additive, MSM can improve animal growth performance and production quality[6–14], enhance immune function [6,8,9,15,16], regulate lipid metabolism

[6,10,13,17–20], and relieve stress [7,13,21,22]. This article mainly reviews the biological functions and applications of MSM in animal production, in order to provide reference for the further development and utilization of MSM in animal husbandry.

2. BRIEF INTRODUCTION OF METHYLSULFONYLMETHANE

MSM is a small sulfur compound with the formula $(CH)_2SO_2$. It appears as a white acicular crystal at room temperature and can be soluble in water (150 g/L at 20°C) and organic solvents such as ethanol [5,6]. MSM is involved in the synthesis of methionine and cysteine and is of great significance for maintaining normal metabolic activities [23]. MSM is mainly absorbed by passive diffusion in the small intestine and can also be converted into sulfate by cecal flora [24]. The metabolites are excreted in urine and can penetrate the blood-brain barrier to protect nerves [24–26]. The synthesis of MSM depends on the metabolite DMSO, which can be rapidly converted into MSM by oral administration [26]. In the natural environment, DMSO is oxidized by ultraviolet light or lightning to generate MSM, forming a sulfur cycle, and artificial synthesis can be achieved by oxidizing DMSO by H_2O_2 or NO_2 [5,26,27]. MSM is a naturally occurring source of sulfate (accounting for 85% of sulfur supply) available in different fruits, vegetables, grains, and animal tissues, and is considered to provide health benefits when used to supplement the diet [6,24]. Cow's milk is the richest source of MSM; other animal feed ingredients containing MSM include Swiss chard (0.05–0.18 ppm), corn (up to 0.11 ppm), and alfalfa (0.07 ppm) [28]. In addition, plants of the *Allium* genus contain a large amount of MSM, including garlic (*Allium sativum* L.), onion (*Allium cepa*), and chive (*Allium tuberosum*) [29]. The content of MSM in common feeds and foods is shown in Table 1 [28].Thus, MSM could also be naturally synthesized in animals fed an MSM-free diet; the natural presence of MSM in animal products might be endogenous,

exogenous, or both [6].

3. BIOGICAL FUNCTIONS AND MECHANISM OF METHYLSULFONYLMETHANE

3.1 Antioxidant

Oxidative stress often causes animals to produce a large amount of reactive oxygen species (ROS), leading to oxidative damage, organ dysfunction, and reduced animal production performance [6]. MSM has been shown to possess strong antioxidant activities in animals such as broiler chickens, laying hens, ducks, and mice [5,6]. The mechanisms of MSM's antioxidant activity includes increasing the activity of superoxide dismutase [6,8,20,30–32], enhancing total antioxidant capacity (TAC) [6–8,10,33,34], reducing malondialdehyde (MDA) [8,10,12,13,20,31,32,35], and regulating the glutathione system (e.g., glutathione synthesis and glutathione peroxidase activity) [7,8,13,20,32,35]. In addition, MSM can inhibit oxidative damage mediated by mitochondrial ROS (superoxide/H_2O_2/HClO), human immunodeficiency virus-1 transcription activator, oxidized oil, $CoCl_2$, heat stress, and ethanol [7,13,21,22,36,37]. Cyclooxygenase-2 (COX-2) and nitric oxide synthase (iNOS) are two key enzymes that induce ROS production [13,38]. MSM can downregulate COX-2/iNOS expression through the nuclear factor kappa-B (NF-κB) pathway and indirectly block ROS generation [13,39]. Furthermore, MSM can regulate the balance between ROS and antioxidant enzymes by controlling other signaling pathways: Janus kinase/signal transducer and activator of transcription [40,41], nuclear factor (erythroid-derived 2)-like 2, and phosphoinositide 3-kinase/protein kinase B [37]. The antioxidant effect of MSM on various animal species is presented in Table 2 below.

3.2 Anti-inflammation

Animal studies on anti-inflammatory effects have mainly demonstrated the inhibitory effects of MSM

on interleukin (IL)-1β, IL-2, IL-6, and tumor necrosis factor alpha (TNF-α) [21,23,35,42–44], though some reports suggested that MSM increased IL-2 and IL-6 in some poultry experiments [6,8,45]. The core mechanisms of MSM anti-inflammatory include: blocking the NF-κB signaling pathway and decreasing the expression of iNOS/COX-2, thereby downregulating the IL-1β, IL-6, and TNF-α [13,39,46]; directly bidirectionally regulating cytokines (inhibiting inflammatory cytokines and promoting anti-inflammatory factors) [47,48]; and regulating the activities of MDA, myeloperoxidase, glutathione, and TAC related to oxidative pathways [35]. In addition, MSM can also exert anti-inflammatory effects by inhibiting extracellular signal-related kinases/Jun amino terminal kinases-mitogen-activated protein kinases and leucine-rich repeat family pyrin domain containing 3 pathways [29,44]. The anti-inflammatory effect of MSM on various animal species is presented in Table 3 below.

3.3 Regulating immunity and intestinal function

Mediating the interaction between oxidative stress and inflammatory response is one of the key mechanisms for MSM to regulate immune response [5,6]. For example, MSM has been shown to increase IL-2 and IL-6 expression levels in poultry [6,8,45], reduce the incidence of lymphadenopathy, splenomegaly, and anemia in mice with immune lymphoproliferative disorders [15], upregulate the mRNA expression of immune-related genes [16], and elevate alanine aminotransferase activity along with the quantity of white blood cells and lymphocytes in broilers [9].

MSM can improve animal intestinal health mainly by enhancing intestinal barrier function (Figure 1). *In vivo* studies have shown that MSM can increase the ileal villus height and villus height-to-crypt ratio [10], regulate the gut microbiota by reducing *Escherichia coli* and increasing *Lactobacillus* populations [9,49], decrease the severity of ethanol/HCl-induced gastric mucosal injury [23], improve intestinal damage [35], and increase the intestinal transport capacity of animals [17]. *In vitro* studies have shown

that MSM inhibits lipopolysaccharide-induced inflammatory cytokines (TNF-α, IL-1β, and IL-6) in chicken and porcine intestinal epithelial cells, while regulating cell proliferation and viability [42,43]. Furthermore, MSM can increase the monolayer transepithelial electrical resistance and upregulate the expression of tight junction proteins (occludin, claudin-1, and zonula occludens-1), while reducing the permeability of porcine intestinal epithelial cells [43]. Overall, these findings illustrate the multifactorial mechanism by which MSM maintains intestinal mucosal homeostasis through structural strengthening, microbial balance, and inflammatory pathway regulation.

3.4 Protect bones and joints

Due to the beneficial anti-inflammatory and immunomodulatory properties of MSM, it is usually used as a dietary supplement to treat diseases such as arthritis, osteoarthritis, rheumatoid arthritis, and knee joint injuries [46–48,50]. Animal studies have demonstrated that MSM can alleviate knee joint and cartilage degeneration in mice, reduce cartilage damage in rheumatoid arthritis rats, protect the articular cartilage surface in rabbits with osteoarthritis, and prevent cartilage erosion in the meniscus of sheep [51–55]. MSM also affects osteogenic differentiation, bone activity, and bone density of cartilage, and exhibits potential for bone induction and conduction in bone regeneration [56–61]. Furthermore, MSM can promote chondrogenesis and osteogenic differentiation in zebrafish by regulating the SRY-box transcription factor 9/RUNX family transcription factor 2 [56], which are key regulatory genes for chondrogenesis and osteogenic differentiation, respectively [56,58,60]. Additionally, MSM can enhance alkaline phosphatase activity in rabbit radius defect repair and regulate collagen cross-linking and mineralization mediated by key enzymes such as transglutaminase-2 [57,58]. These findings demonstrate that the protective mechanism of MSM on animal bones and joints involves the dual pathways of inflammation inhibition and bone metabolism regulation.

3.5 Nourishing the skin and hair

The potential nourishing effects of MSM on skin and hair in animals are hypothesized to be due to its dual mechanisms of supplying sulfur as a critical substrate for the synthesis of structural proteins (methionine, cysteine, and keratin) and exerting antioxidant and anti-inflammatory effects to mitigate tissue damage [3,23,49,62,63]. Experimental evidence demonstrates that MSM can reduce fine lines and wrinkles [64], enhance skin firmness, elasticity, and hydration [65], relieve symptoms of X-linked ichthyosis [66], induce melanin synthesis, and treat skin hypopigmentation diseases such as vitiligo [67]. In studies of animals such as rabbits, guinea pigs, rats, mice, ragdoll kittens, and poodles, MSM has also been shown to have non-irritating effects on the skin and can improve burn skin condition, reduce skin wrinkles caused by ultraviolet radiation B damage, prevent photoaging and reduce the thickness of hair scales [5,49,68].

3.6 Other biological functions

In vitro studies show that MSM induces cell death by inhibiting signal transducer and activator of transcription 3 and 5B [69], inhibiting Janus kinase/signal transducer and activator of transcription [70], and activating caspase pathways [71], and showed anticancer effects against a variety of cancers (breast, esophagus, stomach, liver, colon, bladder, skin, prostate, lung, and endometrial cancers) [5,69–72]. Furthermore, MSM alleviates exercise-induced pathological conditions (e.g., cardiac dysfunction and muscle injury) via oxidative stress protection [16,73], improves cholesterol metabolism by increasing high-density lipoprotein levels in obesity models [74], and combats Alzheimer's disease-like neurotoxicity [75]. These biological properties indicate the potential of MSM in improving animal welfare and quality of life.

4. THE APPLOCATION OF METHYLSULFONYLMETHANE IN PRODUCTION

4.1 Improving animal performance

MSM has biological properties such as anti-inflammatory, antioxidant, and immune and intestinal function regulation. These characteristics are crucial for maintaining a balanced gut microbiota, reducing body oxidation, lowering environmental stress, and ultimately improving animal performance [9,10,12,33]. Reports on the effect of MSM on the growth performance of animals were mostly focused on poultry [6], although the research results are not entirely consistent. Some studies have revealed that dietary MSM has no marked effect on poultry growth performance parameters such as body weight (BW), body weight gain (BWG), feed intake, or feed conversion ratio (FCR) [7,18,20,33]. Additionally, it shows no influence on the production performance or egg quality of laying hens [10,20,30]. Conversely, other studies have demonstrated that MSM, either alone or in combination with other additives, generally exerts a positive effect on certain growth performance indicators in poultry, ragdoll cats, and pigs, for example, by decreasing the FCR [11,12,30,34,49]. A small number of studies have indicated that MSM can notably improve the growth performance of broilers and ducks. Jiao et al. [9] found that the supplementation of 0.20% MSM to broiler diets improved BW and BWG and reduced FCR during a 29-d experiment. Zhang et al. [13] found that the administration of MSM at 1 and 2 g/kg resulted in a linear increase in BWG and a reduction in the FCR during the grower phase (days 10-21) in broilers. Yan et al. [8] indicated that the inclusion of MSM (0.3%) resulted in an increase in final BW and BWG during the periods of days 22-42 and days 1-42, and a reduction in FCR during the period of days 22–42 in Pekin ducks. Lim et al. [45] found that MSM (0.1%) produced significant increases in BW, BWG, and feed intake. Overall, the effects of supplementation of animal diets with MSM have not found any related adverse effects on growth performance [6]. The observed differences in the research results may be

attributed to various confounding variables, including the form of MSM addition, feed formulation characteristics, species-specific metabolic responses, dose optimization challenges, dietary matrix interactions, and feeding environment and period [6–10,13,49]. This complex interplay of factors underscores the necessity for standardized protocols in future nutraceutical research to elucidate MSM's precise mechanisms of action.

4.2 Improve meat quality and reduce lipid peroxidation

In terms of carcass yield, breast meat characteristics, and poultry viscera, in most current studies, there is no difference in the relative weight of carcass, abdominal fat, breast meat, thigh and drumstick, liver, gizzard, pancreas, thymus, bursa of Fabricius, or spleen (the amount of MSM added ranges from 0.025% to 0.3%) [6,8,9,13].

The water-holding capacity (WHC), cooking loss, and drip loss play the key role in the production and processing of meat products by affecting the sensory characteristics and nutritional value of meat, thereby affecting meat quality [13]. Current research predominantly demonstrates that MSM supplementation exerts beneficial effects on these parameters, particularly through its modulatory effects on the pH value of meat [6,13,76]. The characteristic pH decline following muscle fiber contraction after slaughter disrupts protein electrostatic interactions, consequently impairing WHC [77]. Notably, MSM administration (0.3%) has been shown to enhance WHC through pH_{24h} elevation and drip loss reduction [8]. Consistent with this result, a study reported that the supplementation of MSM (0.03%) can improve the WHC of ducks [18]. However, Jiao et al. [9] did not observe a positive effect of MSM (0.05-0.2%) on pH or WHC in broiler chickens, though they observed a linear reduction in drip loss on days 5-7 after slaughter. Similarly, Lee et al. [19] observed a reduction in drip loss in finishing pigs following the addition of MSM (0.03-0.05%) on day 2 post-mortem. Contrastingly, some studies have failed to detect

MSM's influence on drip loss parameters [13]. In addition, changes in storage temperature and cellular structure can also affect the WHC, cooking loss, and drip loss of meat products [77]. However, as of now, research on the impact of MSM in these areas is still rare, and further exploration is needed in future studies.

The color of raw meat is highly susceptible to alterations in feed and the environment [78]. Current research demonstrates that the supplementation of MSM could increase the redness (a*) in finishing pigs [19], broilers [9], and ducks [8,18]. The underlying mechanism may involve two synergistic pathways: First, the inherent antioxidant capacity of MSM may inhibit myoglobin oxidation [8], thereby delaying the conversion of myoglobin to metmyoglobin during storage, which is the main determinant of meat discoloration [78,79]. Second, MSM appears to modulate heme in myoglobin after animal death. Lee et al. [19] observed an increase in iron deposition in the loin of finishing pigs that were fed a diet supplemented with MSM (0.03-0.05%.). This iron enrichment may contribute to improved pigment stability, given the established correlation between iron content and meat redness (a*) [80]. Notably, while significantly influencing redness (a*) parameters, MSM had no significant effect on lightness (L∗) and yellowness (b∗) [8,9,18,19]. Zhang et al. [13] found that birds receiving a 2 g/kg MSM diet had higher rates of moderate white striations, suggesting that the fat content of fillets may be increased with a corresponding decrease in protein percentage [81]. This could lead to changes in the nutritional value of the final meat product.

Lipid composition serves as a critical determinant of meat quality, with MDA constituting a principal biomarker for assessing lipid peroxidation intensity in animal-derived products [6]. As we summarized earlier, the comprehensive analysis of multiple species, including laying hens, broiler chickens, ducks, mice, etc., consistently show that supplementing with MSM significantly inhibited MDA levels,

confirming its ability to alleviate systemic lipid peroxidation [8,10,12,13,20,31,32,35]. The regulatory mechanisms involved include that MSM may alleviate steatosis by regulating the antioxidant defense system (enhancing superoxide dismutase, TAC, and glutathione peroxidase) and inhibiting mitochondrial energy metabolism related genes [20]. Meanwhile, supplementing MSM can significantly reduce the 2-thiobarbituric acid reactive substance (TBARS) in finishing pigs, broiler chickens, and meat ducks [13,18,19]. The presence of elevated levels of unsaturated fat in meat renders it susceptible to oxidation, which can result in the development of rancidity and a deterioration in both flavour and colour [78,82]. TBARS can alter the concentration of secondary lipid oxidation products, which may cause odors in the meat. The decrease in TBARS levels may also be attributed to the strong antioxidant activity of MSM in scavenging free radicals [13]. It is worth noting that in addition to reducing MDA and TBARS, the antioxidant effects of MSM may also help improve the nutritional properties of meat. For example, dietary MSM supplementation in ducks effectively preserves fatty acid integrity [18], while supplementation in pigs has been shown to alter muscle amino acid profiles [19]. Overall, the antioxidant effect of MSM is the primary reason for the improvement in meat quality and reduction of lipid peroxidation observed in livestock and poultry.

4.3 Improve the ability to resist disease and stress

Due to its numerous biological functions, MSM has been shown to enhance animals' disease resistance and environmental stress resistance through anti-inflammatory, antioxidant, and immune-regulating effects [7,12,13,21,22,44]. *Mycoplasma gallisepticum* is a common avian pathogen that frequently causes respiratory diseases in poultry, MSM alleviate inflammatory damage and oxidative stress induced by *Mycoplasma gallisepticum* by inhibiting the NF-κB and extracellular signal-related kinases/Jun amino terminal kinases-mitogen-activated protein kinases signaling pathways in tracheal tissue and

macrophages [44]. Coccidiosis is a parasitic disease in poultry caused by *Eimeria*, which affects the gastrointestinal tract of chickens, reduces the animal's ability to digest nutrients, and leads to malabsorption, affecting the growth performance and animal production [12,33]. In coccidiosis of broilers (*Eimeria* infection), MSM improves growth performance (e.g., elevated BWG), reduces lipid peroxidation (lower TBARS), enhances systemic antioxidant capacity (increased plasma and hepatic TAC), and improves crude ash digestibility, though its direct anti-coccidial efficacy remains limited [12,33]. In addition to disease resistance, as mentioned earlier, MSM has good oxidative stress resistance [7,21,22]. Meanwhile, research has also found that MSM (1 and 2 g/kg) may have a sustained effect on heat-stressed broilers during the finishing period [13]. MSM enhances heat resistance, reduces mortality rate, and improves the oxidative stability of breast meat due to its antioxidant properties [13]. Overall, MSM alleviates pathogen- and stress-induced physiological disorders in poultry primarily by modulating inflammatory signaling and enhancing antioxidant defenses, although its efficacy may vary depending on the disease-specific contexts.

CONCLUSIONS

In summary, MSM is a sulfur-containing organic compound widely existing in nature, which has biological functions, including antioxidant, anti-inflammatory, and immune regulation, etc. MSM participates in various metabolic processes in animals and plays an important role in the efficient production and health maintenance of animals. However, the application of MSM in animal production mainly focuses on the growth performance and the quality of animal products, and its mechanism still needs to be further explored. The functions of MSM in regulating nutrient absorption and metabolism, killing pathogenic microorganisms, and regulating hormone secretion are needed to explore in the future.

At the same time, further studies of different forms and dosages of MSM and their different effects on animal production can provide more and more authoritative data for the promotion of MSM in animal diets and its practical application in animal production.

AUTHOR CONTRIBUTIONS

Conceptualization, Inho Kim.; writing—original draft preparation, Yang Jiao.; writing—review and editing, Xinran Li.; review—supervision, Hengjiang Li. All authors have read and agreed to the published version of the manuscript.

DISCLOSURES

The authors declare that there are no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This article does not require IRB/IACUC approval because there are no human and animal participants.

REFERENCES

1. Liu L, Wang P, Liu S, Yan M, Zhang Q, Clark E, et al. Meta-analyses of the global impact of non-antibiotic feed additives on livestock performance and health. J Adv Res. 2025. https://doi.org/10.1016/j.jare.2025.03.009

2. Richmond VL. Incorporation of methylsulfonylmethane sulfur into guinea pig serum proteins. Life Sci. 1986;39:263–8. https://doi.org/10.1016/0024-3205(86)90540-0

3. Jacob SW, Herschler R. Introductory Remarks: Dimethyl sulfoxide after twenty years. Annals of the New York Academy of Sciences 1983;411. https://doi.org/10.1111/j.1749-6632.1983.tb47276.x

4. U. S. Food and Drug Administration 2004. Guidance for Industry: Botanical Drug products. Accessed Sept. 2018. https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInforma tion/Guidances/ucm070491.pdf.

5. Butawan M, Benjamin R, Bloomer R. Methylsulfonylmethane: applications and safety of a novel dietary supplement. Nutrients. 2017;9:290. https://doi.org/10.3390/nu9030290

6. Kim Y-B, Lee K-W. Role of dietary methyl sulfonyl methane in poultry. Animals (Basel). 2023;13:351. https://doi.org/10.3390/ani13030351

7. Rasheed MSA, Oelschlager ML, Smith BN, Bauer LL, Whelan RA, Dilger RN. Dietary methylsulfonylmethane supplementation and oxidative stress in broiler chickens. Poult Sci. 2020;99:914–25. https://doi.org/10.1016/j.psj.2019.12.010

8. Yan HL, Cao SC, Hu YD, Zhang HF, Liu JB. Effects of methylsulfonylmethane on growth performance, immunity, antioxidant capacity, and meat quality in Pekin ducks. Poultry Science 2020;99:1069–74. https://doi.org/10.1016/j.psj.2019.10.002

9. Jiao Y, Park JH, Kim YM, Kim IH. Effects of dietary methyl sulfonyl methane (MSM) supplementation on growth performance, nutrient digestibility, meat quality, excreta microbiota, excreta gas emission, and blood profiles in broilers. Poult Sci. 2017;96:2168–75. https://doi.org/10.3382/ps/pew480

10. Kim YB, Lee SH, Kim DH, Lee KW. Effects of dietary methyl sulfonyl methane and selenium on laying performance, egg quality, gut health indicators, and antioxidant capacity of laying hens. Anim Biosci. 2022;35:1566–74. https://doi.org/10.5713/ab.21.0564

11. Cho JH, Min BJ, Kwon OS, Shon KS, Jin YG, Kim HJ, et al. Effects of MSM (methyl sulfonyl methane) supplementation on growth performance and digestibility of Ca and N in pigs. J Korean Soc Food Sci Nutr. 2005;34. https://doi.org/10.3746/jkfn.2005.34.3.361

12. Rasheed MSA, Tiwari UP, Jespersen JC, Bauer LL, Dilger RN. Effects of methylsulfonylmethane and neutralizing anti–IL-10 antibody supplementation during a mild Eimeria challenge infection in broiler chickens. Poult Sci. 2020;99:6559–68. https://doi.org/10.1016/j.psj.2020.09.046

13. Zhang H, Majdeddin M, Degroote J, Van Liefferinge E, Van Noten N, Van Kerschaver C, et al. Effect of supplemental methyl sulfonyl methane on performance, carcass and meat quality and oxidative status in chronic cyclic heat-stressed finishing broilers. Poult Sci. 2023;102:102321. https://doi.org/10.1016/j.psj.2022.102321

14. Abdul Rasheed MS, Oelschlager ML, Smith BN, Bauer LL, Whelan RA, Dilger RN. Toxicity and tissue distribution of methylsulfonylmethane following oral gavage in broilers. Poult Sci. 2019;98:4972–81. https://doi.org/10.3382/ps/pez265

15. Morton JI, Siegel BV. Effects of oral dimethyl sulfoxide and dimethyl sulfone on murine autoimmune lymphoproliferative disease. Proc Soc Exp Biol Med. 1986;183:227–30. https://doi.org/10.3181/00379727-183-42409

16. McFarlin BK, Hill DW, Vingren JL, Curtis JH, Tanner EA. Dietary polyphenol and methylsulfonylmethane supplementation improves immune, DAMP signaling, and inflammatory responses during recovery from all-out running efforts. Front Physiol. 2021;12:712731. https://doi.org/10.3389/fphys.2021.712731

17. Lee DY, Lee CY, Shin JN, Oh J-H, Shim SM. Impact of soy lecithin, zinc oxide, and methylsulfonylmethane, as excipient ingredients, on the bioaccessibility and intestinal transport of branched-chain amino acids from animal and plant protein mixtures. Food Funct. 2021;12:11399–407. https://doi.org/10.1039/d1fo01712h

18. Hwang JW, Cheong SH, Kim YS, Lee JW, You BI, Moon SH, et al. Effects of dietary supplementation of oriental herbal medicine residue and methyl sulfonyl methane on the growth performance and meat quality of ducks. Anim Prod Sci. 2017;57:948. https://doi.org/10.1071/AN15134

19. Lee JI, Min HK, Lee JW, Jeong JD, Ha YJ, Kwack SC, et al. Changes in the quality of loin from pigs supplemented with dietary methyl sulfonyl methane during cold storage. Korean J Food Sci Anim Res. 2009;29:229–37. https://doi.org/10.5851/kosfa.2009.29.2.229

20. Wang H, Wang L, Tian C, Rajput SA, Qi D. Effects of methyl sulfonyl methane and selenium yeast on fatty liver syndrome in laying hens and their biological mechanisms. Animals (Basel). 2023;13:2466. https://doi.org/10.3390/ani13152466

21. Amirshahrokhi K, Niapour A. Methylsulfonylmethane protects against ethanol-induced brain injury in mice through the inhibition of oxidative stress, proinflammatory mediators and apoptotic cell death. Int Immunopharmacol. 2022;106:108638. https://doi.org/10.1016/j.intimp.2022.108638

22. Kim SH, Smith AJ, Tan J, Shytle RD, Giunta B. MSM ameliorates HIV-1 Tat induced neuronal oxidative stress via rebalance of the glutathione cycle. Am J Transl Res. 2015;7:328–38

23. Amirshahrokhi K, Khalili AR. Methylsulfonylmethane is effective against gastric mucosal injury. Eur J Pharmacol. 2017;811:240–8. https://doi.org/10.1016/j.ejphar.2017.06.034

24. Wong T, Bloomer RJ, Benjamin RL, Buddington RK. Small intestinal absorption of methylsulfonylmethane (MSM) and accumulation of the sulfur moiety in selected tissues of mice.

Nutrients. 2017;10:19. https://doi.org/10.3390/nu10010019

25. Magnuson BA, Appleton J, Ames GB. Pharmacokinetics and distribution of [35S]methylsulfonylmethane following oral administration to rats. J Agric Food Chem .2007;55:1033–8. https://doi.org/10.1021/jf0621469

26. Layman DL, Jacob SW. The absorption, metabolism and excretion of dimethyl sulfoxide by rhesus monkeys. Life Sci. 1985;37:2431–7. https://doi.org/10.1016/0024-3205(85)90111-0

27. Chen Z, Xu F, Ni L, Jiang J, Yu Y, Pan Y. Investigating semibatch oxidation reaction of dimethyl sulfoxide with hydrogen peroxide: Thermal analysis and process optimization. J Loss Prev Process Ind. 2023;85:105172. https://doi.org/10.1016/j.jlp.2023.105172

28. Pearson TW, Dawson HJ, Lackey HB. Natural occurring levels of dimethyl sulfoxide in selected fruits, vegetables, grains, and beverages. J Agric Food Chem. 1981;29:1089–91. https://doi.org/10.1021/jf00107a049

29. Ahn H, Kim J, Lee MJ, Kim YJ, Cho YW, Lee GS. Methylsulfonylmethane inhibits NLRP3 inflammasome activation. Cytokine. 2015;71:223–31. https://doi.org/10.1016/j.cyto.2014.11.001

30. Kim YB, Lee SH, Kim DH, Lee HG, Jeon YS, Lee SD, et al. Incorporation of dietary methyl sulfonyl methane into the egg albumens of laying hens. Antioxidants (Basel). 2022;11:517. https://doi.org/10.3390/antiox11030517

31. Kamel R, El Morsy EM. Hepatoprotective effect of methylsulfonylmethane against carbon tetrachloride-induced acute liver injury in rats. Arch Pharm Res. 2013;36:1140–8. https://doi.org/10.1007/s12272-013-0110-x

32. Bohlooli S, Mohammadi S, Amirshahrokhi K, Mirzanejad-Asl H, Yosefi M, Mohammadi-Nei A, et al. Effect of methylsulfonylmethane pretreatment on aceta-minophen induced hepatotoxicity in rats. Iran J Basic Med Sci. 2013;16:896–900

33. Jeon YS, Kim YB, Lee HG, Park J, Heo YJ, Chu GM, et al. Effect of dietary organic and inorganic sulfur on the performance of coccidiosis vaccine challenged broiler chickens. Animals (Basel). 2022;12:1200. https://doi.org/10.3390/ani12091200

34. Kim YB, Lee SH, Kim DH, Lee HG, Choi Y, Lee SD, et al. Effect of dietary organic and inorganic sulfur on laying performance, egg quality, ileal morphology, and antioxidant capacity in laying hens. Animals (Basel). 2021;12:87. https://doi.org/10.3390/ani12010087

35. Amirshahrokhi K, Bohlooli S, Chinifroush MM. The effect of methylsulfonylmethane on the experimental colitis in the rat. Toxicol Appl Pharmacol. 2011;253:197–202. https://doi.org/10.1016/j.taap.2011.03.017

36. Beilke MA, Collins-Lech C, Sohnle PG. Effects of dimethyl sulfoxide on the oxidative function of human neutrophils. J Lab Clin Med. 1987;110:91–6

37. Kang DY, Sp N, Bae SW, Jang KJ. Methylsulfonylmethane relieves cobalt chloride-induced hypoxic toxicity in C_2C1_2 myoblasts. Life Sci. 2022;301:120619. https://doi.org/10.1016/j.lfs.2022.120619

38. Dan Dunn J, Alvarez LA, Zhang X, Soldati T. Reactive oxygen species and mitochondria: A nexus of cellular homeostasis. Redox Biol. 2015;6:472–85. https://doi.org/10.1016/j.redox.2015.09.005

39. Kim YH, Kim DH, Lim H, Baek DY, Shin HK, Kim JK. The anti-inflammatory effects of methylsulfonylmethane on lipopolysaccharide-induced inflammatory responses in murine macrophages. Biol Pharm Bull. 2009;32:651–6. https://doi.org/10.1248/bpb.32.651

40. Manea A, Tanase LI, Raicu M, Simionescu M. Jak/STAT signaling pathway regulates nox1 and nox4-based NADPH oxidase in human aortic smooth muscle cells. Arterioscler Thromb Vasc Biol. 2010;30:105–12. https://doi.org/10.1161/ATVBAHA.109.193896

41. S P N, Darvin P, Yoo YB, Joung YH, Kang DY, Kim DN, et al. The combination of methylsulfonylmethane and tamoxifen inhibits the Jak2/STAT5b pathway and synergistically inhibits tumor growth and metastasis in ER-positive breast cancer xenografts. BMC Cancer. 2015;15:474. https://doi.org/10.1186/s12885-015-1445-0

42. Jiao Y, Cheng M, Li H, Yang H, Li X. Effects of Methylsulfonylmethane and epidermal Growth factor receptor-tyrosine kinase inhibitor on cell proliferation, cell cycle and anti-inflammatory effect in chicken intestinal epithelial cells with lipopolysaccharide challenge. Indian J Anim Res. 2023. https://doi.org/10.18805/IJAR.BF-1617

43. Jiao Y, Li H, Ren T, Kim IH. Protective effects of methylsulfonylmethane (MSM) on barrier function injury of porcine intestinal epithelial cells (IPEC-J2) induced by lipopolysaccharide (LPS). Can J Anim Sci. 2023;103:262–72. https://doi.org/10.1139/cjas-2022-0141

44. Miao Y, Niu D, Wang Z, Wang J, Wu Z, Bao J, et al. Methylsulfonylmethane ameliorates inflammation via NF-κB and ERK/JNK-MAPK signaling pathway in chicken trachea and HD11 cells during Mycoplasma gallisepticum infection. Poult Sci. 2022;101:101706. https://doi.org/10.1016/j.psj.2022.101706

45. Lim CI, Ryu KS. Additive Effects of dietary supplementation with zeolite and methyl-sulfonyl-methane on growth performance and interleukin levels of broiler chickens. J Poult Sci. 2023;60:n/a. https://doi.org/10.2141/jpsa.2023003

46. Cheleschi S, Fioravanti A, De Palma A, Corallo C, Franci D, Volpi N, et al. Methylsulfonylmethane and mobilee prevent negative effect of IL-1β in human chondrocyte cultures via NF-κB signaling pathway. Int Immunopharmacol. 2018;65:129-139. doi: 10.1016/j.intimp.2018.10.004.

47. Ma W, Ao S, Zhou J, Li J, Liang X, Yang X, et al. Methylsulfonylmethane protects against lethal dose MRSA-induced sepsis through promoting M2 macrophage polarization. Mol Immunol. 2022;146:69–77. https://doi.org/10.1016/j.molimm.2022.04.001

48. Butawan M, van der Merwe M, Benjamin RL, Bloomer RJ. Chapter 32 - Methylsulfonylmethane: antiinflammatory actions and usage for arthritic conditions. In: Watson RR, Preedy VR, editors.

Bioactive Food as Dietary Interventions for Arthritis and Related Inflammatory Diseases (Second Edition), Academic Press; 2019. p. 553–73. https://doi.org/10.1016/B978-0-12-813820-5.00032-5

49. Guo D, Zhang L, Zhang L, Han S, Yang K, Lin X, et al. Effect of dietary methylsulfonylmethane supplementation on growth performance, hair quality, fecal microbiota, and metabolome in ragdoll kittens. Front Microbiol. 2022;13:838164. https://doi.org/10.3389/fmicb.2022.838164

50. Liu X, Hunter DJ, Eyles J, McLachlan AJ, Adiwidjaja J, Eagles SK, et al. Pharmacokinetic assessment of constituents of Boswellia serrata, pine bark extracts, curcumin in combination including methylsulfonylmethane in healthy volunteers. J Pharm Pharmacol. 2020;72:121–31. https://doi.org/10.1111/jphp.13184

51. Murav'ev IV, Venikova MS, Pleskovskaia GN, Riazantseva TA, Sigidin IA. [Effect of dimethyl sulfoxide and dimethyl sulfone on a destructive process in the joints of mice with spontaneous arthritis]. Patol Fiziol Eksp Ter. 1991:37–9

52. Ezaki J, Hashimoto M, Hosokawa Y, Ishimi Y. Assessment of safety and efficacy of methylsulfonylmethane on bone and knee joints in osteoarthritis animal model. J Bone Miner Metab. 2013;31:16–25. https://doi.org/10.1007/s00774-012-0378-9

53. Amiel D, Healey R, Oshima Y. Assessment of methylsulfonylmethane (MSM) on the development of osteoarthritis (OA): An animal study. The FASEB J. 2008;22. https://doi.org/10.1096/fasebj.22.1_supplement.1094.3

54. Arafa NM, Hamuda HM, Melek ST, Darwish SK. The effectiveness of Echinacea extract or composite glucosamine, chondroitin and methyl sulfonyl methane supplements on acute and chronic rheumatoid arthritis rat model. Toxicol Ind Health. 2013;29:187–201. https://doi.org/10.1177/0748233711428643

55. Maher AD, Coles C, White J, Bateman JF, Fuller ES, Burkhardt D, et al. 1H NMR spectroscopy of serum reveals unique metabolic fingerprints associated with subtypes of surgically induced osteoarthritis in sheep. J Proteome Res. 2012;11:4261–8. https://doi.org/10.1021/pr300368h

56. Dalle Carbonare L, Bertacco J, Marchetto G, Cheri S, Deiana M, Minoia A, et al. Methylsulfonylmethane enhances MSC chondrogenic commitment and promotes pre-osteoblasts formation. Stem Cell Res Ther. 2021;12:326. https://doi.org/10.1186/s13287-021-02396-5

57. Guo Y, Li P, Wang Z, Zhang P, Wu X. Sustained Delivery of methylsulfonylmethane from biodegradable scaffolds enhances efficient bone regeneration. Int J Nanomedicine. 2022;Volume 17:4829–42. https://doi.org/10.2147/IJN.S377036

58. Aljohani H, Senbanjo LT, Chellaiah MA. Methylsulfonylmethane increases osteogenesis and regulates the mineralization of the matrix by transglutaminase 2 in SHED cells. PLoS ONE. 2019;14:e0225598. https://doi.org/10.1371/journal.pone.0225598

59. Aljohani H, Senbanjo LT, Al Qranei M, Stains JP, Chellaiah MA. Methylsulfonylmethane increases the alveolar bone density of mandibles in aging female mice. Front Physiol. 2021;12:708905. https://doi.org/10.3389/fphys.2021.708905

60. Ha S-H, Choung P-H. MSM promotes human periodontal ligament stem cells differentiation to osteoblast and bone regeneration. Biochemical and Biophysical Res Co. 2020;528:160–7. https://doi.org/10.1016/j.bbrc.2020.05.097

61. Ryu JH, Kang TY, Shin H, Kim KM, Hong MH, Kwon JS. Osteogenic properties of novel methylsulfonylmethane-coated hydroxyapatite scaffold. Int J Mol Sci. 2020;21:8501. https://doi.org/10.3390/ijms21228501

62. Hummadi AA, Gany SN, Hadi NR. Evaluation of the Effect of topically applied methylsulfonylmethane and their combination with minoxidil solution for improvement of hair growth in male mice. Wiad Lek. 2022;75:2744–51. https://doi.org/10.36740/WLek202211206

63. Shanmugam S, Baskaran R, Nagayya-Sriraman S, Yong CS, Choi HG, Woo JS, et al. The effect of methylsulfonylmethane on hair growth promotion of magnesium ascorbyl phosphate for the treatment of alopecia. Biomol Ther. 2009;17:241–8. https://doi.org/10.4062/biomolther.2009.17.3.241

64. Anthonavage M, Benjamin R. Effects of oral supplementation with methylsulfonylmethane on skin health and wrinkle reduction. Nat Med J. 2015;Vol 7

65. Muizzuddin N, Benjamin R. Beauty from within: Oral administration of a sulfur-containing supplement methylsulfonylmethane improves signs of skin ageing. International Journal for Vitamin and Nutrition Research 2022;92:182–91. https://doi.org/10.1024/0300-9831/a000643

66. Fleck CA. Managing ichthyosis: a case study. Ostomy Wound Manage. 2006;52:82–6, 88, 90, passim

67. Kim IW, Park WJ, Yun HY, Kim DS. Methylsulfonylmethane promotes melanogenesis via activation of JNK in Mel-Ab cells. Int J Cosmetic Sci. 2024;46:918–26. https://doi.org/10.1111/ics.12988

68. Chu SG, Chang YJ, Ryu JY, Lee JS, Choi KY, Chung HY, et al. Effects of methylsulfonylmethane on UVB-induced skin damage: An experimental study in a mouse model. In Vivo. 2022;36:2714–21. https://doi.org/10.21873/invivo.13007

69. Lim EJ, Hong DY, Park JH, Joung YH, Darvin P, Kim SY, et al. Methylsulfonylmethane suppresses breast cancer growth by down-regulating STAT3 and STAT5b pathways. PLoS One. 2012;7:e33361. https://doi.org/10.1371/journal.pone.0033361

70. Joung YH, Na YM, Yoo YB, Darvin P, Sp N, Kang DY, et al. Combination of AG490, a Jak2 inhibitor, and methylsulfonylmethane synergistically suppresses bladder tumor growth via the Jak2/STAT3 pathway. Int J Oncol. 2014;44:883–95. https://doi.org/10.3892/ijo.2014.2250

71. Kim JH, Shin HJ, Ha HL, Park YH, Kwon TH, Jung MR, et al. Methylsulfonylmethane suppresses hepatic tumor development through activation of apoptosis. World J Hepatol. 2014;6:98–106. https://doi.org/10.4254/wjh.v6.i2.98

72. Kowalska K, Habrowska-Górczyńska DE, Kurczewska D, Domińska K, Urbanek KA, Piastowska-Ciesielska AW. Methylsulfonylmethane sensitizes endometrial cancer cells to doxorubicin. Cell Biol Toxicol. 2021;37:261–75. https://doi.org/10.1007/s10565-020-09542-4

73. Tanner EA, Gary MA, Michalik S, Davis AA, McFarlin BK. Optimized curcumin, pomegranate extract, and methylsulfonylmethane reduce acute, systemic inflammatory response to a half-marathon race. Altern Ther Health Med. 2022;28:72–81

74. Miller L, Thompson K, Pavlenco C, Mettu VS, Haverkamp H, Skaufel S, et al. The effect of daily methylsulfonylmethane (MSM) consumption on high-density lipoprotein cholesterol in healthy overweight and obese adults: A randomized controlled trial. Nutrients. 2021;13:3620. https://doi.org/10.3390/nu13103620

75. Abdel-Rafei MK, Thabet NM. Modulatory effect of methylsulfonylmethane against BPA/γ-radiation induced neurodegenerative alterations in rats: Influence of TREM-2/DAP-12/Syk pathway. Life Sci. 2020;260:118410. https://doi.org/10.1016/j.lfs.2020.118410

76. Gou P, Comaposada J, Arnau J. Meat pH and meat fibre direction effects on moisture diffusivity in salted ham muscles dried at 5°C. Meat Sci 2002;61:25–31. https://doi.org/10.1016/s0309-1740(01)00158-9

77. Warner RD. Chapter 14 - The eating quality of meat: IV—Water holding capacity and juiciness. In: Toldrá F, editor. Lawrie's Meat Science (Ninth Edition), Woodhead Publishing; 2023, p. 457–508. https://doi.org/10.1016/B978-0-323-85408-5.00008-X

78. Faustman C, Suman SP, Ramanathan R. Chapter 11 - The eating quality of meat: I Color. In: Toldrá F, editor. Lawrie's Meat Science (Ninth Edition), Woodhead Publishing; 2023. p. 363–92. https://doi.org/10.1016/B978-0-323-85408-5.00023-6

79. Suman SP, Joseph P. Myoglobin chemistry and meat color. Annu Rev Food Sci Technol. 2013;4:79–99. https://doi.org/10.1146/annurev-food-030212-182623

80. Mortimer SI, van der Werf JHJ, Jacob RH, Hopkins DL, Pannier L, Pearce KL, et al. Genetic parameters for meat quality traits of Australian lamb meat. Meat Sci. 2014;96:1016–24. https://doi.org/10.1016/j.meatsci.2013.09.007

81. Petracci M, Mudalal S, Babini E, Cavani C. Effect of white striping on chemical composition and nutritional value of chicken breast meat. Ital J Anim Sci. 2014;13:3138. https://doi.org/10.4081/ijas.2014.3138

82. Flores M. Chapter 13 - The eating quality of meat: III—Flavor. In: Toldrá F, editor. Lawrie's Meat Science (Ninth Edition), Woodhead Publishing; 2023. p. 421–55. https://doi.org/10.1016/B978-0-323-85408-5.00014-5

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Table 1. The content of MSM in common feed and food (mg/kg).

type	content
alfalfa	0.77
corn	up to 0.11
swiss chard	up to 0.18
tomatoes	up to 0.86
cow's milk	3.30
tea	0.30
coffee	1.60
beer	0.18

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Table 2. Effects of graded levels of dietary MSM on the markers of oxidative stress in animals.

Items[1]	Animals	Sample	Dietary MSM	Time	*p*-Value[2]	Dietary MSM decreased (-) or increased (+) items' concentration compared with the non-supplemented control	Ref.
GPX, U/L CAT, U/mL 8-OHdG, ng/mL	73-week-old laying hens (Lohmann Brown Lite)	serum	0, 0.1, 0.2, 0.3 and 0.4 %	4/8/12 wks	> 0.05	No effects	[30]
SOD, %				12 wks	0.002	+31.24	
TAC, mM				8/12 wks	< 0.05	+0.32/+0.44	
MDA, μM				8 wks	0.025	-6.85	
SOD, %	73-wk-old laying hens (Lohmann Brown-Lite)	serum	0 and 2 g/kg	12 wks	0.014	+18	[10]
TAC,mM					0.068	No effects	
GPX, U/L					0.644		
CAT, U/mL					0.861		
MDA, μM					0.324		
8-OHdG, ng/mL					0.886		
GPX, U/mg		liver			0.199	No effects	
CAT, U/mg					0.920		
TAC, nmol/mg					0.002	+6.19	
MDA, nmol/mg					0.026	-0.51	
GPX, U/mL SOD, %	male Ross 308 broilers	plasma	0, 1 and 2 g/kg	23/25/39 days	> 0.05	No effects	[13]
MDA, mL				25/39 days	< 0.05	-1.6/-2.2	
GSH, μmol/mL		erythrocytes		23/39 days	< 0.05	+0.34/+0.17	
GSSG,μmol/mL GSSG/GSH				23/25/39 days	> 0.05	No effects	
GPX, U/mL		liver		23 days	0.043	-1.0	
SOD, % MDA, mL GSH, μmol/mL GSSG,μmol/mL GSSG/GSH				23/25/39 days	> 0.05	No effects	
MDA, nmol/mL	55-wk-old Jing-fen	serum	0, 350 and 700	4 wks	< 0.05	-	[20]

SOD, U/mL	No.6 laying hens		mg/kg		< 0.05	+	
CAT, U/mL					> 0.05	No effects	
GPX, U/mL							
MDA, nmol/mg		liver			< 0.05	-	
SOD, U/mg mg					< 0.05	+	
CAT, U/mL					> 0.05	No effects	
GPX, U/mg					< 0.05	+	
TAC, mM	broiler chicks (Ross 308)	serum	0 and 2 g/kg	21 days	> 0.05	No effects	[33]
MDA, µM							
TAC, nmol/mg		liver			< 0.05	+13.07	
MDA, nmol/mg					> 0.05	No effects	
TAC, nmol/mg		ileum			> 0.05	No effects	
MDA, µM							
MDA, µM	73-week-old laying hens (Lohmann Brown-Lite)	serum	0 and 2.0 g/kg	12 wks	0.025	-10.05	[34]
SOD, %				4/8/12 wks	> 0.05	No effects	
TAC, mM							
CAT, U/mL							
GPX, U/L							
8-OHdG, ng/mL							
TAC, nmol/mg		liver		12 wks	<0.001	+10.76	
GPX, U/mg					> 0.05	No effects	
CAT, U/mg							
MDA, nmol/mg							
SOD, U/mL	female Pekin ducklings	serum	0, 0.15 and 0.3%	42 days	0.03	+23	[8]
GPX, U/mL					0.02	+33	
MDA, nmol/mL					0.03	-1.14	
TAC, U/mL					0.02	+6.4	
IgG, µg/mL					0.38	No effects	
TAC, mmol/L	Ross 308 male broiler chicks	serum	0 and 0.05%	7 days	0.023	+0.4	[7]
TBARS, µmol/L				7/14/21 days	> 0.05	No effects	
TGSH,µmol/mL							
GPX, nmol/mL							
GR, nmol/mL							

TBARS, μmol/g		liver		7/14/21 days	> 0.05	No effects	
TAC, mmol/g							
TGSH, μmol/g				21 days	0.012	_	
GPX, nmol/mg				21 days	0.003	+	
GR, nmol/mg				7 days	0.004	+	
MDA, μmol	male Ross 308 chicks	serum	0 and 0.4%	21/28 days	< 0.05	-3.34/-3.26	[12]
TAC, mmol				14/21/28 days	< 0.05	-0.4/+0.53/-0.15	
SOD, U/mL	ragdoll kittens	serum	0, 0.2 and 0.4%	0/35/65 days	> 0.05	No effects	[49]
MDA, nmol/mL							
GSH, U							
CAT, U/mL							
TAC , mM							
SOD, U/mg	rats	liver	0, and 400 mg/kg	5 days	< 0.05	+1.74±0.1	[31]
TAC, U/gm						+14.59±0.3	
MDA, μM/g						-5.36±0.1	
MDA, nmol/mg	rats	colonic tissue	0, and 400 mg/kg	4 days	< 0.05	-	[35]
MPO, U/mg						-	
GSH, nM/mg						+	
CAT, nmol/mg						+	
MDA, nmol/mg	rats	liver	0, and 100 mg/kg	7 days	< 0.05	-3.75±0.59	[32]
MPO, U/mg						-1.7±0.4	
SOD, U/mg						+0.8±0.3	
GSH, nmol/mg						+10.32±0.93	

[1]CAT, catalase; GPX, glutathione peroxidase; GR, glutathione reductase; GSH, glutathione; GSSG, glutathione disulphide; IgG, immunoglobulin G; MDA, malondialdehyde; MPO, myeloperoxidase; SOD, superoxide dismutase; TAC, total antioxidant capacity; TBARS, thiobarbituric acid reactive substances; TGSH, total glutathione; 8-OHdG, 8-hydroxydeoxyguanosine.

[2]Significant differences among different levels of dietary MSM were determined at $p<0.05$.

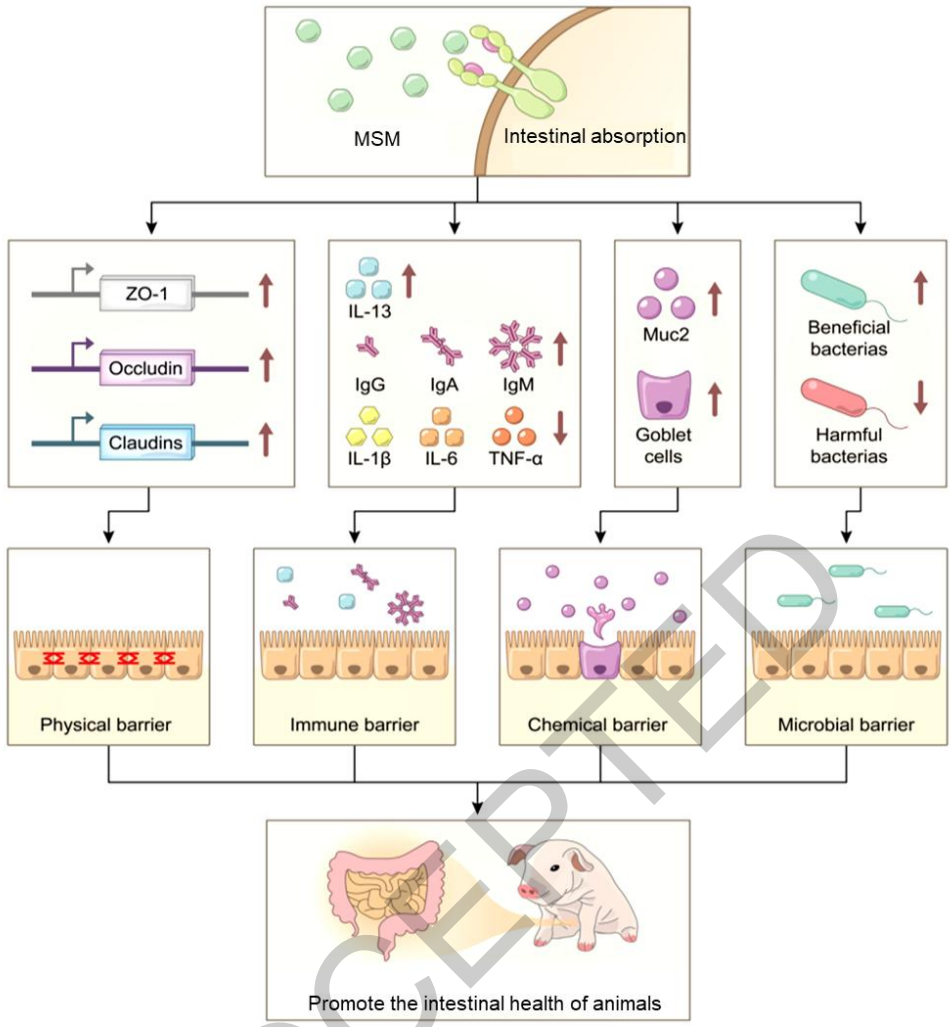
Table 3. Effects of graded levels of dietary MSM on the markers of inflammation stress in animals.

Items[1]	Animals	Sample	Dietary MSM	Time	*p*-Value[2]	Dietary MSM decreased (-) or increased (+) items' concentration compared with the non-supplemented control	Ref.
IL-10 IL-1β IFN-γ	male ross 308 chicks	ceca	0 and 0.4%	12/19 days	> 0.05	No effects	[12]
IL-2, ng/mL	female Pekin ducks	serum	0, 0.15 and 0.3%	42 days	0.03	+14	[8]
IL-6, ng/mL					0.04	+2.9	
IFN-γ, ng/mL					0.02	-2.6	
TNF-α, pg/mL					0.03	-2.7	
IL-2 mRNA	ross broiler chicks	spleen	0 and 0.10%	35 days	0.192	No effects	[45]
IL-2 mRNA		bursa			0.008	+0.686	
IL-2, pg/mL		serum			0.029	+19	
IL-6, pg/mL					0.018	+25	
TNF-α IL-1β IL-6	chickens	intestinal epithelial cells	0 and 100 mM	24 h	< 0.05	-	[42]
TNF-α IL-1β IL-6	white leghorn chickens	chicken like macrophages (HD11 cells)	0 and 200 mmol/L	12 h	< 0.05	-	[44]
IL-8					> 0.05	No effects	
TNF-α IL-6 IL-1	pigs	IPEC-J2 cells	0, 200 and 300 mmol/L	24 h	< 0.05	-	[43]
IL-1β, pg/mg	rats	colonic	400 mg/kg	4 days	< 0.05	-	[35]

TNF-α, pg/mg					> 0.05	No effects	
TNF-α,pg/mg IL-1β, pg/mg IL-6, pg/mg MCP-1, pg/mg	swiss albino mice	gastric tissue	0, 200 and 400 mg/kg	1 h	< 0.05	-	[23]
TNF-α,pg/mg IL-1β, pg/mg IL-6, pg/mg MCP-1, pg/mg	male C57BL/6 mice	brain	0, 200 and 400 mg/kg/day	12 days	< 0.05	-	[21]

[1]IFN-γ, interferon-γ; IL-1β/-2/-6/-8/-10, interleukin (IL)-1β/-2/-6/-8/-10; MCP-1, monocyte chemoattractant protein (MCP)-1; TNF-α, tumor necrosis factor.

[2]Significant differences among different levels of dietary MSM were determined at $p<0.05$.



IL-1β/-6/-13, interleukin (IL)-1β/-6/-13; TNF-α, tumor necrosis factor-α; IgA, immunoglobulin A; IgG, immunoglobulin G; IgM, immunoglobulin M; Muc-2, Mucin2; ZO-1, zona occluden-1.

Figure 1. MSM promotes intestinal health in animals by promoting a variety of intestinal barrier functions.