DIMETHYL SULFOXIDE (DMSO) IN HUMAN HEALTH

REVIEW ARTICLE

Author: Joshua Leisk ©2025 https://bornfree.life

INTRODUCTION

Dimethyl sulfoxide (DMSO) is a small organosulfur molecule (chemical formula (CH3)2SO) best known as a powerful polar solvent. First synthesised in the mid-19th century, DMSO was largely used in industry until medical properties were discovered in the 1950s [1]. It can rapidly penetrate biological membranes and carry other compounds with it [1]. Early research suggested DMSO has diverse biological activities - from reducing inflammation and pain to protecting cells from injury [1]. Its odorless crystalline metabolite, methylsulfonylmethane (MSM, or DMSO2), shares some properties but without DMSO's characteristic garlic odour side effect [12].

Despite initial enthusiasm, DMSO's medical adoption has been contentious. In the 1960s, it was touted as a 'wonder drug' for numerous conditions, but safety concerns (notably eye lens changes in animals) led to regulatory pullback [2]. Today, only a few specific medical uses of DMSO are formally approved, even as many practitioners and patients continue to use it off-label for a wide range of ailments [2]. This review summarises the known therapeutic uses and mechanisms of DMSO, its toxicology profile compared to typical human exposure levels, the realism of achieving toxic doses in practice, its regulatory history and status around the world, and a comparison with MSM in terms of efficacy, safety, and approval status.

THERAPEUTIC USES OF DMSO IN HUMANS

APPROVED AND ESTABLISHED USES

In the United States, DMSO is officially approved only for interstitial cystitis (bladder pain syndrome). A 50% DMSO solution is instilled into the bladder as a therapeutic irrigation to relieve chronic inflammatory bladder pain [2]. This remains the only U.S. Food and Drug Administration (FDA)-approved human medical use of DMSO. Similarly, Health Canada has approved DMSO for chronic inflammatory genitourinary conditions - including interstitial cystitis, radiation cystitis, and painful bladder/prostate conditions - as an intravesical therapy [12].

DMSO is also used under regulatory approval as a cryoprotective agent for preserving cells and tissues (e.g. bone marrow stem cells) prior to transplantation [12].

In Europe, DMSO is recognised in practice as a bladder instillation treatment (featured in urology guidelines) and is often available for this use, although other instillates (such as chondroitin sulphate solutions) are also approved in some countries [17]. No oral DMSO drug products are formally approved in Western countries.

OFF-LABEL AND ALTERNATIVE MEDICINE USES

Beyond bladder instillation, DMSO has been - historically and presently - used (mostly without formal approval) for a remarkable variety of conditions. In the 1960s, Dr. Stanley Jacob and others reported DMSO's potential for treating MUSCULOSKELETAL DISORDERS AND PAIN (such as arthritis, tendon injuries, and muscle strains), SCLERODERMA (SKIN THICKENING), HEADACHES, and even severe conditions like SPINAL CORD INJURY AND STROKE [2] [3].

Topical DMSO applications (often as gels or creams in concentrations ranging 25-70%) have been popular for OSTEOARTHRITIS, BURSITIS, AND SPRAINS, aiming to reduce pain and inflammation. Indeed, a double-blind trial in 1995 found that a 25% DMSO gel significantly reduced joint pain in arthritis patients [12], though some subsequent studies had mixed results. Athletes have used DMSO rubs for sports injuries to speed recovery, capitalising on its analgesic effects [12].

Some clinicians have explored DMSO INTRAVENOUS INFUSIONS for severe infections, PULMONARY CONDITIONS, or CANCER, but such uses remain speculative and unapproved [2].

MECHANISMS OF ACTION

DMSO's broad therapeutic potential is tied to multiple mechanisms:

MEMBRANE PENETRATION AND DRUG DELIVERY

DMSO is a powerful carrier that enhances absorption of other substances through skin and cell membranes [1].

This property underlies its use in topical formulations to drive other active drugs deeper into tissues. For example, DMSO can facilitate transport of compounds like EDTA or antibiotics across biological barriers that would otherwise be impermeable [4].

ANTI-INFLAMMATORY AND ANTIOXIDANT EFFECTS

DMSO exhibits notable anti-inflammatory activity in biological systems. It suppresses the production of pro-inflammatory cytokines (e.g. IL-1, TNF-a) by immune cells. In an ex vivo human blood study, low millimolar concentrations of DMSO significantly reduced endotoxin-stimulated release of IL-6, IL- β and TNF-a from leukocytes [2].

In a mouse model of rheumatoid arthritis, topical 70% DMSO applications twice daily markedly reduced joint swelling and downregulated inflammatory gene expression in the affected tissue [2].

At the molecular level, DMSO scavenges hydroxyl radicals and other reactive oxygen species, thus dampening oxidative stress that drives inflammation [3]. It also inhibits activation of nuclear factor κB (NF-κB) and other pathways in inflammatory cascades, similar to some NSAIDs, though DMSO is not a classic COX inhibitor.

ANALGESIC (PAIN-RELIEVING) ACTION

Rapid pain relief often follows DMSO application, partly due to its reduction of inflammation but also due to a direct effect on nerves. DMSO can block peripheral C-fibre neuronal conduction, acting as a local analgesic. Some studies indicate it increases release of endogenous opioids and modulates substance P, which may contribute to pain relief [2] [12].

Clinically, patients report relief of pain from arthritis, burns, and even neuropathic pain after DMSO application, often within minutes, supporting a genuine analgesic mechanism beyond placebo.

IMPROVED MICROCIRCULATION AND TISSUE PROTECTION

DMSO has vasodilatory properties that can enhance microvascular blood flow in tissues. In animal models, DMSO application prevented microcirculatory disturbances caused by toxins, reduced tissue oedema, and restored normal capillary perfusion [11].

By limiting ischemia and swelling, DMSO may protect tissues from secondary injury after trauma. Additionally, DMSO's unique ability to enter cells and stabilise cell membranes helps cells survive stresses like freezing or hypoxia, which is why it is used to cryopreserve cells without lethal ice crystal formation [2].

In models of CNS AND CARDIAC INJURY, DMSO has been shown to attenuate multiple pathological processes: it restricts excitotoxic damage by limiting glutamate release and NMDA receptor activation, reduces influx of destructive calcium ions into injured cells, and even blocks tissue factor to reduce micro-thrombosis [3]. These combined actions can mitigate the spread of damage in stroke, spinal cord injury, or heart attack, as noted in various preclinical studies [3].

Though human trials are lacking, these properties suggest why some practitioners tried DMSO for acute brain or cord trauma.

OTHER ACTIONS

DMSO has mild MUSCLE RELAXANT effects and can cause histamine release from mast cells at higher concentrations [1], which might paradoxically improve circulation and healing in low doses. It also exhibits broad-spectrum ANTIMICROBIAL AND ANTIBIOFILM ACTIVITY in vitro - for instance, 32% DMSO was able to kill and disperse bacterial biofilms of E. coli, P. aeruginosa, and Salmonella, partly by chemically disrupting the biofilm matrix [8].

Clinically, DMSO is not used primarily as an antibiotic, but this property may contribute to improved wound healing and reducing infection in DMSO-treated injuries. Finally, DMSO has anticholinesterase activity (raising acetylcholine levels) and has been noted to reduce intracranial pressure, both potentially useful effects in certain scenarios [3].

EFFICACY EVIDENCE

The evidence base for many DMSO uses is mixed. Some double-blind trials in OSTEOARTHRITIS found significant pain reduction with DMSO gel, but others had inconclusive outcomes [10].

A systematic review (2008) of DMSO for osteoarthritis identified four controlled trials; half showed pain improvement, but methodological flaws and short durations made conclusions uncertain [10].

By contrast, two small trials of MSM for arthritis in that review showed modest pain relief, hinting that MSM (a related supplement) might also be beneficial [10].

For INTERSTITIAL CYSTITIS, use of intravesical DMSO is supported mainly by case series from the 1970s - patients often report symptom relief, and both American Urological Association (AUA) and European Association of Urology (EAU) guidelines list 50% DMSO instillation as a second-line therapy in refractory cases [17].

WOUND AND ULCER HEALING with topical DMSO has mainly anecdotal support, though its anti-inflammatory and collagen-softening effects have led to experimental use in scleroderma and Peyronie's disease (penile fibrosis). High-

quality modern trials are scarce, in part because DMSO, as an inexpensive generic chemical, attracts little commercial research funding. Still, a "PLOS One" study in 2016 concluded that DMSO's apparent benefits in arthritis and inflammatory conditions warrant renewed investigation in well-controlled studies [2].

TOXICOLOGY AND SAFETY PROFILE OF DMSO

DMSO is often described as a substance of “low intrinsic toxicity”, especially given its long history of use in medicine and research. It is classified by the FDA and International Conference on Harmonisation (ICH) as a Class 3 solvent - the safest category - indicating no evidence of carcinogenicity or genotoxicity and only mild toxicity at most in animal studies [14].

Acute lethal doses are very high: the oral LD50 in rats exceeds 5 g/kg, and dermal LD50 is similarly high, meaning it takes enormous doses to cause death in animals [14]. In practical terms, this would be equivalent to a 70 kg human ingesting over 350 g of DMSO acutely - far above any therapeutic amount. DMSO is NOT A CUMULATIVE TOXIN; it is mostly metabolised to dimethyl sulfone (MSM) or dimethyl sulphide and excreted within a day or two [1].

LOCAL AND SYSTEMIC TOLERANCE

Most people can apply DMSO topically or take it orally at moderate doses with only minor side effects. SKIN IRRITATION is the most common adverse effect of concentrated DMSO. Applications above ~70% can cause burning, itching, and dryness of skin in some individuals [13]. This is partly due to the exothermic reaction when DMSO mixes with water on the skin, releasing heat [13].

At concentrations below 50%, skin reactions are uncommon, and at 10% or less DMSO is not expected to induce irritation [13]. DMSO does not typically cause allergic sensitisation of the skin [13]. OCULAR IRRITATION can occur if DMSO contacts the eyes, warranting flushing with water [13], but in normal use this is avoidable.

The hallmark side effect of systemic DMSO is a GARLIC- OR OYSTER-LIKE ODOR on the breath and skin of the user. This is caused by metabolic conversion of a fraction of DMSO into volatile dimethyl sulphide (DMS) which is exhaled and excreted through sweat [12]. The odour is harmless but can be socially off-putting; it appears shortly after dosing and can linger for days if large doses are taken continuously. GASTROINTESTINAL UPSET (nausea, diarrhea) is occasionally reported with oral DMSO, especially if taken in high concentrations without dilution. Users sometimes mitigate this by taking divided doses or with food.

TOXICITY IN ANIMAL STUDIES

High-dose studies in animals have generally reinforced DMSO's low chronic toxicity. Repeat-dose studies in rodents at the “limit dose” of 1000 mg/kg/day (about 70 g per day for a human) showed "no significant organ toxicity" [13].

DMSO has been found non-carcinogenic and non-teratogenic in lab tests [13]. Notably, unlike many solvents, DMSO was negative in genotoxicity assays [13].

The one famous toxicity finding that halted clinical research in 1965 was the discovery of LENS CHANGES IN THE EYES of animals on high-dose DMSO [2]. Rabbits and dogs given DMSO developed refractive index changes and even cataracts in their ocular lenses, sparking concern that humans might risk eye injury [2]. This prompted the FDA to suspend all DMSO trials in 1965 [2].

However, later investigations showed such effects occurred at doses far above those used clinically, and subsequent primate studies did not replicate significant cataract formation [2]. By 1980 the FDA lifted the ban, acknowledging that moderate DMSO use did not seem to threaten human vision [2]. To date, cataracts have not been reported as an issue in humans using DMSO therapeutically.

Interestingly, one animal study found that injecting a large dose of DMSO triggers an ACUTE PHASE REACTION - an immediate stress/inflammatory response. Rats given an acute DMSO injection showed a rapid spike in cortisol and a dramatic increase in plasma acute phase proteins (cysteine protease inhibitor, fibrinogen, haptoglobin, etc.) within 24 hours [6].

These changes mimicked those seen during severe inflammation (such as from turpentine injection) [6]. This suggests that a sudden high dose of DMSO can stress the system, likely due to DMSO's solvent action disrupting cell membranes or releasing histamine.

In practical terms, RAPID IV INJECTION of concentrated DMSO is known to cause side effects like histamine flush, dizziness, or hypotension. Clinicians using DMSO intravenously (e.g. during Onyx angiographic procedures for aneurysm embolization) recommend slow infusion rates to avoid such reactions.

In one study of 38 patients receiving intra-arterial DMSO as a solvent for Onyx, careful slow injection (with <0.5 mL/min) resulted in NO OBSERVABLE TOXIC REACTION or hemodynamic changes [5]. The only effect was mild transient oxygen desaturation in some patients, likely from exhaled DMS displacing air in the lungs [5].

This demonstrates that "rate and concentration" of DMSO exposure are critical determinants of tolerance.

IN VITRO CELL TOXICITY

In cell culture research, DMSO is commonly used as a solvent for water-insoluble drugs, but scientists know to keep its concentration low (usually =0.1-0.5% v/v) to avoid cytotoxicity. At higher concentrations, DMSO can harm or kill cells in vitro. Notably, a 2014 study reported “UNEXPECTED LOW-DOSE TOXICITY” of DMSO in retinal cells: concentrations above 1% (v/v) induced apoptosis in cultured neuronal cells [9].

The mechanism involved mitochondrial damage and translocation of apoptosis-inducing factor, indicating DMSO can trigger cell death pathways at moderate levels [9]. Concentrations above 10% caused rapid cell membrane pore formation and necrosis [9].

A more recent study in 2019 found that even 0.1% DMSO - a concentration generally considered safe in lab assays - caused DRASTIC CHANGES IN GENE EXPRESSION in human cell-based organoid models [16]. Over 2,000 genes were differentially expressed in cardiac and liver 3D microtissues after prolonged exposure to 0.1% DMSO [16]. Pathways affected included those related to epigenetic regulation and metabolism. This underscores that DMSO, even in seemingly minor amounts, is biologically active and can modulate cell function.

While these in vitro concentrations (0.1-1%) are higher than typical human plasma levels from therapeutic dosing (discussed below), the findings urge caution in assuming DMSO is inert at low doses.

COMMON ADVERSE EFFECTS IN HUMANS

The majority of documented side effects of DMSO in humans are mild and reversible. Besides the garlic odour and skin irritation, some users experience HEADACHE, DIZZINESS, OR SEDATION shortly after dosing - likely due to DMSO's vasodilatory effect and possibly trace impurities.

HYPERSENSITIVITY REACTIONS (allergic rash, anaphylactoid symptoms) are very rare given DMSO's simple structure and prevalence; most people's bodies do not recognise it as a foreign allergen. There are, however, case reports of HAEMOLYSIS or red blood cell damage when DMSO-containing solutions are infused intravenously too concentrated.

For this reason, clinical protocols (e.g. for stem cell infusions containing 10% DMSO cryoprotectant) often recommend diluting the infused product or limiting the infusion rate to prevent haemolysis and cardio-respiratory effects (patients sometimes experience bradycardia, hypertension, or shortness of breath from DMSO-containing infusions) [5].

Such effects are transient and manageable with slowing infusion or supportive care. Overall, NO SERIOUS LONG-TERM TOXICITIES IN HUMANS have definitively been linked to DMSO at therapeutic dosages - a conclusion supported by decades of widespread (if unofficial) use.

EXPOSURE LEVELS

ARE TOXIC CONCENTRATIONS ACHIEVABLE IN HUMANS?

Given the distinctions between concentrations causing toxicity in labs/animals and doses used in people, a key question is whether those “toxic” levels can ever be reached in human systemic circulation via normal therapeutic use. We can compare typical human doses (oral or topical) to the levels known to cause harm in various models:

TYPICAL HUMAN DOSE AND PLASMA LEVELS

A common oral or topical DMSO regimen in alternative medicine is about 5-30 mL of DMSO per day (often taken as 1-2 teaspoons of 50-70% solution, or applied on skin) - roughly equivalent to 5-30 grams of DMSO (density ~1.1 g/mL). Assuming an even distribution in total body water (~42 L in a 70 kg adult), a 5 mL dose (~5.5 g) would yield an initial concentration around 0.13 G/L, and a 30 mL dose (33 g) about 0.79 G/L.

In molar terms, these correspond to ~1.7 mM for the low dose and ~10 mM for the high dose (molecular weight 78.1). Peak plasma levels might be lower if absorption is spread out, or higher if taken all at once; DMSO is well absorbed orally and through skin, so significant systemic absorption does occur [14].

However, DMSO is also metabolised (via oxidation to MSM or reduction to DMS) and excreted relatively rapidly (plasma half-life on the order of hours), so it doesn't indefinitely accumulate.

IN VITRO VS IN VIVO

Toxicity in vitro was noted at 1% (v/v) = ~140 mM for frank cell death [9], and at 0.1% = ~14 mM for subtle gene effects [16]. The "highest" plausible plasma concentration from a huge 30 mL dose (~10 mM) still "barely approaches" the 14 mM level - and that would be transient and in plasma, whereas cells in culture are continuously bathed in DMSO.

More typical doses (5-15 mL) would result in only ~1-5 mM in plasma, well below those in vitro thresholds. Therefore, the concentrations causing cell toxicity in the lab are generally NOT REACHED IN HUMAN SYSTEMIC CIRCULATION under normal dosing. Even at the upper extreme (drinking 30 mL), a person likely would not sustain plasma DMSO at 0.1% for any length of time. This explains why humans don't experience acute organ damage from DMSO, whereas in a petri dish cells show stress at higher exposures.

LOCAL TISSUE CONCENTRATIONS

The situation can differ for local tissues at the application site. Applying 70% DMSO topically delivers a very high local concentration to the skin and underlying tissue before it diffuses. Tissues just under the skin could be transiently exposed to DMSO levels in the tens of percent range. This is why skin irritation is possible and why "localised" toxicity (e.g. blistering or tissue damage) can occur if DMSO is misused (for instance, covering the application site with plastic wrap, which generated heat and rash).

However, systemic distribution quickly dilutes DMSO, and the body's water content ensures no organ is exposed to 70% DMSO internally.

As another example, INTRAVITREAL INJECTION of even a small volume can create locally toxic levels in the retina - the 2014 study injected only 5 µL of 1-8% DMSO into rat eyes and saw retinal cell apoptosis [9]. Such direct exposure is not a typical therapeutic route in humans, so it doesn't occur clinically.

HIGH DOSE SCENARIOS

Could a determined individual ingest enough DMSO to reach truly toxic systemic levels?

It would require extraordinarily large doses. Chronic ingestion of "very" high doses might be self-limited by gastrointestinal intolerance (above ~10-20 g at once, diarrhea and nausea become significant). There are anecdotal reports of patients consuming 50+ mL/DAY (55 g) for chronic pain; even in those cases, apart from bad breath and minor side effects, serious toxicity has not been documented - implying plasma levels still stayed in a tolerable zone. Moreover, the body adapts: DMSO induces increased expression of certain liver enzymes and acute phase proteins at high doses [6], which may help mitigate harm. The "practical" ceiling for achievable plasma concentration is thus much lower than the levels that reliably kill cells or animals.

In summary, *TYPICAL HUMAN SYSTEMIC EXPOSURE TO DMSO IS FAR BELOW THE CONCENTRATIONS KNOWN TO BE CYTOTOXIC OR ORGAN-TOXIC*.

When used in sensible doses (a few grams at a time), DMSO's wide distribution and metabolism prevent accumulation to dangerous levels. The safety margin is large - for instance, one analysis noted that patients undergoing endovascular DMSO use received doses - well under previously implicated doses for systemic toxicity - and showed no toxic signs [5].

That said, caution is warranted in certain scenarios: rapid IV injection or infusion of large volumes can transiently concentrate DMSO in the blood and provoke histamine release or haemolysis. Medical protocols thus limit DMSO infusion rates and volumes.

Topical use also should avoid occlusion and large area coverage with very high concentrations to prevent skin blistering. But IN GENERAL, THE TOXIC CONCENTRATIONS FLAGGED IN VITRO OR IN ANIMAL STUDIES ARE NOT REACHED IN HUMAN SYSTEMIC USE, making severe toxicity very unlikely in practice.

REGULATORY HISTORY AND CURRENT STATUS OF DMSO

UNITED STATES

DMSO's regulatory saga in the U.S. is a tale of initial excitement, abrupt halt, and cautious re-approvals. In 1963-1964, after Dr. Jacob's reports of DMSO's therapeutic promise, the FDA authorised rapid clinical trials. Hundreds of patients

received DMSO for conditions like burns and arthritis. However, in 1965 the FDA "suspended all trials" when laboratory animals developed eye lens changes [2].

For 15 years, DMSO was essentially on hold - no drug approvals, and only limited compassionate use. In 1978, an FDA advisory panel allowed DMSO's use for interstitial cystitis, given lack of other options and apparent safety in that application.

In 1980, the FDA officially lifted its ban on DMSO clinical research [2]. Shortly thereafter (1982), DMSO was formally approved for interstitial cystitis (as RIMSO-50, a 50% solution for bladder instillation). This remains its sole FDA-approved indication [2].

The FDA has since been conservative about other uses: it even maintains a public warning listing DMSO as an unproven treatment for cancer (“fake cancer cure”) [2]. Despite this, the "legal status" of DMSO for other uses is essentially that of an UNAPPROVED DRUG or a DIETARY SUPPLEMENT, depending on how it's marketed. Many companies sell “industrial grade” or “90% pure solvent” DMSO labelled as a solvent (not for drug use), or “Pharmaceutical-grade 99.99%” relatively easily, which customers use medically at their own risk. Compounding pharmacies also prepare DMSO topical gels or eye drops on a physician's order, treating it as an active pharmaceutical ingredient in magistral preparations.

CANADA

Health Canada mirrored the FDA's cautious stance but did approve DMSO for bladder indications. As noted, Health Canada permits DMSO for relief of interstitial cystitis, and this approval extends to similar chronic inflammatory urinary tract conditions like radiation cystitis and possibly prostatitis [12]. DMSO is also cleared for use in preservation of transplant tissues [12]. No other therapeutic claims are approved.

DMSO is not available as an over-the-counter remedy in Canada; it would be obtained through pharmacies or as part of a medical procedure. The Canadian military has issued guidance warning that aside from the officially approved uses, evidence for DMSO is scant and long-term safety unproven [12].

Like the FDA, Health Canada is generally sceptical of unapproved claims and points out the lack of large clinical trials.

EUROPE

In the European Union, there is no centralised marketing authorisation for DMSO as a drug for humans (aside from its presence as an excipient in certain products). However, DMSO is utilised in medical practice. Many EU countries allow intravesical DMSO for bladder pain syndrome either as a pharmacy-compounded instillation or a medical device solution. For example, solutions containing 50% DMSO are used in urology clinics and are recommended by the EAU guidelines for bladder pain [17].

Some European physicians also use DMSO topically for musculoskeletal pain, though these preparations may be obtained as chemical-grade DMSO.

Notably, the EU has a strict regulation for cosmetics that PROHIBITS DMSO IN COSMETIC PRODUCTS (Annex II of EC Regulation 1223/2009) [13]. This means DMSO cannot be an ingredient in consumer skincare/cosmetic items in Europe, likely due to its skin penetration potency and the risk of carrying other substances into the body. Industrial and laboratory use of DMSO in Europe is common (governed by REACH regulations, where DMSO is not particularly restricted given its lower toxicity profile compared to other solvents). Recently, pharmaceutical-grade DMSO has gained acceptance in the EU for use as a solvent in certain approved drug formulations and clinical trial materials; a Certificate of Suitability (CEP) for DMSO was established in 2014, reflecting regulatory comfort with its quality and

safety when produced under GMP [18] [19].

AUSTRALIA

In Australia, DMSO is regulated under the Poisons Standard. It is listed in SCHEDULE 4 (PRESCRIPTION ONLY MEDICINE) when for human therapeutic use, meaning a doctor's prescription is required for any medical use of DMSO above certain concentrations [13]. However, there are exceptions and dual listings. DMSO also appears in SCHEDULE 6 (POISON) for non-therapeutic uses and certain veterinary applications [13].

In 2018, an application to down-schedule DMSO (to make it more freely available) noted its low acute toxicity, lack of chronic toxicity, and safe history in certain formulated products [13].

The outcome maintained that higher concentration DMSO for human use stays prescription-bound (S4), while low concentrations (=10% in a preparation and not for therapeutic use) may be unscheduled or S6 (allowing sale as industrial solvent, etc.) [13].

Australia permits DMSO as an excipient ingredient in various registered products (biologicals, devices, etc.) [13]. For instance, DMSO appears in some veterinary liniments and is used in equine medicine; the Schedule 6 entry allows DMSO in animal treatments under certain conditions (e.g. combined with specific other ingredients in a gel) [13]. Overall, in Australia one cannot legally buy high-concentration DMSO advertised for human therapeutic use without a prescription, but one can obtain “DMSO industrial solvent” (with appropriate warnings) or “Pharmaceutical-grade 99.99%” relatively easily - a regulatory approach to discourage unsupervised medical use while not banning the substance outright.

ALIGNMENT WITH EVIDENCE

Regulatory bodies have often been more conservative than the clinical evidence might suggest. For example, despite some positive trials in osteoarthritis [10] and many decades of patient reports, neither FDA nor EMA approves DMSO for arthritis - largely due to the paucity of large, recent, placebo-controlled studies. Conversely, regulators have allowed DMSO for interstitial cystitis based on older, small studies and clinical need, even though (as critics note) those studies would be considered low-quality today [12].

The disconnect between peer-reviewed evidence and regulation is perhaps most striking in areas like ALTERNATIVE CANCER TREATMENT: peer-reviewed evidence does not support DMSO as a cancer cure, and regulatory agencies actively warn against it [2], yet “fringe” practitioners still promote it. For PAIN AND INFLAMMATION, evidence is mixed - regulators have not approved DMSO for musculoskeletal indications, citing insufficient solid trials, while acknowledging the intriguing findings from some studies (e.g. a well-controlled German trial for arthritis pain) [12].

In summary, global regulators recognise DMSO's unique properties but remain cautious. They tend to PERMIT DMSO WHERE A CLEAR BENEFIT-RISK EXISTS (LIKE IN BLADDER PAIN OR AS A NECESSARY CRYOPROTECTANT), but they WITHHOLD APPROVAL IN MOST OTHER CASES PENDING MORE DEFINITIVE CLINICAL PROOF. This conservative stance sometimes frustrates DMSO advocates, who argue that decades of safe informal use should count as evidence. Nonetheless, the current status is that DMSO is a prescription or otherwise regulated medicine for only a couple of niche uses in most countries, even though it is freely available in non-pharmaceutical grade for other purposes.

DMSO VS. MSM: COMPARING “SIBLING” SULFUR COMPOUNDS

Methylsulfonylmethane (MSM) is a close relative of DMSO - essentially, MSM is DMSO with one additional oxygen (chemical formula (CH3)2SO2). MSM occurs naturally in small amounts in some foods and is also a normal oxidation metabolite of DMSO in vivo [1]. In the body, a portion of any DMSO dose is converted to MSM [1].

MSM is widely marketed as a dietary supplement for joint health, often in combination with glucosamine or chondroitin. Here's how the two compare:

MECHANISMS OF ACTION

MSM and DMSO share anti-inflammatory and antioxidant properties, likely due to their common sulphur moiety. MSM has been shown to reduce inflammatory signalling and oxidative stress in various models [7]

[7]. For instance, MSM (at high concentrations in vitro) inhibited NF-κB activation and lowered production of IL-1β, IL-6, and TNF-a in human monocytes exposed to high glucose [21].

It appears to act upstream on Toll-like receptors and protein kinase C, similarly resulting in reduced cytokine gene expression [21]. DMSO likewise inhibits NF-κB and inflammatory cytokines, as discussed, although DMSO may have additional effects (like membrane penetration and analgesia) that MSM does not strongly exhibit.

Notably, MSM DOES NOT SHARE DMSO'S POTENT SOLVENT CAPABILITIES. While MSM can enhance membrane permeability somewhat [4], it is far less effective than DMSO at carrying other molecules through skin or cells. A study using MSM to transport EDTA into the eye found it did allow some penetration, whereas without MSM the compound could not get in [4]. Thus, MSM can serve as a mild penetration enhancer, but DMSO is the far superior transdermal delivery agent.

One advantage of MSM's extra oxygen is that it cannot be reduced to the volatile sulphide - meaning MSM CAUSES NO GARLIC ODOR. Mechanistically, MSM is sometimes touted as a sulphur donor for building collagen and keratin (hence claims for hair, skin, nail benefits), though the evidence for this biochemical role in humans is not well-substantiated.

THERAPEUTIC APPLICATIONS AND EFFICACY

Both DMSO and MSM have been studied for OSTEOARTHRITIS AND JOINT PAIN. MSM's most common use today is for osteoarthritis as an oral supplement. Clinical trials of MSM (typically 3 grams twice daily) have shown modest improvements in pain and physical function in knee osteoarthritis [10]. While results are not uniformly positive, a couple of randomised trials reported that MSM was superior to placebo in reducing pain and improving mobility in mild to moderate knee arthritis [10]. DMSO, used topically in arthritis, also showed pain relief in some trials but suffers from variability in results.

A systematic review found that the best MSM trials provided “positive but not definitive” evidence of benefit, whereas the DMSO trials were older and had methodological issues, making their positive results less reliable [10]. For SOFT TISSUE INJURIES (sprains, strains), both are used empirically to reduce soreness.

MSM is often taken orally for exercise recovery and claimed to reduce post-exercise muscle damage. Some studies in athletes suggest MSM supplementation can lower markers of oxidative stress and muscle damage after intense exercise [1], aligning with its antioxidant capacity. DMSO, in contrast, might be applied topically by athletes to an acute injury for immediate pain relief. In conditions like ALLERGIC RHINITIS or INTERSTITIAL CYSTITIS (IC), preliminary

evidence hints MSM might help - one small study found oral MSM improved allergy symptoms [1], and MSM has been anecdotally tried in IC (likely orally) with some success, though data are sparse [1]. DMSO remains the standard for IC via instillation; oral MSM is not an established therapy for IC but may support overall anti-inflammatory status.

SAFETY AND TOXICITY

This is where MSM shines. MSM has an excellent safety profile in humans. It is Generally Recognised As Safe (GRAS) by the FDA, and clinical trials have found NO SIGNIFICANT SIDE EFFECTS AT DOSES UP TO 4 GRAMS PER DAY [1]. In fact, MSM is well-tolerated even at higher doses; a toxicity study in rats showed no adverse effects at 5 g/kg/day [22], and similarly high intakes in humans have not produced notable toxicity beyond the occasional mild digestive upset.

Unlike DMSO, MSM causes no breath or body odour. It also causes virtually no skin irritation - indeed, MSM is sometimes included in topical creams as a soothing agent. Rarely, people can have allergic reactions to MSM (since it is often sourced from DMSO or could have residual DMSO impurities), but this is uncommon [15].

DMSO's safety profile is also good, but it has those reversible side effects (odour, skin irritation, etc.) that MSM avoids. Critically, MSM has not been associated with the lens changes or any serious organ toxicities in animals or humans [13]. It is essentially an inert end-product of DMSO metabolism that the body can incorporate or excrete easily. Because of this, MSM is freely sold as a supplement in health stores worldwide, whereas DMSO “with its minor side effects and more potent actions” is treated with more caution by regulators.

REGULATORY STATUS

MSM is UNREGULATED AS A DRUG and sold as a dietary supplement (in the U.S. and many countries). As such, it cannot be marketed with specific disease treatment claims, but it is widely advertised for “joint health” and general wellness. The FDA's GRAS designation (granted in 2007 for a specific MSM product) covers MSM use in foods or supplements and acknowledges its safety at common intake levels [1]. No prescription is needed for MSM, and it is available in capsules, powders, and topical formulations over-the-counter.

DMSO, in contrast, occupies a grey zone: in the U.S., industrial grade DMSO is sold online or in farm supply stores (ostensibly for animal or solvent use), often ending up being used by humans. Medicinal-grade DMSO for intravesical therapy is prescription-only. In many other countries, DMSO for medical use is similarly restricted (prescription or hospital use), whereas MSM is freely available as a supplement.

Essentially, MSM HAS THE REGULATORY STATUS OF A VITAMIN, WHILE DMSO IS TREATED AS A MEDICATION/CHEMICAL SOLVENT. This divergence exists despite MSM sometimes being dubbed “crystalline DMSO” by early proponents, highlighting their chemical kinship [23].

PRACTICAL USE DIFFERENCES

Because DMSO can transport other substances, it is used in scenarios where MSM would be ineffective - for example, as a vehicle in topical drug gels (e.g. certain compounded pain gels use DMSO to drive NSAIDs or corticosteroids through the skin). MSM lacks this strong vehicular ability, but it is sometimes added to creams "with" DMSO to potentially stabilise or add synergistic anti-inflammatory effects.

MSM is often taken in combination with glucosamine for osteoarthritis; DMSO is not taken orally for arthritis in standard practice due to taste and odour issues (when DMSO is taken orally, the garlic taste is quite pronounced). Some arthritis clinics use DMSO intravenously or by injection for severe cases - something not done with MSM. On the other hand, LONG-TERM SUPPLEMENTATION is feasible with MSM (people take it daily for years), whereas long-term

daily use of high-dose DMSO is limited by side effects and practical inconveniences.

In summary, "DMSO and MSM share anti-inflammatory, antioxidant, and potential analgesic activities", but DMSO is more potent in certain pharmacological ways (membrane penetration, acute analgesia) and correspondingly has more notable (though generally mild) side effects. MSM is gentler, with a very high safety margin, making it suitable for supplement use. MSM's efficacy for joint pain and other uses has some supportive evidence but remains not conclusively proven - similar to DMSO's evidence base [10].

Regulatory attitudes reflect these differences: MSM is openly sold as a nutritional supplement touted for arthritis, often by the same advocates who in past decades promoted DMSO. DMSO itself, once hyped as a cure-all, is now a more narrowly applied prescription therapy and laboratory reagent. Both substances continue to be researched - MSM for its possible role in reducing inflammation in metabolic diseases [21], and DMSO for new applications in medicine (e.g. enhancing stem cell delivery or treating traumatic brain injury) [3].

The combination of DMSO and MSM is also sometimes used (e.g. a topical mix for EQUINE TENDON INJURIES or human arthritis), speculating that DMSO drives MSM into tissues where MSM can then exert effects [24]. While more rigorous research is needed for both, the existing literature and usage experience paint DMSO as a powerful but somewhat underutilised medical tool and MSM as a promising supportive supplement - each with overlapping aims of relieving pain and inflammation safely.

CONCLUSION

Dimethyl sulfoxide stands as a unique substance in medicine: at once a solvent, a drug, and a research tool. Its known therapeutic uses in humans - chiefly for bladder inflammation and as a topical analgesic - capitalise on its membrane-penetrating, anti-inflammatory, and analgesic actions. Mechanistically, DMSO can modulate diverse biological processes, from reducing hydroxyl radicals to preventing injury-induced cell death, explaining the myriad conditions it has been applied to. Toxicologically, DMSO is remarkable for its low acute and chronic toxicity, with a safety profile that “aside from manageable nuisances like garlic odour” shows no serious harm at common doses. The toxic doses identified in cell and animal studies are, in practical terms, not attained with typical human use, suggesting a wide margin of safety.

Regulators around the world have been cautious, likely due to the tumultuous history and the paucity of modern large-scale trials. The result is that DMSO's official medical uses remain limited, even as evidence and clinical experience suggest potential benefits in broader contexts (e.g. certain chronic pain or ischaemic injuries) if researched properly. In contrast, MSM, DMSO's close cousin, has enjoyed easier acceptance as a supplement, reflecting its gentler nature despite less potent effects.

For researchers and general readers alike, DMSO offers an intriguing case study of a repurposed industrial compound that became a medical cause celebre. It underscores the need to balance anecdotal success with rigorous evidence. Today, as interest in old drugs for new uses grows, DMSO might warrant a reappraisal under modern clinical trial standards. Likewise, MSM's growing popularity invites further study into how an apparently simple molecule can influence inflammation and joint health.

In conclusion, DMSO IN HUMAN HEALTH IS A STORY OF POTENTIAL AND PRUDENCE - potential in its versatile therapeutic actions, and prudence in its application and regulation until science fully catches up. Both DMSO and MSM hold places in the complementary treatment arsenal for conditions like arthritis, and ongoing research may better define their roles. With careful use guided by scientific and medical insight, DMSO's decades-old promise of a

"versatile pharmacological agent" [2] may yet be more fully realised, supported by the safety record that years of experience have affirmed.

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