Pharmacology and Clinical Use of Dimethyl Sulfoxide (DMSO): A Review

Manjunath Patil1, Shivaprakash B.V.2

1 Krishi Vigyan Kendra, Gulbarga, UAS, Raichur, Karnataka, India
2 Dept. of VSR, Veterinary College, KVAFSU, Bidar, Karnataka, India

Corresponding author email: manjunathpatil2010@rediffmail.com; Authors

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Abstract Dimethyl sulfoxide is having a pyramidal structure, CH3-SO-CH3. It is a dipolar, aprotic and highly hygroscopic solvent. It readily penetrates the skin within 5 minutes after cutaneous application. It enhances penetration of Anaesthetic, cardioactive, anticholinesterase and other not-innocuous therapeutic agents. It is recommended for acute sprains, strains, bursitis and their associated soft tissue swellings and haematoma. Combination therapy of DMSO with antibiotics or steroids enhances the healing of cutaneous habronemiasis or summer sores, bumble foot, acral lick dermatitis, arthritis, and mastitis. It is considered to have a low toxicity. Chronic thermal, chemical exposure of DMSO solvent and higher levels of chemical contaminants with severe electrical burns causes the invasive squamous cell carcinoma of the upper extremities in human beings. The therapeutic intravenous dose is about 1.0 g/kg in 10–45% solution administered slowly in humans, cats, dogs and horses. Intra articular administration of DMSO reduced severity of chemically induced synovitis in horses.

Keywords Pharmacology; Dimethyl sulfoxide (DMSO); Radioscavenging property; Therapeutic applications

1 Introduction

Dimethyl sulfoxide (DMSO), in trace amounts occurs naturally in fresh and ocean water and in rain. It is commercially produced quite inexpensively from lignin, a by product of paper making industry in the United States and coal and petroleum in Europe (Bartfeld and Goldstein, 1975; Jacob and Herschler, 1983). It occurs as a waste product from processing wood pulp (Booth and McDonald, 1982).

The FDA approved therapeutic veterinary preparations are DOMOSO® and SYNOTIC® (Diamond Laboratories Inc., Des Moines, Iowa). While the FDA approved medical preparation is RIMSO-50® (Research Industries Inc.), which contains 50% DMSO solution.

Dimethyl sulfoxide is having a pyramidal structure, CH3-SO-CH3. The sulfur-oxygen bond is quite polar, giving the liquid a high dielectric constant. It is a clear liquid with a boiling point of 189°C at 1 atmosphere pressure and has a specific gravity of 1.0958 at 25°C (Booth and McDonald, 1982).

It is a dipolar, aprotic and highly hygroscopic solvent (MacGregor, 1967; Weissman et al., 1967; David, 1972; Kharasch and Thyagarajan, 1983; Windholz, 1983). Pure DMSO is rapidly diluted to a concentration of 66% to 67% when it is exposed to room air (MacGregor, 1967; Szmant, 1967; Kharasch and Thyagarajan, 1983). Hydration of DMSO is an exothermic reaction, the heat evolved is readily appreciated when DMSO is applied to skin and react with water from air and from underlying tissue (MacGregor, 1967; David, 1972; Jacob and Herschler, 1983; Kharasch and Thyagarajan, 1983).

2 History

Earliest history on Dimethyl sulfoxide can be traced to 1867 when a Russian Chemist, Alexander Saytzeff, described the oxidation of Dimethyl sulfide into Dimethyl sulfoxide and further described some of its remarkable solvent properties (Leake, 1967; Bartfeld and Goldstein, 1975). There was a little interest in DMSO until 1950 when its solvent properties were exploited for use in many industrial processes. Industrial researchers discovered that it is a solvent for many herbicides, fungicides, antibiotics and hormones.
It can greatly enhance their penetrance and efficacy in plants and trees and enhance plant growth by 15% to 20% (Garren, 1967; Kiehl, 1967; Leake, 1967; Leonard, 1967; Scuchetti, 1967; Smale et al., 1975).

Scientists working with DMSO soon reported other unusual properties such as its ability to penetrate skin to produce offensive garlic or oyster halitosis. This smell is due to its metabolite, dimethyl sulfide (Distefano and Klahn, 1965; Brown, 1982).

Robert Herschler and Stanley Jacob were the strong proponents of the early study of DMSO as a therapeutic agent (Leake, 1967; Bartfeld and Goldstein, 1975; Leake, 1975; Douglass and Walker, 1983). DMSO was found to be superior to glycerol for cryopreservation of bovine spermatozoa (Lovelock and Bishop, 1959). It is also used as cryoprotectant added to cell media in order to prevent the cells from dying as they are being frozen (Pegs, 2007). The first report of DMSO as a pharmacologic agent was published in 1964. Investigational new drug (IND) status was then granted by the Food and Drug Administration (FDA) (Harter, 1983).

In November 1965, the FDA terminated clinical studies on DMSO because Rubin demonstrated that DMSO induced lenticular changes in some laboratory animals (Rubin and Barnett, 1967). In 1966, the FDA relaxed the policy to permit clinical evaluation in the treatment of serious conditions such as scleroderma, persistent herpes zoster and severe rheumatoid arthritis, for which no satisfactory therapy was available (Harter, 1983). In 1968, the policy was further relaxed to permit topical application for less than 14 days (Kligman, 1965). In 1970, the FDA approved DMSO for veterinary use in musculoskeletal injuries in horses. In 1972, approval was extended for use in dogs. In 1978, the FDA authorized the use of 50% DMSO (RIMSO-50®) for the treatment of interstitial cystitis in humans (Leake, 1967; and Harter, 1983).

3 Physiological and Pharmacological Properties

3.1 Absorption or penetration of DMSO

Dimethyl sulfoxide readily penetrates the skin within 5 minutes after cutaneous application. Radiolabeled DMSO can be detected in the blood and characteristic garlic halitosis is evident due to reduction of its metabolite called dimethyl sulfide within 20 minutes. It can be found in all the organs of the body and within one hour, radiolabeled DMSO is detected in bones and teeth (Kolb et al., 1967). The penetrating ability of DMSO is believed to be due to its exchange and interchange for water in biological membranes (Szmant, 1967; Weissman et al., 1967; David, 1972; Kharasch and Thygarajan, 1983).

3.2 DMSO as a carrier agent

Dimethyl sulfoxide facilitates penetration of many other substances across the membranes. Cutaneous penetration of various steroids (Dkan and Gunberg, 1967; Maibach and Feldman, 1967; Wood and Wood, 1975), insulin, heparin, sulfadiazine (Potts et al., 1967) and phenylbutazone (Jimenez and Wilkens, 1982) is enhanced by DMSO. Anaesthetic, cardioactive, anticholinesterase and other not-innocuous therapeutic agents may have enhanced penetration or modified activity in the presence of DMSO. Anaesthetic, cardioactive, anticholinesterase and other not-innocuous therapeutic agents may have enhanced penetration or modified activity in the presence of DMSO. Anaesthetic, cardioactive, anticholinesterase and other not-innocuous therapeutic agents may have enhanced penetration or modified activity in the presence of DMSO.

3.3 Radioscavenging property of DMSO

Dimethyl sulfoxide traps free radical hydroxide and its reduction metabolite dimethyl sulfide (DMS) traps the free radical oxygen (Misch and Misch; 1975; Repine et al., 1979; Hill et al., 1983; Rosenblum, 1983). Their free radical scavenging capabilities are believed to be responsible for some of the antiinflammatory, cryoprotective, radioprotective and antiischemic properties when used in vivo, topically or parenterally (Brayton, 1986).

3.4 Enzyme inhibition action of DMSO

Dimethyl sulfoxide inhibits acetylcholinesterase and depresses the diaphragm response to muscle and nerve
stimulation under \emph{in vitro} condition. It causes spontaneous fasciculation, increases gastric smooth muscle tone and the amplitude of contraction of atrial muscle and reduces the cardiac vagal threshold (Sams, 1967). Dimethyl sulfoxide has cardiovascular and vasoactive effects and these are attributed, at least in part, to its anticholinesterase activity (Slafer and Karow, 1975; Hameroff et al., 1983).

3.5 Therapeutic applications of DMSO

The FDA-approved preparation of DMSO, DOMOSO® is recommended for acute sprains, strains, bursitis and their associated soft tissue swellings and haematoma. It relieves pain and swelling and improves the function of the affected part more rapidly than the conventional therapies (Knowles, 1967; Levesque, 1967; Tiegland and Saurino, 1967). Postoperative swelling due to surgical trauma, pain and swelling are reduced and healing is improved (Arno et al., 1967; Kleberger, 1967; Penrod et al., 1967; Riis, 1984).

SYNOTIC® (Diamond Laboratories, Desmoines, Iowa) is recommended for the relief of inflammation and pruritis associated with acute and chronic otitis. RIMSO-50® is recommended for the direct instillation into the urinary bladder in the treatment of refractory interstitial cystitis in human patients (A. M. A. Department of drugs, 1980; Santos et al., 2003; Fourcroy et al., 2004). It can also improve healing by topical application of DMSO to treat oral ulcers (Kutscher et al., 1967), diabetogenic skin ulcers (Miranda-Tirado, 1975), varicose skin ulcers (Sehtman, 1975), chronic skin ulcers (Scott and Walton, 1983), burns (Miranda-Tirado, 1975; and Sehtman, 1975), open wounds (Levesque, 1967; Dubinsky and Skager, 1975), skin grafts (Sehtman, 1975) and corneal ulcers (Perez et al., 1979).

Chronic musculoskeletal conditions such as chronic osteoarthritis and degenerative disc disease in humans (Demos et al., 1967; John and Laudahn, 1967; Paul, 1967; Steinberg, 1967) and scarred or bowed tendon in horses (Tiegland and Saurino, 1967) have been treated with DMSO in clinical trials. Topical application of DMSO gel was evaluated in treating endotoxin induced synovitis in horses (Smith et al., 1998). Intraarticular administration of DMSO reduced severity of chemically induced synovitis in horses (Welch et al., 1991).

Proud flesh is reduced when DMSO is applied to wounds below the equine tarsus or carpus that heal by secondary or tertiary intention (Levesque, 1967). DMSO reduces fibroplasia as a result of its inhibition of fibroblastic proliferation \emph{in vitro} (Alsup and De Bowes, 1984). It would be a valuable adjunct in the treatment of surgical colic cases (Davis, 1984). It decreases the severity of liver damage caused by ischemia-reperfusion after portal vein clamping (Sahin et al., 2004). Its combination with carolina rinse solution would be protective against ischemia-reperfusion injury in the equine jejunum (Dabareiner, 2005).

Combination therapy of DMSO with antibiotics or steroids enhance the healing of cutaneous habronemiasis or summer sores (McMullan, 1982; Faddock and Mullowney, 1983; Moore et al., 1983), bumble foot (Halliwell, 1975), acral lick dermatitis (Scott and Walton, 1983), arthritis and mastitis (Figueiredo et al., 1993). Antifungal and steroids along with DMSO are used for treating scratches (McMullan, 1982) and phytophycos (McMullan, 1983). Topical application of DMSO, phenylbutazone and acetyl salicylic acid ointment is used for the treatment of udder edema (Szalbierz et al., 1996). Topical antiviral agents along with DMSO are used for the treatment of Herpes simplex virus infection (Hamuy and Berman, 1998). Synovial fluid along with DMSO has been tried for treating aseptic arthritis in experimental calves (Tayal et al., 1998 and 2000). The deleterious effect of nicotine was effectively blocked by DMSO in experimental rats (Leite, 2007). Diagnosis of Dermatophytosis of the ear was done by potassium hydroxide and Dimethyl sulfoxide test (Morinaka, 2005).

Acute CNS trauma, inflammation, edema and ischemia have been treated with intravenous DMSO in laboratory (De la Torre et al., 1975; Brown et al., 1980; Rucker et al., 1983) and clinical cases (Lee, 1983; Reed, 1983; Waller et al., 1983; Newton, 1998; Santos et al., 2003). Potential veterinary applications for
DMSO in CNS disorders include intervertebral disc disease in dogs (Lee, 1983), brain and spinal cord trauma in horses (Mayhew and Mackay, 1982; Reed, 1983). Other possible applications of DMSO are the prevention or treatment of post traumatic myocarditis or the myocardial infarctions and consequent arrhythmias that occur secondary to gastric dilatation and torsion in dogs (Finney et al., 1967).

Dimethyl sulfoxide has been tried in human patients to treat various rheumatic diseases such as rheumatoid arthritis (Rosenbaum et al., 1965; Zuckner et al., 1967; Gorog and Kovacs, 1975; Jimenez and Wilkens, 1982; Rosenstein, 1999), renal amyloidosis (Gruys et al., 1981; Jimenez and Wilkens, 1982; Scheinberg et al., 1984; Santos et al., 2003) and scleroderma (Scherbel et al., 1967; Fleischmajer, 1975; Jimenez and Wilkens, 1982; Scherbel, 1983). DMSO’s anticholinesterase activity may help in the treatment of auto immune disorders like myasthenia gravis in which immunologic attack is directed at acetylcholine receptors at neuromuscular junctions (Pestronk and Drachman, 1980).

Intractable pain such as post amputation phantom pain (Rosenbaum et al., 1965), post thoracotomy incisional pain (Penrod et al., 1967), headaches (Blumenthal and Fuchs, 1967) and other painful conditions of various etiologies (Asen, 1967; Blumenthal and Fuchs, 1967; Dubinsky and Skager, 1975; Brown, 1982; Douglass and Walker, 1983) that could not be alleviated by any therapy or could only be alleviated by narcotic analgesia have responded to topical application of DMSO.

DMSO has been classified as a “maturational agent” in some neoplastic cell lines (Borenfreund et al., 1975; Stewart et al., 1975; Patel and Lodish, 1984; Spremulli and Dexter, 1984). DMSO is reported to potentiate cyclophosphamide (Garrido and Lagos, 1975; Warren et al., 1983) and to be effective in a “cytostatic complex” with vinblastin (Setala, 1983).

### 3.6 Toxicity of dimethyl sulfoxide

Dimethyl sulfoxide is considered to have a low toxicity. Median lethal dose (LD-50) of DMSO administered topically, orally or parenterally to laboratory animals are high (Smith et al., 1967; and Rubin, 1975). The therapeutic intravenous dose is about 1.0 g/kg in 10%~45% solution administered slowly in humans (Waller et al., 1983), Cats (Hoerlein et al., 1983), dogs (De la Torre et al., 1975; Rucker et al., 1983) and horses (Mayhew and Mackay, 1982; Reed, 1983). With lethal doses of DMSO, death is usually preceded by prostration, convulsions, dyspnea or tachypnea, hypotension, pulmonary edema and respiratory arrest (Caujolle et al., 1967; Smith et al., 1967; Santos et al., 2003).

Skin sensitivity to topical application of DMSO usually is greater with higher concentrations of DMSO (70%~100%), but 10% DMSO can also cause irritation (Sulzberger et al., 1967; Rubin, 1975). Ocular toxicity due to DMSO has been reported (Rubin and Barnett, 1967; Harter, 1983). In rabbits, dogs and swine, the characteristic changes were altered lucency of the lens and myopia (Kleberger, 1967; Rubin and Barnett, 1967) or function as double focussed lenses (Wood et al., 1967).

Hemolysis is seen both in vitro and in vivo after the use of DMSO (Distefano and Klahn, 1965; Caujolle et al., 1967; Smith et al., 1967; Waller et al., 1983). Nephrotoxicity has been reported with oral and intravenous administration of DMSO in mice, rats, dogs and cats (Caujolle et al., 1967; Smith et al., 1967). Signs of renal damage include hematuria, hemoglobinuria and mild tubular nephrosis or nephritis at postmortem examination (Caujolle et al., 1967; Smith et al., 1967). Its exposure to developing mouse brains @ 0.3 mL/kg can produce brain degeneration (Hanslick et al., 2009). Hepatotoxicity has been reported in chronic toxicity trials involving laboratory animals (Caujolle et al., 1967; Smith et al., 1967; Rubin, 1975). Various toxic agents if present in DMSO solution can readily penetrate rubber gloves and skin (Banthorpe and Lamont, 1967).

In solution with DMSO, effects of some hepatotoxic agents, such as aromatic hydrocarbons are potentiated (Kocsis et al., 1968; and Kocsis et al., 1975). DMSO enhances hepatic binding and metabolism of some carcinogens (Levine, 1975). Teratogenic effects of
DMSO have been reported in birds and mammals (Caujolle et al., 1967). Chronic thermal, chemical exposure of DMSO solvent and higher levels of chemical contaminants with severe electrical burns causes the invasive squamous cell carcinoma of the upper extremities in human beings (Chang, 2011). It requires reduction in exposure to DMSO and reduction in toxic effects before the use of DMSO in stem cell cryopreservation (Windrum et al., 2005).

4 Conclusion
Dimethyl sulfoxide’s effectiveness as a penetrant, penetrant carrier, cryoprotectant, radioprotectent, antiischemic, anti-inflammatory and analgesic agent is well established. Side effects of DMSO such as mast cell degranulation, diuresis and volume depletion may exacerbate patient’s preexisting problems and should be considered before the treatment is initiated. Dimethyl sulfoxide will have a role in veterinary patients for the treatment of sprain, bursitis, proud flesh, synovitis, postoperative swelling, otitis, pruritis, burn, ulcers and pain management if suitable preparation is introduced commercially as a drug in India.

References
A.M.A. Department of Drugs, eds., 1980, Agents Used to Treat Interstitial Cystitis in A.M.A Drug Evaluations, American Medical Association, Chicago, IL 4th ed., pp. 617-618
Alsup E.M., and DeBowes R.M., 1984, Dimethyl sulfoxide, J. Am. Vet. Med. Assoc., 185(9): 1011-1014
PMid:6511636
Arno I.C., Wapner P.M., and Brownstein I.E., 1967, Experiences with DMSO in relief of postpartum episiotomy pain, Annals of the New York Academy of Science, 141: 403-405
http://dx.doi.org/10.1111/j.1749-6632.1967.tb34903.x
PMid:5232252
Asen H., 1967, Dimethyl sulfoxide: A new concept in the treatment of ent diseases, Annals of the New York Academy of Science, 141: 451-456
http://dx.doi.org/10.1111/j.1749-6632.1967.tb34909.x
PMid:5232256
Banthorpe D.V., and Lamont D.M., 1967, Potential Toxicity of Solutions of Dimethyl Sulphoxide, Nature, 215: 1296-1297
http://dx.doi.org/10.1038/2151296a0
PMid:4228231
Bartfeld H., and Goldstein A., 1975, Cell-Mediated Immunity: Its Modulation By Dimethyl Sulfoxide Ann. N. Y. Acad. Sci., 243: 81-90
http://dx.doi.org/10.1111/j.1749-6632.1975.tb25346.x
PMid:1055568
Blumenthal L.S., and Fuchs M., 1967, The clinical use of dimethyl sulfoxide on various headaches, musculoskeletal, and other general medical disorders, Ann. N. Y. Acad. Sci. 141: 572-585
http://dx.doi.org/10.1111/j.1749-6632.1967.tb34927.x
Booth N.H., and McDonald L.E., 1982, Jones Veterinary Pharmacology and Therapeutics, 5th edn., Kalyani Publishers, New Delhi, pp. 662-664
Borenfreund E., Steinglass M., Korngold G., and Bendich A., 1975, Effect of dimethyl sulfoxide and dimethylformamide on the growth and morphology of tumor cells, Ann. N. Y. Acad. Sci., 243: 164-171
http://dx.doi.org/10.1111/j.1749-6632.1975.tb25355.x
PMid:165760
Braude M.C., and Monroe R.R., 1967, Effects of dimethyl sulfoxide and alphaglucocorticoid on pentylenetetrazol convulsive thresholds in mice, Ann. N. Y. Acad. Sci., 141(1): 248-253
http://dx.doi.org/10.1111/j.1749-6632.1967.tb34886.x
PMid:5232234
Brayton C.F., 1986, Dimethyl sulfoxide (DMSO): a review, Cornell Vet., 76: 61-90
PMid:3510103
Brown F.D., Johns L.M., and Mullan S., 1980, J. Neurosurg., 53: 58-62
http://dx.doi.org/10.3171/jns.1980.53.1.0058
PMid:6774065
Brown H.J., 1982, Dimethyl sulfoxide (DMSO)--a unique therapeutic entity, Aviat. Space Environ. Med., 53: 82-88
PMid:7055497
Caujolle F.M.E., Caujolle D.H., Cros S.B., Calvet M. M.J., 1967, Limits of toxic and teratogenic tolerance of dimethyl sulfoxide, Ann. N. Y. Acad. Sci., 141: 110-125
http://dx.doi.org/10.1111/j.1749-6632.1967.tb34871.x
PMid:5232226
Chang B.L., Chang A., Strasser J., Reinhardt J.F., and Guarino M., 2011, An unusual presentation of invasive squamous cell carcinoma of the upper extremities in a patient with a history of severe electrical burns and chronic thermal and chemical exposure, Del. Med. J., 83(5): 137-141
PMid:21710934
Dabareiner R.M., White N.A., Snyder J.R., Feldman B.F., and Donaldson L.L., 2005, Effects of Carolina rinse solution, dimethyl sulfoxide, and the 21-aminosteroid, U-74389G, on microvascular permeability and morphology of the equine jejunal after low-flow ischemia and reperfusion, Amer. J. Vet. Res., 66(3): 525-536
http://dx.doi.org/10.2460/ajvr.2005.66.652
PMid:15822599

David N.A., 1972, The pharmacology of dimethyl sulfoxide, Ann. Rev. Pharm., 12: 353-374
http://dx.doi.org/10.1146/annurev.pa.12.040172.002033
PMid:4556944

DeBowes R.M., and Alsup E.M., Dimethyl sulfoxide, 1984, J. Amer. Vet. Med. Assoc., 185: 1011-1014
PMid:6511636

De la Torre J.C., Kawanaga H.M., Rowed D.W., Johnson C.M., Goode D.J., Kajihara K., and Mullan S., 1975, Dimethyl sulfoxide in central nervous system trauma, Ann. N. Y. Acad. Sci., 243: 362-389
http://dx.doi.org/10.1111/j.1749-6632.1975.tb25377.x
PMid:805559

Demos C.H., Beckloff G.L., Donin M.N., and Oliver P.M., 1967, Dimethyl sulfoxide in musculoskeletal disorders, Ann. N. Y. Acad. Sci., 141: 517-523
http://dx.doi.org/10.1111/j.1749-6632.1967.tb34920.x
PMid:5232264

Distefano V., and Klahn J.J., 1965, Observations on the pharmacology and hemolytic activity of dimethyl sulfoxide, Toxicol. Appl. Pharmacol., 7: 660-666
http://dx.doi.org/10.1016/0041-008X(65)90122-5

Djan T.I., and Gunberg D.L., 1967, Percutaneous absorption of two steroids dissolved in dimethyl sulfoxide in the immature female rat, Ann. N. Y. Acad. Sci., 141: 406-413
http://dx.doi.org/10.1111/j.1749-6632.1967.tb34904.x
PMid:5232253

Douglass W.C., and Walker M., eds., 1983, DMSO, the New Healing Power: how to relieve pain, diminish swelling, reduce inflammation, encourage healing, and restore normal function for a variety of health problems, Devin Adair

Dubinsky M.B., and Skager A.A., 1975, Experience in the use of dimethyl sulfoxide in the diseases of the supporting motor apparatus and general suppressive surgery, Ann. N. Y. Acad. Sci., 243: 494-4996
http://dx.doi.org/10.1111/j.1749-6632.1975.tb25393.x
PMid:1079425

Fadock V.A., and Mullowney P.C., 1983, Dermatological diseases of horses, Part 1. Parasitic dermatoses of the horse, Compend. Cont. Educ. in Vet. Pract., 5: 5615-5623

Feldman W.E., Punch J.D., Holden P.C., 1975, In vivo and in vitro effects of dimethyl sulfoxide on streptomycin-sensitive and -resistant Escherichia coli, Ann. N. Y. Acad. Sci., 243: 269-277
http://dx.doi.org/10.1111/j.1749-6632.1975.tb25365.x
PMid:1093463

Figueiredo J.B., 1993, Control of bovine mastitis through antibiotic therapy aided by dimethyl sulfoxide, Arquivo Brasileiro de Medicina Veterinaria e Zootecnia, 45(5): 465-474

Finney J.W., Urschel H.C., Balla G.A., Race G.I., Jay B.E., Pingree H.P., Dorman H.L., and Mallams J.T., 1967, Ann. N. Y. Acad. Sci., 141: 231-241
http://dx.doi.org/10.1111/j.1749-6632.1967.tb34884.x

Fleischmajer R., 1975, Discussion paper: methodology and techniques in the evaluation of dimethyl sulfoxide for connective tissue disorders, Ann. N. Y. Acad. Sci., 243: 393-394
http://dx.doi.org/10.1111/j.1749-6632.1975.tb25380.x
PMid:1055555

Fourcroy J.L., Jones W.K., Mishell D.R., and Parsons C.L., 2004, Chronic Pelvic Pain of Bladder Origin in Men: A focus on Interstitial cystitis case studies: patients who fail endometriosis therapy, Clinical Courier Newsletters, 22(32): 1-5

Frommhold W., Bublitz G., and Gries G., 1967, The use of dimso for the treatment of postirradiation subcutaneous plaques, Ann. N. Y. Acad. Sci., 141: 603-612
http://dx.doi.org/10.1111/j.1749-6632.1967.tb34930.x
PMid:4962801

Garren R., 1967, Uptake and distribution of labeled dimethyl sulfoxide and its influence on nutritive element transport in plants, Ann. N. Y. Acad. Sci., 141: 127-130
http://dx.doi.org/10.1111/j.1749-6632.1967.tb34873.x

Garrido J.C., and Lagos R.E., 1975, Dimethyl sulfoxide therapy as toxicity-reducing agent and potentiator of cyclophosphamide in the treatment of different types of cancer, Ann. N. Y. Acad. Sci., 243: 412-420
http://dx.doi.org/10.1111/j.1749-6632.1975.tb25384.x
PMid:236715

Gorog P., and Kovacs I.B., 1975, Antiarthritic and antithrombotic effects of topically applied dimethyl sulfoxide, Ann. N. Y. Acad. Sci., 243: 91-97
http://dx.doi.org/10.1111/j.1749-6632.1975.tb25347.x
PMid:805559
Gruys E., Sijens R.J., and Biewenga W.J., 1981, Dubious effect of dimethylsulphoxide (DMSO) therapy on amyloid deposits and amyloidosis, Vet. Res. Commun., 5(1): 21-32.
http://dx.doi.org/10.1007/BF02214964
PMid:7046216

Halliwell W.H., 1975, Bumblefoot infections in birds of prey, J. Zoo An. Med., 6(4): 8-10
http://dx.doi.org/10.2307/20094326

Halliwell W.H., 1975, Bumblefoot infections in birds of prey, J. Zoo An. Med., 6(4): 8-10
http://dx.doi.org/10.2307/20094326

Hamuy R., and Berman B., 1998, Treatment of Herpes simplex virus infections with topical antiviral agents, Eur. J. Dermatol., 8(5): 310-319
PMid:9683881

Hanslick J.L., Lau K., Noquchi K.K., Olney J.W., Zorumski C.F., Mennerick S., and Farber N.B., 2009 Dimethyl sulfoxide (DMSO) produces widespread apoptosis in the developing central nervous system, Neurobiology of Disease, 34(1): 1-10
http://dx.doi.org/10.1016/j.nbd.2008.11.006
PMid:19100327 PMCid:2682536

Harter J.G., 1983, The status of dimethyl sulfoxide from the perspective of the food and drug administration, Ann. N. Y. Acad. Sci., 411: 1-5.
http://dx.doi.org/10.1111/j.1749-6632.1983.tb47277.x
PMid:6349492

Hill P.K., Torre J.C., Thompson S.M., Rosenfield-Wessels S., and Beckett M.L., 1983, Ultrastructural studies of rat fasciculi gracilis unmyelinated fibers after contusion and dmsos treatment, Ann. N. Y. Acad. Sci. 411: 200-217
http://dx.doi.org/10.1111/j.1749-6632.1983.tb47302.x
PMid:6576695

Hoelein B.F., Redding R.W., Hoff E.J., and McGvire J.A., 1983, Evaluation of dexamethasone, DMSO, mammal and solcoseryl in acute spinal cord trauma, J. Amer. An. Hosp. Assoc., 19: 216-226

Jacob S.W., and Herschler R., 1983, Introductory remarks: dimethyl sulfoxide after twenty years, Ann. N. Y. Acad. Sci., 411: 13-17
http://dx.doi.org/10.1111/j.1749-6632.1983.tb47277.x

Jimenez R.A., and Wilkens R.F., 1982, Dimethyl sulfoxide: a perspective of its use in rheumatic diseases, J. Lab. Clin. Med., 100: 489-500

John H., and Laudahn G., 1967, Clinical experiences with the topical application of dmsos in orthopedic diseases: evaluation of 4180 cases, Ann. N. Y. Acad. Sci., 141: 506-516
http://dx.doi.org/10.1111/j.1749-6632.1967.tb34919.x
PMid:5232263

Kharasch N., and Thyagarajan B.S., 1983, Structural basis for biological activities of dimethyl sulfoxide, Ann. N. Y. Acad. Sci., 411: 391-402
http://dx.doi.org/10.1111/j.1749-6632.1983.tb47334.x
PMid:6576721

Keil H.L., 1967, Enhanced bacterial spot control of peach when dimethyl sulfoxide is combined with sprays of oxytetracycline, Ann. N. Y. Acad. Sci., 141(1): 131-138
http://dx.doi.org/10.1111/j.1749-6632.1967.tb34874.x

Kleberger K.E., 1967, An ophthalmological evaluation of dmsos, Ann. N. Y. Acad. Sci., 141: 381-385
http://dx.doi.org/10.1111/j.1749-6632.1967.tb34900.x
PMid:5232248

Kligman A.M., 1965, Topical Pharmacology and Toxicology of Dimethyl Sulfoxide—Part I, J.Amer. Med. Assoc., 193: 796-804
http://dx.doi.org/10.1001/jama.1965.0309010042010
PMid:14329978

Knowles R.P., 1967, Clinical experience with dmsos in small animal practice, Ann. N. Y. Acad. Sci., 141: 478-483
http://dx.doi.org/10.1111/j.1749-6632.1967.tb34914.x
PMid:5232259

Kocsis J.J., 1975, Biological effects of the metabolites of dimethyl sulfoxide, Ann. N. Y. Acad. Sci., 243: 104-109
http://dx.doi.org/10.1111/j.1749-6632.1975.tb25349.x
PMid:1055534

Kocsis J.J., Harkaway S., Santoyo M.C., and Snyder R., 1968, Dimethyl sulfoxide: interactions with aromatic hydrocarbons, Science, 160(3826): 427-428
http://dx.doi.org/10.1126/science.160.3826.427
PMid:5644044

Kolb K.H., Jaenicke G., Kramer M., and Schulze P.E., 1967, Absorption, distribution and elimination of labeled dimethyl sulfoxide in man and animals, Ann. N. Y. Acad. Sci., 141(1): 85-95
http://dx.doi.org/10.1111/j.1749-6632.1967.tb34869.x
PMid:5232278

Kutscher A.H., Zegarelli E.V., and Everett F., 1967, Dmsos in stomatologic research, Ann. N. Y. Acad. Sci., 141: 465-470
http://dx.doi.org/10.1111/j.1749-6632.1967.tb34912.x
PMid:5342262

Leake C.D., 1967, Introductory remarks, Ann. N. Y. Acad. Sci., 141: 1-2
http://dx.doi.org/10.1111/j.1749-6632.1967.tb34859.x
Leake C.D., 1975, Opening remarks, Ann. N. Y. Acad. Sci., 243: 5-6
http://dx.doi.org/10.1111/j.1749-6632.1975.tb25338.x
PMid:1055564

Lee S.W., 1983, DMSO dimethylsulfoxide in treatment for intervertebral disk syndrome in dogs, Vet. Med. Sm. An. Clin., 78(4): 520

Leite M.T., Gomes H.C., Percario S., Russo C.R., and Ferreira L.M., 2007, Dimethyl sulfoxide as a block to the deleterious effect of nicotine in a random skin flap in the rat, Plastic and Reconstructive Surgery, 120(7): 1819-1822
http://dx.doi.org/10.1097/01.prs.0000287134.60766.23
PMid:18090743

Leonard C.D., 1967, Use of dimethyl sulfoxide as a carrier for iron in nutritional foliar sprays applied to citrus, Ann. N. Y. Acad. Sci., 141: 148-157
http://dx.doi.org/10.1111/j.1749-6632.1967.tb34876.x

Levesque F., 1967, Effects of dmso on open wounds in horses, Ann. N. Y. Acad. Sci., 141: 491-492
http://dx.doi.org/10.1111/j.1749-6632.1967.tb34916.x

Levine W.G., 1975, Effect of dimethyl sulfoxide on the hepatic disposition of chemical carcinogens, Ann. N. Y. Acad. Sci., 243: 185-193
http://dx.doi.org/10.1111/j.1749-6632.1975.tb25357.x
PMid:1055538

Lovelock J.E., and Bishop M.W., 1959, Prevention of freezing damage to living cells by dimethyl sulphoxide, Nature, 183: 1394-1395
http://dx.doi.org/10.1038/1831394a0
PMid:13657132

MacGregor W.S., 1967, The chemical and physical properties of DMSO, Ann. N. Y. Acad. Sci., 141(1): 1-2

Maibach H.I., and Feldman R.J., 1967, The effect of dmso on percutaneous penetration of hydrocortisone and testosterone in man, Ann. N. Y. Acad. Sci., 141: 423-427
http://dx.doi.org/10.1111/j.1749-6632.1967.tb34906.x
PMid:5342260

Mayhew I.G., and Mackay R.J., eds., 1982, Equine Medicine and Surgery, 3rd ed., Vol. 2, Santa Barbara, Calif., American Veterinary Publications, pp.1201

McMullan W.C., 1982, Current Therapy in Equine Medicine, Robinson N.E., ed., Philadelphia, Penn.: W.B. Saunders, pp.549-550

Miranda-Tirado R., 1975, Dimethyl sulfoxide therapy in chronic skin ulcers, Ann. N. Y. Acad. Sci., 243: 408-411
http://dx.doi.org/10.1111/j.1749-6632.1975.tb25383.x
PMid:1055558

Misch D.W., and Misch M.S., 1975, The effect of dimethyl sulfoxide on a lysosomal membrane, Ann. N. Y. Acad. Sci., 243: 54-59
http://dx.doi.org/10.1111/j.1749-6632.1975.tb25343.x
PMid:1055566

Moore C.P., Sarazan R.D., Whitley R.D., and Jackson W.F., 1983, Equine ocular parasites: A review, Eq. Vet. J. Sup., 2: 76-85

Morinaka S., 2005, Dermatophytosis of the ear, Otolaryngol Head Neck Surg., 133(1): 113-115
http://dx.doi.org/10.1016/j.otohns.2005.03.029
PMid:16025063

Newton S.A., 1998, Suspected bacterial meningoencephalitis in two adult horses, Vet. Record, 142 (24): 665-669
http://dx.doi.org/10.1136/vr.142.24.665
PMid:9670446

Patel V.P., and Lodish H.F., 1984, Loss of adhesion of murine erythroleukemia cells to fibronectin during erythroid differentiation, Science, 224: 996-998
http://dx.doi.org/10.1126/science.6585955
PMid:6585955

Paul M.M., 1967, Interval therapy with dimethyl sulfoxide, Ann. N. Y. Acad. Sci., 141: 586-598
http://dx.doi.org/10.1111/j.1749-6632.1967.tb34928.x
PMid:5232267

Pegg D.E., 2007, Principles of cryopreservation, Methods in Molecular Biology, 368: 39-57
http://dx.doi.org/10.1007/978-1-59745-362-2_3
PMid:18080461

Penrod D.S., Bacharach B., Templeton III J.Y., 1967, Dimethyl sulfoxide for incisional pain after thoracotomy: preliminary report, Ann. N. Y. Acad. Sci., 141: 493-495
http://dx.doi.org/10.1111/j.1749-6632.1967.tb34917.x
PMid:5232262

Perez, A.L. et al. (1979) Vet. Med. Review. 1: 31 – 39

Pestronk A., and Drachman D.B., 1980, Dimethyl sulphoxide reduces anti-receptor antibody titres in experimental myasthenia gravis, Nature, 288: 733-734
http://dx.doi.org/10.1038/288733a0
PMid:7453805

Post K., and Saunders J.R., 1979, Topical treatment of experimental ringworm in guinea pigs with griseofulvin in dimethylsulfoxide, Can. Vet. J., 20(2): 45-48
PMid:436106 PMCid:1789490

Potts G.E., Rampay J.H., and Benjami F., 1967, The effect of dimethyl sulfoxide (dmso) on antibiotic sensitivity of a group of medically important microorganisms: preliminary report, Ann. N. Y. Acad. Sci., 141: 261-272
http://dx.doi.org/10.1111/j.1749-6632.1967.tb34888.x
Reed S.M., 1983, Current Therapy in Equine Medicine, Robinson N.E., ed., Philadelphia, Penn.: W. B. Saunders, pp.358

Repine J.E., Eaton J.W., Anders M.W., Hoidal J.R., and Fox R.B., 1979, Generation of hydroxyl radical by enzymes, chemicals, and human phagocytes in vitro. Detection with the anti-inflammatory agent, dimethyl sulfoxide, J. Clin. Invest, 64: 1642-1651
http://dx.doi.org/10.1172/JCI109626
PMid:500830 PMcid:371318

Riis R.C., 1984, Contemporary veterinary ophthalmic surgery practice, Proceedings of the 76th Annual Conference for Veterinarians, New York State College of Veterinary Medicine, Ithaca, New York

Rosenbaum E.E., Herschler R.J., and Jacob S.W., 1965, Dimethyl Sulfoxide in Musculoskeletal Disorders, J. Amer. Med. Associ., 192: 309-313
http://dx.doi.org/10.1001/jama.1965.03080170037009

Rosenblum W., 1983, Dimethyl sulfoxide effects on platelet aggregation and vascular reactivity in pial microcirculation, Ann. N. Y. Acad. Sci., 411: 110-119
http://dx.doi.org/10.1111/j.1749-6632.1983.tb47292.x
PMid:6410963

Rosenstein E.D., 1999, Topical agents in the treatment of rheumatic disorders, Rheum. Dis. Clin. North Am., 25(4): 899-918
http://dx.doi.org/10.1016/S0094-0351(08)00408-6

Rubin L.F., 1975, Toxicity of dimethyl sulfoxide, alone and in combination, Ann. N. Y. Acad. Sci., 243: 98-103
http://dx.doi.org/10.1111/j.1749-6632.1975.tb25348.x
PMid:1093466

Rubin L.F., and Barnett K.C., 1967, Ocular effects of oral and dermal application of dimethyl sulfoxide in animals, Ann. N. Y. Acad. Sci., 141: 333-345
http://dx.doi.org/10.1111/j.1749-6632.1967.tb34898.x
PMid:5232245

Rucker N.C., Lumb W.V., Scott R.J., 1983, Combined pharmacologic and surgical treatments for acute spinal cord trauma, Ann. N. Y. Acad. Sci., 411: 191-199
http://dx.doi.org/10.1111/j.1749-6632.1983.tb47301.x
PMid:6576694

Sahin M., Avsar F.M., Ozel H., Topaloqlu S., Yilmaz B., Pasaoglu H., Ayunduk M.C., Erikoqlu M., and Hengirmen S., 2004, The effects of dimethyl sulfoxide on liver damage caused by ischemia-reperfusion, Transplant Proc., 36(9): 2590-2592
http://dx.doi.org/10.1016/j.transproceed.2004.09.057
PMid:15621097

Sams W.M., 1967, The effects of dimethyl sulfoxide on nerve conduction, Ann. N. Y. Acad. Sci., 141: 242-247
http://dx.doi.org/10.1111/j.1749-6632.1967.tb34885.x
PMid:5232233

Santos N.C., Fiqueira-Coelho J., Martins-Silva J., and Saldanha C., 2003, Multidisciplinary utilization of dimethyl sulfoxide: pharmacological, cellular, and molecular aspects, Biochem Pharmacol., 65(7): 1035-1041
http://dx.doi.org/10.1016/S0006-2952(03)00002-9

Scheinberg M.A., Pernambuco J.C., and Benson M.D., 1984, DMSO and colchicine therapy in amyloid disease, Ann. Rheum. Dis., 43: 421-423
http://dx.doi.org/10.1136/ard.43.3.421
PMid:6742905 PMcid:1001363

Scherbel A.L., 1983, The effect of percutaneous dimethyl sulfoxide on cutaneous manifestations of systemic sclerosis, Ann. N. Y. Acad. Sci., 411: 120-130
http://dx.doi.org/10.1111/j.1749-6632.1983.tb47293.x
PMid:6576688

Scott D.W., and Walton D.K., 1984, Clinical evaluation of a topical treatment for canine acral lick dermatitis, J. Amer. An. Hosp. Assoc., 20: 565-570

Scuchetti L.A., 1967, The effects of dmso alone and when combined with various growth regulators on the growth and metabolic products of datura spp., Ann. N. Y. Acad. Sci., 141(1): 139-147
http://dx.doi.org/10.1111/j.1749-6632.1967.tb34875.x
PMid:1055556

Sehtman L., 1975, Dimethyl sulfoxide therapy in various dermatological disorders, Ann. N. Y. Acad. Sci., 243: 395-402
http://dx.doi.org/10.1111/j.1749-6632.1975.tb25381.x
PMid:1055556

Setala K., 1983, Dmso-cytostatic complexes: selective cancer chemotherapy, Ann. N. Y. Acad. Sci., 411: 372-374
http://dx.doi.org/10.1111/j.1749-6632.1983.tb47328.x
PMid:6576717

Shlafer M., and Karow A.M., 1975, Pharmacological effects of dimethyl sulfoxide on the mammalian myocardium, Ann. N. Y. Acad. Sci., 243: 110-121
http://dx.doi.org/10.1111/j.1749-6632.1975.tb25350.x
PMid:236711

Smale B.C., Lasater N.J., and Hunter B.T., 1975, Fate and metabolism of dimethyl sulfoxide in agricultural crops, Ann. N. Y. Acad. Sci., 243: 228-236
http://dx.doi.org/10.1111/j.1749-6632.1975.tb25360.x
PMid:1055542

Smith E.R., Mason M.M., Epstein E., 1967, The influence of dimethyl sulfoxide on the dog with emphasis on the
ophthalmologic examination, Ann. N. Y. Acad. Sci., 141: 386-391
http://dx.doi.org/10.1111/j.1749-6632.1967.tb34901.x
PMid:5232249

Smith G., Bertone A.L., Kaeding C., Simmons E.J., and Apostoles S., 1998, Anti-inflammatory effects of topically applied dimethyl sulfoxide gel on endotoxin-induced synovitis in horses, Am. J. Vet. Res., 59(9): 1149-1152
PMid:9736394

Spremulli D.N., and Dexter D.L., 1984, Polar solvents: a novel class of antineoplastic agents, J. Clin. Onc., 2(3): 227-241
PMid:6321692

Spruance S.L., McKeough M.B., Cardinal J.R., 1983, Dimethyl sulfoxide as a vehicle for topical antiviral chemotherapy, Ann. N. Y. Acad. Sci., 411: 28-33
http://dx.doi.org/10.1111/j.1749-6632.1983.tb47282.x
PMid:6576702

Steinberg A., 1967, The employment of dimethyl sulfoxide as an antiinflammatory agent and steroid-transporter in diversified clinical diseases, Ann. N. Y. Acad. Sci., 141: 532-550
http://dx.doi.org/10.1111/j.1749-6632.1967.tb34922.x
PMid:5232266

Stewart S.E., Kasnic G., Urbanski C., Myers M., and Sreevalsan T., 1975, Studies on the intracisternal a-type particles in mouse plasma cell tumors: induction of maturation of the particles, Ann. N. Y. Acad. Sci., 243: 172-184
http://dx.doi.org/10.1111/j.1749-6632.1975.tb25356.x
PMid:1055537

Sulzberger M.B., Cortese T.A., Fishman L., Wiley H.S., and Peyakovich P.S., 1967, Some effects of dmso on human skin in vivo, Ann. N. Y. Acad. Sci., 141: 437-450
http://dx.doi.org/10.1111/j.1749-6632.1967.tb34908.x
PMid:5232255

Szalbierz M., Malinowski E., and Branicki T., 1996, Analysis of the efficacy of systemic and local treatment of udder oedema in cows, Medycyna Weterynaryjna, 52(2): 120-122

Szman H.H., 1975, Physical properties of dimethyl sulfoxide and its function in biological systems, Ann. N. Y. Acad. Sci., 243 (1): 20-23
http://dx.doi.org/10.1111/j.1749-6632.1975.tb25340.x
PMid:1055540

Tayal R., Chandana I.S., Moulvi B.A., and Singh J., 2000, Comparative evaluation of efficacy of intra-articular administration of dimethylsulfoxide with and without synovial fluid transplant in treatment of aseptic arthritis in calves, Indian J. An. Sci. 70(6): 586-588

Tayal R., Chandana I.S., Moulvi B.A., and Singh J., 1998, Evaluation of topical dimethylsulfoxide with and without synovial fluid transplant for treatment of aseptic arthritis in calves, Indian J. Vet. Surg., 19(2): 96-98

Tiegland M.B., and Saurino V.R., 1967, Clinical evaluation of dimethyl sulfoxide in equine applications, Ann. N. Y. Acad. Sci. 141: 471-477
http://dx.doi.org/10.1111/j.1749-6632.1967.tb34913.x

Van Risjwick F.L., Dunk H.M., and Van’t Hof M.A., 1981, Therapy of acute otitis media: myringotomy, antibiotics, or neither? Lancet, 318: 883-887
http://dx.doi.org/10.1016/S0140-6736(81)91388-X

Waller F.T., Tanabe C.T., and Paxton H.D., 1983, Treatment of elevated intracranial pressure with dimethyl sulfoxide, Ann. N. Y. Acad. Sci., 411: 286-292
http://dx.doi.org/10.1111/j.1749-6632.1983.tb47310.x
PMid:6576703

Warren J., Thuning C.A., and Fanshaw M.S., 1983, Mechanisms of the synergistic effect of oral dimethyl sulfoxide on antineoplastic therapy, Ann. N. Y. Acad. Sci., 411: 150-160
http://dx.doi.org/10.1111/j.1749-6632.1983.tb47297.x
PMid:6576691

Weissman G., Sessa G., and Bevans V., 1967, Effect of dmso on the stabilization of lysosomes by cortisone and chloroquine in vitro, Ann. N. Y. Acad. Sci., 141: 326-332
http://dx.doi.org/10.1111/j.1749-6632.1967.tb34897.x

Welch R.D., Watkins J.P., DeBowes R.M., and Leipold H.W., 1991, Effects of intra-articular administration of dimethylsulfoxide on chemically induced synovitis in immature horses, Am. J. Vet. Res., 52(6): 934-939
PMid:1883099

Windholz M., ed, 1983, The Merck Index: An Encyclopaedia of chemicals, Drugs and Biologicals, ed. 10, Rahway, N.J. Merck & Co., Inc., pp.475

Windrum P., Morris T.C., Drake M.B., Niederwieser D., Ruutu T., and EBMT Chronic Leukaemia Working Party Complications Subcommittee, 2005, Variation in dimethyl sulfoxide use in stem cell transplantation : a survey of EBMT centres, Bone marrow transplantation, 36(7): 601-603
http://dx.doi.org/10.1038/sj.bmt.1705100
PMid:16044141

Wood D.C., and Wood J., 1975, Pharmacologic and biochemical considerations of dimethyl sulfoxide, Ann. N. Y. Acad. Sci., 243: 7-19
Wood D.C., Sweet D., Dolah J.V., Smith J.C., and Contaxis I., 1967, A study of dmso and steroids in rabbit eyes, Ann. N. Y. Acad. Sci., 141: 346-380
http://dx.doi.org/10.1111/j.1749-6632.1967.tb34899.x

Yellowlees P., Greenfield C., and McIntyre N., 1980, Dimethylsulphoxide-induced toxicity, Lancet, 316: 1004-1006
http://dx.doi.org/10.1016/S0140-6736(80)92158-3

Zuckner J., Uddin J., and Gantner G.E., 1967, Local application of dimethyl sulfoxide and dmso combined with triamcinolone acetonide in rheumatoid arthritis, Ann. N. Y. Acad. Sci., 141: 555-559
http://dx.doi.org/10.1111/j.1749-6632.1967.tb34924.x
PMid:5342264

Zuniga A., Burdach R., and Rubio S., 1975, Dimethyl sulfoxide therapy in bronchiolitis, Ann. N. Y. Acad. Sci., 243: 460-467
http://dx.doi.org/10.1111/j.1749-6632.1975.tb25388.x
PMid:1055560