Archives of Dermatological Research
https://doi.org/10.1007/s00403-022-02494-1

REVIEW

# Dimethyl sulfoxide (DMSO): a solvent that may solve selected cutaneous clinical challenges

**Maria Karim[1] · Robert S. Boikess[2] · Robert A. Schwartz[3] · Philip J. Cohen[3,4]**

Received: 18 May 2022 / Revised: 18 November 2022 / Accepted: 28 November 2022


## Abstract

Dimethyl sulfoxide (DMSO) is a clear, odorless liquid, inexpensively produced as a by-product of the wood pulp industry. DMSO's unique chemical properties allow for its broad applications in a wide variety of cutaneous challenges. Widely available in the USA as a solvent, DMSO is FDA-approved only for the treatment of interstitial cystitis and for use as a preservative for organ transplant. DMSO readily penetrates and diffuses through biological membranes. At low concentrations, DMSO exhibits anti-inflammatory, analgesic, diuretic, vasodilator, anti-platelet aggregation, radio-protective, and muscle-relaxing properties. DMSO is also a vigorous scavenger of hydroxyl free radicals, which may explain its observed beneficial effects on skin rejuvenation and recovery from thermal injury. DMSO has a relatively low level of toxicity. DMSO has shown promise in the off-label treatment of basal cell carcinoma, pressure ulcers, scleroderma, herpes simplex, cutaneous fungal infections, and amyloidosis. The potential of DMSO to serve as an independent or adjuvant topical treatment for these conditions is explored in this review.

**Keywords** Dimethyl sulfoxide · DMSO · Pressure ulcers · Basal cell carcinoma · Cutaneous fungal infections · Amyloidosis · Herpes simplex · Scleroderma

## Introduction

Dimethyl sulfoxide, commonly referred to as DMSO, is an organic polar aprotic molecule soluble in both aqueous and organic environments [1, 2] (Fig. 1). It is produced during the conversion of wood into wood pulp and can be formed from the exothermic oxidation of dimethyl sulfide with nitrogen dioxide or oxygen [3, 4] (Fig. 2). Due to its small and compact structure, its capacity to accept hydrogen bonds, and its polar nature, DMSO has the ability to associate with water, proteins, carbohydrates, nucleic acids, ionic substances, hormones, enzymes, and other cellular structures [5]. Thus, hydrogen bonding of DMSO occurs at cell membranes, at transmembrane channels (cell pores), and at the skin's outer surface. DMSO has a high dielectric constant of 47 and a dipole moment of 4.17 D due to separation of charge at the sulfur–oxygen bond, which enables DMSO to associate with a broad range of compounds [4, 6]. Its amphipathic nature makes it highly useful for dissolving polar and nonpolar molecules [2, 7]. The oxygen atom has two lone pairs that facilitate the exchange of electrons and formation of hydrogen bonds. This characteristic enables the molecule to scavenge free radicals, especially hydroxyl radicals [2, 8]. It is this characteristic that potentiates the antioxidant effect of DMSO in ischemic and inflammatory conditions (Table 1).

Currently, DMSO has three major uses: (1) as a solvent in toxicology and pharmacology to enhance the solubility of poorly soluble polar and nonpolar molecules; (2) for cryopreservation of cells by diminishing osmotic stress and cellular dehydration; and (3) as a penetration enhancer in high concentrations for topical treatments employing low molecular weight compounds [7–10]. The molecular basis of the action of DMSO on lipid bilayer membranes contributes to its roles in cryopreservation, membrane fusion, and

✉ Robert A. Schwartz
roschwar@cal.berkeley.edu

[1] Hackensack Meridian School of Medicine, Nutley, NJ, USA

[2] Department of Chemistry and Chemical Biology, Rutgers University New Brunswick, 123 Bevier Rd, Piscataway, NJ 08854, USA

[3] Dermatology, Rutgers-New Jersey Medical School, 185 South, Orange Avenue, Newark, NJ 07103-2714, USA

[4] Dermatology, VA New Jersey Health Care System, East Orange, NJ, USA

Published online: 02 December 2022

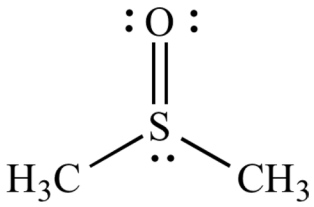

**Fig. 1** Molecular structure of dimethyl sulfoxide (DMSO)

membrane permeability enhancement. DMSO's core three functions are implemented by: (1) making the membrane "floppy"; (2) augmenting lipid–lipid separation in bilayers; and (3) inducing water pores in the membrane [10]. DMSO is a powerful penetrant of cell membranes and biological barriers, facilitating its use as a vehicle for increasing permeability and absorption of biological compounds [2]. Furthermore, in comparing various formulations in the transdermal permeation of tocopherol, Nada et al. discovered that monophasic liquid formulations containing DMSO have higher transdermal permeation than gel, emulsion, and oil-based formulations [11]. When used as a vehicle for delivery of poorly soluble low molecular weight compounds, DMSO potentiates the drug effects, allowing for smaller doses of drug to be used with less toxicity [12, 13]. In examining the percutaneous penetration of hydrocortisone and testosterone dissolved in DMSO, it was concluded that these steroids had a threefold increase in dermal penetration with DMSO.

Notably, after topical application of DMSO, an unpleasant, garlic-like odor is apparent on the breath due to dimethylsulfide, a metabolite of DMSO [14]. (Fig. 3) This feature makes it difficult to perform a truly double-blinded study on DMSO, as breath may be the "giveaway." Occasional side effects of topical DMSO include erythema, dryness, skin irritation, itching, tingling, or burning at the site of application. These effects resolve with cessation of application of DMSO or with lowering of the concentration applied as a more dilute solution in distilled water.

At low concentrations, DMSO exhibits anti-inflammatory, analgesic, vasodilator, anti-platelet aggregation, collagen- dissolving, and radio-protective properties. DMSO is also a vigorous scavenger of hydroxyl free radicals, which may explain its observed anti-inflammatory effects, as well as beneficial effects on recovery from ischemic and thermal injury [15–19].

## Methods

A PubMed database search was done using the terms "DMSO or dimethyl sulfoxide" in combination with the terms "basal cell carcinoma," "pressure ulcers," "scleroderma," "herpes simplex virus," "primary localized cutaneous amyloidosis," "cutaneous fungal infections," and "dermatology." Articles were appraised for methodology and relevance.

## Basal cell carcinoma

Photodynamic therapy using photosensitizers 5-aminolevulinic acid (ALA) and methyl-5-aminolevulinate has been established as an effective treatment for early skin cancers [20]. However, the effectiveness of ALA has been limited by its inability to penetrate the deeper regions of these neoplasms. Thus, methods to enhance the penetration of ALA into all layers of a nodular basal cell carcinoma are being explored. Peng et al. studied the effectiveness of topical 5-aminolevulinic acid (ALA) application with and without the addition of dimethyl sulfoxide/ethylenediaminetetraacetic acid (DMSO/EDTA) by examining its penetration and the fluorescence distribution of ALA-induced porphyrins in patients with basal cell carcinomas. After three hours, both the penetration and fluorescence distribution were observed to be significantly amplified when topical ALA 20% was combined with DMSO 20%/EDTA 4%. Further enhancement of penetration and a tripling of production of ALA-induced porphyrins were seen with prior treatment of 99% DMSO for 15 min, compared to treatment with ALA alone [21].

Additionally, the application of topical DMSO has been shown to improve the remission rate of thin nodular BCCs [22]. In a 1 year follow-up study, 58 patients with 119 nodular basal cell carcinomas who were successfully treated with photodynamic therapy and topical DMSO, were evaluated for cure rate and clinical results. After examination at 12–26 months post-initial successful treatment, 95% of lesions were found to still be in complete response. Microscopic examination of several biopsies from healed areas also did not reveal any signs of damage [23]. These results emphasize the penetration- enhancing capability of DMSO and institute its role in photodynamic therapy.

**Fig. 2** Synthesis of DMSO

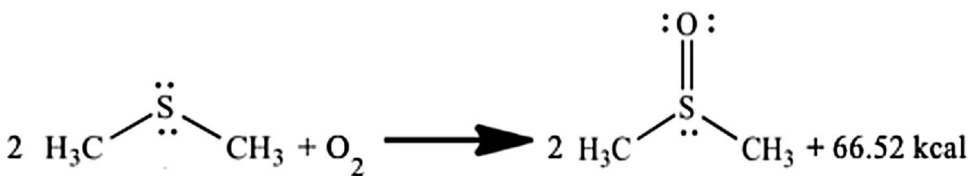

**Table 1** Studies evaluating therapeutic applications of DMSO

| Condition | References | Study type | Patients, *n* | Study methods | Outcome |
|---|---|---|---|---|---|
| Basal cell carcinoma (BCC) | Peng et al. [21] | Prospective cohort study | 22 | The fluorescence distribution of 5-aminolevulinic acid (ALA)-induced porphyrins after topical ALA application with or without DMSO/ethylenediaminetetraacetic acid (EDTA) was investigated in 22 patients with BCC | The penetration of ALA into deep lesions and the production of the ALA-induced porphyrin fluorescence were increased after topical administration of 20% ALA and 20% DMS0/4% EDTA for 3 h. Prior treatment with 99% DMSO for15 minutes further enhanced ALA penetration into the BCC lesions and produced about 3 times more ALA-induced porphyrins compared with those treated with ALA alone |
| | Warloe et al. [22] | Prospective cohort study | 122 | Patients were treated by photodynamic therapy by 5- (ALA) in cream topically applied alone or with (DMSO) and (EDTA), or with DMSO as a pretreatment. After 3 h of cream exposure, 40–200 Joules/cm [2] of 630 nm laser light was given | Fluorescence imaging of biopsies showed significantly improved ALA penetration depth and doubled ALA-induced porphyrin production using DMSO/EDTA. In 363 nodulo-ulcerative lesions the complete response rate increased from 67% to above 90% with DMSO/EDTA for lesions less than 2 mm thickness and from 34% to about 50% for lesions thicker than 2 mm |
| | Soler et al. [23] | Retrospective cohort study | 58 | Topical application of DMSO and 5-ALA acid (20% in cream) for 3 h, after which the lesions were exposed to light | At examination 12–26 months (mean 17 months) after treatment, 113 lesions (95%) maintained complete response |
| Pressure Ulcers | Lishner et al. [25] | Prospective cohort study | 20 | Patients with chronic, resistant perforating ulcers were treated with local application of 25% DMSO solution | Complete healing of ulcers was achieved in 14 patients after 4–15 weeks of daily treatment. Partial resolution was observed in four patients |
| | Duimel-Peeters et al. [26] | Systematic review | 902 | Literature search of the efficacy of DMSO on wound healing which resulted in the identification of 27 publications, 14 of which met the inclusion criteria | DMSO has positive effects on inflammation and wound healing, as well as an analgesic effect at concentrations less than 50% |
| Scleroderma | Scherbel et al. [30] | Prospective cohort study | 42 | Initial application of topical 30–60% DMSO solution, with subsequent increase to 70–100% DMSO, immersion in 50% DMSO, or subcutaneous 1–5% DMSO solution | 26 patients demonstrated "good" or "excellent" improvement<br>16 patients demonstrated "fair" or "poor" response |
| | Engel [31] | Prospective cohort study | 25 | 90% DMSO was applied twice daily to the affected area for 1 year | Increased mobility, pain relief, healing of ulcers, return of sensation and sweating |

**Table 1** (continued)

| Condition | References | Study type | Patients, *n* | Study methods | Outcome |
|---|---|---|---|---|---|
| | Scherbel [32] | Prospective cohort study | 22 | DMSO was applied topically three times daily for 2 weeks. The initial dose was a 35% solution, increased after 2 days to 46%, with applications subsequently reduced as ulcers healed | During a 6 months observation period, improvements in joint mobility, grip strength, and skin softening were noted in 19 patients |
| | Binnick et al. [33] | Prospective cohort study | 19 | Topical DMSO was applied by painting and immersion techniques for 3–15 months<br>Partial control was obtained by using a very low concentration (5%) on one side when involvement was symmetrical | Topical DMSO did not improve the skin induration, range of motion, or Raynaud's phenomenon nor was there a substantial beneficial effect noted on the healing or prevention of ischemic ulcers. Relief of pain was noted in ten of 16 patients |
| | Williams et al. [34] | Randomized double-blind controlled trial | 84 | Comparing DMSO 70% or 0.85% normal saline control for digital ulcers in patients with systemic sclerosis | There were no differences in the number of open ulcers or the combined surface area of ulcers among the 2 treatment groups |
| HSV | Dawber [36] | Randomized double- blind controlled trial | 118 | Idoxuridine 5% in 100% DMSO, applied every 4 h for 4 days compared to idoxuridine 25% alone applied every 2 h | Idoxuridine 5% in 100% DMSO significantly shortened the vesicular phase, healing time, and duration of pain, compared to application of idoxuridine 25% alone |
| | Spruance et al. [37] | In vitro clinical study | 0 | Guinea pigs inoculated with HSV-1 were given 5% acyclovir in DMSO solution or polyethylene glycol (PEG)ointment for twice daily 3 days | The penetration of acyclovir through guinea pig skin in vitro was greater with DMSO than when PEG was the vehicle. 5% acyclovir in DMSO was more effective than 5% acyclovir in PEG in the treatment of herpes simplex infection in the guinea pig |
| Cutaneous fungal infections | Leeyaphan et al. [41] | Randomized controlled trial | 20 | Patients diagnosed with nondermatophyte mold onychomycosis were randomly divided into two groups of 10 patients each: one treated with 0.3% amphotericin B cream in 30% DMSO and the other with 30% DMSO alone | Mycological cure was achieved in 80% of patients treated with amphotericin B cream in DMSO and in 44.4% patients treated with DMSO alone after 36 weeks of treatment. Clinical cure was achieved in 70% patients treated with amphotericin B cream and in 22.2% of patients on the DMSO cream |
| Primary localized cutaneous amyloidosis | Ozkaya-Bayazit et al. [43] | Prospective cohort study | 13 | Patients were treated with a 50% or 100% DMSO solution until pruritus disappeared, and then applied DMSO at increasing intervals to achieve the broadest effective interval for application with maintenance of relief | After a treatment period of 6.5 months, almost 50% remission in pigmentation and > 70% flattening of papules were observed |

**Table 1** (continued)

| Condition | References | Study type | Patients, *n* | Study methods | Outcome |
|---|---|---|---|---|---|
| | Mansoor et al. [44] | Case series | 71 | 70% DMSO was applied to 71 patients with lichen amyloidosis for 6 months | After 6 months of treatment, the appearance of papules and pruritus were eliminated or milder in 66% ($n=47$) of patients |
| | Saki et al. [45] | Randomized single- blinded clinical trial | 18 | Patients with bilateral macular amyloidosis received topical DMSO 50% solution and tretinoin 0.5% cream either on their right or the left side for 20 weeks, daily for the first 4 weeks and every other day after | A significant decline in pigmentation at each follow-up was observed in the DMSO group compared to the tretinoin group (tretinoin − 1.31 vs DMSO − 7.34. The DMSO group exhibited complete relief from itchiness from the first follow-up at 4 weeks ($P=0.003$ for tretinoin and $<0.0001$ for DMSO) |

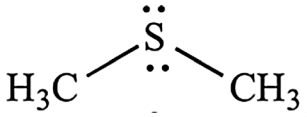


**Fig. 3** Molecular structure of dimethyl sulfide (metabolite of DMSO)

## Pressure ulcers

Pressure ulcers are injuries confined to locally aggravated skin or underlying tissue, defined by their manifestation in situations of restricted mobility due to pressure, stress, or friction over a bony prominence [24]. Previous approaches to the prevention of pressure ulcers include pressure redistributing devices, turning procedures, and application of various topical agents such as emollients. DMSO was found to be effective in preventing the development of pressure ulcers [24]. Moreover, in patients with chronic, resistant perforating ulcers, DMSO induced complete resolution of pressure ulcers after 4–15 weeks of daily treatment [25]. Daily application of DMSO solution decreased the incidence and severity of pressure ulcers in highly susceptible patients, while concurrently providing analgesic benefits. DMSO alleviates the ischemic damage associated with ulcer incidence to promote wound healing [26].

## Scleroderma

The unique organization of the stratum corneum is the major obstacle to topical drug delivery. However, the use of DMSO as a polar solvent has been proven to effectively penetrate the stratum corneum lipid bilayers, potentiating the use of local disease-modifying therapeutics [9, 27]. DMSO reduces the density of collagen fibers in both animals and patients with scleroderma [28, 29]. Scherbel et al. studied 42 scleroderma patients who had exhausted all known therapies without relief. Twenty-six patients showed "good" or "excellent" improvement. They observed healing of ischemic ulcers on fingertips, relief from pain and stiffness, and an increase in strength [30]. Additionally, Engel reported a high rate of success, including the resolution of cutaneous ulcers, in a 2 years study on 25 subjects [31]. Further studies reported resolution of cutaneous ulcers in systemic sclerosis after 2 weeks with DMSO applied topically three times daily. The initial dose was a 35% solution, increased after 2 days to 46%, with applications subsequently reduced, as ulcers healed. During a 6 months observation period, improvements in joint mobility, grip strength, and skin softening were noted in 19 of 22 patients [32].

However, Binnick et al. reported on nineteen patients with systemic scleroderma and five with localized scleroderma treated with topical DMSO by painting and immersion techniques. Partial control was obtained by using a very low

concentration (5%) on one side when involvement was symmetrical. Duration of treatment ranged from 3 to 15 months. Topical DMSO did not improve the skin induration, range of motion, or Raynaud's phenomenon in the scleroderma patients, nor was a substantial beneficial effect noted on the healing of ischemic ulcers. Continuous application of DMSO did not prevent new ulcerations. Relief of pain was noted in ten of 16 patients, most probably due to the local analgesic effect of DMSO [33]. Furthermore, a prospective, randomized, double-blind trial comparing DMSO 70% or 0.85% normal saline control for digital ulcers in 84 patients with systemic sclerosis did not show differences in the number of open ulcers or the combined surface area of ulcers [34].

One of the authors of this manuscript (PJC) has successfully treated scleroderma patients with topical DMSO 2% in a base of hemp oil. Within the first month, lesions were softer in texture with a marked reduction in characteristic woody induration.

## Herpes simplex virus infection

Herpes simplex virus-1 (HSV-1) is an enveloped double-stranded DNA virus characterized by periods of latency and reactivation, which may occur under conditions of stress or spontaneously, resulting in recurrent infection [35]. DMSO enhances the efficacy of idoxuridine in the treatment of viral infections [12]. In a randomized double- blind controlled trial of the efficacy of intermittent topical idoxuridine treatment of herpes infection, idoxuridine 5% in 100% DMSO significantly shortened the vesicular phase, healing time, and duration of pain, compared to application of idoxuridine 25% alone [36]. Spruance et al. studied DMSO as a vehicle for topical anti-viral agents and concluded that the penetration of acyclovir through guinea pig skin in vitro was markedly greater with DMSO than when polyethylene glycol (PEG) was the vehicle. Moreover, when 5% acyclovir in DMSO was compared with 5% acyclovir in PEG in the treatment of herpes simplex infection in the guinea pig, acyclovir with DMSO was found more effective [37].

DMSO has been demonstrated to block infection with herpes simplex virus. Aguilar et al. identified three distinct mechanisms in the relationship between DMSO and the inhibition of HSV viral growth; DMSO (1) inhibited viral DNA replication, (2) decreased virion infectivity, and (3) decreased transcription of HSV-1 genes, including those involved in viral assembly. Thus, in addition to potentiating the effects of anti-viral agents by enhancing permeability, DMSO has been shown to directly affect viral function [38]. Based on these findings, further investigation into the use of DMSO as an adjunctive treatment for herpes simplex virus is warranted.

## Cutaneous fungal infections

Although lower concentrations of DMSO may not possess antifungal properties when used alone, higher concentrations have been shown to inhibit the growth of several fungal species [39]. Kligman found that DMSO applied topically exhibited antifungal properties, reducing the resident microflora by 95% [14, 40]. The effect of 10, 5, 2.5, 1.25, 0.62, 0.31, and 0.15% DMSO on the growth of three strains of dermatophytes (*Trichophyton*, *Epidermophyton*, and *Microsporum*) was investigated by Randhawa. No growth of any dermatophyte was observed at DMSO concentration of 10%. A dose-related decrease in growth was observed between concentrations of 2.5 and 5%, and even concentrations less than 1% significantly inhibited growth [39].

Similarly, Leeyaphan et al. investigated the efficacy of topical 0.3% amphotericin B in 30% DMSO cream compared to 30% DMSO cream alone in patients with subungal onychomycosis. Mycological cure was achieved in 80% of patients treated with amphotericin B cream in DMSO and in 44.4% patients treated with DMSO alone after 36 weeks of treatment. Clinical cure was achieved in 70% patients treated with amphotericin B cream and in 22.2% of patients on the DMSO cream [41].

These results indicate that while topical amphotericin B dissolved in DMSO is efficacious in the treatment non-dermatophyte mold onychomycosis, DMSO alone may also carry some antifungal activity.

## Primary localized cutaneous amyloidosis

DMSO by itself has shown promise in the treatment of primary localized cutaneous amyloidosis. In conducting a systematic review for current reported treatment of primary localized cutaneous amyloidosis, Weidner et al. reported beneficial application of DMSO in two case reports of lichen amyloidosis [42]. Ozkaya-Bayazit et al. investigated the use of topical DMSO in patients with macular and lichen amyloidosis who were refractory to previous treatments with systemic antihistamines and/or topical corticosteroids. Patients were treated with a 50% or 100% DMSO solution until pruritus disappeared, and then applied DMSO at increasing intervals to achieve the broadest effective interval for application with maintenance of relief. After a treatment period of 6.5 months, remarkable results of almost 50% remission in pigmentation and > 70% flattening of papules were observed [43]. Mansoor et al. investigated the efficacy of 70% DMSO in 71 patients with lichen amyloidosis. After 6 months of treatment, the appearance of papules and pruritus were eliminated or milder in 66% ($n = 47$) of patients [44]. This notable clinical improvement may be attributed to the hydroxyl- binding capacity of DMSO, which diminishes the formation of new amyloid fibrils, thus alleviating their

pressure effect on nerve endings. More recently, Saki et al. have investigated the use of topical 50% DMSO solution in comparison to tretinoin 0.5% cream in the treatment of macular amyloidosis in a split- side within- person single-blinded randomized clinical trial. Remarkably, a significant decline in pigmentation at each follow-up was observed in the DMSO group compared to the tretinoin group (tretinoin − 1.31 vs DMSO − 7.34). Furthermore, the DMSO group exhibited complete relief from itchiness from the first follow- up at 4 weeks ($P = 0.003$ for tretinoin and $< 0.0001$ for DMSO) [45].

## Conclusion

DMSO is a solvent of low toxicity that has shown promise in treating a variety of cutaneous disorders. Further investigation of DMSO as a monotherapy and as a transdermal drug transporting agent is merited.

**Author contributions** All authors wrote and reviewed the main manuscript text.

**Funding** None.

### Declarations

**Conflict of interest** The authors declare that they have no conflict of ineterest.

## References


1. Boikess RS (2015) Chemical principles for organic chemistry, 1st edn. CT: Cengage Learning, Stamford, pp 28–29
2. Young VL, Boswell CB, Centeno RF, Watson ME (2005) DMSO: applications in plastic surgery. Aesthet Surg J 25(2):201–209
3. Wu X-F, Natte K (2016) The applications of dimethyl sulfoxide as reagent in organic synthesis. Adv Synth Catal 358(3):336–352
4. Gavrilin MV, Sen'chukova GV, Kompantseva EV (2000) Structure of chemical compounds, methods of analysis and process control for the synthesis and analysis of dimethyl sulfoxide. Pharm Chem J 34(9):490
5. Szmant HH (1975) Physical properties of dimethyl sulfoxide and its function in biological systems. Ann N Y Acad Sci 243:20–23
6. Kharasch N, Thyagarajan BS (1983) Structural basis for biological activities of dimethyl sulfoxide. Ann N Y Acad Sci 411:391–402
7. Verheijen M, Lienhard M, Schrooders Y et al (2019) DMSO induces drastic changes in human cellular processes and epigenetic landscape in vitro. Sci Rep 9(1):4641
8. Pielesz A, Gawłowski A, Biniaś D et al (2018) The role of dimethyl sulfoxide (DMSO) in ex-vivo examination of human skin burn injury treatment. Spectrochim Acta A Mol Biomol Spectrosc 196:344–352
9. Kollerup Madsen B, Hilscher M, Zetner D, Rosenberg J (2018) Adverse reactions of dimethyl sulfoxide in humans: a systematic review. F1000Res 7:1746
10. Notman R, Noro M, O'Malley B, Anwar J (2006) Molecular basis for dimethylsulfoxide (DMSO) action on lipid membranes. J Am Chem Soc 128(43):13982–13983
11. Nada AH, Zaghloul AA, Hedaya MM, Khattab IS (2014) Development of novel formulations to enhance in vivo transdermal permeation of tocopherol. Acta Pharm 64(3):299–309
12. Wood DC, Wood J (1975) Pharmacologic and biochemical considerations of dimethyl sulfoxide. Ann N Y Acad Sci 243:7–19
13. Maibach HI, Feldmann RJ (1967) The effect of DMSO on percutaneous penetration of hydrocortisone and testosterone in man. Ann N Y Acad Sci 141(1):423–427
14. Jacob SW, Wood DC (1967) Dimethyl sulfoxide (DMSO). Toxicology, pharmacology, and clinical experience. Am J Surg 114(3):414–426
15. Ashwood-Smith MJ (1975) Current concepts concerning radioprotective and cryoprotective properties of dimethyl sulfoxide in cellular systems. Ann N Y Acad Sci 243:246–256
16. Del Maestro R, Thaw HH, Björk J, Planker M, Arfors KE (1980) Free radicals as mediators of tissue injury. Acta Physiol Scand Suppl 492:43–57
17. Panganamala RV, Sharma HM, Heikkila RE, Geer JC, Cornwell DG (1976) Role of hydroxyl radical scavengers dimethyl sulfoxide, alcohols and methional in the inhibition of prostaglandin biosynthesis. Prostaglandins 11(4):599–607
18. Haigler HJ, Spring DD (1983) Comparison of the analgesic effects of dimethyl sulfoxide and morphine. Ann N Y Acad Sci 411:19–27
19. Görög P, Kovács IB (1968) Effect of dimethyl sulfoxide (DMSO) on various experimental inflammations. Curr Ther Res Clin Exp 10(9):486–492
20. Ang JM, Riaz IB, Kamal MU, Paragh G, Zeitouni NC (2017) Photodynamic therapy and pain: a systematic review. Photodiagnosis Photodyn Ther 19:308–344
21. Peng Q, Warloe T, Moan J et al (1995) Distribution of 5-aminolevulinic acid-induced porphyrins in noduloulcerative basal cell carcinoma. Photochem Photobiol 62(5):906–913
22. Warloe T, Peng Q, Heyerdahl H et al (1995) Photodynamic therapy with 5-aminolevulinic acid induced porphyrins and DMSO/EDTA for basal cell carcinoma. 5th International Photodynamic Association Biennial Meeting. SPIE 2371: 226–235
23. Soler AM, Warloe T, Tausjø J, Berner A (1999) Photodynamic therapy by topical aminolevulinic acid, dimethylsulphoxide and curettage in nodular basal cell carcinoma: a one-year follow-up study. Acta Derm Venereol 79(3):204–206
24. Moore ZE, Webster J (2018) Dressings and topical agents for preventing pressure ulcers. Cochrane Database Syst Rev 12(12):CD009362
25. Lishner M, Lang R, Kedar I, Ravid M (1985) Treatment of diabetic perforating ulcers (mal perforant) with local dimethylsulfoxide. J Am Geriatr Soc 33(1):41–43
26. Duimel-Peeters IGP, Halfens RJ, Snoeckx LH et al (2003) A systematic review of the efficacy of topical skin application of dimethyl sulfoxide on wound healing and as an anti-inflammatory drug. Wounds 15(11):361–370
27. Ting WW, Sontheimer RD (2001) Local therapy for cutaneous and systemic lupus erythematosus: practical and theoretical considerations. Lupus 10(3):171–184
28. Gries G, Bublitz G, Lindner J (1967) The effect of dimethyl sulfoxide on the components of connective tissue. (Clinical and experimental investigations). Ann N Y Acad Sci 141(1):630–637
29. Frommhold W, Bublitz G, Gries G (1967) The use of DMSO for the treatment of postirradiation subcutaneous plaques. Ann N Y Acad Sci 141(1):603–612
30. Scherbel AL, McCormack LJ, Layle JK (1967) Further observations on the effect of dimethyl sulfoxide in patients with

generalized scleroderma. (Progressive systemic sclerosis). Ann N Y Acad Sci 141(1):613–629
31. Engel MF (1972) Dimethyl sulfoxide in the treatment of scleroderma. South Med J 65(1):71–73
32. Scherbel AL (1983) The effect of percutaneous dimethyl sulfoxide on cutaneous manifestations of systemic sclerosis. Ann N Y Acad Sci 411:120–130
33. Binnick SA, Shore SS, Corman A, Fleischmajer R (1977) Failure of dimethyl sulfoxide in the treatment of scleroderma. Arch Dermatol 113(10):1398–1402
34. Williams HJ, Furst DE, Dahl SL et al (1985) Double-blind, multicenter controlled trial comparing topical dimethyl sulfoxide and normal saline for treatment of hand ulcers in patients with systemic sclerosis. Arthritis Rheum 28(3):308–314
35. Fatahzadeh M, Schwartz RA (2007) Human herpes simplex virus infections: epidemiology, pathogenesis, symptomatology, diagnosis, and management. J Am Acad Dermatol 57(5):737–766
36. Dawber R (1974) Idoxuridine in herpes zoster: further evaluation of intermittent topical therapy. Br Med J 2(5918):526–527
37. Spruance SL, McKeough MB, Cardinal JR (1983) Dimethyl sulfoxide as a vehicle for topical antiviral chemotherapy. Ann N Y Acad Sci 411:28–33
38. Aguilar JS, Roy D, Ghazal P, Wagner EK (2002) Dimethyl sulfoxide blocks herpes simplex virus-1 productive infection in vitro acting at different stages with positive cooperativity. Application of micro-array analysis. BMC Infect Dis. https://doi.org/10.1186/1471-2334-2-9
39. Randhawa MA (2006) The effect of dimethyl sulfoxide (DMSO) on the growth of dermatophytes. Nippon Ishinkin Gakkai Zasshi 47(4):313–318
40. Kligman AM (1965) Topical pharmacology and toxicology of dimethyl sulfoxide—part 1. JAMA 193:796–804
41. Leeyaphan C, Suiwongsa B, Komesmuneeborirak P et al (2021) Effectiveness and safety of topical amphotericin B in 30% dimethyl sulfoxide cream versus 30% dimethyl sulfoxide cream for nondermatophyte onychomycosis treatment: a pilot study [published online ahead of print, 2021 Oct 26]. Indian J Dermatol Venereol Leprol. https://doi.org/10.25259/IJDVL_359_2021
42. Weidner T, Illing T, Elsner P (2017) Primary localized cutaneous amyloidosis: a systematic treatment review. Am J Clin Dermatol 18(5):629–642
43. Ozkaya-Bayazit E, Kavak A, Güngör H, Ozarmagan G (1998) Intermittent use of topical dimethyl sulfoxide in macular and papular amyloidosis. Int J Dermatol 37(12):949–954
44. Mansoor M, Kapadia N, Talat H et al (2017) Lichen amyloidosis: evaluation of the efficacy of topical dimethyl sulfoxide (DMSO) 70% in Abbasi Shaheed hospital. Karachi Professional Med J 24(7):1020–1026
45. Saki N, Ahramiyanpour N, Heiran A, Alipour S, Parvizi MM (2020) Efficacy of topical dimethyl sulfoxide (DMSO) 50% solution vs tretinoin 0.5% cream in treatment of patients with primary macular amyloidosis: a split-side single-blinded randomized clinical trial. Dermatol Ther 33(3):13305–8. https://doi.org/10.1111/dth.13305