DMSO: Many Uses, Much Controversy

Maya Muir

Abstract

Dimethyl sulfoxide (DMSO), a by-product of the wood industry, has been in use as a commercial solvent since 1953. It is also one of the most studied but least understood pharmaceutical agents of our time--at least in the United States. According to Stanley Jacob, MD, a former head of the organ transplant program at Oregon Health Sciences University in Portland, more than 40,000 articles on its chemistry have appeared in scientific journals, which, in conjunction with thousands of laboratory studies, provide strong evidence of a wide variety of properties. (See Major Properties Attributed to DMSO) Worldwide, some 11,000 articles have been written on its medical and clinical implications, and in 125 countries throughout the world, including Canada, Great Britain, Germany, and Japan, doctors prescribe it for a variety of ailments, including pain, inflammation, scleroderma, interstitial cystitis, and arthritis elevated intercranial pressure.

Yet in the United States, DMSO has Food and Drug Administration (FDA) approval only for use as a preservative of organs for transplant and for interstitial cystitis, a bladder disease. It has fallen out of the limelight and out of the mainstream of medical discourse, leading some to believe that it was discredited. The truth is more complicated.

DMSO: A History of Controversy

The history of DMSO as a pharmaceutical began in 1961, when Dr. Jacob was head of the organ transplant program at Oregon Health Sciences University. It all started when he first picked up a bottle of the colorless liquid. While investigating its potential as a preservative for organs, he quickly discovered that it penetrated the skin quickly and deeply without damaging it. He was intrigued. Thus began his lifelong investigation of the drug.

The news media soon got word of his discovery, and it was not long before reporters, the pharmaceutical industry, and patients with a variety of medical complaints jumped on the news. Because it was available for industrial uses, patients could dose themselves. This early public interest interfered with the ability of Dr. Jacob--or, later, the FDA--to see that experimentation and use were safe and controlled and may have contributed to the souring of the mainstream medical community on it.

Why, if DMSO possesses half the capabilities claimed by Dr. Jacob and others, is it still on the sidelines of medicine in the United States today?

"It's a square peg being pushed into a round hole," says Dr. Jacob. "It doesn't follow the rifle approach of one agent against one disease entity. It's the aspirin of our era. If aspirin were to come along today, it would have the same problem. If someone gave you a little white pill and said take this and your headache will go away, your body temperature will go down, it will help prevent strokes and major heart problems--what would you think?"

Others cite DMSO's principal side effect: an odd odor, akin to that of garlic, that emanates from the mouth shortly after use, even if use is through the skin. Certainly, this odor has made double-blinded studies difficult. Such studies are based on the premise that no one, neither doctor nor patient, knows which patient receives the drug and which the placebo, but this drug announces its presence within minutes.

Others, such as Terry Bristol, a Ph.D. candidate from the University of London and president of the Institute for Science, Engineering and Public Policy in Portland, Oregon, who assisted Dr. Jacob with his research in the 1960s and 1970s, believe that the smell of DMSO may also have put off the drug companies, that feared it would be hard to market. Worse, however, for the pharmaceutical companies was the fact that no company could acquire an exclusive patent for DMSO, a major consideration when the clinical testing required to win FDA approval for a drug routinely runs into millions of dollars. In addition, says Mr. Bristol, DMSO, with its wide range of attributes, would compete with many drugs these companies already have on the market or in development.

The FDA and DMSO

In the first flush of enthusiasm over the drug, six pharmaceutical companies embarked on clinical studies. Then, in November 1965, a woman in Ireland died of an allergic reaction after taking DMSO and several other drugs. Although the precise cause of the woman's death was never determined, the press reported it to be DMSO. Two months later, the FDA closed down clinical trials in the United States, citing the woman's death and changes in the lenses of certain laboratory animals that had been given doses of the drug many times higher than would be given humans.

Some 20 years and hundreds of laboratory and human studies later, no other deaths have been reported, nor have changes in the eyes of humans been documented or claimed. Since then, however, the FDA has refused seven applications to conduct clinical studies, and approved only 1, for intersititial cystitis, which subsequently was approved for prescriptive use in 1978.

Dr. Jacob believes the FDA "blackballed" DMSO, actively trying to kill interest in a drug that could end much suffering. Jack de la Torre, MD, Ph.D., professor of neurosurgery and physiology at the University of New Mexico Medical School in Albuquerque, a pioneer in the use of DMSO and closed head injury, says, "Years ago the FDA had a sort of chip on its shoulder because it thought DMSO was some kind of snake oil medicine. There were people there who were openly biased against the compound even though they knew very little about it. With the new administration at that agency, it has changed a bit." The FDA recently granted permission to conduct clinical trials in Dr. de la Torre's field of closed head injury.

DMSO Penetrates Membranes and Eases Pain

The first quality that struck Dr. Jacob about the drug was its ability to pass through membranes, an ability that has been verified by numerous subsequent researchers.1 DMSO's ability to do this varies proportionally with its strength--up to a 90 percent solution. From 70 percent to 90 percent has been found to be the

most effective strength across the skin, and, oddly, performance drops with concentrations higher than 90 percent. Lower concentrations are sufficient to cross other membranes. Thus, 15 percent DMSO will easily penetrate the bladder.2

In addition, DMSO can carry other drugs with it across membranes. It is more successful ferrying some drugs, such as morphine sulfate, penicillin, steroids, and cortisone, than others, such as insulin. What it will carry depends on the molecular weight, shape, and electrochemistry of the molecules. This property would enable DMSO to act as a new drug delivery system that would lower the risk of infection occurring whenever skin is penetrated.

DMSO perhaps has been used most widely as a topical analgesic, in a 70 percent DMSO, 30 percent water solution. Laboratory studies suggest that DMSO cuts pain by blocking peripheral nerve C fibers.3 Several clinical trials have demonstrated its effectiveness,4,5 although in one trial, no benefit was found.6 Burns, cuts, and sprains have been treated with DMSO. Relief is reported to be almost immediate, lasting up to 6 hours. A number of sports teams and Olympic athletes have used DMSO, although some have since moved on to other treatment modalities. When administration ceases, so do the effects of the drug.

Dr. Jacob said at a hearing of the U.S. Senate Subcommittee on Health in 1980, "DMSO is one of the few agents in which effectiveness can be demonstrated before the eyes of the observers....If we have patients appear before the Committee with edematous sprained ankles, the application of DMSO would be followed by objective diminution of swelling within an hour. No other therapeutic modality will do this."

Chronic pain patients often have to apply the substance for 6 weeks before a change occurs, but many report relief to a degree they had not been able to obtain from any other source.

DMSO and Inflammation

DMSO reduces inflammation by several mechanisms. It is an antioxidant, a scavenger of the free radicals that gather at the site of injury. This capability has been observed in experiments with laboratory animals7 and in 150 ulcerative colitis patients in a double-blinded randomized study in Baghdad, Iraq.8 DMSO also stabilizes membranes and slows or stops leakage from injured cells.

At the Cleveland Clinic Foundation in Cleveland, Ohio, in 1978, 213 patients with inflammatory genitourinary disorders were studied. Researchers concluded that DMSO brought significant relief to the majority of patients. They recommended the drug for all inflammatory conditions not caused by infection or tumor in which symptoms were severe or patients failed to respond to conventional therapy.9

Stephen Edelson, MD, F.A.A.F.P., F.A.A.E.M., who practices medicine at the Environmental and Preventive Health Center of Atlanta, has used DMSO extensively for 4 years. "We use it intravenously as well as locally," he says. "We use it for all sorts of inflammatory conditions, from people with rheumatoid arthritis to people with chronic low back inflammatory-type symptoms, silicon immune toxicity syndromes, any kind of autoimmune process.

"DMSO is not a cure," he continues. "It is a symptomatic approach used while you try to figure out why the individual has the process going on. When patients come in with rheumatoid arthritis, we put them on IV DMSO, maybe three times a week, while we are evaluating the causes of the disease, and it is amazing how free they get. It really is a dramatic treatment."

As for side effects, Dr. Edelson says: "Occasionally, a patient will develop a headache from it, when used intravenously--and it is dose related." He continues: "If you give a large dose, [the patient] will get a headache. And we use large doses. I have used as much as 30ÝmlÝIV over a couple of hours. The odor is a problem. Some men have to move out of the room [shared] with their wives and into separate bedrooms. That is basically the only problem."

DMSO was the first nonsteroidal anti-inflammatory discovered since aspirin. Mr. Bristol believes that it was that discovery that spurred pharmaceutical companies on to the development on other varieties of nonsteroidal anti-inflammatories. "Pharmaceutical companies were saying that if DMSO can do this, so can other compounds," says Mr. Bristol. "The shame is that DMSO is less toxic and has less int he way of side effects than any of them."

Collagen and Scleroderma

Scleroderma is a rare, disabling, and sometimes fatal disease, resulting form an abnormal buildup of collagen in the body. The body swells, the skin--particularly on hands and face--becomes dense and leathery, and calcium deposits in joints cause difficulty of movement. Fatigue and difficulty in breathing may ensue. Amputation of affected digits may be necessary. The cause of scleroderma is unknown, and, until DMSO arrived, there was no known effective treatment.

Arthur Scherbel, MD, of the department of rheumatic diseases and pathology at the Cleveland Clinic Foundation, conducted a study using DMSO with 42 scleroderma patients who had already exhausted all other possible therapies without relief. Dr. Scherbel and his coworkers concluded 26 of the 42 showed good or excellent improvement. Histotoxic changes were observed together with healing of ischemic ulcers on fingertips, relief from pain and stiffness, and an increase in strength. The investigators noted, "It should be emphasized that these have never been observed with any other mode of therapy."10 Researchers in other studies have since come to similar conclusions.11

Does DMSO Help Arthritis?

It was inevitable that DMSO, with its pain-relieving, collagen-softening, and anti-inflammatory characteristics, would be employed against arthritis, and its use has been linked to arthritis as much as to any condition. Yet the FDA has never given approval for this indication and has, in fact, turned down three Investigational New Drug (IND) applications to conduct extensive clinical trials.

Moreover, its use for arthritis remains controversial. Robert Bennett, MD, F.R.C.P., F.A.C.R., F.A.C.P., professor of medicine and chief, division of arthritis and rheumatic disease at Oregon Health Sciences University (Dr. Jacob's university), says other drugs work better. Dava Sobel and Arthur Klein conducted their own

informal study of 47 arthritis patients using DMSO in preparation for writing their book, Arthritis: What Works, and came to the same conclusion.12

Yet laboratory studies have indicated that DMSO's capacity as a free-radical scavenger suggests an important role for it in arthritis.13 The Committee of Clinical Drug Trials of the Japanese Rheumatism Association conducted a trial with 318 patients at several clinics using 90 percent DMSO and concluded that DMSO relieved joint pain and increased range of joint motion and grip strength, although performing better in more recent cases of the disease.14 It is employed widely in the former Soviet Union for all the different types of arthritis, as it is in other countries around the world.

Dr. Jacob remains convinced that it can play a significant role in the treatment of arthritis. "You talk to veterinarians associated with any race track, and you'll find there's hardly an animal there that hasn't been treated with DMSO. No veterinarian is going to give his patient something that does not work. There's no placebo effect on a horse."

DMSO and Central Nervous System Trauma

Since 1971, Dr. de la Torre, then at the University of Chicago, has experimented using DMSO with injury to the central nervous system. Working with laboratory animals, he discovered that DMSO lowered intracranial pressure faster and more effectively than any other drug. DMSO also stabilized blood pressure, improved respiration, and increased urine output by five times and increased blood flow through the spinal cord to areas of injury.15-17 Since then, DMSO has been employed with human patients suffering severe head trauma, initially those whose intracranial pressure remained high despite the administration of mannitol, steroids, and barbiturates. In humans, as well as animals, it has proven the first drug to significantly lower intracranial pressure, the number one problem with severe head trauma.

"We believe that DMSO may be a very good product for stroke," says Dr. de la Torre, "and that is a devastating illness which affects many more people than head injury. We have done some preliminary clinical trials, and there's a lot of animal data showing that it is a very good agent in dissolving clots."

Other Possible Applications for DMSO

Many other uses for DMSO have been hypothesized from its known qualities hand have been tested in the laboratory or in small clinical trials. Mr. Bristol speaks with frustration about important findings that have never been followed up on because of the difficulty in finding funding and because "to have on your resume these days that you've worked on DMSO is the kiss of death." It is simply too controversial. A sampling of some other possible applications for this drug follows.

DMSO as long been used to promote healing. People who have it on hand often use it for minor cuts and burns and report that recovery is speedy. Several studies have documented DMSO use with soft tissue damage, local tissue death, skin ulcers, and burns.18-21

In relation to cancer, several properties of DMSO have gained attention. In one

study with rats, DMSO was found to delay the spread of one cancer and prolong survival rates with another.22 In other studies, it has been found to protect noncancer cells while potentiating the chemotherapeutic agent.

Much has been written recently about the worldwide crisis in antibiotic resistance among bacteria (see Alternative & Complementary Therapies, Volume 2, Number 3, 1996, pages 140-144) Here, too, DMSO may be able to play a role. Researcher as early as 1975 discovered that it could break down the resistance certain bacteria have developed.23

In addition to its ability to lower intracranial pressure following closed head injury, Dr. de la Torre's work suggests that the drug may actually have the ability to prevent paralysis, given its ability to speedily clean out cellular debris and stop the inflammation that prevents blood from reaching muscle, leading to the death of muscle tissue.

With its great antioxidant powers, DMSO could be used to mitigate some of the effects of aging, but little work has been done to investigate this possibility. Toxic shock, radiation sickness, and septicemia have all been postulated as responsive to DMSO, as have other conditions too numerous to mention here.

DMSO in the Future

Will DMSO ever sit on the shelves of pharmacies in this country as a legal prescriptive for many of the conditions it may be able to address? Will the studies we need to discover when this drug is most appropriate ever be done? Given the difficulties the drug has run into so far and the recent development of new drugs that perform some of the same functions, Mr. Bristol is doubtful. Others, however, such as Dr. Jacob and Dr. de la Torre, see the FDA approval of DMSO for interstitial cystitis and the more recent FDA go-ahead for DMSO trials with closed head injury as new indications of hope. The cystitis approval means that physicians may use it at their discretion for other uses, giving DMSO a new legitimacy.

Dr. Jacob continues to believe that DMSO should not even be called a drug but is more correctly a new therapeutic principle, with an effect on medicine that will be profound in many areas. Whether that is true cannot be known without extensive a publicly reported trials, which are dependent on the willingness of researchers to undertake rigorous studies in this still-unfashionable tack and of pharmaceutical companies and other investors to back them up. That this is a live issue is proved by the difficulty the investigators with approval to test DMSO for closed head injury clinically are having finding funds to conduct the trials.

In 1980, testifying before the Select Committee on Agin of the U.S. House of Representatives, Dr. Scherbel said, "The controversy that exists over the clinical effectiveness of DMSO is not well-founded--clinical effectiveness may be variable in different patients. If toxicity is consistently minimal, the drug should not be restricted from practice. The clinical effectiveness of DMSO can be decided with complete satisfaction if the drug is made available to the practicing physician. The number of patient complaints about pain and the number of phone calls to the doctor's office will decide quickly whether or not the drug is effective."

It may be premature to call for the full rehabilitation of DMSO, but it is time to call

for a full investigation of its true range of capabilities.

References

1. Kolb, K.H., Jaenicke, G., Kramer, M., Schulze, P.E. Absorption, distribution, and elimination of labeled dimethyl sulfoxide in man and animals. *Ann NY Acad Sci* 141:85-95, 1967.
2. Herschler, R., Jacob, S.W. The case of dimethyl sulfoxide. In: Lasagna, L. (Ed.), *Controversies in Therapeutics*. Philadelphia: W.B. Saunders, 1980.
3. Evans, M.S., Reid, K.H., Sharp, J.B. Dimethyl sulfoxide (DMSO) blocks conduction in peripheral nerve C fibers: A possible mechanism of analgesia. *Neurosci Lett* 150:145-148, 1993.
4. Demos, C.H., Beckloff, G.L., Donin, M.N., Oliver, P.M. Dimethyl sulfoxide in musculoskeletal disorders. *Ann NY Acad Sci* 141:517-523, 1967.
5. Lockie, L.M., Norcross, B. A clinical study on the effects of dimethyl sulfoxide in 103 patients with acute and chronic musculoskeletal injures and inflammation. *Ann NY Acad Sci* 141:599-602, 1967.
6. Percy, E.C., Carson, J.D. The use of DMSO in tennis elbow and rotator cuff tendinitis: A double-blind study. *Med Sci Sports Exercise* 13:215-219, 1981.
7. Itoh, M., Guth, P. Role of oxygen-derived free radicals in hemorrhagic shock-induced gastric lesions in the rat. *Gastroenterology* 88:1126-1167, 1985.
8. Salim, A.S., Role of oxygen-derived free radical scavengers in the management of recurrent attacks of ulcerative colitis: A new approach. *J. Lab Clin Med* 119:740-747, 1992.
9. Shirley, S.W., Stewart, B.H., Mirelman, S. Dimethyl sulfoxide in treatment of inflammatory genitourinary disorders. *Urology* 11:215-220, 1978.
10. Scherbel, A.L., McCormack, L.J., Layle, J.K. Further observations on the effect of dimethyl sulfoxide in patients with generalized scleroderma (progressive systemic sclerosis). *Ann NY Acad Sci* 141:613-629, 1967.
11. Engel, M.F., Dimethyl sulfoxide in the treatment of scleroderma. *South Med J* 65:71, 1972.
12. Sobel, D., Klein, A.C. *Arthritis: What Works*. New York: St. Martins Press, 1989.
13. Santos, L., Tipping, P.G. Attenuation of adjuvant arthritis in rats by treatment with oxygen radical scavengers. *Immunol Cell Biol* 72:406-414, 1994.
14. Matsumoto, J. Clinical trials of dimethyl sulfoxide in rheumatoid arthritis patients in Japan. *Ann NY Acad Sci* 141:560-568, 1967.
15. de la Torre, J.C., et al. Modifications of experimental spinal cord injuries using dimethyl sulfoxide. *Trans Am Neurol Assoc* 97:230, 1971.
16. de la Torre, J.C., et al. Dimethyl sulfoxide in the treatment of experimental brain compression. *J Neurosurg* 38:343, 1972.
17. de la Torre, J.C., et al. Dimethyl sulfoxide in the central nervous system trauma. *Ann NY Acad Sci* 243:362, 1975.
18. Lawrence, H.H., Goodnight, S.H. Dimethyl sulfoxide and extravasion of anthracycline agents. *Ann Inter Med* 98:1025, 1983.
19. Lubredo, L., Barrie, M.S., Woltering, E.A. DMSO protects against adriamycin-induced skin necrosis. *J. Surg Res* 53:62-65, 1992.
20. Alberts, D.S., Dorr, R.T. Case report: Topical DMSO for mitomycin-C-induced skin ulceration. *Oncol Nurs Forum* 18:693-695, 1991.
21. Cruse, C.W., Daniels, S. Minor burns: Treatment using a new drug deliver

system with silver sulfadiazine. *South Med J* 82:1135-1137, 1989.
22. Miller, L., Hansbrough, J., Slater, H., et al. Sildimac: A new deliver system for silver sulfadiazine in the treatment of full-thickness burn injuries. *J Burn Care Rehab* 11:35-41, 1990
23. Salim, A. Removing oxygen-derived free radicals delays hepatic metastases and prolongs survival in colonic cancer. *Oncology* 49:58-62, 1992.
24. Feldman, W.E., Punch, J.D., Holden, P. In vivo and in vitro effects of dimethyl sulfoxide on streptomycin-sensitive and resistant *Escherichia coli*. *Ann Acad Sci* 141:231, 1967.

Source: Alternative & Complementary Therapies, July/August 1996, pages 230-235. DMSO Organization would like to thank the publisher for permission to place this fine article on the World Wide Web.