DIMETHYLSULPHOXIDE : A PROMISING COMPOUND FOR PHARMACOLOGICAL AND MOLECULAR UTILIZATION

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Dimethylsulfoxide (DMSO) us an organosulfur compound with the formula $(CH_3)_2SO$. This colourless liquid is an important *polar* aprotic solvent that dissolves both polar and non polar compounds and is miscible in a wide range of organic solvents as well as water. It has a relatively high melting point. It is a polar aprotic solvent and is less toxic than other members of this class, such as di-methyl formamide, di-methyl acetamide, N-methyl-2-pyrrolidone, and HMPA. It is frequently used as a solvent for chemical reactions involving salts, most notably Finkelstein reactions and other nucleophilic substitutions. It is also extensively used as an extractant in biochemistry and cell biology. The use of DMSO as an alternative treatment for cancer is of particular concern, as it has been shown to interfere with a variety of chemotherapy drugs, including cisplatin, carboplatin and oxaliplatin. DMSO is reported to enhance the production of several platlet specific proteins and platlet activation dependent granule eternal membrane protein.

KEYWORDS : DMSO, Dimethyl sulfoxide, Heart disease, Stents, Stroke, Traumatic Brain Injury, Spinal cord Trauma.

INTRODUCTION

DMSO is an aprotic solvent molecule with a highly polar domain and two non polar methyl groups; making it soluble in both aqueous and organic media. A clear odourless liquid; inexpensively produced as a by-product in the paper industry. It is being frequently used as a solvent in biological studies (both in vivo and in vitro) and also serves as a vehicle for drug therapy.

Being an efficient hydrogen bond disruptor, it is an efficient solvent for water insoluble compounds. Therapeutic and toxic agent's insoluble in water finds solubility in DMSO. Deuterated DMSO (DMSO-d_6) , finds use as a solvent for NMR spectroscopy, again due to its ability to dissolve a wide range of analytes , the simplicity of its own spectrum, and its suitability for high-temperature NMR spectroscopic studies. Though it has some disadvantages also like its high viscosity, which broadens signals, and its hygroscopicity, which leads to an overwhelming H_2O resonance in the ^1H NMR spectrum. Keeping in mind the multi- disciplinary effects of DMSO brought into knowledge by various studies; its therapeutic and pharmacological properties finds immense utilization in pharmacology, toxicology and in trauma diseases. DMSO is found to induce differentiation and function of leukemic and other malignant cells. DMSO has prophylactic radio protective properties and

cryoprotective actions. Primary pharmacological action of DMSO includes anti- inflammation, analgesia, diuresis, enhancement of resistance to infection, vasodilatation, muscle relaxation, hyper cholesterolemia.

Properties	
Chemical formula	C_2H_6OS
Molar mass	78.13 g·mol^{-1}
Appearance	Colourless liquid
Density	1.1004 g cm^{-3}
Melting point	19 °C (66 °F; 292 K)
Boiling point	189 °C (372 °F; 462 K)
Solubility in water	Miscible
Solubility in diethyl ether	very soluble
Acidity (pK_a)	35
Refractive index(n_D)	1.479 $\varepsilon_r = 48$
Viscosity	1.996 c P at 20 °C

Over the past 40 years, more than 10,000 articles on the biological implications and 30,000

Articles on the Chemistry of DMSO have appeared in the scientific literature. Although DMSO was known since 19th century due to its main use in wood industry, its biological properties were discovered in 1960's. Since then, it founds major use for laboratory and pharmacological purposes It is a by- product of Kraft pulping (sulphate process) which converts wood into wood pulp leaving almost cellulose fibres. The process simply involves treatment of wood chips with a mixture of sodium hydroxide and sodium sulphide known as white liquor, breaking the bonds which link lignin to cellulose. DMSO is a very simple compound but has stimulated many researchers to work with it in a different context. Due to its strong affinity for water; it is rapidly diluted on exposure to air. The most important therapeutic effect includes its own rapid penetration and enhanced penetration of other substances across biological membranes. It is clear odourless liquid, inexpensively produced as a by-product of the paper industry, intercellular, electrical uncoupler, solubilising agent used in sample preparation for electron microscopy. It has also been reported as an antidote to the extravagation of vesicant anticancer agents. Additionally, it had found extensive use in the treatment of brain oedema, schizophrenia and interstitial cystitis. High concentrations of DMSO find application in cutaneous manifestations of scleroderma. An interesting finding reports that dermal application of DMSO seems to provide rapid temporary relief or pain in patients with arthritis and connective tissue injuries.

We aim to throw some more light on its cellular, toxicological and pharmacological aspects. DMSO received its approval in treatment of interstitial cystitis by intervesicular instillation by FDA, USA in 1978 [2].

PRIMARY PHARMACOLOGICAL ACTIONS

1. Membrane Penetration : DMSO readily crosses biological membranes. Kolbe *et. al.* [3] evaluated the absorption and distribution of DMSO is lower animals (rat) and man. After cuticle administration, radioactivity in blood was measured which appeared after 5 minutes of application, further was detected after one hour in the bones. Denko [4] and his associates applied 35S-labeled DMSO to the skin of rats. Within 2 hour a wide range of radioactivity was distributed in all organs studied. The highest values occurred in decreasing order in the following soft tissues; spleen, stomach, lung, vitreous humor, thymus, brain, kidney, sclera, colon, heart, skeletal muscle, skin, liver, aorta, adrenal, lens of eye, and cartilage. Rammler and Zaffaroni [5] illustrated the chemical properties of DMSO and suggested that the rapid movement of this molecule through the skin, a protein occurring when DMSO substitutes for water.

2. Membrane Transport : Low molecular weight non ionized molecule transports easily through the skin though high molecular weight compounds like insulin do not pass through the skin. Nadd *et al* [6]suggested that DMSO enhanced penetration of infections agent in experimental leukaemia of guinea pigs.

3. Anti- inflammation : DMSO showed no anti-inflammatory effect when studied in experimental inflammation induced in rabbit eye by mustard oil in the rat ear by croton oil [7]. Suckest [8] has demonstrated anti- inflammatory effects with intra- articular DMSO in rabbits following the creation of experimental (croton oil) arthritis.

4. Nerve blockade (Analgesia) : DMSO injected subcutaneously in 10% concentration. into cats produced a total loss of the central pain response. Two ml of 50% DMSO injected into the cerebrospinal fluid led to total anaesthesia of animal and complete recovery of animal occurred without apparent 14 effect [9].

5. Muscle Relaxation : On applying DMSO topically to the skin of patients, it is reported to produce electro myographic muscle relaxation 1 hour after application [10].

6. Hydroxyl radical scavenger : When oxygen supply is not completely abolished, per oxidation of cellular membrane bound lipids occur resulting in enhancement of hydroxyl free radicals. DMSO is reported as an effective hydroxyl radical scavenger [11, 12, 13]. It is known to improve mitochondrial oxidative phosphorylation, which gets affected during ischemial injury.

7. Therapeutic effects: DMSO was introduced as a potential therapeutic agent for the treatment of head and spinal cord injury for stroke in early 1970's by De la Torre and his group [14] Zhang and Eyzaguirre [15] reported that rise in intracellular Ca^{+2} concentration induced by hypoxia in mouse glomous cells is blunted by presence of DMSO. Michael [16] showed that in DMSO treated human erythroleukemia cells, Calcium elevations by adrenaline and neuropeptide Y were reduced significantly. N.C. Santos *et al* reported that DMSO prevents the ionophore- induced calcium loading of human erythrocytes. The combination of DMSO and haematoxylin was being used as a cure for cancer in study reported DMSO potentiating therapy (DPT) as the magic bullet for cancer. (Webster Kehr , 22 Feb. 2015).

A 1978 study concluded that DMSO brought significant relief to the majority of the 213 patients with inflammatory genitourinary disorders that were studied [28]. The authors recommended DMSO for genitourinary inflammatory conditions not caused by infection or tumour in which symptoms were severe or patients failed to respond to conventional therapy.

Reported Effects of DMSO:

DMSO is reported to enhance the production of several platelet specific proteins; platelet activation dependent granule eternal membrane protein [16]. Also, it inhibits inter lewkin-8 production in a dose-dependent manner, directly at the transcriptional level, preventing adhesion of neutrophils to endothelium, converges ClO^{-} and possibly reduces NADPH-oxidase activity [17] . DMSO is also reported to arrest the cell cycle of several human and mouse lymphoid cell lines at G phase [18] DMSO leads to the collapse of mitochondrial membrane potential, release of cytochrome C from mitochondria and activation of capase- 9 & 3 but not of capase-8 [19]. In lipid metabolism DMSO is reported to increase the transfer of unspecified cholesterol between membranes [20,] reduces the accumulation of cholesterol in vascular and extra vascular tissues, and partially prevents the development of dietary cholesterol induced atherosclerosis. On cryopreservation of human platelets; DMSO induces K^{+}, Ca^{+2} and lactate dehydrogenase release from the intracellular space to the extracellular space DMSO also plays an important role in hydrogen bound disruption action [21]. Because of its strong scavenging effects, it should be used with caution as a solvent in chemiluminescence studies [22].

DMSO is reported to enhance the penetration of chemicals and is added to fixatives to improve cell preservation. In 1978, it got approval from FDA (USA) for use in interstitial cystitis treatment. Its successful application is treatment of dermatological urinary and pulmonary, rheumatic and renal manifestation of amyloidosis. It finds extensive use in much gastrointestinal disease due to its non-inflammatory reactive oxygen scavenging actions. It reality clones blood-brain barrier and has been effective in treating brain oedema. Interestingly, it has been suggested for treatment of Alzheimer's disease [25].

Most significant side affect of DMSO is greater like breast odour due to pulmonary selection of small % of DMSO as dimethyl sulphide. DMSO may also be used as a cryoprotectant, added to cell media to reduce ice formation and thereby prevent cell death during the freezing process [29]. Approximately 10% may be used with a slow-freeze method, and the cells may be frozen at −80 °C (−112 °F) or stored in liquid nitrogen safely.

Cellular (Molecular Effects):

DMSO has radio protective properties against lethal and mutagenic effects of X- rays in cells, cellular systems and whole animals. It also has cryoprotectant properties, meaning that it is capable of protecting against injury due to freezing. As a source of sulphur, DMSO aids in heavy metal detoxification. Sulphur bind with toxic heavy metals (Hg, Pb, Al, Cd, Ar, Ni) and eliminates then via urination, defection and sweating. Though, some systematic side effects from use of DMSO are added to fixatives to improve cell preservation [23].

Side Effects:

Besides, several pharmacological applications in treatment of different diseases. DMSO use pose side effects like vomiting, nausea, diarrhoea, rashes, flushing, bronchospasm, lever failure, hyper tension, heart attack, and cardiac arrest [26, 27].

Pathological Activity	**Effect of DMSO**
Intracranial Pressure Increase (ICP)	Decreases
Inflammation	Suppresses
Cerebral Ischemia	Increases the flow
Free Radical formation	Scavenges
Cerebral oedema	Reduces

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