

# Amelioration of COVID-19 Course using Inhalation of Dimethylsulfoxide (DMSO) and Ethanol Solution

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## Abstract

The overwhelming incidence, the frightening mortality, the economic burden and social life consequences of COVID-19 has put the human being on the edge of an unprecedented catastrophe. In spite of fully-featured pandemic and thorough knowledge regarding the SARS-COV-2 virology, epidemiology, pathogenesis and heterogeneous clinical course of the disease, nothing has been done so far with respect to a noticeable improvement in our treatment strategies, except fighting for face mask, gown and ventilator, of course. A pre-primitive particle, barely visible even through electron microscope, with a brain of only 29.0 kb, is about to demolish the entire life aspects of highly civilized mankind, pushing them down their chambers in panic and absolute despair. I understand a fellow virologist has named the virus an evil genius primordial life entity. He is right somehow, but I would suggest, confrontation with such an evil thing necessitates an inherent, intuitive and holistic approach. It sounds like we are hypnotized by dreadful spiky silhouette of the virus and become totally distracted from looking towards the weaknesses and fragilities that the virus might have. So far, we have been merely amused with those scanty surface proteins and the tiny genome of the virus. The extremely fragile and pathetically frail virus bilayer phospholipid envelope has been vaguely neglected. We have barely addressed the enormous influence of virus lipid coat on its infective capabilities. We have never thought that even a subtle effort that brings about some biophysical changes in virus lipid envelope may lead to a major achievement reducing the virulence of the bug, and taming the fire-spitting dragon, SARS-COV-2. Enjoying an unstable and ever changing genome, the coronavirus species have been playing hide and seek with us for so many years, and we are still showing renewed enthusiasm to develop enduring vaccine or monoclonal antibodies. It does look somehow eccentric indeed. And so is the fantasy concerning the whole bunch of feeble and failing antiviral agents, old and new. It is a nightmare coming true when we hear that the patients recovered from COVID-19 are still virus shedder and remain positive while retested for RT-PCR. Therefore, counting on convalescent plasma therapy might also be a minor chance if ever. Putting all together, we must look at the problem from an entirely opposite angle. We know beyond doubt that the entire herd of SARS-COV-2 is well within our reach inside the upper and lower respiratory tract. And, the time is tight hence, we are supposed to think about our currently available armaments and use them against the weakest structural aspect of the brand new coronavirus, SARS-COV-2. Based on strong unquestionable biophysical and biological data, I would like to suggest a safe and powerful remedy for COVID-19. Let's play the "Odysseus", and make use of a wooden "Trojan horse" to enter the SARS-COV-2 castle.

**Keywords:** COVID-19, Lipid envelope, Management, Dimethylsulfoxide, Ethanol, Aerosol

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## Introduction

Most viruses including coronavirus species are wrapped in a lipid bilayer called envelope, where the functionally important virus surface proteins are implanted. This lipid bilayer is largely made of phospholipids derived from hosting cell. The physicochemical characteristics of the viral lipid envelope not only help the virus to maintain its spherical structure but also play a pivotal role as a concrete foundation for its vital surface proteins [1]. Even trivial and hardly detectable changes in these ultra-structural properties would deeply affect the virus infectivity and virulence [2]. A matter of utmost importance is that, the lipid envelopes of these virus species are highly sensitive to desiccating chemical agents and lipid solvating substances. That is why the enveloped viruses are much easier to sterilize compared to non-enveloped viruses. Desiccation is the state of extreme dryness or the process exerting an extreme drying. A desiccant chemical is a hygroscopic substance that induces or sustains such a state (extreme dryness) in its vicinity. A hygroscopic substance is able to absorb water from its surroundings. Dimethylsulfoxide (DMSO), ethyl alcohol and ether are typical mediums of powerful hygroscopic and lipid solubilizing properties. Dimethylsulfoxide (DMSO) is known as an organic co-solvent used commercially for over forty years. DMSO is a powerful antioxidant frequently applied in wide range of antimicrobial studies and as a unique ingredient of topical medicaments to facilitate penetration of a drug to deeper compartments of the skin [3].

DMSO is an aprotic polarity solvent that effectively solubilizes a wide variety of organic and inorganic chemicals including lipids with an unquestionable safety profile even at high molar Concentration [4]. It looks as if, even smaller proportions of DMSO are still of drastic effect on inducing dehydration of the lipid membrane surfaces. DMSO desiccates and weakens the bio-membrane of cells and microorganisms lipid sheet. In a comprehensive and professionally designed biochemical study, regarding DMSO inducing dehydration near lipid membrane surfaces, C-Y. Cheng concludes that; DMSO "sprayed" on lipid surfaces, even at low molar concentrations induces profound dehydration of lipid membranes, leading to marked physicochemical changes. He states that physicochemical effects of DMSO on lipid surfaces are complex and significant at a broad range of DMSO concentrations [5]. He notifies that DMSO is not only clearly affects the lipid membranes, but also directly modulates the hydration water at the lipid membrane surfaces, imposing a strong hygroscopic effect, causing desiccation of lipid bilayers [4]. DMSO is known to interact with phospholipid bilayers as well. Molecular dynamics simulations of DMSO-dipalmitoylphosphatidylcholine systems demonstrate that DMSO modulates the mechanical properties of lipid bilayers, reducing both the area compressibility, thickness and bending moduli, hence making the lipid layer more floppy and affecting its stability and solidarity [6]. DMSO Causes significant changes on phospholipid bilayer of cultured skin fibroblast cells and disturbs the quality of membrane lipid matrix.

Numerous biophysical studies clearly demonstrate that DMSO can induce phospholipid bilayer thinning and creates pores through membrane lipid structures. These findings lend support

and shed light onto the facts behind antimicrobial and antiviral effects of DMSO. It has been shown that topical DMSO blocks lipid enveloped, ds DNA containing, herpes simplex virus transcription-replication process acting as a direct antiviral agent [7]. DMSO has been shown to potentiate the antiviral effects of all disinfectants. DMSO is among the low toxicity solvents expressing strong free radical scavenger activities. An impressive research work by researcher reveals that DMSO decreases cell proliferation and TNF- $\alpha$ , IFNs, and IL-2 production in cultures of peripheral blood lymphocytes. This study signifies the appreciable anti-inflammatory effects and cytokines storm preventing capabilities of DMSO [8].

A CDC guideline regarding chemical disinfectants states that "ethanol has generally been underrated as a potent virucidal agent inactivating and disinfecting all enveloped lipophilic viruses". The widely accepted explanation for virucidal action of ethyl alcohol is denaturation of viral proteins and bilayer phospholipid envelop. In a recent study published by G. Kampf, ethanol at 80% solution was highly effective killing all tested 21 enveloped viruses within only 30 seconds. Another report elucidates that ethyl alcohol disinfects the lipid coated viruses in no time, instantly, only in 10 seconds! Here is the critical question; "what really happens to lipid enveloped viruses to become inactive in such a short period of time?" [9]. Ten seconds is the time between only two blinks. The answer would be quite straightforward; the denaturation of viral lipid coat and displacement of surface proteins. The instantaneous desiccation and partially dissolved lipid layer terminates the infective abilities of the virus. To disinfect a virus, it is not necessary to smash it down to pieces [10]. A momentary desiccation of viral envelop is all we need. Desiccation of virus lipid layer would simply loosen the imbedded or implanted functional viral proteins inside the viral envelop. It would be a reasonable expectation that even low concentrations of a desiccating substance and a powerful lipid solvent, if used as a synergistic combined formulation, execute this desirable impact on enveloped viruses. Kampf specifies that the powerful antiviral effects of ethyl alcohol were not as remarkable in virus species lacking lipid bilayer coat.

## Literature Review

We all know that we are right in the middle of a historic battle against an all-out enemy, the SARS-COV-2. Although called a new corona virus but it is now well-known to all of us, warts and all. We understand that the virus spreads from one person to another, and almost always *via* respiratory droplets while talking, sneezing or coughing [11]. It is crystal clear that the virus introduces itself as an obsessed inhabitant of nasal cavity mucosa, throat, pharynx and eventually the lower respiratory tract epithelium and capillary endothelium, obviously being reluctant to go further beyond the alveoli. We have learned that the SARS-COV-2 has no noticeable desire to present overt viremia and high blood viral load, particularly as an intact and fully developed particle. SARS-COV-2 uses Angiotensin- Converting Enzyme (ACE) as the major binding site to enter the cells, and we know that upper and lower respiratory tract possess the highest concentrations of this protein. Thus, SARS- COV-2 is commonly regarded as a restricted inhabitant of our respiratory tract, an organ system within our

easy reach for aerosolized drug delivery [12]. Now you can tell what I mean!! It was mentioned earlier that, the corona virus, having a bilayer phospholipid envelop embracing all functional proteins, would be extremely vulnerable to lipid solvating and hygroscopic substances. Imagine the entire bunch of breeding bug being gathered on an open land, under your direct sight. I see that even a puff of aerosol composed of DMSO and ethanol would suffice to instantly cause a thrilling turmoil in the herd. I can understand that my proposal sounds too good to be true, but going through what I reviewed and reasoned might convince some of clinicians and researchers who fight at the front lines of this battle, desperately seeking out a faint beam of light finding their way through this absolute darkness [13]. We all feel totally disarmed regarding the current disaster, but it should not force us to test the measures which have been tested and failed over and over again. What I suggest is not a strange and unprecedented issue at all. Ethanol has been known to human being for more than a thousand year. It has been used for long as a potent disinfectant. Inhalation of 50% ethyl alcohol-water solution used to be a routine practice to treat acute pulmonary edema for years without any noticeable drawback, perhaps for its unique hygroscopic properties. Hence, the younger colleagues should feel comfortable in terms of ethyl alcohol aerosol inhalation, particularly at concentrations up to 50% [14].

Ethyl alcohol as a lipid solvent and unique virucidal agent and DMSO as a superb hygroscopic solution, lipid layer modulator and a smooth vehicle for better penetration of ethanol into the deeper epithelial and endothelial cells of respiratory system would help us to get access to the headstream of corona virus replication and infectivity. As mentioned earlier, DMSO acts as a potent free oxygen radical scavenger and inhibitor of cytokines release [15]. Hygroscopic properties (absorbing and dragging water and moist from surrounding environment leading to local dryness and desiccation) in addition to remarkable anti-inflammatory capabilities of DMSO (scavenging the hazardous free radicals and considerable capacity inhibiting cytokines generation) might break the vicious cycle of "cytokines storm" that cause ARDS and multiple-organ failure. Owing to simplicity of the therapeutic trial and absence of expected complication, a sagacious and thoughtful scientist would easily figure out that, in case of hypothesis failure, not much would have been lost [16]. We are already the loser in the battle with COVID-19, and we clearly know that we have played all of old, ragged cards and no miraculous aces to bring it out of our large sleeves [17]. There is not much uncertainty regarding potential untoward side effects concerning the mentioned substances. In terms of feasibility of this clinical trial, we have millions of desperate patients in absolute misery close at hands and all we need is a bottle of ethyl alcohol and a jar of DMSO and, a metered-dose inhaler for mild cases, or a nebulizer for critically ill patients [18].

## Discussion

The entire COVID-19 patients from terminally ill cases, asymptomatic individuals who tested positive, mild cases managed at home and even convalescents, who might be still virus shedder, could all be subjected to this clinical trial. Drug delivery to rhino-oral cavity and down the respiratory tract has

been known to humans for thousands of years to treat regional or systemic diseases [19]. Inhalation therapy allows us to use smaller doses of a particular medicine with much less side effects. Proper formulation of medicaments and the right delivery devices are essential for effective drug conveyance to the tracheobronchial tree and alveoli. Devices currently in use for this purpose are pressurized Metered-Dose Inhaler (MDI) and nebulizers [20]. The MDI would be perfect for out-patient subjects and nebulizers for in-patient critically ill individuals. Having enough experience and basic knowledge about the clinical picture of COVID-19, the suggested initial doses to be utilized could be one metered dose from 40% ethanol combined with 5% Dimethylsulfoxide (DMSO) solution. For researchers' information, the optimal concentration for topical DMSO applications is 5%-10%, but it might be used up to 50% without noticeable untoward effects. Considering the highly volatile nature of ethanol and to a lesser degree DMSO, we are logically allowed to repeat the same metered dose every hour for six hours. Whilst checking out any evidence of assumptive side effects, if clinical picture shows no vivid improvement, then we can double the dose that is, giving two puffs per hour. Observing any hint of amelioration in patient's general condition, we can switch to two puffs every other hour [21]. The therapeutic program could actually be more flexible depending on the severity of the disease and according to improving clinicians' experience to titrate the amount of constituents (DMSO and ethanol) in the aerosolized solution. In less galloping, milder cases with no threatening signs of extensive lung involvement, we can modify the drug delivery protocol to less frequent doses.

In case of unimpressive clinical results with highest applicable doses of sub ether and DMSO alcohol solution, we can fuel the formulation by adding sub-sedating doses of ether. It is known that hygroscopic and lipid modulating properties of ether is comparable to DMSO and ethyl alcohol. With regard to fetid smell of DMSO, if really annoying, adding some oral deodorants like mint herb and eucalyptus extract might do the trick. We are not expecting a full scale miracle, though it might, but all we need is to unsettle the virus environment and reduce the infectivity, virulence and the unleashed transmission of the bug. The least logical outcome of this simple, safe, inexpensive and practical intervention could be the deceleration of this overwhelming pandemic avalanche [22]. We plan to impose constant pressure on the virus *via* disturbing its simple replication milieu in upper and lower respiratory tract and disruption of the ongoing chain of transmission. We wish to be able to behave like an intruder to virus territory, the same as it intruded into our life. It would be enough to make the virus feels unease and unsafe for a period of time. We want the virus to go back to what it used to be, a simple common cold viral agent. We are now aware of the sole port of entrance into the virus fortress, its lipid envelope, and a sensible hint regarding the functioning key. Let's think about it. Let's put this simple measure to test.

## Conclusion

We hope that, inhalation of small but frequent doses of an aerosolized solution composed of Dimethylsulfoxide (DMSO) and ethanol would turn into a major breakthrough to help the human beings out of current health dilemma and the dire days. We pray

faithfully to almighty God to be merciful towards us sinners, and help us to overcome the current human health disaster.

## Conflict of Interest

Hereby I declare no conflict for any possible interest.

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