## Silver is A Broad Spectrum Anti-Viral

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Silver has been understood from antiquity to have anti-infective properties.<sup>i</sup> In our time various silver based preparations and formulations are commonly employed as wound dressings, as treatment for topical infections and for water purification. The anti-fungal,<sup>ii</sup> anti-protozoal<sup>iii</sup> and broad spectrum anti-bacterial properties<sup>iv</sup>,<sup>v</sup> of silver have been well-researched and documented in medical studies. Somewhat more recently the broad spectrum anti-viral activity of silver has become more widely recognized and documented. This review will examine the peer-reviewed medical literature relating to the anti-viral properties of silver with specific attention paid to anti-viral activity of silver against enveloped viruses and, in light of the recent COVID-19 viral pandemic, what studies may be available specifically concerning the activity of silver against coronaviruses.

Before beginning a brief note concerning terminology is appropriate. The majority of studies referenced, refer to the activity of "nano" particles of silver. Nanosilver is a somewhat nebulous term, but generally is seen to refer to silver particles with diameters in the 10-100 angstrom (nanometer) range or sometimes 1-100 angstroms. Such silver nanoparticles may be generated by a variety of chemical, biological and physical means, to include electrolysis. Particles of silver of sufficiently small diameter, nano particles, when placed in water will, due to Brownian motion and the repelling action of like charges, remain dispersed in solution for a long time to indefinitely. Such a solution is termed a colloidal solution of silver particles, (colloquially, "colloidal silver"). As silver, if unbound to other elements has a positive charge one also occasionally hears the term "ionic silver" employed.

In 1975 Chang et al.<sup>vi</sup>, documented *in-vitro* activity of silver sulfadiazine against Herpesvirus hominis virus, noting drug activity was proportional to duration of exposure and concentration of silver sulfadiazine. Herpesvirus is an enveloped DNA virus. Similarly, in 1999, Stozkowska<sup>vii</sup> and Wroczyńska-Pałka researched the activity of silver sulfathiazole against Herpes virus stating, *"This drug suppresses or completely inactivates the infectivity of virus. The antiviral effect is directly related to concentration of the drug and duration of exposure."* The researchers also noted a similar activity with silver nitrate while sulfathiozole alone, without silver, did not show anti-viral activity.

Human immunodeficiency virus (HIV), the well-known cause of AIDS, is an enveloped, RNA retrovirus virus. Viral cell entry is mediated by the interaction of a glycoprotein,

gp120, embedded in the viral membrane with the cluster of differentiation (CD4) receptor protein found on the surface of immune cells. In 2005, Elechiguerra et al. published, "Interaction of silver nanoparticles with HIV-1". viii Silver nanoparticles produced from three different approaches were found, *in-vitro*, to prevent cell entry of the HIV virus. The authors state, "For all three nanoparticle preparations, at silver concentrations above 25 µg/mL, viral infectivity was reduced to an extent that it could not be detected by syncytium formation". Through electron microscopy scanning studies the authors concluded that particles in the size range of 1 to 10 nanometers were binding to the virus and responsible for preventing viral cell entry. Further, the binding of the silver particles was not random but was selective for the protruding gp120 glycoproteins most likely in the area of dilsulfide bonds on this protein. The resulting steric hindrance from the attached silver prevented viral entry into the cell. While, as will be noted later, there appear to be additional mechanisms of anti-viral action mediated by silver, this research, in addition to documenting the absence of HIV viral cell entry, provides a plausible mechanism of action for how silver might block cell entry of enveloped viruses. COVID-19 is an enveloped virus whose cell entry is mediated, per early research, by interaction of the viral membrane spike glycoprotein with the Angiotensin II Converting Enzyme(ACE II) receptor protein.<sup>ix</sup>

Hepatitis B is a small double stranded, enveloped DNA virus. In 2009 Lu et al.<sup>x</sup> reported the results of *in-vitro* study examining the interaction of silver nanoparticles and the hepatitis virus. These silver particles were created chemically from silver nitrate and designed to have particle diameters of either approximately 10 nanometers or approximately 50 nanometers. The researchers found that both sizes of particles reduced extracellular virus formation by greater than 50%. While silver did not have an effect on intracellular viral DNA, it did inhibit the formation of viral RNA from this DNA template, a necessary step in infection. The authors conclude, "*Silver nanoparticles could inhibit the in vitro production of HBV RNA and extracellular virions. We hypothesize that the direct interaction between these nanoparticles and HBV double-stranded DNA or viral particles is responsible for their antiviral mechanism." As silver was found to inhibit formation of messenger RNA post viral infection, this would indicate a second possible mechanism of action of silver against viruses in addition to the blockage of viral cell entry, as the authors speculate, perhaps mediated by interaction of silver with viral DNA.* 

Human respiratory syncytial virus (RSV) is an enveloped RNA virus. In 2008 Sun et al<sup>xi</sup> reported results of in vitro research finding that PVP coated silver nanoparticles at low concentrations inhibited RSV infection by 44%. Monkeypox virus is an enveloped RNA virus within the orpthopox virus genus. While the virus generally infects animals it may cause zoonotic infections in humans leading to a disease somewhat similar in

presentation and course to smallpox. Rogers et al. reported results on research examining inhibition of monkeypox viral plaque formation from exposure to silver nanoparticles<sup>xii</sup>. Nano particles created from plasma gas synthesis and polysaccharide-coated silver nanoparticles in ranges from 10 to 100 nanometers were examined at dosages ranging from 25 - 200 ug/ml. No concentration of nanosilver exhibited cytotoxicity at the dosages examined. Silver nanoparticles of 55 nanometers and polsaccharide coated silver particles of 25 nanometers demonstrated a statistically significant dose dependent decrease in viral plaque formation. Other particle sizes did not lead to statistical significance with some sizes and dosages leading to non-significant increases in plaque formation.

Following the earlier work of Chang and Stozkowska, Baram-Pinto et al.<sup>xiii</sup> created silver nanoparticles capped with mercaptoethane sulfonate and studied their effect on Herpes simplex virus. These silver nanoparticles led to the blockage of viral entry into cells and "*prevention of subsequent infection*". Mercaptoethane sulfonate alone showed no anti-viral activity. Vijayakumar and Prasad reported on results of creation of silver nanoparticles embedded in a carbonaceous matrix<sup>xiv</sup> "*This carbonaceous matrix embedded silver nanoparticles showed antimicrobial properties against both bacteria (Gram-positive and Gram-negative) and virus (M 13 phage virus). The bactericidal effects were noticed even after washing and repeated exposure of these carbon supported silver nanoparticles to fresh bacterial cultures, revealing their sustained activity*". Similarly, De Gusseme et al.<sup>xv</sup> created silver nanoparticles in the 0.9-11.2 nanometer range. This nanosilver when applied to a carbon filter led to a 3.8 log reduction in water with murine (mouse) norovirus. The authors conclude, "*This is* 

the first report to demonstrate the antiviral efficacy of extracellular biogenic  $Ag^0$  and its promising opportunities for continuous water disinfection".

Arenaviruses are a family of non-enveloped RNA viruses responsible for a variety of serious viral hemorrhagic fevers. Speshock et al<sup>xvi</sup> examined the interaction of silver nanoparticles with the Tacribe, arenavirus. Silver did not inhibit viral entry into Vero cells grown in culture for these non-enveloped viruses. However, silver nanoparticles in the size range of 25-50 nanometers "dramatically reduced" viral RNA expression leading to a significant reduction in progeny virus. The authors conclude, "Silver nanoparticles are capable of inhibiting a prototype arenavirus at non-toxic concentrations and effectively inhibit arenavirus replication when administered prior to viral infection or early after initial virus exposure".

Silver has been examined by multiple researchers for its effect on influenza virus. Mehrbod et al<sup>xvii</sup> reported nanosilver inhibited viral entry of this enveloped virus. Xiang et al<sup>xviii</sup> reported that silver nanoparticles in the 10 nm range inhibited influenza A as evidenced through a variety of assays. For instance, the hemagllutination assay is a commonly employed method for quantifying the concentration of influenza virus. The authors state, "*In the presence of silver-nps, the ability of H1N1 influenza A virus to agglutinate erythrocytes was either reduced or completely inhibited*". Mori et al.<sup>xix</sup> created silver nanoparticles complexed with chitosan (lobster shell) with particles sizes ranging from 3.5 to 12.9 nanometers. All sizes of particles exhibited a dose dependent inhibition of influenza A, while chitosan alone demonstrated no anti-viral activity.

Since 2013 research on the antiviral properties of nanosilver has increased greatly. Adenoviruses are non-enveloped DNA viruses that are a frequent cause of the common cold. Chen et al<sup>xx</sup> report a dose dependent decrease in adenovirus type 3 viral DNA in cultures treated with nanosilver, concluding, *"the present study indicates silver nanoparticles exhibit remarkably inhibitory effects on Ad3 in vitro"*.

Vaccinia virus, a large enveloped DNA virus closely related to Smallpox virus, has been well studied as the viral agent responsible for the eradication of smallpox disease through vaccination. Trefry et al.<sup>xxi</sup> report that 25-nm silver nanoparticles inhibited viral entry into cells, "*The silver nanoparticles caused a 4- to 5-log reduction in viral titer at concentrations that were not toxic to cells. Virus was capable of adsorbing to cells but could not enter cells in the presence of silver nanoparticles"*.

Xiang et al.<sup>xxii</sup> reported results on research into silver nanoparticles and human H3N2 influenza virus. The unconjugated nanosilver was created chemically through an oxidation-reduction reaction of silver nitrate with sodium carbonate and tannic acid. No information is provided on the resulting silver particle sizes. At dosages from 6.25 to 50 ug/ml there was no observed cytotoxicity to the examined cell lines. Silver nanoparticles were shown to decrease to a statistically significant degree growth of influenza virus as indicated by the hemagglutination assay and likewise to decrease cell apoptosis (death). Electron microscopy studies found destruction of morphological viral structures through interaction with silver particles starting from 30 to 120 minutes post exposure. This study is also notable for the report of animal *in-vivo* results. Mice inoculated intranasally with nanosilver demonstrated significantly enhanced survival after exposure to H3N2 influenza virus, specifically none of the control group mice survived while 75% of those inoculated with nanosilver intranasally survived. Treated mice also showed *"lower lung viral titer levels and minor pathologic lesions in lung tissue"*.

Gaikwad et al.<sup>xxiii</sup> reported on *in-vitro* results of nanosilver's effects against Herpes simplex virus types I and II and Human Parainfluenza virus type 3. Nanoparticles in this instance were produced from a fungus based approach. Average particle size was

estimated to vary from 20 to 50 nanometers. The Vero cell assay was used to determine cytotoxicity of silver to cells. Antiviral activity was measured at concentrations ranging from 0.1, to 10 µg/mL by observing the number of viral plaques in Vero cell monolayers as compared to controls. Cell cytotoxicity was not observed at the concentrations evaluated. Treatment showed a consistent decrease in replication efficiency for Herpes simplex type I and Parainfluenza virus and a minor effect on Herpes simplex type II virus. Interestingly, the particular fungal species used in preparing the nanosilver had a considerable effect on anti-viral activity. The authors speculate that the differences may be due to variations in particles size and/or zeta potential (charge) from samples prepared from different fungi. They write, "From the present study it was observed that AgNPs were capable of controlling viral infectivity, most likely by blocking interaction of the virus with the cell, which might be dependent on the size and zeta potential of the AgNPs".

Moving on to 2014, the following study, "Inhibitory effect of silver nanomaterials on transmissible virus-induced host cell infections" by Lv et al. xxiv is notable in the present context. The authors state that, "transmissible gastroenteritis virus (TGEV) is an economically significant coronavirus that can cause severe diarrhea in pigs". The authors note that human corona viral infections including the recent MERS and SARS outbreaks are a public health concern and so the researchers chose TGEV Coronavirus as a model for human Coronavirus infection. Four types of silver nanoparticles were examined to include silver nanowires of 60 and 400 nanometers and silver nanoparticles of 10 and 20 nanometers. Swine testicle (ST) cells were cultured in Dulbecco's modified Eagle's medium and cell viability determined using the "MTT" assay. PCR, Western Blot, immunofluorescence and flow cytometry assays were also performed. The silver nanowires and 20 nm nanosilver particles decreased cell apoptosis (death) from corona virus infection. The MMT assay demonstrated that these three silver formulations also led to a dose dependent reduction in viral titers. Interestingly, the 10 nm silver particles did not show an anti-viral effect. However the Polyvinylpyrrolidone capping agent used as a stabilizer was 4 fold higher in the 10 nm silver particles as compared with the 20 nanometer particles and the authors speculate this may have had an effect on the anti-viral activity as compared with the other three silver formulations. Through further research the authors find that one plausible mechanism of action for silver's anti-viral activity in this study was from interaction with the p38/mitochondriacaspase-3 signaling pathway which plays a role in mediation of cell apoptosis.

The authors conclude from their research, "Our data indicate that Ag NMs are effective in prevention of TGEV-mediated cell infection as a virucidal agent or as an inhibitor of viral entry".

Hu et al.<sup>xxv</sup> confirmed the anti-viral activity of silver nanoparticles against Herpes simplex virus type II as evaluated through plaque formation assay and MMT assay stating, "*Therefore, 100*  $\mu$ g/mL Ag-NPs could completely inhibit HSV-2 replication. Ag-NPs at nontoxic concentrations were capable of inhibiting HSV-2 replication when administered prior to viral infection or soon after initial virus exposure."

Khandelwal et al.<sup>xxvi</sup> demonstrated that silver nanoparticles derived from silver nitrate and with a size range of 5-30 nanometers at a nontoxic concentration inhibited replication of a Morbillivirus that may afflict livestock. Orlowski et al.<sup>xxvii</sup> reported that tannic acid modified silver nanoparticles in the size range of 13 to 46 nanometers inhibited Herpes simplex type II viral infection *in-vitro* and *in-vivo* in mice. Closing out 2014, Swathy et al<sup>xxviii</sup> published research on a surprising synergism between silver nanoparticles and carbonate ions. The researchers, "*discovered that 50 parts per billion* (*ppb*) of Ag(+) released continuously from silver nanoparticles confined in nanoscale cages is enough to cause antimicrobial activity in conditions of normal water." By way of context, sodium fluoride is often added to water supplies at a level of 1-2 parts per million, so this is a concentration of silver some 1/20th to 1/40th that of added fluoride. The authors go on to state, "the antibacterial and antiviral activities of Ag(+) can be enhanced ~1,000 fold, selectively, in presence of carbonate ions " While not discussed by the authors baking soda is an extremely inexpensive source of carbonate ions.

Sujitha et al.<sup>xxix</sup> 2015 reported success in controlling Dengue fever viral infection *in*vitro with silver nanoparticles. Treatment with 20ug/ml silver nanoparticles led to a greater than 4 log reduction in viral titers after six hours. "AgNP were highly effective against the dengue vector A. aegypti". Elbeshehy et al<sup>xxx</sup> report that silver nanoparticles in the size range of 72-92 nanometers show activity against Bean Yellow Mosaic Virus. Fatima et al<sup>xxxi</sup> report in 2106 that silver nanoparticles created using Cinnamomum cassia as a reducing agent effectively and non-toxically inhibited H7N3 Influenza A virus infection of a cultured Vero cell line. Somewhat similarly, Yang et al.xxxii also report in 2106 that silver nanoparticles using curcumin as a reducing agent showed a, "highly efficient inhibition effect against respiratory syncytial virus (RSV) infection, giving a decrease of viral titers about two orders of magnitude ... no toxicity was found to the host cells". Bekele et al<sup>xxxiii</sup> examined the activity of silver nanoparticles of 10, 75, and 110 nanometers against feline calicivirus. At dosages of 50 and 100 ug/ml the 10 nanometer particles, "inactivated the FCV (feline calicivirus) beyond the limit of detection". The larger 75 and 110 nanometer particles did not show anti-viral activity. Borrego et al.<sup>xxxiv</sup> report that a proprietary formulation of silver nanoparticles was effective in preventing Rift Valley fever viral infection of a Vero cell line.

Also in 2016 Chen et al.<sup>xxxv</sup> created silver nanoparticle impregnated graphene oxide sheets. This material was tested for activity against infectious bursal disease virus and feline coronavirus (FcoV). The silver impregnated sheets reduced viral infection by feline coronavirus by 25% as compared to 16% for graphene oxide alone. While certainly not a dramatic result this is a second confirmatory study that silver has anti-viral activity against viruses of the corona virus family.

Another interesting study from 2016 was published by Li et al.<sup>xxxvi</sup>. The researchers describe "decorating" the surface of the antiviral drug oseltamivir (Tamiflu) with silver nanoparticles and comparing the *in-vitro* efficacy of this combination to silver alone and oseltamivir alone for ability to inhibit H1N1 influenza. Quoting the researchers, "Compared to silver and oseltamivir, oseltamivir-modified AgNPs (Ag@OTV) have remarkable inhibition against H1N1 infection, and less toxicity was found for MDCK cells by controlled-potential electrolysis (CPE), MTT, and transmission electron microscopy (TEM). Furthermore, Ag@OTV inhibited the activity of neuraminidase (NA) and hemagglutinin (HA) and then prevented the attachment of the H1N1 influenza virus to host cells." This finding is significant in that oseltamivir is one of the drugs currently being researched and utilized as a possibly useful treatment for COVID-19 infection. In this study regarding influenza virus, silver was seen to have a synergistic effect with oseltamivir.

While there are further positive studies of anti-viral activity from 2017 to the present, due to constraints of time the literature review will be truncated here. It is trusted that to a reasonable reader the above suffices to convincingly make the case that silver is a potent and broad spectrum anti-viral. It should also be noted that by no means have these studies been "cherry picked". While there are some studies with less dramatic findings, some studies where some of the particular dosages, particle sizes or formulations in a given study were not effective, in this literature review I have not seen a single article reporting absence of anti-viral activity against any virus that was researched.

The above research was almost uniformly *in-vitro* (test-tube) studies, it is unfortunate that more *in-vivo* data is not available at this time for this very promising anti-viral. Further, many issues relating to the *in-vitro* studies, how do we prevent the silver from clumping in the growth media we are using, for instance, are not at all directly applicable to the *in-vivo* system, where the question would instead by what is the behavior of nanosilver in the albumin rich milieu of blood plasma.

There are literally dozens of approaches to generating nanosilver with one recent article reviewing a number of physical, chemical and biologically oriented approaches<sup>xxxvii</sup>. One means of generating nanosilver has been conspicuously absent from the studies

published in the literature to date, namely the way the great scientist and experimenter, Michael Faraday first created colloidal metals nearly two hundred years ago, through electrolysis. This approach is not at all complicated, for instance to create colloidal silver one would start with two wires or strips of 99.9% pure silver. One silver wire is connected to the positive of a DC voltage source, say a nine volt battery, the other wire to the negative of the battery. The two wires, and only the wires, are placed in water separated by a distance of 1/8th to one half inch to allow the water to act as a resistor. Over the course of a few minutes a cloud of microscopic silver is seen to appear in the water. Over time this silver would eventually electroplate on the negative electrode, however, due to the like positive charges on the small silver particles, and the Brownian motion of water, the majority of the silver stays in solution as a colloid. If one has a total dissolved solids meter, costing perhaps 20 dollars, one can document the concentration in parts per million of colloidal silver as the process proceeds. If one starts with tap water with 200 ppm dissolved minerals and impurities when one reads 220 ppm dissolved solids one knows one has 20 ppm silver in that water. In a pinch, if one has two 99.9% pure silver dollars, one could also use those to create colloidal silver following the same procedure. Two silver wires weighing only a few grams and costing a few dollars could produce literally tens of gallons of colloidal silver before themselves being dissolved through electrolysis. This treatment would cost pennies per day.

When one sees a slight cloudy white tinge to tap water, this is generally a concentration in the range of 10-40 ppm. Hence, even if one does not have a dissolved parts meter one can eyeball a reasonable concentration by observing a very slight cloudy tinge to the water. If, as will be discussed further, one uses distilled water one will see a slight cloudy yellow tinge to the water instead of whitish, again consistent with a 10-40 ppm concentration.

Peter Lindemann, PhD, has published non peer-reviewed results of characterization of silver particles produced through electrolysis.<sup>xxxviii</sup> By electron microscopy characterization, low voltage electrolysis of silver in tap water is reported as generating particles in the size range of 50 to 150 nanometers. While on the large size of those particles showing efficacy in the previously reviewed literature, this is within the size range of particles that showed anti-viral activity in some studies. Silver generated by electrolysis in distilled water was found to have a particle size of around 4 nanometers. This smaller particle size, secondary to the Tyndall effect shows a yellowish tinge, reflective of the small particle size. As smaller particle sizes were generally associated with greater antiviral activity in the above review, I concur with Dr. Lindemann's position that ideally one might wish to create colloidal silver with distilled water. There is a caveat to that position however, which again refers to use of silver i*n-vivo*. Unfortunately, the pharmacodynamics and pharmacokinetics of nanosilver are for the

most part uncharacterized in peer-reviewed literature at this time. Nonetheless, one point is fairly obvious. About the first thing colloidal silver taken by mouth will encounter is stomach acid. Stomach acid is primarily hydrochloric acid. Silver dissolves in hydrochloric acid. Hence, while colloidal silver created with tap water has a slightly larger particle size than one might wish when considering the previous literature, it would seem a fairly safe bet that due to the activity of hydrochloric acid on silver, the particle sizes reaching the blood stream would comprise a range consisting of particles smaller than those ingested. More simply, I would say, do not despair about making useful anti-viral colloidal silver if one doesn't have distilled water. While it would be nice to have distilled water, clinically the two approaches may likely yield similar results. I would further recommend Dr. Lindemann's write-up on this topic as a useful guide to creating colloidal silver. Again, however, do not be intimidated, one doesn't have to "overthink" this. Take two strips of pure silver connect them to a nine volt battery stick the strips (not touching each other) in a glass of water. Make sure only silver is in the water as one is not trying to create colloidal alligator clip. In 2-5 minutes or so with tap water one will see a slightly cloudy tinge, one is done. If using distilled water at nine volts this will take 1-2 hours and one will see a slight yellowish tinge. Dr. Lindemann mentions using, I believe, a tablespoon or two of 10-20 ppm colloidal silver, I am perhaps a bit more radical as every couple weeks I brew up 8 ounces of 10-20 ppm colloidal silver made from twice filtered tap water and gulp it down, it is some of the best tasting water you will come across. I also make a second glass and pour it through a carbon (Britta) water filter and use that filter for my drinking water for the next two weeks.

Colloidal silver, made from a variety of means has been used as a health tonic by hundreds of thousands of people by this time. The primary, and only that I am aware of, concerning health side effect reported from this usage appears to be a very rare occurrence of bluish skin discoloration known as argyria. While it is arguable, whether argyria is seen only with ingestion of silver salts such as silver nitrate or also with prolonged use of colloidal silver, yes, if one drank gallons of 100 ppm colloidal silver for years and never looked in a mirror, one might theoretically find a serious problem with skin discoloration. This side effect might be compared with the, still widely used antibiotic, gentamicin, which causes a rare, acute, sometimes irreversible hearing loss. Further, some commonsense is in order, two strips of wire weighing a few grams will suffice to make tens if not hundreds of gallons of colloidal silver before themselves fully dissolving. This is not at all like a child munching down chips of lead based paint, this is a very, very small amount of silver, likely a dose orders of magnitude less than the 50 mg of elemental zinc one might take, and correctly so, as a supplement without a second thought. In addition to a reasonable safety profile established through years of use by at minimum hundreds of thousands of people, there are numerous testimonies of health benefits, sometimes dramatic, from individuals using colloidal silver made electrolytically from tap water and possibly distilled water as well. I will not delve into this literature as there are I realize some readers who might find the presentation lessened if evidence is expanded outside of the peer-reviewed literature. I would just pose as a philosophical question, if one can identify the identity of an individual patient and has no reason to suspect a financial or other bias to their reporting, should the patient's description of their own symptomatology and disease course be considered more or less authoritative than the second hand case report written up by their physician in a medical journal? As a corollary, who would be expected to more often have a financial or emotional bias to distort results of a health intervention, a patient or a health practitioner? These are questions far outside the scope of this write-up except to note that the evidence presented has been solely from the peer-reviewed medical literature to keep from turning away those purists who feel strongly that this is all that should be taken into consideration.

Lastly, in addition to taking colloidal silver internally, if one knew they were not going to be able to wash their hands with soap and water for a time, applying colloidal silver water topically might help to prevent spread of disease in the same way that silver impregnated wound dressings are used as anti-infectives for difficult to treat wounds. One might also consider making a concentrated glass of colloidal silver and pouring it into the end of a wash cycle for laundry, or simply soaking laundry in colloidal silver before drying, so as to have silver impregnated clothing. The literature for silver as an effective antibacterial against both gram positive and negative bacteria is more voluminous than what has been presented here for its' anti-viral activity. It bears noting that what often is fatal for someone acquiring a viral pneumonia is the injured lungs developing a superseding bacterial infection which the patient in a weakened condition is unable to fight off.

In summary, silver is well-documented in the peer reviewed medical literature to be a broad spectrum anti-viral, silver is also a broad spectrum anti-bacterial. Two *in-vitro* studies have documented activity of silver against animal corona viruses. In the current context of COVID-19 spread it is urgent and imperative that health researchers and authorities examine the *in-vitro* and *in-vivo* activity of silver against this novel corona virus. One reasonable mechanism of action by which silver interferes with viral entry is by binding to the thiol residue disulfide bridges of surface glycoproteins of enveloped viruses as documented in the literature. Silver has demonstrated highly selective viral toxicity *in-vitro*. Colloidal silver, used appropriately and reasonably, has a track record of years of safe use. Colloidal silver with particle sizes identical to those showing

activity in the medical litrature may be generated cheaply and easily through electrolysis.

One should not provide a false hope, one is also and perhaps more culpable, for failing to disclose a reasonable hope. Colloidal silver may or may not be effective against COVID-19, those studies need to be performed, the above provides a reasonable hope that it could be effective. Hospitals overwhelmed with viral illness will be hard pressed to provide appropriate care to all but the most ill, while someone with a common cold who goes to a hospital to be tested for COVID-19 runs a very high risk of now being infected with this highly contagious bug even if they weren't before they visited the hospital. Colloidal silver has a track record of safe use, costs a couple cents or less for per eight ounce glass, and can be made in a few minutes with a nine volt battery and a couple strips of 99.9% pure silver. Perhaps the most appropriate question one might ask is, what have you got to lose?

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- i Alexander JW. History of the medical use of silver. Surg Infect (Larchmt). 2009 Jun;10(3):289-92.
- ii Burduşel AC, Gherasim O, Grumezescu AM, Mogoantă L, Ficai A, Andronescu E. Biomedical Applications of Silver Nanoparticles: An Up-to-Date Overview. Nanomaterials (Basel). 2018 Aug 31;8(9)
- iii Rai M, Kon K, Ingle A, Duran N, Galdiero S, Galdiero M. Broad-spectrum bioactivities of silver nanoparticles: the emerging trends and future prospects.

Appl Microbiol Biotechnol. 2014 Mar;98(5):1951-61.

- Sánchez-López E, Gomes D, Esteruelas G, Bonilla L, Lopez-Machado AL, Galindo iv R, Cano A, Espina M, Ettcheto M, Camins A, Silva AM, Durazzo A, Santini A,
- Garcia ML, Souto EB. Metal-Based Nanoparticles as Antimicrobial Agents: An Overview. Nanomaterials (Basel). 2020 Feb 9;10(2)
- Franci G, Falanga A, Galdiero S, Palomba L, Rai M, Morelli G, Galdiero M. v Silver nanoparticles as potential antibacterial agents. Molecules. 2015 May 18;20(5):8856-74.

vi Chang T-W, Weinstein L. In vitro activity of silver sulfadiazine against Herpesvirus hominis. J Infect Dis. 1975 Jul;132(1):79-81.

vii Stozkowska W, Wroczyńska-Pałka M. [Studies on the antiviral activity of silver sulfathiazole]. Med Dosw Mikrobiol. 1999;51(1-2):167-74. Polish. PubMed PMID: 10865442.

viii Elechiguerra JL, Burt JL, Morones JR, Camacho-Bragado A, Gao X, Lara HH, Yacaman MJ. Interaction of silver nanoparticles with HIV-1. J Nanobiotechnology. 2005 Jun 29;3:6

Hoffmann M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, Erichsen S, ix Schiergens TS, Herrler G, Wu NH, Nitsche A, Müller MA, Drosten C, Pöhlmann S. SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinicallv

Proven Protease Inhibitor. Cell. 2020 Mar 4.

Lu L, Sun RW, Chen R, Hui CK, Ho CM, Luk JM, Lau GK, Che CM. Silver Х nanoparticles inhibit hepatitis B virus replication. Antivir Ther. 2008;13(2):253-62.

xi Sun et al. Silver Nanoparticles Inhibit Replication of Respiratory Syncytial Virus. Journal of Biomedical Nanotechnology 4(2):149-158 · June 2008

xii Rogers, J.V., Parkinson, C.V., Choi, Y.W. et al. A Preliminary Assessment of Silver Nanoparticle Inhibition of Monkeypox Virus Plaque Formation. Nanoscale Res Lett 3, 129 (2008)

Baram-Pinto D, Shukla S, Perkas N, Gedanken A, Sarid R. Inhibition of herpes xiii simplex virus type 1 infection by silver nanoparticles capped with mercaptoethane sulfonate. Bioconjug Chem. 2009 Aug 19;20(8):1497-502. doi: 10.1021/bc900215b. Epub 2009 Jul 8. xiv Vijayakumar PS, Prasad BL. Intracellular biogenic silver nanoparticles for the

generation of carbon supported antiviral and sustained bactericidal agents. Langmuir. 2009 Oct 6;25(19):11741-7

- xv De Gusseme B, Sintubin L, Baert L, Thibo E, Hennebel T, Vermeulen G, Uyttendaele M, Verstraete W, Boon N. Biogenic silver for disinfection of water
  - contaminated with viruses. Appl Environ Microbiol. 2010 Feb;76(4):1082-7
- xvi Speshock JL, Murdock RC, Braydich-Stolle LK, Schrand AM, Hussain SM. Interaction of silver nanoparticles with Tacaribe virus. J Nanobiotechnology. 2010 Aug 18;8:19

xvii Mehrbod P., Motamed N., Tabatabaian M., Soleimani Estyar R Amini E., Shahidi M., Kheiri M.T. In Vitro Antiviral Effect of "Nanosilver" on Influenza Virus. DARU Vol 17, No. 2 2009

xix Mori Y, Ono T, Miyahira Y, Nguyen VQ, Matsui T, Ishihara M. Antiviral activity of silver nanoparticle/chitosan composites against H1N1 influenza A virus. Nanoscale Res Lett. 2013 Feb 20;8(1):93. doi: 10.1186/1556-276X-8-93.

xx Chen N, Zheng Y, Yin J, Li X, Zheng C. Inhibitory effects of silver nanoparticles against adenovirus type 3 in vitro. J Virol Methods. 2013 Nov;193(2):470-7.

xxi Trefry JC, Wooley DP. Silver nanoparticles inhibit vaccinia virus infection
by
preventing viral entry through a macropinocytosis-dependent mechanism. J

Biomed

Nanotechnol. 2013 Sep;9(9):1624-35.

xxii Xiang D, Zheng Y, Duan W, Li X, Yin J, Shigdar S, O'Connor ML, Marappan M, Zhao X, Miao Y, Xiang B, Zheng C. Inhibition of A/Human/Hubei/3/2005 (H3N2) influenza virus infection by silver nanoparticles in vitro and in vivo. Int J Nanomedicine. 2013;8:4103-13

xxiii Gaikwad S, Ingle A, Gade A, Rai M, Falanga A, Incoronato N, Russo L, Galdiero S, Galdiero M. Antiviral activity of mycosynthesized silver nanoparticles against herpes simplex virus and human parainfluenza virus type 3. Int J

Nanomedicine. 2013;8:4303-14. doi: 10.2147/IJN.S50070. Epub 2013 Nov 6.

xxiv Lv X, Wang P, Bai R, Cong Y, Suo S, Ren X, Chen C. Inhibitory effect of silver nanomaterials on transmissible virus-induced host cell infections. Biomaterials.

2014 Apr;35(13):4195-203. doi: 10.1016/j.biomaterials.2014.01.054. Epub 2014 Feb 10.

xxv Hu RL, Li SR, Kong FJ, Hou RJ, Guan XL, Guo F. Inhibition effect of silver nanoparticles on herpes simplex virus 2. Genet Mol Res. 2014 Mar 19;13(3):7022-8. doi: 10.4238/2014.March.19.2.

xxvi Khandelwal N, Kaur G, Chaubey KK, Singh P, Sharma S, Tiwari A, Singh SV, Kumar N. Silver nanoparticles impair Peste des petits ruminants virus replication. Virus Res. 2014 Sep 22;190:1-7. doi: 10.1016/j.virusres.2014.06.011. Epub 2014 Jun 28.

xxvii Orlowski P, Tomaszewska E, Gniadek M, Baska P, Nowakowska J, Sokolowska J, Nowak Z, Donten M, Celichowski G, Grobelny J, Krzyzowska M. Tannic acid modified silver nanoparticles show antiviral activity in herpes simplex virus type 2 infection. PLoS One. 2014 Aug 12;9(8):e104113.

xxviii Swathy JR, Sankar MU, Chaudhary A, Aigal S, Anshup, Pradeep T. Antimicrobial silver: an unprecedented anion effect. Sci Rep. 2014 Nov 24;4:7161.

xxix Sujitha V, Murugan K, Paulpandi M, Panneerselvam C, Suresh U, Roni M, Nicoletti M, Higuchi A, Madhiyazhagan P, Subramaniam J, Dinesh D, Vadivalagan C, Chandramohan B, Alarfaj AA, Munusamy MA, Barnard DR, Benelli G. Greensynthesized silver nanoparticles as a novel control tool against dengue virus (DEN-2) and its primary vector Aedes aegypti. Parasitol Res. 2015 Sep;114(9):3315-25.

xxx Elbeshehy EK, Elazzazy AM, Aggelis G. Silver nanoparticles synthesis mediated by new isolates of Bacillus spp., nanoparticle characterization and their activity against Bean Yellow Mosaic Virus and human pathogens. Front Microbiol. 2015 May 13;6:453

xxxi Fatima M, Zaidi NU, Amraiz D, Afzal F. In Vitro Antiviral Activity of Cinnamomum cassia and Its Nanoparticles Against H7N3 Influenza A Virus. J Microbiol Biotechnol. 2016 Jan;26(1):151-9

xxxii Yang XX, Li CM, Huang CZ. Curcumin modified silver nanoparticles for highly

efficient inhibition of respiratory syncytial virus infection. Nanoscale. 2016 Feb 7;8(5):3040-8.

xxxiii Bekele AZ, Gokulan K, Williams KM, Khare S. Dose and Size-Dependent Antiviral Effects of Silver Nanoparticles on Feline Calicivirus, a Human Norovirus Surrogate. Foodborne Pathog Dis. 2016 May;13(5):239-44.

xxxiv Borrego B, Lorenzo G, Mota-Morales JD, Almanza-Reyes H, Mateos F, López-Gil E,de la Losa N, Burmistrov VA, Pestryakov AN, Brun A, Bogdanchikova N. Potential application of silver nanoparticles to control the infectivity of Rift Valley fever virus in vitro and in vivo. Nanomedicine. 2016 Jul;12(5):1185-92.

xxxv Chen YN, Hsueh YH, Hsieh CT, Tzou DY, Chang PL. Antiviral Activity of Graphene-Silver Nanocomposites against Non-Enveloped and Enveloped Viruses. Int J

Environ Res Public Health. 2016 Apr 19;13(4):430.

- xxxvi Li Y, Lin Z, Zhao M, Xu T, Wang C, Hua L, Wang H, Xia H, Zhu B. Silver Nanoparticle Based Codelivery of Oseltamivir to Inhibit the Activity of the
- H1N1 Influenza Virus through ROS-Mediated Signaling Pathways. ACS Appl Mater Interfaces. 2016 Sep 21;8(37):24385-93
- xxxvii Wei L, Lu J, Xu H, Patel A, Chen ZS, Chen G. Silver nanoparticles: synthesis, properties, and therapeutic applications. Drug Discov Today. 2015 May;20(5):595-601.

xxxviii Colloidal Silver: "A Closer Look" By Peter A. Lindemann, <u>https://www.elixa.com/colloidal-silver-a-closer-look/</u> accessed 3/21/2020