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Letter to Editor

Could curcumin modified silver nanoparticles treat COVID-19?

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Dear Editor,

Silver nanoparticles (AgNPs) have been widely used for diagnostic and therapeutic applications in the treatment of wound healing, arthritic as well as infectious diseases. The size of silver nanoparticles are extremely small ranged from 1 nm to 100 nm which provides a large surface area to enhance their solubility, chemical stability, and catalytic activity for its functions.[1] Anti-viral and anti-bacterial are the two common properties of silver nanoparticles. These are attracted lots of scientist's investigation for a long time.

AgNPs have an anti-viral potential because it's against many types of viruses including human immunodeficiency virus, hepatitis B virus, herpes simplex virus, monkeypox virus, and respiratory syncytial virus.[2] In 2008, Sun L et al. reported that the respiratory syncytial virus is inhibited by silver nanoparticles capped with the poly(N-vinyl-2-pyrrolidone) (PVP), bovine serum albumin (BSA), and a recombinant F protein from RSV (RF 412). AgNPs bind to the viral surface, block the interaction with G-protein, and distribute on the viral envelope to suppress its combination. AgNPs have less than 20% cytotoxicity for a concentration of 100 μg/mL to inhibit the virus infection.[3]

There is similar research from Morris D et al. proved that AgNPs exist of anti-viral and immunomodulatory activities in respiratory syncytial virus (RSV) infection of mice. It inhibits

the virus replication and decreases the level of pro-inflammatory cytokines (i.e., IL-1α, IL-6, TNF-α) and pro-inflammatory chemokines (i.e., CCL2, CCL3, CCL5). The number of neutrophil increases and re-activates in the lung tissue. This is non-toxic when silver nanoparticles size within 12 nm and dose below 50 micrograms/mL.[4]

Besides, AgNPs also have anti-bacterial potential as it prevents the respiratory virus infection such as methicillin-resistant *Staphylococcus aureus* (MRSA). Ip M et al. identified that silver ions release in the wound dressings from the AgNPs. These interact with the thiol groups of enzymes and proteins of bacteria lead to affect cell respiration and kills the virus. It's inhibited by the 1 μg/mL of silver ions only.[5] Another study from Duncan et al. demonstrated that the antibacterial activity of AgNPs in Gram-positive and Gram-negative bacteria. The AgNPs anchor on the bacterial cell undergo lysis and release the silver ion into the cytoplasm to inhibit an electron transport chain in the cell; inactivate the bacterial protein synthesis; inhibit the DNA replication; activate the generation of reactive oxygen species (ROS) to destroy the membrane protein making the bacterial cell death.[6]

Recently, Zachar O et al. reported that AgNPs are effective to suppress viral and bacterial respiratory infections in a minimal inhibitory concentration (MIC) for the prevention and treatment of COVID-19. The concentration of AgNPs colloids are around 10 μg/mL and the particle sizes between 3 nm to 7 nm. However, these formulations only investigate at the early stages for COVID-19. It's required to work more before going on to the next stages.[7] Basically, the pathogenesis of COVID-19 is caused by a SARS-CoV-2 virus. It binds to epithelial cells in the nasal cavity and replication in the angiotensin-converting enzyme 2 (ACE-2) receptor. The SARS-CoV-2 virus migrates down the respiratory tract, infection the airway, and trigger the immune response. It would be further reached to the lung causing damage, apoptosis of its alveoli cells, and finally, lead to lung inflammation. If the SARS-CoV-2 virus continuous self-replication in the angiotensin-converting enzyme 2 (ACE-2) receptor, this becomes more severe scarring and fibrosis in the lung.[8] AgNPs are an anti-viral and anti-bacterial agent to block the active site of angiotensin-converting enzyme 2 (ACE-2) for suppressing the SARS-CoV-2 virus replication.

Nowadays, traditional Chinese herb is widely used within the COVID-19 outbreak such as "Curcumin". It possesses anti-viral and anti-bacterial properties. However, curcumin is lower solubility and absorption in the human body. AgNPs are the best tools for curcumin to improve its limitations and enhance the original function. A proposed pharmacological mechanism of AgNPs encapsulated with curcumin is the same as AgNPs itself. Curcumin blocks the active site of angiotensin-converting enzyme 2 (ACE-2) and attaches to the viral envelope lead to inhibit its replication, prevent the infection of the respiratory tract.

In the past, it has several shreds of evidence for AgNPs encapsulated with curcumin. It would increase the function of anti-viral and anti-bacterial properties but this is still not used in the treatment of COVID-19. This is including (1) Yang XX et al. discovered that curcumin acts as reducing and capping agents in the synthetic route of AgNPs. It's modified by curcumin to have a stronger anti-viral property and higher efficient inhibition effect against respiratory syncytial virus (RSV) infection. This decreases the viral trigger, inhibits the virus to host interaction, and without toxicity to the host cell.[9] (2) Gupta A et al. also developed that AgNPs use curcumin-cyclodextrins loaded into bacterial cellulose-based hydrogels for wound dressing applications. These silver nanoparticle-loaded bacterial cellulose hydrogels have a strong anti-bacterial property with high cytocompatibility. It's inhibited three of the common wound-infecting pathogenic microbes including *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Candida auris*.[10]

All of the above information demonstrates that AgNPs or it's encapsulated with curcumin may possible for the treatment of COVID-19. However, much more work needs to be done such as basic cell culture, cytotoxicity, animal models, clinical trials as well as the safety assessments in the human.

Ethical Issues
Not applicable.

Conflict of Interest
Authors declare no conflict of interest in this study

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