

The Potential Utilization of Virucidal Nanoparticles As “Nano-Traps” In Development of Potential Therapeutics Against the Emerging SARS-Cov-2 Variants

Mirza Niaz Zaman Elin

Founder, MedTheme Corporation

Abstract:

The rapid spreading of emerging variants and sub-variants such as the delta and omicron variants and the relevant sub-variants of SARS-CoV-2 and associated mortality is truly alarming. Considering the current situation, development of effective countermeasures is an urgent need. Utilization of nano particle based therapeutics can be proven as an effective option which can be developed in shortest possible period of time. When suspended in a preprocessed protein filled solution, metal nano particles such as Silver nanoparticles (AgNPs), Gold nanoparticles (AuNPs) have an innate nature to facilitate attachment of the surrounding protein structures on their surfaces. This phenomenon is known as protein corona formation. The proposal is to utilizing this innate nature of the metal nano particles to synthesize virucidal nano particles which can be used as a medical countermeasure the emerging variants of SARS-CoV-2.

Keywords: Nanoparticles, Metal, Therapeutics, SARS-CoV-2, Coronavirus, Complex, Spike proteins

INTRODUCTION:

Development of medical countermeasures against the emerging variants of SARS-COV-2 has become a true necessity as the rapid spreading of the emerging variants and associated mortality is truly alarming. Utilization of nano particle based therapeutics can be proven as an effective option which can be developed in shortest possible period of time. Gold nanoparticle-Recombinant human ACE2(Angiotensin Converting Enzyme-2) protein- Recombinant Human TMPRSS2(Transmembrane Protease, Serine-2) protein(AuNP-RHACE2P-RHTMPRSS2P) is hypothesized and proposed as a potential virucidal nanoparticle model that can be utilized as a potential countermeasure against the emerging variants.

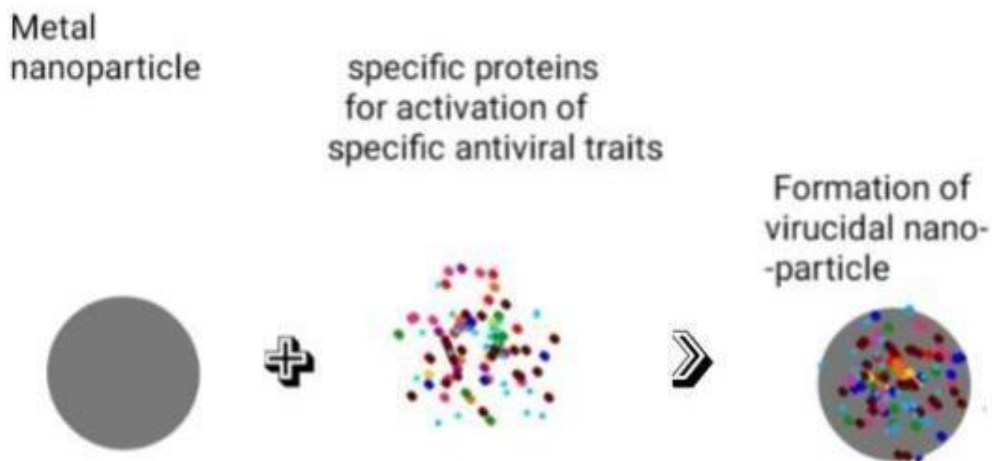


Figure: Graphic presentation of abstract

1.1 MATERIALS AND METHODS:

When suspended in a preprocessed protein filled solution, metal nano particles have an innate nature to facilitate attachment of the surrounding protein structures on their surfaces[1]. This phenomenon is known as protein corona formation[2,3]. The proposal is to utilize this innate nature of the metal nano particles to synthesize virucidal nano particles which can be used as a medical counter measure against SARS-CoV-2. For the above mentioned purpose, Gold nano particles (AuNPs), recombinant human ACE2 (RHACE2) protein and recombinant human transmembrane protease 2 (RHTMPRSS2) protein can be used.

1.2 Potential mechanisms:

The Virucidal Nanoparticle Model: AuNPs-RHACE2P-RHTMPRSS2P protein corona complex :

It is known that SARS-CoV-2 along with all of its variants, despite the changes in spike protein features, requires TMPRSS2 for spike protein activation and uses ACE2 as receptor for the purpose of entry to the target cell. ACE2 is most abundant in the respiratory tract epithelial cells. Thus administration of AuNPs-RHACE2P-RHTMPRSS2P corona complex through inhalation formula could potentially translate into inducing nano-traps which will attract the virus, activate its spike protein and bind it to the complex thus deactivating them eventually as Au nano particles are proven to be highly lethal to microbes in general as they easily become attached to the outer protein structures thus deactivate the microbes. Therefore, potential virucidal activity induced inhibition of viral replication can be achieved.

1.3 Potential results:

Due to the synthetic nature of the AuNP-RHACE2P-RHTMPRSS2P complex, it is unlikely that viruses will develop resistance against it, thus in modified form it has potential to be utilized during any possible future outbreak.

AuNPs are known to be highly lethal to microbes but non toxic to humans considering a non toxic dosage. Due to inhibitory effects to microbes which results from attachment of viral surface protein components to the nanoparticles due to high surface tension, upon interactions viral deactivation occurs rapidly[4]. The explained phenomenon opens up potential new path for therapeutic development against emerging

variants of SARS-CoV-2. To evaluate the efficacy, rigorous in-vitro, in-vivo and clinical studies on human subjects are required prior to opt out for clinical trials on human subjects.

DISCUSSION:

For maximum potentiation, spherical shaped AuNPs with diameter of 70 nm range should be chosen thus the diameter of the AuNPs-RHACE2P-RHTMPRSS2P protein corona complex will eventually be in the 120 nm range[5,6]. This parameters are important for the purpose of enhanced virucidal nano particles-virus interaction.

In the case of evaluation of the efficacy of the protein corona complex, it has to be determined that whether the viral spike protein has specific affinity towards ACE2 as host cell receptor. Different capping agents such as, polyvinylpyrrolidone (PVP), polyethylene glycol (PEG) can be used to reduce any possible toxicity resulted from Au nanoparticles.

Some other nanoparticles such as silver nanoparticles, silver sulfide nanoparticles (Ag₂SNPs), zinc oxide nanoparticles (ZnONPs), Iron oxide nanoparticles (Fe₂O₃NPs) also have the ability to facilitate attachment of surrounding protein structures on their surfaces when suspended in a preprocessed protein-filled solution[7,8,9,10], therefore, can also be utilized to construct virucidal nanoparticles via protein corona formation[11,12].

The hypothetical virucidal nanoparticle model can be utilized to discover new applications of nanoparticles in the field of vaccine development and drug discovery. It addressed not only potential medical countermeasures against the emerging variants of SARS-CoV-2 but also any possible future threat as in modified form the hypothesized virucidal nanoparticle model can be potentially utilized against any virus regardless their ability to develop resistance.

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