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Bio-Nanotechnology-Enhanced Nasal Prophylaxis: A Computational Approach for Targeting SARS-CoV-2 Variants

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INTRODUCTION & AIM

The global COVID-19 pandemic highlighted the urgent need for novel antiviral strategies beyond vaccines and conventional therapeutics.

Metallic nanoparticles, particularly gold nanoparticles (AuNPs) and silver nanoparticles (AgNPs), have demonstrated broad-spectrum antiviral properties.

Their potential arises from their ability to interfere with viral entry, protein function, and replication pathways.

This study aimed to computationally investigate the interactions of AuNPs, AgNPs, and the phytochemical Beta-escin with key SARS-CoV-2 structural and nonstructural proteins, as well as to propose a nanoparticle-based intranasal formulation for preventive intervention.

METHOD

Target proteins analyzed:

•Spike receptor-binding domains (RBDs) of **five variants**: Alpha, Beta, Delta, Omicron, Gamma

•Human ACE2 receptor

•Viral enzymes: Main protease (Mpro) and RNA-dependent RNA polymerase (RdRp)

Computational tools:

•**Docking**: AutoDock 4.2, HDOCK

•**Molecular dynamics simulations**: To assess stability of interactions

•**Quantum-level analysis**: To refine binding predictions

Proposed formulation: A composite intranasal spray combining AuNPs, AgNPs, and Beta-escin for synergistic antiviral action at mucosal entry sites.

CONCLUSION

Gold and silver nanoparticles, when combined with Beta-escin, demonstrate synergistic antiviral activity against SARS-CoV-2 across multiple viral targets.

The proposed nanoparticle-based intranasal formulation could act as a first-line preventive measure against evolving variants.

Next steps: Experimental validation (in vitro, in vivo) and translational studies are essential to advance this strategy toward real-world application.

FUTURE WORK / REFERENCES

1. Zatla, I., & Boublenza, L. (2025). Battling COVID-19 leveraging nanobiotechnology: Gold and silver nanoparticle–B-escin conjugates as SARS-CoV-2 inhibitors. *Open Life Sciences*, *20*(1), 20221047.
2. Zatla, I., & Boublenza, L. (2025). Green-Synthesized Colloidal Metal–B-Escin Bioconjugates for Nasal Delivery: A Hypothetical Prophylactic and Therapeutic Product Against SARS-CoV-2 Variants. *Trends in Sciences*, *22*(6), 9826-9826.
3. Zatla, I., & Boublenza, L. (2024). A Computational Study on Gold and Silver Nanoparticles against SARS-CoV-2 Proteins. *Proceedings*, *103*, 23.

RESULTS & DISCUSSION

Nanoparticle–protein binding:

•AuNPs: Strong interactions with Spike–ACE2 interface, especially Omicron variant (tightest binding).

•AgNPs: Higher affinity toward RdRp, suggesting potential to block viral replication.

•Both AuNPs and AgNPs showed favorable binding with Mpro, disrupting viral proteolysis pathways.

Beta-escin: Enhanced stability of nanoparticle–protein complexes and contributed to synergistic effects.

Formulation model: Predicted to block viral entry and replication by targeting both the Spike–ACE2 interaction and enzymatic activity.

Computational validation: Molecular dynamics and quantum analysis confirmed stable, high-affinity interactions.

AuNPs and AgNPs exhibit complementary antiviral profiles:

•AuNPs are effective at the entry stage (blocking Spike–ACE2 binding).

•AgNPs are stronger at the replication stage (inhibiting RdRp).

Beta-escin enhances nanoparticle interactions, adding anti-inflammatory and antiviral benefits.

The intranasal delivery route is advantageous due to:

•Direct targeting of the viral entry site (nasal mucosa).

•Non-invasive administration.

•Potential for prophylactic use in high-risk populations.

While results are in silico, they provide a foundation for experimental studies and clinical translation.