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Biological Synthesis of Nanoparticles and Evaluation of Their Synergistic Antimicrobial Effects with Algae Extract Against Multidrug-Resistant Bacteria: A Policy Summary and Applied Approach

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Abstract
Selenium nanoparticles (SeNPs) were biosynthesized using the bacterium *Kocuria*, isolated from the Hera mangrove ecosystem in Iran. After confirming their structural and chemical properties, the SeNPs were tested—both alone and in combination with *Chlorella vulgaris* crude extract against multidrug-resistant bacteria. The combination effectively inhibited the growth of *Escherichia coli, Staphylococcus epidermidis,* and *Staphylococcus saprophyticus*, but did not affect *A. baumannii*. Cytotoxicity tests showed that while SeNPs and *Chlorella vulgaris* individually had low toxicity, their combination increased cytotoxic effects. Overall, the SeNPs- *Chlorella vulgaris* combination shows promise as a novel approach to combat resistant bacteria, though further optimization and safety evaluations are needed.
Keywords: Selenium Nanoparticles, *Kocuria*, *Chlorella vulgaris*, Antimicrobial Activity, Multidrug-Resistance, Bioremediation

1. Background

Mangrove ecosystems are unique habitats that support diverse salt-tolerant microorganisms. These environments, marked by high salinity, fluctuating tides, and nutrient-rich sediments, promote the growth of microbes with special metabolic abilities.[1] Some bacterial strains, such as *Kocuria*, can convert selenium into selenium nanoparticles (SeNPs) through biological processes. This transformation reduces selenium toxicity and enhances nanoparticle stability, making them suitable for biomedical uses. SeNPs are known for their antimicrobial, antioxidant, and anticancer properties. They inhibit pathogen growth, neutralize free radicals, and induce cancer cell death.[2] They also aid in bioremediation by detoxifying polluted environments. Meanwhile, *Chlorella vulgaris*, a microalga, produces bioactive compounds like proteins, phenolics, and antioxidants with antimicrobial effects. Its crude extracts can synergistically enhance nanoparticle activity against drug-resistant bacteria. This synergy offers a promising strategy to tackle multidrug-resistance (MDR), a major challenge in modern medicine.[3]

2. Methods

A selenite-resistant strain of Cocoria (Bm3) was isolated from the Hera mangrove ecosystem and used for the biosynthesis of selenium nanoparticles (SeNPs). The nanoparticles were quantified by standard analytical techniques and a crude extract of *Chlorella vulgaris* was prepared. The antimicrobial activity of SeNPs, their extracts and their combinations was tested against MDR clinical isolates and cytotoxicity was assessed on MCF-7 cells.

3. Results

The antimicrobial potential of the synthesized SeNPs was systematically investigated, both as individual agents and in combination with crude extracts derived from the microalga *Chlorella vulgaris*. The evaluation was carried out against a panel of MDR bacterial strains, which represent a major challenge in clinical settings due to their ability to withstand conventional antibiotics. The combined treatment of SeNPs with CE demonstrated clear synergistic effects, particularly in inhibiting the growth of *Escherichia coli*, *Staphylococcus epidermidis*, and *Staphylococcus saprophyticus*.

4. Discussion and Conclusion

The present study highlights the potential of integrating

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microbial biotechnology with algal bioactive compounds to combat antibiotic resistance by demonstrating the synergistic antimicrobial effect of selenium nanoparticles (SeNPs) synthesized by *Kocuria* strain Bm3 with a crude extract of *Chlorella vulgaris*. The enhanced efficacy of the combination therapy is likely due to the phenols, proteins, and chlorophyll present in *Chlorella vulgaris* that may facilitate the penetration of nanoparticles and disrupt bacterial defense mechanisms.[4]

From a clinical and management perspective, these findings suggest that SeNPs in synergy with algal extracts could serve as complementary strategies to standard therapies and offer new avenues for the management of resistant infections. However, the cytotoxicity results, showing reduced survival of MCF-7 cells under combination treatment, suggest that safety concerns should be addressed before clinical application. Long-term toxicology studies, dose optimization, and *in vivo* testing are essential to ensure therapeutic benefits without compromising patient safety.

5. Policy Messages and Management Implications

1. Integrate novel antimicrobial strategies: Military and public health systems should consider SeNPs combined with *Chlorella vulgaris* extract as complementary tools against MDR infections.
2. Prioritize safety assessment: Comprehensive toxicology assessments and long-term safety studies should be conducted before clinical acceptance.
3. Support sustainable biomanufacturing: Investment in microbial and algal biotechnology can enhance environmentally friendly therapeutic production.
4. Strengthen preventive health programs: Military health care should emphasize routine screening and surveillance for resistant pathogens to reduce infection risks.
5. Research funding guidance: Policymakers should allocate resources to enhance biosynthetic methods, explore synergistic compounds, and conduct *in vivo* testing.

In conclusion, while SeNPs alone showed modest antimicrobial activity, their combination with *Chlorella vulgaris* extract significantly improved outcomes against selected resistant pathogens. This dual approach not only advances therapeutic innovation but is also in line with sustainable bioremediation strategies. Future research should prioritize biosynthetic methods, explore synergistic formulations with other bioactive compounds, and validate clinical application through comprehensive trials.

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Author Contributions

Authors contributed equally to this work.

Conflict of Interest Disclosures

All authors declared that they have no conflict of interest.

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