**Identifying selectively antimicrobial metal and metal-oxide nanoparticles**

**for targeted eradication of pathogenic bacteria**

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Microbial infections caused by bacteria, viruses, or fungi pose significant health risks, with antibiotics being the primary treatment. However, their non-selective nature and overuse contribute to antibiotic resistance [1]. Inorganic nanoparticles (NPs) offer a promising alternative due to their ability to combat infections by disrupting bacterial metabolism, damaging cell membranes, and inhibiting biofilm formation [2]. At the same time, size, shape, roughness, surface charge, and other specific properties of NPs facilitate varied interactions with bacteria compared to antibiotics which have a specific mechanism of action. This diversity in mechanisms of action of NPs poses challenges in developing a generalized theory to predict the antimicrobial effects across various bacterial strains [3]. The need becomes more pronounced when considering selectively toxic nanoparticles tailored to exert antimicrobial activity exclusively against pathogenic bacteria. These challenges spur investigations into developing theoretical models based on a data-driven approach, allowing correlation among poorly formalized parameters. Although machine learning has been used for predicting antimicrobial activity of NPs, overall, to our knowledge, no study has evaluated its capability to discover selectively antimicrobial NPs.

Our approach involved compiling comprehensive databases to characterize nanoparticles and their antibacterial activity. We trained CatBoost regressor model on unique datasets consisting of 489 samples for minimal concentration prediction. The ML model achieved a mean cross-validation R2 score of 0.82 with RMSE of 0.46 respectively. Subsequently, we combined ML with genetic algorithm (GA), a screening platform that enables high-throughput identification of NPs with selective antimicrobial activity. With this platform we for the first time identified CuO NPs exhibiting selective antimicrobial against pathogenic *Staphylococcus aureus.* CuO NP with key parameters including NP synthesis with green methods, nanorods in shape, average NP size of 30 nm, and reaction time of 2 hours showed a minimal bactericidal concentration (MBC) of 62.52 µg/ml against *Staphylococcus aureus* whereas it achieved MBC of 455.37 µg/ml for non-pathogenic *Bacillus subtilis*. Hence, the selectively antimicrobial CuO NP demonstrated higher toxicity against pathogenic *Staphylococcus aureus* compared to non-pathogenic *Bacillus subtilis*, with a concentration difference of 392.85 µg/ml. The antimicrobial selectivity of NPs is attributed to a complex interaction between the NPs and diverse microbial strains. The findings of this study present a novel and promising methodology for identifying selectively antimicrobial NPs capable of eradicating pathogenic bacteria without harming non-pathogenic ones.

**Reference**

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