

# INPLASY

## Investigation of how the cytotoxicity and antibacterial effect influenced by the physical-chemical parameters of the nanoparticles

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### ADMINISTRATIVE INFORMATION

**Support** - This research was supported by NKFIH FK 137749.

**Review Stage at time of this submission** - Preliminary searches.

**Conflicts of interest** - None declared.

**INPLASY registration number:** INPLASY2024100043

**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 10 October 2024 and was last updated on 10 October 2024.

### INTRODUCTION

**R** eview question / Objective SPICE.

**Condition being studied** in vitro antibacterial and cytotoxicity tests.

### METHODS

**Search strategy** Keywords: silver, nanoparticles, magnetite, copper, zinc, gold, antibacterial, cytotoxicity, MIC, inhibition, viability.  
Databases: PubMed, ScienceDirect, Semantic Scholar.

**Participant or population** Bacteria, mammalian cell lines.

**Intervention** Nanoparticles.

**Comparator** Negative control - no nanoparticles.

**Study designs to be included** In vitro experimental studies.

**Eligibility criteria** Missing data - material category, bacterial strain, cell type.  
Language criteria - only english studies.  
Articles before 2005.

**Information sources** Published articles in electronic databases, in case of missing data we will try to contact the authors of the studies.

**Main outcome(s)** In case of cell cytotoxicity tests: viability.  
In case of antibacterial tests: inhibition zone, MIC (minimal inhibitory concentration).

**Data management** Search results will be exported to EndNote, after merging duplicate removal two members of the project team will carry out the title/abstract, and subsequently the full text selection independently. Disagreements will be resolved using a third member. Data extraction from the included studies will be carried out by two

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members of the research team independently using a standardized data extraction excel sheet. Disagreements will be resolved using a third member.

**Quality assessment / Risk of bias analysis** The quality assessment of the included studies will be assessed by ToxRTool. Two independent reviewers will perform the assessment, and an independent third investigator will resolve the disagreements. Publication bias will be assessed by visual inspection of the Funnel-plots, and Egger's test will be carried out if possible.

**Strategy of data synthesis** Both qualitative and quantitative synthesis of the data will be performed. The minimum number of studies will be three for performing a meta-analysis. A random-effects model will be used to pool effect sizes using a frequentist approach. For the continuous outcomes, the mean will be used as effect size measure with 95% confidence interval. Inverse variance weighting method will be used to calculate the pooled mean. Heterogeneity will be assessed by both the tau-square and the Higgins and Thompson  $I^2$  statistics. We will summarize our findings in forest plots. Where applicable, we will report the prediction intervals of results. Model fitting parameters, potential outlier publications will be explored using different influence measures and plots. The statistical analysis will be conducted using the R software (R Core Team).

**Subgroup analysis** If enough and well structured data will be available, we plan to analyze subgroups or regression or variable importance by available parameters of the nanoparticles (eg. material, concentration, size, shape), the bacteria (eg. strain, species) and the cell lines (eg. origin, line).

**Sensitivity analysis** Sensitivity of the pooled effect size to potentially influential studies will be carried out using leave-one-out sensitivity analysis and other measures and plots of influence.

**Language restriction** English.

**Country(ies) involved** Hungary.

**Keywords** nanoparticles, cytotoxicity, antibacterial effect, inhibition zone, minimal inhibition concentration, viability, silver, copper, magnetite, zinc, gold.

#### **Contributions of each author**

Author 1 - Sarolta Halmoczki - The author provided all the searches and collected the data, created the

data tables and figures. She also provided the writing part of the manuscript. The author contributed to the development of the selection criteria, and the risk of bias assessment strategy.

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Author 2 - Gergely Agócs - The author provided statistical expertise.

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Author 3 - Angela Jedlovszky-Hajdu - The author provided the search and supervised the project, she is the funding holder. She also provided the writing part of the manuscript. The author contributed to the development of the selection criteria.

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