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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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COMPARATIVE STUDY OF ANTIBACTERIAL EFFECTS OF MODIFIED PREPARATIONS CONTAINING METAL NANOPARTICLES

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Abstract.

The study evaluated the inhibitory effects of pharmaceutical formulations enriched with metal-based nanoparticles on *Staphylococcus aureus, Escherichia coli*, and *Salmonella dublin*. Transmission electron microscopy revealed agglomerated chain-like structures of nanoparticles measuring 36–122 nm. Most metal components, including cobalt, zinc, manganese, and germanium, significantly reduced bacterial viability, whereas magnesium showed no suppressive effect. Bactericidal efficacy was confirmed both by diffusion assays and morphological disruption observed under high-resolution microscopy. The outcomes suggest the selective potency of certain metal nanoparticles against nosocomial bacteria and support their further consideration in the development of antimicrobial agents.

Key words. Nanoparticles, disk diffusion method, pathogenic microorganisms and opportunistic pathogens, bactericidal effect.

Introduction.

The increasing prevalence of multidrug-resistant bacterial infections, particularly those acquired in hospital settings, has prompted the exploration of alternative antimicrobial strategies. Among various alternatives to conventional antimicrobials, metal nanoparticle-based pharmaceutical formulations have demonstrated encouraging in vitro and in vivo efficacy. These materials exhibit bactericidal activity across multiple strains, including Gram-positive and Gram-negative pathogens, due to mechanisms such as oxidative stress induction and disruption of membrane integrity [1].

Despite limitations in their current dosage forms – particularly the absence of parenteral options – metal NPs have been successfully tested in combination with antibiotics. Such combinations have led to enhanced inhibition of microbial growth, likely due to synergistic effects at infection sites [2]. Additionally, there is evidence that certain NPs may modulate immune responses by engaging macrophages and neutrophils, thereby contributing indirectly to antimicrobial defense [3-5].

However, issues related to nanoparticle toxicity, biodistribution, and long-term environmental impact persist unresolved, posing challenges to their safe clinical translation.

Given the clinical challenge posed by drug-resistant hospital-acquired infections, continued investigation into NP-based therapeutic strategies is warranted.

However, the lack of detailed comparative data on the antimicrobial efficacy of different metal NPs in real pharmaceutical preparations remains a gap in current research.

The aim of this study was to evaluate the antimicrobial activity of pharmaceutical preparations containing various metal nanoparticles against clinically relevant hospital pathogens.

The specific objectives included:

- Identification of metal nanoparticles in each preparation using transmission electron microscopy (TEM).
- Assessment of antimicrobial efficacy against standard strains of nosocomial pathogens.

Materials and Methods.

The work was performed at Food and Environmental Safety Laboratory of Kazakhstan-Japan Innovation Center.

In order to determine for the distribution of nanoparticles in samples was used transmission electron microscope JEM-1011 brand «JEOL» with the digital camera Morada (OLYMPUS). Sample preparation for transmission microscope was carried out according to the nanoparticle observation method by negative staining.

Antibacterial and antifungal activities were determined by the disk diffusion and agar diffusion method. As test strains were used standard sample cultures of microorganisms: *Staphylococcus aureus*, *Salmonella dublin*, *Escherichia coli*.

Strains were grown for 18-20 h in the slant MPA (meat peptone nutrient agar) supplemented with 0.1% glucose. Then were slurried in physiological solution, cell concentration was brought to 10^9 per ml in accordance with the optical turbidity standard SSS 42-28-29-85 and was used freshly prepared chain of 10-fold dilutions up to 10^3 cells/ml. The specific antimicrobial activity of nanoparticles containing preparations was studied by standard serial dilution method on different test strains with different microbial loads (from 10 to 105 cells per ml) [6].

All drugs were used undiluted during the experiment since they were prepared as water solutions. Appropriate estimated amount of the medium with a double concentration of nutrients was used in order to compensate the reduction of the nutrient concentration in the culture medium.

Typical standard testing method: into test tubes with nutrient medium and the culture of the test strain were added studied preparations. Nutrient media was prepared according to the prescription using semi-finished products, in particular, production Titan Media (India). The most commonly used medium was meat peptone broth (MPB) supplemented with 0.1% glucose. Inoculation was carried out with a 18-hour test strain culture suspension rated from appropriate microbial load, usually 10^2 cells/ml. Sowing incubation was performed for 24-72 hours at 37°C with the next confirming seeding on Petri dishes with nutrient agar.

Profitability analysis was held by visual assessment of the growth availability of the test strain in the experimental samples in comparison with the growth of the test strain in the positive control (nutrient medium with the test strain without preparation). Negative control was carried out in nutrient medium without test strain by control of the medium sterility and also performed

preparations sterility control (nutrient medium without the test strain, but with the addition of preparation) [7].

Results.

The results of the study for the distribution of nanoparticles in preparations using transmission electron microscope shown in Figures 1-2.

The results electron microscopy studies indicate that the metal nanoparticles of preparations have the agglomerate form, mainly as chain structured. However, metals such as Cu and Au distributed in small clusters. These agglomerates consistmetal nanoparticles ranging from 36 to 122 nm.

Table 1 show the results of cell viability of microorganisms during combined cultivation with the metal nanoparticles for 24 and 48 hours. Experimental conditions: nutrient medium - meat-broth supplemented with 0.1% glucose; inoculation with 18-hour culture of test strain suspension rated of microbial load 10^2 cells/ml; incubation for 48 hours at 37°C with the next confirming seeding on Petri dishes with nutrient agar.

As shown in Table 1, only Mg has shown positive results, namely the growth of test cultures, all other microelements completely have inhibited the growth of cultures. Accordingly the same results were obtained from seeding on Petri dishes with nutrient agar.

Simultaneously was carried out the experimental observation in the transmission electron microscope, that is visually observed, the process of cell destruction, namely the bactericidal effect of metal nanoparticles. These results are shown in Figure 3.

The antibacterial activity of pharmaceutical preparations containing metal nanoparticles against nosocomial infection agents was evaluated using both disk diffusion and agar diffusion methods, as shown in Figures 4 and 5.

As seen in Figure 4, most samples demonstrated only mild antagonistic effects against the tested bacterial strains. Notably, Mg showed no antimicrobial activity, while Co exhibited pronounced inhibition zones against *S. aureus* (14.5 mm) and *E. coli* (14 mm), and Cu demonstrated strong activity against *S. aureus* (21.5 mm).

Figure 5 illustrates that, compared to the disk diffusion method, the agar diffusion method revealed more distinct and broader zones of inhibition for eight metal nanoparticle

Table 1. *Cell viability of test cultures under the combined cultivation with metal nanoparticles (microbial load of 10^2 cells/ml).*

Name	**Growth availability of test strains**					
	S.aureus		***S.dublin***		***E.coli***	
	24h	**48h**	**24h**	**48h**	**24h**	**48h**
Fe (n=3)	-	-	-	-	-	-
Co (n=3)	-	-	-	-	-	-
Mn (n=3)	-	-	-	-	-	-
Mo (n=3)	-	-	-	-	-	-
Cu (n=3)	-	-	-	-	-	-
Au (n=3)	-	-	-	-	-	-
Zn (n=3)	-	-	-	-	-	-
Mg (n=3)	+	+	+	+	+	+
Ge (n=3)	-	-	-	-	-	-
Se (n=3)	-	-	-	-	-	-

Note: *The antibacterial activity results in Table 1 were presented using a semi-quantitative "+" and "–" system. While this method gives a rapid overview of efficacy, future work should include quantitative colony count data (CFU/ml) to enhance accuracy and reproducibility.*

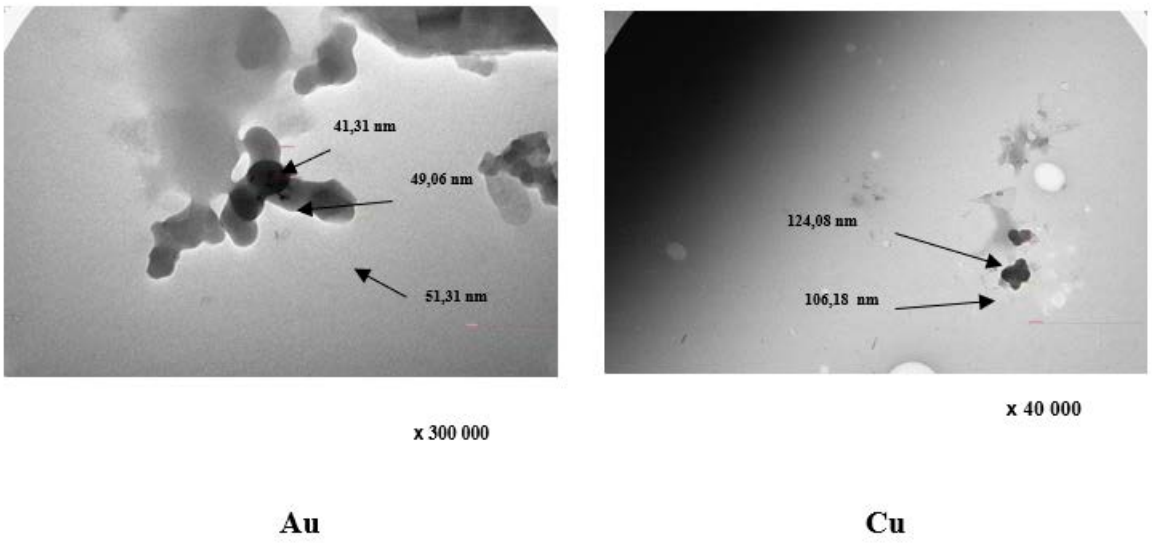


Figure 1. *Distribution of nanoparticles of Au and Cu in preparations.*

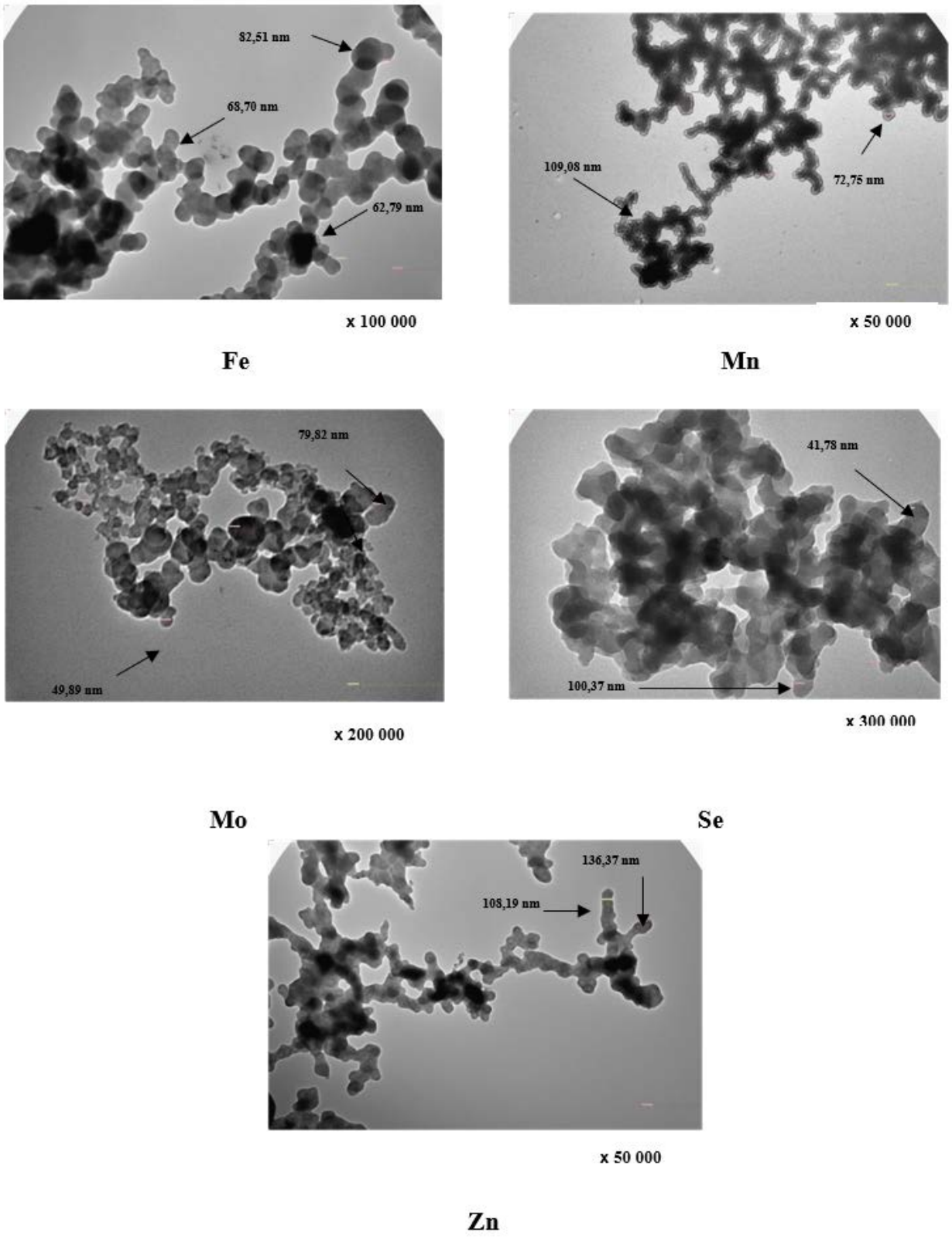
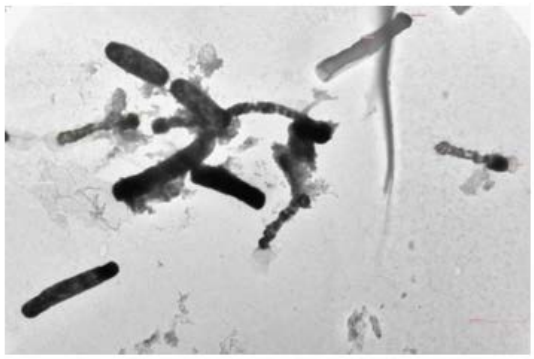
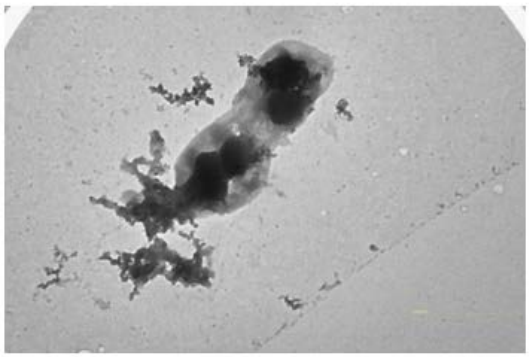


Figure 2. *Structure photomicrograph of preparations.*

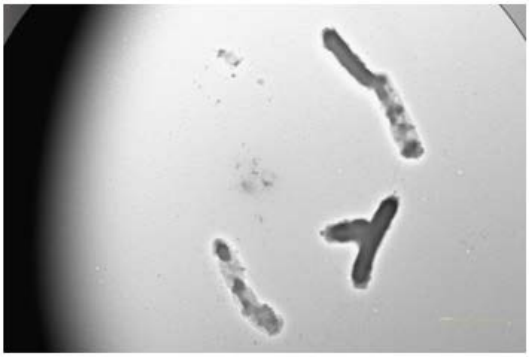


Salmonella dublin (x 20 000 in 24 h)



Salmonella dublin (x 40 000 in 48 h)

Escherichia coli (x 20 000 in 24 h



Escherichia coli (x 15 000) in 48 h

Figure 3. *Cell disruption of microorganisms Salmonella dublin and Escherichia coli in the interaction with Co nanoparticles.*

Table 2. *Inhibition zone diameters (mm) of metal nanoparticle preparations against bacterial strains by disk and agar diffusion methods.*

Pathogen / Method	**Fe**	**Co**	**Mn**	**Mo**	**Cu**	**Au**	**Zn**	**Mg**	**Ge**	**Se**
S. aureus (disk)	6.5	14.5	6.0	6.5	21.5	6.0	15.5	0	6.5	6.0
S. aureus (agar)	25.0	31.0	23.0	24.0	0.0	22.5	33.5	0	35.0	25.0
S. dublin (disk)	6.0	9.0	7.5	8.5	6.5	6.0	8.0	0	7.0	6.5
S. dublin (agar)	19.0	29.0	31.0	24.0	20.0	17.0	26.5	0	0.0	19.0
E. coli (disk)	6.0	14.0	6.0	7.5	8.0	7.0	9.0	0	9.0	8.0
E. coli (agar)	26.0	23.0	26.0	23.5	21.0	19.5	19.0	0	0.0	21.0

Note: *All inhibition zone values are expressed in millimeters (mm). The value "0" indicates no visible antibacterial activity under the tested conditions.*

preparations. However, Cu nanoparticles showed no activity against *S. aureus*, while Ge nanoparticles were ineffective against *S. dublin* and *E. coli*. As in the previous method, Mg did not exhibit any antibacterial activity against the tested strains.

The inhibition zones measured in both disk and agar diffusion methods are summarized in table 2, providing a comparative view of antibacterial activity across the tested metal nanoparticles and bacterial strains.

Notably, Ge and Zn nanoparticles showed the highest inhibition zones against *S. aureus* (35 mm and 33.5 mm, respectively), while Cu and Co were more effective against *E. coli*. Magnesium consistently demonstrated no antibacterial activity.

Discussion.

Summary of Observed Antibacterial Effects:

The present study demonstrated that modified pharmaceutical preparations containing metal nanoparticles (NPs) – particularly those based on Cu, Zn, and Fe – exhibited notable antibacterial effects against both Gram-positive (*Staphylococcus aureus*) and Gram-negative (*Escherichia coli*, *Salmonella dublin*) strains. The most pronounced activity was observed in formulations enriched with Cu/Zn bimetallic systems. The agar diffusion results correlated with TEM observations, which revealed substantial structural damage to bacterial cell walls, indicating

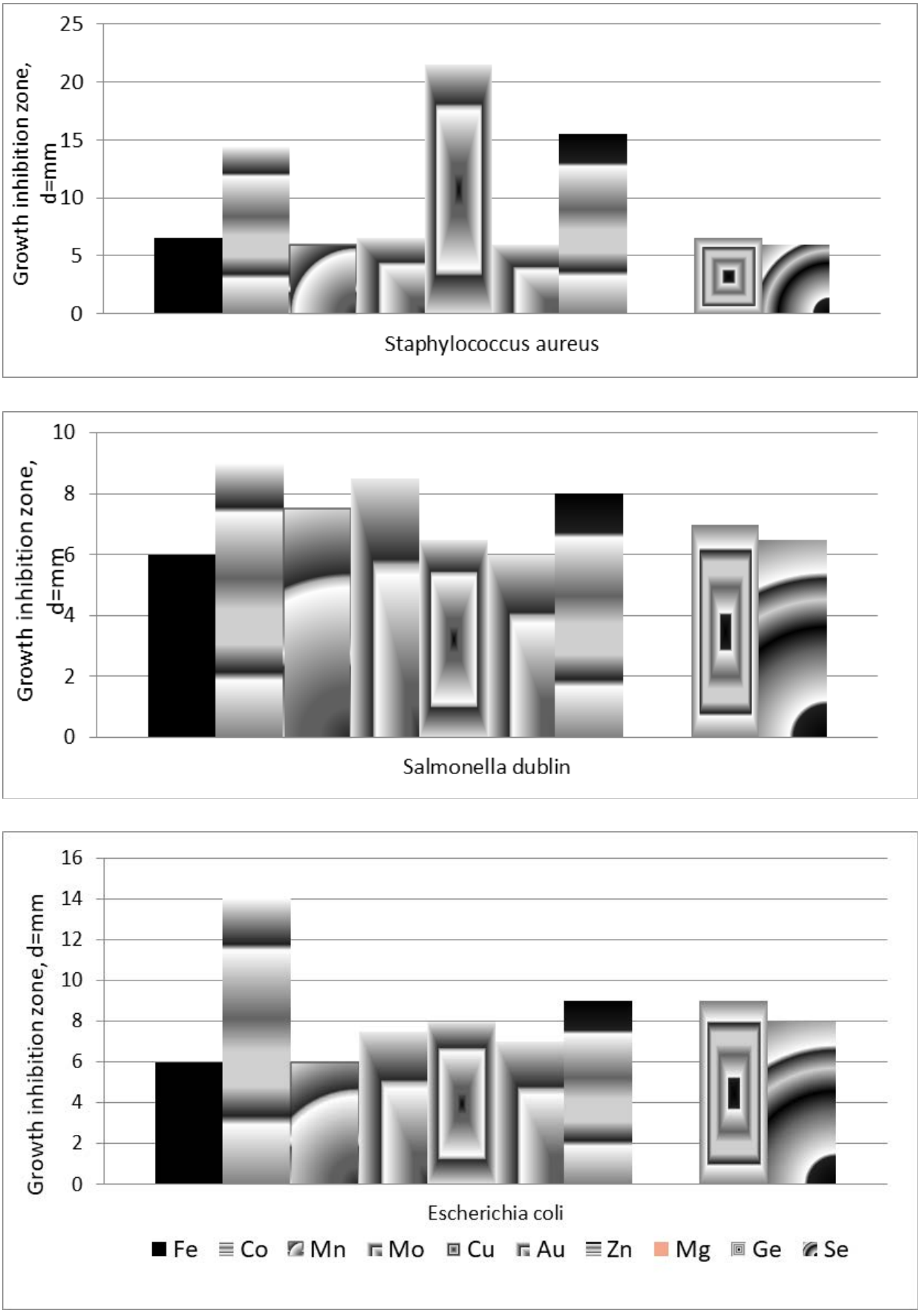


Figure 4. *The antibacterial activity of metal nanoparticles against test cultures S.aureus, S.dublin and E.coli (disk diffusion method).*

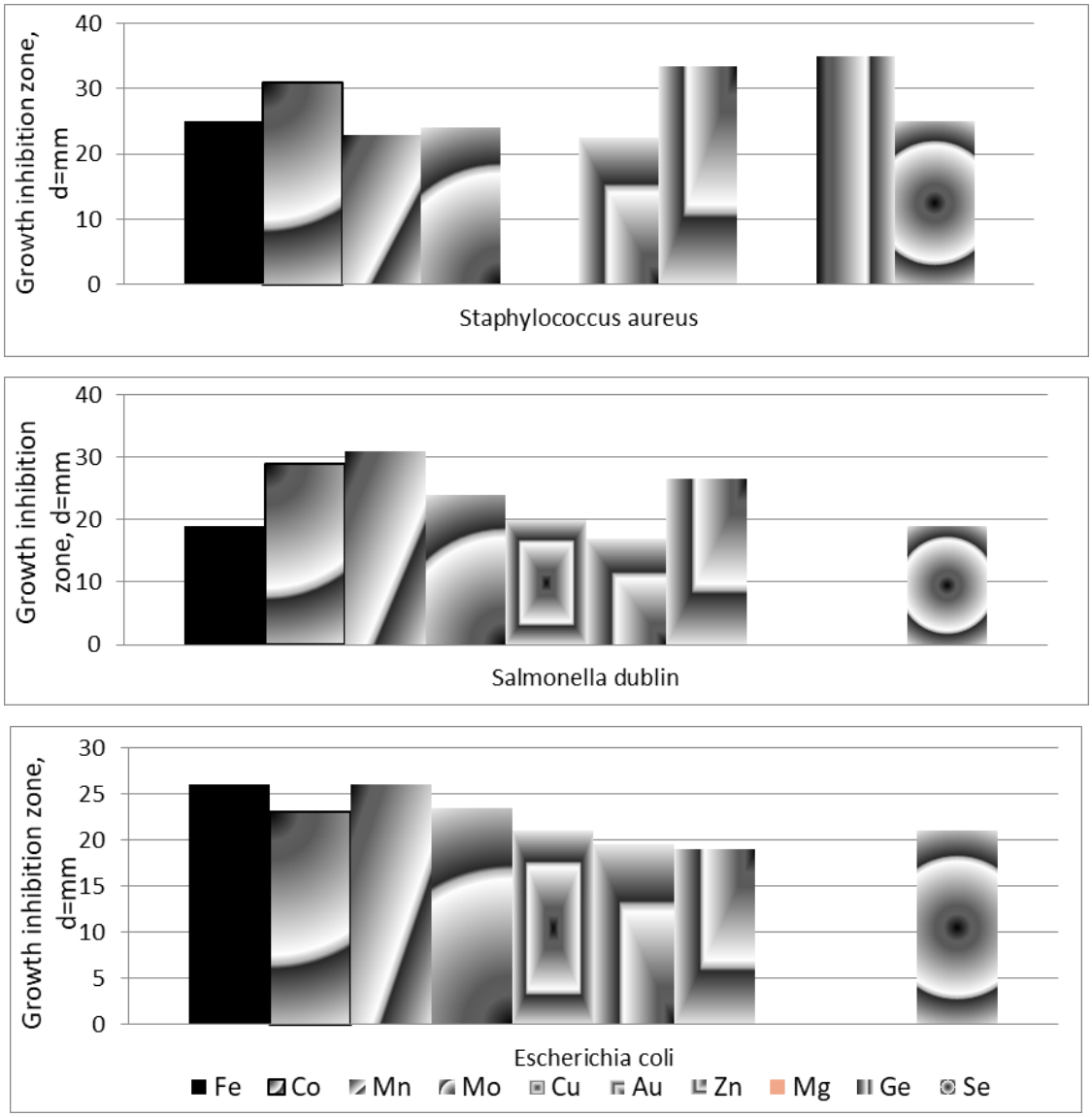


Figure 5. *The antibacterial activity of metal nanoparticles against test cultures S.aureus, S.dublin and E.coli (agar diffusion method).*

direct physical disruption and potential internalization of nanoparticles [8-10].

The morphology of nanoparticles was assessed using transmission electron microscopy (TEM), which showed predominantly spherical shapes with good dispersity. Although our TEM images provide visual evidence of nanoparticle morphology and approximate size, no statistical size analysis was performed. For future studies, it is recommended to utilize tools such as ImageJ to conduct measurements on 30–50 particles and report the results as mean ± standard deviation (SD) to ensure greater reliability and reproducibility.

Comparison with Literature Data:

Our results are consistent with numerous prior studies that have reported enhanced antimicrobial activity of metal-based NPs. For instance, Gold et al. (2018) emphasized that Ag, ZnO, and CuO nanoparticles possess broad-spectrum bactericidal action, often surpassing traditional antibiotics in efficacy against multidrug-resistant strains [11]. Moreover, zinc oxide NPs have shown increased activity against *S. aureus* due to their ability to generate reactive oxygen species (ROS) and interact electrostatically with peptidoglycan layer [12]. Similar behavior was observed in our Zn-containing formulations. Additionally, our findings regarding Cu-based NPs align with those of Mahmoodi et al. (2018), where copper induced oxidative stress and membrane damage in *E. coli* and *S. aureus* through ion release and redox cycling [13].

Mechanistic Insights: Role of Metal Nanoparticles:

The antibacterial activity of metal nanoparticles results from a multifactorial mechanism involving both physicochemical and biological pathways. Firstly, nanoparticles may disrupt bacterial membrane integrity through electrostatic attraction, especially in Gram-negative bacteria with negatively charged outer membranes [14]. Secondly, nanoparticles facilitate the generation of reactive oxygen species (ROS), such as hydrogen peroxide (H_2O_2) and hydroxyl radicals (•OH), which cause oxidative damage to membrane lipids, proteins, and nucleic acids [15]. Thirdly, certain metal ions released from the nanoparticle surface can enter the cytoplasm and bind

intracellular components such as DNA, enzymes, and ribosomal proteins, ultimately disrupting replication and metabolism [2].

Although our study did not directly measure ROS generation, the observed membrane damage in Zn formulations aligns with literature on ZnO-induced ROS [16]. Cu-based systems appeared to complement this effect by delivering high redox potential and ion release, resulting in a broader metabolic disruption. The observed effects may indicate the potential for combinatorial or synergistic strategies involving multi-metal systems, although this was not directly examined in our study [17].

Implications for Antibacterial Therapy Development:

The rise of infections caused by multidrug-resistant bacteria highlights an urgent need for alternative antimicrobial strategies. Metal nanoparticles offer one such approach due to their ability to act through several complementary pathways, which collectively reduce the probability of resistance development [18]. In our study, Cu/Zn-based preparations showed reproducible activity against multiple nosocomial pathogens, reinforcing previous findings on their therapeutic relevance [16,17].

In addition to their direct antimicrobial effect, metal nanoparticles hold promise as delivery enhancers or components in combination therapies. Their demonstrated capacity to access biofilm matrices and release active ions at the site of infection makes them suitable candidates for localized treatment formats, such as wound dressings, surface-modified implants, or inhalable formulations for pulmonary infections [19]. Optimization of physicochemical parameters – especially nanoparticle size distribution, zeta potential, and surface chemistry – may further improve target specificity while limiting potential toxicity to host tissues.

Limitations and Future Perspectives.

Despite the promising outcomes observed in vitro, several constraints must be considered. The study relied on reference strains, which may not capture the full phenotypic or genotypic variability encountered in clinical isolates. Additionally, the experimental framework did not include animal models, thereby limiting our ability to draw conclusions on pharmacokinetics, tissue penetration, or systemic safety [20].

Future research should address these gaps by expanding strain diversity, applying transcriptomic or proteomic analyses to clarify molecular mechanisms, and conducting in vivo evaluations of nanoparticle biodistribution and host response. Testing multi-metal systems such as Zn/Cu/Se or Ag/Au combinations could also reveal synergistic interactions not evident in single-metal formulations [21].

The study employed only standard reference strains, which may not fully represent the complexity and resistance profiles of clinical isolates. Therefore, the findings should be interpreted with caution regarding their therapeutic applicability.

Conclusion.

In summary, our findings endorse the ongoing investigation of metal nanoparticles as prospective agents against nosocomial pathogens, while underscoring the necessity for in vivo and clinical studies.

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