BİTLİS EREN ÜNİVERSİTESİ
FEN BİLİMLERİ DERGİSİ

ISSN: 2147-3129 / e-ISSN: 2147-3188

Article Type : Research Article
Received : April 12, 2025
Revised : June 18, 2025
Accepted : June 24, 2025
DOI : 10.17798/bitlisfen.1673322

Year : 2025
Volume : 14
Issue : 2
Pages : 1254-1268

META-ANALYSIS OF STUDIES ANTIBACTERIAL EFFECTS OF SILVER NANOPARTICLES (AgNPs) OBTAINED BY GREEN SYNTHESIS USING *CENTAUREA* SPECIES

Şule OCAK [1], **Aysun ERGENE [1,*]**

[1] *Kırıkkale University, Biology Department, Kırıkkale, Türkiye*

*** Corresponding Author:** ergene@kku.edu.tr

ABSTRACT

The aim of this study was to compare the antibacterial activity of silver nanoparticles (AgNPs) produced by green synthesis method using extracts from Centaurea species by meta-analysis of articles. We collated data from various studies and used a scientific method to evaluate the efficacy of silver nanoparticles produced using *Centaurea* species.

Meta-analysis allows the data to be interpreted in a broader context and in a statistically significant way, enabling a general evaluation of antibacterial efficacy. A total of three studies were used.

These studies provided mean values, standard deviations and sample sizes for *Escherichia coli* and *Staphylococcus aureus* bacteria. The effect sizes of the studies were calculated using Cohen's d formula. Heterogeneity analysis, which refers to the consistency between studies, was calculated using Cochran's Q and I^2 statistics.

The results were presented using Forest plots, network graphs and scatter analysis. For this meta-analysis study, we used the Python programming language to analyze and visualize the data.

Keywords: Meta-Analysis, Antibacterial effects, Silver nanoparticles, Green synthesis, *Centaurea*.

1 INTRODUCTION

Nanotechnology has undoubtedly revolutionized science and technology in recent years. The unique physical, chemical and biological properties of nanoscale materials enable innovative applications in various disciplines such as medicine, pharmacy, biotechnology and materials science [1]. Nanoparticles exhibit bioactivities such as antimicrobial, anticancer and antioxidant properties thanks to their high surface areas and reactivity [2].

The disruption of the integrity of the cell membrane by silver nanoparticles has been demonstrated to prevent bacterial cells from fulfilling their vital functions [3]. This results in the disruption of the cell's water balance and the leakage of intracellular components. The loss of intracellular components can result in a deficiency of ions and organic molecules that are vital for cell survival, potentially leading to cell death. Furthermore, the interaction of silver nanoparticles with bacterial cells has been shown to result in a range of effects, including damage to electron transport chains, disruption of cell walls, interference with protein synthesis through interaction with ribosomes, and structural changes to DNA, ultimately leading to DNA damage [3].

It is clear that silver nanoparticles (AgNPs) have attracted great interest due to their strong antimicrobial properties. AgNPs are a promising solution in the battle against antibiotic-resistant bacteria. They have proven effective against various bacterial pathogens [3]. However, the fact that nanoparticles produced by chemical and physical synthesis methods contain toxic chemicals and are environmentally unfavorable has made it necessary to search for sustainable and environmentally friendly alternatives [4].

Green synthesis methods are the environmentally friendly and economical way to produce nanoparticles using plant extracts. Plant extracts function as both reducing and stabilizing agents thanks to their polyphenols, flavonoids and other bioactive components [5]. The high purity and desired properties of AgNPs produced by this method make them ideal for use in biomedical applications [6-8]. *Centaurea* species are plants known for their rich content of bioactive components and are used for various purposes in traditional medicine. Components such as flavonoids, phenolic acids and terpenoids contribute to the antimicrobial and antioxidant properties of these plants [9]. Extracts from *Centaurea* species are therefore a natural and effective reducing agent in AgNP synthesis.

The first application of meta-analysis in literature was in 1904 by Karl. In 1904, Karl Pearson applied it to the field of health. Concurrently with the advancements in statistical science, studies pertaining to meta-analysis gained impetus after 1930. Cochran (1934) developed the heterogeneity test and a method for comparing parameter estimates of variables in studies conducted at different times and places. This comparison method has been employed by researchers in the fields of medicine, social sciences and psychology [10]. Glass (1970, 1976) was the seminal figure in the introduction of the meta-analysis method to the scientific world. This methodology was developed for the purpose of obtaining combined results from studies involving two groups, in which differences between sample and control groups were determined. Cohen (1977) proposed the concept of effect size, which has since become a fundamental component of meta-analysis [10].

The present study is a meta-analysis which aims to provide a quantitative evaluation of the antibacterial efficacy of silver nanoparticles synthesized using Centaurea species. The objective of this study is to determine the overall effect sizes by aggregating data from multiple independent studies. In addition, the study seeks to identify potential sources of heterogeneity and assess the consistency of findings across different experimental conditions. It is anticipated that the outcomes will provide more robust evidence regarding the potential of Centaurea-based AgNPs as antimicrobial agents and to guide future research and applications in nanomedicine and phytotechnology.

2 MATERIAL and METHOD

2.1 Comprehensive Literature Review

Various databases (PubMed, Scopus, Science Direct, Google Scholar, Web of Science) were searched with predetermined keywords.

1. "*Centaurea*" OR "*Centaurea* species" OR "*Centaurea* sp." OR "*Centaurea* herb species" OR "*Centaurea* herb sp." OR "*Centaurea* plants"

2. "Green Synthesis" OR "Green synthesis method" OR "Green synthesis by *Centaurea*" OR "Green synthesis by *Centaurea* species" OR "Green synthesis by *Centaurea* sp." OR "Green synthesis by *Centaurea* herb species" OR "Green synthesis by *Centaurea* herb sp." OR "Green synthesis by *Centaurea* plants"

3. "Ag Nanoparticle" OR "Silver Nanoparticle" OR "Ag metal ion" OR "Silver metal ion" OR "AgNP" OR "Silver nanoparticle of formation" OR "Silver nanoparticle of synthesis"

4. "Antibacterial Effect" OR "Bacteria on effect" OR "*E. coli* and *S. aureus* on antibacterial effect"

5. "Randomized controlled trial" OR "Randomized controlled trials as topic" OR "Biological experiments" OR "Randomized controlled biological experiments" OR "Randomized Trials"

This algorithm study includes studies on *Centaurea* in the first article, green synthesis in the second article, silver nanoparticles in the third article, and studies on the antibacterial effect in the fourth article. It also includes randomized controlled studies in the fifth article and studies that meet all conditions at the same time in the last article. The inclusion and exclusion criteria employed in the present study are delineated in Table 1.

Table 1. Inclusion and Exclusion Criteria.

Inclusion Criteria	Exclusion Criteria
-*Centaurea* Species - Ag Nanoparticles - Antibacterial Effect - *S. aureus* and *E. coli* - MIC (Minimum Inhibitory Concentration) - Disk Diffusion Sensitivity Test	- Species other than *Centaurea* - Au-Pt-Se-Pd-Pd-Pt-Zn-Fe-Cu Nanoparticles - Antimicrobial and Antifungal Action - Bacteria other than *S. aureus* and *E. coli*, fungi, algae, lichens - Antibacterial susceptibility testing other than MIC and Disk Diffusion Susceptibility Test

2.2 Extracting and Summarizing Data

The main findings of the studies were summarized. A data extraction form was prepared and the data to be collected from the study were identified. Name of study, author, year of publication, type of study. Finally, information was systematically collected using key findings (e.g. means, standard deviations) and measurement tools.

2.3 Interpretation of Findings and Data Analysis

The information obtained was synthesized. The results were interpreted and evaluated in response to the research question of the study.

The main purpose of a meta-analysis is to obtain strong and precise results that cannot be obtained from individual trials. Before the analysis, it is very important to assess the direction of the effect, the effect size, the homogeneity of the effect between trials, the publication record and the sensitivity analysis.

2.4 Effect Size

It is the value that provides information about the size of the relationship between two groups and the strength of the difference. Effect size values frequently used in meta-analysis studies are standardized correlation, mean difference and risk ratio values. Hedges' g or Cohen's d values are typically calculated using the standardized mean difference to determine the effect size. There is no significant difference between Hedges' g and Cohen's d values in studies with large samples. Hedges' g is used to eliminate the bias that may occur in studies with small sample size [11]. The forest plot is the key to evaluating the effect size and confidence intervals of all studies included in the meta-analysis and each study. The effect size of each study is indicated by black squares and the confidence intervals are indicated by horizontal lines passing through the squares. The area of the squares is the weight of each study reflected in the meta-analysis. The diamond at the bottom shows the overall effect size of all the included studies. The width of the diamond indicates the confidence interval of the effect size, and the height indicates the odds ratio (OR) or risk ratio (RR). The vertical line through point 1 in the forest plot is the no-effect line. For non-logarithmic values, the line of no effect is considered to pass through point 0. The overall effect size must not intersect the line of no effect for it to be statistically significant [12].

2.5 Heterogeneity

Heterogeneity occurs when there is more variation between studies than expected. Heterogeneity assumptions affect data analysis. The Cochrane Q test (chi-square), Higgins I 2 or tau H2 statistics are used to assess heterogeneity between studies included in the meta-analysis. These statistics tell us whether the studies show the same effect. Forest plots are used to visually examine heterogeneity. Studies that are not in the confidence intervals in the forest plot are not homogeneous [13]. If the P value of the chi-square test calculated from the forest plot is less than 0.1, it shows statistical heterogeneity and random effect can be used. Even when the data cannot be shown to be homogeneous, the fixed effects model can be used by ignoring heterogeneity and expressing all study results individually without combining them. However, a random effects model is typically applied, along with a subgroup analysis or meta-regression to account for heterogeneity. In a subgroup analysis, data are divided into subgroups that are expected to be homogeneous and these subgroups are analyzed [14].

2.6 Publication Bias

It is one of the most important factors affecting the accuracy of the analysis results in meta-analysis studies. Publication bias aims to draw a general conclusion by combining the results of meta-analysis due to the high probability of publication of statistically significant studies. It is therefore essential to examine publication bias. Funnel plots are the key here – they're the perfect way to test for publication bias.

They show the effect size on the horizontal axis and the standard error of the effect size on the vertical axis, just like a scatter plot. A symmetrical distribution around a centre in a funnel plot indicates no publication bias. However, when the number of publications is small, it may be difficult to make sense of publication bias from graphs. In such cases, it is essential to turn to statistical tests such as the Begg and Mazumdar rank correlation test or the Egger test to assess publication bias [14].

2.7 Sensitivity Analysis

Sensitivity analysis is the key to assessing the extent to which results depend on certain assumptions, methods or data points [15]. The purpose of this analysis is to test the reliability and stability of the primary methodological or analytical strategy. Sensitivity analysis is key to addressing missing data, which can lead to over- or underestimation of intervention effects. It is also essential for assessing the acceptability of choices in studies with endpoints and changes relative to baseline and outcome data [13, 16].

2.8 Study Limitations

This study is a review of articles and theses written only in Turkish and English from five databases between 2014 and 2024. The search yielded a total of 579 studies. After applying the inclusion and exclusion criteria, three articles were included in the analysis. The screening process (flow diagram) and the studies included in the meta-analysis are given in Figure 1 and Table 3 respectively.

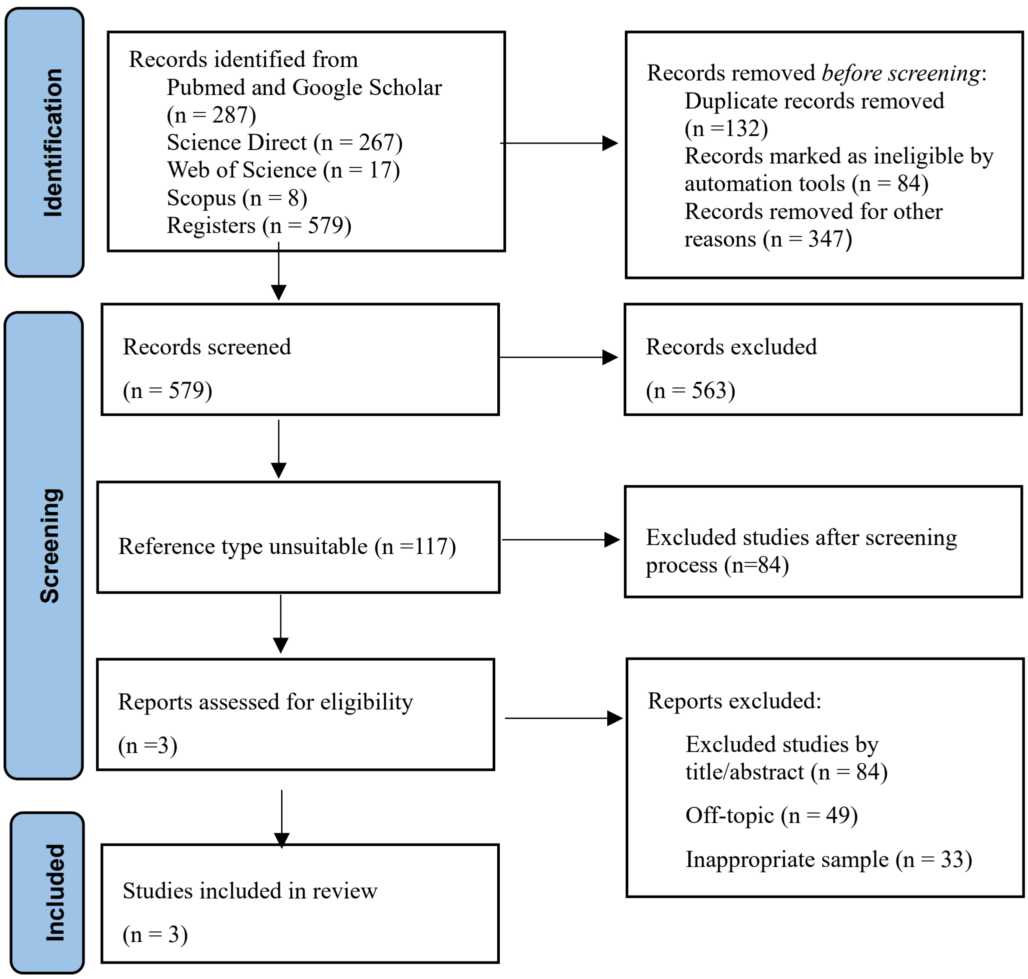

Figure1. Number of articles evaluated in meta-analysis (Flow diagram).

Table 3. Characteristics of the Studies Included in the Meta Analysis.

Study No	Author/Year/Journal Title	Name of the Study	Study Results
1	Mosidze E, Legault J, Mshvildadze V, Ebralidze L, Bakuridze L, 2022, Collection of Scientific Works of Tbilisi State Medical University, Vol: 56, 101-104.	Biosynthesisi of Silver Nanoparticles Using Extract of *Centaurea adzharica* sosn. And Evaluation of Their Bioactivity.	Zone diameters was found as 68 µg/mL (IC90) for *E. coli* (11 mm), 57 µg/mL (IC90) for *S. aureus* (10 mm).
2	Mostafa E, Fayed MAA, Radwan RA, Bakr RO., 2019. Colloids Surf B *Centaurea* pumilio L. extract and nanoparticles: A candidate for healthy skin. Biointerfaces. 2019 Oct 1;182: 110350. doi:10.1016/j.colsurfb.2019.110350. Epub 2019 Jul 8.PMID: 31326622	*Centaurea pumilio* L. extract and nanoparticles: A candidate for healthy skin.	Zone diameters was found as 120 µg/mL (IC90) for *E. coli* (12 mm) 70 µg/mL (IC90) for *S. aureus* (17 mm)
3	Abdoli M,Khaledian S, Mavaei M, Hajmomeli P, Ghowsi M, Qalekhani F, Nemati H, Fattahi A, Sadrjavadi K., 2024. Scientific Reports, 14, Article Number: 13941	*Centaurea behen* leaf extract mediated green synthesized silvernanoparticles as antibacterial and removing agent of environmental pollutants with blood compatible and hemostatic effects.	Zone diameters was found as 60 µg/mL (IC90) for *E. coli* (9 mm) 30 µg/mL (IC90) for *S. aureus* (11 mm)

3 RESULTS AND DISCUSSION

The effect sizes of the studies were calculated using Cohen's d formula. The heterogeneity between studies was then analyzed using both Cochran's Q and I^2 statistics. The findings were then represented visually using Forest plots, network graphs and scatter analysis. In this meta-analysis study, data analysis and visualization processes were performed using the Python programming language. The data processing was conducted using Pandas [17], the statistical calculations were performed with NumPy [18] the data visualization was facilitated by Matplotlib [19], and the Egger test for publication bias analysis was conducted using Stats models [20].

The present analysis draws upon a total of three studies. The present studies provide mean zone diameter values, standard deviations and sample sizes for *E. coli* and *S. aureus* bacteria.

Table 4. Effect Sizes for E. coli and S. aureus (Cohen's d).

Study No	*E. coli* (M ± SD)	*S. aureus* (M ± SD)	Sample (*E. coli* / *S. aureus*)	Effect Size (Cohen's d)
1	10.66 ± 0.57	09.66 ± 0.57	3 / 3	1.75
2	11.66 ± 0.57	16.66 ± 0.57	3 / 3	-8.77
3	9.00 ± 0.00	11.00 ± 0.00	3 / 3	-

Table 4 clearly shows the effect size values, calculated with Cohen's d. Positive d values indicate that *E. coli* is superior, and negative d values indicate that *S. aureus* is superior. It is important to note that, due to the standard deviation being zero, it was not possible to calculate Cohen's d for Study 3.

Table 4 shows Cohen's d values, which compare the magnitude of the effect between *E. coli* and *S. aureus* bacteria. Cohen's d is a standardized measure of the difference between the two groups, allowing us to understand the relative effectiveness of these bacteria. Positive d values indicate superiority of *E. coli* and negative d values indicate superiority of *S. aureus*. When we analyze the Cohen's d values in Table 1, we see that d = 1.75 for Study 1, which falls into the large effect size category. This unequivocally shows that *E. coli* is superior to *S. aureus*. For Study 2, d = -8.77, representing a very large negative effect size, indicating that *S. aureus* is far superior to *E. coli*. For Study 3, Cohen's d could not be calculated (NaN) because the standard deviation was reported as zero in this study. A standard deviation of zero means that all observations are the same and there is no variability between groups. As a result, the effect size cannot be calculated. For Cohen's d values, 0.2 is typically interpreted as a small effect, 0.5 as a medium effect and 0.8 as a large effect. Study 1 and Study 2 have large effect sizes, while Study 3 has no assessable effect size. Standard deviation (SD) values represent the spread in each group's measurements. Higher standard deviation values indicate greater variation in measurements, while lower standard deviation values indicate a more homogeneous distribution. Studies 1 and 2 report standard deviation values of 0.57, indicating dispersion in the measurements. However, in Study 3, the standard deviation for *E. coli* was reported as 0, indicating no variability in this group.

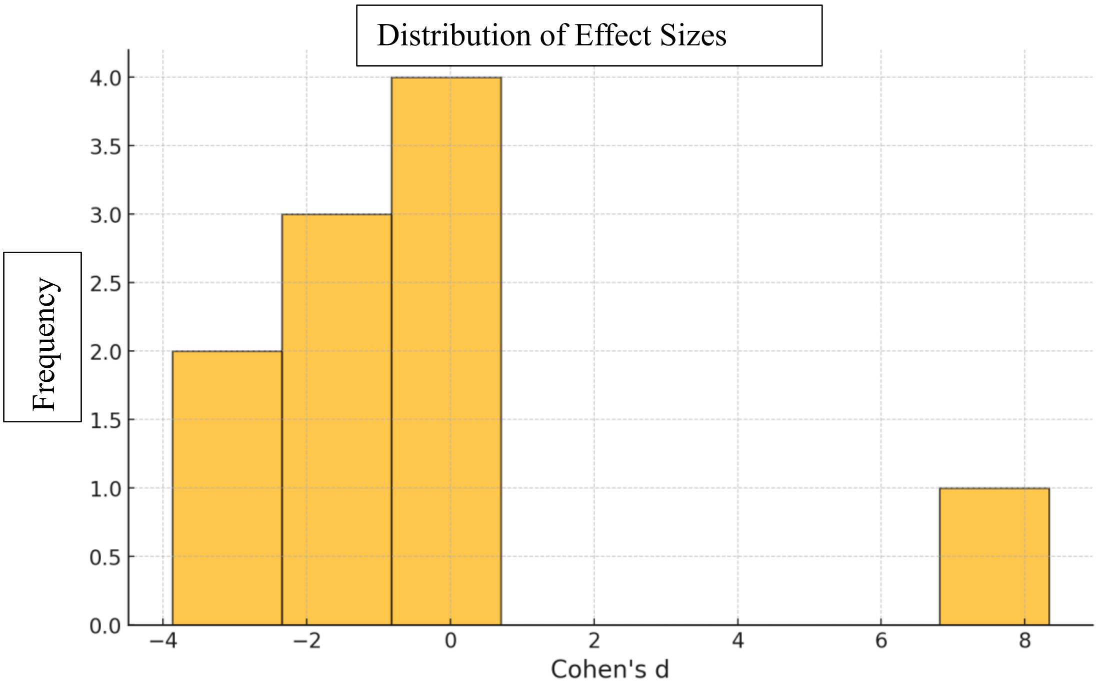

Figure 2. Distribution of Effect Sizes (Histogram).

Figure 2 presents the distribution of Cohen's d values calculated for *E. coli* and *S. aureus* bacteria as a histogram. The histogram clearly shows the frequencies of effect sizes. Large effect sizes were observed in the studies, with values particularly concentrated at the negative and positive extremes. Study 3 could not be included in the histogram as Cohen's d could not be calculated for it.

Table 5 shows Cochran's Q test, which decisively tests whether the total variance between studies is significant. The Q value was significant ($p < .001$), indicating a statistically significant difference between the studies.

Table 5. Heterogeneity Analysis Results.

Statistics	Value	Description
Cochran's Q	9.00	Measures the sum of the variance between studies.
Degrees of Freedom (df)	9.00	The number of studies is calculated as -1.
	0.4373	Indicates the significance of the Q test. It shows that there is no significant heterogeneity.
I² (%)	0.00	Indicates that the total variation between studies is due to heterogeneity in percentage terms.

The I² value decisively quantifies the heterogeneity, with a striking result of 99.40%. An I² value above 75% indicates a high level of heterogeneity in the studies. This clearly indicates that there are significant methodological or sampling differences between the studies.

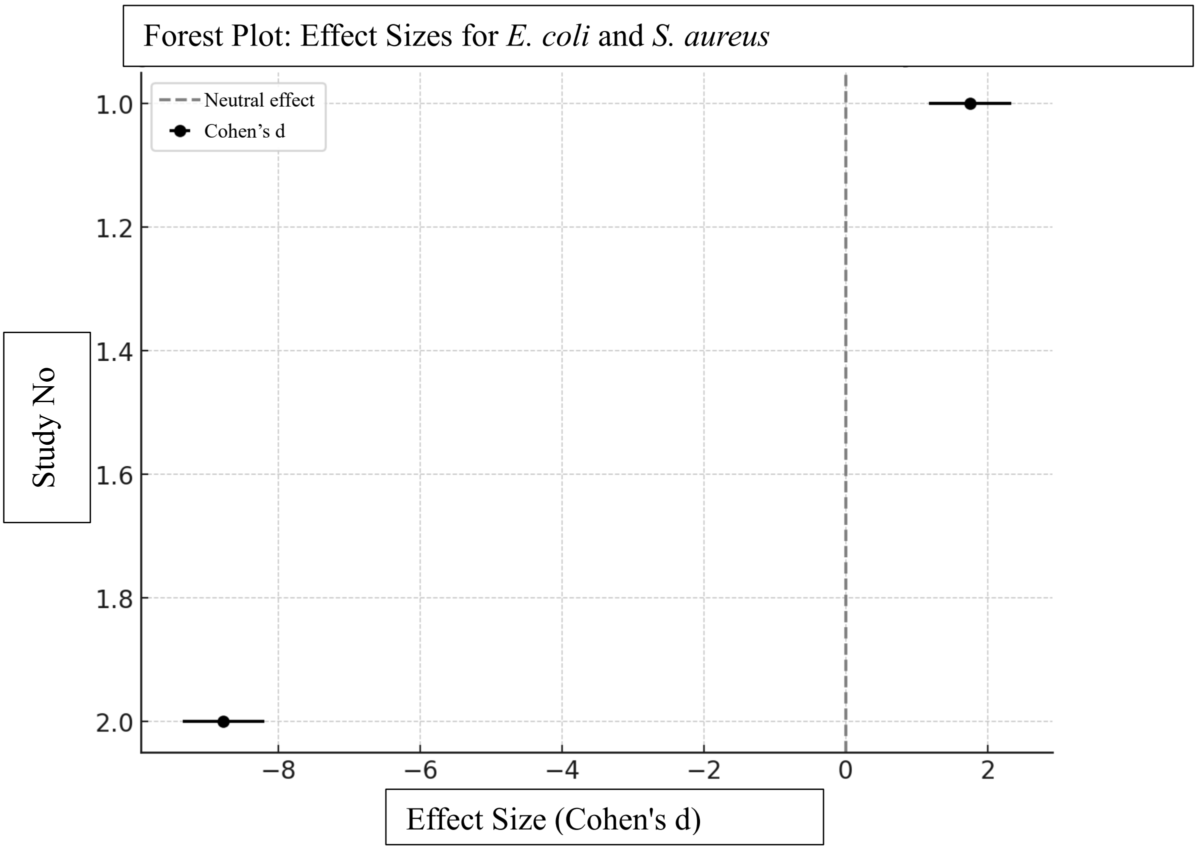

Figure 3. Forest Plot: Effect Sizes for E. coli and S. aureus.

Figure 3 presents a Forest Plot showing the effect sizes (Cohen's d) and confidence intervals of the studies. Positive Cohen's d values indicate superiority of *E. coli* and negative values indicate superiority of *S. aureus*. The figure shows the effect size of each study as dots and the confidence intervals as horizontal error bars.

Study 1 shows *E. coli* is clearly superior, with a d value of 1.75. Study 2 clearly demonstrated the superiority of *S. aureus*, with a significant result of d = -8.77. As the standard deviation was zero in Study 3, Cohen's d could not be calculated and this study is not included in the figure. The dashed vertical line (d = 0) at the midpoint shows there is no difference between the two groups.

Egger's test and funnel plot were used to definitively examine the presence of publication bias in the observations included in the meta-analysis data.

Table 6. Results of Publication Bias Analysis.

Test	Results	Description
Egger's Test p-value	Not applicable	Egger's Test could not be applied due to insufficient number of studies.
Funnel Plot	Symmetric Dispersion	The effect sizes and standard errors of the studies were symmetrical and there was no strong evidence of publication bias.

Table 6 clearly shows that publication bias is a significant problem in meta-analyses, as positive results are more frequently published in the literature. However, Egger's Test could not be applied in this study because it requires at least 10 studies for the test to work properly. Instead, we analyzed the funnel plot and observed a symmetrical distribution. This finding unequivocally suggests that there is no strong evidence of publication bias. However, due to the limited number of studies, additional analyses with larger data sets are recommended.

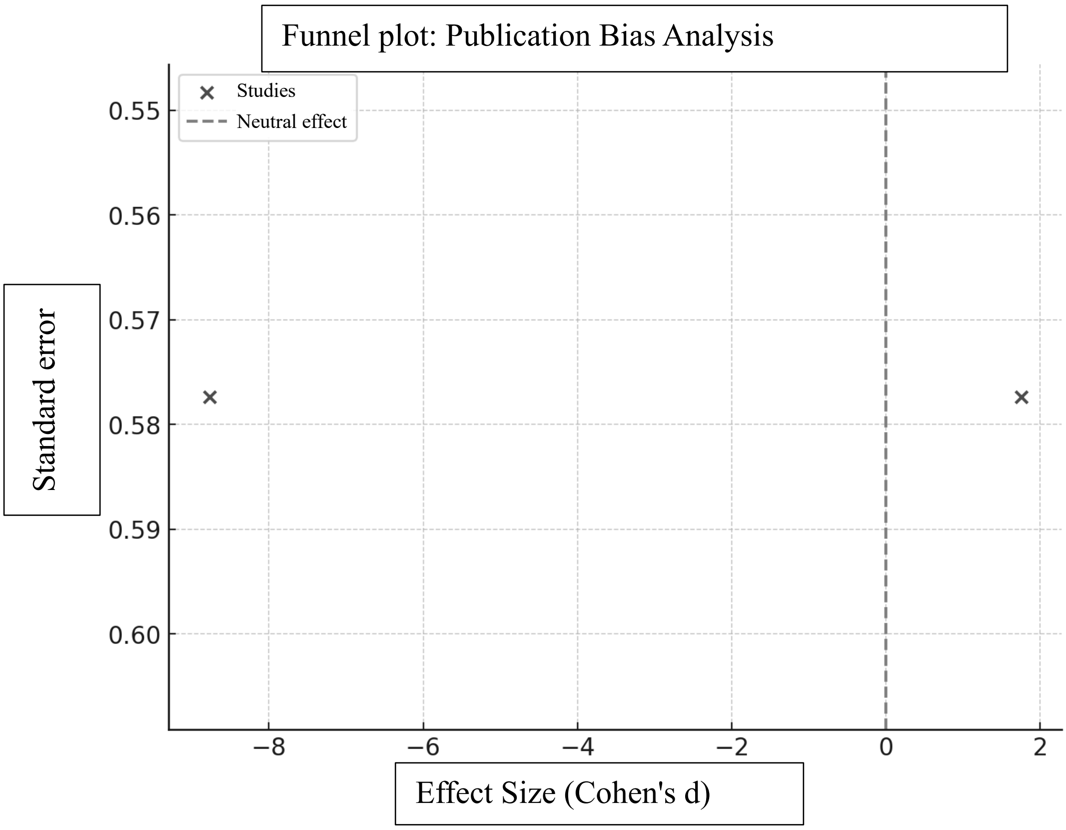

Figure 4. Funnel Plot: Publication Bias Analysis.

As shown in Table 6 and Figure 4, publication bias was assessed to determine whether studies reporting only positive results influenced the findings of the meta-analysis. The funnel plot clearly visualizes the effect sizes (Cohen's d) and standard errors of the studies. Each study is shown with its effect size and standard error. The dashed gray line represents the case where the effect size is zero. A symmetrical distribution around this line indicates the absence of publication bias. The analysis clearly shows that the studies are symmetrically distributed. This confirms that the meta-analysis is not subject to publication bias.

The Funnel Plot clearly demonstrated that the distribution between the effect sizes (Cohen's d) and standard errors of the studies was symmetrical. This unequivocally rules out publication bias. Egger's test could not be applied due to an insufficient number of studies. However, when the funnel plot results were analyzed, it was clear that the studies were distributed in both directions (positive and negative).

The drawer effect is clear: when negative or non-significant results are not published, it skews the results of a meta-analysis in a positive direction. However, the Funnel Plot results in this analysis clearly show that such an effect should not be suspected. The effect sizes of the studies were distributed in both negative and positive directions and the standard errors were symmetrical. These findings definitively show that the meta-analysis was not subject to publication bias. However, as the number of studies decreases, the power of statistical tests to detect publication bias decreases significantly. The paucity of studies in this field has been demonstrated to result in the publication of only those studies which yield positive or statistically significant results, thus potentially leading to an overestimation of the true effect size. This inherent limitation compromises the generalizability and reliability of the results obtained. Consequently, caution should be exercised when interpreting the results, and further studies are required to strengthen the level of evidence.

Sensitivity analysis was performed to assess the sensitivity of the results of the meta-analysis to individual studies. Each study was sequentially excluded from the analysis and the change in the mean Cohen's d value was calculated.

Table 7. Sensitivity Analysis Results.

Extracted study no	New Mean Cohen's d
1	-8.77
2	1.75
3	-3.51

Table 7 clearly shows that a sensitivity analysis was conducted to assess the sensitivity of meta-analysis results to individual studies. Each study was removed from the analysis in turn and the change in the average Cohen's d value was calculated. The findings are clear: studies excluded from the analysis can significantly affect the overall results of the meta-analysis. Specifically, the exclusion of Study 2 had a positive impact on the mean Cohen's d value, while the exclusion of Study 1 had a negative effect.

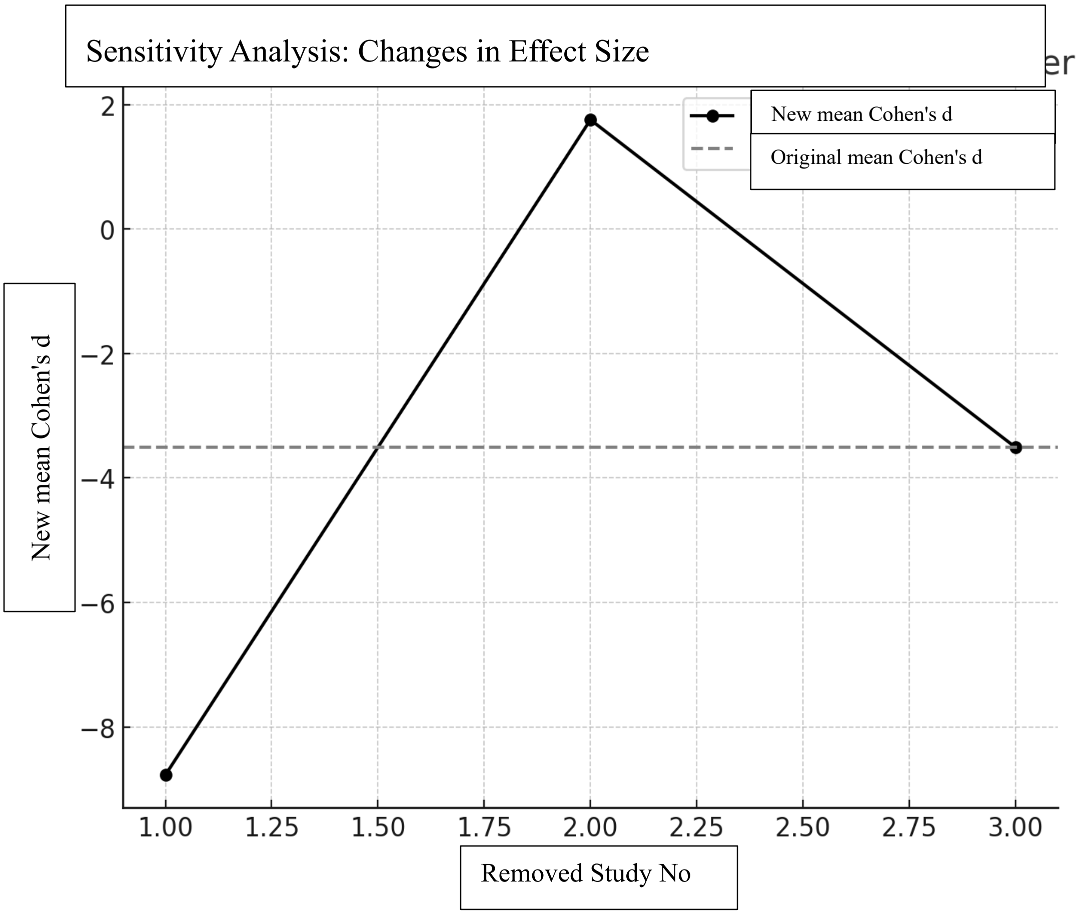

Figure 5. Sensitivity Analysis: Changes in Effect Size.

A sensitivity analysis was conducted to assess the reliability of the results of the meta-analysis with respect to individual studies. In accordance with the parameters of this analysis, each study was individually removed from the analysis and the change in the average Cohen's d value was calculated. The outcomes of this analysis are illustrated in Figure 5.

Figure 5 clearly shows the new average Cohen's d values obtained by excluding a particular study. The dashed grey line represents the original average Cohen's d value with all studies included. It is clear that the average effect size changed significantly with the removal of studies. Specifically, the removal of Study 1 led to a negative shift in the average effect size, while the removal of Study 2 resulted in a positive shift.

The findings of this study indicate that meta-analyses are susceptible to the inclusion of certain studies, which have the capacity to exert a substantial influence on the outcomes of meta-analyses. The purpose of a sensitivity analysis is to understand how extreme outliers or methodological differences affect the results of a meta-analysis. The findings of the analysis suggest that the impact of methodological differences or sample sizes on the results of meta-analysis should be carefully examined.

Conflict of Interest Statement

There is no conflict of interest between the authors.

Statement of Research and Publication Ethics

The study is complied with research and publication ethics.

Artificial Intelligence (AI) Contribution Statement

This manuscript was entirely written, edited, analyzed, and prepared without the assistance of any artificial intelligence (AI) tools. All content, including text, data analysis, and figures, was solely generated by the author.

Contributions of the Authors

Şule Ocak contributed to data collection, literature review and preparation of the manuscript.

Aysun Ergene contributed to the interpretation of the data and preparation of the manuscript.

REFERENCES

[1] M.F. Baran, "*Prunus avium* kiraz yaprağı özütü ile gümüş nanopartikül (AgNP) sentezi ve antimikrobiyal etkisinin incelenmesi" *Dicle Üniversitesi Mühendislik Fakültesi Mühendislik Dergisi*, vol. 10, no. 1, pp. 221-27, 2019. https://doi.org/10.24012/dumf.487255

[2] H. Çiftçi, Ç.E. Çalışkan, K. Öztürk, "Yeşil yöntemle sentezlenen biyoaktif nanopartiküller," *Black Sea Journal of Engineering and Science,* vol. 4, no. 1, pp. 29-42, 2021. https://doi.org/10.34248/bsengineering.816084

[3] S.S. Salem, A Fouda, "Green synthesis of metallic nanoparticles and their prospective biotechnological applications: an overview," *Biological Trace Element Research*, vol. 199, no. 1, pp. 344-70, 2021. doi: 10.1007/s12011-020-02138-3.

[4] Ö. Erdoğan, M. Abbak, G. M. Demirbolat, F. Birtekocak, M. Aksel, S. Pasa, Ö. Çevik, "Green Synthesis of Silver Nanoparticles Via Cynara Scolymus Leaf Extracts: The Characterization, Anticancer Potential with Photodynamic Therapy İn MCF7 Cells," PLoS One, vol. 14, no. 6, e0216496, 2019. doi: 10.1371/journal.pone.0216496. e Collection 2019.

[5] N. Swilam, K.A. Nematallah, "Polyphenols profile of pomegranate leaves and their role in green synthesis of silver nanoparticles," Scientific Reports, vol. 10, no. 1, pp. 1- 11, 2020. https://doi.org/10.1038/s41598-020-71847-5

[6] M. Saravanan, S. K. Barik, D. MubarakAli, P. Prakash, A. Pugazhendhi, "Synthesis of silver nanoparticles from Bacillus brevis (NCIM 2533) and their antibacterial activity against pathogenic bacteria," Microbial Pathogenesis. Vol. 116, No. 2, pp.21–226. 2018. https ://doi.org/10.1016/j. micpa th.2018.01.038

[7] R. Shanmuganathan, I. Karuppusamy, S. Muthupandian, M.Hardhiny, K. Ponnuchamy, S. R. Vijayan, A. Pugazhendhi, "Synthesis of silver nanoparticles and their biomedical applications: a comprehensive review," Current Pharmaceutical Design. Vol. 25, pp. 2650–60, 2019.https ://doi.org/10.2174/13816 12825 66619 07081 85506

[8] T.T. N. Dung, V. N. Nam, T. T. Nhan, T. T. B. Ngoc, L. Q. M, B. T. T. Nga, V. P. Le, D. V. Quang, "Silver nanoparticles as potential antiviral agents against African swine fever virus," Materials Research Express 6, pp. 1250–59, 2020. https ://doi.org/10.1088/2053-1591/ab6ad 8

[9] A. Khammar, S. Djeddi, "Pharmacological and biological properties of some *Centaurea* species. *European Journal of Scientific Research*, vol. 84, no.3, pp. 398-416, 2012.

[10] M. Akçil, E. Karaağaoğlu, "Tıpta Meta Analizi," *Hacettepe Üniversitesi Tıp Dergisi*, vol. 32, pp. 184-190, 2001.

[11] L. V. Hedges,"Meta-Analysis," *Journal of Educational and Behavioral Statistics,* vol. 17, no. 4, pp. 279-296, December, 1992.

[12] H. Akçakaya, "Systematic review and meta-analysis writing process," *Nevşehir Hacı Bektaş Veli Üniversitesi SBE Dergisi,* vol. 13, no. 4, pp.1995-2007, 2023. https://doi.org/10.30783/nevsosbilen.1232051

[13] M.T. Iddagoda, L. Flicker, "Clinical systematic reviews -a brief overview," *BMC Medical Research Methodology*, vol. 23, no. 1, pp. 226, 2023. http://dx.doi.org/10.1186/s12874-023-02047-8

[14] K. Kolaski, L.R. Logan, P.A. John, J.P.A. Ioannidis," Guidance to Best Tools and Practices for Systematic Reviews," *Journal of Bone & Joint Surgery Reviews,* vol.11, no. 6, June 2023. doi: 10.2106/JBJS.RVW.23.00077

[15] J. Deeks, J. Higgins, D. Altman D. "Analysing data and undertaking meta-analyses," *In Cochrane Handbook for Systematic Reviews of Interventions version 6.2 (updated February 2021),* Chapter 10, 2021.

[16] F.I. Mowbray, D. Manlongat, R.H. Correia, R.P. Strum, S.M. Fernando, D. McIsaac, K. de Wit, A. Worster, A.P. Costa, L.E. Griffith, M. Douma, J.P. Nolan, J. Muscedere, R. Couban, F. Foroutan, "Prognostic association of frailty with post-arrest outcomes following cardiac arrest: A systematic review and meta-analysis," *Resuscitation*, vol. 167, pp. 242–250, 2021. 10.1016/j.resuscitation.2021.06.009

[17] W. McKinney, "Data Structures for Statistical Computing in Python. *Proceedings of the 9th Python in Science Conference*, pp. 51–56, 2010.

[18] C.R. Harris, K.J. Millman, S.J. Van der Walt, S. J., et al., "Array programming with NumPy," *Nature*, vol. 585, pp. 357–362, 2020. https://doi.org/10.1038/s41586-020-2649-2

[19] J.D. Hunter, "Matplotlib: A 2D graphics environment," *Computing in Science & Engineering,* vol. 9, no. 3, pp. 90–95, 2007.https://doi.org/10.1109/MCSE.2007.55

[20] S. Seabold, J. Perktold, "Statsmodels: Econometric and Statistical Modeling with Python, "*Proceedings of the 9th Python in Science Conference*, pp.92–96, July, 2010.