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OPEN PEER REVIEW

Study One-Pot Synthesis of Nanoparticles Omeprazole-Silver and Omeprazole Sulfide-Silver and Their Antibacterial Properties

Arezoo Ravanan, Nosrat Mahmoodi, Bahman Sharifzadeh, Atefeh Ghavidast, Maryam Mohammadbeigi, Fahime Majlesi

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About this report

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1 Original submission

2 comments · 24 Jul 2024 – 26 Jul 2024

Mohammad Mahdi Zangeneh Reviewer

MAJOR REVISION 24 Jul 2024

Dear authors.
The recent manuscript has been written, and the following comments need to be addressed before acceptance in the "Jundishapur Journal of Natural Pharmaceutical Products":
Title:
Don't use abbreviations in the title.
The title is short.

Abstract:
Please define the following abbreviations:
TEM
FT-IR
DRS
XRD
What is the average size of the nanoparticles? Please mention it in the Abstract.
Mention the results of UV-Vis in the Abstract.
The Conclusion section of the Abstract is weak.

Keywords
Enhance the Keywords.

Introduction
The objectives and aim of the Introduction are weak.
Talk more about the antibacterial efficacies of silver nanoparticles in the Introduction.
Improve the third paragraph of the Introduction.

Methods and Materials
Add the Materials section to this part.
The Chemical characterization section should include more details.
Please explain the following section in more detail:
The Synthesis of NPs Whit Omeprazole and Omeprazole Sulfid (One-Put)
Add the Statistical analysis section to this part.

Results
Explain all results in more detail.
Show the peaks on the UV-Vis diagrams.
Add the FT-IR results.
Increase the resolution of Figure 6.
Rewrite the following sentence:
"In another experiment, according to what can be seen in Figure 6a, 6b and 6c following the cultivation of bacteria on a pure agar medium, the synthesized products, namely silver-omeprazole and silver-omeprazole sulfide, were cultured on agar medium. While the combination of silver and the drug resulted in limited growth in certain instances and no growth in others, as depicted in the accompanying images"

Discussion
This part is so weak. All data from this study must be thoroughly compared with those from previous studies.

Conclusion
I can't see the conclusion section.
Add sentences related to suggestions for future studies.
Add sentences related to future prospects.
Add sentences related to the limitations.

References
All references must be prepared according to the style of the journal.
The number of references for an original article is so low. Please use articles published in the "Jundishapur Journal of Natural Pharmaceutical Products" related to the antibacterial efficacies of silver nanoparticles.

I suggest that an English language professor read the manuscript and correct all grammatical errors.

Referee 1 Reviewer

MAJOR REVISION 26 Jul 2024

Dear Editor
Have a nice day.
The author studied the synthesis of Omeprazole@AgNPs and Omeprazole sulfide@AgNPs and considered their antibacterial properties.
I would suggest reconsidering the manuscript for publication only after the following major revision. It should be completely restructured to be published.
1. A DLS test is necessary for the synthesized nanoparticles.
2. The method of synthesis should be described in the abstract section.
3. Figure 1 should be modified for omeprazole and omeprazole sulfide.
4. The proposed mechanism is required for the synthesis pathway.
5. What is the role of PVP in the synthesis process?
6. The antibacterial effects of silver nanoparticles should be evaluated.
7. In the antibacterial test, the effect of the solvent must be evaluated.

2

Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Manuscript ID: 150851

Answer to reviewers

Answer:
Dear referee
Thank you for reading my article. I tried to fix all the bugs you mentioned.
I changed the title of the article and corrected the abbreviations and changes in the abstract.
Added details for results section.
Representation of peaks in UV-Vis plots: highlighted in red.
FT-IR is wrongly mentioned in the article and omitted from the text.
Rewrite the following sentence: Done..
In another experiment, the synthesized products, i.e., omeprazole silver and omeprazole silver sulfide, were cultured on agar medium, as seen in Figures 6a, 6b, and 6c following bacterial culture on pure agar medium. while the combination of silver and drug resulted in limited growth in certain cases and no growth in others, as shown in the accompanying figures.
Discussion
In this section, I tried to enter the data and the result of the review in a summary form and tried to make changes in it according to your opinion.
I have given the answers to other questions as follows and in full detail in the following text:

Reviewer 1:

Title:
Don’t use the abbreviation words in the Title.
Title is short.

Answer:
Title is corrected as bellow:
Study one-pot synthesis of nanoparticles omeprazole-silver and omeprazole sulfide-silver and their antibacterial properties

Abstract:
Please describe the following abbreviation words:
TEM
FT-IR
DRS
XRD

Answer:
Title is corrected as bellow:
the synthesis of omeprazole and omeprazole sulfide drugs was completed on silver nanoparticles and the resulting nanoparticles were characterized by transmission electron microscopy (TEM), diffuse reflectance spectroscopy (DRS), Fourier

Transform Infrared Spectrometer (FT-IR) and X-ray Diffraction (XRD) was investigated and the results were reported.

What is average size of nanoparticles? Please mention in Abstract.

Answer:
Briefly, the size of omeprazole nanoparticles is less than 40 nm and the length of omeprazole sulfide nanoparticles is less than 60 nm.

Mention the results of UV-Vis in Abstract.

Answer:
In the UV_Vis spectrum have been observed that The pure Omps appear as λmax at 400 nm corresponding to the n→η* motion of the S-Omps molecule, while the Ag@Omps arrangement appears as λmax at 300 nm.

Conclusion section of Abstract part is weak.
Answer:
is corrected as bellow:
the green synthesis of silver nanoparticles with omeprazole and omeprazole sulfide has been investigated for their antibacterial properties. The nanoparticles were characterized using various techniques. The results indicate that the size of omeprazole nanoparticles is less than 40 nm, while the length of omeprazole sulfide nanoparticles is less than 60 nm. The omeprazole@AgNPs (Ag@Omp) and omeprazole sulfide@AgNPs (Ag@Omps) have shown antibacterial properties, with the UV-Vis spectrum showing distinct peaks for the different arrangements. Overall, the study demonstrates the potential of utilizing silver nanoparticles in combination with omeprazole and omeprazole sulfide for enhanced antibacterial activities.

Keywords
Enhance the Keywords.

Answer:
Green synthesis, Nanocrystalline silver particles, Omeprazole, Omeprazole sulfide, Antibacterial properties, Characterization techniques, Drug-delivery systems

Introduction

Objectives and aim of the Introduction is weak.
Talk more about the antibacterial efficacies of silver nanoparticles in Introduction.
Ameliorate the third paragraph of Introduction.
Answer:

specific goal of precisely controlling atoms and molecules to create products on a larger scale. Nanoparticles use chemical processes including dangerous chemicals (2), and reducing agents, and by reducing the size of the material to the nanoscale, various properties such as melting point, chemical properties, boiling temperature, magnetic properties, light absorption, catalytic activity, and thermal conductivity are changed.

Silver nanoparticles (AgNPs) are an important class of nanomaterials with diverse applications in both industrial and biomedical sectors. The distinct chemical properties of AgNPs make them a potential method for drug delivery to specific cells or genes. The increasing use of silver nanoparticles as drug carriers, with their reliable antibacterial properties, emphasizes their importance. In addition, advances in synthetic techniques for drug preparation with nanoparticles are also discussed in this context.

The purpose of this reading is to investigate and synthesize medicine with the help of silver nanoparticles and have a better effect on the body. In addition, with the progress of science, the use of various drugs to treat diseases has decreased due to side effects, and medical science is looking for new solutions such as drug carriers.

Green synthesis of reactive silver nanoparticles together with omeprazole and omeprazole sulfide. Synthesized silver nanoparticles were characterized by different analytical tools, and in the end, antibacterial properties were tested in different situations.

Methods and Materials
Add the Materials section to this part.
Chemical characterization section should be mention with more details.
Please explain more the following section:
The Synthesis of NPs Whit Omeprazole and Omeprazole Sulfid (One-Put)
Add the Statistical analysis section to this part.

Answer:

The Synthesis of NPs Whit Omeprazole and Omeprazole Sulfid (One-Put)

A solution containing 0.082 g of $AgNO_3$ in 10 mL of water was combined with 0.03 g of PVP in 5 mL of water. This mixture was then placed in an ice bath for 30 minutes. Subsequently, the solution was removed from the ice bath, and 0.018 g of $NaBH_4$ was added drop by drop to the solution over a period of 30 minutes. This resulted in a sudden color change from yellow to brown and black. After the complete addition of $NaBH_4$, 0.331 mmol of Omeprazole in 10 mL of EtOH was introduced to the solution and allowed to react for 4 hours. Following the completion of the reaction time, the solution was centrifuged, washed with distilled water to remove impurities and excess EtOH. The resulting precipitate was separated, dried, and prepared for spectral analysis.

The resulting suspension was centrifuged at 10,000 rpm for 15 minutes, and the resulting precipitate was washed three times with double distilled water to eliminate any water-soluble impurities. Subsequently, the precipitate underwent three washes through dispersion and centrifugation using ethanol to remove any excess Omeprazole and reducing agent. The precipitate was then dried in an oven at 60°C for 10 hours, resulting in the acquisition of a pale grey powder.

Results
Explain with more details all results.
Show the peaks on the UV-Vis diagrams.
Add the FT-IR results.
Increase the resolution of Figure 6.
Rewrite the following sentence:
“In another experiment, according to what can be seen in Figure 6a, 6b and 6c following the cultivation of bacteria on a pure agar medium, the synthesized products, namely silver-omeprazole and silver-omeprazole sulfide, were cultured on agar medium. While the combination of silver and the drug resulted in limited growth in certain instances and no growth in others, as depicted in the accompanying images”

Reply

4.1. Fourier Transform Infrared Spectrometer (FT-IR)

The interaction of the drug omeprazole (OMP) with the surface of silver nanoparticles and the synthesis of Ag@OMP nanodrug were investigated by recording and comparing the Fourier transform infrared spectra of OMP and Ag@OMP. Figure 2 shows the infrared spectrum of OMP (lower-blue band) and Ag@OMP (upper-red band).

Figure 2. Fourier transform infrared spectrum of OMP (bottom-blue band) and Ag@OMP (top-red band)

The interaction of the drug omeprazole sulfide (OMPS) with the surface of silver nanoparticles and the synthesis of the nanodrug Ag@OMPS in Figure 3.

Figure 3. Fourier transform infrared spectrum of OMPS (bottom blue bar) and Ag@OMPS (top red bar).

Also, the interaction of the two drugs OMPS and OMPS with the surface of silver nanoparticles and the synthesis of Ag@OMP-OMPS nano drug was investigated by recording the Fourier transform infrared spectrum (Figure 4).

Figure 4. Fourier transform infrared spectrum of Ag@OMP-OMPS

Therefore, in Figures 2, 3 and 4, the appearance of similar signals with a change in their position and intensity proves the successful binding of drugs to the surface of silver nanoparticles and is recorded in the table below (Table 1).

4.2. X-Ray Diffraction

The powder X-ray diffraction (XRD) patterns of Ag@Omp (a) and Ag@Omps (b) are depicted in Figure 5. In Figure 5a, the peak position at 2θ = 38˚-80˚ corresponds well with Ag@Omprazole. In Figure 2b, the distinctive peaks of AgNPs were observed at 2θ = 38˚-80˚, identified as (111), (200), and (220) reflection lines of the face-centered cubic (fcc) structure of metallic silver. The average crystallite size, D, was determined using Scherrer's equation to be 58 nm in Ag@Omp (5a) and 28 nm in Ag@Omps (5b), where D = Kλ/(β cosθ), with λ representing the wavelength of Cu-Kα radiation used (λ = 1.54 Å), β as the full width at half maximum (0.31) of the diffraction peak, θ as the Bragg angle for the measured peak, and K as a constant equal to 0.94. This value aligns well with the TEM image. The intensity of peaks indicates the high degree of crystallinity of the AgNPs.

Figure 5. X-ray diffraction patterns of the (a) Ag@Omp and (b) Ag@Omps.

4.2. UV-Vis Absorption Spectra

Figure 6, outlines the UV-Vis assimilation spectra of Ag@Omp and Ag@Omps in EtOH arrangement. The pure Omp appears as a λmax at 400 nm corresponding to the n→η* move of the molecule O-Omp, while a solution of Ag@Omp appears as a λmax at 300 nm retention surface plasmon reverberation retention band (SPRAB) of AgNPs, individually. also, the pure Omps appears as a λmax at 400 nm corresponding to the n→η* move of the molecule S-Omps, whereas an arrangement of Ag@Omps appears as a λmax at 300 nm.

Figure 6. UV-Vis absorption spectra of Ag@Omp and Ag@Omps , Ag@Omp-Omps.

Within the final shap, UV-Vis assimilation spectra of Ag@Omp-Omps in EtOH arrangement. shows a λmax at 400 nm compared to the n→η* move of the molecule O-Omp and S-Omps assimilation surface plasmon reverberation retention band (SPRAB) of AgNPs. with compared to the assimilation band of free drugs at 400 nm, affirms a lower concentration of drugs on AgNPs. The appearance of two new peaks at 300 nm is related to the Ag-Drugs complex.

5.3. Transmission Electron Microscopy (TEM)

The TEM of Ag@Omp (fig 7a,b) image reveals that particles are spherical shape with approximate size of <40 nm; Scherrer’s calc. = 28 nm.

Figure 7. TEM image of the (a,b) Ag@Omp , (c,d) Ag@Omps.

The TEM of Ag@Omps (fig 7c,d) image reveals that particles are spherical shape with approximate size of <60 nm; Scherrer’s calc. = 58 nm.

6.4. Antibacterial Properties

In the experiment, Agar Mueller Hinton, tubes containing half McFarland, tubes containing DMSO, antibiogram discs, and pure bacteria in a suitable culture medium were utilized. The process involved using a swab, loop, flame, hood, and lamp. The bacteria strains Pseudomonas, Staphylococcus, E. coli, Bacillus, Enterococcus, and

Micrococcus were employed. Various studies have investigated the therapeutic effects of omeprazole in combination with antibiotics for patients with duodenal ulcers and Helicobacter pylori infection(16).

In this particular study, the antibacterial activities of Ag@Omp, Ag@Omps, and Ag@Omp-Omps were assessed using the MIC and disc diffusion methods.

4.4.1. Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC)

To prepare the drug reference tube, 1 g of Ag@Omp was dispersed in 5 ml of DMSO. For determining the Minimum Inhibitory Concentration (MIC), ten tubes containing 1 ml of Trypticase Soy Broth (TSB) were used. Initially, 1 ml of the drug reference tube was added to the first tube. Subsequently, 1 ml from the first tube was transferred to the second tube, and this process was repeated until the tenth tube, from which the final 1 ml was selected. Each tube was then inoculated with 5×105 -106 (CFU)/ml colony-forming units of bacteria and incubated at 37°C for 18-24 hours(17).

Gram-positive bacteria (Staphylococcus aureus ATCC27853, Bacillus subtilis ATCC1715, Micrococcus luteus ATCC1408) and gram-negative bacteria (Pseudomonas aeruginosa ATCC1310, Escherichia coli ATCC25922, and Enterococcus faecalis ATCC29212) were used in this experiment. Subsequently, each tube was streaked and incubated on an agar plate at 37°C for 18-24 hours. Due to the turbidity observed in the test tubes during the MIC and MBC methods, making it difficult to determine the lowest drug concentration inhibiting bacterial growth, the results obtained from this test were presented in the form of a graph or report. The results of these tests can be seen in Figure 8a and 8b.

Figure 8. Growth of bacteria in the presence of pure omeprazole(a), pure omeprazole sulfide(b)

In another experiment, according to what can be seen in Figures 9a, 9b, and 9c, following the cultivation of bacteria in pure agar medium, silver omeprazole and silver omeprazole sulfide were added to the agar medium. The combination of silver and the drug leads to limited growth in certain cases of non-growth in other media of the bacteria, as shown in the accompanying images.

Discussion

This part is so weak. All data of this study must be compared with the previous studies completely.

5. Discussion

At a glance, the synthesis of silver nanoparticles with the drugs omeprazole and omeprazole sulfide was successful, demonstrating enhanced antibacterial properties and improved drug characteristics. Omeprazole sulfide exhibited superior antibacterial properties compared to omeprazole silver, with the combination of both drugs showing moderate effectiveness.

The study revealed that the drugs alone did not possess antibacterial effects, but when combined with nano-silver, they exhibited enhanced efficacy.

The interaction of the drug omeprazole (OMP) with the surface of silver nanoparticles and the synthesis of Ag@OMP nanodrug were investigated by recording and comparing the Fourier transform infrared spectra of OMP and Ag@OMP. (lower-blue band) and Ag@OMP (upper-red band). also the interaction of the drug omeprazole sulfide (OMPS) with the surface of silver nanoparticles and the synthesis of the nanodrug Ag@OMPS in Figures 2, 3 and 4, the appearance of similar signals with a change in their position and intensity proves the successful binding of drugs to the surface of silver nanoparticles. The powder X-ray diffraction (XRD) patterns of Ag@Omp (a) and Ag@Omps (b) are depicted the peak position at $2\theta = 38^{\circ}$-80° corresponds well with Ag@Omprazole.

the distinctive peaks of AgNPs were observed at $2\theta = 38^{\circ}$-80°, identified as (111), (200), and (220) reflection lines of the face-centered cubic (fcc) structure of metallic silver.

The TEM of Ag@Omps image reveals that particles are spherical shape with approximate size of <60 nm; Scherrer’s calc. = 58 nm.

These experiments showcase the potential for developing new nano-drugs and enhancing the antimicrobial properties of existing medications, aligning with advancements in nanomedicine production and aiding in the treatment of various medical conditions.

Conclusion
I can’t see the conclusion section
Add the sentences related to the suggestion for the future studies.
Add the sentences related to the future prospective.
Add the sentences related to the limitations.

6. Conclusions

the green synthesis of silver nanoparticles with omeprazole and omeprazole sulfide has been investigated for their antibacterial properties. The nanoparticles were characterized using various techniques. The results indicate that the size of omeprazole nanoparticles is less than 40 nm, while the length of omeprazole sulfide nanoparticles is less than 60 nm. The omeprazole@AgNPs (Ag@Omp) and omeprazole sulfide@AgNPs (Ag@Omps) have shown antibacterial properties, with the UV-Vis spectrum showing distinct peaks for the different arrangements. Overall, the study demonstrates the potential of utilizing silver nanoparticles in combination with omeprazole and omeprazole sulfide for enhanced antibacterial activities.

References
All references must be prepared according to the style of journal.
The number of references for an original article is so low. Please use the articles published in the “Jundishapur Journal of Natural Pharmaceutical Products” related to the antibacterial efficacies of silver nanoparticles.

Refernce

It’s reviewed and correct as Vanover citation method

I suggest that an English language professor read and edited all grammatical errors of this manuscript.

It is corrected.

Reviewer 2:
Hi
Dear Editor
The manuscript is approved and the following corrections are made
1.Check the reaction mechanism
2. Calculate the reaction efficiency
3. FT-IR spectrum should be taken and interpreted

4. SEM should be taken and interpreted
5. Elemental analysis should be taken
6. What did you do to optimize this reaction and increase efficiency?
7. Many works have been done in this field, what is the reason for its innovation?

Answer:

Dear referee 2

This mechanism was prepared by my supervisor, Mr. Dr. Nosratollah Mahmoodi, according to him, the mechanism is easier and easier to understand than the synthesis process.

2. Calculate the yield of the reaction

yield of 92 % is calculated and writed.

3. FT-IR spectrum should be taken and interpreted:

added

4. SEM should be taken and interpreted:

the synthesis product was low and not sufficient for investigation in all areas.

5. Elemental analysis should be done

the synthesis product was low and not sufficient for investigation in all areas.

6. What did you do to optimize this reaction and increase efficiency?

In order to optimize the reaction and bring the reaction process closer to green synthesis, the use of plant extracts instead of Na B H 4 has been the continuation of this study, which has been published in another journal. To read more, you can read with the following ID: https://doi.org/10.22034/ijnc.2023.2011981.1359

7. A lot of work has been done in this field, what is the reason for its innovation?

Perhaps it can be said that the use of nanotechnology as drug carriers, which is widely used in the treatment of diseases today, was the reason for this study.

Reviewer 3:
answer:

Dear Judge 3:

Thanks for reading my article and have a nice day.

1. DLS testing is necessary for synthesized nanoparticles:
   due to the lack of the final product, it was not possible to perform all the tests in question.
2. The synthesis method should be explained in the abstract section:
   done.

3. Figure 1 should be revised for omeprazole and omeprazole sulfide:
   the drug figure was omitted.
4. Proposed mechanism required for the synthesis route:
   The mechanism is shown in scheme 1 and this mechanism was prepared by my supervisor, Mr. Dr. Nosratollah Mahmoodi, according to him, the mechanism is easier and easier to understand than the synthesis process.
5. What is the role of PVP in the synthesis process?
   It was to prevent clumping of the final product.
6. Antibacterial effects of silver nanoparticles should be evaluated.
   In some articles, the antibacterial effect of silver nanoparticles was investigated, and this study continued the synthesis based on them.
7. The effect of the solvent must be evaluated in the antibacterial test.
   In the antibacterial test, since the general goal was to show the antibacterial effects of the drug with and without silver nanoparticles, an ineffective solvent was used as a result.

With the best regard

2 Revision 1

1 comment · 24 Aug 2024

Referee 1 Reviewer

REJECT 24 Aug 2024

Dear Editor
Have a nice day.
The authors investigated the one-pot synthesis of omeprazole-silver and omeprazole sulfide-silver nanoparticles and their antibacterial properties.
In my opinion, this manuscript cannot be considered for publication, because the comments have not been properly reviewed.

3

Revision 2

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Manuscript ID: 150851

Answer to reviewer 2

Reviewer 2:
Hi
Dear Editor
The manuscript is approved and the following corrections are made
1.Check the reaction mechanism
2. Calculate the reaction efficiency
3. FT-IR spectrum should be taken and interpreted
4. SEM should be taken and interpreted
5. Elemental analysis should be taken
6. What did you do to optimize this reaction and increase efficiency?
7. Many works have been done in this field, what is the reason for its innovation?

Answer:

Dear referee

The requested changes have been modified in the text of the article according to your opinion and inserted in purple color. It is hoped that it will be approved by your Excellency.

1.Check the reaction mechanism

A proposed mechanism for the synthesis of Omeprazole sulfide@AgNPs actonization starts by electrophilic reaction with Ag+ and oxygen's polyvinylpyrrolidone that generating the zwitterionic intermediate. NaBH4 as a Blocking agent prevent from nxt accumulation. This zwitterionic intermediate ready to place its silver ion in a one-way reaction as an electrophile to the sulfur of omeprazole. And finally, the silver popper bond is formed in the final product.

2. Calculate the yield of the reaction

yield of 92 % is calculated and writed.

3. FT-IR spectrum should be taken and interpreted:

It was added in the main file of the article at the time of modification.

4. SEM should be taken and interpreted:

According to your opinion, it was said that the SEM spectrum should be taken, the truth is that the synthesis was not enough and it was not enough to examine all the areas and also the size of the particles in this reaction was important for it. We solved it with the same TEM spectrum.

5. Elemental analysis should be done

the synthesis product was low and not sufficient for investigation in all areas.

6. What did you do to optimize this reaction and increase efficiency?

In order to optimize the reaction and bring the reaction process closer to green synthesis, the use of plant extracts instead of $NaBH_4$ has been the continuation of this study, which has been published in another journal. To read more, you can read with the following ID: https://doi.org/10.22034/ijnc.2023.2011981.1359

7. A lot of work has been done in this field, what is the reason for its innovation?

It can be said that the use of nanotechnology as a drug carrier is widely used in the treatment of diseases. Also, using a nanoparticle as a carrier to carry multiple drugs and reduce the use of different drugs separately to treat diseases. This study can be a prerequisite for more extensive studies on multidrug carriers.

With the best regard

Manuscript ID: 150851

Answer to reviewer 1

Reviewer 1:

Title:
Don’t use the abbreviation words in the Title.
Title is short.

Answer:
Title is corrected as bellow:
Study one-pot synthesis of nanoparticles omeprazole-silver and omeprazole sulfide-silver and their antibacterial properties

Abstract:
Please describe the following abbreviation words:
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FT-IR
DRS
XRD

Answer:
Title is corrected as bellow:
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What is average size of nanoparticles? Please mention in Abstract.

Answer:
Briefly, the size of omeprazole nanoparticles is less than 40 nm and the length of omeprazole sulfide nanoparticles is less than 60 nm.

Mention the results of UV-Vis in Abstract.

Answer:
In the UV_Vis spectrum have been observed that The pure Omps appear as λmax at 400 nm corresponding to the n→η* motion of the S-Omps molecule, while the Ag@Omps arrangement appears as λmax at 300 nm.

Conclusion section of Abstract part is weak.
Answer:
is corrected as bellow:
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Keywords
Enhance the Keywords.

Answer:
Green synthesis, Nanocrystalline silver particles, Omeprazole, Omeprazole sulfide, Antibacterial properties, Characterization techniques, Drug-delivery systems

Introduction

Objectives and aim of the Introduction is weak.
Talk more about the antibacterial efficacies of silver nanoparticles in Introduction.
Ameliorate the third paragraph of Introduction.
Answer:
specific goal of precisely controlling atoms and molecules to create products on a larger scale. Nanoparticles use chemical processes including dangerous chemicals (2), and reducing agents, and by reducing the size of the material to the nanoscale, various properties such as melting point, chemical properties, boiling temperature, magnetic properties, light absorption, catalytic activity, and thermal conductivity are changed.

Silver nanoparticles (AgNPs) are an important class of nanomaterials with diverse applications in both industrial and biomedical sectors. The distinct chemical properties of AgNPs make them a potential method for drug delivery to specific cells or genes. The increasing use of silver nanoparticles as drug carriers, with their reliable antibacterial properties, emphasizes their importance. In addition, advances in synthetic techniques for drug preparation with nanoparticles are also discussed in this context.

The purpose of this reading is to investigate and synthesize medicine with the help of silver nanoparticles and have a better effect on the body. In addition, with the progress of science, the use of various drugs to treat diseases has decreased due to side effects, and medical science is looking for new solutions such as drug carriers.

Green synthesis of reactive silver nanoparticles together with omeprazole and omeprazole sulfide. Synthesized silver nanoparticles were characterized by different analytical tools, and in the end, antibacterial properties were tested in different situations.

Methods and Materials
Add the Materials section to this part.
Chemical characterization section should be mention with more details.
Please explain more the following section:
The Synthesis of NPs Whit Omeprazole and Omeprazole Sulfid (One-Put)
Add the Statistical analysis section to this part.

Answer:

The Synthesis of NPs Whit Omeprazole and Omeprazole Sulfid (One-Put)

A solution containing 0.082 g of $AgNO_3$ in 10 mL of water was combined with 0.03 g of PVP in 5 mL of water. This mixture was then placed in an ice bath for 30 minutes. Subsequently, the solution was removed from the ice bath, and 0.018 g of $NaBH_4$ was added drop by drop to the solution over a period of 30 minutes. This resulted in a sudden color change from yellow to brown and black. After the complete addition of $NaBH_4$, 0.331 mmol of Omeprazole in 10 mL of EtOH was introduced to the solution and allowed to react for 4 hours. Following the completion of the reaction time, the solution was centrifuged, washed with distilled water to remove impurities and excess EtOH. The resulting precipitate was separated, dried, and prepared for spectral analysis.

The resulting suspension was centrifuged at 10,000 rpm for 15 minutes, and the resulting precipitate was washed three times with double distilled water to eliminate any water-soluble impurities. Subsequently, the precipitate underwent three washes through dispersion and centrifugation using ethanol to remove any excess Omeprazole and reducing agent. The precipitate was then dried in an oven at 60°C for 10 hours, resulting in the acquisition of a pale grey powder.

Results
Explain with more details all results.
Show the peaks on the UV-Vis diagrams.
Add the FT-IR results.
Increase the resolution of Figure 6.
Rewrite the following sentence:
“In another experiment, according to what can be seen in Figure 6a, 6b and 6c following the cultivation of bacteria on a pure agar medium, the synthesized products, namely silver-omeprazole and silver-omeprazole sulfide, were cultured on agar medium. While the combination of silver and the drug resulted in limited growth in certain instances and no growth in others, as depicted in the accompanying images”

Reply

4.1. Fourier Transform Infrared Spectrometer (FT-IR)

The interaction of the drug omeprazole (OMP) with the surface of silver nanoparticles and the synthesis of Ag@OMP nanodrug were investigated by recording and comparing the Fourier transform infrared spectra of OMP and Ag@OMP. Figure 2 shows the infrared spectrum of OMP (lower-blue band) and Ag@OMP (upper-red band).

Figure 2. Fourier transform infrared spectrum of OMP (bottom-blue band) and Ag@OMP (top-red band)

The interaction of the drug omeprazole sulfide (OMPS) with the surface of silver nanoparticles and the synthesis of the nanodrug Ag@OMPS in Figure 3.

Figure 3. Fourier transform infrared spectrum of OMPS (bottom blue bar) and Ag@OMPS (top red bar).

Also, the interaction of the two drugs OMPS and OMPS with the surface of silver nanoparticles and the synthesis of Ag@OMP-OMPS nano drug was investigated by recording the Fourier transform infrared spectrum (Figure 4).

Figure 4. Fourier transform infrared spectrum of Ag@OMP-OMPS

Therefore, in Figures 2, 3 and 4, the appearance of similar signals with a change in their position and intensity proves the successful binding of drugs to the surface of silver nanoparticles and is recorded in the table below (Table 1).

4.2. X-Ray Diffraction

The powder X-ray diffraction (XRD) patterns of Ag@Omp (a) and Ag@Omps (b) are depicted in Figure 5. In Figure 5a, the peak position at $2\theta = 38^{\circ}$-80° corresponds well with Ag@Omprazole. In Figure 2b, the distinctive peaks of AgNPs were

observed at 2θ = 38˚-80˚, identified as (111), (200), and (220) reflection lines of the face-centered cubic (fcc) structure of metallic silver. The average crystallite size, D, was determined using Scherrer's equation to be 58 nm in Ag@Omp (5a) and 28 nm in Ag@Omps (5b), where D = Kλ/(β cosθ), with λ representing the wavelength of Cu-Kα radiation used (λ = 1.54 Å), β as the full width at half maximum (0.31) of the diffraction peak, θ as the Bragg angle for the measured peak, and K as a constant equal to 0.94. This value aligns well with the TEM image. The intensity of peaks indicates the high degree of crystallinity of the AgNPs.

Figure 5. X-ray diffraction patterns of the (a) Ag@Omp and (b) Ag@Omps.

4.2. UV-Vis Absorption Spectra

Figure 6, outlines the UV-Vis assimilation spectra of Ag@Omp and Ag@Omps in EtOH arrangement. The pure Omp appears as a λmax at 400 nm corresponding to the n→η* move of the molecule O-Omp, while a solution of Ag@Omp appears as a λmax at 300 nm retention surface plasmon reverberation retention band (SPRAB) of AgNPs, individually. also, the pure Omps appears as a λmax at 400 nm corresponding to the n→η* move of the molecule S-Omps, whereas an arrangement of Ag@Omps appears as a λmax at 300 nm.

Figure 6. UV-Vis absorption spectra of Ag@Omp and Ag@Omps , Ag@Omp-Omps.

Within the final shap, UV-Vis assimilation spectra of Ag@Omp-Omps in EtOH arrangement. shows a λmax at 400 nm compared to the n→η* move of the molecule O-Omp and S-Omps assimilation surface plasmon reverberation retention band (SPRAB) of AgNPs. with compared to the assimilation band of free drugs at 400 nm, affirms a lower concentration of drugs on AgNPs. The appearance of two new peaks at 300 nm is related to the Ag-Drugs complex.

5.3. Transmission Electron Microscopy (TEM)

The TEM of Ag@Omp (fig 7a,b) image reveals that particles are spherical shape with approximate size of <40 nm; Scherrer’s calc. = 28 nm.

Figure 7. TEM image of the (a,b) Ag@Omp , (c,d) Ag@Omps.

The TEM of Ag@Omps (fig 7c,d) image reveals that particles are spherical shape with approximate size of <60 nm; Scherrer’s calc. = 58 nm.

6.4. Antibacterial Properties

In the experiment, Agar Mueller Hinton, tubes containing half McFarland, tubes containing DMSO, antibiogram discs, and pure bacteria in a suitable culture medium were utilized. The process involved using a swab, loop, flame, hood, and lamp. The bacteria strains Pseudomonas, Staphylococcus, E. coli, Bacillus, Enterococcus, and Micrococcus were employed. Various studies have investigated the therapeutic effects of omeprazole in combination with antibiotics for patients with duodenal ulcers and Helicobacter pylori infection(16).

In this particular study, the antibacterial activities of Ag@Omp, Ag@Omps, and Ag@Omp-Omps were assessed using the MIC and disc diffusion methods.

4.4.1. Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC)

To prepare the drug reference tube, 1 g of Ag@Omp was dispersed in 5 ml of DMSO. For determining the Minimum Inhibitory Concentration (MIC), ten tubes containing 1 ml of Trypticase Soy Broth (TSB) were used. Initially, 1 ml of the drug reference tube was added to the first tube. Subsequently, 1 ml from the first tube was transferred to the second tube, and this process was repeated until the tenth tube, from which the final 1 ml was selected. Each tube was then inoculated with 5×105 -106 (CFU)/ml colony-forming units of bacteria and incubated at 37°C for 18-24 hours(17).

Gram-positive bacteria (Staphylococcus aureus ATCC27853, Bacillus subtilis ATCC1715, Micrococcus luteus ATCC1408) and gram-negative bacteria (Pseudomonas aeruginosa ATCC1310, Escherichia coli ATCC25922, and Enterococcus faecalis ATCC29212) were used in this experiment. Subsequently, each tube was streaked and incubated on an agar plate at 37°C for 18-24 hours. Due to the turbidity observed in the test tubes during the MIC and MBC methods, making it difficult to determine the lowest drug concentration inhibiting bacterial growth, the results obtained from this test were presented in the form of a graph or report. The results of these tests can be seen in Figure 8a and 8b.

Figure 8. Growth of bacteria in the presence of pure omeprazole(a), pure omeprazole sulfide(b)

In another experiment, according to what can be seen in Figures 9a, 9b, and 9c, following the cultivation of bacteria in pure agar medium, silver omeprazole and silver omeprazole sulfide were added to the agar medium. The combination of silver and the drug leads to limited growth in certain cases of non-growth in other media of the bacteria, as shown in the accompanying images.

Discussion

This part is so weak. All data of this study must be compared with the previous studies completely.

5. Discussion

At a glance, the synthesis of silver nanoparticles with the drugs omeprazole and omeprazole sulfide was successful, demonstrating enhanced antibacterial properties and improved drug characteristics. Omeprazole sulfide exhibited superior antibacterial properties compared to omeprazole silver, with the combination of both drugs showing moderate effectiveness.

The study revealed that the drugs alone did not possess antibacterial effects, but when combined with nano-silver, they exhibited enhanced efficacy.

The interaction of the drug omeprazole (OMP) with the surface of silver nanoparticles and the synthesis of Ag@OMP nanodrug were investigated by recording and comparing the Fourier transform infrared spectra of OMP and Ag@OMP. (lower-blue band) and Ag@OMP (upper-red band). also the interaction of the drug omeprazole sulfide (OMPS) with the surface of silver nanoparticles and the synthesis of the nanodrug Ag@OMPS in Figures 2, 3 and 4, the appearance of similar signals with a change in their position and intensity proves the successful binding of drugs to the surface of silver nanoparticles. The powder X-ray diffraction (XRD) patterns of Ag@Omp (a) and Ag@Omps (b) are depicted the peak position at 2θ = 38˚-80˚ corresponds well with Ag@Omprazole.

the distinctive peaks of AgNPs were observed at 2θ = 38˚-80˚, identified as (111), (200), and (220) reflection lines of the face-centered cubic (fcc) structure of metallic silver.

The TEM of Ag@Omps image reveals that particles are spherical shape with approximate size of <60 nm; Scherrer's calc. = 58 nm.

These experiments showcase the potential for developing new nano-drugs and enhancing the antimicrobial properties of existing medications, aligning with advancements in nanomedicine production and aiding in the treatment of various medical conditions.

Conclusion
I can't see the conclusion section
Add the sentences related to the suggestion for the future studies.
Add the sentences related to the future prospective.
Add the sentences related to the limitations.

6. Conclusions

the green synthesis of silver nanoparticles with omeprazole and omeprazole sulfide has been investigated for their antibacterial properties. The nanoparticles were characterized using various techniques. The results indicate that the size of omeprazole nanoparticles is less than 40 nm, while the length of omeprazole sulfide nanoparticles is less than 60 nm. The omeprazole@AgNPs (Ag@Omp) and omeprazole sulfide@AgNPs (Ag@Omps) have shown antibacterial properties, with the UV-Vis spectrum showing distinct peaks for the different arrangements. Overall, the study demonstrates the potential of utilizing silver nanoparticles in combination with omeprazole and omeprazole sulfide for enhanced antibacterial activities.

References
All references must be prepared according to the style of journal.
The number of references for an original article is so low. Please use the articles published in the “Jundishapur Journal of Natural Pharmaceutical Products” related to the antibacterial efficacies of silver nanoparticles.

Refernce

It’s reviewed and correct as Vanover citation method

I suggest that an English language professor read and edited all grammatical errors of this manuscript.

It is corrected.

Manuscript ID: 150851

Answer to Reviewer 3

Dear Judge 3:

Thanks for reading my article and have a nice day.

1. DLS testing is necessary for synthesized nanoparticles:
   due to the lack of the final product, it was not possible to perform all the tests in question.
2. The synthesis method should be explained in the abstract section:
   done.
3. Figure 1 should be revised for omeprazole and omeprazole sulfide:
   the drug figure was omitted.
4. Proposed mechanism required for the synthesis route:

The mechanism is shown in scheme 1 and this mechanism was prepared by my supervisor, Mr. Dr. Nosratollah Mahmoodi, according to him, the mechanism is easier and easier to understand than the synthesis process.

5. What is the role of PVP in the synthesis process?
   It was to prevent clumping of the final product.
6. Antibacterial effects of silver nanoparticles should be evaluated.
   In some articles, the antibacterial effect of silver nanoparticles was investigated, and this study continued the synthesis based on them.
7. The effect of the solvent must be evaluated in the antibacterial test.
   In the antibacterial test, since the general goal was to show the antibacterial effects of the drug with and without silver nanoparticles, an ineffective solvent was used as a result.

3 Revision 2

1 comment · 30 Oct 2024

Referee 1 Reviewer

MINOR REVISION 30 Oct 2024

Dear Editor
Have a nice day.
The author studied the one-pot synthesis of omeprazole-silver and omeprazole sulfide-silver nanoparticles and their antibacterial properties.
The manuscript is recommended for acceptance for publication after the following minor changes.
1. Please rewrite the introduction section based on recent studies.
2. Please mention the source of all materials used.
3. Please provide valid references for the method section.
4. Please correct the typographical errors in the text.

4

Revision 3

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Manuscript ID: 150851

Answer to reviewer 2

Reviewer 2:
Hi
Reviewer 1:

Dear Editor

Have a nice day.

The author studied Study one-pot synthesis of nanoparticles omeprazole-silver and omeprazole sulfide-silver and their antibacterial properties.

It is recommended to be accepted for publication after the following minor changes.

1. Please rewrite the introduction section based on the recent studies.

2. Please mention the source of all materials used.

3. Please mention the valid references for the method section.

4. Please correct the typo mistakes in the text.

Answer:

Dear referee

1. Please rewrite the introduction section based on recent studies.

Sincerely... After reading, a part of the text was rewritten and corrected.

2. Please cite the source of all materials used.

All the details are explained in this section. If you think any changes are needed, I will fix it.

3. Please cite authoritative references in the method section.

Changes are displayed in red text.

4. Please correct typographical errors in the text.

By checking the text, I tried my best to fix typographical errors.

4 Revision 3

0 comments

No public comments in this round.