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Colloidal Silver Nanoparticles Obtained via Radiosynthesis: Synthesis Optimization and Antibacterial Application

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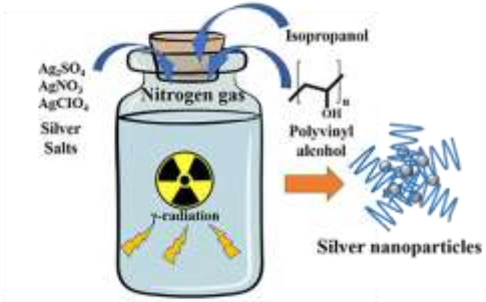
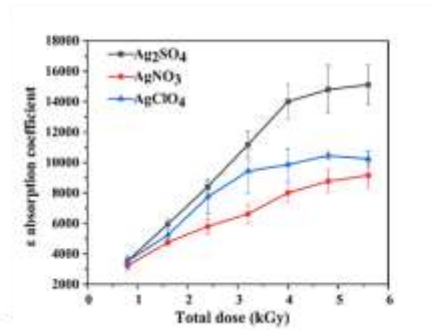
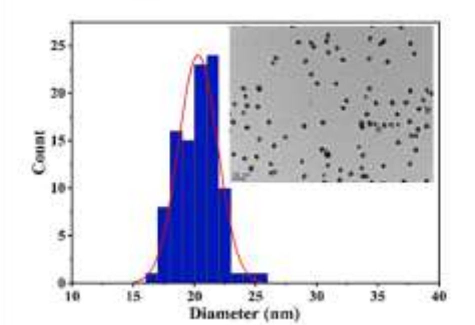
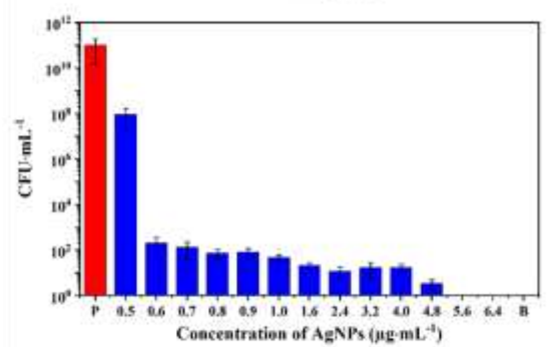








Abstract:

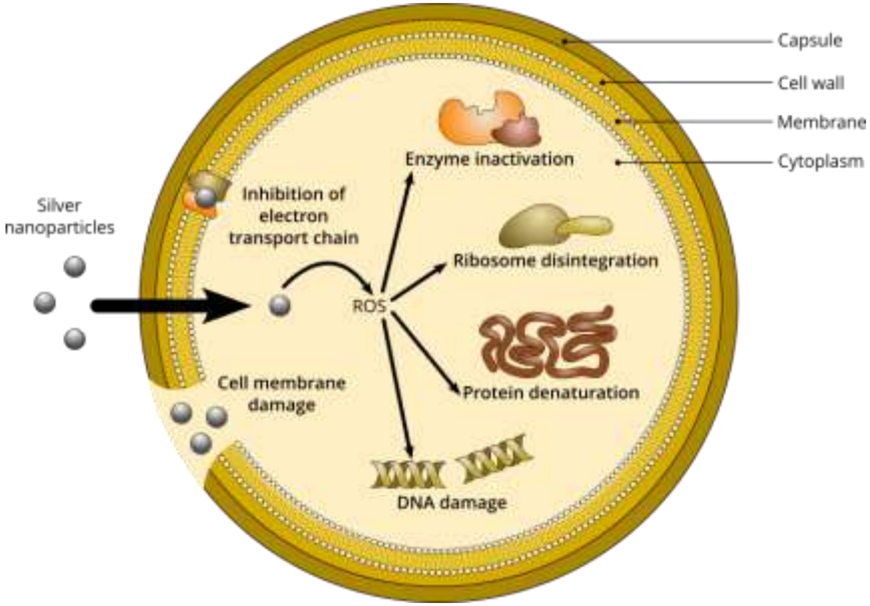
Silver nanoparticles (AgNPs) with broad-spectrum antimicrobial properties are gaining increasing interest in fighting multidrug-resistant bacteria. Herein we describe the synthesis of AgNPs stabilized by polyvinyl alcohol (PVA) with high purity and homogeneous sizes using radiolysis. Solvated electrons and reducing radicals are induced from solvent radiolysis and no other chemical reducing agents are needed to reduce the metal ions. Another advantage of this method is that it leads to sterile colloidal suspensions, which can be directly used for medical applications. We systematically investigated the effect of the silver salt precursor on the optical properties, particle size and morphology of the resulting colloidal AgNPs. With Ag_2SO_4 precursor, the AgNPs displayed a narrow size distribution (20 ± 2 nm). In contrast, $AgNO_3$ and $AgClO_4$ precursors lead to inhomogeneous AgNPs of various shapes. Moreover, the optimized AgNPs synthesized from Ag_2SO_4 were stable upon storage in water and phosphate-buffered saline (PBS) and were effective in inhibiting the growth of Staphylococcus. aureus (*S. aureus*) at a concentration of 0.6 $\mu g \cdot mL^{-1}$ and completely eradicated it at a concentration of 5.6 $\mu g \cdot mL^{-1}$. When compared with various conventional methods and other different strategies, the remarkable bactericidal ability against *S. aureus* of the AgNPs produced here opens up new avenues for further applications in medicine and other domains.

Keywords: Silver nanoparticles; radiosynthesis; antibacterial property; *S. aureus*; sterile colloidal suspensions

Background and Objective

Q: Bacterial resistance caused by the widespread use of antibiotics.

A: Colloidal AgNPs with broad-spectrum antibacterial activity are employed to fight multidrug-resistant bacteria.

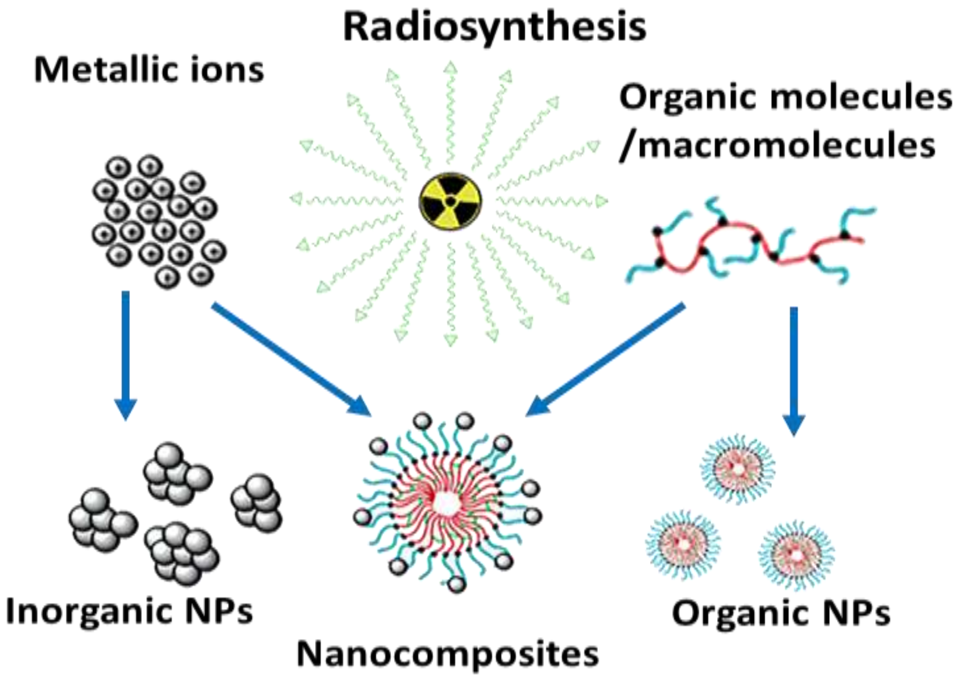


Mechanisms of silver's antibacterial properties: [1-2]

A. AgNPs lead to direct damage to cell wall and cell membrane.
B. AgNPs generate reactive oxygen species (ROS).
C. The cell uptake of free silver ions is followed by disruption of protein production, DNA replication and enzyme activation.

[1] *J. Nanoparticle Res.* **2010**, 12, 1531–1551; [2] *Int. J. Nanomedicine.* **2020**, 15, 2231–2258

AgNPs Radiosynthesis

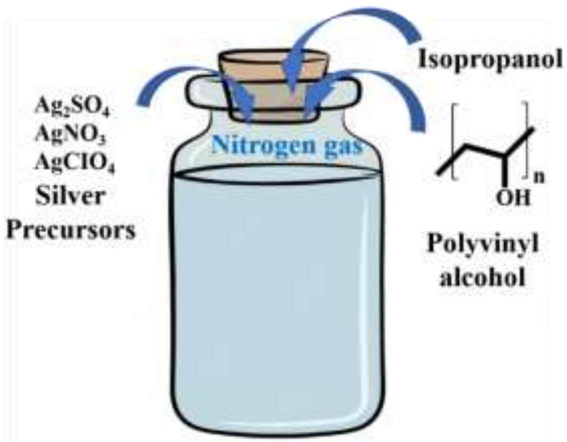


ADVANTAGES

- Green, straightforward & environmentally friendly.
- Controlled synthesis of AgNPs without using toxic reducing agent like $NaBH_4$.
- Metal NPs with monodispersed in a fully reduced, highly pure and highly stable state.
- A powerful synthesis method at room temperature.
- An unique method to obtain sterile formulations to be directly used in medical applications.

[3] *Prog. Org. Coat.* **2023**, 176, 107393; [4] *Physica. E.* **2009**, 42, 132–135

Synthesis Mechanism



(a) Preparation of silver NPs precursor

(b) The formation of AgNPs via radiosynthesis

(1) $H_2O \xrightarrow{\gamma\text{-ray}} \bar{e}_{aq}, H_3O, H^{\bullet}, OH^{\bullet}, H_2, H_2O_2, H_3O^{+}$

(2) $Ag^{+} + e^{-}_{aq} \longrightarrow Ag^{0}$

(3) $OH^{\bullet}$ (or $H^{\bullet}$) + $(CH_3)_2CHOH \longrightarrow (CH_3)_2C^{\bullet}OH + H_2O$ (or H_2)

(4) $Ag^{+} + (CH_3)_2C^{\bullet}OH \longrightarrow [Ag(CH_3)_2C{\bullet}OH]^{+}$

$[Ag(CH_3)_2C{\bullet}OH]^{+} + Ag^{+} \rightarrow Ag^{+}{}_{2} + (CH_3)_2CO + H^{+}$

(5) $Ag^{0}{}_{m} + Ag^{0} \rightarrow Ag^{0}{}_{m+1}$

(6) $Ag^{0}{}_{m+1} + Ag^{+} \rightarrow Ag^{+}{}_{m+2}$

(7) $Ag^{+}{}_{m+2} + e^{-}_{aq} \rightarrow Ag^{0}{}_{m+2}$

(8) $Ag^{0}{}_{m} + Ag^{0}{}_{n} \rightarrow Ag^{0}{}_{m+n}$

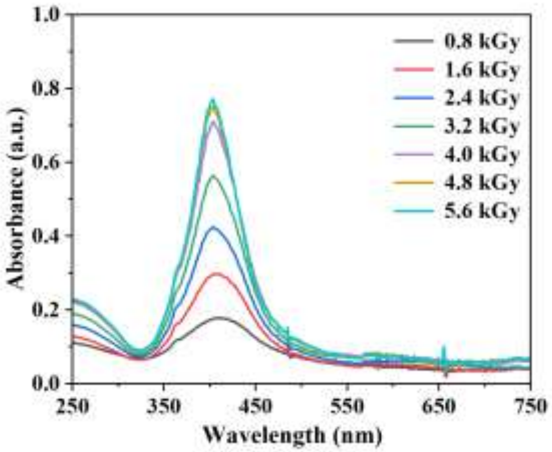
(9) $PVA^{\bullet} + PVA^{\bullet} \rightarrow$ PVA-PVA

Radiolysis of water (1); Radicals formation (1, 3); Nucleation (2, 4); Agglomeration (5–8); Aggregation Restriction (9) [5] [6]

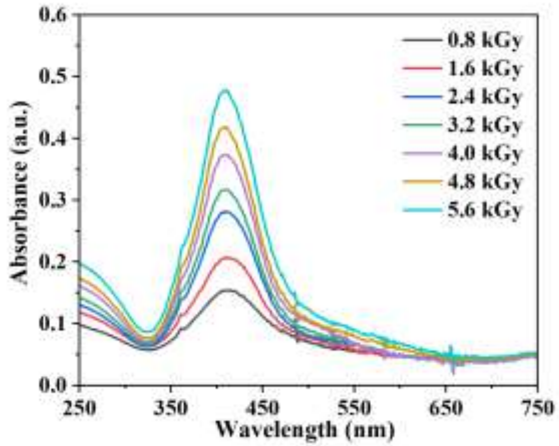
[5] *Int. J. Mol. Sci*. **2013**, 14, 7880-7896. [6] *Pharmaceutics*. **2023**, 15, 1787.

Synthesis Optimization of AgNPs

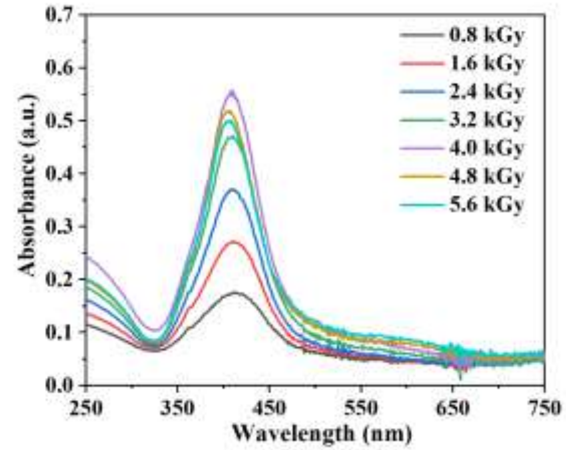
Ag_2SO_4 precursor

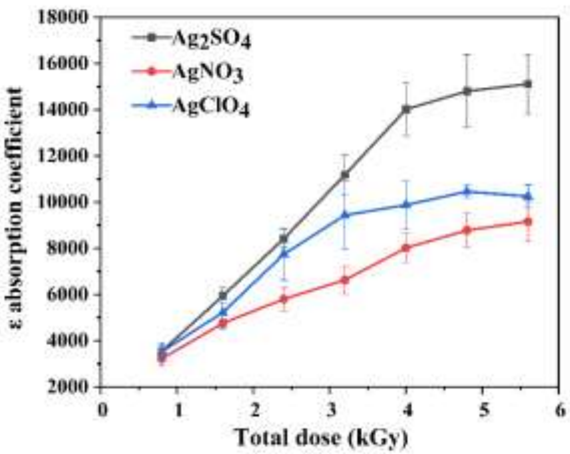


$AgNO_3$ precursor



$AgClO_4$ precursor



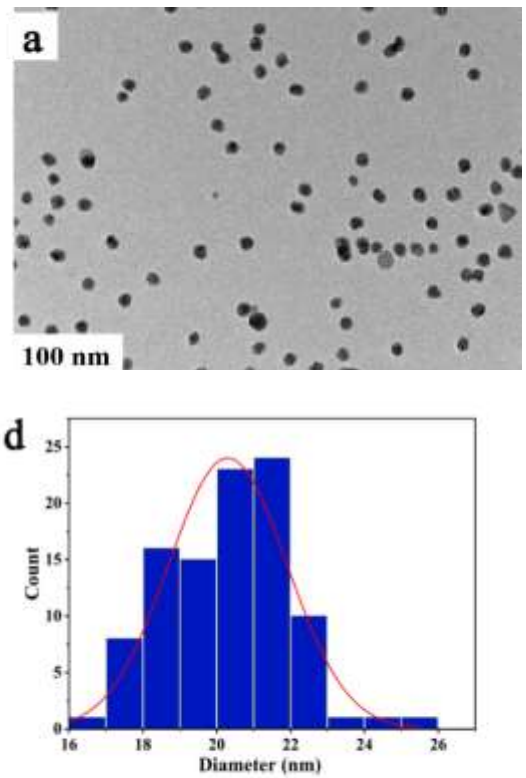


- Plasmon resonance absorption of silver cluster around 400 nm.
- AgNPs are formed with increasing radiation dose.
- Full reduction of Ag+ ions into AgNPs when the absorbance reaches a plateau.
- Best results for AgNPs using Ag_2SO_4

[6]]*Pharmaceutics.* **2023**, 15, 1787.

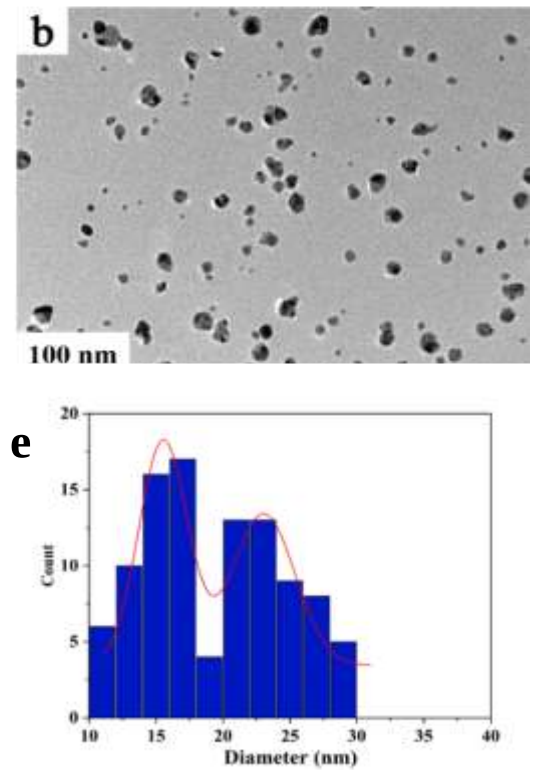
Morphology and Size Distribution of AgNPs

Ag_2SO_4 precursor



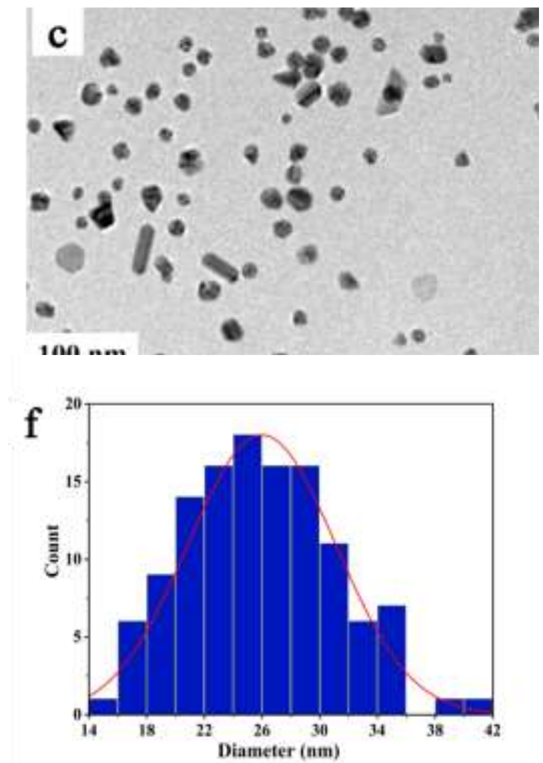
Ave: 20 ± 2 nm. Uniform;
DLS size, 26 ± 3 nm
Zeta potential, −16 mV

$AgNO_3$ precursor



Ave: 19 ± 5 nm. Irregular

$AgClO_4$ precursor



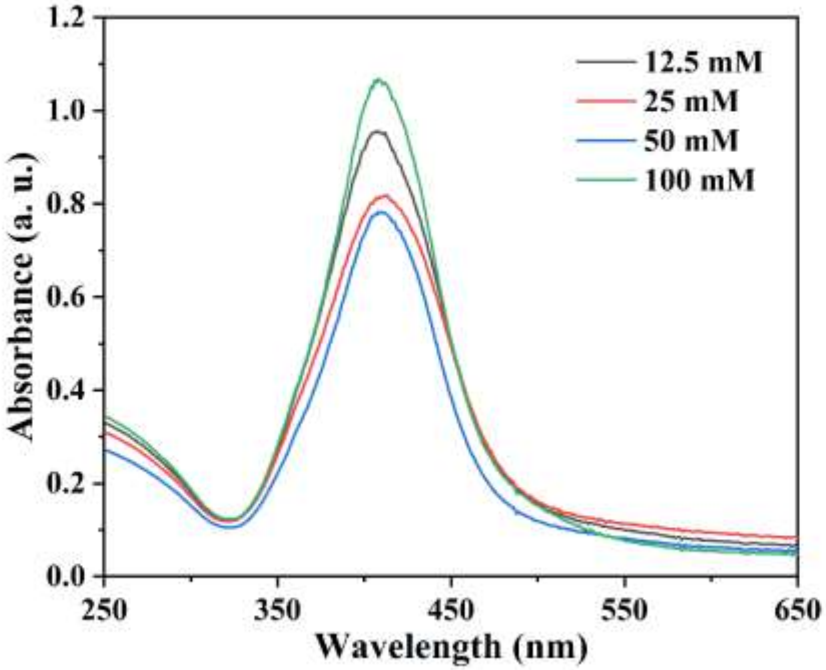
Ave: 26 ± 6 nm. Irregular

- Different sizes and shapes are obtained, depending on the type of salt precursor, related to the crystal nucleation and growth rate.

[6]]*Pharmaceutics.* **2023**, 15, 1787.

Influence of Surfactant Concentration

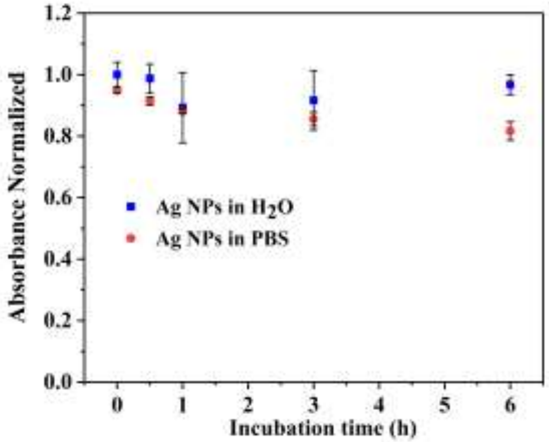
PVA concentration

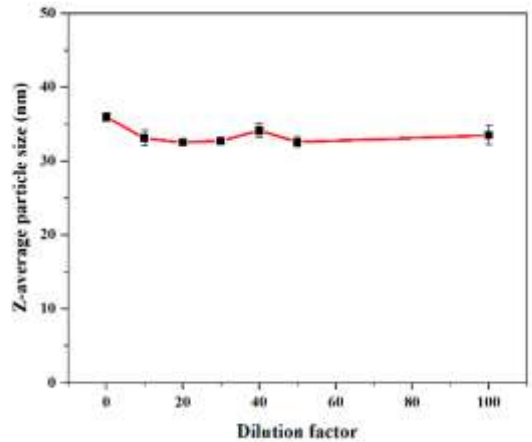


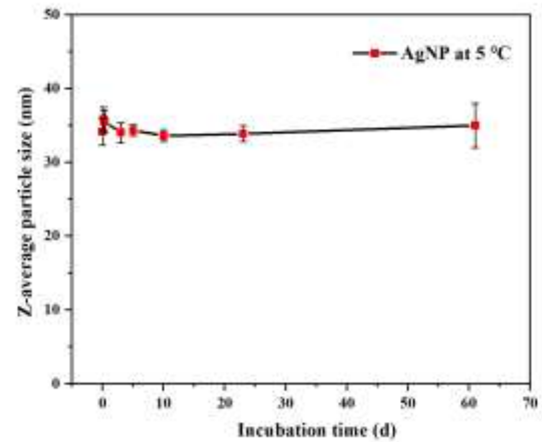
- PVA concentration has a slight influence on NP formation.
- The optimal AgNPs are stabilized by the PVA with concentration of 100 mM.

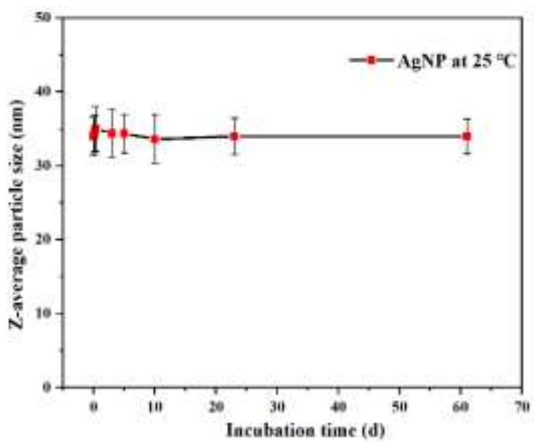
[6]]*Pharmaceutics.* **2023**, 15, 1787.

AgNPs' Stability Study









- The optimized AgNPs are good stable upon storage, either in water, or in PBS (10X) for short-term (6 h).
- The optimized AgNPs have good stability on the particle size in water for long-term (2 months).

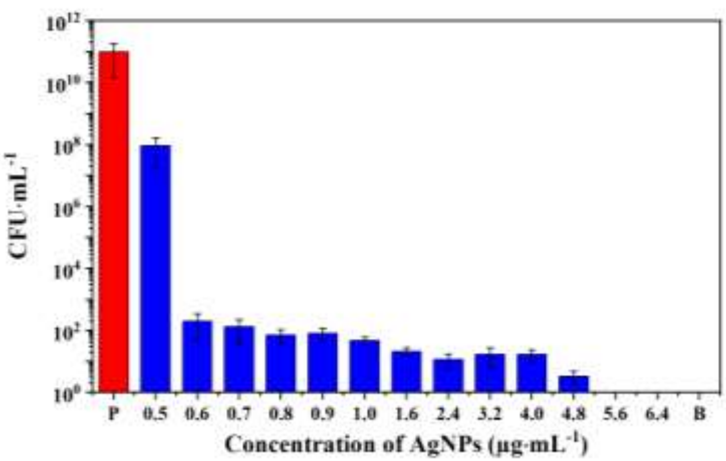
[6]]*Pharmaceutics.* **2023**, 15, 1787.

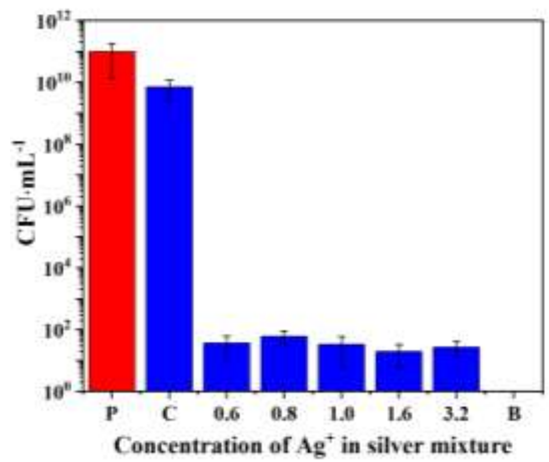
Antibacterial Study for AgNPs

S. aureus + AgNPs (0.5 µg·mL^{-1})/ LB broth (Red circle)

S. aureus + AgNPs (0.6 µg·mL^{-1})/ LB broth (Red circle)

S. aureus + AgNPs (5.6 µg·mL^{-1})/ LB broth (Red circle)





Minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) against *S. aureus* are 0.6 and 5.6 µg·mL^{-1}, respectively.

[6]]*Pharmaceutics*. **2023**, 15, 1787.

Conclusions

- AgNPs were obtained using three different precursors (Ag_2SO_4, $AgNO_3$, and $AgClO_4$)
- AgNPs (Ag_2SO_4, 2 mM) exhibit the best optical property, together with a uniform size distribution of (20 ± 2 nm).
- Conversely, AgNPs obtained with the other precursors have diverse morphologies.
- The optimized AgNPs are stable upon storage in water and PBS for short-term (6h) and long-term (2 months).
- They have good antibacterial properties (*S. aureus*) : MIC of 0.6 $\mu g \cdot mL^{-1}$ and MBC of 5.6 $\mu g \cdot mL^{-1}$.

Acknowledgments

Supervisor

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Collaborators

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PhD. Aisara Amanova
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Supplementary

Silver from	Method	Size data	Bacterial strain	MIC	MBC
Ag NPs - Myramistin	Chemical reduction	8.5 nm	S. Aureus INA 00761	5 $\mu g \cdot mL^{-1}$	-
Lignin-Ag NPs	Chemical reduction	~20 nm	S. Aureus MDR	10 $\mu g \cdot mL^{-1}$	10 $\mu g \cdot mL^{-1}$
			S. Aureus ATCC700788	5 $\mu g \cdot mL^{-1}$	10 $\mu g \cdot mL^{-1}$
PSS-Ag NPs	Chemical reduction	5 nm	S. Aureus ATCC29213	1.14 $\mu g \cdot mL^{-1}$	-
Dendrimer-encapsulated-Ag NPs	Chemical reduction	3.33 nm	S. Aureus USA300	128 $\mu g \cdot mL^{-1}$	-
Carboxy methyl cellulose-Ag NPs	Chemical reduction	5–15 nm	S. Aureus ATCC43300	60 $\mu g \cdot mL^{-1}$	60 $\mu g \cdot mL^{-1}$
AgNPs-Tannic acid	Chemical reduction	4.69 ± 1.56 nm	S. Aureus ATCC 25923	8–16 $\mu g \cdot mL^{-1}$	16-32 $\mu g \cdot mL^{-1}$
Zeolite containing silver and zinc	Chemical reduction	ND	S. Aureus ATCC 25923	-	39 $\mu g \cdot mL^{-1}$
Ag NPs-Cotyledon orbiculate	Biosynthesis reduction	106–137 nm ± 2	S. Aureus ATCC 25923	20 $\mu g \cdot mL^{-1}$	40 $\mu g \cdot mL^{-1}$
Ag NPs-A. esculentus flower extract	Biosynthesis reduction	5.52–24.65 nm; average 18.24	S. Aureus ATCC29213	85 $\mu g \cdot mL^{-1}$	90 $\mu g \cdot mL^{-1}$
Ag NPs-lyophilized hydroalcoholic extract of S. Cumini seeds	Biosynthesis reduction	36.25–77.01 nm	S. Aureus ATCC25923	125 $\mu g \cdot mL^{-1}$	-
Ag NPs-Artemisia haussknechtii leaf aqueous extract	Biosynthesis reduction	10.69 nm	S. aureus ATCC 43300	10 $\mu g \cdot mL^{-1}$	60 $\mu g \cdot mL^{-1}$
AgNPs-Sucrose	Saccharide-based reduction	25 ± 5 nm	S. Aureus	0.057 $\mu g \cdot mL^{-1}$	0.23 $\mu g \cdot mL^{-1}$
AgNPs- Soluble starch	Saccharide-based reduction	25 ± 5 nm	S. Aureus	0.34 μg/mL	1.62 μg/mL
Ag NPs-PVA(72000)	γ-Radiation reduction	~28 nm	S. Aureus	-	-
AgNPs-Chitosan-derived CQDs	γ-Radiation reduction	25 nm	S. Aureus	100 $\mu g \cdot mL^{-1}$	-
AgNPs-PVA(1700-1800)	γ-Radiation reduction	31.2–50.8 nm	S. Aureus ATCC29213	-	-
AgNPs-PVA(30000 ~ 70000) (this work)	γ-Radiation reduction	20 nm	S. Aureus ATCC 27217	0.6 $\mu g \cdot mL^{-1}$	5.6 $\mu g \cdot mL^{-1}$