Synthesis of PVA Encapsulated Silver Nanoparticles as a Drug Delivery System for Doxorubicin and Curcumin

Nhi Nguyen, Cam Huong Le

53 Nguyen Du, Dist. 1, Ho Chi Minh City, 700000, Vietnam ; nhituyet6788@gmail.com

ABSTRACT: Silver nanoparticles, of great significance in drug delivery, are unstable due to agglomeration. To address this problem, we examined the effectiveness of polyvinyl alcohol (PVA) as a cheap, environmentally-friendly biomaterial in stabilizing and increasing the efficiency of drug-loaded silver nanoparticles. In this study, we have successfully synthesized *in situ* PVA-coated nanoparticles with a particle size of 70.1 nm measured by DLS and 46.7nm measured using SEM by chemical reduction method using silver nitrate (AgNO₃), sodium borohydride (NaBH₄), and PVA. Drug loading efficiency of AgNPs-PVA reached 91.95% for Doxorubicin and 99.24% for Curcumin, which is higher than the drug loading efficiency of uncoated silver nanoparticles. Additionally, we have determined the antibacterial activity of AgNPs-PVA and AgNPs-PVA-Cur on strains of gram (+) *Bacillus cereus* and gram (-) *E. coli* and a concentration of 5 ppm and above yield zones of inhibition greater than 10 mm in diameter. Given time and additional equipment, we hope to conduct further studies that examine the anticancer properties of AgNPs-PVA-Dox on cancer cells and the burn treatment applications of AgNPs-PVA-Cur on mice.

KEYWORDS: Nanomedicine; Drug Loading; PVA-coated Silver Nanoparticles; Breast Cancer Therapeutics; Burns Treatment.

■ Introduction

Over the past decades, silver nanoparticles have attracted great attention from scientists around the world due to their unique properties and wide applicability. Specifically, silver nanoparticles have been studied and used as catalysts¹ and biological probes.² In particular, thanks to their effective antimicrobial activity,^{3,4} silver nanoparticles are believed to be a potential solution to the problem of biological infection.

Throughout the world, the production of silver nanoparticles has been carried out by different methods such as chemical reduction methods, physical reduction methods, biological reduction methods, etc. The FM Gutierrez team used chemical agents to reduce silver ions to silver; the resulting silver nanoparticles were smaller than 100 nm.⁵ H. Jiang *et al.* used high-energy electromagnetic waves such as gamma rays, ultraviolet rays, and lasers to synthesize silver nanoparticles.⁶ Some studies used chemical reducing agents such as sodium borohydride,⁷ ascorbic acid⁸ to reduce silver ions to silver nanoparticles. In this study, we employed a chemical reduction method using sodium borohydride as a reducing agent because the method is the least time-consuming and requires minimal laboratory equipment.

Doxorubicin (Dox) is an active ingredient that is commonly used in breast cancer treatment today. However, Dox causes many serious side effects. Treatment with doxorubicin often leads to undesirable reactions that need to be closely monitored. Undesirable effects often depend on the route of administration, dosage, administration's speed and frequency. Nausea, vomiting and hair loss are common in many patients. Impaired bone marrow function is a very common adverse reaction to dose limits. One more side effect worth noting is

the accumulation of cardiotoxins in the patient's body.⁹ Silver nanoparticles in drug delivery, especially for Doxorubicin as a breast cancer treatment, are of great significance in the biochemistry field for their ability to bypass the cell membrane via endocytosis and to localize into the lysosomes. Here, the NPs release the drug directly, damaging cell's DNA and lead to cell death.¹⁰ Thus, AgNPs lead the drug to its destination, reducing dosage and side effects.¹¹

Curcumin is a bright yellow chemical produced by *Curcuma longa* plants. It is the principal curcuminoid of turmeric (*Curcuma longa*), a member of the ginger family, Zingiberaceae. Research by scientists in the late twentieth century has determined that curcumin plays an important role in the biological activities of turmeric. Based on *in vitro* and animal studies, scientists have proven that curcumin has antibacterial and anti-scar wound healing properties.^{12,13}

Burns are conditions of the skin due to heat damage which are very common in real life. First degree burns result in pain and reddening of the epidermis (outer layer of the skin) while second-degree burns (partial thickness burns) affect the epidermis and the dermis (lower layer of skin, causing pain, redness, swelling, and blistering which can lead to infection. At the nanoscale, silver increases its antiseptic activity by up to 50000 times greater compared with that of silver in ionic size. Silver nanoparticles can continually release silver ions and owing to electrostatic attraction and affinity to sulfur proteins, silver ions can adhere to the cell wall and cytoplasmic membrane. The adhered ions can enhance the permeability of the cytoplasmic membrane and lead to disruption of the bacterial envelope.¹³ Therefore, the use of silver nanoparticles in combination with Curcumin with its antibacterial and anti-scar wound healing

properties is also seen as a potential approach in treating burns, which are easily infected and result in severe skin scarring.

In order for nanoparticles to disperse well in the solvent without agglomeration, a coating with a surfactant or an electrostatic method that causes the nanoparticles' surface to have the same charge and repel each other is used.¹⁴ Nanoparticles formed by these methods are usually less than 100 nm in size. In this study, we examined the effectiveness of PVA as a biocompatible, water-soluble, inexpensive and non-toxic surfactant in stabilizing and increasing the efficiency of drug-loaded silver nanoparticles.¹⁵ While Doxorubicin-loaded and Curcumin-loaded nanoparticles have been previously studied such as that of Y. Du *et al.* on Doxorubicin-loaded gold nanoparticles¹⁶ and S. Ravindra *et al.* on Curcumin-loaded silver nanoparticles hydrogels¹⁷ and PVA has previously been used in combination with silver nanoparticles as a stabilizer,¹⁸ using PVA to stabilize and increase the efficiency of silver nanoparticles for loading and delivering doxorubicin and curcumin specifically is new. The first goal of our study is, by chemical reduction methods, to develop PVA-coated silver nanoparticle (AgNPs-PVA) synthesis process with NaBH_4 as the reducing agent and determine the physicochemical properties of silver nanoparticles that formed: structure, particle size, and distribution. Next, we compared the drug loading effectiveness of AgNPs-PVA for Doxorubicin and Curcumin to uncoated silver nanoparticles. The ultimate goal is to test anticancer properties of Doxorubicin-loaded AgNPs-PVA (AgNPs-PVA-Dox) on cancer cells, and antibacterial properties of Curcumin-loaded AgNPs-PVA (AgNPs-PVA-Cur) on mice and implement them for treatments on humans.

■ Result and Discussion

Analysis of Physicochemical Properties:

In this study, we proceeded to coat silver nanoparticles with polyvinyl alcohol by *in situ* method, which means that AgNPs-PVA nanoparticle synthesis process is in parallel with AgNPs granulation process.

Figure 2.1: Structural properties of AgNPs-PVA.

One of the roles of PVA as a coating agent in the synthesis of silver nanoparticles is to protect them from self-aggregation in solution. Structural flexibility and conformational dynamics of a stabilizing agent backbone or a polymer chain, adsorbed onto a nanoparticle surface, play an important role in colloidal stabilization, shape-controlled growth, as well as the water-protecting effect of silver nanoparticles.¹⁹ To gain a better understanding of non-bonded interactions, occurring at the organic/inorganic interface between PVA, the AgNP core, and the surrounding water molecules, a scheme of possible interactions is given in Figure 2.1.

When conducting spectroscopy of the samples, each sample had a defined peak spectral height like the standard UV-vis spectrum of silver nanoparticles from which the silver nanoparticles could be determined. In this case, the occurrence of silver nanoparticles could be detected if the UV-vis spectrophotometer result showed the absorption peak around wavelengths of 430 nm. Simultaneously, the higher the peak is on the absorbance axis, the more of the light with this particular wavelength is absorbed, indicating higher concentration of silver nanoparticles in aqueous solution. Thus, this property helps determine if the silver nanoparticles synthesis process had happened and make preliminary prediction of the concentration of silver nanoparticles formed.²⁰

Figure 2.2: UV-Vis spectra of AgNPs-PVA solution over stirring time of 15 minutes, 30 minutes, 45 minutes, 60 minutes, and 90 minutes.

Based on this ground work, we varied the stirring time of each batch from 15 to 90 minutes in order to examine the occurrence and concentration of our silver nanoparticles suspended in water at room temperature. We measured each batch with a UV-vis spectrophotometer, whose spectrum range was set from 350 nm to 700 nm, and obtained absorption peaks at 400 to 409 nm with absorbance of 0.075 to 0.25. This result indicated that silver nanoparticles were formed although the concentration of nanoparticles in solutions was quite low. However, the most optimal stirring was determined at 15

Figure 2.3: Particle size distribution of AgNPs-PVA measured by DLS.

minutes, which yielded the maximum peak wavelength at 409 nm and highest absorbance at 0.25 (Figure 2.3).

With the formation of silver nanoparticles confirmed and optimal stirring time determined, we synthesized more batches and sent them to Academy of Chemical Engineering-Vietnam Academy of Science and Technology. Our aim was to measure the particle size distribution AgNPs-PVA by dynamic light scattering (DLS), which determines a relaxation time for the decay of the autocorrelation function of the scattered light. From that, a diffusion coefficient inversely proportional to particle size can be extracted. Results of the size distribution of AgNPs-PVA nanoparticles by DLS showed that the nanoparticles formed were, in average, approximately 70.1 nm in size (Figure 2.5).

Figure 2.4: FTIR spectra of AgNPs-PVA nanoparticles.

Consequently, to confirm that the silver nanoparticles have been coated with PVA, we conducted analysis of AgNPs-PVA by FTIR spectroscopy at wavenumbers 4000 – 400 cm^{-1} . Figure 2.4 shows that FTIR spectrum of AgNPs-PVA appears to have characteristic peaks at wavenumbers 3348 cm^{-1} , 1638 cm^{-1} , 659 cm^{-1} , which corresponds to the O-H, C-C bond, and the torsional fluctuations of the OH group. This indicated the presence of PVA coating on the surface of AgNPs and bonds between PVA and AgNPs.

Figure 2.5: SEM measurement results of AgNPs-PVA.

The final method of chemical analysis we employed was scanning electron microscopy (SEM), which scans a focused electron beam over of the nanoparticles. The electrons in the beam interact with the sample, producing various signals that can be used to obtain information about the surface topography and composition. SEM results showed that the AgNPs-PVA formed were spherical (Figure 2.5), the total number of particles was 394 and the average particle size was 46,764 nm

(Table 3.1), which is smaller than the size measured by the DLS (Figure 2.5).

The reason for the difference in the two methods lies in the mechanism of DLS, which does not measure size but, instead, diffusivities of AgNPs-PVA in an aqueous solution. If given monodisperse size distribution, i.e. all particles of the same size, then a size measurement by SEM should give a size similar to that measured by DLS. If a distribution of particle sizes exists in a solution, DLS weights the distribution differently compared to SEM, by size to the power of 6, essentially giving a z-average distribution. Larger particles are, therefore, given more weight, making the "average" size look larger than SEM's. Hence, the SEM result is a more reliable indicator of AgNPs-PVA size.

Drug Loading Efficiency of AgNPs-PVA:

Figure 2.6: AgNPs-PVA-Dox solution (left), AgNPs-PVA-Cur (right).

We proceeded to load Doxorubicin and Curcumin onto AgNPs-PVA with concentration of 200 ppm by shaking and centrifuge. Based on Figure 2.1 in which the solid silver core is coated with dispersed PVA particles, the drug is expected to coat and be absorbed on the PVA surface of the AgNPs-PVA.

Figure 2.7: Calibration curve showing the relationship between concentration and loading efficiency of Doxorubicin.

A standard calibration curve was constructed for AgNPs-PVA-Dox and AgNPs-PVA-Cur in order to obtain the linear equation which was further used to calculate the drug-loading efficiency. We prepared stock Doxorubicin and Curcumin solutions with a concentration of 100 ppm. From these two

stock solutions, suitable dilutions were prepared at 5 ppm, 10 ppm, 15 ppm, 20 ppm, and 25 ppm. All the dilutions were analyzed by UV-Visible Spectrophotometer. The values of absorbance were then recorded and a standard curve was constructed by plotting absorbance against concentration. From this curve a regression line equation was obtained in MS Excel format.

Once the calibration curve for Doxorubicin was obtained, we analyzed our 200 ppm AgNPs-PVA-Dox, which was synthesized beforehand, by UV-Visible Spectrophotometer. The absorbance was recorded at 0.2632, which was then plotted into the equation of the calibration curve to calculate the unloaded Doxorubicin amount of 16.2090 ppm. This experimental result showed that Doxorubicin drug loading efficiency of AgNPs-PVA reached 91.9455% (Figure 2.7).

Figure 2.8: Calibration curve showing the relationship between concentration and loading efficiency of Curcumin.

Once the calibration curve for Curcumin was obtained, we analyzed our 200 ppm AgNPs-PVA-Cur, which was synthesized beforehand, by UV-Visible Spectrophotometer. The absorbance was recorded at 1.9679, which was then plotted into the equation of the calibration curve to calculate the unloaded Curcumin amount of 7.4883 ppm. This experimental result showed that Curcumin drug loading efficiency of AgNPs-PVA reached 96.2559% (Figure 2.8).

Antibacterial Properties of AgNPs-PVA and AgNPs-PVA-Cur:

a) Bacteria *Bacillus cereus* (gram positive) b) *E. coli* bacteria (gram negative)

Figure 2.9: Petri dishes showing zones of inhibition against bacteria *Bacillus cereus* (gram positive) and *E. coli* bacteria (gram negative) for AgNPs-PVA concentrations of 5 ppm, 10 ppm, 20 ppm, 30 ppm, 40 ppm.

The experimental results showed that AgNPs-PVA became antibacterial at the concentration of 5 ppm. At a concentration of 5 ppm, diameters of the zones of inhibition of AgNPs-PVA in both bacteria were greater than 10mm. The greatest diameters recorded were 20mm from the concentration of 40 ppm for *Bacillus cereus* and 20mm from the

concentration of 40 ppm for *E. coli*. This confirms the antibacterial potential of AgNPs-PVA (Figure 2.9).

a) Bacteria *Bacillus cereus* (gram positive) b) *E. coli* bacteria (gram negative)

Figure 2.10: Petri dishes showing zones of inhibition against bacteria *Bacillus cereus* (gram positive) and *E. coli* bacteria (gram negative) for AgNPs-PVA concentrations of 5 ppm, 10 ppm, 20 ppm, 30 ppm, 40 ppm.

The experimental results showed that AgNPs-PVA-Cur became antibacterial at a concentration of 5 ppm. At a concentration of 5 ppm, the zone of inhibition of AgNPs-PVA-Cur is greater than 15mm. The greatest diameters recorded were 23mm from the concentration of 40 ppm for *Bacillus cereus* and 21mm from the concentration of 40 ppm for *E. coli*. This confirms the antibacterial potential of AgNPs-PVA-Cur and shows an improvement in antibacterial potential of AgNPs-PVA-Cur when compared with AgNPs-PVA (Figure 2.10).

Conclusion

In this study, we have successfully synthesized AgNPs-PVA with particle size of 70.1nm measured by DLS and 46.7nm measured by SEM. We proceeded to examine the drug loading efficiency of AgNPs-PVA for Doxorubicin and Curcumin, which reached 91.9455% and 99.2411%, respectively. We have tested the antibacterial activity of AgNPs-PVA and AgNPs-PVA-Cur on gram (+) *Bacillus cereus* and gram (-) *E. coli* for concentrations of 5 ppm, 10 ppm, 20 ppm, 30 ppm, 40 ppm and found that AgNPs-PVA and AgNPs-PVA-Cur become antibacterial at the concentration of 5 ppm and above. Hence, AgNPs-PVA-Dox was found to have the potential to be tested on breast cancer cells and be implemented into breast cancer therapeutics due to their high drug loading efficiency. Furthermore, AgNPs-PVA-Cur was found to have the potential to be tested on burns spots on mice due to their antibacterial activity.

Methods

Materials:

Chemicals included silver nitrate (AgNO_3), sodium borohydride (NaBH_4), and polyvinyl alcohol (PVA) obtained from Scharlau Chemicals (Spain), Curcumin from Ho Chi Minh City University of Agriculture and Forestry, and Doxorubicin hydrochloride (10 mg/5 ml) from Fresenius Kabi.

We used gram-positive bacteria *Bacillus cereus*, gram-negative *E. coli* from Ho Chi Minh City University of Natural Sciences to investigate the antibacterial properties of AgNPs-PVA and AgNPs-PVA-Cur.⁶

The Process of Synthesizing AgNPs-PVA from AgNO_3 , NaBH_4 :

The silver nanoparticle synthesis process was carried out as follows. A 0.001M AgNO_3 solution was dripped into 50 ml of 2% PVA solution. Then, while the mixture was being

stirred for 15 minutes in the dark, 0.001M NaBH₄ was added dropwise until the solution turned pale yellow. The reacted solution was centrifuged at 13000 rpm and washed three times with deionized distilled water. The obtained AgNPs-PVA was stored at 4°C.²¹

Diagram 1.1: The process of particle synthesis AgNPs- PVA.

The Process of Loading Doxorubicin and Curcumin into AgNPs-PVA:

1 ml of Dox / Cur solution (0.2 mg / mL) was added to 9 ml of AgNPs-PVA solution (2 mg / ml) at pH = 7.4. The reaction mixture was shaken with a shaker at temperature 37 ° C for 24 hours in the dark. Then, the reaction mixture was centrifuged for 15 minutes.²²

Diagram 1.2: The process of synthesizing AgNPs- PVA-Dox and AgNPs-PVA-Cur.

Chemical Analysis Methods:

Ultraviolet-visible spectroscopy (UV-Vis) is a quantitative analysis method, based on the absorption effect that occurs when matter molecules interact with electromagnetic radiation. The radiation region used in this study is the infrared region with wavelengths from 350 to 700 nm. The phenomenon of electromagnetic radiation absorption complies with the Bouguer - Lambert - Beer law. In this study, we used the model UV-Vis Biochrom S60 from Ho Chi Minh City Pedagogical University.

Dynamic light scattering (DLS) is a technique that can be used to determine the size distribution profile of small particles in suspension or polymers in solution. Fourier-transform infrared spectroscopy (FTIR) is a technique used to obtain an infrared spectrum of absorption or emission of a solid, liquid, or gas. Scanning electron microscope (SEM) is a type of electron microscope that produces images of a sample by scanning

the surface with a focused beam of electrons. In this study, we sent the silver nanoparticles to Pharmaceutical Chemistry Research Center - Vietnam Academy of Science and Technology to be analyzed by DLS, FTIR, and SEM.

Data Analysis Methods:

Particle size: we used ImageJ software to analyse the particle size of AgNPs-PVA from SEM results. The count in the section was 394 particles, with total area of 18425. Therefore, the average size of nanoparticles calculated was 46.764nm.

Drug loading efficiency:

-A standard calibration curve was constructed for AgNPS-PVA-Dox and AgNPs-PVA-Cur in order to obtain the linear equation which was further used to calculate the drug-loading efficiency. For this purpose, stock Doxorubicin and Curcumin solutions were prepared with a concentration of 100 ppm. From this stock solution, suitable dilutions were prepared at 5 ppm, 10 ppm, 15 ppm, 20 ppm, and 25 ppm. All the dilutions were analyzed by UV-Visible Spectrophotometer (UV-Vis Biochrom S60). The values of absorbance were recorded and a standard curve was constructed by plotting absorbance against

Table 1: Absorbance values of Doxorubicin solution at 1 ppm, 2 ppm, 3 ppm, 4 ppm, 5 ppm.

C (ppm)	Abs
5	0.0666
10	0.1551
15	0.2436
20	0.3321
25	0.4206

Table 2: Absorbance values of Curcumin solution at 1 ppm, 2 ppm, 3 ppm, 4 ppm, 5 ppm.

C (ppm)	Abs
1	0.26343
2	0.52613
3	0.78883
4	1.05153
5	1.31423

concentration. From this curve a regression line equation was obtained in MS Excel format.

-We proceeded to analyze our 200 ppm AgNPs-PVA-Dox/Cur, which was synthesized beforehand, by UV-Visible Spectrophotometer. The absorbance was recorded, which was then plotted into the equation of the calibration curve to calculate the unloaded amount of Doxorubicin and Curcumin. Consequently, the loading efficiencies were obtained.

-The efficiency of Doxorubicin loading is calculated by the formula below:²³

$$\text{Doxorubicin Loading Efficiency (\%)} = \frac{(\text{Initial amount of Doxorubicin}) - (\text{Unloaded amount of Doxorubicin})}{(\text{Initial amount of Doxorubicin})} \times 100\%$$

$$\frac{200 - 16.1090}{200} \times 100\% = 91.9455\%$$

$$\text{Curcumin Loading Efficiency (\%)} = \frac{(\text{Initial amount of Curcumin}) - (\text{Unloaded amount of Curcumin})}{(\text{Initial amount of Curcumin})} \times 100\%$$

$$\frac{200 - 7.4883}{200} \times 100\% = 96.2559\%$$

cumin to be 50µg for 5 ppm, 100µg for 10 ppm, 200µg for 20 ppm, 300µg for 30 ppm, and 400µg for 4 ppm.

Acknowledgements

Big thanks for Mr. Tran Duc Thanh for always staying by our side and supporting us the best that he could.

Deepest gratitude to the Vietnam Academy of Science and Technology, Ho Chi Minh City Pedagogical University, and Ho Chi Minh University of Natural Sciences for letting us use your laboratory equipment and space.

References

1. N. Pradhan, A. Pal, T. Pal (2002), *Silver nanoparticle catalyzed reduction of aromatic nitro compounds*, *Colloid. Surf. A*, 196, 247-257.
2. JN Anker, WP Hall, o. Lyandres, NC Shah, J. Zhao, RP Van Duyne (2008), *Biosensing with plasmonic nanosensors*, *Nat. Mater.*, 7, 442-453.
3. KS Lee, MA El-Sayed (2006), *Gold and silver nanoparticles in sensing and imaging: sensitivity of plasmon response to size, shape, and metal composition*, *J. Phys. Chem. B*, 110, 19220-19225.
4. KH Cho, JE Park, T. Osaka, SG Park (2005), *The study of antimicrobial activity and preservative effects of nanosilver ingredients*, *Electrochim. Acta*, 51, 956-960.
5. DK Lee and YS Kang, 2004. *Synthesis of silver nanocrystallites by a new thermal decomposition method and their characterization*. *ETRI Journal*, 26 (3), 252-256.
6. B. Taneja, B. Ayyub, and R. Chandra, 2002. *Size dependence of the optical spectrum in nanocrystalline silver*. *Physical Review B*, 65, 1-6.
7. Zhang, RC Patel, R. Kothari, CP Johnson, SE Friberg, PA Aikens (2000), *Stable silver clusters and nanoparticles prepared in polyacrylate and inverse micellar solutions*, *J. Phys. Chem. B*, 104, 1176-1182.
8. GJ Lee, SI Shin, YC Kim, SG oh (2004), *Preparation of silver nanorods through the control of temperature and pH of reaction medium*, *Mater. Chem. Phys.*, 84, 197-204.
9. Lê Thi My Hanh (2017), *Nghiên cứu bào chế nano doxorubicin đa chức năng*.
10. Elbaz, Nancy & Ziko, Laila & Siam, Rania & Mamdouh, Wael. (2016). *Core-Shell Silver/Polymeric Nanoparticles-Based Combinatorial Therapy against Breast Cancer In-vitro OPEN*. *Scientific Reports*. 6. 10.1038.
11. Patra, J. K., Das, G., Fraceto, L. F., Campos, E. V. R., Rodriguez-Torres, M. del P., Acosta-Torres, L. S., Shin, H.-S. (2018). *Nano based drug delivery systems: recent developments and future prospects*. *Journal of Nanobiotechnology*, 16(1).
12. Rahmani AH, Alsahli MA, Aly SM, Khan MA, Aldebasi YH (2018). *Role of Curcumin in Disease Prevention and Treatment*. *Adv Biomed Res*, 7:38.
13. Yin, I. X., Zhang, J., Zhao, I. S., Mei, M. L., Li, Q., & Chu, C. H. (2020). *The Antibacterial Mechanism of Silver Nanoparticles and Its Application in Dentistry*. *International journal of nanomedicine*, 15, 2555-2562.
14. Pfeiffer C, Rehbock C, Hühn D, Carolina Carrillo-Carrion, Dorleta Jimenez de Aberasturi, Vivian Merk, Stephan Barcikowski, Wolfgang J Parak (2014). *Interaction of colloidal nanoparticles with their local environment: the (ionic) nanoenvironment around nanoparticles is different from bulk and determines the physico-chemical properties of the nanoparticles*. *J R Soc Interface*. 2014;11(96):20130931.
15. Gaaz TS, Sulong AB, Akhtar MN, Kadhum AA, Mohamad AB, Al-Amiry AA (2015). *Properties and Applications of Polyvinyl Alcohol, Halloysite Nanotubes and Their Nanocomposites*. *Molecules*. 2015;20(12):22833-22847.
16. Du Y, Xia L, Jo A, Davis RM, Bissel P, Ehrich MF, Kingston DGI. *Synthesis and Evaluation of Doxorubicin-Loaded Gold Nanoparticles for Tumor-Targeted Drug Delivery*. *Bioconjug Chem*. 2018 Feb 21;29(2):420-430.
17. Ravindra, S., A. Mulaba-Bafubandi, V. Rajinkanth, K. Varaprasad, N. Reddy, K. Mohana Raju. *Development and Characterization of Curcumin Loaded Silver Nanoparticle Hydrogels for Antibacterial and Drug Delivery Applications*. *Journal of Inorganic and Organometallic Polymers and Materials* 22 (2012): 1254-1262.
18. Mahmudin, L., Suharyadi, E., Utomo, A. B. S., & Abraha, K. (2016). *Influence of stabilizing agent and synthesis*

temperature on the optical properties of silver nanoparticles as active materials in surface plasmon resonance (SPR) biosensor.

19. Kyrychenko, A., Pasko, D. A., & Kalugin, O. N. (2017). *Poly(vinyl alcohol) as a water protecting agent for silver nanoparticles: the role of polymer size and structure*. Physical Chemistry Chemical
20. K.A. Juby, Charu Dwivedi, Manmohan Kumar, Swathi Kota, H.S. Misra, P.N. Bajaj, *Silver nanoparticle-loaded PVA/gum acacia hydrogel: Synthesis, characterization and antibacterial study*, *Carbohydrate Polymers*, Volume 89, Issue 3, 2012, Pages 906–913.
21. Khanna, P. K., Singh, N., Charan, S., Subbarao, V. V. V. S., Gokhale, R., & Mulik, U. P. (2005). *Synthesis and characterization of Ag/PVA nanocomposite by chemical reduction method*. *Materials Chemistry and Physics*, 93(1), 117–121.
22. Kayal, S., & Ramanujan, R. V. (2010). *Doxorubicin loaded PVA coated iron oxide nanoparticles for targeted drug delivery*. *Materials Science and Engineering: C*, 30(3), 484–490.
23. Papadimitriou, S., & Bikiaris, D. (2009). *Novel self-assembled core-shell nanoparticles based on crystalline amorphous moieties of aliphatic copolyesters for efficient controlled drug release*. *Journal of Controlled Release*, 138(2), 177–184.

■ Author

Nhi Nguyen, the main contributor and translator of this research paper, is a senior at Tran Dai Nghia High School. She has a consuming passion for chemistry and loves nothing more than working in her kitchen and her lab. Her intended major is Chemical Engineering.