

SYSTEMATIC LITERATUR REVIEW: SYNTHESIS OF SILVER NANOPARTICLES (AgNPs) USING SECONDARY METABOLITES OF FRUIT PEEL EXTRACT

Indana Lazulfa¹, Erindyah Retno Wikantyasning²*

¹Magister Farmasi, Universitas Muhammadiyah Surakarta, Surakarta, Indonesia ²Fakultas Farmasi, Universitas Muhammadiyah Surakarta, Surakarta, Indonesia *Email Corresponding : erindyah.rw@ums.ac.id

Submitted: 26 August 2023 Revised: 12 September 2023 Accepted: 19 September 2023

ABSTRACT

The synthesis of silver nanoparticles (AgNPs) using secondary metabolites of biological materials is a simple, cost-effective, and environmentally friendly method compared to physical synthesis methods. The secondary metabolites of the fruit peel extract can be used to synthesize AgNPs. Researchers chose experimental research articles with the theme of silver nanoparticle synthesis using fruit peels for review and selected journals published from 2018 to 2022 from web searches PubMed, Google Schoolar, Scopus, and ScienceDirect. The researchers screened and selected 28 articles according to the inclusion and exclusion criteria. The synthesis of AgNPs using fruit peel extracts can produce stable nanosized AgNPs. Silver nanoparticles synthesized using fruit peels showed stable silver nanoparticle synthesis results in terms of zeta potential and polydispersity index (PDI) values and obtained an average size of 2–200 nm with a spherical shape.

Keywords: Silver Nanoparticles, Fruit Peel Extract, Antibacterial agent

INTRODUCTION

Nanotechnology is a modern exploratory field involving the design, synthesis, and use of particles ranging in size from approximately one to 100 nm. Several metals, including Au (gold), Ag (silver), Ce (cerium), Pt (platinum), Pd (palladium), and Zn (zinc), can be used to create metal nanoparticles (Das, Patra, Debnath, et al., 2019) (Annu et al., 2018). In this study, silver salts were used. Silver is an antimicrobial agent that has been used since ancient times and was approved as an antibacterial agent in the early 1990s (Das, Patra, Debnath, et al., 2019) (Perveen et al., 2018). In addition, silver-based compounds are cheaper than goldbased ones. This compound also has a unique ability to fight infectious diseases by preventing the growth of bacteria, fungi, and germs, so silver nanoparticles are a popular component in many health products and devices (Yahya dan Abid, 2022). AgNPs can be prepared by reducing silver salts, usually with silver nitrate. Silver nanoparticle material can be formed using two approach, namely the "top-down" and "bottom-up" approach. The "topdown" approach involves breaking down large pieces of a material to produce the required nanostructures. The "bottom-up" approach forms nanoparticles by assembling single materials or molecules into larger nanostructures (Song et al., 2020). The "top-down" approach involves the mechanical grinding of the bulk metal with subsequent stabilization using colloidal protective agents. "Bottom-up" approach, such as chemical reduction methods, electrochemical methods, and others (Zhang et al., 2016).

AgNPs can be prepared using various types of nanoparticle synthesis methods, namely physical, chemical, and biological methods (Nguyen, 2020). In contrast to physical and chemical methods, nanoparticle synthesis uses biological methods or green nanoparticle synthesis, which is environmentally friendly, cost-effective, and stable for a long time, and can produce various forms of nanoparticles (such as spherical, spherical, prismatic, or plate) with sizes ranging from 1 to 100 nm. The combination of small size and high surface-to-volume ratio is the reason for the effectiveness of nanoparticle preparations (Alkhulaifi et al., 2020).

Open Journal Systems STF Muhammadiyah Cirebon : ojs.stfmuhammadiyahcirebon.ac.id

Certain plants have historically been recognized as good sources of medicinal chemicals and have been used in herbal medicine to treat various diseases (Yahya and Abid 2022). Plant biomass may also prove useful for the sustainable manufacture of nanoparticles. The 'green' way is also considered very effective in synthesizing nanomaterials for new product development. Nanoparticles synthesized with secondary metabolites of biological materials are considered relatively safe, environmentally friendly, harmless, and non-toxic (Das, Patra, Basavegowda, et al., 2019). Secondary metabolites at biological materials function as reducing agents to reduce silver salts, silver nitrate (AgNO3), so that in the bio method, the formation of silver nanoparticles is made using the 'Bottom-up" approach.

Extracts from various plant components, including algae, fungi, and microbes, can be used to create green nanoparticles (Patra, Das and Shin, 2019). The demand for environmentally friendly and non-toxic nanoparticle manufacturing techniques has fueled interest in biological approaches that avoid the use of hazardous chemicals as byproducts. Biological engineering has a high probability of being environmentally and economically advantageous. Biological methods involve the production of nanoparticles using microorganisms or medicinal plants (Yahya dan Abid, 2022).

To obtain important products and to further reduce or eradicate the waste materials produced, the green synthesis of nanoparticles is currently a very attractive research area. Biological synthesis of AgNPs is also considered advantageous because it is easier for mass production. AgNPs synthesized from secondary metabolites of biological materials are biocompatible and can be safely used for various therapeutic applications. Utilization of agricultural fruit peel waste in the synthesis of AgNPs is also an environmentally friendly opportunity (Das, Patra, Debnath, et al., 2019). With improved biodegradability and reduced toxicity, AgNPs offer remarkable anticancer, antiviral, antibacterial, and anti-inflammatory properties. An approach that is affordable and safe for the environment is the biosynthesis of silver NP (Das, Patra, Basavegowda, et al., 2019).

Silver nanoparticles (AgNPs) possess unique chemical, optical, electrical, magnetic, and mechanical properties. This unique feature can be useful in drug delivery applications (Yahya and Abid, 2022). AgNPs are commonly utilized in goods, including household antiseptic sprays, wound dressings, and antimicrobial coatings for medical devices, and are used to sterilize textiles and air surfaces because of their broad-spectrum antibacterial capabilities (Das, Patra, Debnath, *et al.*, 2019).

RESEARCH METHOD

This study was conducted using a systematic literature review. This systematic review presents the results of nanoparticle synthesis using various biological ingredients from fruit peels. This systematic literature review was conducted using several electronic databases, namely ScienceDirect, Scopus, PubMed, and Google Scholar, using the keywords biosynthesis, nanoparticles, silver, and fruit peels. The study was conducted using the following inclusion criteria: the research theme was the biological synthesis of AgNPs using fruit peels, studies provide variable results that confirm the formation and stability of AgNPs, and articles are available free of charge.

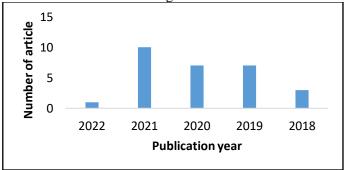


Figure 1. Number of articles publication year

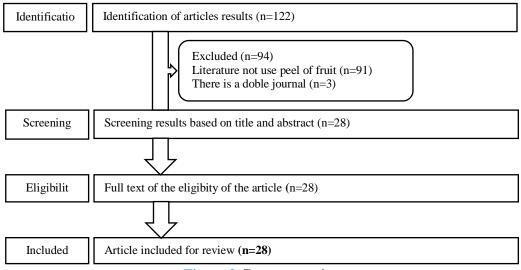


Figure 2. Data extraction

Research Procedure

The research strategy for studies or journal articles was selected using the following data: type of fruit peel used, resulting nanoparticle size results, resulting nanoparticle shape results, color results showing the formation of nanoparticles, and several variables of the resulting nanoparticle stability, such as polydispersity index (PDI), zeta potential, and yield. The following lists the criteria used to evaluate the methodological quality of the studies. To analyze the potential of silver bionanoparticles synthesized using fruit peels, we examined all selected articles, namely, the size characterization of the synthesized nanoparticles, the shape of the resulting nanoparticles, the color results showing the formation of nanoparticles, and the stability of the resulting nanoparticles. Articles that report a correlation between the concentration of the reducing agent and the reduced material, as well as the size of the resulting nanoparticles, are considered to be of higher methodological quality.

RESULTS AND DISCUSSION

The domains of biology, medicine, and engineering are all included in the expanding field of nanotechnology research. However, using a green strategy, the unique multidisciplinary field of nano-biotechnology makes it possible to utilize nanoparticles in biomedical settings. AgNPs can be produced from agricultural fruit peel waste in an environmentally friendly process (Das, Patra, Debnath, *et al.*, 2019).

N o	Fruit identity	conc	nple entrat on	con	NO ₃ centr ion	NP Size	NP Shap e	Colo r	Zeta Pote ntial	PDI	Referen ces
1	Citrus sinensis (a) Citrus limonum (b) Citrus reticulata (c)	50, and g/ml	100, 150	2 AgN 10 mM		75,67 nm	spher ical	brow n	-	-	(Yahya dan Abid, 2022)

Table I. Study of th	Biogynthesis	Characteristics of	f Silvor	Nononarticles
Table I. Study of th	e Diosviitilesis	Characteristics o	I Sliver	nanoparticles

2	Citrus par adisi	10 %	9 mL AgNO ₃ (0, 0,625, 1, 1,25, 2,5, 5, dan 10 mM)	160.5± 1.74 nm	-	reddi sh brow n	-	-	(Arsène <i>et al.</i> , 2021)
3	Citrus maxima Merr.	2,5 %	AgNO ₃ 0,1 M	13 ± 6 nm	spher ical	red – dark brow n	-	-	(Nguyen , 2020)
4	Citrus limon	10 %	50 mL AgNO ₃ 1 mM	59,74 nm	spher ical and rod- like	brow n	-	-	(Alkhul aifi <i>et</i> <i>al.</i> , 2020)
5	Citrus macropter a	10 %	40 mL AgNO ₃ 2 mM	11 nm	spher ical	Yello wish oran ge	-20. 8 mV	0,252	(Saha <i>et al.</i> , 2021)
6	Citrus limetta	40 %	0.001 N AgNO ₃	18 nm	spher ical	brow n	-	0,25 mon odisp ersi	(Dutta, Ghosh, <i>et al.</i> , 2020)
7	Citrus limon (a) Citrus tangerine (b) Citrus sinensis (c)	10 %	40 ml AgNO ₃ 1 mM	10 - 70 nm (a) 5 - 80 nm (b) 10 - 50 nm (c)	spher ical, trian gle, hexa gonal , rod	reddi sh brow n / golde n	-	-	(Niluxss hun, Masilam ani dan Mathive nthan, 2021)
8	Citrus sinensis	40 %	0.001 N AgNO ₃	22 nm	spher ical	brow n	-	0,226 mon odisp ersi	(Dutta, Chattop adhyay, <i>et al.</i> , 2020)
9	<i>Citrus</i> <i>reticulata</i> Blanco (Kinnow)	10 %	150 ml AgNO ₃ 1 mM	10–35 nm; 10,7 nm	spher ical	Dark brow n	-	-	(Jaast dan Grewal, 2021)
1 0	Citrus paradisi	30 %	80 mL AgNO ₃ 1 mM	14.84 ± 5 nm	spher ical	brow n	-	polid isper si	(Ayinde, Gitari dan Samie, 2019)
1	Citrus reticulum	40 %	2 mM AgNO ₃	10–19 nm; 14,6 nm	spher ical / oval	Dark brow n	-22,3 mV	0,197	(Omran <i>et al.</i> , 2021)
1 2	Ananas comosus	22 %	100 mL AgNO ₃	37,32 %	Nearl v	Redd ish	-	-	(Das, Patra,

Medical Sains : Jurnal Ilmiah Kefarmasian Vol. 8 No. 3, July – September 2023, Page. 1289-1304

	(L.)		1 mM		spher ical	brow n			Debnath , <i>et al.</i> , 2019)
1	Ananas	40 %	10 mM	11,61	spher	Dark	-	-	(Baran
3	comosus		AgNO ₃	nm	ical	brow n			<i>et al.</i> , 2021)
1 4	Punica granatum (black skin)	10 %	6 mM AgNO ₃	15.6 nm	spher ical	Dark brow n / redne ss	-39,6 mV	0,32	(Khorra mi, Zarepou r dan Zarrabi, 2019)
1	Punica	33 %	1 mM	15-30	spher	Dark	31,2	0,321	(Khan et
5	granatum		AgNO ₃	nm; 20 nm	ical	brow n	± 0,3 mV		<i>al.</i> , 2021)
1	Punica	10 %	1 mM	57.7 -	spher	Dark	-	-	(Joshi et
6	granatum		AgNO ₃	142.4 nm	ical	brow n	68.9 3 mv		<i>al.</i> , 2018)
1 7	Punica granatum	10 %	AgNO ₃ 0.1 mM	20 - 40 nm; 26,95 nm.	spher ical	brow n	-	-	(Devane san <i>et</i> <i>al.</i> , 2018)
1 8	Punica granatum L Citrullus lanatus	7 % pomegran ate (PP) and watermel on (WP)	100 ml silver AgNO ₃ 1 mM	PPAg NPs : 15 - 70 nm; 61 nm WPAg NPs : 20 - 85 nm; 75 nm	spher ical	Dark brow n	PPA gNPs : - 25.4 6 mV WPA gNPs : - 21.3 3 mV	-	(Saad <i>et</i> <i>al.</i> , 2021)
1 9	Vitis vinifera	20 %	AgNO ₃	30–65 nm	spher ical	Dark brow n	-28.4 mV	-	(Hashim <i>et al.</i> , 2020)
2 0	Vitis vinifera	10 %	90 mL AgNO ₃ 1 mM	10–50 nm; 30 nm	spher ical and nearl y spher ical	reddi sh brow n	-	polid isper si	(Kowsal ya <i>et al.</i> , 2019)
2 1	Ipomoea batatas (L.)	40 %	500 mL AgNO ₃ 1 mM	-	spher ical	reddi sh brow n	-	-	(Das, Patra, Basaveg owda, <i>et</i> <i>al.</i> , 2019)
2 2	Pisum sativum L.	25 %	100 mL AgNO ₃ 1 mM	10 - 25 nm; 16,18	spher ical	reddi sh brow	-	-	(Patra, Das dan Shin,

Systematic Literatur Review: Synthesis of Silver Nanoparticles (AgNPs) ... (Lazulfa et al.)

				nm		n			2019)
2 3	Benincasa hispida	40%	1 mM AgNO ₃	26±2 nm	spher ical	brow nish yello w	28 mV	-	(Solima n <i>et al.</i> , 2020)
2 4	Litchi chinensis	0,5 %	0.1 mM AgNO ₃	3-10 nm	spher ical	light yello w	-	-	(Pervee n <i>et al.</i> , 2018)
2 5	Magifera indica	10 %, 15 %, 20 %, 25 %, 30 %, and 35 %	25 mL of 2.0 mM/L AgNO ₃	25-70 nm; 23.7 nm	spher ical, oval, irreg ular	reddi sh brow n	-	-	(Xing <i>et</i> <i>al.</i> , 2021)
2 6	Stenocere us queretaro ensis	1 %	2 mM AgNO ₃ solution	60 - 200 nm; 98,96 nm	spher ical	reddi sh brow n	-	-	(Padilla- Camber os <i>et al.</i> , 2021)
2 7	Opuntia ficus- indica	40 %	90 mL 1 mM AgNO ₃	20– 60 nm	spher ical	brow n	-	-	(Kamara j <i>et al.</i> , 2020)
2 8	Aegle marmelos	1 % (a), 5 % (b), 10 % (c)	1 mM AgNO ₃	(a,b) 12- 30 nm (c) 10- 15 nm	spher ical	dark red brow n	-14.2 mV (a) -20.3 mV (b) -21.9 mV (c)	(a,b) Polid isper si (c) mon odisp ersi	(Kushw ah <i>et al.</i> , 2019)

A. Factors that determine the success of making silver nanoparticles

Different synthetic processes produce different forms of AgNPs. The various forms of AgNPs are round, triangular, square, cubic, rectangular, stem, oval, and flowered (Akter *et al.*, 2018). The nanoparticle formation depends on the concentration of the reducing agent used. Spherical forms were formed at lower concentrations, and other forms were formed at higher concentrations. The shape of stable nanoparticles tends to be spherical because spheres have the least surface per unit volume, so the interfacial energy is minimal (Liu *et al.*, 2012). Temperature, dispersion agents, surfactants, and other variables can all affect the consistency and amount of nanoparticles produced (Yaqoob, Umar and Ibrahim, 2020).

1. Concentration of dispersed substance AgNP : silver nitrate (AgNO₃)

The concentration of AgNO₃ greatly influenced the success of the AgNP synthesis. Commonly used concentrations of silver nitrate (AgNO₃) were 1, 2, and 10 mM. The synthesis of silver nanoparticles (NP) causes a color change from yellow to brown. The use of a AgNO₃ solution with a higher concentration in the AgNP synthesis process produces a more concentrated colloidal NP color. This indicates that an increasing number of NPs are formed or that the concentration of NPs formed is also higher (Masykuroh and Puspasari, 2022). In other words, the greater the silver nitrate (AgNO₃) concentration, the deeper is the color of the solution. A solution containing 2 mM AgNO₃ had a lighter hue than a solution

containing 10 mM AgNO₃. Additionally, the absorbance value increased with increasing silver nitrate concentration. Thus, AgNPs may be affected by fluctuations in the concentration of silver nitrate (AgNO₃) (Mulwandari, 2022) (Masykuroh dan Puspasari, 2022).

The formation of AgNPs can be observed visually from the color change and the appearance of a peak at a wavelength in the range of 400-450 nm which is the wavelength of AgNPs. The use of the same reducing agent with a greater precursor concentration can cause the silver reduction process to take a shorter time, as seen from the color change to dark brown and the increase in absorbance intensity. Qualitatively, the higher the absorbance value, the greater the number of nanoparticles formed or the higher the concentration of nanoparticles in the solution (Mulwandari, 2022). The greater the concentration of AgNO₃ used in the synthesis, the greater the amount of Ag^+ that must be reduced resulting in greater agglomeration and resulting in a larger size distribution of the AgNPs (Nalawati, Suyatma and Wardhana, 2021). Increasing the concentration of AgNO₃ resulted in a smaller AgNP size. This is related to the high surface area per unit volume, which can further increase particle connectivity and electrical conductivity (Htwe *et al.*, 2019).

2. Concentration of dispersing agent

Aqueous polymers were used to create AgNPs, which had a restricted diameter range and a typical diameter of approximately 10 nm. However, compared to aqueous polymer-based AgNPs, silver nanoparticles prepared using low-molecular-weight dispersion agents are smaller and have a lighter distribution of species (Yaqoob, Umar and Ibrahim, 2020). In addition, AgNPs synthesized with a higher concentration of the dispersing agent had a darker solution color than a solution with a smaller concentration of the dispersing agent (Mulwandari, 2022).

It is believed that the phytochemical elements included in the dispersion agents reduce AgNPs or serve as reducing agents in the production of AgNPs, including polyphenols. Through a charge transfer process, the hydroxyl groups found in polyphenols can function as reducing agents. In addition, vitamins, such as ascorbate, can transform atmospheric oxygen into water, a process that is accelerated by the presence of metal ions and light. The synthesis of AgNPs can be enhanced by increasing the reducing power of ascorbic acid through oxidation to dehydroascorbic acid (Omran et al., 2021).

Alkaloids, terpenoids, and certain coenzymes are examples of phenolic compounds with reducing properties. The coenzymes include nicotinamide adenine dinucleotide (NAD), NADH, and NAD⁺. NADH is transformed into an electron donor and aids in the transport of electrons during redox processes, whereas NAD⁺ is an oxidizing and reducing substance that functions as an electron acceptor (Omran *et al.*, 2021). Compounds such polyphenols, flavonoids, tannins, and ascorbic acid; in addition to serving as an antioxidant, they have the ability to convert Ag^+ into AgNP, which might lead to the efficient synthesis of AgNPs in industrial production (Saha *et al.*, 2021).

Phenolics and flavonoids contain aromatic rings and hydroxyl groups (Kushwah *et al.*, 2019). The functional groups in the essential oils contained in reducing agents, apart from functioning as reducing agents, are also responsible for their stability. This functional group is responsible for the reduction of Ag⁺ ions to AgNPs (Mulwandari, 2022). Various phenolic compounds, such as geraniol, hotrieniol, carveol, linalool, and menthol, can also reduce Ag⁺ ions and stabilize AgNPs (Dutta, Chattopadhyay, *et al.*, 2020) (Dutta, Ghosh, *et al.*, 2020). Various phenolic compounds act as reducing and stabilizing agents (Dutta, Chattopadhyay, *et al.*, 2020). When plant extracts are used for biosynthesis, AgNPs are captured and covered with phenolic compounds. Phenolic compounds can capture AgNPs and prevent their contact and possible agglomeration (Liu, Chang dan Chen, 2018).

Additionally, proteins, polysaccharides, terpenoids, organic acids, and polyphenols can attach to the free carboxylic ions of amino acids or amine groups, function as stabilizing agents for AgNPs, and bind to AgNPs (Omran *et al.*, 2021) (Hashim *et al.*, 2020).

3. Temperature

Temperature has the greatest impact on material synthesis (Crisan *et al.*, 2021). Heating and incubating AgNO₃ solutions can be useful for reducing Ag⁺ ions to produce silver nanoparticles (AgNPs) (Jaast and Grewal, 2021). According to research by Crisan et al., 2021, at lower temperatures, nanoparticles cannot be produced. The reaction for the formation or synthesis of AgNPs can be affected by the temperature. The reaction temperature has an important effect because an increase in the reaction temperature results in a decrease in the particle size, while a decrease in the reaction temperature can result in an increase in the particle size. When the reaction for the formation of nanoparticles is carried out at low temperatures, the resulting silver particles are larger (Elamawi, Al-Harbi and Hendi, 2018) (Yaqoob, Umar and Ibrahim, 2020).

As the temperature was increased, the absorbance increased. At room temperature, the AgNP reaction rate was sluggish; however, by increasing the temperature of the reaction mixture, the reaction rate could be increased. Ag+ ions are rapidly reduced as the reaction temperature increases, and the subsequent homogenous nucleation of Ag nuclei can result in the formation of small AgNPs (Khalil et al., 2014). According to Crisan et al., 2021, the synthesis of AgNPs at 80 °C results in the formation of metal nanoparticles. However, if the synthesis is carried out at temperatures up to 100 °C, the rate of the reaction becomes very high and can inhibit particle growth. This is caused by the very high temperature of the production of nanoparticle preparations, which can increase the reaction rate, resulting in unwanted reactions. However, the rate of reaction was slow at low temperatures, and after three hours the color of the solution began to change (Yaqoob Umar and Ibrahim, 2020).

Temperature affects the form of the nanoparticles. If the process for the creation of AgNPs is conducted at an insufficient temperature, the resultant AgNPs will not have a spherical shape (Yaqoob, Umar and Ibrahim, 2020). The formation of AgNPs at low temperatures can produce small spherical particles and nanorods, whereas at higher temperatures, platelet nanoparticles are formed (Crisan *et al.*, 2021).

4. The pH of the solution AgNP

The pH of the solution can affect the formation of AgNPs. There is a possibility of agglomeration owing to changes in the pH of the solution (Selvamani, 2019). Given that the pH affects the surface charge characteristics of the catalyst, the initial pH of the solution is a crucial variable affecting color deterioration. AgNPs become negatively charged at pH values greater than 8. However, at a pH lower than 5, AgNPs have a positive charge. The rate of degradation from the starting pH of the catalyst solution indicated that the degradation processes were efficient at pH 6.5. With a solution of H₂SO₄ (to acidify) and NaOH (to alkalinize), the pH of the reaction may change (Nagar and Devra, 2019). According to research by Crisan et al., 2021, at pH 5, a silver nanoparticle synthesis process occurs at a low rate, whereas at pH 9, the silver nanoparticle synthesis process occurs at an intensive rate. Meanwhile, a research by Gontijo et al., 2020 found that when processes with a pH range of 3–7 are utilized, the aggregation for the creation of nanoparticles is significant. The use of a pH range of 3–7 causes aggregation, which leads to the production of small nanoparticles (Gontijo *et al.*, 2020).

Changes in pH during the preparation of nanoparticle solutions can cause changes in absorbance. The absorbance increased with increasing pH from 2 to 8 and then decreased. By changing the pH of the reaction mixture, it was possible to

control the size and form of the biosynthesized nanoparticles. The ability of reaction pH to alter the electrical charge of biomolecules may have a significant impact on their capacity for capping and stability, which may subsequently affect the development of nanoparticles. In comparison to an alkaline medium, the particle size is anticipated to be greater in acidic media. With a spherical form, the particle size at pH 3 was larger than that at pH 8. The capacity to decrease and stabilize nanoparticles was improved in an alkaline pH environment. It is crucial to monitor the rate of AgNPs at pH 8 and room temperature, because the reaction occurs more quickly. The number of nuclei and size of the resultant AgNPs were mediated by the extract at pH 8. Owing to the enhanced reactivity of reducing agents, the number of nuclei increases with increasing pH, causing the absorption peak of the product to shift with increasing pH, which is accompanied by a reduction in the size of silver nanoparticles (Khalil *et al.*, 2014).

5. The Photochemistry

Visible light can also be used for photochemical processes. Visible light includes sunlight, artificial white light, and monochromatic light (e.g. blue light, red light, etc.). Visible light is defined as radiation that excites the human visual system. Spectrum variations depend on the amount of radiation energy that reaches the retina, with a lower limit of 360–400 nm and an upper limit of 760–830 nm. Visible light that can be utilized in photochemical processes such as sunlight, artificial white light, and monochromatic light (e.g. blue light, red light, etc.) (Jara et al., 2021).

The 'photo' process variable can also influence the nanoparticle synthesis approach. The 'photo' process variable refers to the synthesis of AgNP, which is accomplished by photoreducing AgNO3 in a suspension of layered inorganic clay, which serves as a stabilizer to prevent nanoparticle aggregation. A relatively constant size and diameter distribution may be achieved using this irradiation approach to reduce the size of AgNPs using a single distribution mode. However, this approach requires expensive equipment and appropriate experimental settings (Natsuki and Hashimoto, 2015).

6. The Surfactant

Research by Yaqoob et al. in 2020 indicated that polyvinylpyrrolidone (PVP) is an effective surfactant employed in the manufacture of AgNPs. PVP is frequently employed as a dispersant because it can slow the formation of nanoparticles and create balanced colloidal nanoparticles. PVP significantly affected the application of the AgNPs. Agglomeration occurs when a small amount of PVP is employed, which may lead to partial coating of the PVP particles. To produce smaller-sized silver particles, PVP and AgNO3 ratios should be balanced. Therefore, PVP was applied to the surface of the particles. The sizes of the metal nanoparticles increased with the addition of PVP. Therefore, a significant quantity of PVP did not result in smaller colloidal particles. High volumes may be detrimental to particle creation, and hence, they are not advantageous. Silver nanoparticles with oxygen or nitrogen in PVP were described by FT-IR spectra as a coating on the surfaces of metal particles. Consequently, the coating prevented particle aggregation and generated spherical particles. Additionally, sodium gluconate (C5H11O5COONa) was present as a dispersing element, as confirmed by FT-IR. It has been demonstrated that $C_5H_{11}O_5COO$ may create a shield on the surface of metal nanoparticles. This layer can prevent the AgNPs from forming large spherical particles and tiny clumps (Yaqoob Umar and Ibrahim, 2020).

B. Variables indicating successful formation of good silver nanoparticles

1. Particle size

Small particle sizes may tolerate particle aggregation, which can increase the potential stability of nanoparticle preparation. The spherical shape and particle size of AgNPs affect their degrading activity because as the size decreases, the active site

and surface area increase, increasing the binding area (Jaast and Grewal, 2021). The resulting particle size affects the performance of the material. A small particle size results in a large surface area, which accelerates the absorption of these particles. The optimal formula for AgNPs produced a particle size distribution with one peak. The peak of the curve represents the particle size distribution area, indicating good uniformity of the particle size (Mulwandari, 2022). The concentration of AgNO3 that increases during synthesis is used, the resulting particle size will be smaller so that in the end it allows for an increase in activity (Masykuroh dan Puspasari, 2022).

Particle size obtained from the synthesis of nanoparticles using secondary metabolites from fruit peels, 3–200 nm. The secondary metabolites of lychee (Litchi chinensis) produced the smallest particle size, between 3 and 10 nm. The secondary metabolites of the cactus fruit (Stenocereus quercetaroensis) produced the largest particle size, between 60 and 200 nm. In addition, in research Kushwah et al., 2019, the greater the amount of extract solution used, the smaller was the resulting particle size. This was proven using 1–5 ml of Aegle marmelos extract, and the researchers obtained particle sizes of 12-30 nm. Meanwhile, with 10 ml of Aegle marmelos extract, researchers obtained particle sizes of 10-15 nm. The color of the synthesis of AgNPs with secondary metabolites indicates the successful formation of AgNPs, namely red brown to dark brown. A color change from colorless to brown, or yellow to reddish brown, indicates the reduction of silver Ag+ ions to silver nanoparticles (AgNPs) (Niluxsshun, Masilamani dan Mathiventhan, 2021) (Arsène et al., 2021). The synthesis of AgNPs from various biological materials, on average, produces spherical nanoparticles.

The size of the silver particles can influence antibacterial activity; the smaller the nanoparticles, the higher the antibacterial impact (Nalawati Suyatma and Wardhana, 2021). According to a study by Crisan et al., 2021, nanoparticle preparations with particle sizes below 10 nm have a significant increase in antibacterial activity. Nanoparticles of smaller dimensions are related with better bacterial cell wall penetration and more severe destruction due to the buildup of reactive oxygen species (ROS). Small- and medium-sized AgNPs have a significant influence on mitochondrial electron transport, phagocytosis, autophagy, organelle integrity, and organization (e.g., microtubules). Transcriptional responses to medium-sized AgNPs were also detected. AgNPs can readily pass through the kidneys and are eliminated from the body via the urinary system because of their modest hydrodynamic diameter (less than 6 nm), which considerably minimizes the danger of long-term toxicity.

2. Zeta potential (ZP)

The zeta potential (ZP) is a parameter that expresses the electrochemical equilibrium between particles and liquids, such as colloidal nanoparticle (NP) solutions used in medicine, pharmaceuticals, chemical manufacturing, mineral processing, and water and soil cleaning. ZP is a physicochemical property that indicates the stability of a colloidal particle system owing to the presence of charged groups/molecules on the surface of the material, which may alter its performance and processing properties in suspension. Process control, quality, and product standards are all affected by the ZP values (Lunardi et al., 2021). The ZP value of an aqueous solution of AgNPs determines the stability of the preparation (Farzeen and Kumar, 2022).

A low zeta potential induces repulsion rather than attraction and the dispersion breaks and flocculates (Chitradevi, Jestin Lenus and Victor Jaya, 2019). In general, the zeta potential value of nanoparticle preparations can be said to reach a good level of stability, that is, when the preparation has a zeta potential greater than +25 mV and less than -25 mV (Omran et al., 2021). Another study has reported that the zeta potential of stable AgNPs should be at least 30 mV. The stabilizing effect of this

zeta potential value can produce nanoparticles with a narrow size distribution index (Farzeen and Kumar, 2022). Meanwhile, some of the studies analyzed yielded zeta potential values of 14.2 - 68.93 mV. According to Kushwah et al., 2019, the greater the amount of extract solution used, the higher the zeta potential obtained, thus showing more stable NP results. In addition, the electrical conductivity of the synthesized AgNPs decreases with increasing AgNO3 concentration (Htwe et al., 2019).

Extreme positive or negative zeta potential values of nanoparticle solutions can produce strong repulsive forces. The higher the zeta potential value (negative or positive), the smaller the possibility of particle aggregation owing to electrical repulsion. However, if the particles have a lower zeta potential value (negative or positive), then the particles will not have the power to prevent the particles from coming together, and flocculation will occur (Sulaiman *et al.*, 2020) (Pradita and Wahyuni, 2023).

Potential Zeta Value	Stability				
>30 mV	Good stability				
>60 Mv	Excellent stability				
20 mV	Short term stability				
-5 mV dan 5mV	Fast aggregation occurs				
(Sulaiman <i>et al.</i> , 2020)					

 Table II. Potential Zeta Value based on

3. Polydispersity index (PDI) value

The value of the polydispersity index or PDI is used to describe the uniformity of particle sizes and to estimate the range of particle size distribution present in a sample. PDI can be used to determine whether aggregation occurs in the sample. The polydispersity index value in nanoparticle preparations has meaning, namely the value "0" represents the highest level of monodispersion, while the value "1" represents the distribution of polydispersity particles (Omran et al., 2021). Monodisperse systems are more stable than polydisperse systems, and polydisperse systems tend to form aggregates because they do not have the same molecular weight. The formulation is considered to be more stable in a monodisperse system because it is more homogeneous with a certain size (Danaei et al., 2018).

The articles analyzed showed PDI values of 0.197–0.321. The results obtained, on average, show monodisperse PDI results, which are approximately ± 0.200 , indicating a better level of distribution. The polydispersity index determines the uniformity of the size of the nanoparticles so that they can provide greater opportunities to interact with compounds or bait organisms in activity tests (Masykuroh and Puspasari, 2022).

CONCLUSION

AgNPs synthesized using secondary metabolites of fruit peel extract can produce nanoparticles with good quality and quantity. The quality and quantity of the nanoparticle synthesis results can be supported by increasing the concentration of the dispersed substance, silver salts (AgNO₃), and a large number of secondary metabolites in fruit peel extracts, such as the phenolic group in the dispersing agent. In addition, the use of a synthesis temperature of 80 °C, an optimal pH (usually use a pH that tends to be alkaline), controlling environmental light, and using additives such as surfactants like PVP to help prevent particle agglomeration. Good AgNP results, in addition to producing particles with nano sizes, variables that indicate the successful formation of AgNPs are such as zeta potential values of more than +30 mV and less than -30 mV, the high zeta potential value indicates that the possibility of particle aggregation due to electrical repulsion is smaller. The values of PDI also show homogeneity particle size of AgNP, monodisperse homogeneity indicates the uniformity of the particles produced with the possibility of small interactions between particles.

REFERENCES

- Akter, M. *et al.* (2018) "A systematic review on silver nanoparticles-induced cytotoxicity: Physicochemical properties and perspectives," *Journal of Advanced Research*, 9, hal. 1–16. doi: 10.1016/j.jare.2017.10.008.
- Alkhulaifi, M. M. et al. (2020) "Green synthesis of silver nanoparticles using Citrus limon peels and evaluation of their antibacterial and cytotoxic properties," Saudi Journal of Biological Sciences, hal. 3434–3441. doi: https://doi.org/10.1016/j.sjbs.2020.09.031.
- Annu *et al.* (2018) "Fruit waste (peel) as bio-reductant to synthesize silver nanoparticles with antimicrobial, antioxidant and cytotoxic activities," *Journal of Applied Biomedicine*, 16(3), hal. 221–231. doi: 10.1016/j.jab.2018.02.002.
- Arsène, M. M. J. et al. (2021) "Antibacterial activity of grapefruit peel extracts and greensynthesized silver nanoparticles," Veterinary World, 14(5), hal. 1330–1341. doi: 10.14202/vetworld.2021.1330-1341.
- Ayinde, W. B., Gitari, W. M. dan Samie, A. (2019) "Optimization of microwave-assisted synthesis of silver nanoparticle by Citrus paradisi peel and its application against pathogenic water strain," *Green Chemistry Letters and Reviews*, 12(3), hal. 225–234. doi: 10.1080/17518253.2019.1627427.
- Baran, A. et al. (2021) "Ecofriendly Synthesis of Silver Nanoparticles Using Ananas comosus Fruit Peels: Anticancer and Antimicrobial Activities," *Bioinorganic Chemistry and Applications*, 2021. doi: 10.1155/2021/2058149.
- Chitradevi, T., Jestin Lenus, A. dan Victor Jaya, N. (2019) "Structure, morphology and luminescence properties of sol-gel method synthesized pure and Ag-doped ZnO nanoparticles," *Materials Research Express*, 7(1). doi: 10.1088/2053-1591/ab5c53.
- Crisan, C. M. *et al.* (2021) "Review on silver nanoparticles as a novel class of antibacterial solutions," *Applied Sciences (Switzerland)*, 11(3), hal. 1–18. doi: 10.3390/app11031120.
- Danaei, M. *et al.* (2018) "Impact of particle size and polydispersity index on the clinical applications of lipidic nanocarrier systems," *Pharmaceutics*, 10(2), hal. 1–17. doi: 10.3390/pharmaceutics10020057.
- Das, G., Patra, J. K., Basavegowda, N., *et al.* (2019) "Comparative study on antidiabetic, cytotoxicity, antioxidant and antibacterial properties of biosynthesized silver nanoparticles using outer peels of two varieties of ipomoea batatas (L.) lam," *International Journal of Nanomedicine*, 14, hal. 4741–4754. doi: 10.2147/JJN.S210517.
- Das, G., Patra, J. K., Debnath, T., *et al.* (2019) "Investigation of antioxidant, antibacterial, antidiabetic, and cytotoxicity potential of silver nanoparticles synthesized using the outer peel extract of Ananas comosus (L.)," *PLoS ONE*, 14(8), hal. 1–19. doi: 10.1371/journal.pone.0220950.
- Devanesan, S. *et al.* (2018) "Antimicrobial and Cytotoxicity Effects of Synthesized Silver Nanoparticles from Punica granatum Peel Extract.," *Nanoscale research letters*, 13(1), hal. 315. doi: 10.1186/s11671-018-2731-y.
- Dutta, T., Chattopadhyay, A. P., *et al.* (2020) "Biogenic silver nanoparticle synthesis and stabilization for apoptotic activity; insights from experimental and theoretical studies," *Chemical Papers*, 74(11), hal. 4089–4101. doi: 10.1007/s11696-020-01216-z.
- Dutta, T., Ghosh, N. N., et al. (2020) "Green synthesis of antibacterial and antifungal silver nanoparticles using Citrus limetta peel extract: Experimental and theoretical studies," *Journal of Environmental Chemical Engineering*, 8(4), hal. 104019. doi: 10.1016/j.jece.2020.104019.

- Elamawi, R. M., Al-Harbi, R. E. dan Hendi, A. A. (2018) "Biosynthesis and characterization of silver nanoparticles using Trichoderma longibrachiatum and their effect on phytopathogenic fungi," *Egyptian Journal of Biological Pest Control*, 28(1), hal. 1–11. doi: 10.1186/s41938-018-0028-1.
- Farzeen, S. dan Kumar, A. (2022) "Synthesis of silver nanoparticles (AgNPs) of leaves extract of Rhynchoglossum notonianum wall. for enhancing its bioavailability and antibacterial activity," *International journal of health sciences*, 6(March), hal. 6947– 6961. doi: 10.53730/ijhs.v6ns2.6756.
- Gontijo, L. A. P. *et al.* (2020) "pH effect on the synthesis of different size silver nanoparticles evaluated by dls and their size-dependent antimicrobial activity," *Revista Materia*, 25(4), hal. 1–10. doi: 10.1590/S1517-707620200004.1145.
- Hashim, N. *et al.* (2020) "Green mode synthesis of silver nanoparticles using Vitis vinifera's tannin and screening its antimicrobial activity / apoptotic potential versus cancer cells," *Materials Today Communications*, 25(March), hal. 101511. doi: 10.1016/j.mtcomm.2020.101511.
- Htwe, Y. Z. N. et al. (2019) "Effect of silver nitrate concentration on the production of silver nanoparticles by green method," *Materials Today: Proceedings*, 17, hal. 568–573. doi: 10.1016/j.matpr.2019.06.336.
- Jaast, S. dan Grewal, A. (2021) "Green synthesis of silver nanoparticles, characterization and evaluation of their photocatalytic dye degradation activity," *Current Research in Green and Sustainable Chemistry*, 4(August), hal. 100195. doi: 10.1016/j.crgsc.2021.100195.
- Jara, N. et al. (2021) "Photochemical synthesis of gold and silver nanoparticles-a review," *Molecules*, 26(15), hal. 1–24. doi: 10.3390/molecules26154585.
- Joshi, S. J. et al. (2018) "Green synthesis of silver nanoparticles using pomegranate peel extracts and its application in photocatalytic degradation of methylene blue," Jundishapur Journal of Natural Pharmaceutical Products, 13(3), hal. 0–4. doi: 10.5812/jjnpp.67846.
- Kamaraj, M. et al. (2020) "Rapid Green Synthesis of Silver Nanoparticles Using Ethiopian Cactus Pear Fruit Peel Infusions and Evaluation of Its In Vitro Clinical Potentials," *Journal of Inorganic and Organometallic Polymers and Materials*, 30(9), hal. 3832– 3836. doi: 10.1007/s10904-020-01549-y.
- Khalil, M. H. et al. (2014) "Green synthesis of silver nanoparticles using olive leaf extract and its antibacterial activity," Arabian Journal of Chemistry, 7(6), hal. 1131– 1139. doi: 10.1016/j.arabjc.2013.04.007.
- Khan, A. A. *et al.* (2021) "Pomegranate peel induced biogenic synthesis of silver nanoparticles and their multifaceted potential against intracellular pathogen and cancer," *Saudi Journal of Biological Sciences*, 28(8), hal. 4191–4200. doi: 10.1016/j.sjbs.2021.06.022.
- Khorrami, S., Zarepour, A. dan Zarrabi, A. (2019) "Green synthesis of silver nanoparticles at low temperature in a fast pace with unique DPPH radical scavenging and selective cytotoxicity against MCF-7 and BT-20 tumor cell lines," *Biotechnology Reports*, 24, hal. e00393. doi: 10.1016/j.btre.2019.e00393.
- Kowsalya, E. *et al.* (2019) "Biocompatible silver nanoparticles/poly(vinyl alcohol) electrospun nanofibers for potential antimicrobial food packaging applications," *Food Packaging and Shelf Life*, 21(September 2018), hal. 100379. doi: 10.1016/j.fpsl.2019.100379.
- Kushwah, M. et al. (2019) "Antibacterial and Antioxidant Activity of Biosynthesized Silver Nanoparticles Produced by Aegle marmelos Fruit Peel Extract," Analytical Chemistry Letters, 9(3), hal. 329–344. doi: 10.1080/22297928.2019.1626279.
- Liu, Y. *et al.* (2012) "The shape of things to come: Importance of design in nanotechnology for drug delivery," *Therapeutic Delivery*, 3(2), hal. 181–194. doi: 10.4155/tde.11.156.
- Liu, Y. S., Chang, Y. C. dan Chen, H. H. (2018) "Silver nanoparticle biosynthesis by using phenolic acids in rice husk extract as reducing agents and dispersants," *Journal of*

Food and Drug Analysis, 26(2), hal. 649–656. doi: 10.1016/j.jfda.2017.07.005.

- Lunardi, C. N. *et al.* (2021) "Experimental methods in chemical engineering: Zeta potential," *Canadian Journal of Chemical Engineering*, 99(3), hal. 627–639. doi: 10.1002/cjce.23914.
- Masykuroh, A. dan Puspasari, H. (2022) "Antibacterial Activity of Silver Nano Particles Biosynthesized Using Alocasia macrorrhizos Extract Against Staphylococcus aureus and Escherichia coli," *Bioma : Jurnal Biologi Makassar*, 7(1), hal. 76–85. doi: 10.20956/bioma.v7i1.19350.
- Mulwandari, M. (2022) Synthesis Of Silver Nanoparticles Using Citronella Oil (Cymbopogon Nardus L. Rendle)To Inhibit The Growth Of Lichen On Temple Stones. Universitas Islam Indonesia.
- Nagar, N. dan Devra, V. (2019) "A kinetic study on the degradation and biodegradability of silver nanoparticles catalyzed Methyl Orange and textile effluents," *Heliyon*, 5(3), hal. e01356. doi: 10.1016/j.heliyon.2019.e01356.
- Nalawati, A. N., Suyatma, N. E. dan Wardhana, D. I. (2021) "Synthesis of Silver Nanoparticle (NPAg) using Seed Aqueous Extract of Jatropha Curcas L and Their Anti-Bacterial Activity Assessment," Jurnal Teknologi dan Industri Pangan, 32(1), hal. 98–106. doi: 10.6066/jtip.2021.32.2.98.
- Natsuki, J., Natsuki, T. dan Hashimoto, Y. (2015) "A Review of Silver Nanoparticles: Synthesis Methods, Properties and Applications," *International Journal of Materials Science and Applications*, 4(5), hal. 325. doi: 10.11648/j.ijmsa.20150405.17.
- Nguyen, V. T. (2020) "Sunlight-Driven Synthesis of Silver Nanoparticles Using Pomelo Peel Extract and Antibacterial Testing," *Journal of Chemistry*, 2020. doi: 10.1155/2020/6407081.
- Niluxsshun, M. C. D., Masilamani, K. dan Mathiventhan, U. (2021) "Green Synthesis of Silver Nanoparticles from the Extracts of Fruit Peel of Citrus tangerina, Citrus sinensis, and Citrus limon for Antibacterial Activities.," *Bioinorganic chemistry and applications*, 2021, hal. 6695734. doi: 10.1155/2021/6695734.
- Omran, B. A. *et al.* (2021) "Biovalorization of mandarin waste peels into silver nanoparticles and activated carbon," *International Journal of Environmental Science and Technology*, 18(5), hal. 1119–1134. doi: 10.1007/s13762-020-02873-z.
- Padilla-Camberos, E. *et al.* (2021) "Biosynthesis of silver nanoparticles using stenocereus queretaroensis fruit peel extract: Study of antimicrobial activity," *Materials*, 14(16). doi: 10.3390/ma14164543.
- Patra, J. K., Das, G. dan Shin, H. S. (2019) "Facile green biosynthesis of silver nanoparticles using Pisum sativum L. outer peel aqueous extract and its antidiabetic, cytotoxicity, antioxidant, and antibacterial activity," *International Journal of Nanomedicine*, 14, hal. 6679–6690. doi: 10.2147/IJN.S212614.
- Perveen, S. et al. (2018) "Antibacterial evaluation of silver nanoparticles synthesized from lychee peel: individual versus antibiotic conjugated effects," World Journal of Microbiology and Biotechnology, 34(8). doi: 10.1007/S11274-018-2500-1.
- Pradita, E. Y. dan Wahyuni, S. (2023) "Nanogel Synthesis Of Chitosan-Alginate-Siam Orange (Citrus nobilis Lour) Extract and Its Antibacterial Activity," *Indonesian Journal of Chemical Science*, 12(1). Tersedia pada: http://journal.unnes.ac.id/sju/index.php/ijcs.
- Saad, A. M. *et al.* (2021) "Polyphenolic extracts from pomegranate and watermelon wastes as substrate to fabricate sustainable silver nanoparticles with larvicidal effect against Spodoptera littoralis: Polyphenolic extracts from pomegranate and watermelon wastes," *Saudi Journal of Biological Sciences*, 28(10), hal. 5674–5683. doi: 10.1016/j.sjbs.2021.06.011.
- Saha, P. *et al.* (2021) "Biogenic Synthesis and Catalytic Efficacy of Silver Nanoparticles Based on Peel Extracts of Citrus macroptera Fruit," *ACS Omega*, 6(28), hal. 18260– 18268. doi: 10.1021/acsomega.1c02149.

Selvamani, V. (2019) Chapter 15 - Stability Studies on Nanomaterials Used in Drugs. In

Characterization and Biology of Nanomaterials for Drug Delivery, Characterization and Biology of Nanomaterials for Drug Delivery: Nanoscience and Nanotechnology in Drug Delivery. Diedit oleh S. S. S. R. Mohapatra et al. Elsevier Inc. doi: 10.1016/B978-0-12-814031-4.00015-5.

- Soliman, W. E. *et al.* (2020) "Therapeutic applications of biostable silver nanoparticles synthesized using peel extract of benincasa hispida: Antibacterial and anticancer activities," *Nanomaterials*, 10(10), hal. 1–13. doi: 10.3390/nano10101954.
- Song, H. *et al.* (2020) "Ga-Based Liquid Metal Micro/Nanoparticles: Recent Advances and Applications," *Small*, 16(12), hal. 1–21. doi: 10.1002/smll.201903391.
- Sulaiman, G. M. *et al.* (2020) "Hesperidin Loaded on Gold Nanoparticles as a Drug Delivery System for a Successful Biocompatible, Anti-Cancer, Anti-Inflammatory and Phagocytosis Inducer Model," *Scientific Reports*, 10(1), hal. 1–16. doi: 10.1038/s41598-020-66419-6.
- Xing, Y. *et al.* (2021) "Characterization and Antimicrobial Activity of Silver Nanoparticles Synthesized with the Peel Extract of Mango.," *Materials (Basel, Switzerland)*, 14(19). doi: 10.3390/ma14195878.
- Yahya, M. Q. dan Abid, K. Y. (2022) "Evaluation of Antimicrobial Effects of Citrus Peel Extracts and Its Silver Nanoparticles Against Multiple Pathogens," *Military Medical Science Letters*, 91(3), hal. 244–255. doi: 10.31482/mmsl.2021.052.
- Yaqoob, A. A., Umar, K. dan Ibrahim, M. N. M. (2020) "Silver nanoparticles: various methods of synthesis, size affecting factors and their potential applications-a review," *Applied Nanoscience (Switzerland)*, 10(5), hal. 1369–1378. doi: 10.1007/s13204-020-01318-w.
- Zhang, X. F. *et al.* (2016) "Silver nanoparticles: Synthesis, characterization, properties, applications, and therapeutic approaches," *International Journal of Molecular Sciences*, 17(9). doi: 10.3390/ijms17091534.

Medical Sains : Jurnal Ilmiah Kefarmasian Vol. 8 No. 3, July – September 2023, Page. 1289-1304