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Research Article

Nano antioxidant serum ethanol extract lime peel (*Citrus aurantifolia* S.)

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ABSTRACT

Serum is a cosmetic that has received great attention from the industry, but the main challenges are appearance, transparency and public acceptance of herbal active ingredients. On the other hand, herbal cosmetics, such as those using lime peel, are also growing. This study aims to determine the antioxidant activity of lime peel made in a nano extract serum preparation. The method for making nano extracts uses ionic gelation with PSA (Particle Size Analyzer) and Zeta Potential characterization. The concentration of nano serum of lime peel ethanol extract used was 0.5%; 1%; and 3%. Meanwhile, the antioxidant activity testing method uses DPPH and data analysis applied one-way ANOVA then by Tukey test. The results of the nano extract serum formulation using organoleptic testing are transparent, thick and liquid, odorless, and feel moist on the skin. The results of nanoparticle characterization using PSA measurements with three replications were 295.1; 320.3; 385.4 nm and the results of testing the zeta potential of nanoparticles with three replications, namely 3.2; 3.4; 6.0mV. Furthermore, the results of the antioxidant activity test on the basis of the preparation formula are classified as weak (IC50 value of 156.22 µg/mL); Meanwhile, preparation formula with a concentration of 0.5%; 1%; 3% are considered very strong (IC50 value of 46.39 µg/mL; 41.06 µg/mL; 36.27 µg/mL). The results of data analysis consider significance of p value below 0.05. The conclusion is nano lime peel extract meets the requirements and the serum preparation meets the requirements and has antioxidant activity.

1. Introduction

Beauty is something that is paid a lot of attention to appearance, especially skin by women throughout the world, including in Indonesia as a tropical country in Southeast Asia with air temperatures between 25-30˚C, many use cosmetics to care for and make skin brighter (Sumule et al., 2020). Recently, the use of herbal cosmetics or herbal ingredients has received widespread attentionin society. Herbal cosmetics are products formulated using various herbal ingredients which are used to provide certain cosmetic benefits (Permana et al., 2022).

One herbal ingredient that can be used to care for skin is lime peel. According to previous research, lime peel contains several active compounds such as flavonoids, alkaloids, saponins, tannins and polyphenols (Nafisa et al., 2021). The high flavonoid content can be used as an antioxidant which can capture free radicals and inhibit the lipid oxidation process (Nurisyah et al., 2020). One of the skin care cosmetic innovations currently developing is serum. Serum is a preparation that has a low viscosity, so serum is categorized as an emulsion preparation (Febriani et al., 2022). Serum has the advantage of having a high concentration of active ingredients, so it is quickly absorbed by the skin to provide a comfortable effect (Aprilia et al., 2022). High concentrations of active ingredients in serums can cause irritation to sensitive skin (Hidayah et al., 2021), to overcome this problem it was created in the form of nanoparticles to control the release of active ingredients gradually and selectively which can reduce the risk of irritation and feel softer (Abdassah, 2017). Therefore, lime peel (*Citrus aurantifolia* S.) is considered to have the potential to be developed into an antioxidant serum made from nano-extract active ingredients.

2. Materials and Methods

Lime peel extraction

The extraction process was carried out using the maceration method with 70% ethanol solvent. The ratio of simplicia powder to 70% ethanol solvent used is 1:5 for 400 g of simplicia and 2 L of 70% ethanol. Maceration and remaceration were carried out for 2 days with the same stirring. The filtrate obtained was then concentrated using an evaporator at a temperature of 50°C. The concentrated solution was evaporated in a water bath at 60°C until a thick lime peel extract was obtained (Liza et al., 2022).

Phytochemical Screening

Phytochemical screening is aimed at determining the presence of flavonoids, phenols, tannins, saponins, alkaloids, steroids and terpenoids using methods that have been carried out in previous research (Nisa, 2019).

Determination of Total Phenol

A gallic acid solution with a concentration of 1000 ppm was made by taking 10.0 mg of gallic acid, then dissolving it in 10 ml of methanol pa. A gallic acid solution with a concentration of 10 was made; 50; 100; 250; and 500 ppm to find the calibration curve. A sample of 10.0 mg was weighed, dissolved in 10 mL of methanol, then 0.1 mL was taken and put into a test tube. Add 7.9 mL of distilled water and 0.5 mL of Follin-Ciocalteu solution then vortex. Then 0.5 mL of 10% sodium carbonate solution was added. It was incubated for 30 minutes and the absorbance was measured at a known maximum wavelength (Najihah et al., 2018). Three measurements were replicated. The sample concentration values obtained were then substituted into the following total phenol content calculation formula:

$$\text{Total phenol content (mg GAE/g)} = \frac{x.\ V.\ Fp}{m}$$

Information :
x = Concentration (µg/mL)
V = volume of sample solution (mL)
Fp = Solution dilution factor (mL)
m = Sample weight (g)

Determination of Total Flavonoids

A quercetin solution with a concentration of 1000 ppm was made by taking 10.0 mg of quercetin, then dissolving it in 10 ml of methanol. A quercetin solution with a concentration of 10 was made; 50; 100; 250; and 500 ppm to find the calibration curve. A sample of 10.0 mg was weighed, dissolved in 10 mL of methanol, then 0.1 mL of each was taken and put into a test tube. Added 0.1 mL of 10% solution and 0.1 mL of 10% sodium acetate solution. Then add 2.8 mL of distilled water. It was incubated for 30 minutes and the absorbance was measured at a known maximum wavelength. Three measurements were replicated $AlCl_3$ (Najihah et al., 2018). The sample concentration values obtained were then substituted into the following formula for calculating total flavonoid levels:

$$F = \frac{c.V.Fp.}{m} x\ 100\%$$

Information :
F = Total flavonoid content
c = Quercetin equivalent (µg/mL)
V = volume of sample solution (mL)
Fp = Solution dilution factor (mL)
m = Sample weight (g)

Making Nanoparticles

The process of making lime peel extract nanoparticles is carried out by mixing 0.2 g of chitosan in 100 mL of 1% acetic acid solution (0.2% chitosan solution). A total of 1 g of lime peel extract was dissolved in 50 mL of ethanol: water (7:3) mixed with 0.2% chitosan solution. A total of 0.1 g of NaTPP dissolved in 100 mL of distilled water (0.1% NaTPP solution) was added gradually, stirring using a magnetic stirrer at a temperature of 60°C with a speed of 2,000 rpm until the solution was homogeneous. Next, the extracted nanoparticles were characterized using PSA and zeta potential.

Making Serum Preparations

The process of making serum preparations using a carbomer base of 0.5 grams is developed with hot water in a ratio of (1:20). Then add TEA, stir until homogeneous. Next, add sodium benzoate and disodium EDTA which have been dissolved in distilled water, stir until homogeneous. Then add glycerin, stir continuously until homogeneous, then add nano ethanol extract of lime peel, slowly stir until homogeneous (Yuniarsih et al., 2022). The formulation of the serum preparation used can be seen in table 1.

Table 1. Formulation of nano serum preparations from lime peel ethanol extract

Material	Function	Concentration			
		F0 (%)	F1 (%)	F2 (%)	F3 (%)
Nano ethanol extract of lime peel	Active substance	0	0.5	1	3
Carbomer	Gelling agent	0.5	0.5	0.5	0.5
Glycerin	Humectant	5	5	5	5
Triethanolamine	pH neutralizer	1	1	1	1
Na Benzoate	Preservative	0.15	0.15	0.15	0.15
Disodium EDTA	Chelating agents	0.2	0.2	0.2	0.2
Aquadest	Solvent	Ad 100	Ad 100	Ad 100	Ad 100

Information : F0: Formula with 0% active substance; F1: Formula with 0.5% active substance; F2: Formula with 1% active substance; F4: Formula with 3% active substance

Physical Evaluation of Serum Preparations

Serum preparations are evaluated by organoleptic observations such as odor, color, shape and homogeneity, measuring pH, viscosity, spreadability, stickiness both before and after the cycling.

Antioxidant Activity Testing

Before further research was carried out, the extract was oriented towards antioxidant activity to obtain good antioxidant activity values at each concentration. From the results of orientation carried out using the DPPH method, antioxidant activity results were obtained at concentrations of 0.5%, 1% and 3% (Slamet et al., 2022).

Data analysis

Data analysis in research regarding the antioxidant activity of lime peel extract and lime peel extract nano gel on antioxidant activity was carried out quantitatively using the OneWay type ANOVA test. This ANOVA test is used to evaluate differences between concentration groups in experiments involving more than two groups. This method is included in the parametric test, which requires that the data must have a normal distribution, homogeneity of variance, and be taken from a randomly selected sample. To determine differences between groups, Tukey testing was carried out on the Post Hoc Test menu with SPSS.

3. Results and Discussions

Simplicia Standardization

Simplicia standardization is carried out to guarantee the quality and safety standards of simplicia (Sutomo et al., 2021). Determination of quality standards includes specific and non-specific parameters. The results of standardization of lime peel simplicia can be seen in table 2.

Table 2. Simplicia standardization results

Testing	Results (%)	Condition (%)
Drying shrinkage	1.35*	<10
Water content	6.23*	<10
Total ash content	1.25*	<7.0
Water soluble ash content	5.85*	-

Testing	Results (%)	Condition (%)
Acid insoluble ash content	0.35*	<0.4
Ethanol soluble essence content	1.96*	<18.0
Water soluble essence content	21.32*	<25.6

Remarks (*): meets the requirements according to the literature

Results of Lime Peel Extraction

The results of extracting lime peel simplicia from the weight of dried simplicia produce a dark brown colored extract. The weight of the thick extract obtained was 35.33 grams with an extract yield of 8.83% and a water content of 0.24%. Extract yield is calculated based on the comparison of extract weights.

Phytochemical Screening Results

Phytochemical screening aims to determine the content of secondary metabolite compounds contained in lime peel extract *(Citrus aurantifolia* S.*)* using the color reaction method (Nurjannah et al., 2022). Based on the results of the phytochemical screening examination of lime peel extract, the results obtained were in accordance with previous research conducted by Nisa (2019), which can be seen in table 3.

Table 3. Results of phytochemical screening of lime peel ethanol extract

Active Compound Group	Results
Alkaloids with dragendroff	+
Alkaloids with mayer	+
Alkaloids with Wagner	+
Flavonoids	+
Terpenoids	+
Steroids	-
Tannin	+
Saponin	+
Phenol	+

Information :
+ : detected to contain a compound
- : detected does not contain compounds

Results of determining total phenol

Determination of the total phenol content in the sample was carried out by reacting the sample using the Folin-Ciocalteu reagent, and then measuring the absorbance at a wavelength of 783 nm (Antasionasti et al., 2020). The results obtained can be seen in table 4.

Table 4. Results of measuring total phenol levels

Sample	Average (mg GAE/g extract)
Ethanol extract of lime peel	183.9 ± 6.55
Nano ethanol extract of lime peel	1115 ± 2.75

Testing for total phenol levels shows a calibration curve with the equation y = 0.001x + 0.0391 and a correlation coefficient (r) of 0.9996 at a wavelength of 783 nm, indicating a linear and accurate analysis method (Sukmawaty et al., 2019). Table 4 shows an average phenol content of 183.9 ± 6.5 mgGAE/g in the ethanol extract of lime peel and 1115 ± 2.7 mgGAE/g in the extract nanoparticles, with the higher phenol content in the nanoparticles possibly due to differences in sample levels after the extract is converted into nanoparticles.

Determination of total flavonoids

Determination of total flavonoid levels aims to determine the total flavonoid compound content contained in lime peel extracts and nano extracts.(Fikayuniar et al., 2020). Determination of total flavonoid levels was carried out using colorimetry, then measured at a wavelength of 432.5 nm. The results obtained can be seen in table 5.

Table 5. Results of determining total flavonoid levels

Sample	Average (mg QE/g extract)
Ethanol extract of lime peel	54.69 ± 3.09
Nano ethanol extract of lime peel	262.8 ± 1.19

Determination of flavonoid levels using a standard solution of quercetin at a wavelength of 432.5 nm produced a calibration curve with the equation y = 0.0021x + 0.0658 and a correlation coefficient (r) of 0.9999, indicating an accurate linear analysis (Wahid et al., 2020). The results of measuring flavonoid levels in table 5 show that the average flavonoid content in the extract was 54.69 ± 3.09 mgQE/g and in the nanoparticles 262.8 ± 1.19 mgQE/g, with a higher flavonoid content in the nanoparticles due to the difference in levels. sample after the extract is converted into nanoparticles (Liza et al. , 2022).

Nanoparticle Characterization Results

Making nanoparticles from ethanol extract of lime peel produces a yellow solution. Next, the nanoparticles were tested using particle size, polydispersity index, and zeta potential to evaluate their characteristics and stability (Antasionasti et al., 2020). The characterization results can be seen in table 6.

Table 6. Results of characterization of nanoparticles from ethanol extract of lime peel

Types of Nanoparticle Characterization	Results
Particle size (nm)	333.6 ± 46.5
Polydispersity Index	0.447 ± 0.1
Zeta Potential (mV)	4.2 ± 1.5

Making nanoparticles using chitosan, sodium tripolyphosphate (Na TPP), and lime peel extract was carried out using the ionic gelation method. The resulting nanoparticles were tested using particle size analysis, polydispersity index, and zeta potential. The Particle Size Analyzer results show an average size of 333.6 ± 46.5 nm, these results are included in the nanoparticle range, namely 10-1000 nm (Putri at al., 2019). Characterization results: The polydispersity index is 0.447 ± 0.1, indicating a moderate and homogeneous size distribution (Wirasti et al., 2021). Then the Zeta potential characterization results averaged 4.2 ± 1.5 mV which shows dispersion stability, even though this value is below ± 30 mV, lime peel extract nanoparticles are considered stable (Prasetyaningrum et al., n.d.).

Serum Preparation Evaluation Results

Organoleptic Test

Organoleptic tests are carried out to determine the physical properties of serum preparations by observing the preparation through the five senses (Setyawardhani et al., 2021). The parameters observed were smell, shape and color. Organoleptic testing was carried out before and after the cycling test. Based on the test results on base serum preparations, serum concentrations of 0.5%, 1% and 3% were obtained in a thick liquid form, colorless (transparent) and odorless.

The organoleptic test results before and after the cycling test showed that the shape, color, odor and taste remained consistent, indicating the physical stability of the serum preparation during long-term storage (Ningrum et al., 2020).

Homogeneity

Homogeneity is an important parameter and is a measure of the quality of the preparation because the active ingredients used are evenly. The results of homogeneity in the base serum preparation, serum concentrations of 0.5%, 1% and 3% obtained a homogeneous preparation marked by the absence of lumps on the slide.

Test the homogeneity to determine the distribution of particles and the effectiveness of the therapeutic preparation (Marlina, 2020). The test results before and after the cycling test, which were observed under light, showed that there were no coarse lumps, indicating that the serum preparation had good homogeneity (Febriani et al., 2022).

Test pH

pH test to see the acidity or alkalinity level of the preparation. The pH results can be seen in Figure 1.

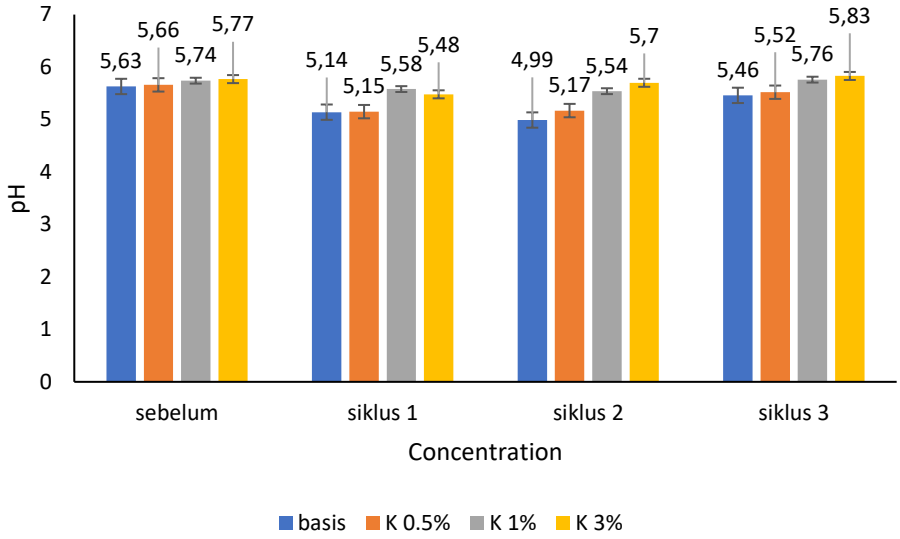

Figure 1 serum pH test results

Measure the pH to ensure the suitability of the preparation to the physiological pH of the skin, avoiding irritation or dry skin (Anggraeni et al., 2021). The pH diagram in Figure 1 shows the preparation value according to the standard, with the addition of lime peel nanoextract which is acidic, it increases the pH

(Thakre, 2017). After the cycling test, the pH decreased due to the reaction of carbon dioxide with water, with a range of 4.99 to 5.83, still within the good range for serum 4.5 to 6.5 (Yuniarsih et al., 2022).

Spreadability Test

The purpose of carrying out a spreadability test is to see the ability of the preparation to spread well on the skin(Pogaga et al., 2020). The results of the spreadability test can be seen in Figure 2.

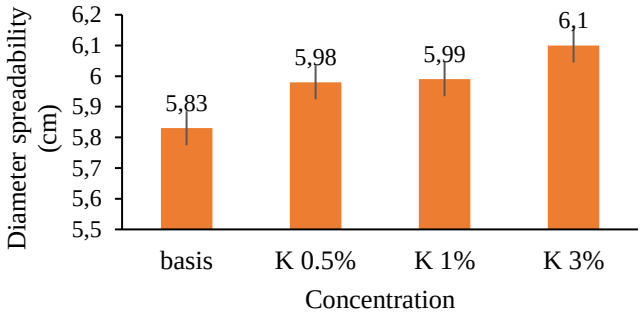

Figure 2 Serum spreadability test result

The spreadability test assesses the speed of spread of the serum on the skin, with an effective serum that is easy to apply and distributes the active substance evenly. Increasing the extract concentration increases the spreading diameter, while high viscosity reduces the spreading power; more dilute preparations spread better. The spreadability test results in Figure 2 show that the preparation meets the standards, with a spread of between 5 and 7 cm.

Adhesion Test

Adhesion testing is carried out to see the time it takes for the preparation to stick to the skin. The results of the adhesion test can be seen in Figure 3.

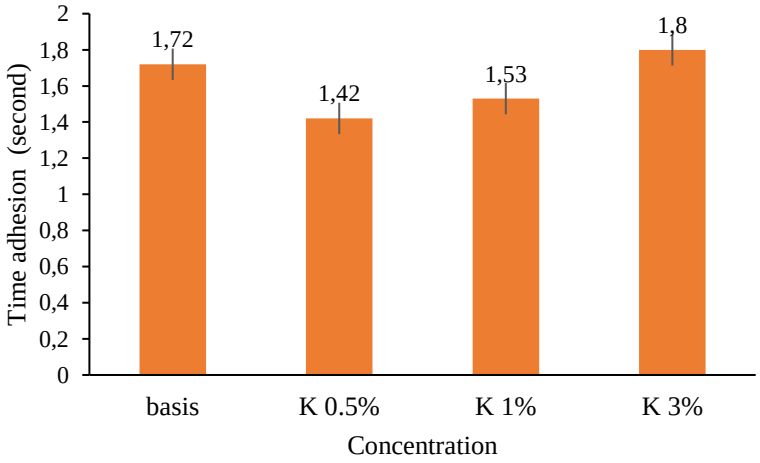

Figure 3 Serum adhesion test result

The adhesion test, assesses how long the serum can stick to the skin, increasing the effectiveness of drug delivery (Anggraeni et al., 2021). The requirement for good serum adhesion is more than one second

(Rohmani et al., 2019). The results of the serum adhesion test can be seen in Figure 3 showing that the preparation has good adhesion, because it lasts for more than one second (Anindita et al., 2022).

Viscosity Test

The viscosity test is carried out with the aim of seeing the consistency of the preparation which can affect the spreadability and application of the preparation such that it is easy to remove from the container but is unlikely to flow from the hand (Yuniarsih et al., 2022). The viscosity results can be seen in Figure 4.

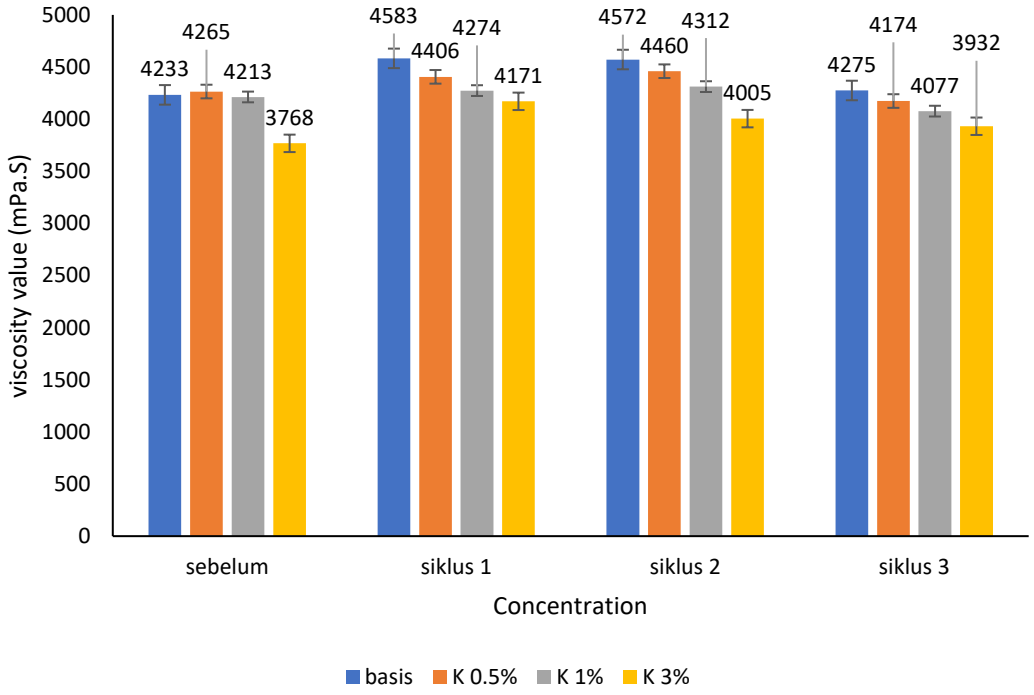

Figure 4 Serum viscosity test results

The viscosity test assesses the consistency of the preparation which affects spreadability and ease of application. The viscosity test results can be seen in Figure 4 showing that the viscosity decreases with increasing concentration of the active substance, in line with the spreadability (Sumule et al., 2020). At a concentration of 0.5% (F2), the viscosity increases possibly because the active substance has not completely dissolved. Figure 4 shows a decrease in viscosity during the 3 cycles of the cycling test, possibly due to temperature changes and polymer reactions, but still within the appropriate range, namely 200-5000 mPa.s (Anindita et al., 2022).

Antioxidant Activity Test

Antioxidant activity testing was carried out using the DPPH method by looking at the IC value results$_{50}$ which is obtained (Sukweenadhi et al., 2020). The IC50 value can be seen in Figure 5.

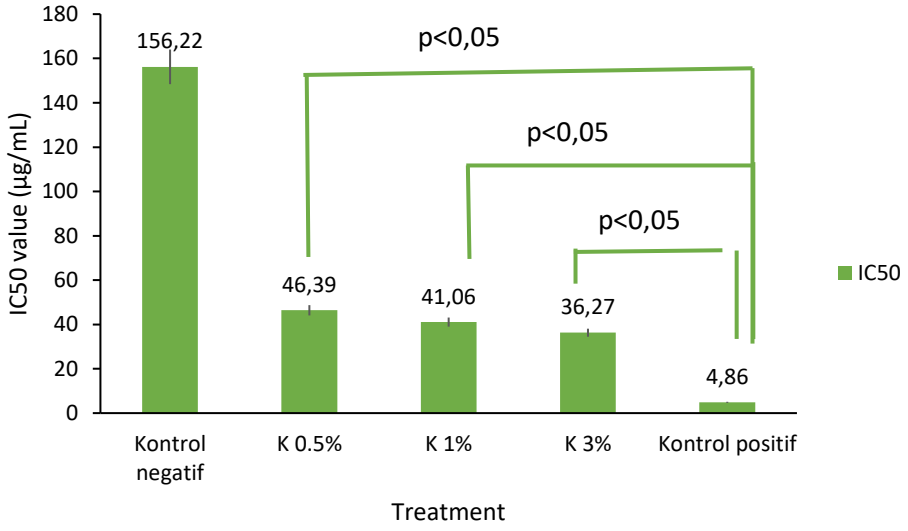

Figure 5 Results of Antioxidant Activity Data Analysis

Information :
K 0.5%: Serum active ingredient concentration 0.5%
K 1%: Serum active ingredient concentration 1%
K 3%: Serum active ingredient concentration 3%
P<0.05: there is a significant difference

This study measured the antioxidant activity of lime peel extract (*Citrus aurantifolia* S.) using the DPPH (2,2-Diphenyl-1-Picrylhydrazyl) method. Antioxidant potential was calculated from the IC_{50} value and compared with vitamin C (Khasanah et al., 2021). The DPPH method, which utilizes a UV-Vis spectrophotometer at a wavelength of 451 nm, is effective for rapid and sensitive analysis. Figure 5 shows that extracts with concentrations of 0.5%, 1%, and 3% have very strong antioxidant activity, with IC_{50} less than 50 µg/mL (Khasanah et al., 2021). A compound is said to be a very strong antioxidant if the IC50 value is less than 50 µg/mL (very strong), if the IC50 value is between 50-100 µg/mL (strong), if the IC50 value is around 100-150 µg/mL (moderate), if the IC50 ranges from 150-200 µg/mL (weak), and if the IC50 value is more than 200 µg/mL (very weak) (Rizkayanti et al., 2017). Based on the results of the analysis, it can be seen that in the positive control with treatment concentrations of 0.5%, 1% and 3% concentration, there were significant differences. This means that the test group treatment has different activity from the positive control, indicated by a sig value <0.05 (Sari et al., 2022). In this case, all concentrations can be formulated properly in serum preparations.

4. Conclusions

Ethanol extract of lime peel (*Citrus aurantifolia* S.) showed antioxidant activity with an IC_{50} value of 37.30 µg/mL, including the strong category. This extract can be made into nanoparticles with particle sizes of 295.1 nm, 320.3 nm, and 385.4 nm and zeta potentials of 3.2 mV, 3.4 mV, and 6.0 mV. Physical evaluation of the serum showed that the nano ethanol extract of lime peel met the requirements and could be used as a serum preparation. This nano extract serum has antioxidant activity with a serum base IC_{50} value of 156.22

µg/mL (weak category), and serum IC_{50} concentrations of 0.5%, 1% and 3% respectively 46.39 µg/mL, 41 .06 µg/mL, and 36.27 µg/mL (very strong category).

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