Determination of hydroquinone levels in whitening serum circulating at market place x using the uv-vis Spectrophotometric method

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Abstract

Hydroquinone is a dangerous substance in cosmetic products that has been banned for use on the face and skin, even though hydroquinone is relatively high in society. This study aimed to determine the hydroquinone content in whitening serum circulating in the marketplace using the UV-Vis spectrophotometry method. This type of research is descriptive and non-experimental. Samples of 12 whitening serums circulating in marketplace X were selected by purposive sampling. Qualitative analysis of organoleptic tests and color tests using FeCl3. Quantitative analysis of the determination of hydroquinone levels in whitening serum by UV-Vis spectrophotometry. The wavelength detection of 295 nm resulted from a linear regression formula of Y = 0.0331x + 0.0697 with a correlation coefficient (r) = 0.9997. Qualitative analysis of the organoleptic tests showed that 4 of the 12 samples were positively hydroquinone in samples S1, S2, S11 and S12 with a sticky to very sticky texture and a pungent odor. The results of the color test showed that 2 of the 12 samples suspected of being positive for hydroquinone in samples S3 and S11 showed a dark brown color. Method validation in the specificity test has a maximum wavelength of 294 nm at 4, 10, and 14 ppm concentrations. Precision test yields % RSD 0.10%. The accuracy test produces a %recovery value of 77.98%. The quantitative analysis test results for determining hydroquinone levels in whitening serum circulating in marketplace X using the UV-Vis spectrophotometry method showed that all 12 serum samples contained hydroquinone with levels ranging from 2.20 to 3.77%. From this study, it can be concluded that all bleach serum samples circulating in marketplace X contained hydroquinone levels that did not meet the Food and Drug Supervisory Agency requirements.

Keywords: prescribing patterns; antihypertensive ; agents ; PHC Clinic

Introduction

With the development of science and technology, people's living needs are also increasing. This need is not only for clothing, food and education; the need for appearance has become a daily need, especially for women. Some women want clean, smooth, firm and beautiful skin (Adriani & Safira, 2019). One of the many forms of cosmetic preparations that have been developed recently is serum. Because serum has a high concentration of active ingredients, the effect is more easily absorbed, spreads quickly on the surface of the skin and can brighten facial skin (Carolin, 2020).

From June 2020 to September 2021, Badan Pengawas Obat dan Makanan (Food and Drug Administration of Indonesia) found 72 dangerous products circulating on the market, 18 of which were cosmetic products containing dangerous ingredients, namely hydroquinone (BPOM, 2021). Based on this statement, it has been proven that the use of hydroquinone is still high on the face and skin in the community and does not meet the requirements of the Food and Drug Supervisory Agency. In this case, it is vital to carry out this research to ensure that cosmetic products without a BPOM distribution permit registration number containing the dangerous substance hydroquinone are not suitable for use on the skin, especially whitening serums circulating in marketplaces in Bekasi Regency.

According to Putri and Wahyudiani (2021), hydroquinone has unwanted effects when used for a long time, including irritative dermatitis, contact dermatitis, and ochronosis. Hydroquinone can treat skin problems caused by melanin accumulation hyperpigmentation, such as the appearance of uneven black spots on the skin. Research conducted by Arwibiyantari (2018) analyzed hydroquinone in whitening serum using UV-Vis spectrophotometry in 2 samples with results of 0.146% and 0.138%. In this study, the UV-Vis spectrophotometric method was used to determine serum levels of bleach circulating on the market because it has the advantage of being used for the analysis of various organic and inorganic substances, being selective, having high accuracy with a relative error of 1 - 3%, being able to determine the quantity of the substance. Which is small, and the results are accurate because the numbers listed are read directly, recorded automatically and printed in digital numbers (Rohmah *et al.*, 2021). Therefore, research regarding determining hydroquinone levels in whitening serum circulating in the marketplace using the UV–vis spectrophotometric method is fundamental.

Methods

The design of this research is non-experimental descriptive. This research was conducted at the Mitra Keluarga STIKes Pharmaceutical Chemistry Laboratory, Bekasi, West Java Province, from January to April 2023. The sample population in this study were all cosmetic shops in the Bekasi Regency area, which were in marketplace X. The tools

used include analytical scales, steam cups, measuring cups, beaker glasses, funnels, 50 mL measuring flasks, 10 mL measuring flasks, 100 mL measuring flasks, watch glasses, stir sticks, micropipettes, tips, cuvettes, glass, filter paper. , test tube, test tube rack, drip plate, spatula, dropper pipette, Erlenmeyer 50 mL, and UV–vis spectrophotometry.

The first way of working is organoleptic qualitative analysis; samples were subjected to organoleptic testing using the body's senses. The parts of the body that have a role are the eyes, ears, sense of taste, sense of smell, and sense of touch (Simaremare, 2019), and the second way of working in qualitative analysis is the color test on hydroquinone using FeCl3 by pipetting 5 mL of serum sample and dissolving 5 mL of methanol p.a until dissolved, adding 1% FeCl3 reagent. Five drops. The sample can be concluded to be positive for hydroquinone if the color changes from green to black (Rahmadari *et al.*, 2021). Next, the first quantitative analysis is carried out: making a standard hydroquinone solution by weighing 50 mg of hydroquinone, putting it into a 50 mL measuring flask, and dissolving it with methanol p.a. until the limit mark. The solution was shaken until homogeneous, and a concentration of 1000 ppm was obtained. The second quantitative analysis, the preparation of a 20 ppm hydroquinone standard solution, is carried out with a concentration of 1000 ppm that has been made. A 50 mL volumetric flask is prepared, then 2 mL of input is taken, which is taken using a pipette. Add methanol p.a to the mark and shake until dissolved. Then, 20 ppm of standard hydroquinone solution is obtained (Sahumena, 2019).

Determination of the maximum wavelength was carried out by inserting a standard solution of 20 ppm into a cuvette using a blank solution, namely methanol p.a. absorbance was measured with a wavelength of 200-400 nm. The maximum wavelength is determined by looking at the highest absorbance value. A 20 ppm standard curve was made by pipetting 2, 3, 4, 5, 6 and 7 mL of 20 ppm standard solution, each put into a 10 mL volumetric flask, adding methanol p.a. to the limit mark. The concentrations obtained were 4, 6, 8, 10, 12, and 14 ppm. Each of these concentrations was measured at the previously obtained wavelength using a blank methanol solution. The standard standard curve is obtained by plotting the concentration with absorbance (Sahumena, 2019).

In this research, a method validation test was carried out. The specificity test was carried out with hydroquinone concentrations of 4.10 and 14 ppm inserted into the cuvette to see the absorption spectrum formed at the maximum wavelength obtained (Guy, 2006). Linearity test was carried out with concentrations of 4, 6, 8, 10, 12 and 14 ppm measured maximum wavelength. Linear regression optimization made a relationship curve between the x-axis hydroquinone levels, namely absorbance. The results obtained were selected with good correlation coefficient relations and carried out three replications. The accuracy test was carried out using the addition method. A sample of 1 mL of whitening serum is taken, put into a 100 mL volumetric flask and added methanol p.a until the mark is marked and shaken until dissolved. Then take as much as 10 mL using a measuring pipette, put it into a 50 mL volumetric flask and add 100 ppm standard hydroquinone, pipettes 2, 4, and 6 mL to produce concentrations of 4, 8, and 12 ppm. In a 50 mL volumetric flask containing each - methanol p.a was added to each concentration along with the sample to the limit mark, the absorbance value obtained by UV-Vis spectrophotometry was measured and carried out three times. The absorbance value obtained was plotted with the linear regression equation and can produce hydroquinone concentrations, which will be determined as % recovery. The precision test was carried out with a hydroquinone solution with a concentration of 4 ppm, and then the absorbance measurement was carried out at the maximum wavelength with six replications (Sahumena, 2019).

Then, the final test of quantitative analysis, namely the determination of hydroquinone levels, was carried out by taking 1 mL of bleaching serum sample, adding methanol p.a to 100 mL in a measuring cup, then filtering the solution and taking 10 mL and adding methanol p.a in a 50 mL volumetric flask to the mark limit. Then, fill it into a cuvette and measure it using UV-Vis spectrophotometry at a wavelength of 295 nm. Each sample was carried out three times.

Results and Discussions

This study obtained samples of whitening serum products from shops in Bekasi Regency at marketplace X at a price of Rp. 3,000 – Rp. 30,000, which had sold ≥100 pcs and did not have a BPOM permit number, then 12 samples were analyzed based on the inclusion criteria. The organoleptic test is a test using the body's senses, which consist of the sense of sight, the sense of taste, the sense of smell and the sense of touch (Simaremare, 2019). In **Table 1**, the organoleptic test results can be seen.

Table 1. Organoleptic test results for whitening serum

Sample Code	Color	Scent	Texture
S1	Pink	Fragrant and pungent	Thick and sticky
S2	Bright Pink	Fragrant and pungent	Very thick and sticky
S3	Bright Yellow	Fragrant and pungent	Thick, slightly runny and not overpowering
S4	Clear White	Fragrant and not	Thick and a little sticky

		stinging	
S5	Bright Pink	Fragrant and pungent	Runny and a little sticky
S6	Yellow	Fragrant and pungent	Thick, slightly runny and not sticky
S7	Deep Pink	Fragrant and pungent	Thick and not sticky
S8	Pink	Fragrant and pungent	Thick, a little runny and sticky
S9	Yellow	Fragrant and pungent	Thick and not sticky
S10	Pink	Fragrant and pungent	Watery and not sticky
S11	Cloudy Pink	Fragrant and pungent	Thick and sticky
S12	Clear White	Fragrant and pungent	Thick and sticky

In **Table 1.** The organoleptic test of samples S1, S11, and S12 smells good, does not sting and has a sticky, thick texture. Sample S2 smells good and stings. The texture is thick and sticky. Research by Yusuf *et al*. (2017) showed that serum preparations that did not contain hydroquinone showed clear organoleptic test results, had no odor and had a thick texture. The results of a study by Simaremare (2019) show that hydroquinone samples have a sticky texture and a pungent odor. This color test aims to determine the presence of phenol groups in hydroquinone, which reacts with FeCl3. The color test in this study can be seen **Figure 1** ; **Table 2.**

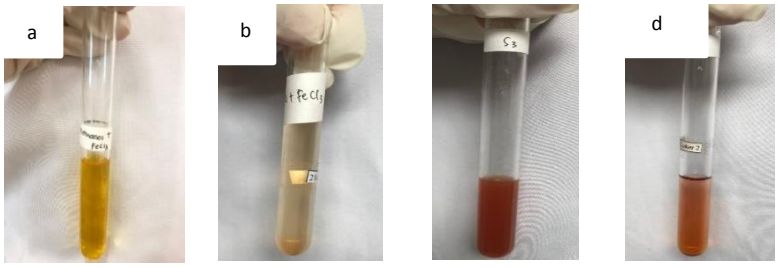

Figure 1. Results of the bleach serum color test with 1% FeCl3. a) Negative control, b) Positive control, c) sample S3, d) sample S11

Table 2. Color Test Results with 1% FeCl3

Sample code	**Color before addition of $FeCl_3$**	**Color after addition of $FeCl_3$**	**Results**
Control +	Clear	Brown	+
Control -	Clear	Dark Yellow	-
S1	Pink	Orange	-
S2	Bright Pink	Yellow	-
S3	Bright Yellow	Deep Brown	+
S4	Clear White	Yellow	-
S5	Bright Pink	Dark Pink	-
S6	Yellow	Yellowish Brown	-
S7	Deep Pink	Orange	-
S8	Pink	Dark Pink	-
S9	Yellow	Yellow	-
S10	Pink	Orange	-
S11	Cloudy Pink	Dark Brown	+
S12	Clear White	Yellow	-

Using a cuvette that already contains a blank solution, namely methanol pro analysis, the absorbance is set to 0 (zero) absorbance. The blank solution is a different solution to the sample, but is made in the same way for the purpose of comparison. The blank solution is entered into UV-Vis spectrophotometry for each absorbance measurement, with the aim being that only the absorbance or uptake of the desired substance is measured (Mustika, 2018). The maximum wavelength obtained is 295.0 nm. This is included in the theoretical requirements, according to USP (2020)

hydroquinone has a theoretical wavelength of 293 nm ± 2 nm. The maximum wavelength chosen is 295 nm, because methanol has a UV cut off of 215 nm, if the maximum wavelength chosen is close to the solvent's UV cut off, it will interfere with the wavelength reading of the analyte.

Determination of Hydroquinone Standard Curve

In the test, a standard curve for hydroquinone is then created by measuring the absorbance of the standard hydroquinone solution in maximum wavelength that has been obtained. Absorbance (y) obtained is then plotted against the concentration of the standard solution (x). Determining sample levels using the linear regression method is a parametric method with the independent variable (sample concentration) and the dependent variable (sample absorbance) using the curve regression line equationstandard solution. The sample concentration can then be calculated based on the standard curve equation obtained (Arifiyana *et al.*,2019)

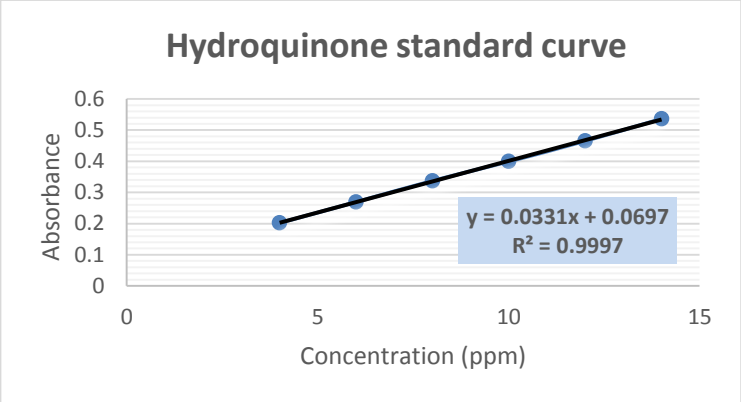

Figure 3. Hydroquinone Standard Standard Curve

Hydroquinone standard curves were prepared with concentrations of 4, 6, 8, 10, 12 and 14 ppm. Based on standard curve measurements, it was found that the equation results from the three replications had a correlation that met the requirements. The results of the linear regression equation Y = 0.0331x + 0.0697 were found.

Linearity Test

Linearity is a measure of how well the standard curve relates response (y) to concentration (x). Linearity is calculated statistically through a correlation coefficient (r) (Rahmadari *et al.*, 2021). This study produces a correlation coefficient of r = 0.9997. The value of r ≥ 0.99 indicates that there is a linear relationship between the concentration of the analyte and the measured absorbance based on Lambert Beer's law (Miller, 2014). The increasing levels of hydroquinone in solution, therefore the absorption also increases, because of the correlation relationship what happens is linear then the Lambert-Beer Law is in place materialized (Saraswati, 2022). This proves that the curve Hydroquinone calibration provides good linearity and a reliable method used appropriately to determine hydroquinone levels in whitening serum.

Specificity Test

Based on Table 3, it can be seen that with an increase in concentration there is also an increase in the absorbance value with a fixed maximum wavelength value in the specificity test.

Table 3. Specificity Test Results

Hydroquinone concentration (ppm)	Maximum absorbance value	Average± SD	Maximum wavelength
4	0,155	0,159 ± 0,0050	294 nm
	0,156		294 nm
	0,166		294 nm
10	0,511	0,521 ± 0,0069	294 nm
	0,524		294 nm
	0,527		294 nm
14	0,735	0,772 ± 0,0261	294 nm
	0,786		294 nm
	0,794		294 nm

The specificity test uses concentrations of 4, 10 and 14 ppm, because they represent the lowest, medium to highest concentrations and are carried out three times to get accurate results. From the research that has been carried out, it can be concluded that the higher the concentration, the greater the absorbance and the higher the concentration, the maximum wavelength will not shift towards bathochromic or hypsochromic. According to USP (2020) the maximum wavelength of hydroquinone is 293 nm ± 2 nm.

Accuracy Test

Based on Table 4. The results of the accuracy test determination showed that the % recovery value was 73.64 – 83.80% with an average value of 77.98%.

Table 4. Accuracy Test Results

Concentration (ppm)	Absorbance (sample)	addition	Absorbance (sample rate)	addition	Measurable standard	% *recovery*	Average % *recovery* ± SD
	0,210	0,320	4,24	7,56	3,32	83,08	
4	0,216	0,325	4,42	7,71	3,29	82,33	82,07 ± 0,942
	0,221	0,328	4,57	7,80	3,23	80,82	
	0,210	0,405	4,24	10,13	5,89	73,64	
8	0,216	0,414	4,42	10,40	5,98	74,77	74,90 ± 1,083
	0,221	0,423	4,57	10,67	6,10	76,28	
	0,210	0,516	4,24	13,48	9,24	77,04	
12	0,216	0,520	4,42	13,60	9,18	76,54	76,96 ± 0,314
	0,221	0,528	4,57	13,85	9,27	77,29	
			Average (% *Recovery*)				**77,98**

Accuracy is the thoroughness of the analysis method used or closeness measurement results with the values accepted by Fahira *et al.*, (2021). Accuracy itself is a statement as a percentage of acquisition return (% recovery) of the added analyte. In this research using the standard addition method (standard addition), addition method a known standard solution is added to the sample which are reviewed to reduce errors caused by various matris (Sahumena, 2019). Based on research conducted at concentrations of 4, 8 and 12 ppm, an average % recovery value was found to be 77.98%. These results can be said to be in accordance with the requirements for good accuracy, namely 60 – 115%. This proves that the method used has accurate measurements by showing the degree of equality of the average compared to the actual value and that the method has good accuracy.

Precision Test

Based on Table 5. The results of the precision test showed that % RSD was 0.10%. According to Syahriana *et al.* (2019) a method is declared precise if the percent RSD value is ≤2%.

Table 5. Precision Test Results

No	Concentration (ppm)	Absorbance at λ 295 nm	Measurable levels (ppm)
1	4	0,226	4,72
2	4	0,245	5,30
3	4	0,254	5,57
4	4	0,265	5,90
5	4	0,273	6,14
6	4	0,283	6,44
		Average	**5,68**
		SD	**0,57**
		RSD (%)	**0,10**

In this study, precision was determined by measuring the absorbance of one concentration of a 4 ppm hydroquinone standard solution for 6 replications, because to determine whether the repeatability value was good or not. Based on the research that has been carried out, the results of the precision test show that the %RSD value is 0.10%.

Determination of Hydroquinone Levels

The results of determining hydroquinone levels in whitening serum circulating in market places in Bekasi Regency ranged from 2.20 – 3.77%. Of the 12 samples, they did not meet the requirements set by the Food and Drug Supervisory Agency. In **Table 6.** it can be seen as follows.

Table 6. Results of Determination of Hydroquinone Content

Sample	Replication	Absorbance	X (ppm)	Analyte mass (ug)	% rate (b/v)	Average (%) ± SD
S1	1	0,210	4,24	21,19	2,12	2,20 ± 0,068
	2	0,216	4,42	22,10	2,21	
	3	0,221	4,57	22,85	2,29	
S2	1	0,260	5,75	28,75	2,87	3,06 ± 0,137
	2	0,274	6,17	30,86	3,09	
	3	0,282	6,41	32,07	3,21	
S3	1	0,223	4,63	23,16	2,32	2,60 ± 0,218
	2	0,245	5,30	26,48	2,65	
	3	0,258	5,69	28,44	2,84	
S4	1	0,247	5,36	26,78	2,68	2,80 ± 0,105
	2	0,254	5,57	27,84	2,78	
	3	0,265	5,87	29,35	2,94	
S5	1	0,253	5,54	27,69	2,77	3,06 ± 0,218
	2	0,275	6,20	31,01	3,10	
	3	0,288	6,60	32,98	3,30	
S6	1	0,205	4,09	20,44	2,04	2,19 ± 0,131
	2	0,213	4,33	21,65	2,16	
	3	0,226	4,72	23,61	2,36	
S7	1	0,212	4,30	21,50	2,15	2,42 ± 0,222
	2	0,230	4,84	24,21	2,42	
	3	0,248	5,39	26,93	2,69	
S8	1	0,311	7,29	36, 45	3,65	3,77 ± 0,120
	2	0,317	7,47	37,36	3,74	
	3	0,330	7,86	39,32	3,93	
S9	1	0,218	4,48	22,40	2,24	2,69 ± 0,561
	2	0,225	4,69	23,46	2,35	
	3	0,300	6,69	34,79	3,48	
S10	1	0,255	5,60	27,99	2,80	2,96 ± 0,124
	2	0,266	5,93	29,65	2,97	
	3	0,275	6,20	31,01	3,10	
S11	1	0,229	4,81	24,06	2,41	2,51 ± 0,080
	2	0,236	5,02	25,12	2,51	
	3	0,242	5,21	26,03	2,60	
S12	1	0,273	6,14	30,71	3,07	3,21 ± 0,111
	2	0,283	6,44	32,22	3,22	
	3	0,291	6,69	33,43	3,34	

After carrying out method validation tests with the aim of prove that these parameters have met the requirements its use (Sahumena, 2019). The next testing stage is in progress The final step is determining hydroquinone levels. Hydroquinone levels were determined using long-wavelength UV-Vis spectrophotometry 295.0 nm where each sample was measured three time with the aim of showing more accurate results. According to the results of measurements and calculations that have been carried out, Hydroquinone levels were found in all twelve whitening serum samples obtained from the marketplace in Bekasi Regency with a range 2.20 – 3.77%. It can be shown that these 12 samples do not enter into the conditions set by BPOM. From 12 samples what has been analyzed are products that circulate freely in marketplace, this is conveyed by marking the product no there is a batch number, BPOM permit number and other markings only include the product name. Based on **Table 2.** The results of the color test using FeCl3 out of 12 samples only 2 samples showed a dark brown color so that the sample was suspected to be positive for hydroquinone. Based on research conducted by Simaremare (2019) the color test using FeCl3 6 from 8 samples was suspected to be positive for hydroquinone which produced a green to black color.

Conclusions

It can be concluded that the results of the qualitative organoleptic test of 4 of the 12 samples were suspected to be positive for hydroquinone and the color test for 2 of the 12 samples was suspected to be positive for hydroquinone with

a dark brown color change. Quantitative test using UV-Vis spectrophotometry for all 12 serum samples was positive for hydroquinone with levels ranging from 2,20 to 3,77%, meaning that the samples did not meet BPOM requirements number 17 of 2022 concerning Technical Requirements for Cosmetic Ingredients.

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