ANALYSIS OF HYDROQUINONE CONTENT IN WHITENING CREAM CIRCULATED IN GORONTALO CITY USING UV-VIS SPECTROPHOTOMETRY

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ABSTRACT

This study aims to determine the content of hydroquinone in whitening cream circulating in the city of Gorontalo and to determine the level of hydroquinone in bleaching cream circulating in the city of Gorontalo.

This research method is a design*mixed methods,* which is a rare research by combining two forms of approach in research, namely qualitative and quantitative. This study began with a qualitative analysis using FeCl3 and Benedict's reagents so that the results were obtained that from 8 samples of whitening cream (A, B, C, D, E, F, G, H) there were 2 samples of whitening cream containing hydroquinone, namely cream A and C. then continued with a quantitative test using UV VIS spectrophotometry.

The result is that sample A contains 41,976 mg/g and sample C 28,430 mg/g then proceeds with the validation of the analytical method, the validation parameters include linearity, limit of detection (LOD) and limit of quantification (LOQ). carried out with the value of the correlation coefficient R = 0.9999 and LOD = 18.642 PPM, LOQ = 62.142 PPM.

Keywords: Hydroquinone, UV-VIS spectrophotometry, benedict, FeCl3

INTRODUCTION

Along with the development of science and technology so that the needs of people's lives are also growing. Needs are not only about food, clothing and education, but the need to support daily appearance has also become a special need especially for women. Not surprisingly, some of them are competing to get various kinds of cosmetics for their skin to make it look beautiful. Against most women with clean, soft, light-colored skin that is free from blemishes including skin beautifully. Cosmetics are used solely for a temporary appearance, but the effect on the future is not considered [16].

Cosmetics can be called by preparations that are used in the outermost part of the human body. The outermost part of the body that is targeted is the epidermis, lips, hair, nails, outermost genitals, teeth, and mucous membranes, in the mouth area. Cosmetics have benefits where in cleansing the outer part of the body, scenting the outside of the body, changing appearance, as well as efforts to maintain and maintain the body [7].

In accordance with the tests carried out by the Food and Drug Administration (BPOM), the number of
Whitening cosmetic ingredients that are very widely distributed contain hydroquinone in the Regulation of the Head of the Food and Drug Supervisory Agency number KH.03.1.23.08.11. 07517 of 2011 concerning the Technician Requirements for Hydroquinone Cosmetics Materials are already prohibited

Submit: May 28th, 2022 Accepted: June. 19th, 2022 Published: June. 29th, 2022

from being used for whitening cosmetics. Hydroquinone is sufficient for cosmetic use on artificial nails in a concentration of 0.02% [6].

Hydroquinone is a substance that is always used in whitening cosmetics. Excessive use can cause harmful effects on the skin because it can cause skin cancer [13]. Hydroquinone is an active compound that can control skin pigmentation which is dark brown in color, until black spots or spots appear on the skin. Hydroquinone is used in the brightness of skin that looks dark due to freckles or has not aged. Mild side effects where too much use of hydroquinone causes redness of the facial skin as well as when exposed to sunlight [10].

Cosmetics forming creams containing hydroquinone are often used in reducing dark spots on the face. The bleaching effect of hydroquinone is longer and can be very short at very high levels. High levels can produce unexpected side effects such as the appearance of several diseases, such as vitiligo (skin pigment disappears to form white areas such as phlegm) to ochronosis (skin that turns black or blue with skin such as burning and itching). The use of hydroquinone for years can also cause cancer symptoms (Ibrahim, et al., 2004) disorders in the kidneys, cell proliferation, also has the potential to be carcinogenic as well as teratogenic [17].

Hydroquinone can peel the outermost skin and prevent the formation of melanin which regulates skin color, the use of hydroquinone on the skin cannot exceed 2% hydroquinone cannot be used for a long period of time and if the use exceeds 2% it is always under the control of a doctor [4]. Since 2007 the use of hydroquinone is no longer justified if it exceeds a concentration of 2% based on the decision of BPOM HK.00.05.42.1018 the use of hydroquinone is prohibited in cosmetic preparations, but it is still recommended for its use by professionals in the condition that the recommended level does not exceed 2%. However, it is suspected that the spread of cream preparations still contained hydroquinone used by professionals in excess of 2%. Hydroquinone more than 2% belongs to a group of hard drugs whose use always uses a doctor's prescription. Hydroquinone levels that reach 5% can cause redness with a burning sensation in the skin. The danger of using these hard drugs not under the supervision of a doctor can cause skin irritation, skin redness, burning, kidney disorders, blood cancer and liver cancer. Excessive use can cause skin irritation, but if stopped immediately can be bad. Hydroquinone levels in creams spread on the market are quite permitted 2%, above that it is used for drugs (BPOM RI, 2007). but if stopped immediately can be bad. Hydroquinone levels in creams spread on the market are quite permitted 2%, above that it is used for drugs [5]. but if stopped immediately can be bad. Hydroquinone levels in creams spread on the market are quite permitted 2%, above that it is used for drugs [5].

Based on several studies that have been carried out previously by [3] regarding the quantitative analysis of hydroquinone on cosmetic ingredients of whitening cream which are circulated in the area of central Surabaya and northern Surabaya in the UV VIS spectro procedure, it shows that all samples of the whitening cream contain hydroquinone with the largest concentration obtained in the whitening cream. sample G which produces a hydroquinone content of 0.0331%. Meanwhile, research conducted by [15] in Jayapura City on the analysis of hydroquinone and mercury in whitening cream circulating in Jayapura showed that the quantitative test data using UV-VIS spectro six samples of positive cream contained hydroquinone in the concentration of sample A amounting to 5.143 ppm; B in the amount of 5.413 ppm;

E amounted to 5.511 ppm; F of 5.542 ppm; G amounted to 5.534 ppm; with H amounting to 5.542 ppm.

Based on this, to prove the safety of the whitening cream circulating in the city of Gorontalo, an analysis of the hydroquinone content in the whitening cream circulating in the city of Gorontalo was conducted using UV VIS spectrophotometry.

RESEARCH METHODS

This research is a laboratory experimental research with a research design*mixed methods,*where a rare observation in combining two forms of approach to observation, namely qualitative and quantitative [8].

The equipment used for these observations is analytical balance, UV-VIS spectro, beaker, measuring cup, measuring flask, test tube, volume pipette, watch glass, stirring rod, and dropper pipette. The materials used in this research are:The products used in these observations were samples of facial whitening cream, standard hydroquinone, aquades and methanol, Benedict's reagent and FeCl3 solution..

The population in this study were whitening creams circulating in the city of Gorontalo, while the samples used in this study were 8 brands of facial whitening creams. The technique of sample collection is done by purposive sampling

This research is a laboratory experimental study to determine whether whitening creams are circulating in the city of Gorontalo.

Hydroquinone Qualitative Test

a. Color Reagent Test using 1% $FeCl_3$ reagent

   The hydroquinone color reaction test using 1% FeCl3 reagent will undergo an oxidation reduction reaction, if it is positive it contains hydroquinone a green/yellow color will be formed (Carissa, 2015). Each sample of whitening cream was weighed as much as 1gr then dissolved with 5mL of 96% ethanol, and added 4 drops of 1% FeCl3.

b. Color reagent test using Benedict's reagent

   The hydroquinone color reaction test using Benedict's reagent will undergo an oxidation reduction reaction, if it is positive it contains hydroquinone it will form a brick red color (Carissa, 2015). Each sample of whitening cream was weighed as much as 1gr then dissolved with 5mL of 96% ethanol, and added 4 drops of Benedict.

Hydroquinone quantitative test

a. Preparation of standard solution

   Weighing 5 mg of pure hydroquinone by dissolving in 50 mL of methanol, then shaking the solution until homogenized. Until the standard strength of hydroquinone is 100 ppm against methanol. The standard liquid formed will be used in the determination of the wavelength and the formation of the standard curve.

b. Determination of Wavelength

   The determination of the maximum wavelength is carried out by scanning the hydroquinone standard liquid from a wavelength of 280-300 nm. So that the spectrophotometry tool will display wavelength data by producing a very maximum absorbance value.

c. Standard Curve Creation

   Taking a standard solution of 100 ppm as much as 2mL, 2.5mL, 3mL, 4mL, 5mL, and 6mL each was put into a measuring cup then added 25mL of methanol with shaking until homogeneous. Produced liquids in strengths of 8 ppm, 10 ppm, 12 ppm, 16 ppm, 20 ppm, and 24 ppm. Then measure the absorbance in terms of the maximum resulting wavelength in measuring the initial wavelength. The method in forming a standard curve is to plot the concentration and absorbance

obtained in measurements with concentrations of 8 ppm, 10 ppm, 12 ppm, 16 ppm, 20 ppm, and 24 ppm..

d. Determination of Hydroquinone levels in Whitening Cream

Weigh each sample of 25 mg of whitening cream by dissolving in 50 mL of methanol, then shake until mixed. Pipette 1mL by inserting it into a cuvette and then measuring using UV-VIS spectro in the maximum wavelength. Quantitative testing, the absorbance is calculated through the test analyte by being identified in the qualitative test in the maximum wavelength then calculating the concentration according to the regression similarity obtained in the standard curve determination.

Method Validation

a. linearity

Linearity is the strength of an analytical system that produces a good direct response and helps transform mathematics well, proportional to the strength of the analyte as well as the sample. Linearization is calculated in a statistical way through the correlation coefficient (r). Certain additions can be carried out by entering the concentration and absorbance of the standard liquid [9]. The value of the correlation coefficient (r) with close to 1 reveals a linear relationship to the strength of the obtained absorption, in another sense the increase in the absorption price of the analyte is directly proportional to the increase in strength based on the characteristics of yielding the correlation coefficient (r) where appropriate is r 0.999 [12]

a. Limit of Detection (LOD) and Limit of Quantification (LOQ)

The limit of detection (LOD) is the lowest amount of analyte in the sample that can be detected that still produces a significant response, but the quantitation limit is included in the parameters in the analysis for the lowest amount of analyte in the sample that can still match the characteristics carefully and accurately. The limit of detection by quantitation is calculated in a statistical way from a linear line formed through its standard curve. If the detection limit obtained shows a value of < 1.1211 ppm so that certain data can be trusted where the resulting signal includes a hydroquinone signal. However, if the concentration obtained is >1.1211 ppm, the signal obtained is not a signal from hydroquinone. While the quantity limit if the measurement results are not <3.7370 ppm then the measurement results can be said to be accurate [12].

The determination of the LOD price with the LOQ is carried out by entering the absorbance of the standard liquid calculation data into the resulting linear regression equation. Determination of LOD and LOQ values can be set in the next equation [12].

$$\mathbf{LOD} = \frac{\mathbf{3}\ \boldsymbol{X}\ \boldsymbol{SD}}{\boldsymbol{b}}$$

$$\mathbf{LOQ} = \frac{\mathbf{10}\ \boldsymbol{X}\ \boldsymbol{SD}}{\boldsymbol{b}}$$

Note:LOD= smallest amount of analyte
LOQ= Quantity Limit
SD = Foreign exchange standard
B = Coefficient of Variable X
A = Constant

RESEARCH RESULT

1. Qualitative Analysis

Qualitative testing of hydroquinone aims to identify whether facial whitening cream contains hydroquinone. The results of the qualitative test are presented in Table 1 below:

Table 1 Hydroquinone qualitative test

No	Sample	Efficacy	Color Change FeCl3	Color Change Benedict	Results
Control + Hydroquino			Yellow	Brick Red	+ C6H4(OH)2
1	Sample A	enlighten	Yellow	brick red	+ C6H4(OH)2
2	Sample B	enlighten	purple blue	Pink orange	- C6H4(OH)2
3	Sample C	enlighten	Yellow	brick red	+ C6H4(OH)2
4	Sample D	enlighten	Orange	Blue	- C6H4(OH)2
5	Sample E	enlighten	Orange	Blue	- C6H4(OH)2
6	Sample F	enlighten	Orange	Puti	- C6H4(OH)2
7	Sample G	enlighten	Blue	Pale yellow	- C6H4(OH)2
8	H . sample	enlighten	Blue	Yellow	- C6H4(OH)2

Hydroquinone Quantitative Test

a. Determination of the maximum wavelength.

Table 2 The results of determining the maximum wave length

No	P/V	Wavelength	Absorbance
1	(↑)	294.05	0.282

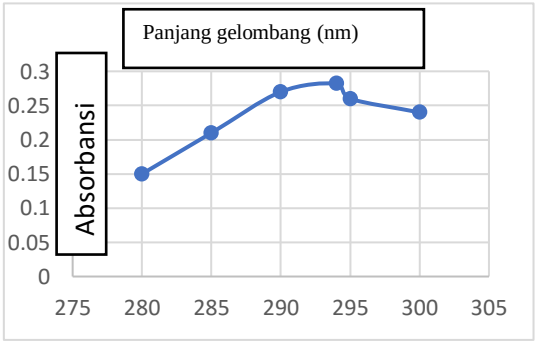

Figure 1. Maximum Wavelength Measurement Curve

b. Determination of the Hydroquinone Standard Curve

Determination of the standard curve in this study was carried out by plotting the concentration and absorbance obtained in the measurement using the maximum wavelength (294 nm). calculation data is shown in table 3

Table 3. Analytical results of hydroquinone

NO	Sample ID	absorbent
1	Blank	0.0000
2	Series 1 (8ppm)	O,2261
3	Series 2 (10ppm)	0.2826
4	Series 3 (12ppm)	0.3376
5	Series 4 (16ppm)	0.4541
6	Series 5(20ppm)	0.5643
7	Series 6 (24ppm)	0.6795

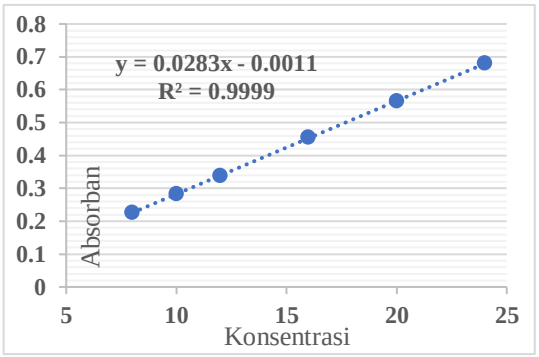

Figure 2 Hydroquinone standar curve

c. Test Sample

Table 4. Sample Test Results

Sample	absorbance	Concentration (ppm)	Hydroquinone (%)
A1	0.2917	250 ppm	2.794%
A2	0.2814	250 ppm	2.894%
C1	0.4014	500 ppm	3.981%
C2	0.4121	500 ppm	4,087%

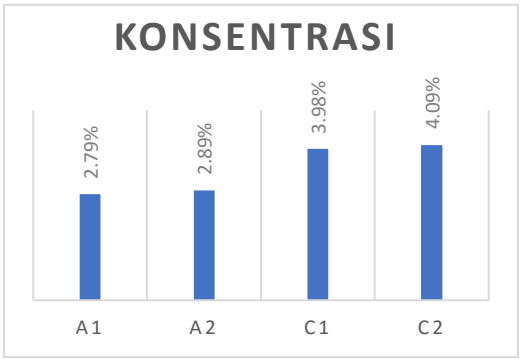

Figure 3 Sampel Analysis Result

d. Determination of Hydroquinone Levels in cream

Data analysis of hydroquinone levels in samples of facial whitening cream scattered in the city of Gorontalo using UV-VIS spectrophotometry in the

maximum wavelength obtained 4.19% hydraquinone in sample A and 2.84% hydroquinone in sample C.

Method Validation

a. linearity

The similarity of the standard curve lines can be seen in Figure 4.2 The regression equation obtained in the manufacture of the hydraquinone standard curve where Y = 0.0283X - 0.0011 in the correlation coefficient (r) = 0.9999

b. Limit of Detection (LOD) and Limit Of Quantification (LOQ)

The following are the measurement results of Limit of Detection (LOD) and Limit of Quantification (LOQ).

Table 5. Standard Division

No	X	Y	Y	(Y Y)	(YY¯)^2
1	8	0.2261	0.424083	-0.19798333	0.0391974
2	10	0.2826	0.424083	-0.14148333	0.020017534
3	12	0.3376	0.424083	-0.08648333	0.007479367
4	16	0.4541	0.424083	0.030016667	0.000901
5	20	0.5643	0.424083	0.140216667	0.019660714
6	24	0.6798	0.424083	0.255716667	0.065391014
Total					0.152647028
S					0.030529
SD					0.174727
LOD (PPM)					18,642 ppm
LOQ (PPM)					62.142ppm

DISCUSSION

Hydroquinone Qualitative Analysis

The qualitative analysis of hydroquinone aims to identify whether facial whitening creams contain hydroquinone. In the qualitative test using color reagents, where the reagents used are FeCl3 and bededic reagents. FeCl3 reagent is used and Benedict's reagent because if hydroquinone is added the reagent will undergo an oxidation-reduction reaction. Based on Table 1, obtained 2 samples (HQM and BWS) showed positive results of hydroquinone which was indicated by a color change. FeCl3 and benedict were used for qualitative analysis of hydroquinone because FeCl3 and benedict reagents function to bind hydroquinone so as to produce color changes in samples A and C [4]; [2]. In the identification of samples using FeCl3, namely as an indicator, the presence of a hydroxyl group in the sample will react to produce a yellow color when FeCl3 is added where FeCl3 will form a complex compound, a complex compound is formed because the element O in hydroquinone reacts with FeCl3 to form a reaction that produces a yellow color. Identification using Benedict's reagent where Benedict's reagent serves to identify the presence of an aldehyde or ketone group so that a brick red color will be formed.

The next procedure to determine the levels of hydroquinone in the HQM and BWS samples was quantitative test using UV-VIS spectrophotometry. The following is an oxidation reduction reaction of hydroquinone with FeCl3 and Benedict's reagent.

$C_6H_6O_2$ (Hydroquinone) + Fe^{3+} ⟶ $C_6H_4O_2$ (Quninon) + Fe^{2+}

$C_6H_6O_2$ (Hydroquinone) + Cu^{2+} ⟶ $C_6H_4O_2$ (Quninon) + Cu

Quantitative Analysis using UV-VIS . Spectrophotometry

a. Formation of Standard Solution

A standard liquid is a liquid with a known concentration of elements or compounds. The manufacture of the hydroquinone raw liquid can be used in determining the maximum wavelength by forming a standard curve In this study, the standard liquid made was a standard solution of hydroquinone in a strength of 100 ppm. By dissolving 5 mg of hydroquinone with 50 mL of methanol to obtain a concentration of 100 ppm.

b. Determination of the Maximum Wavelength of Hydroquinone

In determining the wavelength analyzed using UV-VIS spectro in the wavelength of 280-300 nm. Calculation

data in table 4.2 where hydroquinone has a maximum wavelength of 294 nm in an absorbance value of 0.282. According to the Ministry of Health (2014) the maximum wavelength of hydroquinone is 293 ± 2. In accordance with certain conditions, the wavelength produced by absorption breaks through the range of 0.2-0.8 based on Lambert Beer's law. According to Lambert Beer's law absorption is directly proportional to strength [9]

c. Standard Curve Determination

The standard curve is one of the curves in adding the number of compounds indirectly, the determination of the standard curve aims to obtain the Y equation and the regression value that will be used in determining the concentration of a compound [11].

Based on the results of hydroquinone analysis using a wavelength of 294 nm and the resulting absorbance is not 0.2 and not 0.8 because according to Lambert Beer's law the appropriate absorbance price is 0.2-0.8 (Suhartati 2013). According to Suhartati 2013, if the absorbance value obtained is >0.8 or <0.2, the absorbance is no longer zero. The standard curve of hydroquinone is presented in figure 4.2

d. Determination of hydroquinone levels in facial whitening cream

In looking at the levels of hydroquinone in facial whitening creams that are spread in Gorontalo City without a distribution permit using UV VIS spectrophotometry, each sample is counted twice in order to produce very accurate data [2]. Determination of hydroquinone levels in the sample is done by taking 0, 25 mg of whitening cream was then dissolved using 50 mL of methanol so that a 500ppm cream concentration was obtained, then 1 mL of the test solution was taken, then 20 mL of methanol was added and a hydroquinone concentration of 250ppm was obtained and then analyzed using UV VIS spectrophotometry at a maximum wavelength of 294 nm. Each sample is repeated twice (duplo) to ensure very accurate data.

Through the test data, it was found that the hydroquinone content in the whitening cream exceeded the predetermined limit [7]. Hydroquinone cream A with C has a concentration of 4.19% and 2.84%, the level set is >2%. The use of hydroquinone in facial whitening creams that are used for a long period of time has not been allowed or its use is prohibited because it can cause harmful effects to the skin.

Hydroquinone is a substance that is always used in whitening cosmetics. Excessive use can cause harmful effects on the skin because it can cause skin cancer [13]. Hydroquinone is an active compound that can control skin pigmentation which is dark brown in color, until black spots or spots appear on the skin. Hydroquinone is used in the brightness of skin that looks dark due to freckles or has not aged. Mild side effects where too much use of hydroquinone causes redness of the facial skin as well as when exposed to sunlight [10].

The use of hydroquinone in whitening cream will damage the melanin layer on the skin because hydroquinone works by inducing the tyrosinase enzyme by preventing the enzymatic oxidation reaction of tyrosine 3,4dihydroxyphenylalanine. Tyrosinase is an important enzyme in the formation of melanin. Until when the enzyme work is inhibited so that the amount of melanine pigment in the skin becomes low, so the skin becomes very white [14]. Melanin is a pigment that makes up the color of the skin (white, black, and brown). So that the use of hydroquinone in the long term at the

highest levels will damage the pigment in the skin [2] If the skin pigment is damaged there will be redness and burning of the skin, and irritation of the skin and if it is stopped immediately it will have a worse effect [5] .

Method Validation

Validation of analytical procedures is one of the assessment measures in these parameters, in accordance with laboratory testing, in proving where certain parameters are in accordance with the requirements for their users [10].

Validation of analytical methods is a process carried out through laboratory experiments where the characteristics of a procedure meet the requirements for analytical applications. Validation of a method is very important because it ensures that the procedures used meet the standards [10].

a. Linearity

Linearity is the strength of analytical procedures in generating responses directly or through mathematical transformations accordingly, proportional to the strength of the analyte in the sample. Determination of the linearity of the hydroquinone standardized curve according to the absorption value in the hydroquinone range of 8 to 24 ppm. The similarity of the standard curve lines can be seen in Table 4.2. The regression similarity produced in the formation of the standard curve for hydraquinone is Y = 0.0283X - 0.0011 at the correlation coefficient (r) = 0.9999. The correlation coefficient (r) close to 1 reveals a strong correlation. linear between the concentration in the absorption obtained,

The linearity test aims to determine whether two variables have a linear relationshipor not significantly, this examiner sees how variable x affects variable y, whether the effect is directly proportional or inversely proportional. This test is usually used as a requirement in correlation analysis or linear regression.

Based on the results obtained, it shows that there is a linear relationship between the coefficients and the resulting absorption.

b. Limit of Detection (LOD) and Limit of Quantification (LOQ)

The limit of detection through an analytical procedure is the value of the limit test parameter where the smallest analyte concentration can be detected. Meanwhile, LOD through one of the analytical procedures is the determination price for the quantitative determination of substances in the lowest concentration in the matrix such as contamination in drug raw materials [9].

The limit of detection is defined as the lowest concentration of analyte that can still be detected although it cannot always be quantified. While the limit of quantification as the lowest concentration of analyte in the sample that can be determined [9]

Based on table 4.5, the hydroquinone values obtained are LOD = 18.642 ppm and LOQ = 62, 142 ppm. The results of the LOD and LOQ validation of this study showed very good results. This refers to the results of the detection limit where the results obtained are > 1.1211 ppm and the quantity limit is < 1.1211 ppm. according to [12] If the detection limit obtained shows a value of more than 1.1211 ppm so that certain data can be trusted where the resulting signal includes a hydroquinone signal. However, if the concentration obtained is <1.1211 ppm, the signal obtained is not a signal from hydroquinone. While the quantity limit when the calculation data is not below 3.7370 ppm so that the calculation data can be said to be accurate.

CONCLUSION

In accordance with the observational data that has been carried out, it can be concluded that:

1. Qualitative test data in eight samples of whitening cream that were spread in Gorontalo City there were two positive samples containing hydroquinone where sample A and sample C.
2. Quantitative test data using UV VIS spectrophotometry two samples of whitening cream contained hydroquinone in the concentration of sample A amounting to 41.976 mg/g or 4.1976% and sample C of 28.430 m/g or 2.843% in accordance with the test data carried out, it is known where the levels of hydroquinn in sample exceeds the level limit that has been determined by BPOM is <2%.

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