

Article History

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nandaraudhatil@umbandung.ac.id**QUALITATIVE AND QUANTITATIVE ANALYSIS OF HYDROQUINONE CONTENT IN MARKETPLACE FACIAL WHITENING CREAMS****Zaman Ruchiyat^a, Nanda Raudhatil Jannah^{a*}, Ayu Shalihah^a**^a Pharmacy Study Program, Faculty of Science and Technology, Universitas Muhammadiyah Bandung**Abstract**

Hydroquinone is one of the dangerous ingredients in facial whitening cream cosmetics which can cause skin irritation, skin redness and a burning feeling. The purpose of this study was to determine the hydroquinone content in facial whitening cream cosmetics sold in the marketplace. The method used in this study was a qualitative test using a colour reagent test and the Thin Layer Chromatography (TLC) method with toluene:glacial acetic acid as the mobile phase (5:5) and Silica Gel254 Plate as the stationary phase. Quantitative analysis used the UV - Vis spectrophotometry method at a wavelength of 541 nm. The results of the qualitative test in the TLC test showed that 4 samples tested positive for hydroquinone in samples A, B, D, and E, with a range of R_f values of 0.44, 0.5, 0.52, and 0.5, respectively. The results of the quantitative test showed that 9 samples contained hydroquinone with a sample content range of 0.22 - 3.62 ppm with an LoD value of 0.637 ppm and an LoQ of 2.124 ppm. The results of this study indicate that there are still cosmetics containing hydroquinone, these results are not following the Regulation of Badan Pengawas Obat dan Makanan (BPOM) No. KH. 00.01.43.2503 of 2009 where the use of this hydroquinone ingredient is prohibited for use in facial whitening creams because it can endanger health.

Keywords: Analysis; Hydroquinone; TLC; Whitening Cream

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INTRODUCTION

Life is expanding at the same time as science and technology is becoming more complex. It is not just about the need for clothing, food, housing, education, and health when using more complex science and technology; it is also about the desire to beautify oneself, which has always been a top priority in sustaining everyday looks. Utilizing cosmetics is one approach to transforming or improving oneself. In today's society, using cosmetics is primarily done to maintain personal hygiene, improve one's appearance with makeup, boost one's sense of calm and self-confidence, protect one's skin and hair from ultraviolet rays and other environmental toxins, delay the ageing process, and generally help one enjoy and appreciate life more [1].

Face whitening or face lightening creams are frequently used cosmetic products that are applied to the face. Regardless of the safety of the substances used or the ingredients, many women and men desire attractive, white, and clean face skin. Mercury, hydroquinone, retinoic acid, and artificial dyes like rhodamine B and permanent orange are only a few of the substances that cannot be utilized to make cosmetics [2]. The Republic of Indonesia's Minister of Health's Regulation No. 445/MENKES/PER/V/1998 forbade the usage of these materials back in 1998. Hydroquinone-containing creams will build up in the skin, which can result in mutations and damage, suggesting that long-term usage could be carcinogenic

[3]. The Head of BPOM issued a warning letter with the number KH. 00.01.43.2503 of 2009 on cosmetics that include harmful or illegal substances, such as hydroquinone, where their use in cosmetic preparations can be harmful to human health and is not permitted.

Since 2008, the use of hydroquinone in face whitening cosmetics has been prohibited and is only permitted in amounts that do not exceed 0.02% on artificial nails [3]. More than 2% of hydroquinone falls within the category of hard drugs that require a prescription from a doctor to be used. Without a doctor's supervision, using this potent medication has risks that might result in skin rashes, skin redness, and burning sensations. Additionally, it can result in liver cell cancer (hepatocellular adenoma), blood cancer (leukemia), and abnormalities in the kidneys (nephropathy). More frequent usage may irritate skin, however stopping it right away can worsen the problem [1]

According to Research [7], there are 8 samples circulating in Jayapura, with 3 samples coming from medical offices and 5 samples coming from commercial beauty establishments, with an average hydroquinone level in the 6 samples ranging from 5,143 ppm to 5,542 ppm [4]. Using the qualitative color test technique and the quantitative UV-Vis Spectrophotometric test, research by Fahira et al (2021) discovered that 8 out of 10 samples of whitening cream obtained from several marketplaces in Mataram City tested positive for

hydroquinone. The average hydroquinone level in the 8 samples ranged from 3,130% to 4,292%, according to the data [5].

On the basis of the aforementioned background, it is vital to examine the amounts of hydroquinone in cosmetic samples of facial whitening creams, particularly those that are available in the market but are not registered with BPOM RI. Using UV-Vis spectrophotometry and thin layer chromatography, analysis was done qualitatively.

RESEARCH METHODS

Materials

The materials used were 10 samples of whitening cream, distilled water, ethanol 96%, stationary phase (GF 254 silica plate), mobile phase (toluene: glacial acetic acid), iron (III) chloride, 1% fluroglucin, sodium hydroxide, and standard hydroquinone. All chemicals were purchased from Merck Germany and were used without further purification.

Equipments

The equipment used was glassware, analytical balance, 254nm UV lamp, oven, water bath, capillary tube, drip plate, and UV-Vis spectrophotometer (Shimadzu UV-2600, Japan).

Procedure

A Qualitative Analysis of Hydroquinone

1. Color Reaction Method

1 gram of cream sample was weighed and then placed on the drip plate. Then 3 drops of 5% FeCl₃ reagent were added to the drop plate and the color change was observed. Positive samples containing hydroquinone are indicated by a change in color from green to black [5].

2. Qualitative Analysis with TLC

Hydroquinone standards and cream samples (A, B, C, D, E, F, G, H, I, J) weighed as much as 2 grams each. Then put in a 25 mL volumetric flask and diluted with 96% ethanol up to the mark line. The mixture was homogenized over a water bath at 60 °C for 10 minutes while stirring, and cooled. The filter results can be used for TLC analysis using a TLC plate that has been saturated with toluene:glacial acetic acid as the mobile phase. The separated stains were observed under UV254 nm light and then the R_f value was calculated [6].

Estimation of The Sample's Hydroquinone Concentration

In a beaker, add 5 mL of 96 ethanol and 100 milligrams of bleaching cream. The mixture was stirred and homogenized over a water bath for 10 minutes at 60 °C before being chilled. After filtering with Whatman paper and pouring 96% ethanol to the mark in a 10 mL volumetric flask. A test tube containing 5 mL of the

mixture was then filled, to which 1 mL of 1% phloroglucin reagent and 1 mL of 0.5 N NaOH were added. The test tube was then heated in a water bath at 70 °C for 50 minutes. The solution was then cooled, 10 mL of 96% ethanol was added, and the absorbance was determined using a UV-Vis spectrophotometer set to the maximum wavelength. Based on the regression equation that was created by establishing the standard curve, the amount of hydroquinone in the sample was estimated [5].

Method Validation

- Linearity

The results of the absorbance measurements are gathered to identify the correlation coefficient (r) value based on the hydroquinone standard curve that has been determined [7].

$$y = bx + a$$

where :

y = dependent variable

a = intercept

b = slope

x = concentration

- LoD and LoQ Test

The smallest concentration that can still be detected (LoD) and detected in quantity (LoQ) is calculated statistically through a linear line from the standard curve [7].

- Detection Limit (LoD)

$$\text{LoD} = \frac{3 \cdot \text{SD}}{b}$$

- Quantity Limit (LoQ)

$$\text{LoQ} = \frac{10 \cdot \text{SD}}{b}$$

RESULTS AND DISCUSSION

Organoleptic Test of Whitening Cream Samples

Samples of 10 brands of face whitening creams with a minimum rating of 4, the most customer reviews, prices ranging from Rp. 4,000 to Rp. 60,000, and no BPOM registration numbers were obtained. The findings of the organoleptic testing on 10 samples of face whitening cream are shown in Table 1 below. Each cream purchased in the market has a different appearance color. The inclusion of additional compounds that produce darker colors may be the cause of the color variation. similar to how hydroquinone is described as readily becoming black when exposed to light. Some of the cream samples had pungent qualities. The 10 samples of whitening cream did not have BPOM registration numbers. This is a sign that cream sample analysis is necessary to detect the

presence of potentially hazardous chemicals like hydroquinone [8].

Table 1. Organoleptic test of samples

Sample	Color	fragrance	Texture
A	Faded pink	Creamy scent (stings)	Sticky
B	White	Creamy scent	Sticky with air bubbles
C	<i>Cream</i>	Creamy scent (stings)	Firm and sticky
D	<i>Cream</i>	Creamy scent	Sticky with air bubbles
E	White	Creamy scent	Sticky
F	<i>Cream</i>	Creamy scent (stings)	Sticky with air bubbles
G	White	Creamy scent	Sticky
H	White	Creamy scent	Sticky with air bubbles
I	Pale yellow	Creamy scent	Sticky with air bubbles
J	Spotted white	Creamy scent	Sticky

Qualitative Analysis Using Color Reagent Method and Thin Layer Chromatography (TLC) Method

FeCl_3 reagent is one of the specific color reagents for hydroquinone. Of the 10 samples of facial whitening cream cosmetics tested, 9 samples experienced discoloration as shown in Figure 1. Some samples produce a black color after reacting with FeCl_3 . The color formation reaction can be seen in Figure 2. The presence of FeCl_3 will form a complex with hydroquinone in the sample, resulting in a green-to-black color change. [4]

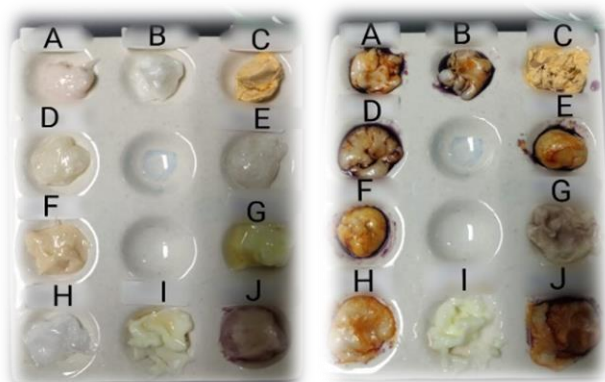


Figure 1. The changes in a facial whitening cream cosmetic test sample before (left) and after the addition of the FeCl_3 reagent (right)

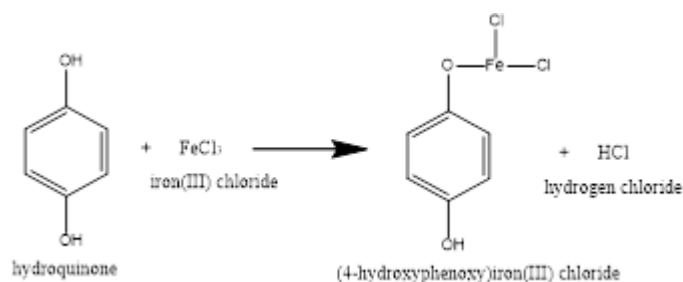


Figure 2. Chemical reaction of hydroquinone with FeCl_3

Figure 2 depicts the chemical reaction between FeCl_3 and hydroquinone producing 4-hydroxyphenoxy)iron(III) chloride while generating hydrochloric acid as a byproduct. As the reaction occurs the detection of the hydroquinone is possible to be conducted via spectrophotometric detection due to color change. Table 2 shows the R_f data from the analysis using TLC on the nine samples compared to the hydroquinone standard R_f . The results are declared positive if the color of the sample spots, the positive control and the sample R_f values are close to each other with a value difference of ≤ 0.2 cm, while the value ≥ 0.2 cm is declared negative [8]. This phenomenon could be driven by several factors, including the activation of the plate, the thickness and flatness of the plate, the solvent, the number of spots, and the steam in the developer's vessel used [9].

Table 2. Qualitative analysis using Thin Layer Chromatography

Sample	Hydroquinone standard R_f value	R_f value of the Cream sample
A	0.34	0.44
B	0.44	0.50
C	0.50	ND
D	0.50	0.52
E	0.34	0.50
F	0.50	ND
G	0.34	ND
H	0.56	ND
J	0.34	ND

ND=Not Detected

Using TLC and a 5:5 toluene:glacial acetic acid eluent/mobile phase ratio, a qualitative analysis of the cream sample was performed. The comparison of the R_f values of the standard and cream samples revealed that 4 of the 9 samples were believed to be hydroquinone positive. The other 5 samples' findings, however, were negative or undetectable since no stains showed up on the TLC plate. The results are declared positive if the color of the sample spots, the positive control and the sample R_f values are close to each other with a value difference of ≤ 0.2 cm, while the value ≥ 0.2 cm is declared negative [8]. The nine samples were

examined using a UV-Vis spectrophotometer to more clearly demonstrate whether or not hydroquinone was present in the samples. In another study, TLC has been used as an identification method for a hydroquinone range 1.9 – 3.3 µg/g in whitening cream [11]. This shows that TLC is still commonly used for the initial detection of hydroquinone.

Quantitative Analysis of Hydroquinone

This quantitative test was carried out using a UV-Vis spectrophotometer at a wavelength of 541 nm. The maximum wavelength obtained is relevant to previous research by Sarah, 2014 [6]. Hydroquinone Standard Solution and Cream Samples were reacted with the addition of 1% phloroglucinol reagent as a complexing agent so that absorption of the solution could be observed at visible light wavelengths. From the measurement of the absorption of the hydroquinone standard solution in Figure 3., the regression equation $y = 0.0437x + 0.0315$ is obtained with a value of $r^2 = 0.987$. The requirement for linearity is when the value of r is close to 1 indicating a linear relationship between the hydroquinone concentration and the measured absorbance [4]. Based on Table 3, the hydroquinone concentration in 9 samples ranged from 0.220 – 3.628 ppm.

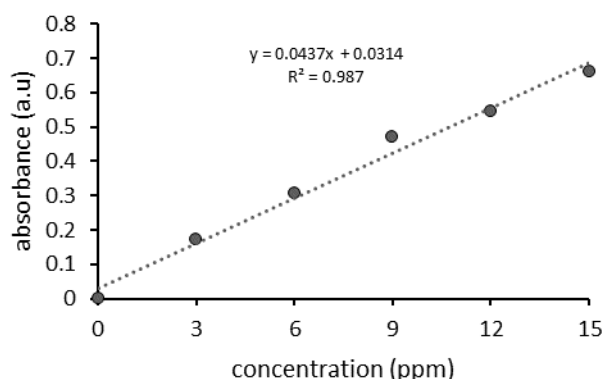


Figure 3. Hydroquinone Standard Solution Calibration Curve

Table 3. The results of determining hydroquinone levels in cosmetic samples of facial whitening creams

No	Sample Code	Concentration (ppm)
1	A	3.628
2	B	1.120
3	C	0.676
4	D	0.612
5	E	0.517
6	F	0.771
7	G	0.993
8	H	0.898
9	J	0.220

The limit of detection (LoD) and quantity (LoQ) tests for measuring hydroquinone levels obtained successive results of 0.637 and 2.124 ppm. Based on

the data in Table 3, it was found that seven samples (A, B, C, F, G and H) are above the LoD value. However, only sample A is above the LoQ value. It is safe to assume that the signal obtained is a signal from hydroquinone if the analysis findings are higher than the LoD and LoQ values. If the findings, however, are less than the LoD and LoQ, then they were not produced by hydroquinone signals or it is not detected specifically as hydroquinone. The smaller the LoD and LoQ values, the more sensitive the equipment is to detecting the content of the analyte accurately and precisely [7].

According to the Head of BPOM Number 18 of 2015 concerning technical requirements for cosmetic ingredients, the use of hydroquinone or the allowable hydroquinone content in cosmetic preparations is 0.02% in nail polish. Meanwhile, the level of hydroquinone in facial whitening cream cosmetics is 0% or not allowed, according to the Regulation of the Minister of Health of the Republic of Indonesia No. 445/MENKES/V/1998 and according to Drug and Food Regulations (BPOM) based on PUBLIC WARNING/WARNING No KH.00.01.43.2503 dated 11 June 2009 [10]. And it can also be observed from the risks associated with using hydroquinone, which can irritate the skin, cause it to turn red and feel burnt [1].

Apart from online sales, hydroquinone is still found in samples of whitening creams in traditional markets in Indonesia [12]. Not only in Indonesia, the identification of hydroquinone in whitening creams in other countries is still being carried out, even large concentrations have been found, such as in China and the US, which reach 41-42 ppm [13]. This should be the concern of all parties, to continue carrying out supervision and education to consumers. Due to its dangerous side effects [14], hydroquinone considers to be replaced with more effective and safer agents as the comparative studies have shown that arbutin was more effective than hydroquinone as a whitening agent [15].

CONCLUSION

According to the findings of the hydroquinone content test performed on 10 cosmetic samples of face whitening cream purchased from the market, 4 of the 10 cosmetic samples tested positive for hydroquinone using the TLC test, which had an R_f value of 0,44 – 0,52. With the use of quantitative analysis, hydroquinone concentrations of 0.637 and 2.124 ppm, were sample A above the LoD and LoQ limits. It is better to learn more about hydroquinone in various cosmetic face whitening creams that are marketed on the market given that it is still used in the preparation of many cosmetic face whitening products.

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