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APPLICATION D-OPTIMAL METHOD ON THE OPTIMIZATION OF FORMULATION OF KINTAMANI ARABICA COFFEE GEL (*Coffea arabica* L.)

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ABSTRACT

Arabica coffee (Coffea arabica L.) kintamani is a superior agricultural product from Bali. Arabica coffee (Coffea arabica L.) contains many compounds, one of which is caffeine beneficial for health and beauty. This study aims to formulate kintamani arabica coffee beans into a gel dosage form. The formula optimization was made using the D-Optimal method using a combination of HPMC and propylene glycol as observation variables and spreadability, pH, and viscosity of the gel preparation as experimental responses. The study of caffeine from the gel preparation was carried out using a Franz diffusion cell. The spectrophotometric method determines caffeine content in the gel preparation and its release.The results showed that the amount of HPMC used would increase the viscosity value (+14113.92) and decrease the spreadability (-0.29) and pH (-6.59167E-003) of the gel. The greater the amount of propylene glycol used will decrease the viscosity value (-2484.54) and increase the spreadability value (+0.30) and pH (+0.31802) of the gel. The conclusion of this study is the use of a combination of HPMC and propylene glycol (6%:17%) resulted in the optimum formula with a viscosity value of 44,070 cps, a spreadability value of 3.6 cm, and a pH value of 5.32. The caffeine content obtained in the gel preparation was 188.47 g and the amount of caffeine released from the gel preparation for 6 hours of testing was 4.95%.

Keywords: Arabica Coffee; HPMC; Propylene glycol; D-Optional mixture design

1. INTRODUCTION

Kintamani arabica coffee (*Coffea arabica* L.) is well known internationally because it is considered to have better quality beans than other types of coffee such as robusta coffee (*Coffea canephora*) and it has a complex aroma and taste (Mangku et al., 2018). Arabica coffee (Coffea arabica L.) contains many compounds such as caffeine, chlorogenic acid, trigonelline, carbohydrates, fats, amino acids, organic acids, volatile aromas, and minerals (Farhaty, 2012). Caffeine in coffee is useful as an antioxidant that counteracts free radicals (Gebeyehu & Bikila, 2015). In addition, caffeine in coffee has pharmacological effects that are clinically useful, such as stimulating the nervous system, relaxing smooth muscles, especially bronchial smooth muscles, and stimulating cardiac muscles (Dewi et al., 2017).

Gels, sometimes called jellies, are semisolid systems consisting of suspensions made up of small inorganic particles or large organic molecules, penetrated by a liquid (Kemenkes RI, 2020). Gel has the advantage that it has high viscosity and adhesion so it does not flow easily on the surface of the skin. The gel has thixotropic properties so that it is easy to apply evenly, does not leave marks, produces a thin film-like layer when apply is easily washed off with water, and gives a cooling sensation after use. Gels can penetrate better than creams, are very good for hair areas, and are preferred cosmetically (Rosida et al., 2018).

Several studies related to coffee gel formulations have been carried out. For example, research conducted by (Fitria & Chandra, 2018) shown that arabica coffee bean extract (*Coffea arabica* L.) which is given topically can reduce stretch marks. The use of HPMC as a gel base has been widely carried out. (Ardana et al., 2015) states that HPMC gel base with a concentration of 7% meets good requirements for viscosity tests, pH tests, and spreadability tests. The addition of propylene glycol in the formulation of gel preparations plays a role in increasing the spreadability of the gel and the penetration rate of the active substance (Putra, 2016) (Qisti et al., 2018). Research on the optimization of the Arabica coffee (Coffea arabica L.) gel formula using the D-Optimal mixture design has not been found. This method has advantages such as the number of trials is smaller, it can analyze the relationship between factors and experimental responses simultaneous (Ittiqo & Anderiani, 2017). The optimal formula was determined using Design-Expert software version 7 by looking the desirability value (Setyawan et al., 2012). Based on the description above, it is necessary to conduct research to optimize the kintamani Arabica (*Coffea arabica* L.) coffee gel formula using the D-optimal method.

2. METHODS

2.1. Tools and Materials

2.1.1. Tools

UV-Vis Spectrophotometer (*Shimadzu type UV-1280 UV-Vis Spectrophotometer*) is used to determine the levels of caffeine in gel dosage form and caffeine released during time periods. Release study is conducted by Franz diffusion cell.

2.1.2. Materials

Arabica coffee (*Coffea arabica* L.) beans is harvested from Catur Village, Kintamani, Bali. HPMC K100 was given from PT. Colorcon, propylene glycol purchased from Bratachem. All materials used are of pharmaceutical grade.

2.2. Extraction Process

Roasted arabica coffee bean extraction was carried out by taking 1 g of coffee bean sample, then dissolved in 150 mL of hot distilled water, later on filtered and the filtrate was taken (Fajriana & Fajriati, 2018). Furthermore, the extract mixture was filtered using filter paper with the help of a vacuum. The filtrate poured into a separating funnel. Liquid-liquid extraction was carried out with 45 mL ethyl acetate solvent with 5 times replications. The ethyl acetate fraction was evaporated over a water bath (Wilantari et al., 2018).

2.3. Gel Formulation

The gel base was formulated using HPMC with distilled water, then allowed to stand for approximately 24 hours. Furthermore, the coffee extract was mixed with propylene glycol, methylparaben, and propylparaben. Then gel base added to the mixture, and crushed until homogeneous and gel preparation was formed. Gel formulations were manufactured by following table below (**Table 1**).

2.4. Physical Properties Gel Test

2.4.1. Viscosity Test

Viscosity measurements were carried out with a viscometer (*Brookfield type DV-E*) with spindle number 7 at a speed of 60 rpm. The gel base was put into a glass beaker then the viscosity value was measured on the instrument (Ardana et al., 2015).

Table 1. Formulation of Arabica Coffee Gel (*Coffea arabica* L.) Using the D-Optimal Method

Run No	Arabica Coffee Extract (%)	HPMC (%)	Propyleneglycol (%)	Methylparaben (%)	Propylparaben (%)	Aquadest (%)
1	2	6.00	17.00	0,075	0,025	150
2	2	6.25	16.75	0,075	0,025	150
3	2	6.50	16.50	0,075	0,025	150
4	2	7.00	16.00	0,075	0,025	150
5	2	7.00	16.00	0,075	0,025	150
6	2	7.00	16.00	0,075	0,025	150
7	2	6.00	17.00	0,075	0,025	150
8	2	6.50	16.50	0,075	0,025	150
9	2	6.00	17.00	0,075	0,025	150
10	2	6.75	16.25	0,075	0,025	150
11	2	6.50	16.50	0,075	0,025	150

2.4.2. Spreadability Test

Sample placed on a round glass with a diameter of 15 cm, another glass was placed on it. After that, added 150 g of additional load and allowed to stand for 1 minute. Then the constant diameter was measured (Astuti et al., 2010). The spreadability of 3-5 cm shows a semisolid consistency which is very comfortable to use (Garg et al., 2002).

2.4.3. pH Test

The pH measurements of the preparation were carried out using a pH meter. The instrument was calibrated using a neutral pH buffer solution (pH 7.00) and an acidic pH buffer solution (pH 4.00) until the instrument shows the pH value. Then the electrodes were washed with distilled water. Furthermore, the electrode was dipped into the gel base, until the tool shows a constant pH value (Ardana et al., 2015). The number shown by the pH meter is the pH value of the preparation (Rawlins, 2002). The pH of the gel base preparation must be following the skin pH, namely 4.5-6.5 (Tranggono & Latifah, 2007).

2.5. Data Analysis

The optimal formula for arabica coffee gel (*Coffea arabica* L.) was analysed by multi-variant analysis with a mathematical model approach (linear, quadratic, special cubic). The optimum formula was determined based on the desirability value. The desirability value is a value that illustrates the correlation between the observation data and model prediction.

2.5.1. Formula Optimization

The optimum formula was determined based on the physical properties of the gel, which consisted of a spreadability test of 5-7 cm (Garg et al., 2002), a pH test of 4.5-6.5 (Tranggono & Latifah, 2007), and desirability value of the model.

2.5.2. Caffeine Release Study

The release of caffeine compounds was carried out using the Franz Diffusion Cell method using phosphate-buffered saline dissolution medium pH 7.4. The membrane used was filter paper. The temperature of the dissolution medium was 37ºC with a sampling volume of 2 ml, the sampling time was 6 hours.

The UV-Vis spectrophotometric method was used to determines caffeine content in the gel preparation and its release. A calibration curve of a standard caffeine solution with a concentration of 0 was made; 2; 4; 6; 8; 10 mg/L. The sample solution was measured for absorbance at a maximum wavelength of 272.5 nm. The resulting absorbance was entered into the standard curve series.

3. RESULTS AND DISCUSSION

3.1. Extraction and Gel Preparation Result

The extraction process resulted in a yield of 8.76 g. Furthermore, the extract that has been obtained were tested for water content. The recommended dry extract moisture content is less than 5% (Voigt et al., 1994). The results of the water content test on the coffee extract showed a value of 4.95%, which means it has met the requirements. The resulting arabica coffee gel is shown in the following picture (**Figure 1**).

Figure 1. Arabica Coffee Gel Formulation

3.2. Viscosity Test

HPMC gel base was made with a concentration according to the designed formula. Propylene glycol functions as a humectant and emollient that can maintain moisture in the preparation and increase the amount of water when the preparation is applied and is able to increase the solubility of methylparaben and propylparaben which functions as a preservative (Rowe et al., 2015). The results of the viscosity test are shown in the following **Figure 2**.

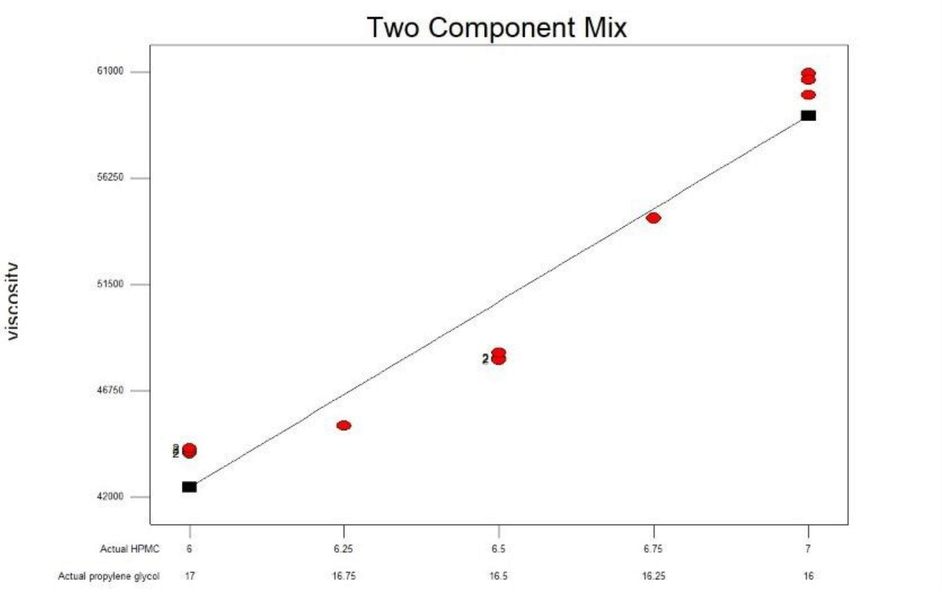

Figure 2. Correlation between the Combination of HPMC and Propylene Glycol on Viscosity value

The viscosity test showed that the greater concentration of HPMC in the gel formulation will increase the viscosity value. Runs 1, 7, and 9 with HPMC concentration of 6% yielded an average value of 44073 ± 105.039 cp. While run 4, 5, 6 with HPMC concentration of 7% which is the highest concentration produces an average viscosity value of 60510 ± 491.121 cp. Viscosity in pharmaceutical products generally has a viscosity of more than 30 dPas (Sinko, 2011). The increase use of HPMC will cause fluid to be retained and bound (Arikumalasari et al., 2013). From the viscosity response data, a graph of the viscosity test of the Kintamani Arabica Arabica (Coffea arabica L.) gel was generated which showed significant results which can be seen from the p-value <0.0001 (less than 0.05). This value explains that the equation model used was able to describe the actual condition of the viscosity measurement results. This is supported by an insignificant model prediction error of 0.0591 (more than 0.05).

3.3. Spreadability Test

The results of the dispersion test show that the less use of HPMC in the run formula will increase the dispersion value. This happens because HPMC will increase the viscosity of the gel so that the strength of the gel to spread when applied will decrease. The diameter of semi-solid preparations that are good for topical use are in the diameter value range of 3-5 cm or it can be stated that the dispersion area is between 7,605-19,625 cm2 (Garg et al, 2002). The results of the spreadability test are shown in the following **Figure 3**.

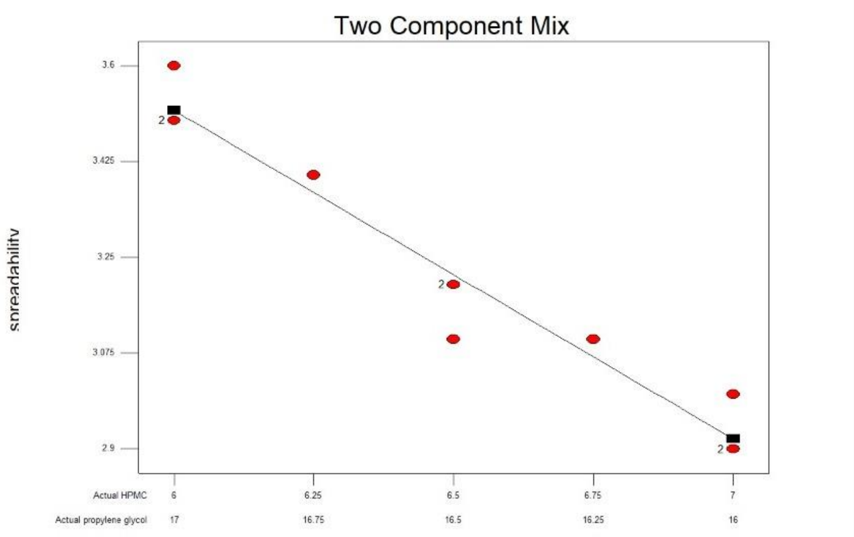

Figure 3. Correlation between the Combination of HPMC and Propylene Glycol on Spreadability Value

Preparations that are difficult to spread or too easily spread will reduce the level of effectiveness and comfort when the gel preparation is applied (Irianto et al., 2020). Based on the test results, 2 out of 11 runs produced a dispersion value outside expected range, namely runs 4 and 5 with a dispersion value of 2.9 cm. This is because the amount of HPMC in the high formula causes the viscosity value to increase and the dispersion value to decrease (Arikumalasari et al., 2013). Based on the response data of the dispersion test, a graph of the dispersibility test of the Kintamani Arabica Arabica (Coffea arabica L.) gel was produced which showed significant results which can be seen from the p-value <0.0001 (less than 0.05). This value explains that the equation model used is able to describe the actual condition of the dispersion response. This is supported by an insignificant model prediction error of 0.407 (more than 0.05).

3.4. pH Test

The purpose of the coffee gel pH being made to resemble the pH of the skin is so as not to cause irritation when using coffee gel. The results of the pH test are shown in the following **Figure 4**.

The pH test showed that all the formulas made were in the skin pH range of 4.5-6.5 (Tranggono & Latifah, 2007). Based on the test results, increasing the concentration of HPMC in the run formula variation will reduce the pH value of the preparation, but the pH changes that occur are not significant and are still within the normal pH range of the skin. Similar research results were also shown in the research of Pramita et al. 2017 where in his research the higher the concentration of HPMC formulated, the lower the resulting pH value. Based on the pH test response data, a linear graph of the pH test of Arabica coffee (*Coffea arabica* L.) Kintamani was produced which showed significant results which can be seen from the p-value of 0.0216 (less than 0.05). This value explains that the equation model used is able to describe the actual conditions of the pH test response. This is supported by an insignificant model prediction error of 0.1229 (more than 0.05).

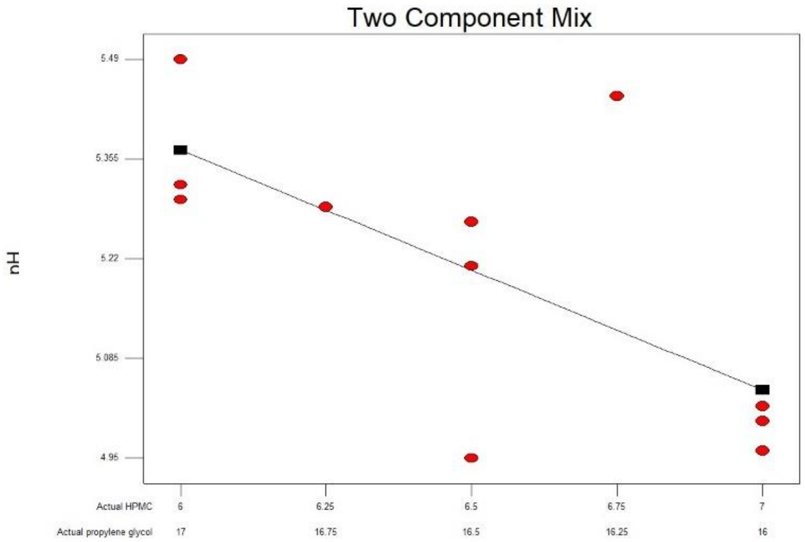

Figure 4. Correlation between the Combination of HPMC and Propylene Glycol on pH value

3.5. Data Analysis

The digital software used to analyze the coffee gel test data is *Design Expert 7.1.5*. With the use of this software, the gel test result data will be automatically processed and produce the optimum formula for arabica coffee gel.

3.6. Optimum Formula

The digital software used to analyze the coffee gel is Design Expert 7.1.5. The gel test result data will be automatically processed and produce an optimal run formula for Arabica coffee gel. The following is the resulting optimal run formula (**Figure 5** and **Table 2**):

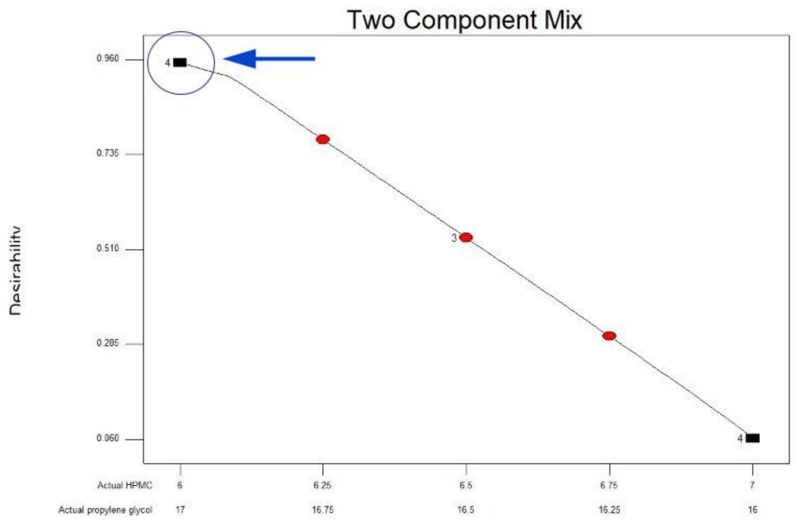

Figure 5. Combination of HPMC and propylene glycol (6:17) as the optimum formula with a desirability value of 0.95.

Table 2. Prediction of Optimum Formula

No	Extract	HPMC	Propyleneglycol	Viscosity	Spreadability	pH	Desirability	
1	2	6	17	42446.2	3.51	5.36	0.951	Selected

The results of the optimum gel formula made 3 replications (R1, R2, R3). The results of the physical test of the replicated samples produced the average values of viscosity, spreadability, and pH are 42444.33 cps, 3.53 cm, 5.35, respectively. The test results were analyzed using an open stat-single sample test comparison. The probability values generated for the viscosity, spreadability, and pH tests are 0.519, 0.556, and 0.742, respectively, which indicates each parameter generated by the expert design model is not significantly different from the observation results.

3.7. Caffeine Release Test

The caffeine content in the coffee gel sample was tested using a Franz diffusion cell. The process began with making a phosphate buffer saline solution of pH 7.4 (Putri et al., 2019). Preparation of standard solution of 1000 ppm caffeine, 100 ppm standard solution, and a series solution of 4 ppm, 6 ppm, 8 ppm, 10 ppm, 12 ppm, and 15 ppm were carried after. The maximum wavelength resulting from the test is 273 nm. The resulting caffeine standard curve with a linear regression value of 0.9977 indicates good linearity. The resulting LoD value is 13.48 µg/mL, and the resulting LoQ value is 44.95 µg/mL. Linear regression graph shown in **Figure 6**.

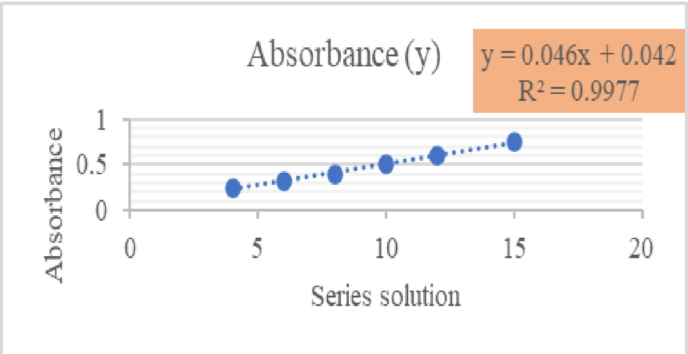

Figure 6. Linear Regression Graph

The assay of the sample was carried out by weighing 1 g of the gel sample and then dissolving it in 10 mL of phosphate saline buffer. The solution was centrifuged for 5 minutes at 1000 rpm. The supernatant was pipetted, and the absorbance value was measured using UV-vis spectrophotometry at the maximum wavelength. The amount of caffeine obtained is 183.96 ± 15.83 (n=4).

Caffeine content release test results aims to measure the amount of caffeine that has been successfully penetrated into the skin. The absorbance value is used to calculate the amount of caffeine penetrated into the skin. Measurement of caffeine content in samples using UV-vis spectrophotometry method. The caffeine content obtained is a description of the amount of caffeine absorbed per unit area in a unit of time which depends on the solubility of the drug and distribution characteristics, differences in drug concentration across the membrane, carrier properties and thickness of the stratum corneum (Astuti et al., 2012). The value of the caffeine content produced is listed in the following **Table 3**.

Penetrated caffeine was detected at 15 minutes because it takes time for the active substance to dissolve in the donor compartment system. The average value of caffeine content obtained at the 15th minute was 0.29 ± 0.062 mg/gram sample. The highest concentration of caffeine that was penetrated was in the 240th minute with an average value of 0.67 ± 0.243 mg/gram sample. then decreased in the 360th minute. This is in accordance with Chandra's, 2019 research where there was a decrease in the level of penetrated caffeine because the active substances contained in the preparation began to decrease. The graph of the level of the penetrated caffeine is shown in **Figure 7**.

Table 3. Total Percentage of Caffeine Released during 6 Hours.

Formula	Caffein Level (µg)	Percentage (%)
Optimum Formula (F1)	9.10 ± 0.99 (n=4)	4.95
Replication 1 (R1)	7.06 ± 0.99 (n=4)	3.84
Replication 2 (R2)	8.19 ± 0.99 (n=4)	4.45
Replication 3 (R3)	9.17 ± 0.99 (n=4)	4.98
Average	7.63 ± 0.99 (n=4)	4.55

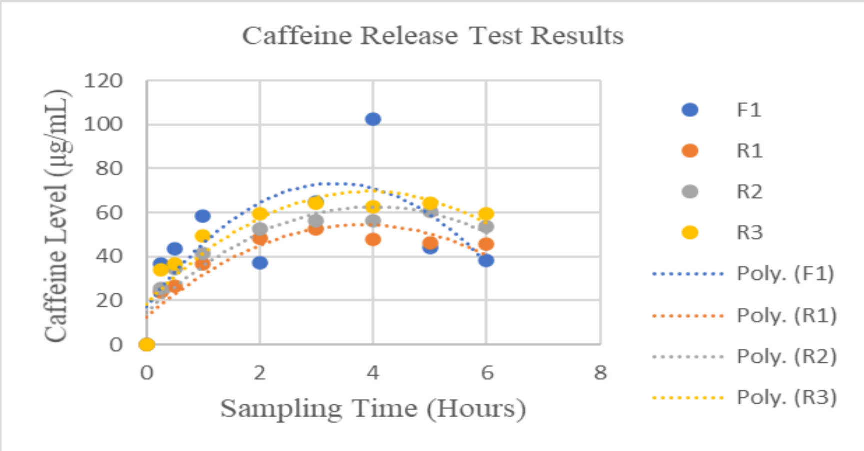

Figure 7. Levels of Caffeine Released after 6 Hours of Testing (F1= optimum formula; R1 = replication 1; R2 = replication 2; R3 = replication 3).

4. CONCLUSION

Coffee gel with a concentration of 6% HPMC and 17% propylene glycol became the optimum formula because it produced the best correlation values for viscosity, spreadability, and pH tests. The desirability value between the prediction model in Design-Expert and actual observation is 0.951. The results of the caffeine release test showed that the release was 9.10 µg (4.95%). This data will be useful as a reference for further research on testing the stability of kintamani arabica coffee gel. Future research needs to be considered for formulation development and evaluation of kintamani arabica coffee nanogels.

5. ACKNOWLEDGMENT

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6. CONFLICT OF INTEREST

The author declares that there no competing conflicts of interest.

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