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Optimization of Kolang-Kaling Seed Galactomannan Serum Using Response Surface Methodology

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ABSTRACT

Background: Ultraviolet (UV) exposure promotes free radical formation, leading to oxidative stress, lipid peroxidation, inflammation, and hyperpigmentation. Galactomannan derived from kolang-kaling (Arenga pinnata) exhibits antioxidant activity with potential protective effects against UV-induced damage. In serum formulations, carbomer and triethanolamine (TEA) are commonly combined as gelling agents to achieve desirable physicochemical properties. **Objective:** This study aimed to optimize a galactomannan-based facial serum by determining the most effective Carbomer–TEA concentration combination using Response Surface Methodology (RSM). **Methods:** A formulation optimization study was conducted employing the RSM approach with Design Expert software to evaluate the interaction effects of Carbomer and TEA concentrations on serum characteristics. **Results:** The optimal formulation predicted by the model consisted of 0.100% (w/v) Carbomer and 1.047% (w/v) TEA. **Conclusion:** Response Surface Methodology successfully optimized the galactomannan facial serum formulation. The identified combination of Carbomer and TEA is expected to provide suitable serum properties while supporting the antioxidant potential of galactomannan against UV-induced oxidative damage.

Keywords: Carbomer; Galactomannan; Optimization; Response Surface Methodology (RSM); Triethanolamine

INTRODUCTION

Ultraviolet (UV) radiation exposure can trigger a range of damaging effects on the skin, including premature aging, skin cancer, and a weakened immune response. These adverse effects are closely associated with the formation of reactive oxygen species (ROS), which are induced by UV radiation exposure (Jain & Jain, 2010).[1] Free radicals are highly reactive molecules characterized by unpaired electrons, enabling them to attack cellular components such as proteins, lipids, and DNA (Bogdan Allemann & Baumann, 2008).[2] This damage can persist as long as metabolic processes or external oxidative stressors continue to induce radical formation.

With increasing age, the production of free radicals tends to rise, while endogenous defense mechanisms gradually decline. This imbalance contributes to progressive structural damage at the cellular level, eventually accelerating cellular aging2. Antioxidant compounds can protect the body against both endogenous and exogenous oxidative stress by scavenging free radicals, thereby inhibiting oxidative reactions.[2,3]

Galactomannan extract has demonstrated antioxidant activity, with an IC_{50} value of 20.45 ppm.[4,5] A lower IC_{50} value indicates stronger antioxidant activity. Compounds with an IC_{50} below 50 ppm are considered to have very strong antioxidant activity, while values between 50–100 ppm indicate active antioxidants. Compounds with IC_{50} values between 101–250 ppm are classified as having moderate activity, 250–500 ppm as weak, and above 500 ppm as inactive.

Topical gel formulations, particularly serums, are widely used in cosmetic and pharmaceutical products. Carbomer is a polymer

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commonly utilized as a thickening agent in commercial skincare formulations based on gel systems. The addition of a neutralizer such as triethanolamine (TEA) can alter the polymer's conformation and the viscosity of the dispersed system. When the polymer structure is disrupted by hydrogen bonding or electrostatic interactions, a gel network is formed. However, TEA is an alkalizing agent with a high pH (approximately 8–10.5)[6], whereas carbomer typically has a pH range of 2.5–4.07. To achieve optimal viscosity, the pH of carbomer should be adjusted to a range between 6.0 and 11.07.

METHOD

The research method contains the way the research is carried out. Each of the research procedures that have been carried out must be clearly elaborated. In this subsub-section, write a description of the ethics test certificate if the research involves experimental animals.

1. Extraction of galactomannan *from Arenga pinnata* seed (kolang kaling)

Kolang-kaling (sugar palm fruit) was washed thoroughly with clean water, then homogenized using a blender. A total of 200 grams of kolang-kaling seeds were blended with 2000 mL of distilled water. The mixture was stored at a cold temperature (4°C) for 24 hours. Subsequently, the mixture was centrifuged at 9500 rpm for 15 minutes, yielding supernatant A. The remaining residue was added to 750 mL of distilled water and centrifuged under the same conditions to obtain supernatant B.

Supernatants A and B were then combined with 96% (v/v) ethanol in a 1:2 ratio and stored at a cold temperature for the next 24 hours. The resulting precipitate was separated using filter paper. The residue was soaked in 100 mL of 96% ethanol for 24 hours, followed by filtration, and then soaked again in another 100 mL of ethanol for an additional 24 hours. The final residue obtained after the second filtration was collected and stored.[3]

2. Preparation of galactomannan serum

The galactomannan serum formulation was optimized through varying proportions of carbomer 934 and triethanolamine (TEA). The formulation design was created using Design Expert version 13, applying a Response Surface Methodology (RSM) optimal design model. According to FDA guidelines, the concentration range for Carbomer 934 is 0.1–1%, while TEA is used in the range of 0.03–6%. The composition of the formulations can be seen in Table 1.

3. Physical assay of serum formulations[7]
    a. Organoleptic Evaluation
    The serum formulations were evaluated descriptively for color, aroma, and texture.
    b. pH assay
    The pH of each serum formulation was analyzed by comparing it to the normal pH range of facial skin (4.5–6.5).
    c. Viscosity assay
    Viscosity was measured and compared with the standard viscosity range for facial serums, which is 800–3,000 cPs.
4. Optimization using Design Expert – Response Surface Methodology (RSM)

Data analysis was conducted using the Analysis of Variance (ANOVA) method, with each response analyzed individually. The ANOVA results included the significance (p-value) of the model, lack-of-fit testing, comparison between the adjusted R-squared and predicted R-squared values, and an evaluation of adequate precision.

Following response analysis, optimization was conducted using predefined factors and response variables by assigning priority scales. After determining the optimal formulation, verification was performed to confirm that the experimental results were consistent with the software's predicted outcomes.

Table 1. Galactomannan serum formulation with design expert software

Materials / Run (%)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Galactomannan	10	10	10	10	10	10	10	10	10
Carbomer 934	1	0.55	0.1	0.55	0.55	1	0.55	0.1	0.55
Triethanolamin	6	6	3.0001	0.06	3.0001	0.06	0.06	0.06	3.0001
Glycerin	4	4	4	4	4	4	4	4	4
Ethylhexylglicerin	0.075	0.075	0.075	0.075	0.075	0.075	0.075	0.075	0.075
Phenoxyethanol	0.675	0.675	0.675	0.675	0.675	0.675	0.675	0.675	0.675
Aquadest (Ad)	100	100	100	100	100	100	100	100	100

The verification data were then compared against the 95% confidence interval (CI) or prediction interval (PI). If the data fell within the CI or PI, it was concluded that the model was in agreement with the software's prediction.

RESULTS

The extracted galactomannan from kolang-kaling weighed 33.38 grams and was characterized by a white color and semisolid form. The pH of each galactomannan serum formulation was measured using a pH meter, with three replications for each formula. Based on the pH measurements of the nine galactomannan serum formulations, as shown in Table 2, all formulas exhibited acceptable pH values within the normal skin pH range of 4.5–6.58.

Table 2. Viscosity test results of galactomannan serum preparation

Formulations	Viscosity (cPs) Mean±SD
F1	3827.67±163.76
F2	2691.00±93.95
F3	1501.00±133.50
F4	1113.00±133.32
F5	1815.00±123.74
F6	1595.67±17.91
F7	1121.00±75.38
F8	987.67±31.94
F9	1576.00±268.39

The viscosity measurement results indicated that formulas F1 to F9 were within the standard range for gel serum preparations (800–3000 cPs). Formulations within this viscosity range possess characteristics that allow for easy topical application. A higher viscosity reduces the spreadability of the serum on the skin, while a lower viscosity causes the formulation to flow too rapidly. The differences in viscosity among the formulations were due to varying ratios of carbomer and TEA.

Formula optimization was designed using Design Expert version 13, by varying the concentrations of Carbomer and TEA to evaluate their effects on pH and viscosity responses. The method used was Response Surface Methodology (RSM). The optimization design data are presented in Table 3.

Table 3. Optimization design data

Run	TEA (%)	*Carbomer* (%)
1	6	1
2	6	0.55
3	3	0.1
4	0.06	0.55
5	3	0.55
6	0.06	1
7	0.06	0.55
8	0.06	0.1
9	3	0.55

DISCUSSION

As shown in Table 3, the highest pH response was obtained in Run 1, with 6% TEA and

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1% Carbomer. In comparison, Run 2, which used the same TEA concentration but a lower Carbomer concentration, showed a pH value of 6.81 (Table 4). The lowest pH response was observed in Run 5, with a pH value of 6.42, where the TEA concentration was 3% and the Carbomer concentration was 0.55%.

Based on Figure 1, the interaction curve between the components indicates that the pH response is influenced by the interaction of TEA and carbomer. The variation in color represents different concentration combinations of TEA and carbomer, which affect the pH of the serum formulation. The red area indicates that the combination of TEA and carbomer yields the highest pH value. The blue area represents the lowest pH values resulting from the interaction of the two components, while the green area indicates a moderate pH response — neither too high nor too low.

Table 4. The results of pH value

Run	TEA (%)	*Carbomer* (%)	pH
1	6	1	6.81
2	6	0.55	6.85
3	3	0.1	6.44
4	0.06	0.55	6.69
5	3	0.55	6.42
6	0.06	1	6.65
7	0.06	0.55	6.61
8	0.06	0.1	6.53
9	3	0.55	6.45

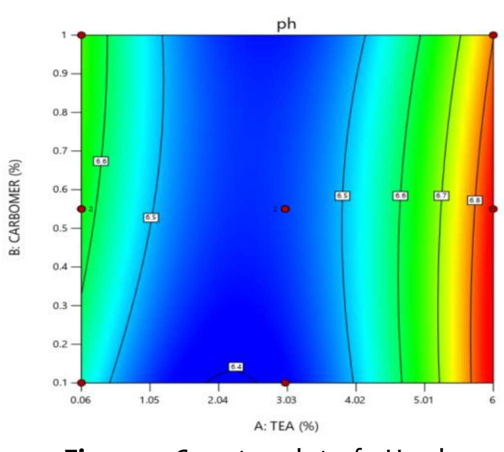

Figure 1. Counter plot of pH value

The optimization model of carbomer and TEA on the pH response is illustrated using a quadratic model, represented by the following equation:

Y = 0.1150 (A) + 0.0069(B) – 0.0470 (AB) + 0.2987 (A2) – 0.0239 (B2)

Given : A = TEA

B = Carbomer

Y = pH

The quadratic model equation indicates that the pH response is influenced by both TEA and carbomer, as well as the interaction between them. TEA had a greater influence, with a coefficient of 0.1150, while the coefficient for carbomer (B) was 0.0069. The interaction between TEA and Carbomer decreased the pH, as indicated by the negative coefficient of AB (–0.0470).

Carbomer tends to form gels when added to aqueous solutions, as its polymer chains become hydrated, unravel, and swell up to approximately 1000 times their original size. Carbomer is an anionic polymer and remains acidic in its non-neutralized state; therefore, it must be neutralized with a base to exhibit its gelling capability.[7]

The optimal pH range for carbomer to effectively form a gel is typically between pH 6 and 117. When dissolved in water at a concentration of 0.2%, carbomer itself has a pH of approximately 2.5–4.07. A stirred carbomer solution remains acidic and does not yet form a well-structured gel matrix. When TEA is added to a mixture containing carbomer, a chemical interaction occurs between TEA and the polymer. Upon neutralization by an alkalizing agent such as TEA, the polymer absorbs and retains water, resulting in negative charges along the polymer chain due to the ionization of carboxylic acid groups.[8] As a result, the polymer chains crosslink to form a stable gel mass. However, if the pH is adjusted too low or too high, carbomer may fail to form a proper gel.

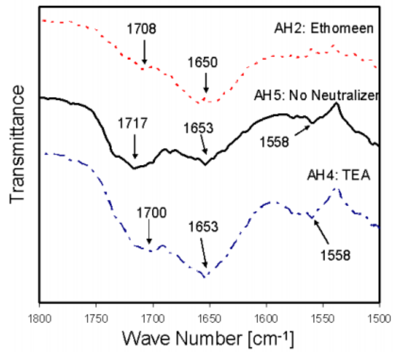

Figure 2. The comparison of FTIR spectrum carbomer in different neutralizers

The FTIR spectrum can be seen in Figure 2, which examines the functional groups of carbopol (carbomer) in combination with TEA, shows that when carbomer is neutralized with TEA, the percentage of hydrogen-bonded carboxyl groups increases. As a result, the absorption band at 1653 cm^{-1} becomes more dominant than the band at 1710 cm^{-1} 12. The carboxyl band becomes ionized due to the formation of amine salts from the carbopol polymer dissolved in a polar solvent. The intensity of the absorption peaks increases in line with the increasing concentration of TEA in the gel formulation.

The ANOVA results from Design Expert (Table 5) indicate the significance of the response analysis among variables and help determine the most suitable model recommended by the software. The choice of ANOVA model is based on a high R^2 value, which indicates a strong model fit. However, in addition to R^2, other factors such as the Lack of Fit F-value and model p-value also influence the selection of the appropriate model.[9]

Table 5. The results of ANOVA in pH response

Response	Significancy p-value	Lack of Fit p-Value	R^2	Pred R2	Adeq
pH	0.0177	0.3592	0.97	0.1611	12.026

The ANOVA results showed that the variable components had a significant effect on reducing the FFA conversion value when the lack of fit (F-value) was less than 0.05. Conversely, a value greater than 0.05 indicates that the lack of fit is not significant. A non-significant lack of fit value suggests that the model provides a good fit to the response data. The model p-value was 0.0177, which is less than 0.05, indicating that the model is statistically significant. The lack of fit F-value was 1.39, indicating a non-significant result. The Predicted R^2 value was 0.1611, which did not reach the expected level of accuracy when compared to the adjusted R^2 value of 0.9184. The difference between the two values exceeds 0.2, which may indicate a significant block effect or potential issues with the model and/or the data. The adequate precision value was 12.0262, which exceeds the desired threshold of 4, indicating an adequate signal. Therefore, this model can be used effectively to navigate the design space.

Viscosity response analysis

The highest viscosity response was observed in Run 1, where 6% TEA and 1% carbomer produced a viscosity of 3827.67 cPs (Table 6). In comparison, Run 2, which used the same TEA concentration but a lower carbomer concentration, showed a viscosity of 2691 cPs.

The lowest viscosity response was observed in Run 4, with a value of 520.67 cPs, obtained from a formulation containing 0.06% TEA and 0.55% Carbomer.

Based on Figure 3, the interaction curve between the components indicates that viscosity response is influenced by the interaction between TEA and carbomer. The different colors represent various concentration combinations of TEA and carbomer, which affect the viscosity of the serum formulation. The red area indicates that the combination of TEA and carbomer produces the highest viscosity values. The blue area represents the lowest viscosity values, while the green area shows a moderate viscosity response neither too high nor too low.

Table 6. The results of viscocity value

Run	TEA (%)	*Carbomer* (%)	Viiscocity(cPs)
1	6	1	3827.67
2	6	0.55	2691
3	3	0.1	1501
4	0.06	0.55	520.67
5	3	0.55	1815
6	0.06	1	1550
7	0.06	0.55	573.67
8	0.06	0.1	716.33
9	3	0.55	1576

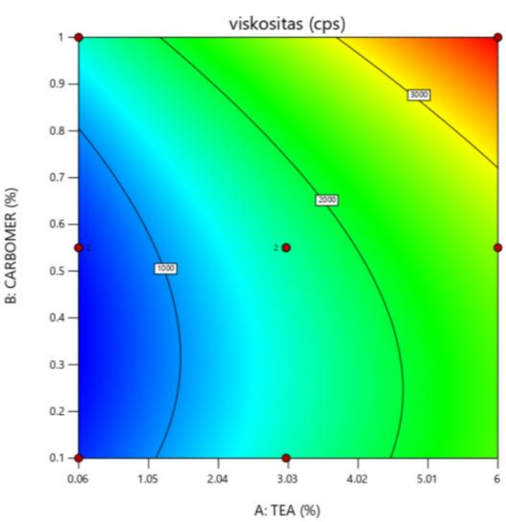

Figure 3. Counter plot of viscosity value

The quadratic model equation for the optimization of TEA and Carbomer on viscosity response is expressed as follows:

$$Y = 1029.47 (A) + 577.28 (B) + 143.19 (AB) - 43.99 (A2) + 483.84 (B2) + 1671.70$$

Given :A =TEA
B = Carbomer
Y = Viscosity

Based on the quadratic model equation, the viscosity response is influenced by both TEA and carbomer, as well as the interaction between them. The effect of TEA on increasing viscosity is greater compared to that of carbomer, as indicated by the coefficient for TEA (A), which is 1029.47, while the coefficient for carbomer (B) is 577.28. This suggests that the concentration of TEA is the more dominant factor in enhancing the viscosity of the formulation.

The combination of TEA and carbomer also contributes to an increase in viscosity, as shown by the positive coefficient for their interaction term (AB), which is +143.19.

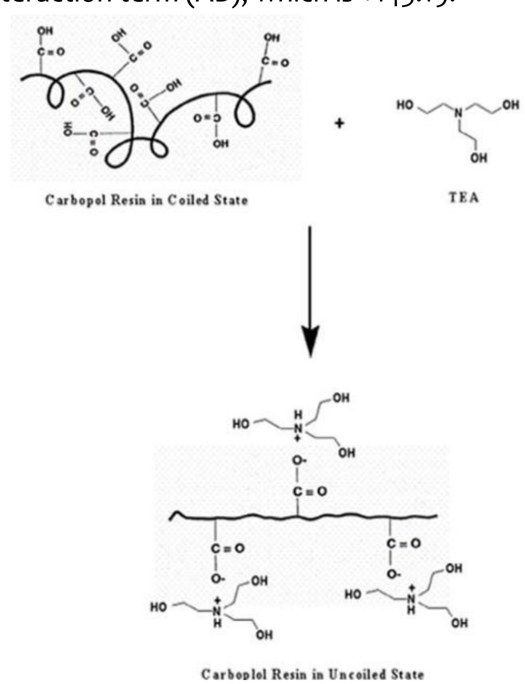

Figure 4. Neutralization structure of carbopol (carbomer) with TEA

The addition of a neutralizing agent such as TEA can alter the polymer conformation and the viscosity of the dispersion. The neutralizer primarily works by forming ion pairs.[11] During the neutralization process, the polymer structure in carbomer is disrupted and forms a gel system (Figure 4), which is believed to occur through hydrogen bonding and ionization of the carboxyl groups.

Table 7. The results of ANOVA in viscosity response

Response	Significancy p-value	Lack of Fit p-Value	R^2	Pred R2	Adeq
Viscosity	0.0014	0.3643	0.99	0.8503	30.869

The ANOVA test results presented in Table 7 show a p-value of less than 0.05, indicating statistical significance. The Lack of Fit value was not significant, suggesting a good model fit. The Predicted R^2 value of 0.8503 was reasonably close to the Adjusted R^2 value of 0.9854, with a difference of less than 0.2. Adequat Precision is a measure of the signal-to-noise ratio, with a desirable value greater than 4. A value of 30.869 indicates that the signal generated by the model is more than adequate.

Formula Optimization

The determination of the optimal formula was based on the desirability value approaching 1, as a value closer to 1 indicates higher accuracy in the optimization process. This desirability value reflects how well the predefined criteria have been achieved. Optimization was conducted by setting goals for the desired response criteria, taking into account the feasible range for each parameter. The output of the optimization process yielded several new formulations identified as optimal by the software.

The response data obtained were then further analyzed using a numerical optimization method. This method was selected because two variables were involved in the study, and numerical optimization can determine a specific optimal formulation based on the selected response input parameters.

Table 8. Numerical method setting

Name	Goal	Lower Limit	Upper Limit	Lower Weight	Upper Weight	Importance
TEA	*minimize*	0.06	6	1	1	3
Carbomer	*In range*	0.1	1	1	1	3
pH	*minimize*	4.5	6.5	1	1	1
Viskositas	*minimize*	800	3000	1	1	5

Table 9. The composition of optimum formula

Number	TEA	Carbomer	pH	Viscocity	Desirability	
1	**1.047**	**0.1**	**6.442**	**966.824**	**0.607**	**Selected**
2	1.077	0.1	6.440	976.571	0.607	
3	1.117	0.1	6.437	989.195	0.607	

Table 10. Confirmation test of optimum formula

Formula	Response	Prediction	Verification	95% PI low	95% PI high
1	pH	6.44	6.39	6.30	6.58
	Viskositas	966.82	967.68	580.54	1353.11

The minimum selection for TEA (Table 8) was intended to ensure that the selected formulation does not have an excessively high pH, as higher concentrations of TEA can increase pH values. TEA is an alkalizing agent that functions to neutralize the acidity of carbomer.[6]

Three solutions were generated, as shown in Table 9. Each formulation has a desirability value of 0.607, which indicates a good level of desirability. The selected formulation is a combination of 1.047% TEA and 0.1% carbomer, which meets the goal of minimizing TEA with an importance level of 3. This formula also predicts the lowest viscosity among the other options. The importance level for viscosity was set to the highest setting, as the goal was to optimize the formulation by achieving the lowest possible viscosity.

The optimized formulation was re-prepared in triplicate and tested for pH and viscosity to proceed with confirmation testing. As shown in Table 10, the pH and viscosity values obtained from the verification data were not significantly different from the predicted values. The results also fell within the Prediction Interval (PI) range, indicating that the model is consistent with the predictions provided by the software.

Carbomer has the ability to easily bind and disperse in water, forming hydrogen bonds. To form a stable gel mass, a neutralizing agent such as TEA is required. In this interaction, TEA ionizes the carbomer, generating negatively charged ions along the polymer backbone, which leads to electrostatic repulsion.[12] This repulsion results in an extended three-dimensional network that forms a dense gel matrix. The amount of carbomer used determines the viscosity of the resulting gel formulation. The more carbomer added, the higher the viscosity; conversely, reducing the amount of Carbomer will decrease the viscosity.

CONCLUSION

The optimization of TEA and Carbomer resulted in an optimal formulation at a concentration of 1.047% TEA and 0.1% Carbomer. In this formulation, Carbomer was able to form an effective gel with a viscosity of 967.68 cPs and a pH of 6.44.

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