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Optimization and Characterization of Serum of Red Onion Skin Extract and Antioxidant Activity

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Abstract: Red onion (*Allium cepa* L.) skin is enriched with flavonoids, steroids, and phenolic compounds, which possess the potential to promote hair growth. The present investigation sought to optimize gelling agent concentrations within hair serum formulations incorporating red onion peel extract (Allium cepa L.) for its antioxidant properties. Formula optimization was executed employing the Regular Two-Level Factorial Design methodology utilizing Design Expert® 13 software. Two independent variables were examined: carbomer 940 concentration ranging from 0.1–0.3% and sodium alginate concentration ranging from 0.5–1%. Through factorial analysis of physical properties, formula 2 emerged as optimal, containing carbomer 940 at 0.3% and sodium alginate at 1%. The resultant formulation demonstrated the following physicochemical characteristics: pH of 6.14±0.01, viscosity of 854.35±12.87 cP, spreadability of 7.26±0.70 cm, adhesiveness of 8.02±0.19 cm, and additional adhesion metrics of 8.69±0.27 cm, 4.17±0.23 s, and 3.35±0.26 s. Accelerated stability assessment via cycling protocols revealed preservation of organoleptic integrity, absence of phase separation or syneresis, and constancy in pH and viscosity parameters. The optimal red onion peel extract serum formulation demonstrated an IC50 value of 84.00 ppm, reflecting substantial antioxidant capacity and considerable promise for further pharmaceutical development as an antioxidant agent.

Keywords: antioxidant; carbomer 940, red onion, serum, sodium alginate

1. INTRODUCTION

Hair constitutes a significant component of personal appearance, as the quality and health of hair substantially contribute to individual self-confidence [1]. Hair loss represents one of the most prevalent and troubling dermatological concerns affecting populations globally. Androgenetic alopecia (AGA), the most common form of non-scarring hair loss, affects up to 50% of men and approximately 19% of women, with prevalence rising sharply with age and reaching as high as 80% of men and 50% of women by the age of 70 [2], [3]. Although AGA is not associated with direct mortality, it exerts a considerable psychosocial burden, being frequently linked to diminished self-esteem, anxiety, and depression, which underscores the continuing demand for safe and effective therapeutic options [3], [4].

At present, the pharmacological management of hair loss relies predominantly on synthetic agents such as topical minoxidil and oral finasteride. However, both are constrained by notable limitations. Minoxidil demonstrates efficacy in fewer than 40-60% of patients and is commonly associated with scalp irritation, itching, dryness, and contact dermatitis at the site of application [5], [6]. Finasteride, a systemic 5α-reductase inhibitor, has been linked to adverse effects including decreased libido, erectile dysfunction, and ejaculatory disorders, and is contraindicated in women of childbearing potential owing to its teratogenic risk [6], [7]. Concern regarding these agents has been further heightened by a 2025 safety alert from the U.S. Food and Drug Administration (FDA) regarding compounded topical finasteride products, following reports that systemic adverse effects may persist even after discontinuation [8]. These limitations provide a clear rationale for exploring natural, plant-derived alternatives with favorable safety profiles.

This trend is reflected in the growing global preference for naturally derived ingredients in cosmetic and pharmaceutical formulations. The natural cosmetic ingredients market was valued at approximately USD 10.56 billion in 2025 and is projected to reach USD 21.68 billion by 2023 (CAGR ≈ 9.5%), with botanical extracts constituting the largest segment, driven by consumer demand for clean-label, multifunctional products and by growing concern over the adverse effects of synthetic compounds [9]. Red onion (*Allium cepa* L.) epidermis contains quercetin, a predominant phytochemical demonstrating marked hair growth-stimulating properties. The quercetin constituent present in red onions functions by suppressing androgen gene expression, thereby attenuating overall androgen activity. Furthermore, quercetin exhibits potent antioxidant properties that promote hair growth by regulating the anagen phase and enhancing circulatory perfusion to hair follicular structures [10], [11].

Red onion skin extract (Allium cepa L.) was formulated into a hair serum to optimize its topical therapeutic potential. A serum was selected as the delivery system because it is applied directly to the scalp as a leave-on preparation and requires no rinsing after use. Serum preparation can prolong contact between the active ingredient and the scalp, is lightweight and non-greasy, and is readily absorbed, thereby improving user comfort and compliance while supporting effective delivery of bioactive constituents to the hair follicle [12]. Serums also offer greater versatility than hair masks: their comparatively low viscosity permits daily application and uniform distribution across the scalp. At the same time, their viscosity is higher than that of aqueous preparations such as hair tonics, allowing the formulation to remain at the application site without dripping while helping to protect the hair shaft and retain moisture [13].

Serum preparations exhibit elevated viscosity compared to solution-based preparations, consequently demonstrating enhanced physicochemical stability. The viscosity parameter of serum formulations represents a critical factor influencing scalp penetrability, a consideration necessitated by the scalp's distinctive dermatological architecture characterized by elevated hair follicle density, averaging approximately 100,000 follicles per unit area [14]. To establish optimal serum viscosity, systematic variation of gelling agent concentrations in the red onion skin (*Allium cepa* L.) hair serum formulation becomes requisite to yield preparations with superior physicochemical characteristics. The synergistic combination of carbomer 940 and sodium alginate has demonstrated substantial positive effects on preparation properties. Exclusive utilization of carbomer 940 at elevated concentrations can precipitate excessive acidification of the preparation, potentially inducing dermal irritation. Conversely, sodium alginate application at high concentrations can compromise spreadability characteristics and produce an excessively rigid formulation consistency, thereby impeding active ingredient penetration through successive epidermal layers [15], [16].

Given these considerations, the present investigation formulates a hair serum preparation derived from red onion skin extract (*Allium cepa* L.). This research encompasses optimization and comprehensive characterization of red onion skin extract hair serum, utilizing gelling agent concentration as the primary independent variable. The strategic combination of multiple gelling agents, specifically carbomer 940 and sodium alginate, produces serum preparations demonstrating substantially improved physicochemical properties in comparison with formulations employing single gelling agent systems.

2. MATERIALS AND METHODS

2.1. Materials

Materials used in this research include red onion skin (*Allium cepa* L.), 96% ethanol, (Emsure®), sodium alginate (Akshar Exim®), carbomer 940 (Corel Pharma Chem®), triethanolamine (Petronas®), methyl paraben (Ueno Fine Chemicals®), propyl paraben (Ueno Fine Chemicals®), glycerin (Wilmar®), quercetin (Sigma-Aldrich®), alumunium chloride ($AlCl_3$) (Emsure®), potassium acetate (SAP Chemicals®), concentrated sulfuric acid (H_2SO_4) 2N (Emsure®), bismuth nitrate (Emsure®), potassium chloride (Emsure®), iodine (Emsure®), mercury chloride ($HgCl_2$) (Emsure®), glacial acetic acid (Emsure®), anhydride acetic acid (Emsure®), magnesium powder (Rofa®), hydrochloric acid

(HCl) 37% (Emsure®), ferric chloride ($FeCl_3$) (Emsure®), blue tip (Onemed®), filter paper (Whatman®), and chloroform p.a. (Emsure®).

2.2. Tools

Equipment used in this research includes analytical balance 0.0001 g (Ohaus®), oven (Memmert®), pH meter (Lutron® pH Electrode PE-03), rotary evaporator (Biobase®), grinder (Inima®), UV-Vis spectrophotometer (Biobase® BK-UV1900PC), magnetic stirrer (IKA® C-MAG HS4), magnetic stirrer (IKA® C-MAG HS7), cup and bob viscometer (Grace Instrument® M3400), micropipette 100-1000 µL (Dragon Lab®), refrigerator (RSA®), furnace (Muffle Furnaces Nuve®), 40 mesh sieve (d = 425 mm) (Setrch®), vortex (IKA® 153-010), spin bar (RCC®), tube rack (Rofa®), spatula (Phtc®), 50 mL glass vials (Packaging 007®), and glassware (Pyrex® and Iwaki®).

2.3. Extraction of red onion skin

Red onion skin simplicia was subjected to extraction via maceration methodology. The powdered red onion skin simplicia was macerated over a period of three days by dissolving in 96% ethanol at a 1:7.5 (w/v) ratio [17], [18]. The extraction process was maintained at ambient temperature with mechanical agitation performed twice daily at designated intervals. Upon completion of the three-day maceration period, the resulting mixture underwent filtration using filter paper, followed by a secondary maceration cycle extending three days. The combined filtrate was subsequently concentrated using rotary evaporation at 50°C until a concentrated extract was obtained [17], [18].

2.4. Characterisation of red onion skin extract

The characterisation parameters for this research's extract include organoleptic properties, moisture content, drying loss, water-soluble extract content, ethanol-soluble extract content, total ash content, and acid-insoluble total ash content [17].

2.5. Phytochemical screening

The phytochemical screening method used was qualitative, based on observing colour reactions. Test parameters conducted included the identification of flavonoids, saponins, alkaloids, phenolics, steroids, and triterpenoids [17].

2.6. Determination of total flavonoid content in red onion skin extract

The determination of quercetin's maximum wavelength was conducted through spectroscopic scanning of quercetin solutions across the wavelength range of 400-800 nm [11]. Initial preparation involved dissolving 10 mg of quercetin in 10 mL of 96% ethanol to establish a stock solution at 1000 ppm concentration. Subsequent serial dilution of 1 mL of this stock solution with 10 mL of 96% ethanol yielded a standard solution at 100 ppm. From this standard solution, a series of concentrations was prepared at 6, 8, 10, 12, and 14 ppm. Calibration samples were prepared by pipetting volumes of 0.2 mL (2 ppm), 0.4 mL (4 ppm), 0.6 mL (6 ppm), 0.8 mL (8 ppm), and 1 mL (10 ppm) into separate vessels. Each calibration sample received the addition of 3 mL of 96% ethanol, 0.2 mL of 10% aluminium chloride, and 0.2 mL of 1% potassium acetate, followed by volume adjustment to 10 mL with distilled water using volumetric flasks and subsequent incubation at ambient temperature for 30 minutes [19].

Sample preparation followed an analogous protocol, wherein 10 mg of the extract was dissolved in 10 mL of 96% ethanol to achieve a concentration of 1000 ppm. A 1 mL aliquot of this solution was then diluted to 10 mL with 96% ethanol, resulting in a 100 ppm concentration. Subsequently, 1 mL of this diluted solution was transferred to a 10 mL volumetric flask and treated with 3 mL of 96% ethanol, 0.2 mL of aluminium chloride, and 0.2 mL of 1% potassium acetate. The volume was adjusted to the mark with distilled water, and the resulting sample was incubated at ambient temperature for 30 minutes [19].

2.7. Hair serum formulation of red onion skin extract

The serum formulation design was determined using Design-Expert® 13 software. Formula optimisation was conducted using the Regular Two-Level Factorial Design method in Design-

Expert® 13. Four formulas were used in this research, with two factors: carbomer 940 and sodium alginate at low and high levels. The formulas can be seen in Table 1.

The formulation of red onion skin extract hair serum commences with the preparation of the base matrix. Carbomer 940 is initially dispersed in distilled water at an elevated temperature of 90 °C utilising magnetic agitation until complete dispersion is achieved. Concurrently, sodium alginate undergoes dispersion in distilled water at ambient temperature through continuous magnetic stirring. Subsequently, the dispersed sodium alginate and carbomer components are combined in a glass beaker and mixed until a homogeneous phase is obtained. Thereafter, propyl paraben and methyl paraben are solubilised in glycerin prior to incorporation into the base formulation until homogeneity is attained. The remaining glycerin is introduced incrementally. Triethanolamine (TEA) is subsequently added to the base, followed by the red onion skin extract and distilled water, with the final volume adjusted to 100 mL [20], [21].

Table 1. The formula of red onion skin extract hair serum

Ingridients	Amount of Ingredients in the Formula			
	F1	F2	F3	F4
Red onion skin extract (g)	1.10	1.10	1.10	1.10
Carbomer 940 (g)	0.33	0.33	0.11	0.11
Sodium alginate (g)	0.55	1.10	1.10	0.55
Glycerin (ml)	11.00	11.00	11.00	11.00
Methyl paraben (g)	0.02	0.02	0.02	0.02
Propyl paraben (g)	0.19	0.19	0.19	0.19
TEA (ml)	0.11	0.11	0.11	0.11
Aquadest (ml)	Ad100	Ad100	Ad100	Ad100

2.8. Evaluation of hair serum

2.8.1. Organoleptic test

Organoleptic testing is a direct observational method that involves objectively assessing the form, colour, and odour [20].

2.8.2. Homogeneity test

The preparation is sampled at three different points and spread onto transparent glass. The test preparation is homogeneous with no coarse particles [20].

2.8.3. pH test

pH is measured using a pH meter by preparing a 0.5 g sample in 50 mL of distilled water. The solution is then immersed in the pH meter electrode, and the reading is recorded on the monitor [20].

2.8.4. Viscosity test

Viscosity testing is performed using a cup and bob viscometer. A 30 mL sample is filled into the cup, and the viscometer rotor is placed precisely at the centre of the cup. The device speed is 60 rpm, and the viscosity indicator needle moves to the right. Viscosity is read after the indicator needle stabilises on the rotor scale [20].

2.8.5. Adhesion test

The adhesion test uses 0.25 g of serum, places it on an object glass, and covers it with another glass. The object glass is pressed with a 1 kg weight for 5 minutes. The weight is lifted, and the object glass is mounted on an adhesion test device. The testing device is equipped with 50- and 100-gram weights, and the time required for the serum to separate between the two glass objects is recorded [20].

2.8.6. Spreadability test

Prepare a flat glass and place 0.5 grams of serum in it. Then place another glass on top and add weights of 50, 100, and 150 grams for 1 minute. Measure the diameter formed [20].

2.8.7. Stability test

The red onion skin extract serum preparation is incubated at 4°C for 24 hours, followed by incubation at 40°C for the next 24 hours. This treatment constitutes a single 48-hour cycle. Testing is conducted over six cycles, and physical changes in the serum preparation, including organoleptic properties, pH, and viscosity, are monitored at the beginning and end of each cycle [22].

2.8.8. Determination of optimum formula

The optimal formula is selected using Design-Expert® 13, based on desirability values approaching 1 and response parameters for pH, viscosity, spreadability, and adhesion.

2.9. Antioxidant activity testing using the DPPH method

2.9.1. Preparation of red onion skin extract serum

The serum is prepared as sample solutions at 80, 100, 200, 400, 600, 800, and 1000 ppm. Sample solution, DPPH, and ethanol are pipetted at 2 mL each into separate test tubes. They are then vortexed for 2 minutes and left for 30 minutes, then measured for absorbance using a UV-Vis spectrophotometer [23].

2.9.2. Calculation of inhibition concentration (IC_{50})

Antioxidant activity data are analysed using a linear regression model (y = bx + a) to obtain the IC_{50} value. Determination of antioxidant activity is based on the absorption of DPPH radicals by samples through calculation of inhibition percentage using the following formula:

$$\% \text{ Inhibition} = \frac{\text{Abs.standard} - \text{Abs.sample}}{\text{Abs.standard}} \times 100\% \quad \ldots\ldots (1)$$

2.9.3. Data analysis

Serum preparation evaluation data are analysed using factorial design calculations in Design-Expert® 13. Analysis is performed by calculating coefficient values for each factor, namely, carbomer and sodium alginate, to obtain equations showing the relationship between factors and responses. Based on these equations, the influence of each factor and their combination on the evaluation results for serum preparation can be observed. Data analysis for the cycling test on serum preparations is performed using SPSS® 25. Analysis is conducted using the paired sample t-test method.

3. RESULTS AND DISCUSSION

3.1. Onion skin extraction

The extraction of onion peel yielded a concentrated extract weighing 150.5 grams, corresponding to a 15.05% yield. The yield percentage reflects the efficiency of the extraction process, defined as the ratio of the weight of the extract obtained to the initial material weight. It also demonstrates the effectiveness with which active compounds were isolated from raw materials [24]. The yield percentage of the concentrated onion peel extract met the requirement of being at least 10%.

3.2. Extract characterisation

The characterisation of the extract was: organoleptic properties were a thick extract, dark red with a characteristic odour; water content of 8.33%±0.011; water-soluble extract content of 28.33%±2.886; ethanol-soluble extract content of 76.67%±2.886; and total ash content of 5%±1.

Phytochemical screening of onion peel extract aimed to identify bioactive compounds with potential antioxidant activity, such as flavonoids. These compounds can scavenge free radicals and protect cells from oxidative damage. The findings revealed that onion peel extract contains flavonoids, phenolics, and triterpenoids. Flavonoids in onion peel extract play a vital role in reducing oxidative stress and improving hair health [25].

3.3. Determination of total flavonoids in onion skin extract

A quercetin standard solution at a concentration of 1000 ppm demonstrated maximum absorption at 433 nm, yielding an absorbance value of 2.0366. The absorbance graph produced a linear regression equation of y = 0.0099x + 0.1971, with a correlation coefficient of r = 0.9909. The proximity of this correlation coefficient to unity, substantially exceeding the 0.5 threshold, establishes

a robust linear relationship between absorbance and compound concentration. This mathematical relationship indicates that flavonoid concentrations within the onion peel extract exhibit a proportional increase in corresponding absorbance measurements.

The derived calibration curve equation facilitated the quantification of total flavonoid content within the extract. Triplicate analysis of total flavonoid content produced mean absorbance measurements of 0.328, 0.330, and 0.324, respectively. Application of these values to the total flavonoid quantification formula yielded replicate concentrations of 132.22, 134.24, and 128.18 mg QE/g extract. The mean total flavonoid content determined in the onion peel extract was 13.15%, exceeding the previously reported value of 10.82% [25].

3.4. Evaluation of hair serum preparation

The evaluation of the onion peel extract hair serum included organoleptic testing, homogeneity, viscosity, spreadability, and adhesiveness. Measured parameters, including viscosity, pH, spreadability, and adhesiveness, were optimised using a factorial design in Design-Expert® 13. An analysis model is considered good if the p-value is less than 0.05, R2 is greater than 0.7, and the difference between Adjusted R2 and Predicted R2 is no more than 0.2. The adequate precision value exceeds 4. The coefficients for each response included an intercept, factors A and B, and the interaction between them. Additionally, the p-values for each factor and response were obtained. The % contribution of each response was analysed using ANOVA.

Table 2. Evaluation results of red onion peel extract serum

Evaluation	Formula			
	F1	**F2**	**F3**	**F4**
Organoleptic	Colour: dark red Odour: red onion skin extract Texture: Viscous	Colour: dark red Odour: red onion skin extract Texture: Viscous	Colour: dark red Odour: red onion skin extract Texture: Viscous	Colour: dark red Odour: red onion skin extract Texture: Slightly viscous
Homogeinity	Homogeneous	Homogeneous	Homogeneous	Homogeneous
pH	6.12±0.01	6.14±0.02	6.49±0.01	6.42±0.01
Viscosity (cPs)	527.47±12.86	854.35±12.87	490.335±0.00	22.88±0.00
Spreadability (cm)				
50 gr	8.26±0.22	7.26±0.70	7.32±0.45	9.56±0.34
100 gr	8.62±0.23	8.02±0.19	8.46±032	9.94±0.19
150 gr	9.30±0.04	8.69±0.27	9.94±0.19	11.44±0.51
Adhesiveness (s)				
50 gr	2.65±0.30	4.16±0.424	2.63±0.67	2.39±0.24
100 gr	1.62±0.17	3.35±0.27	1.73±0.46	1.29±0.28

3.4.1. Organoleptic test

Organoleptic evaluation was performed to systematically assess the hair serum's physical characteristics, encompassing colour, odour, and textural properties. Such sensory assessment constitutes a vital methodological component, as these observable attributes directly influence user satisfaction and acceptability during product application. Following organoleptic examination of the red onion peel extract serum formulations, all tested formulas demonstrated a distinctly red colouration accompanied by the characteristic aromatic profile inherent to red onion peel extract. The textural analysis revealed a consistently thick consistency across all formulations, with this variation in texture attributable to differential concentrations of the gelling agent employed in each formula, which modulates the overall viscosity and consistency of the preparation. The comprehensive formulation specifications for the red onion peel extract serum are presented in Figure 1.



Figure 1. Serum of Red Onion Peel Extract

3.4.2. Homogeneity

The homogeneity of the onion peel extract hair serum formulation was evaluated through visual examination utilising transparent glass vessels. The assessment demonstrated that all formulated variants exhibited homogeneous characteristics, with no coarse particulate aggregates and a uniformly distributed chromatic appearance. The attainment of homogeneous serum consistency signifies optimal distribution of constituent components throughout the preparation, thereby enhancing the potential for dermal absorption and amplifying antioxidant efficacy.

3.4.3. The pH test

The serum's pH is related to the stability of active compounds, the serum's properties, and user comfort. Cosmetic products, including serums, must not be excessively acidic, as this can cause skin irritation, nor excessively alkaline, as this can lead to dry skin [26]. The required pH range for topical formulations is 4.5–6.5. The differences in pH among the formulas can be explained by the varying concentrations of the two gelling agents. Carbomer 940 is a cross-linked polyacrylic acid polymer containing a high proportion of carboxylic acid groups, so it is inherently acidic; increasing its concentration lowers the pH of the preparation [27]. Sodium alginate, in contrast, is the sodium salt of alginic acid and tends to be mildly basic in aqueous dispersion, so increasing its concentration slightly raises the pH [28]. These results confirm that carbomer 940 was the dominant determinant of serum pH, whereas sodium alginate contributed only marginally to pH modulation. This behaviour is consistent with the physicochemical properties of carbomer, whose carboxylic acid groups largely dictate the acidity of aqueous gel systems. In contrast, sodium alginate primarily functions as a viscosity-enhancing polymer, with only a limited contribution to pH variation. From a formulation perspective, these findings suggest that optimisation of serum pH should be achieved primarily by adjusting carbomer 940 concentration, while sodium alginate may be varied to tailor rheological properties with minimal impact on pH. Combining the two gelling agents therefore allowed the final pH to be balanced so that it did not become too acidic, and the residual acidity of carbomer 940 was further neutralised by the addition of triethanolamine [20]. Overall, the pH of all formulas was compatible with the scalp and skin, supporting the physicochemical stability of the active compounds.

3.4.4. Viscosity

The viscosity of the serum was measured to assess the thickness of the serum preparation. Higher serum viscosity indicates greater thickness and reduced spreadability of the serum preparation. Serum preparations require low viscosity values for good spreadability [29]. The viscosity requirement for serum is 230-1150 cPs. Low serum viscosity facilitates application and provides user comfort. The differences in viscosity values across formulas are influenced by the concentration of the gelling agent used in each formula. The viscosity of each formula was governed by the concentrations of the two gelling agents, carbomer 940 and sodium alginate, both of which increase the viscosity of a preparation as their concentration rises. This relationship is clearly reflected in the results, when the sodium alginate level was held constant, increasing the amount of carbomer

940 markedly raised the viscosity. Likewise, when the carbomer 940 level was held constant, increasing the sodium alginate amount also raised the viscosity[20], [30].

3.4.5. Spreadability

Spreadability testing of the serum was conducted to assess its ability to spread upon application to the skin's surface. Higher spreadability values indicate easier and broader distribution of the active ingredients on the skin, influencing the absorption and release of active substances from the serum. A good spreadability value for serum ranges between 5–7 cm [29]. The spreadability test was performed using weights of 50, 100, and 150 grams to measure spread diameter and assess the consistency of the formulation. The results demonstrate that serum spreads over a larger area as weight increases, indicating its capacity to distribute active ingredients evenly across the skin. The outcomes of the spreadability test at weights of 50 grams, 100 grams, and 150 grams reveal a consistent trend: the lower the gelling agent concentration, the greater the serum spreadability.
This deviation can be explained by the physical nature of the preparation and by the gelling agent concentrations. Spreadability is inversely related to viscosity, the lower the viscosity of a preparation, the more widely it spreads. Unlike a semisolid gel, a serum is intentionally formulated to be more fluid so that it can be applied easily to the scalp as a leave-on product and distributed evenly without rinsing, this lower viscosity inherently produces higher spreadability. Moreover, the gelling agent concentrations used in this study were relatively low, which further reduced the viscosity and increased the spread [31].

It should be noted that the commonly cited spreadability range of 5-7 cm is largely based on semisolid gel and cream formulations, while the optimal spreadability reported in the literature varies depending on the dosage form, with a recommended range of 5-7 cm. For a fluid leave-on scalp serum, a relatively greater spreadability may be advantageous, as it facilitates more uniform scalp coverage and enhances the distribution of the active ingredient across the application area. However, excessively high spreadability may reduce the formulation residence time on the scalp, potentially limiting prolonged contact with the target site. Therefore, optimisation of spreadability should aim to balance ease of application and sufficient retention. This can be achieved by increasing the concentration of the gelling agent, particularly carbomer 940, which demonstrated greater thickening efficiency than sodium alginate [31].

3.4.6. Adhesion strength

The adhesion strength test assesses the serum's ability to adhere to the skin before washing or rinsing with water. A good serum formulation should have an adhesion strength greater than 1 second [18]. Variations in gelling-agent concentration affect adhesion strength across serum formulations. Higher concentrations of gelling agents result in thicker formulations with longer adhesion times. This study used two weights, 50 g and 100 g, in the adhesion strength tests.

The results of adhesion strength tests at 50 grams and 100 grams showed a consistent pattern: the lower the gelling agent concentration, the lower the adhesion strength. A lower adhesion strength reduces the viscosity of the formulation. Serum adhesion affects its therapeutic efficacy. The longer the serum remains on the skin, the greater the absorption of active ingredients, resulting in prolonged therapeutic effects and improved efficacy [20].

3.4.7. Model Analysis for Process Optimization

Prior to initiating the optimization procedure, comprehensive model analysis is essential. The dependent variables selected for formulation optimization encompassed pH, viscosity, spreadability, and adhesion properties. The analytical outcomes for these four response variables are presented in Table 3. Model adequacy is established through satisfaction of specific statistical criteria, including a p-value below 0.05, an R^2 coefficient exceeding 0.7, a disparity between adjusted R^2 and predicted R^2 values not exceeding 0.2, and adequate precision values surpassing 4.

Table 3. The Results of Response Model Analysis

Respons	Parameter				
	R2	Adjusted R2	Predicted R2	Adequate Precision	P-value
pH	0.99	0.99	0.99	56.00	<0.0001
Viscosity	0.99	0.99	0.99	120.21	<0.0001
Spreadability					
50 g	0.86	0.81	0.68	8.59	0.0009
100 g	0.93	0.91	0.85	14.07	<0.0001
150 g	0.94	0.92	0.85	15.65	<0.0001
Adhesiveness					
50 g	0.82	0.75	0.59	7.60	0.0024
100 g	0.91	0.87	0.79	11.38	0.0002

3.4.8. Analysis

A comprehensive investigation was conducted to evaluate the impact of carbomer 940 (A) and sodium alginate (B) concentrations, along with their interaction (AB), on four critical pharmaceutical responses: pH, viscosity, spreadability, and adhesion. Design Expert 13 software was employed to execute a systematic analysis of these response variables. The analytical findings pertaining to all four responses are presented in Table 4. The regression coefficients derived from each factor were subsequently utilised to formulate mathematical expressions representing the response relationships, with the resulting equations documented in Table 5. The directional sign of the regression coefficients indicates the nature and magnitude of the relationship between predictor variables and the response variable. A positive (+) coefficient denotes a direct proportionality between the factor and the response outcome, whereas a negative (-) coefficient indicates an inverse proportionality, wherein an increase in the factor corresponds to a decrease in the response variable.

Table 4. Analysis of pH, Spreadability, and Adhesion

Respon		Intercept	A (Carbomer 940)	B (Sodium alginate)	AB-Interaction
pH	Coefisien	6.29	-0.16	0.02	-0.01
	P-value		<0.0001	0.0001	0.0081
	%Contribution		97.19	1.98	0.50
Viscosity	Coefisien	523.76	167.16	148.58	14.86
	P-value		<0,0001	<0.0001	0.0005
	%Contribution		55.56	43.90	0.44
Spreadability 50 gram	Coefisien	8.10	-0.34	-0.81	0.31
	P-value		0.04	0.0003	0.05
	%Contribution		11.36	64.95	9.53
100 gram	Coefisien	8.76	-0.44	-0.52	0.22
	P-value		0.0002	<0.0001	0.01
	%Contribution		35.43	49.11	8.66
150 gram	Coefisien	9.85	-0.85	-0.53	0.22
	P-value		<0.0001	0.0003	0.04
	%Contribution		64.77	25.25	4.40
Adhesiveness 50 gram	Coefisien	2.96	0.45	0.44	0.32
	P-value		0.0050	0.01	0.0251
	%Contribution		33.11	31.89	16.99
100 gram	Coefisien	2.00	0.49	0.54	0.32
	P-value		0.0007	0.0003	0.01
	%Contribution		33.98	41.82	14.87

Table 5. The Response of Equation

Response	Parameter
pH	y= 6.29 – 0.1633A + 0.0233B – 0.0117AB
Viscosity	y= 523.76 + 167.16A + 148.58B + 14.86AB
Spreadability	y= 8.10 – 0.3386A – 0.8098B + 0.3103AB
Adhesion	y= 2.96 + 0.4467A + 0.4383B + 0.3200AB

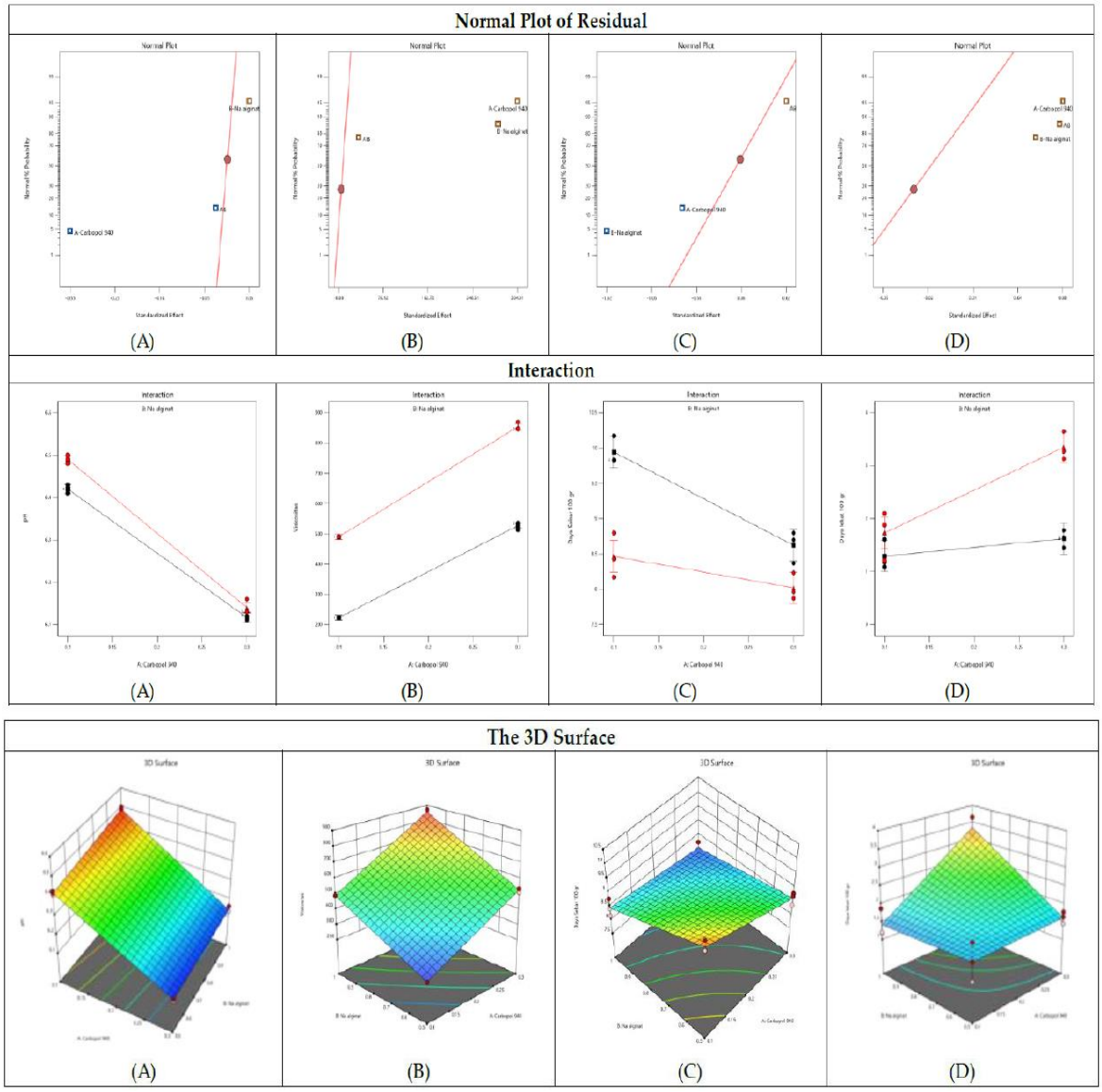


Figure 1. Normal plot of residual, interaction, and the 3D surface of pH (A), viscosity (B), spreadability (C), adhesion (D)

In the pH response, Factors A, B, and AB significantly affect the pH response, as evidenced by p-values < 0.05. Factor A has the most significant influence, followed by factors B and AB, which contribute 97.19%, 1.98%, and 0.50%, respectively. Factor B has a positive correlation, as the point in Figure 1 (A) is located to the right of the diagonal line. This indicates that increasing the concentration raises the pH value when Sodium Alginate acts independently. In contrast, Factor A shows a negative correlation: its point lies below the diagonal line, indicating that when Carbomer acts independently, increasing its concentration lowers the pH. The interaction between factors A and B further reduces pH because Carbomer has a more acidic pH than Sodium Alginate and has a greater contribution to the response, as confirmed by the ANOVA analysis results.

In the viscosity response, the interaction between factors A and B can also be illustrated in the interaction curve shown in Figure 1 (B). Based on Figure 1 (B), the interaction between factor A and factor B demonstrates two parallel lines. The curve shows that higher concentrations of carbomer and sodium alginate yield higher viscosity. This is further supported by the 3D surface plot in Figure 8(b), which indicates that the lowest viscosity, represented in the blue region, occurs at a carbomer concentration of 0.1% and a sodium alginate concentration of 0.5%. Factors A, B, and their interaction (AB) significantly influence the viscosity response, as their p-values are less than 0.05. Among these, factor A has the greatest effect, accounting for 55.56%, followed by factor B at 43.90% and the AB interaction at 0.44%. Factors A, B, and AB positively correlate with viscosity, as the regression coefficients and the equation indicate. This implies that lower concentrations result in lower viscosity values when factors A, B, or AB stand alone.

The interaction between sodium alginate and carbomer 940 is depicted in Figure 1 (B). Figure 1 (B) shows that the carboxyl group (-COOH) of carbomer interacts with the hydroxyl group (-OH) of sodium alginate, forming a strong intermolecular hydrogen bond network that enhances the cohesion between polymer chains. Figure 1 (B) illustrates that Na^+ ions in sodium alginate act as bridges between the carboxylate groups of carbomer and sodium alginate, thereby creating a denser structure that increases the viscosity of the formulation [20].

In the spreadability response with a 50-gram weight, the interaction between A and B can also be illustrated in the interaction curve shown in Figure 1 (C). Based on Figure 1 (C), the interaction between factors A and B is represented by two parallel lines. This curve reveals that higher concentrations of sodium alginate and carbomer reduce the formulation's spreadability. The 3D surface graph in Figure 1 (C) indicates that a low carbomer concentration of 0.1% and a low sodium alginate concentration of 0.5% result in higher spreadability, as noted in the red region. Factors A, B, and AB significantly influence the spreadability response, as their p-values are less than 0.05. Factor B has the most significant impact, accounting for 64.95%, followed by factor A (11.36%) and the AB interaction (9.53%).

In the spreadability response with a 100-gram weight, Factors A, B, and AB significantly influence the spreadability response, as indicated by p-values < 0.05 for all three. Factor B has the most significant impact, accounting for 49.11%, followed by factor A (35.43%) and the AB interaction (8.66%). The positive value of factor AB is due to its position to the right of the diagonal line in Figure 1 (C), indicating that the interaction between factors A and B increases spreadability. Factors A and B exhibit a negative correlation, with points below the diagonal, suggesting that higher individual concentrations of either factor are associated with lower spreadability.

In the spreadability response with a 150-gram weight, Factors A, B, and AB significantly influence the spreadability response, as indicated by p-values < 0.05 for all three. Factor A has the most significant impact, contributing 64.77%, followed by factor B at 25.25% and the AB interaction at 4.40%. The positive value of factor AB is due to its position to the right of the diagonal line in Figure 1 (C), indicating that the interaction between factors A and B increases spreadability. Factors A and B exhibit a negative correlation, with points below the diagonal indicating that higher individual concentrations of either factor are associated with lower spreadability.

In the adhesion response with a 50-gram weight, Factors A, B, and AB significantly influence the pH response, as indicated by p-values < 0.05 for all three. Factor A has the most significant influence, contributing 33.11%, followed by factor B at 31.89% and the AB interaction at 17.00%. Factors A, B, and AB all have positive values, as shown in Figure 1 (C), where they lie to the right of the diagonal line. This indicates that the interaction between factors A and B, as well as their individual contributions, results in increased adhesion strength at higher concentrations.

In the adhesion response with a 100-gram weight, Factors A, B, and AB significantly influence the pH response, as indicated by p-values < 0.05 for all three. Factor B has the most significant influence, accounting for 41.82%, followed by factor A (33.98%) and the AB interaction (14.87%). Factors A, B, and AB have positive coefficients, as shown in Figure 23(a), where they are positioned to the right of the diagonal line. This indicates that the interaction between factors A and B, as well

as the individual contributions of each factor, results in increased adhesion strength at higher concentrations.

3.4.9. Optimal formula determination

The numerical data indicate that the second formula, with 1% sodium alginate and 0.3% carbomer 940, achieves the highest desirability value of 0.866. The desirability value indicates the program's ability to predict the optimal formula given the specified criteria. As the desirability value approaches 1, the program's ability to generate the desired formula approaches perfection.

3.5. Total flavonoid content in the optimal serum formula

The total flavonoid content in serum was measured using the standard linear regression equation for quercetin, y = 0.0099x + 0.1971 (r = 0.9909). Measurements were performed in triplicate for onion peel extract serum, yielding an average absorbance of 0.316. By substituting this absorbance value into the total flavonoid formula, the result was 120.77 mg QE/g extract. This translates to a total flavonoid content of 12.07% in the onion peel extract serum. The percentage of total flavonoid content tested using UV-Vis spectrophotometry in formulations containing extracts is generally lower than in pure extracts. This reduction is attributed to the presence of excipients in the formulation that dilute the flavonoid concentration. The formulation process may also cause partial degradation of flavonoids due to heat exposure, pH changes, or interactions with other components [32], [33].

3.6. Antioxidant activity test

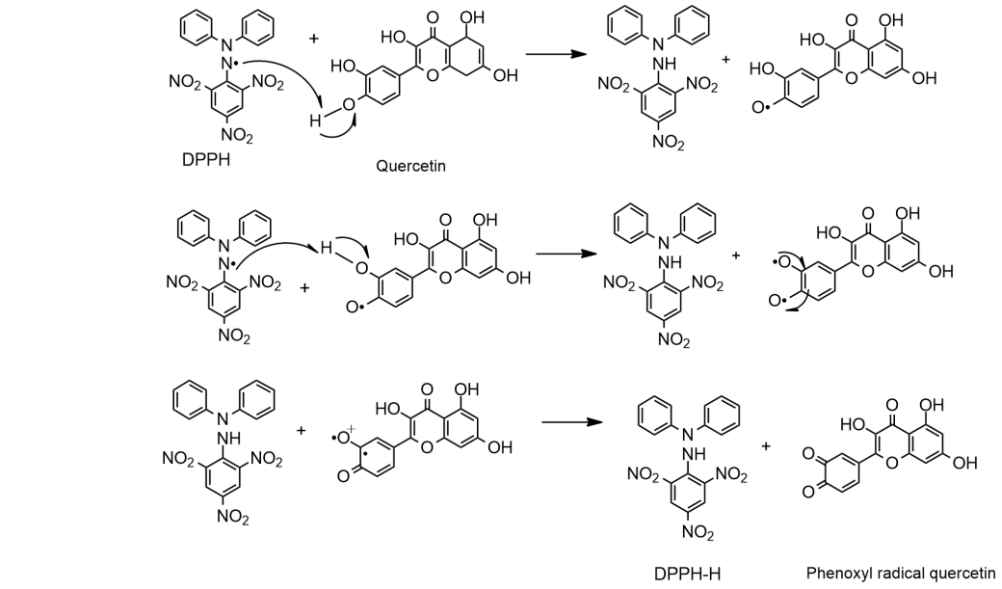
The antioxidant activity test was conducted using the DPPH method. The percentage inhibition (% inhibition) was used to determine the IC_{50} value, defined as the extract concentration (ppm) required to inhibit oxidative stress by 50%. The results showed a decrease in absorbance with increasing solution concentrations. This reduction in absorbance is due to the higher number of antioxidant compounds donating electrons to DPPH at higher solution concentrations [25].

The IC_{50} values for antioxidant activity of onion peel extract and its serum were determined, with quercetin as the reference. The DPPH assay was employed to assess the antioxidant activity of the onion peel extract. The study results indicate that onion peel extract exhibits very strong antioxidant activity (IC_{50} = 11.62 ppm), whereas quercetin exhibits even stronger activity (IC_{50} = 4.72 ppm). These findings align with reported antioxidant activity of 15.44 ppm, classifying onion peel extract as a very strong antioxidant [34].

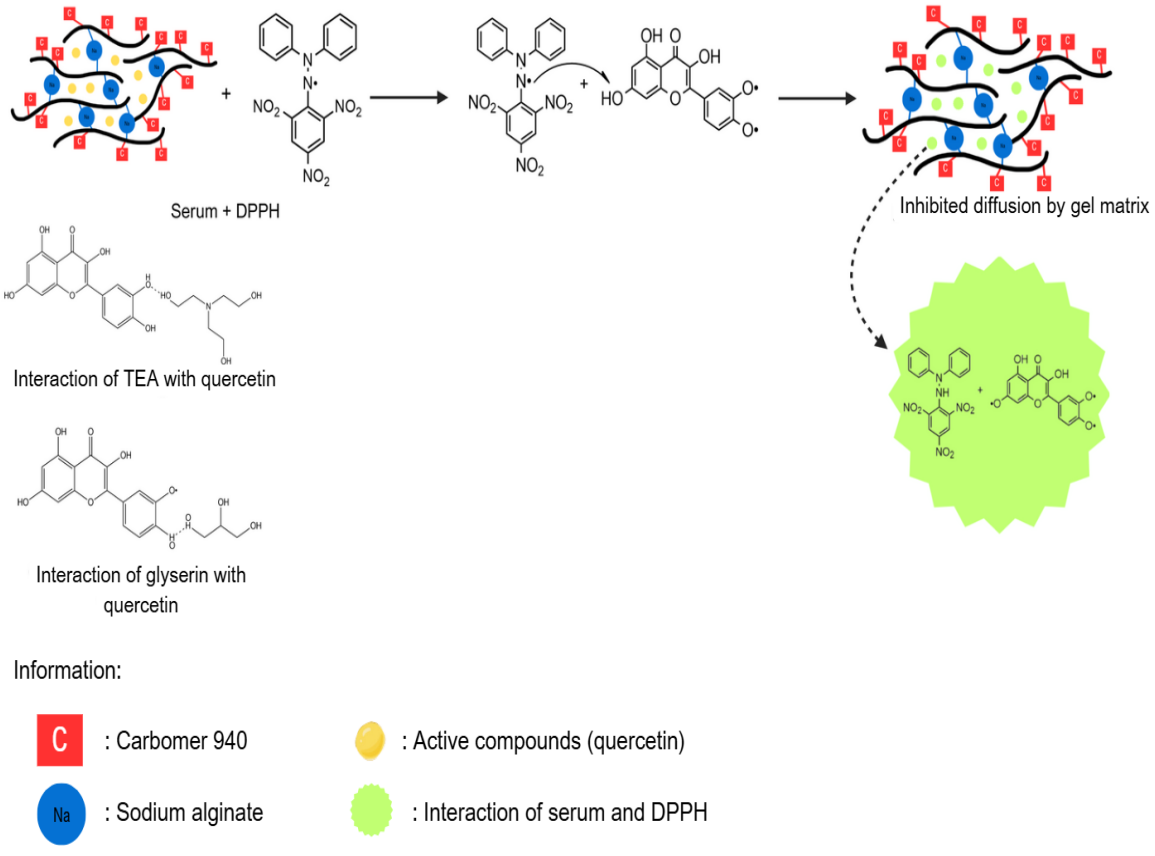
Onion peel extract contains several bioactive compounds contributing to its antioxidant activity, including flavonoids, phenolics, and triterpenoids[35]. Flavonoids, particularly quercetin, are the primary compounds responsible for high free radical scavenging capability and protection against oxidative stress[36], [37]. The lower IC_{50} value of pure quercetin compared with the ethanol extract of onion peel may result from the complexity of the extract's composition, which contains various other compounds. Not all these compounds have equivalent antioxidant activity; some may interact, reducing overall effectiveness[38], [39].

The IC_{50} value of the onion peel extract serum is 84.00 ppm, higher than that of the extract alone, indicating strong antioxidant activity. This is consistent with the finding that serums containing extracts generally have lower antioxidant activity than pure extracts. Formulations such as serums often include additives, including thickeners, preservatives, and humectants, which may reduce the effectiveness of active compounds by decreasing their bioavailability or their reactivity with free radicals. This effect is illustrated in Figure 2.

Interactions between glycerin or TEA and quercetin can reduce the availability of quercetin's active groups to scavenge DPPH radicals. Additionally, sodium alginate and carbomer 940 may form a gel matrix that slows the diffusion of antioxidants, necessitating higher concentrations to achieve the same effect [40].



(a)



(b)

Figure 2. (a) Reaction of DPPH with quercetin (b) Reaction of DPPH with quercetin in serum

3.7. Stability testing of the optimum formula

Stability testing of the optimal serum formula was conducted using the cycling test method. This test aims to evaluate potential changes in pH, viscosity, color, and syneresis over six cycles.

Table 6. Cycling test results

Formula	Parameter	Results	
		Before	**After**
Optimal	Organoleptic	Colour: dark red Odor: red onion skin extract Texture: Viscous	Colour: dark red Odor: red onion skin extract Texture: Viscous
	pH	6.14±0.02	6.56±0.02
	Viskosity (Cp)	854.35±12.86	653.76±25.73
	Sineresys	-	-

Based on Table 10, the optimal serum formula exhibited no organoleptic changes in color, odor, or texture. The cycling test also confirmed the absence of syneresis in the formula, as no phase separation occurred due to water expulsion within the serum structure. The lack of syneresis is attributed to the stable matrix formed by the combination of carbomer and sodium alginate as gelling agents, which prevents the solvent from separating or surfacing in the serum.



Figure 3. Organoleptic of cycling test

A pH change was observed in the optimum serum formula after the cycling test, increasing from 6.14 before testing to 6.56, a difference of 0.41. Statistical analysis using the SPSS Paired-Samples T-Test indicated a significant difference in pH before and after testing ($p < 0.001$). The pH variations of ±0.5 to 1.0 relative to the initial value are generally considered acceptable for topical formulations, as the serum remains within a safe pH range for skin application. The increase in pH may result from O_2 interactions with water in the serum [41], [42].

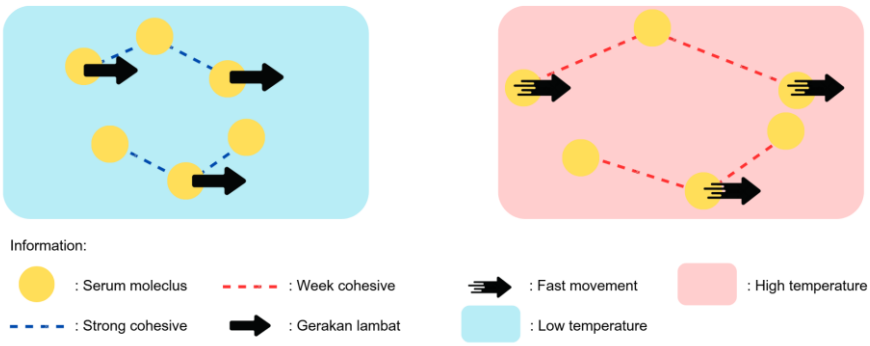


Figure 4. Illustration of the cycling test for viscosity

The viscosity of the serum formula decreased after the cycling test, dropping from 854.35 cP to 653.76 cP, a reduction of 200.59 cP. The SPSS Paired-Samples T-Test confirmed a significant difference in viscosity before and after testing ($p = 0.004$; <0.005). The decrease in viscosity is likely due to temperature effects. At elevated temperatures, molecular kinetic energy increases, leading to faster molecular motion. This diminishes molecular cohesive forces, ultimately lowering serum viscosity [42].

4. CONCLUSION

The optimal formulation identified by factorial design optimization consisted of 0.3% carbomer 940 and 1% sodium alginate, with close agreement between observed and predicted data. The concentrations of carbomer and sodium alginate significantly affected pH, viscosity, spreadability, and adhesiveness. Increasing carbomer and sodium alginate concentrations enhanced viscosity and adhesiveness but reduced pH and spreadability. The stability of the red onion peel extract serum was assessed for organoleptic properties, pH, viscosity, and syneresis. The optimal formula of the red onion peel extract serum exhibited strong antioxidant activity, with an IC50 value of 84.00 ppm.

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