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Physical Evaluation and Stability of HPMC-Based Bromelain Enzyme Gel Preparation

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ABSTRAK

Bromelain merupakan enzim proteolitik dari tanaman nanas (*Ananas comosus*) yang berpotensi sebagai bahan aktif dalam sediaan topikal. Pengembangan bromelain dalam bentuk gel memerlukan basis yang sesuai untuk menghasilkan sediaan dengan karakteristik fisik dan stabilitas yang baik. *Hydroxypropyl methylcellulose* (HPMC) dipilih sebagai basis gel karena mampu membentuk gel yang stabil, homogen, dan sesuai untuk penggunaan topikal. Penelitian ini bertujuan untuk memformulasikan dan mengevaluasi karakteristik fisik serta stabilitas sediaan gel enzim bromelain berbasis HPMC. Penelitian dilakukan secara eksperimental melalui optimasi basis gel HPMC pada konsentrasi 1%, 2%, dan 3%. Basis terpilih digunakan untuk membuat sediaan gel enzim bromelain dengan konsentrasi bromelain 2% (F1), 4% (F2), dan 8% (F3). Evaluasi meliputi uji organoleptik, homogenitas, pH, viskositas, daya sebar, daya lekat, identifikasi kualitatif bromelain, serta stabilitas menggunakan metode *temperature stress test*. Hasil optimasi menunjukkan bahwa HPMC 2% merupakan basis yang paling sesuai karena menghasilkan gel homogen dengan nilai pH, viskositas, daya sebar, dan daya lekat yang memenuhi persyaratan. Uji Biuret positif pada bromelain murni dan seluruh formula gel, yang menunjukkan protein bromelain masih terdeteksi setelah formulasi. Evaluasi fisik menunjukkan bahwa seluruh formula homogen, berbau khas bromelain, serta memenuhi persyaratan pH, viskositas, daya sebar, dan daya lekat. Uji stabilitas menunjukkan bahwa seluruh formula tidak mengalami perubahan organoleptik yang nyata. Namun, pH dan viskositas menurun seiring peningkatan suhu, dengan penurunan viskositas terbesar pada F3. Berdasarkan hasil penelitian, sediaan gel enzim bromelain berbasis HPMC menunjukkan karakteristik fisik yang baik, dengan HPMC 2% sebagai basis gel yang paling sesuai. Namun, suhu penyimpanan perlu diperhatikan untuk menjaga stabilitas fisik sediaan.

Kata Kunci: *Bromelain; Gel; HPMC; Evaluasi fisik; Stabilitas.*

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ABSTRACT

Bromelain is a proteolytic enzyme derived from pineapple (Ananas comosus) and has potential as an active ingredient in topical preparations. The development of bromelain in gel form requires a suitable base to produce a preparation with good physical characteristics and stability. Hydroxypropyl methylcellulose (HPMC) was selected as the gel base because it can form a stable, homogeneous gel suitable for topical use. This study aimed to formulate and evaluate the physical characteristics and stability of an HPMC-based bromelain enzyme gel preparation. The study was conducted experimentally by optimizing HPMC gel bases at concentrations of 1%, 2%, and 3%. The selected base was used to prepare bromelain enzyme gel with bromelain concentrations of 2% (F1), 4% (F2), and 8% (F3). The evaluation included organoleptic properties, homogeneity, pH, viscosity,

spreadability, adhesiveness, qualitative identification of bromelain, and stability using the temperature stress test method. The optimization results showed that 2% HPMC was the most suitable base, as it produced a homogeneous gel with pH, viscosity, spreadability, and adhesiveness values that met the requirements. The Biuret test was positive in pure bromelain and all gel formulas, indicating that bromelain protein remained detectable after formulation. Physical evaluation showed that all formulas were homogeneous, had a characteristic bromelain odor, and met the requirements for pH, viscosity, spreadability, and adhesiveness. The stability test showed no noticeable organoleptic changes in all formulas. However, pH and viscosity decreased as temperature increased, with the greatest viscosity reduction observed in F3. Based on the results, the HPMC-based bromelain enzyme gel preparation showed good physical characteristics, with 2% HPMC as the most suitable gel base. However, storage temperature should be considered to maintain the physical stability of the preparation.

Keywords: *Bromelain; Gel; HPMC; Physical evaluation; Stability.*

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1. Introduction

Gel is a semisolid dosage form that is widely used for topical application. Gels have several advantages, including ease of application, good spreadability on the skin surface, a cooling sensation, non-sticky properties, and ease of removal with water [1]. In addition, gels can improve user comfort because they are able to maintain contact between the active substance and the skin surface for a certain period of time [2]. These characteristics make gel a suitable dosage form for the topical delivery of active ingredients.

In gel formulation, the gelling agent plays an important role in determining the physical quality of the preparation. One gelling agent that is commonly used is hydroxypropyl methylcellulose (HPMC). HPMC is a hydrophilic cellulose-derived polymer that can form clear and stable gels and has good compatibility with various active ingredients and excipients [3]. HPMC is also non-toxic, does not irritate the skin, and can produce gels with good consistency, making it widely used as a base in topical formulations [4].

Bromelain is a natural proteolytic enzyme obtained from pineapple (*Ananas comosus*), mainly from the fruit, stem, and leaves [5]. This enzyme belongs to the thiol endopeptidase group, which is able to break peptide bonds in proteins into simpler peptides and free amino acids [6]. Bromelain is known to have various biological activities, including fibrinolytic, antiedema, antithrombotic, and anti-inflammatory activities. Therefore, it has potential to be developed as a natural active ingredient in topical preparations [7],[8].

Several previous studies have developed bromelain in topical preparations. Wiyono and Mustofani reported that a gel containing crude bromelain extract from pineapple peel with Carbopol 940 as the base had good physical characteristics and showed potential in supporting the healing of bruises [9]. Another study by Thomas *et al*., showed that a bromelain enzyme gel using Carbopol 940 as the base could be formulated as a topical preparation and had activity in burn wound healing [10]. However, these studies mostly focused on Carbopol-based formulations, crude bromelain extract, or certain polymer combinations. Studies on bromelain enzyme gel formulations using HPMC as the base, especially those related to physical evaluation and stability, still need to be further developed.

The development of bromelain in an HPMC base needs to consider the physical characteristics and stability of the preparation. This is because bromelain is an enzymatic protein compound whose stability can be affected by formulation

conditions, pH, temperature, and the excipients used [11]. Therefore, evaluation of organoleptic properties, homogeneity, pH, viscosity, spreadability, adhesiveness, and stability is necessary to ensure that the preparation meets the quality requirements of a topical gel. Based on this background, this study was conducted to formulate and evaluate the physical properties and stability of an HPMC-based gel preparation containing bromelain enzyme. This formulation is expected to produce a gel preparation with good physical characteristics, stable properties, and suitability for topical use.

2. Methods

This study used a true experimental design and was conducted at the Chemistry and Pharmaceutical Analysis Laboratory and the Pharmaceutical Technology Laboratory, Department of Pharmacy, Faculty of Sports and Health, Universitas Negeri Gorontalo. This study aimed to formulate and evaluate the physical properties and stability of an HPMC-based gel preparation containing bromelain enzyme.

Materials and Equipment

The equipment used in this study consisted of a stirring rod, porcelain dish, climatic chamber, beakers (Pyrex®), measuring cylinders (Pyrex®), caliper, glass slides, mortar and pestle, analytical balance, pH meter, dropper pipettes, spatula, stopwatch, test tubes (Pyrex®), and Brookfield viscometer. The materials used included 70% alcohol, distilled water, bromelain enzyme, hydroxypropyl methylcellulose (HPMC), methyl paraben, sodium hydroxide (NaOH), propylene glycol, and copper(II) sulfate ($CuSO_4$).

Optimization of the HPMC Gel Base

Optimization of the gel base was carried out by preparing an HPMC gel base without the addition of an active ingredient. HPMC was prepared in three concentration variations, namely 1%, 2%, and 3%. Each HPMC concentration was dispersed in distilled water up to 100 mL and then allowed to stand for approximately 24 hours until a homogeneous gel base was formed. The obtained gel bases were then physically evaluated for organoleptic properties, homogeneity, pH, viscosity, spreadability, and adhesiveness to determine the most optimal HPMC concentration as the gel base [3].

Formulation of Bromelain Enzyme Gel Preparation

The bromelain enzyme gel was prepared in three formulas with different bromelain concentrations, namely F1 2%, F2 4%, and F3 8%. HPMC was used as the gel base, methyl paraben as a preservative, propylene glycol as a humectant, and distilled water as the solvent. The formula of the bromelain enzyme gel preparation is shown in Table 1.

Table 1. Formula of bromelain enzyme gel preparation

Materials	Concentration (%)		
	F1	F2	F3
Bromelain enzyme	2	4	8
HPMC	2	2	2
Methyl paraben	0,2	0,2	0,2
Propylene glycol	10	10	10
Distilled water	ad 100 mL	ad 100 mL	ad 100 mL

Preparation of Bromelain Enzyme Gel

The gel was prepared by first setting up the required equipment and materials. HPMC was placed into a mortar containing a portion of distilled water, then allowed to swell and stirred until homogeneous. Methyl paraben and propylene glycol were added to the gel base and mixed until homogeneous. The bromelain enzyme was first dissolved in distilled water, then added gradually to the gel base while continuously stirring until homogeneous. Distilled water was then added to make up the volume to 100 mL, and the mixture was stirred again until a homogeneous gel preparation was formed.

Qualitative Test of Bromelain

The qualitative test of bromelain was carried out using the Biuret method to identify the presence of protein in pure bromelain enzyme before formulation and in the bromelain enzyme gel preparation after formulation. The sample was prepared under alkaline conditions by adding NaOH solution, followed by the addition of diluted $CuSO_4$ solution. A positive result was indicated by the formation of a violet-blue or violet-red color, which shows the presence of peptide bonds in the protein [9].

Evaluation of the Formulation

Organoleptic Test

The organoleptic test was carried out using the senses or by visual observation. This test was performed by observing the color, odor, and texture of the prepared gel formulation [12].

pH Test

The pH test was carried out using a pH meter, which was inserted into the gel sample. After the electrode was fully immersed, the pH meter displayed the corresponding pH value. The acceptable pH range for a preparation that does not irritate the skin is 4.5–6.5 [13].

Viscosity Test

The viscosity test was carried out using a Brookfield viscometer with spindle number 7. This test aimed to determine the consistency of the preparation, which affects its topical application. According to SNI 16-4399-1996, the standard viscosity requirement for gel preparations is 6,000–50,000 cP or 6–50 Pa.S [10].

Spreadability Test

The spreadability test was carried out to determine the spreading area of the prepared gel. A greater spreadability value indicates better spreading ability of the preparation. The required spreadability range for semisolid preparations is 5–7 cm [13].

Adhesion Test

The adhesion test was carried out to determine the ability of the preparation to adhere to the skin. The test was performed by placing 0.5 g of the preparation on a Petri dish, then covering it with another Petri dish in an inverted position and applying a 150 g load on top for 5 minutes. After that, the time required for the two glass surfaces to separate was recorded. An effective adhesion time is more than 4 seconds [14].

Stability Test (Temperature Stress Test)

The stability test was carried out using the temperature stress test method to determine the effect of temperature on the physical stability of the gel preparation. The gel samples were placed in closed containers and stored in a climatic chamber at various cold temperatures of 2°C, 4°C, 6°C, 8°C, and 10°C, as well as high temperatures of 40°C, 50°C, 60°C, 70°C, and 80°C. Observations were made every 1 hour. After the temperature treatment was completed, the samples were evaluated for changes in organoleptic properties, pH, and viscosity.

3. Results and Discussion

Optimization of the HPMC Gel Base

Optimization of the HPMC gel base was carried out to determine the most suitable HPMC concentration as the base for a bromelain enzyme gel formulation. The HPMC concentrations used were 1%, 2%, and 3%. Evaluation of the gel base included organoleptic properties, homogeneity, pH, viscosity, spreadability, and adhesiveness. The results of the HPMC gel base optimization are presented in Table 2.

Table 2. Results of HPMC gel base optimization

Evaluation Type	HPMC Concentration		
	1%	2%	3%
Color	Clear	Clear	Clear
Odor	Typical HPMC odor	Typical HPMC odor	Typical HPMC odor
Texture	Slightly viscous	Viscous	Highly viscous
Homogeneity	Homogeneous	Homogeneous	Homogeneous
pH	5,69	5,78	5,81
Viscosity (cP)	480	12.560	28.560
Spreadability (cm)	7,85	5,71	5,31
Adhesiveness (second)	64	20	11

Source: Processed primary data, 2026

Based on Table 2, all variations of the HPMC gel base showed a clear appearance, a characteristic HPMC odor, and homogeneous properties. These results indicate that HPMC was well dispersed in distilled water, resulting in a uniform gel base. The main difference was observed in the texture, where 1% HPMC had a slightly viscous texture, 2% HPMC was viscous, and 3% HPMC was highly viscous. The increase in viscosity occurred along with the increasing concentration of HPMC. This is because a higher HPMC concentration allows more polymer chains to become hydrated and form a gel network, resulting in a thicker base consistency [15].

The pH values of the HPMC gel bases ranged from 5.69 to 5.81. These values are still within the acceptable pH range for topical preparations, which is 4.5–6.5. An appropriate pH in topical preparations is required to reduce the risk of skin irritation [16]. Increasing the HPMC concentration did not cause a significant change in pH, indicating that HPMC was relatively stable in the gel base system prepared.

The viscosity test results showed that increasing the HPMC concentration increased the viscosity of the gel base. The viscosity values of 1%, 2%, and 3% HPMC were 480 cP, 12,560 cP, and 28,560 cP, respectively. The viscosity of 1% HPMC did not meet the viscosity requirement for gel preparations because it was too low, whereas 2% and 3% HPMC were within the acceptable viscosity range for gels, namely 6,000–50,000 cP [10]. This increase in viscosity indicates that HPMC concentration affects the consistency of the gel base [17].

The spreadability of the gel base decreased as the HPMC concentration increased. The spreadability values of 1%, 2%, and 3% HPMC were 7.85 cm, 5.71 cm, and 5.31 cm, respectively. The spreadability of 1% HPMC exceeded the required range for gels, which is 5–7 cm, while 2% and 3% HPMC remained within this range. The decrease in spreadability is related to the increase in viscosity, as a more viscous gel base has greater flow resistance, resulting in a lower spreading ability [18].

The adhesiveness test results in Table 2 showed that all gel bases had an adhesiveness value of more than 4 seconds, thus meeting the adhesiveness requirement for topical preparations [14]. The adhesiveness values of 1%, 2%, and 3% HPMC were 64 seconds, 20 seconds, and 11 seconds, respectively. Although all bases met the requirement, adhesiveness decreased as the HPMC concentration increased. This may occur because a gel base with a higher HPMC concentration has a denser gel structure, which may reduce its ability to make contact with the surface [19].

Based on the optimization results, the 2% HPMC gel base was selected as the most suitable base for the bromelain enzyme gel formulation. The 2% HPMC gel base showed good physical characteristics, including a clear appearance, homogeneous properties, an appropriate pH, viscosity that met the requirement, spreadability within the acceptable range, and adhesiveness that still fulfilled the required criteria. Therefore, 2% HPMC was used as the gel base in the bromelain enzyme gel formulation.

Qualitative Test of Bromelain

The qualitative test for bromelain was carried out using the Biuret method to identify the presence of protein in pure bromelain enzyme before formulation and in the bromelain enzyme gel preparation after formulation. The results of the qualitative bromelain test are presented in Table 3 and Figure 1.

Table 3. Qualitative test of bromelain

Sample	Test Result	Color Change	Interpretation
Pure bromelain enzyme	Positive (+)	Violet blue	Indicates the presence of protein
F1	Positive (+)	Violet blue	
F2	Positive (+)	Violet blue	
F3	Positive (+)	Violet blue	

Source: Processed primary data, 2026

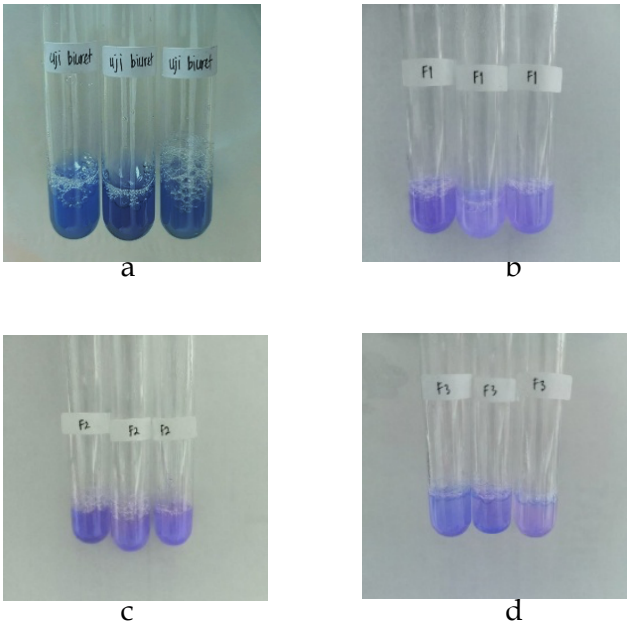

Figure 1. Biuret test. a) Pure bromelain enzyme, b) Formula 1 (F1), c) Formula 2 (F2), and d) Formula 3 (F3)

Based on Table 3 and Figure 1, the Biuret test on the pure bromelain enzyme showed a positive result, indicated by the formation of a violet-blue color. Similar results were also observed in the bromelain enzyme gel preparations of formulas F1, F2, and F3. This color change indicates the presence of protein in the samples through the formation of a complex between Cu^{2+} ions and peptide bonds in bromelain protein.

The Biuret test is a qualitative method used to identify the presence of peptide bonds in proteins. Under alkaline conditions, Cu^{2+} ions derived from $CuSO_4$ react with peptide bonds to form a violet-colored complex. The formation of this violet color indicates the presence of two or more peptide bonds in the protein structure [20],[21]. The positive result in the pure bromelain enzyme confirms that the active ingredient used contains protein, which is consistent with the characteristic of bromelain as a proteolytic enzyme. This finding is in line with the study by Wiyono and Mustofani, which reported that bromelain gave a positive reaction in the Biuret test, as shown by the formation of a violet-blue color indicating the presence of peptide bonds in protein [9]. The result for the pure bromelain enzyme is shown in Figure 1a.

The positive Biuret results in formulas F1, F2, and F3 indicate that bromelain protein could still be identified after being formulated into an HPMC-based gel preparation. These results also suggest that the gel formulation did not cause complete degradation of the bromelain protein structure [22]. This indicates that the formulation process using HPMC, methylparaben, propylene glycol, and distilled water did not qualitatively eliminate the presence of bromelain protein. The results for the gel formulas are shown in Figure 1b, c, and d.

Evaluation of the Formulation

The physical evaluation of the bromelain enzyme gel preparation was carried out to determine the physical characteristics of each formula. The gel preparations were prepared in three formulas with varying concentrations of bromelain enzyme,

namely F1 containing 2% bromelain, F2 containing 4% bromelain, and F3 containing 8% bromelain. The evaluation parameters observed included organoleptic properties, homogeneity, pH, viscosity, spreadability, and adhesiveness. The results of the physical evaluation of the bromelain enzyme gel preparations are presented in Table 4.

Table 4. Physical evaluation results of bromelain gel

Evaluation Type	F1	F2	F3
Color	Clear, slightly cloudy	Clear, slightly cloudy	Clear and cloudy
Odor	Characteristic bromelain odor	Characteristic bromelain odor	Characteristic bromelain odor
Texture	Thick	Thick	Thick
Homogeneity	Homogeneous	Homogeneous	Homogeneous
pH	5,86	5,75	5,68
Viscosity (cP)	16.720	14.560	14.080
Spreadability (cm)	5,52	5,59	6,27
Adhesiveness (second)	75	55	42

Source: Processed primary data, 2026

Based on Table 4, the evaluation results of the bromelain enzyme gel preparation showed that formulas F1, F2, and F3 had relatively similar physical characteristics, with differences observed in pH, viscosity, spreadability, and adhesion. Organoleptically, all formulas had a characteristic bromelain odor, a thick texture, and were homogeneous. Formulas F1 and F2 appeared clear and slightly cloudy, whereas F3 appeared clear but cloudy. This difference in turbidity may be influenced by the increased concentration of bromelain in the preparation. This finding is in accordance with the study by Thomas *et al.*, which reported that bromelain enzyme gel has a cloudy appearance, a characteristic odor, and a homogeneous texture [10]. Homogeneity indicates that the active ingredient and excipients are evenly dispersed in the gel base, thereby supporting the distribution of the active substance in the topical preparation [23].

The pH values of the bromelain enzyme gel preparations in F1, F2, and F3 were 5.86, 5.75, and 5.68, respectively, as shown in Table 4. These values remain within the quality requirement range for topical preparations according to SNI 16-4399-1996, namely 4.5–8.0, and are also suitable for skin pH, which ranges from 4.5-7 [17],[23]. The pH values slightly decreased from F1 to F3, which may be influenced by the increased concentration of bromelain. Bromelain is an enzymatic protein that contains functional groups such as carboxyl (-COOH), amino (-NH_2), and sulfhydryl (-SH) groups, which may affect the balance of H^+ and OH^- ions in the preparation [11]. Nevertheless, all formulas remained within the safe range for topical use.

The viscosity test results in Table 4 showed that the viscosity values of F1, F2, and F3 were 16,720 cP, 14,560 cP, and 14,080 cP, respectively. These three formulas met the viscosity requirement for gel preparations, which is 6,000–50,000 cP or 6–50 Pa.S [10]. Viscosity decreased from F1 to F3, indicating that an increase in bromelain concentration may affect the consistency of the preparation. Viscosity is important because it is related to the ease of removing the preparation from its container, its ability to spread on the skin, and the duration of contact at the application site. A gel that is too viscous will be difficult to remove from the container, whereas a gel that is too fluid will not remain on the skin for a sufficient period during use [24].

The spreadability test results showed that F1, F2, and F3 had spreadability values of 5.52 cm, 5.59 cm, and 6.27 cm, respectively. As shown in Table 4, all formulas

met the acceptable spreadability range for gel preparations, namely 5–7 cm [25]. The increase in spreadability from F1 to F3 was consistent with the decrease in viscosity of the preparation. Spreadability is inversely related to viscosity. A lower viscosity reduces flow resistance, allowing the gel to spread more easily on the skin surface [16]. The increased spreadability of F3 was presumably associated with the higher concentration of bromelain, which affected the physical characteristics of the gel. A study by Hasson showed that bromelain gel formulations may have different physical and pharmaceutical characteristics depending on the composition and gel base used [26].

The adhesion test results showed that F1 had the highest adhesion value, namely 75 seconds, followed by F2 at 55 seconds and F3 at 42 seconds. Based on Table 4, all formulas met the adhesion requirement for topical preparations, which is more than 4 seconds [14]. The decrease in adhesion from F1 to F3 was consistent with the decrease in viscosity, since adhesion is directly proportional to viscosity. The higher the viscosity of a preparation, the longer its adhesion ability tends to be. Adhesion plays an important role in maintaining contact between the preparation and the skin, thereby supporting the delivery of the active substance to the application site [27].

Overall, the physical evaluation results showed that the three HPMC-based bromelain enzyme gel formulas had good physical characteristics. All formulas met the requirements for organoleptic properties, homogeneity, pH, viscosity, spreadability, and adhesion. Differences in bromelain concentration may affect the pH, viscosity, spreadability, and adhesion of the preparation.

Stability Test (Temperature Stress Test)

The temperature stress test was conducted to determine the effect of temperature variation on the physical stability of the bromelain enzyme gel preparation. The test was carried out at low temperatures of 2°C, 4°C, 6°C, 8°C, and 10°C, as well as high temperatures of 40°C, 50°C, 60°C, 70°C, and 80°C. The observed parameters included organoleptic properties, pH, and viscosity.

All formulas showed relatively good organoleptic stability during the temperature treatment. F1, F2, and F3 remained clear and cloudy in appearance, had a characteristic bromelain odor, and maintained a thick texture at all temperature variations. These results indicate that exposure to extreme temperatures did not cause any noticeable organoleptic changes in the bromelain enzyme gel preparation.

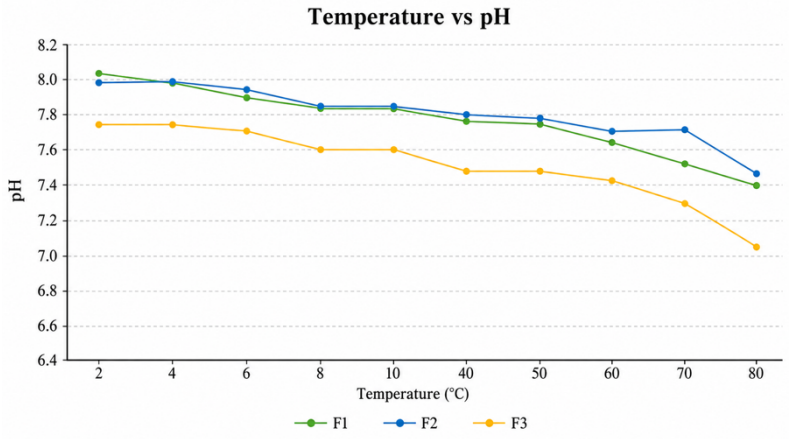

Figure 2. pH test results

Although the preparation remained organoleptically stable, the pH values decreased as the temperature increased. The pH of F1 decreased from 8.03 at 2°C to 7.37 at 80°C. F2 showed a decrease from 7.97 to 7.45, while F3 decreased from 7.73 to 7.04. The changes in pH values for each formula can be seen in Figure 2.

Figure 2 shows that all formulas experienced a decrease in pH after being exposed to increasingly higher temperatures. This decrease may occur because an increase in temperature can raise the kinetic energy of molecules and accelerate chemical reactions within the preparation. Excessively high temperatures may affect drug stability and cause changes in chemical activity, including changes in pH values [28]. F3 showed the lowest pH value across almost the entire temperature range, which is presumed to be related to its higher bromelain concentration compared with F1 and F2.

The pH values obtained in this stability test differed from the initial pH values observed during the physical evaluation of the preparation. In the initial physical evaluation, the pH values ranged from 5.68 to 5.86, whereas after the temperature stress test, the pH values ranged from 7.04 to 8.03. This difference may be influenced by exposure to extreme temperatures, which can alter the physical condition of the gel system. Temperature changes may affect the polymer chains in the gel. At high temperatures, the polymer chains may undergo disentanglement, resulting in decreased viscosity, while at low temperatures, the polymer chains tend to undergo entanglement, which may also affect the physical characteristics of the preparation [29].

In addition to pH, the viscosity of the preparations also changed after temperature treatment. The viscosity of all formulas decreased as the temperature increased. F1 showed a decrease in viscosity from 18,960 cP at 2°C to 4,480 cP at 80°C. F2 decreased from 18,880 cP to 4,480 cP, while F3 showed the greatest decrease, from 16,880 cP to 960 cP. The changes in viscosity values for each formula can be seen in Figure 3.

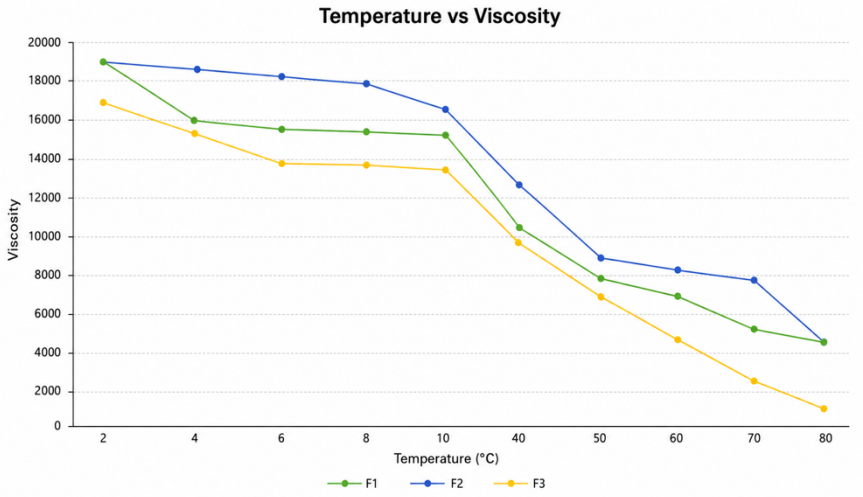

Figure 3. Viscosity test results

Figure 3 shows that an increase in temperature caused a decrease in viscosity in all formulas. The decrease in viscosity at high temperatures may be caused by the weakening of intermolecular interactions and HPMC polymer chains, resulting in a less compact gel structure and a more fluid preparation. At higher temperatures, molecular movement increases, which weakens intermolecular forces and reduces flow resistance [30]. This condition indicates that storage temperature may affect the

physical quality of gel preparations, particularly in terms of viscosity [31]. F3 showed the greatest decrease in viscosity compared with F1 and F2. This suggests that the formula with a higher bromelain concentration tends to be more sensitive to temperature changes. An excessive decrease in viscosity may affect the consistency of the preparation, its ability to adhere to the skin, and user comfort during application.

Overall, the results of the temperature stress test showed that the HPMC-based bromelain enzyme gel preparation remained organoleptically stable under various temperature conditions, but changes occurred in pH and viscosity. These changes indicate that temperature affects the physical characteristics of the gel preparation. Therefore, storage at an appropriate temperature should be considered to maintain the physical quality of the bromelain enzyme gel preparation during storage.

4. Conclusion

Based on this study, an HPMC-based bromelain enzyme gel can be formulated with physical characteristics that meet the requirements for topical preparations. The formulation containing 2% bromelain showed the best results, producing a homogeneous gel with a pH suitable for the skin, acceptable viscosity, good spreadability, and good adhesion. F1, F2, and F3 showed good physical quality. However, differences in bromelain concentrations affected the pH, viscosity, spreadability, and adhesion of the gel preparation. The temperature stress test showed that the gel remained stable in terms of organoleptic properties. However, exposure to high temperature may cause changes in pH and a decrease in viscosity. Therefore, the HPMC-based bromelain enzyme gel has potential to be used as a topical preparation, provided that the bromelain concentration and storage conditions are properly considered to maintain the physical quality of the formulation.

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