

A LITERATURE REVIEW ON THE FORMULATION, CHARACTERIZATION, AND STABILITY OF CINNAMOMUM BURMANNII EMULGEL EXTRACT AS AN ANTIOXIDANT AND SUNSCREEN

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INTISARI

Ekstrak kulit kayu manis memiliki aktivitas antioksidan dan tabir surya serta dapat diformulasikan menjadi sediaan emulgel. Emulgel merupakan sediaan semisolid yang mengombinasikan bentuk emulsi dan gel. Emulgel dapat meningkatkan penghantaran obat sehingga dapat lebih mudah menembus kulit dan meningkatkan aktivitas farmakologisnya. Komponen bahan penyusun nanoemulgel merupakan faktor penting yang berperan dalam menentukan karakteristik fisik, stabilitas dan aktivitas farmakologis dari sediaan nanoemulgel. Perbedaan variasi konsentrasi ekstrak dan gelling agent dapat berpengaruh pada karakteristik fisik, stabilitas dan aktivitas farmakologis dari emulgel. Review ini bertujuan menentukan konsentrasi ekstrak dan gelling agent yang paling efektif pada formula emulgel. Metode yang digunakan adalah studi literatur terhadap artikel penelitian formulasi sediaan emulgel ekstrak kulit kayu manis dengan variasi konsentrasi ekstrak dan gelling agent dengan aktivitas antioksidan dan tabir surya. Formulasi yang disarankan adalah formula yang memenuhi syarat karakteristik fisik, stabilitas dan aktivitas farmakologisnya. Formula emulgel yang paling memenuhi syarat adalah yang mengandung ekstrak kulit kayu manis konsentrasi 1% dengan gelling agent Viscolam MAC 5%.

Kata kunci: antioksidan, ekstrak kulit kayu manis, emulgel, karakteristik fisik, tabir surya

ABSTRACT

Cinnamon bark extract possesses antioxidant and sunscreen properties, making it suitable for incorporation into an emulgel formulation. Emulgel is a hybrid formulation that combines the characteristics of both emulsions and gels. Emulgel enhances drug delivery by facilitating deeper skin penetration and augmenting its pharmacological efficacy. The emulgel ingredients are crucial for determining the physical characteristics, stability, and pharmacological activity of the emulgel preparations. Variations in the concentration of extracts and gelling agents can impact the physical properties, stability, and pharmacological activity of the emulgel. The objective of this review is to ascertain the optimal concentrations of extracts and gelling agents in emulgel formulations for enhanced efficacy. The method used was a literature study of research articles on the formulation of cinnamon bark extract emulgel preparations with varying extract concentrations and gelling agents with antioxidant and sunscreen activity. The recommended formula meets the requirements for physical characteristics, stability, and pharmacological activity. The emulgel formulation that best meets the specified criteria consists of 1% concentration of cinnamon bark extract in combination with the gelling agent Viscolam MAC 5%.

Keywords: antioxidant, cinnamon bark extract, emulgel, sunscreen, physical characteristics

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INTRODUCTION

The skin can experience adverse effects due to an overabundance of ultraviolet (UV) rays, including hyperpigmentation, premature aging, erythema, and the potential development of skin cancer (Utami et al., 2016). The adverse impacts of sunlight typically arise from exposure to the UV-A and UV-B electromagnetic spectra. These negative effects can be attributed to the ability of UV-A and UV-B rays to stimulate the production of reactive oxygen species (ROS). The generation of reactive oxygen species (ROS) can induce oxidative stress, leading to cellular apoptosis, injury, and, ultimately, cell demise (Pizzino et al., 2017). One potential measure to mitigate the adverse consequences of UV radiation involves utilizing photoprotective agents and antioxidants. The inclusion of photoprotective agents in sunscreen formulations serves to either absorb or reflect ultraviolet (UV) rays. At the same time, the presence of antioxidants aims to mitigate the detrimental consequences of reactive oxygen species (ROS) generation (Lin et al., 2019; Widyastuti et al., 2016).

Cinnamon bark, derived from the *Cinnamomum burmannii* plant, is recognized as a natural ingredient possessing pharmacological properties, specifically functioning as an antioxidant and sunscreen agent. The pharmacological activity of cinnamon bark is significantly influenced by the presence of the cinnamaldehyde compound (Priani et al., 2014). The incorporation of cinnamon bark into an emulgel formulation has the potential to enhance both the comfort and efficacy of the product.

The emulgel is a pharmaceutical formulation that integrates the characteristics of both emulsions and gels. Emulgels have been identified as a potential solution for facilitating the delivery of hydrophobic drugs. This is achieved through encapsulation, wherein the drugs are enclosed within the emulgel matrix. Subsequently, a carrier is employed to facilitate the penetration of the emulgel and the subsequent release of the encapsulated drugs into the skin (Srivastava et al., 2020). Emulgel formulations offer certain advantages compared to emulsions; specifically, a gelling agent in the emulsion system enhances its stability by increasing the viscosity of the aqueous phase (Kumar et al., 2016; Sreevidya, 2019). Emulsions and gels possess distinct characteristics; however, gel formulations encounter constraints when administering hydrophobic pharmaceutical agents. The constraint mentioned above can be addressed by using a gelling agent, wherein an emulsion is incorporated into the base gel to form an emulgel formulation (Sreevidya, 2019).

The physical characteristics, stability, and pharmacological activity of gelling agents and cinnamon bark extract can be influenced by their use and concentration variations. Developing efficacious emulgel formulations must be created by optimizing the selection of gelling agents and appropriate extract concentrations. This is crucial to achieve desired physical properties that align with the specified requirements and enhance the overall activity of the emulgel. This literature provides an overview of variations in extract concentrations and the utilization of productive gelling agents commonly employed in the formulation of cinnamon bark extract emulgel products, and their potential for antioxidants and sunscreens. This literature review examines the physical attributes of emulgel formulations, including organoleptic assessments, pH levels, spreadability measurements, centrifugation tests, homogeneity evaluations, and viscosity analyses.

METHOD

The methodology employed for article screening involves conducting a comprehensive review of pertinent literature. The search for relevant articles was performed using a set of keywords, including emulgel, cinnamon bark, formulation, physical characteristics, and sunscreen activity. The inclusion criteria for this literature review consist of research articles that address specific topics using relevant keywords, original articles, articles published between 2012 and 2023, and research

articles written in both Indonesian and English. The articles that were not accessible in the full text were considered exclusion criteria.

The methodology employed in compiling this review consists of four distinct stages. Initially, a comprehensive search was conducted on the PubMed, Science Direct, and Google Scholar databases, employing appropriate keyword variations. Additionally, the process involves filtering the article titles based on the literature review's objectives, followed by assessing the appropriateness of the abstracts of the selected papers for inclusion in the literature review. Next, the relevant articles are downloaded in their entirety as PDF files.

RESULT AND DISCUSSION

Emulgel

The emulgel is a pharmaceutical formulation created by combining a gel and an emulsion, intended for topical application on the skin. Emulgel formulations are created by incorporating a gelling agent into the aqueous phase, which induces modifications in the emulsion preparation. Oil-in-water (O/W) emulsions are employed to administer lipophilic pharmaceutical compounds, whereas water-in-oil (W/O) emulsions are utilized to deliver hydrophilic drugs. The emulgel formulation involves the conversion of an emulsion into a gel by incorporating the emulsion into a gel base (Aisyah et al., 2017; Haneefa et al., 2013). Emulgel preparations offer several advantages in the field of pharmaceutical formulations. These advantages include thixotropic properties, facilitating easy application, and ensuring a longer duration of contact. Additionally, emulgel preparations exhibit improved stability and enable the incorporation of hydrophobic drugs. Notably, the preparation process does not require intensive sonication, further enhancing its appeal (Sreevidya, 2019).

The emulgel formulation comprises two distinct phases: a minor phase of emulsified oil and a major phase of organic matter that forms a gel-like structure when dispersed in water. Including an oil phase in the emulsion formulation confers certain advantages to the emulgel preparation compared to the gel preparation alone. The edges of the product exhibit enhanced spreadability, adhesion, ease of application, and comfort for patients during wear (Sari et al., 2015).

Formula

In addition to the active substance, emulgel formulations contain various components such as carriers, oils, aqueous ingredients, gelling agents, emulsifiers, humectants, and enhancers. The carrier material must possess specific attributes that enable it to effectively store, distribute, release, and deliver the drug to the intended site while ensuring its therapeutic efficacy is sustained over an extended duration. Mineral oil serves as a constituent of the oil phase within emulsions. The utilization of oil, either independently or in conjunction with solid or liquid paraffin, is a common practice in pharmaceuticals for drug delivery. Non-biodegradable oils, such as castor, fish, and other mineral oils, are frequently used in oral preparations (Begum et al., 2019). The aqueous phase refers to a constituent comprising substances soluble in water. Alcohol and water are two examples of materials in the aqueous phase. The gelling agent is a substance employed to enhance the viscosity of formulations and serve as a thickening agent. The efficacy of drug release from the formulation can be influenced by the concentration of the gelling agent employed in its preparation. The gelling agents used in emulgel formulations consist of Hydroxypropyl methylcellulose (HPMC) and carbopol (Charyulu et al., 2021; Yassin, 2014). The emulsifier, also known as the emulsifying agent, expedites the emulsification procedure during production and sustains stability throughout storage to prevent the emulsion from undergoing separation.

Polyethylene Glycol 40, Tween 80, Span 80, Stearic acid, and Sodium stearate are frequently employed emulsifying agents. Humectants or wetting agents are used in formulations to mitigate water loss. Humectants are utilized to minimize the drying process of emulgels, thereby ensuring the preservation of their consistency and facilitating the application of emulgels. Glycerin, triethanolamine (TEA), and propylene glycol are used as humectants in various applications. Enhancers promote the transdermal delivery of drugs by augmenting the permeability of the skin membrane. The enhancement of drug absorption via the dermal route can be achieved by employing

carriers that increase the permeability of the stratum corneum, thereby optimizing drug delivery. The enhancers used in the study were sodium lauryl sulfate and oleic acid (Shokri et al., 2012; Yassin, 2014). The formulation for the emulgel preparation containing cinnamon bark extracts is provided in Table I.

The gelling agents employed in emulgel formulations, as indicated in Table 1, encompass Carbopol, HPMC, and Viscolam MAC. At concentrations ranging from 0.5% w/v to 2% w/v, Carbopol can undergo expansion, forming three-dimensional microgels. Carbopol can form complexes with specific polymeric excipients that are influenced by pH. Hydroxypropyl methylcellulose (HPMC) is a cellulose derivative characterized by its acid and base neutrality and its exceptional viscosity stability. HPMC exhibits numerous advantages compared to other cellulose derivatives due to its extensive pH stability range from 3 to 11 (Yati et al., 2018). Viscolam MAC, employed as a gelling agent, possesses various merits, specifically its liquid form, which facilitates the mixing process. Viscolam MAC can potentially serve as an emollient for topical delivery (Priani et al., 2021).

Table I. The various emulgel formulations containing cinnamon bark extract

Formulas	Composition			References
	F1	F2	F3	
Cinnamon Bark Extract	2 g	4 g	6 g	
Liquid paraffin	10	10	10	
Methyl paraben	0,4	0,4	0,4	
Propyl paraben	0,6	0,6	0,6	
Tween 80	20	20	20	(Paramawidhita et al., 2016)
Span 80	20	20	20	
Propylene glycol	20	20	20	
HPMC	6	6	6	
Aquadest (ad)	200g	200g	200g	
Cinnamon Bark Extract	1 (%)			
Sodium lauryl sulfate	0,75			
Carbopol gel 934 2%	12,5			
TEA	qs			
Methylparaben	0,08			(Priani et al., 2014b)
Propylparaben	0,02			
Olive oil	20			
Alpha-tocopherol	0,03			
Ketostearyl alcohol	6,75			
Aquadest (ad)	100			
Cinnamon bark extract	1 (%) w/w	1 (%) w/w	1 (%) w/w	
Grape seed oil	20	20	20	
Tween 80	4,39	4,39	4,39	
Span 80	5,61	5,61	5,61	
Viscolam MAC	1	3	5	(Venchenkov et al., 2020)
TEA	qs	qs	qs	
Propylene glycol	10	10	10	
Aquadest (ad)	100	100	100	
Cinnamon bark extract	1 %	1 %	1 %	
Olive oil	20	20	20	
Natrium lauril sulfat	0,75	0,75	0,75	
Sodium lauryl sulfate	6,75	6,75	6,75	
Carbomer gel 2%	-	-	12,5	
HPMC Gel 5%	20	40	-	(Priani et al., 2014a)
Methylparaben	0,18	0,18	0,18	
Propylparaben	0,02	0,02	0,02	
Tocopherol	0,03	0,03	0,03	
Propylene glycol	10	10	10	
Aquadest (ad)	100	100	100	

The emulsifiers employed in the emulgel formulations documented in Table 1 consist of Tween 80 and Span 80. Using tween and span emulsifiers is commonly employed in conjunction due to their ability to produce stable emulsions in emulgel experiments. Tween 80 functions as an emulsifier, exhibiting the ability to dissolve in water and form an oil-in-water (O/A) type emulsion. A blend of Span 80, which possesses a prominent lipophilic moiety and exhibits non-ionic characteristics, generates an emulsion of enhanced stability (Rusli et al., 2022).

The formula in Table 1 incorporates the utilization of humectants, specifically TEA and propylene glycol. According to Hendradi et al. (2013), propylene glycol and TEA possess wetting agent properties due to their ability to bind water, stabilize preparations, and moisturize the skin. Sodium lauryl sulfate (SLS) is a compound known for enhancing drug penetration through the stratum corneum, facilitating their entry into the skin (Fatmawati et al., 2016).

Physical Characterization

Variations in the concentration of the extract and gelling agent employed can lead to variations in the physical characteristics of the emulgel. Table II displays the findings about the physical attributes of emulgel formulations containing cinnamon bark.

The evaluation of emulgel preparations encompassed organoleptic analysis, which involved the assessment of attributes such as color, odor, and flavor. The test outcomes indicated that the emulgel formulations exhibited a light or pale brown hue, possessed a distinct scent, and were semisolid. The results presented in Table 2 of the study conducted by (Paramawidhita et al., 2016) indicate that variations in the concentrations of cinnamon bark extract utilized in the emulgel preparations did not yield discernible variations in terms of color, odor, and flavor, as determined through organoleptic testing. The utilization of gelling agents, specifically 1% w/w and 2% w/w HPMC and 0.25% w/w Carbomer, did not yield divergent outcomes regarding organoleptic testing results (Priani et al., 2014a).

The experiment involved assessing the pH value of the emulgel preparation about varying concentrations of cinnamon bark extract. The results indicated that as the concentration of cinnamon bark extract increased, there was a corresponding decrease in the pH of the emulgel preparation. This is attributed to the acidic nature of the cinnamon extract. The pH values of all emulgel preparations comply with the established pH range for normal skin, which is 4.5-7. Excessive acidity in the pH level can lead to irritation, whereas an elevated alkaline pH level can result in dryness and scaliness of the skin (Purwanti et al., 2022).

The results obtained from evaluating emulgel preparations indicate an inverse relationship between the concentration of cinnamon bark extract and the gelling agent and the spreadability value. Specifically, an increase in the concentration of these components leads to a decrease in spreading power. This phenomenon can be attributed to the positive correlation between the concentration of the extract and its spreading ability, as well as the extract's consistency (Kharisma & Safitri, 2017). Variations in the concentration of the gelling agent can impact the spreadability of the preparation. The range of spreadability values that satisfies the specified criteria is between 5 and 7 centimeters. An inverse relationship exists between the concentration of the gelling agent and the spreadability of the preparation. The observed phenomenon can be attributed to the heightened concentration of the gelling agent, resulting in an augmented viscosity of the preparation (Ali Khan et al., 2020).

The objective of the centrifugation test is to assess the emulgel preparation's stability concerning the effects of gravitational force. The centrifugation test demonstrated the stability of the emulgel formulation, as evidenced by the absence of phase separation (E. Utami et al., 2020). A homogeneity test was conducted to ascertain the uniform distribution of the active substance and to identify the lack of any lumps within the emulgel formulation. The homogeneity test results indicated that the emulgel formulation containing cinnamon bark extract exhibited homogeneity (Goji et al., 2022; Wibowo et al., 2021).

The viscosity testing was conducted to ascertain the consistency and thickness of the prepared emulgel formulations. The concentration of the gelling agent employed can influence the viscosity of the preparation. It has been observed that an increase in the concentration of the gelling agent leads to a corresponding increase in the viscosity of the preparation (Ali Khan et al., 2020; E. Utami et al., 2020).

Table II. The results of the physical characterization of emulgel preparations of cinnamon bark extract with variations in the concentration of the extract and gelling agent

Active substance	Gelling agent	Organoleptic	pH	Spreadability	Centrifugation	Homogeneity	Viscosity	Reference
Cinnamon bark extract 1% (w/w)	Viscolam MAC10 1%	Light brown, enough viscous, odorless	7 ± 0	6,03 ± 0,153	Stable	Homogeneous	-	(Venchenkov et al., 2020)
	Viscolam MAC10 3%	Light brown, enough viscous, odorless	7 ± 0	5,1 ± 0,1	Stable	Homogeneous	-	
	Viscolam MAC10 5%	Light brown, enough viscous, odorless	7 ± 0	4,63 ± 0,153	Stable	Homogeneous	-	
Cinnamon bark extract 1% (w/w)	HPMC 1%	Semisolid, brown, characteristic odor	-	-	Stable	-	-	(Priani et al., 2014a)
	HPMC 2%	Semisolid, brown, characteristic odor	-	-	Stable	-	-	
	Carbomer 0,25%	Semisolid, brown, characteristic odor	5,259 ± 0,053	-	Stable	-	-	
Cinnamon bark extract 1%		Brown in color, fine grained texture, characteristic aroma	6,79 ± 0,09	0,34 ± 0,08 g/cm	-	-	1786,67 ± 400,67 cps	
Cinnamon bark extract 2%	HPMC 3%	Brown in color, fine grained texture, characteristic aroma	6,75 ± 0,23	0,28 ± 0,02 g/cm	-	-	2226,67 ± 688,57 cps	(Paramawidhita et al., 2016)
Cinnamon bark extract 3%		Brown in color, fine grained texture, characteristic aroma	6,74 ± 0,05	0,18 ± 0,05 g/cm	-	-	2400 ± 1139,12 cps	
Cinnamon bark extract 1%	Carbopol 934 2%	Semisolid, cream color, characteristic odor	5,23 ± 0,07	-	Stable	-	2155 ± 22,9 cps	(Priani et al., 2014b)

Stability

The stability test aims to prove the stability of the quality of preparation to change within a certain period due to environmental influences such as light, temperature, and environment. The results of the stability test can be seen in Table III.

The results of the stability test of the cinnamon bark extract emulgel preparation in Table 3 showed that the preparation was stable at room temperature ($25^{\circ}\text{C} \pm 2^{\circ}\text{C}$) and temperature ($40^{\circ}\text{C} \pm 2^{\circ}\text{C}$) for 28 days. There was no statistically significant difference in the pH and viscosity values with a significance value ($p>0.05$). The Freeze-Thaw test results showed no phase separation in the emulgel after being tested at 4°C and 48°C for 48 hours to 5 cycles, respectively. The results of the stability test showed the selection of materials used in the emulgel formulation was correct. Cinnamon bark extract has pharmacological activity as an antioxidant so that it can reduce the risk of oxidation by air and light and stability is maintained (Cahyani et al., 2020; Ratnapuri et al., 2019; Supriadi et al., 2022).

Table III. Stability of cinnamon bark extract emulgel preparations

Active Ingredients	Method	Stability Test Results	References
Cinnamon bark extract 1%	Freeze Thaw	There was no phase separation in the emulgel after being tested at 4°C and 48°C for 48 hours to 5 cycles, respectively.	(Priani et al., 2014a)
Cinnamon bark extract 1%	Accelerated stability	There were no significant differences in the pH and viscosity values stored at room temperature and 40°C on day 0 and day 28 ($p>0.05$). Product remains stable.	(Priani et al., 2014b)

Antioxidant and sunscreen effect

Cinnamon bark extract has pharmacological activity, namely as an antioxidant agent and sunscreen (Priani et al., 2021; Venchenkov et al., 2020). Cinnamon bark extract is formulated into an emulgel preparation to enhance pharmacological effects through the skin delivery system. The antioxidant and sunscreen effects of cinnamon bark extract emulgel preparations can be seen in Table IV.

Table IV. Antioxidant and sunscreen effects of cinnamon bark extract emulgel preparations

Title	Active Substance	Gelling Agent	Antioxidant	Sunscreen	References
Formulation of Antioxidant Emulgel and Sunscreen Cinnamon Bark Extract (<i>Cinnamomum Burmanni</i> (Nees & T.Nees) Blume) and Grape Seed Oil (<i>Vitis vinifera L.</i>)	Cinnamon Bark Extract 1%	Viscolam MAC 5%	11.46 ± 0.36 (Very strong)	18.13 ± 0.24 (Ultra Protection)	(Venchenkov et al., 2020)
Antioxidant Emulgel Preparation Formulation Containing Ethanol Extract of Cinnamon Bark (<i>Cinnamomum burmanni</i> Nees Ex. Bl.)	Cinnamon Bark Extract 1%	Carbome 0,25%	10.40 ± 0.08 (Very strong)	-	(Priani et al., 2014a)
Development of Sunscreen Emulgel Containing <i>Cinnamomum Burmannii</i> Stem Bark Extract	Ekstrak kulit kayu manis 1%	Carbopol 934 2%	-	4.383 ± 0.063 (Moderate Protection)	(Priani et al., 2014b)

According to the data presented in Table IV the emulgel preparations containing 1% w/w cinnamon bark extract exhibit a strong antioxidant activity, as indicated by the IC_{50} value of 11.46 ± 0.36 . The antioxidative properties of cinnamon bark extract can be attributed to the presence of cinnamaldehyde compounds. The presence of cinnamaldehyde in cinnamon bark extract facilitates

the transfer of a hydrogen atom to the DPPH free radical, resulting in the conversion of DPPH into a non-radical compound known as DPPH-H (Priani et al., 2021). Emulgel preparations containing Viscolam MAC at extract concentrations of 1% and 5% exhibit a sunscreen value with an SPF value of 18.13 ± 0.24 , indicating their inclusion in the category of “ultra protection”. The efficacy of sunscreen can be attributed to the aromatic groups present in its active ingredients. Including the aromatic group within the molecule enables it to absorb UV radiation of high energy effectively and subsequently emit it at a lower energy level. This mechanism protects the skin from potential damage caused by UV radiation (Adamson & Shinkai, 2019).

CONCLUSION

The review findings indicate that using various ingredients in the formulation of cinnamon bark extract emulgel formula will result in diverse outcomes regarding physical characterization, stability, antioxidant activity, and sun protection properties. The emulgel formulation that best satisfies the specified criteria consists of a 1% w/w concentration of cinnamon bark extract in combination with the gelling agent Viscolam MAC 5% w/w.

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