CHAPTER I
INTRODUCTION

1. 1 Background

Many Indonesian women experience signs of premature aging. An online survey conducted by the skincare brand Olay found that around 76% of women have experienced symptoms of premature skin aging,[1] and 57% have noticed signs of aging as early as 25 years old.[2] Premature aging is a skin aging process that occurs faster than it should. It can happen to anyone, especially in Indonesia, which has a tropical climate with abundant sunlight.[3]

Premature aging of the skin is primarily triggered by external factors such as sunlight, free radicals, smoking, excessive alcohol consumption, and poor diet, as well as internal factors including heredity, psychological condition, overall health, and immune status.[4] The most common cause is exposure to free radicals in the form of ultraviolet radiation.[5] Prevention can be carried out through the use of orally consumed supplements, such as chewable tablets containing vitamin C and natural antioxidant sources.[6] Chewable tablets form a smooth mass after disintegration, have a pleasant taste, and do not diminish flavor perception, so they can be taken without drinking water. Their disintegration occurs in the mouth, allowing gradual absorption in the gastrointestinal tract and providing a faster onset of effect.[7]

Red guava fruit *(Psidium guajava* L.*)* is a natural ingredient that contains vitamin C at approximately 42.9 mg per 100 grams of fresh fruit, equivalent to 0.429

[1] Anna Rizkyah and Salsabila Nurul Karimah, "Literature Review : Penuaan Dini Pada Kulit : Gejala , Faktor Penyebab Dan Pencegahan," *JGK: Jurnal Gizi Dan Kesehatan* 3, no. 2 (2023): 107–16, doi:10.36086/jgk.v3i2.2029.

[2] Novita Arya Cahyani, Herri S Sastramihardja, and Siska Nia, "Scoping Review : Efek Pegagan *(Centella asiatica)* Dalam Sediaan Topikal Terhadap Pencegahan Penuaan Dini," *Medical Science* 2 (2022): 207–16.

[3] Siti Aizah, "Antioksidan Memperlambat Penuaan Dini Sel Manusia," *Prosiding Semnas Hayati IV*, 2020, 182–85.

[4] Ibid.

[5] Ibid.

[6] Wida Ningsih, Firmansyah, and Nova Jumaynah, "Formulasi Tablet Kunyah Kalsium Laktat Dengan Variasi Konsentrasi HPMC Sebagai Bahan Pengikat Terhadap Sifat Fisiknya," *Jurnal Ilmu Farmasi & Farmasi Klinik* 14, no. 1 (2017): 30–36.

[7] Aina Haque et al., "Formulasi Dan Evaluasi Fisik Sediaan Tablet Kunyah Minyak Atsiri Jeruk Kalamansi *(Citrus macrocarpa Bunge)* Dengan Variasi Pemanis Laktosa," *Jurnal Ilmu Kefarmasian* 4, no. 1 (2023): 149–53.

grams, based on vitamin C content determination using the *Na-2,6-dichlorophenol indophenol* (DCIP) titration method.[8] It also contains antioxidant compounds such as flavonoids, ellagic acid, gallic acid, leucocyanidin, and quercetin, all of which exhibit antioxidant activity. The IC_{50} value indicates that a concentration of 194.22 ppm of fresh red guava extract is required to inhibit 50% of DPPH free radicals, which falls into the *moderate* category of antioxidant activity.[9] In addition, red guava fruit extract has been shown to exhibit antimicrobial activity against *Escherichia coli, Staphylococcus aureus, and Shigella dysenteriae.*[10]

In formulating chewable tablets from red guava fruit extract, an appropriate binder is required because the characteristics of chewable tablets differ from those of conventional tablets. The binder used in this study is HPMC *(Hydroxypropyl Methylcellulose)*. HPMC functions to bind powder particles into granules, increase tablet compactness and hardness, and facilitate granule formation so that they can be easily compressed into tablets. HPMC is a cellulose derivative binder that offers several advantages, including improving the flow properties of granules, resulting in compact tablets, and being chemically inert. It is inert toward many substances, compatible with packaging components, and readily available.[11]

Chewable tablets are formulated using the wet granulation method because it effectively produces granules with good flow properties and binding capacity, resulting in chewable tablets with optimal, stable physical quality throughout the manufacturing process. Specifically, wet granulation improves the cohesiveness and compressibility of powders, enhances the distribution and uniformity of the active ingredient within the tablet, and prevents segregation of components during

[8] Septipianus Arung Padang and Rasnita Maharani Maliku, "Penetapan Kadar Vitamin C Pada Buah Jambu Biji Merah *(Psidium guajava L.)* Dengan Metode Titrasi Na-2,6 Dichlorophenol Indophenol (DCIP)," *Media Farmasi* XIII, no. 2 (2017).

[9] Rahmayani Hasibuan and M Idris, "Perbandingan Uji Kadar Vitamin C Dan Antioksidan Buah Jambu Biji Merah *(Psidium guajava L .,)* Segar Dan Dalam Kemasan Menggunakan Metode DPPH Di Kecamatan Marbau," *JB&P : Jurnal Biologi Dan Pembelajarannya* 11 (2024): 173–81.

[10] Muhammad Rijal et al., "Uji Efektivitas Ekstrak Etanol Buah Jambu Biji Merah *(Psidium guajava L.)* Dalam Menghambat Pertumbuhan Bakteri Porphyromonas Gingivalis Penyebab Periodontitis," *Indonesian Journal of Dentistry*, 2023, 31–37.

[11] Christine Citra Dewi and Nyi Mekar Saptarini, "Review Artikel: Hidroksi Propil Metil Selulosa Dan Karbomer Serta Sifat Fisikokimianya Sebagai Gelling Agent," *Farmaka* 14 (2014): 1–10.

compression.[12] The principle of wet granulation involves transforming a mixture of the active ingredient and excipients into larger, stronger granules by adding a binding solution so that the powder particles agglomerate into cohesive granules.[13]

Chewable tablets are expected to help prevent and slow premature aging through their vitamin C and natural antioxidants, which neutralize free radicals that damage collagen and elastin in the skin.[14] Based on the description above, this study aims to develop an oral pharmaceutical dosage form that is practical and easy to consume, thereby improving user compliance in the prevention of premature aging, particularly in tropical regions such as Indonesia, which are exposed to high levels of ultraviolet radiation. This is carried out by formulating chewable tablets containing red guava *(Psidium guajava* L.*)* fruit extract with variations in HPMC concentration as the binding agent.

1. 2 Problem Formulation

The research problems in this study are as follows:

1. How does the variation in HPMC concentration as a binding agent affect the chewable tablet formulation of red guava *(Psidium guajava* L.*)* extract?
2. Does the physical quality of the chewable tablet preparation of red guava *(Psidium guajava* L.*)* extract with varying concentrations of HPMC as a binding agent comply with the standards of the Indonesian Pharmacopoeia?

1. 3 Research Objectives

This research pursues the following objectives:

1. To analyze the effect of varying HPMC concentrations as a binding agent on the chewable tablet formulation of red guava *(Psidium guajava* L.*)* extract.
2. To determine the physical quality of the chewable tablet preparation of red guava *(Psidium guajava* L.*)* extract with varying concentrations of HPMC

[12] Ayu Aprilia et al., "Review: Formulasi Tablet Effervescent Berbahan Dasar Alami," *Agrointek : Jurnal Teknologi Industri Pertanian* 15, no. 4 (2021): 992–1000, doi:10.21107/agrointek.v15i4.9031.

[13] Haque et al., "Formulasi Dan Evaluasi Fisik Sediaan Tablet Kunyah Minyak Atsiri Jeruk Kalamansi *(Citrus macrocarpa Bunge)* Dengan Variasi Pemanis Laktosa."

[14] Shannaz N Yusharyahya, "Mekanisme Penuaan Kulit Sebagai Dasar Pencegahan Dan Pengobatan Kulit Menua Skin Aging Mechanism as A Basic Prevention and Treatment of Skin Aging," *EJKI* 9, no. 2 (2021).

as a binding agent that meets the standards of the Indonesian Pharmacopoeia.

1. 4 Research Benefits

1. Theoretical Benefits

The results of this study are expected to make a scientific contribution to the field of herbal pharmacy, particularly to the formulation of chewable tablets from red guava *(Psidium guajava* L.*)* extract of the effects of the wet granulation method and variations in binding agents on the physical characteristics of chewable tablets, such as hardness, size uniformity, and disintegration time. The findings of this study may serve as a reference for the development of chewable tablet formulations derived from other natural materials and enrich the existing literature on patient-friendly pharmaceutical formulation technology.

2. Practical Benefits

The outcomes of this research are anticipated to provide an alternative pharmaceutical dosage form that is easier to consume, particularly for patients who have difficulty swallowing conventional tablets. This chewable tablet is anticipated to enhance patient comfort and adherence in the use of herbal medicines containing red guava *(Psidium guajava* L.*)* extract, which is rich in vitamin C and antioxidants. The wet granulation method employed in this formulation can produce tablets with stable physical quality that meet standard requirements, thereby facilitating the production and distribution processes on an industrial scale.

1. 5 Originality of the Research

The development of chewable tablet formulations containing red guava (Psidium guajava L.) extract has been investigated by several researchers, as summarized in Table 1.

Table 1. Originality of the Research

Research Title	Research Method	Variables	Results	Research Differences
Formulation of Chewable Tablets of	Experimental	**Dependent:**	The results from the three formulas indicate that Formula I, containing 5.0%	**Dependent:**

Roselle *(Hibiscus sabdariffa* L.*)* Calyx Extract with Variations in PVP Concentration as a Binder on Their Physical Properties[15]		Physical characteristics of the tablets **Independent:** Variation in PVP concentration as a binder	PVP, was the best formulation. This is because the lowest concentration of PVP was sufficient to meet the required physical properties of the chewable tablets as well as sensory evaluation of taste.	Physical quality of the chewable tablet preparation **Independent:** Wet granulation method and variation of binders in the formulation
Effect of *Hydroxypropyl Methylcellulose* (HPMC) Concentration as a Binder in Tablet Formulations of Red Ginger *(Zingiber officinale var. rubrum)* Rhizome Extract[16]	Experimental	**Dependent:** Physical characteristics of the tablets **Independent:** Variation in HPMC concentration as a binder	Based on the study findings, it can be inferred that Hydroxypropyl Methylcellulose (HPMC) used as a binder affects the characteristics of lozenge tablets formulated with red ginger rhizome extract (*Zingiber officinale Var. Rubrum*) at concentrations of 4%, 5%, and 6%. Higher concentrations of HPMC result in better uniformity of tablet weight and increased tablet hardness; however, tablet friability tends to decrease.	**Dependent:** Physical quality of the chewable tablet preparation **Independent:** Wet granulation method and variation of binders in the formulation
Effect of Corn Starch *(Zea mays* L.*)* Concentration as a Binder in the Formulation of Effervescent Granule Preparations[17]	Experimental	**Dependent:** Evaluation of physical quality of granules **Independent:** Concentration of corn starch as a binder	Based on the results of the study, it can be concluded that the formulation of effervescent granules using corn starch affects the physical properties of the granules, including flow time, angle of repose, compressibility index, granule dissolution time, pH, and drying shrinkage. Among all the formulations, the best physical properties were	**Dependent:** Physical quality of the chewable tablet preparation **Independent:** Wet granulation method and variation of binders in the formulation

[15] Tiyas Repining Sawiji, Murrukmihadi Mimiek, and Siti Aisyah, "Formulasi Tablet Kunyah Ekstrak Kelopak Bunga Rosella *(Hibiscus sabdariffa L.)* Dengan Variasi Konsentrasi Pvp Sebagai Bahan Pengikat Terhadap Sifat Fisiknya," *Acta Holist. Pharm* 1, no. 1 (2019): 1–8.

[16] Nur AIn Thomas et al., "Pengaruh Konsentrasi Hydroxypropyl Methylcellulose Sebagai Bahan Pengikat Pada Sediaan Tablet Ekstrak Rimpang Jahe Merah *(Zingiber officinale Var. Rubrum.)*," *Indonesian Journal of Pharmaceutical Education* 1, no. 3 (2021): 158–67, doi:10.37311/ijpe.v1i3.11667.

[17] Dewi Yuniharni, Wardatul Husna, and Vivi Faradilla, "Pengaruh Konsentrasi Pati Jagung *(Zea mays L.)* Sebagai Bahan Pengikat Pada Formulasi Sediaan Granul Effervescent," *Eksplorasi: Jurnal Sains Dan Teknologi* 1, no. 1 (2023): 1–9.

			observed in Formula III, which contained 15% corn starch.	
Review of the Effect of Binders on the Physical Properties of Chewable Tablet Formulations[18]	Literatur review	**Dependent:** Physical properties of chewable tablets **Independent:** Effect of binders	Variation in binder composition, such as mannitol and amylum manihot, significantly affects the physical properties of tamarind turmeric chewable tablets. Tablets composed of 100% mannitol (F1) exhibited lower friability and relatively better disintegration compared to tablets containing other binder mixtures. The advantage of this study is that it provides useful information for formulating tamarind turmeric tablets using more natural and economical raw materials. However, further research is needed to explore the long-term effects of these binders on stability and consumer acceptability. Future development could focus on taste testing, shelf life, and the potential use of alternative binder variations.	**Dependent:** Physical quality of the chewable tablet preparation **Independent:** Wet granulation method and variation of binders in the formulation
Evaluation of the Use of Canna Starch *(Canna edulis Kerr.)* as a Binder in Chewable Tablets of Ethanolic Extract of Moringa *(Moringa oleifera* L.*)* Leaves Prepared	Based on book literature	**Dependent:** Evaluation of physical quality of chewable tablets **Independen:** Concentration of ganyong starch as a binder	The study produced tablets that met the requirements in both granule and tablet evaluations. Among the three formulas, the optimal starch content was achieved at 10% amylum, corresponding to Formula III. The granule evaluation results were as follows: moisture content 0.00%, compressibility index 7.89%, angle of repose 32.21º, and flow rate 4.59 seconds. The tablet	**Dependent:** Physical quality of the chewable tablet preparation **Independent:** Wet granulation method and variation of binders in the formulation

[18] Sakinah Pokhrel, "Review Pengaruh Binder Terhadap Sifat Fisik Pada Formulasi Sediaan Tablet Kunyah," *Αγαη* 15, no. 1 (2024): 37–48.

by the Wet Granulation Method[19]		evaluation results included: no physical damage, organoleptic test showing a slightly sweet-bitter taste, uniformity of size with a diameter of 12.00 mm and thickness of 4.69 mm, weight uniformity with an average of 507.9 mg, hardness 5.16 kg, friability 0.36%, and disintegration time of 4 minutes 30 seconds.

[19] Maryatul Kiptiyah et al., "Evaluasi Penggunaan Pati Ganyong *(Canna edulis Kerr.)* Sebagai Bahan Pengikat Pada Tablet Kunyah Ekstrak Etanol Daun Kelor *(Moringa oleifera L)* Dengan Metode Granulasi Basah," *Seminar Nasional Kesehatan*, 2021, 2188–2206.