THE EFFICACY OF POLY-D, L-LACTIC ACID (PDLLA) FOR HAND REJUVENATION

THATARATH DENSRISEREEKUL

MASTER OF SCIENCE
IN
DERMATOLOGY

SCHOOL OF ANTI-AGING AND REGENERATIVE MEDICINE
MAE FAH LUANG UNIVERSITY
2025

THE EFFICACY OF POLY-D, L-LACTIC ACID (PDLLA) FOR HAND REJUVENATION

THATARATH DENSRISEREEKUL

THIS THESIS IS A PARTIAL FULFILLMENT OF
THE REQUIREMENTS FOR THE DEGREE OF
MASTER OF SCIENCE
IN
DERMATOLOGY

SCHOOL OF ANTI-AGING AND REGENERATIVE MEDICINE
MAE FAH LUANG UNIVERSITY
2025

THESIS APPROVAL

MAE FAH LUANG UNIVERSITY

FOR

MASTER OF SCIENCE IN DERMATOLOGY

Thesis Title: The Efficacy of Poly-D, L-Lactic Acid (PDLLA) for Hand Rejuvenation

Author: Thatarath Densrisereekul

Examination Committee:

Tanomkit Pawcsuntorn, M. D.	Chairperson
Paisal Rummaneethorn, M. D.	Member
Associate Professor Wongdyan Pandii, Dr. P. H.	Member

Advisor:

Paisal

.....Advisor

(Paisal Rummaneethorn, M. D.)

Dean:

Karnt W.

.....

(Karnt Wongsuphasawat, Ph. D.)

ACKNOWLEDGEMENTS

The completion of this thesis was made possible with the invaluable assistance and guidance of many esteemed individuals. First and foremost, I would like to express my heartfelt gratitude to my advisor, Dr. Paisal Rummaneethorn, for his insightful consultations and steadfast support throughout the research process. I am also deeply thankful to Prof. Tanomkit Pawcsuntorn (chairperson) and Assoc. Prof. Dr. Wongdyan Pandii, for their exceptional suggestions, which significantly contributed to the successful completion of this thesis.

I would like to express my sincere gratitude to Mae Fah Luang University for its generous sponsorship throughout my research. With your unwavering support, I was able to complete my thesis and contribute more knowledge to the field of medicine.

Furthermore, I would like to extend my sincere appreciation to my parents, friends, and the staff at the School of Anti-Aging and Regenerative Medicine, Mae Fah Luang University, for their continuous support and encouragement.

Thatarath Densrisereekul

Thesis Title	The Efficacy of Poly-D, L-Lactic Acid (PDLLA) for Hand Rejuvenation
Author	Thatarath Densrisereekul
Degree	Master of Science (Dermatology)
Advisor	Paisal Rummaneethorn, M. D.

ABSTRACT

Hand rejuvenation, essential for a natural look in cosmetic procedures, is often overlooked despite hands being highly visible and prone to aging signs like prominent veins and tendons due to subcutaneous atrophy. Aging hands show atrophy, volume loss, and skin changes such as wrinkles and pigmentation issues, becoming noticeable from the fourth decade of life due to UV exposure, pollutants, and stress.

Autologous fat grafting and dermal fillers are key techniques for restoring youthful volume and skin quality. Fat grafting, refined since the 1980s, offers natural, long-lasting results but is complex and time-consuming. Common dermal fillers like hyaluronic acid, polynucleotides, calcium hydroxylapatite (CaHA) which is FDA-approved in 2015, and poly-lactic acid (PLA) stimulate collagen synthesis and augment skin volume.

While other dermal fillers are well researched, PDLLA still remains questionable on efficacy for hand rejuvenation

Objective: The study aims to evaluate the efficacy of poly-D,L-lactic acid (PDLLA) for hand rejuvenation, improving hand elasticity, melanin levels, transepidermal water loss, oiliness, and moisture levels.

Material and Methods: 15 thai women and men volunteers, age between 45-65 years old were enrolled in this study. Hands of each participant were treated with Poly-D, L-lactic acid (PDLLA). All volunteers were treated for 2 times with spacing 4 weeks interval and following up 3 times with spacing 4 weeks interval. The level of smoothness, wrinkle, elasticity, melanin, moisture, oiliness, transepidermal water loss were measured at every visit. Moreover, the patient satisfaction score and the side effect were recorded.

Results: Statistically significant improvements were observed in hydration (from 41.8 ± 10.5 to 55.5 ± 11.1; $P < 0.001$) and TEWL (from 23.5 ± 16.0 to 20.6 ± 16.6; $P = 0.048$)

by week 16, indicating improved skin barrier function. Elasticity showed the greatest improvement, rising from 0.82 ± 0.04 at baseline to 1.00 ± 0.03 at week 16 ($P < 0.001$), with a mean percentage change of 21.51 ± 7.92. Melanin levels decreased significantly at week 12 ($P = 0.049$), although percentage changes were not statistically significant. Oiliness fluctuated transiently, peaking at week 12 ($P = 0.040$) and normalizing by week 16. Adverse effects were minimal and self-limiting, with no reported cases of scarring or dyspigmentation. Satisfaction scores significantly improved in smoothness ($P = 0.01$), wrinkle reduction ($P = 0.01$), and moisture ($P = 0.03$).

Conclusions: PDLLA is a safe and effective biostimulatory filler for hand rejuvenation, demonstrating significant improvements in skin hydration, elasticity, and patient satisfaction with minimal side effects. These findings support its clinical application in aesthetic dermatology for hand aging.

Keywords: Poly-D,L-lactic Acid (PDLLA), Hand Rejuvenation

TABLE OF CONTENTS

TABLE OF CONTENTS

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

CHAPTER 1

INTRODUCTION

1.1 Background

Natural-appearing outcomes in aesthetic medicine are characterized by harmonious integration with anatomical regions that prominently reveal signs of aging. While facial rejuvenation has been extensively investigated, supported by a robust body of literature and clinical experience, rejuvenation of other anatomically significant regions—particularly the hands—remains comparatively underexplored. This is despite the hands' critical role in the overall aesthetic perception and their economic relevance within the cosmetic field.

The dorsal hands are among the most visible and expressive parts of the human body. With age, they exhibit characteristic signs of senescence, including subcutaneous atrophy and volume depletion, resulting in the increased visibility of underlying structures such as veins, extensor tendons, and osseous contours. Although cultural practices emphasize hand aesthetics through manicures and the wearing of jewelry, the dorsal hands are frequently neglected as targets for cosmetic intervention.

Age-related changes in the hands manifest as dermal thinning, loss of elasticity, and textural irregularities. Clinically, the skin often presents with wrinkling, heterogeneous pigmentation, and a range of photodamage-related lesions, including mottled dyspigmentation, solar lentigines, seborrheic keratoses, actinic keratoses, and in some cases, cutaneous malignancies. Moreover, the aging skin of the hands tends to be more susceptible to trauma and ecchymosis (Bidic et al., 2010).

Aging of the hands becomes noticeable as early as the fourth decade of life. Chronic exposure to ultraviolet radiation, pollutants, irritants, and mechanical stress causes visible senescence in the hands. Superficial damage, including discoloration, textural variation, and the development of neoplastic lesions, is often seen. Aging of the hands also involves changes to underlying structures, and in certain diseased states, aberrant microcirculation can exacerbate the aging process.

Aging of the Hands: Anatomical Changes and Rejuvenation Strategies

The aging process of the hands is multifactorial, involving progressive anatomical, histological, and aesthetic alterations. Three principal features characterize hand aging: increased visibility of extensor tendons due to diminished subcutaneous volume in the intermetacarpal spaces, enhanced tortuosity and prominence of dorsal veins, and the presence of actinic and seborrheic keratoses. These visible signs are accompanied by changes in dermal thickness and tissue elasticity, which contribute significantly to the aged appearance of the hands.

Quantitative measurements highlight the progression of tissue atrophy with age. Soft tissue thickness on the dorsum of the hand declines markedly—from an average of 3.12 mm during adolescence to approximately 1.6 mm in individuals older than 45 years. Similarly, cutaneous thickness decreases with age, from about 1.2 mm at 25 years to 0.75 mm at 70 years, reflecting the cumulative degradation of dermal collagen and elastin. Gender differences are also evident, with men generally exhibiting thicker dorsal hand skin, although this difference narrows with age. The reduction in soft tissue volume leads to characteristic concavities between metacarpals and greater skeletal definition. Additionally, age-associated pigmentary and textural changes such as lentigines, dyschromia, and epidermal roughness become more pronounced.

Several intrinsic and extrinsic factors accelerate the cutaneous aging of the hands, including genetic predisposition, chronic ultraviolet exposure, mechanical overuse, exposure to environmental toxins, substance abuse, and systemic conditions such as rheumatologic disease (Bidic et al., 2010). In contrast, youthful hands are defined by even skin tone, firm and well-hydrated dermis, and minimal visibility of subdermal structures such as veins, tendons, or bone contours.

A perception-based study by Bains et al. demonstrated that the visibility of dorsal hand veins plays a significant role in perceived age. When participants were shown digitally altered images of female hands, those with reduced vein prominence were consistently rated as younger than their unaltered counterparts, indicating the strong aesthetic impact of vascular visibility—greater than other enhancements like manicures or jewelry.

Volumization of the dorsal hand is a key component of rejuvenation strategies. Restoring volume helps camouflage prominent subdermal structures and improves the

skin's texture and tone. One established method is autologous fat grafting, wherein fat is harvested from a donor site and injected into the dorsal hand. Since its inception in the 1980s, the technique has undergone substantial refinement. Early approaches, such as Fournier's single-bolus injection technique, often produced inconsistent results. Subsequent innovations by Coleman introduced the use of cannulas and small-volume, multi-tunneled injections, significantly enhancing graft survival and aesthetic outcomes (Coleman, 2002). Despite its efficacy and biocompatibility, fat grafting remains a technically demanding and time-intensive procedure with extended recovery time, largely due to the harvesting process.

In addition to autologous grafting, a variety of dermal fillers are used for non-surgical hand rejuvenation. These include hyaluronic acid (HA), polynucleotides (PN), calcium hydroxylapatite (CaHA), and poly(lactic acid) (PLA). PLA refers to a family of stereoisomers such as poly(D-lactic acid) (PDLA), poly(L-lactic acid) (PLLA), poly-D,L-lactic acid (PDLLA), and racemic PLA. These agents not only restore volume but also stimulate neocollagenesis via controlled inflammatory responses. Biostimulatory fillers like PLA derivatives induce a low-grade granulomatous reaction, initiating a cascade that includes M2 macrophage polarization and increased interleukin-10 (IL-10) secretion. This microenvironment promotes fibroblast migration and upregulates transforming growth factor-beta (TGF-β), ultimately enhancing collagen synthesis and dermal remodeling (Oh, 2023).

1. Calcium Hydroxyapatite (CaHA):

In 2015, CaHA received FDA approval for hand rejuvenation following a pivotal study involving 113 patients. Initially recommended for use with 0.3 cc of 1% lidocaine and a 25-gauge needle, current protocols prefer higher dilutions and a 22- or 25-gauge cannula. Both proximal and distal entry sites are effective, resulting in minimal bruising. Studies indicate high satisfaction among patients and physicians. Common side effects such as swelling, pain, redness, and bruising typically resolve within two weeks. Post-treatment care may include ice packs, massage, and corticosteroids. Research by Wu et al. demonstrated that triamcinolone injections post-CaHA treatment significantly reduced swelling and adverse events without compromising long-term efficacy.

2. Poly-Lactic Acid (PLA):

Poly-Lactic Acid (PLA) diluted with anesthetic was used in two European studies for soft tissue augmentation of the hands over multiple sessions, followed by post-treatment massage to ensure even distribution. However, nodules formed and persisted even one year after the intervention. Higher dilutions of water and lidocaine reduced nodule formation, but unevenness still persisted. Due to the anatomical complexity of the hand, deeper injections are often not feasible. While PLA can be used off-label for dorsal hand rejuvenation, it's not the preferred biostimulator because of the high risk of nodule formation, especially in the dynamic environment of the hand's tendons. To mitigate this risk, PLA must be deposited carefully in the subcutaneous layer, particularly in the intermetacarpal spaces, avoiding muscle involvement. (Redaelli, 2006)

1.2 Research Question

1.2.1 Primary Research Question

Does poly-D,L-lactic acid (PDLLA) effectively rejuvenate aging hands by improving hand skin parameters?

1.2.2 Secondary Research Question

Are there any significant side effects or complications associated with PDLLA treatment for hand rejuvenation, and how satisfied are patients with the outcomes?

1.3 Objectives

1.3.1 Primary Objective

The study aims to evaluate the efficacy of poly-D,L-lactic acid (PDLLA) for hand rejuvenation, improving hand skin parameters, using the Cutometer MPA 580.

1.3.2 Secondary Objective

To investigate the side effects and complications associated with using the efficacy of poly-D,L-lactic acid (PDLLA) for hand rejuvenation.

To assess patient satisfaction with the efficacy of poly-D,L-lactic acid (PDLLA) for hand rejuvenation.

1.4 Research Hypothesis

1.4.1 Primary Hypothesis

Poly-D,L-lactic acid (PDLLA) treatment significantly improves hand skin parameters in individuals with signs of hand aging.

1.4.2 Secondary Hypothesis

PDLLA treatment for hand rejuvenation results in no significant increase in adverse effects or complications, while maintaining a high level of patient satisfaction.

1.4.3 Scope of Research

1. Population: Thai adults aged 45-65 years old who exhibit signs of hand aging.

2. Experimental group: Thai adults aged 45-65 years old who exhibit signs of hand aging.

1.5 Conceptual Framework

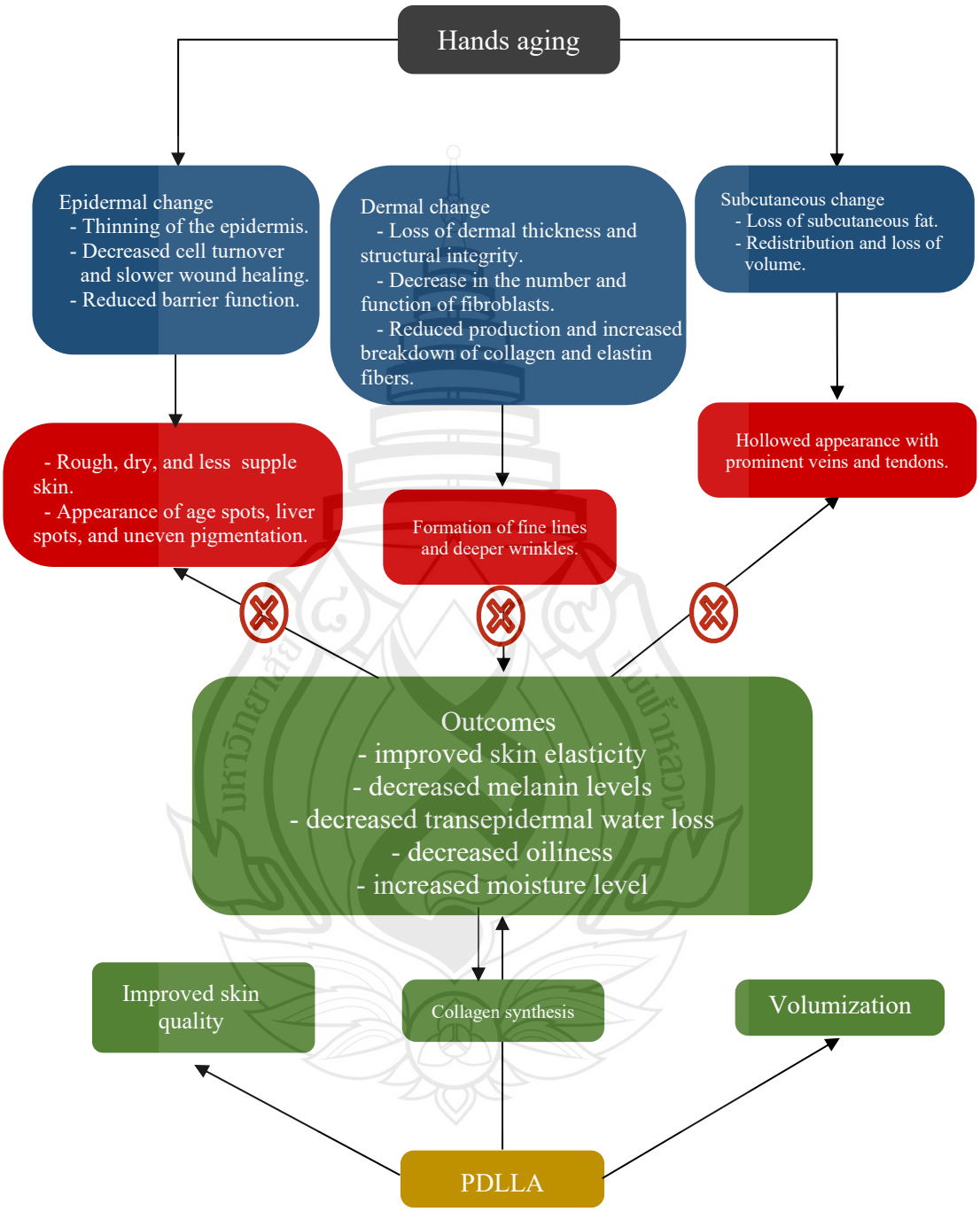


Figure 1.1 Conceptual Framework

1.6 Operational Definitions

Figure 1.2 Cutometer MPA 580

1.6.1 Poly-D,L-lactic acid (PDLLA)

PDLLA is a synthetic biodegradable polymer commonly used in medical and cosmetic applications. It is a mixture of poly-D-lactic acid and poly-L-lactic acid. PDLLA is widely used in dermal fillers and other biostimulatory agents to promote collagen production. This results in long-lasting volumization and structural support for treated areas.

1.6.2 Cutometer MPA 580

The Cutometer MPA 580 is a device equipped with a multi-probe adaptor. It measures various biomechanical parameters of the skin. These parameters include elasticity, melanin levels, transepidermal water loss, oiliness, and moisture levels.

1.6.3 Efficacy of Treatment

Injecting PDLLA into the dorsal hand leads to improvements in hand elasticity, melanin levels, transepidermal water loss, oiliness, and moisture levels.

1.6.4 Side Effects and Complications

Potential side effects include pain, swelling, bruising, scarring, infections, and vascular complications.

Score 0: None

Score 1: Mild (side effects resolved within 1 week: pain, swelling, bruising)

Score 2: Moderate (side effects requiring intervention: chronic swelling, nodules, overcorrection)

Score 3: Severe (severe side effects requiring immediate treatment: infections, vascular complications)

1.6.5 Skin Parameters

Skin parameters measured from cutometer MPA 580 including skin elasticity, melanin levels, hydration and transepidermal water loss, and oiliness

Table 1.1 Common Adverse Events Following Dermal Filler Injections with Corresponding Preventive and Management Approaches

Adverse Event	Preventive Measures and Clinical Management
Localized Injection Reactions (e.g., redness, swelling, discomfort, ecchymosis)	- Advise patients to withhold anticoagulant or antiplatelet agents prior to treatment (e.g., aspirin) - Opt for blunt-tipped cannulas to limit trauma to vasculature - Employ fine-gauge needles to decrease pain and bruising - Apply cold therapy post-procedure - Consider IPL or vascular laser for persistent bruising
Subcutaneous Nodularity, Linear Beading, Tyndall Phenomenon	- Prevent by avoiding superficial dermal placement - Use steady, uniform injection technique - Treat with gentle massage or aspiration - For HA-based fillers, hyaluronidase may be used - Surgical excision may be required in resistant cases
Persistent Papular Lesions	- Product-dependent protocols: • Bellafill®: consistent and smooth injection method • Sculptra®: ensure sufficient product dilution • Silicone: utilize the microdroplet technique

Table 1.1 (continued)

Adverse Event	Preventive Measures and Clinical Management
Post-Procedural Infection	- Meticulously disinfect skin using antiseptic solutions (e.g., chlorhexidine) - Manage infections with antibiotics and/or surgical drainage
Reactivation of Herpes Simplex Virus	- Initiate prophylactic antiviral therapy in patients with history of herpes labialis - Avoid procedures during active episodes
Allergic or Hypersensitivity Reactions	- Contraindicated in individuals with known filler allergies - Pre-administration skin testing for animal-derived products - HA filler reactions may resolve spontaneously; treat with tacrolimus, corticosteroids, hyaluronidase, or drainage
Delayed-Onset Nodules	- Employ strict aseptic technique prior to injection - If nodules develop, pursue drainage with culture and histopathology
Vascular Injury or Embolic Events (e.g., tissue necrosis, visual impairment)	- Possess detailed knowledge of facial vascular pathways - Always aspirate prior to injection - Use cannulas or fine needles in high-risk zones - Inject slowly with minimal pressure - Cease injection if blanching, pain, or vision changes occur - Initiate warm compresses, massage, and oral aspirin - Use hyaluronidase promptly if HA filler is involved

Table 1.2 Filler-Specific Vascular Compromise Management Strategies

Complication	Prevention and Management Strategies
Hyaluronic Acid Filler without Visual Compromise	- Discontinue injection immediately upon signs of vascular reflux or blanching - Administer high-dose hyaluronidase at the suspected site of occlusion and surrounding areas - Use substantial units, potentially in repeated pulses - Adjunctive therapies: gentle massage, corticosteroids, warm compress, oral aspirin, and hyperbaric oxygen therapy
Calcium Hydroxylapatite	- Preliminary evidence supports the use of sodium thiosulfate (0.1–0.2 mL of 250 mg/mL) for potential filler dissolution - Clinical efficacy in vascular occlusion remains under investigation

Source Jones et al. (2021)

1.7.6 Volunteer Satisfaction Score

Score 0: Unsatisfied

Score 1: Mildly satisfied

Score 2: Moderately satisfied

Score 3: Very satisfied

Score 4: Extremely satisfied

1.7.7 Signs of Aging Hands

1. Atrophy and loss of subcutaneous tissue
2. Wrinkled skin and heterogeneous color/texture
3. Mottled dyspigmentation, solar lentigines, seborrheic keratoses
4. Vulnerable skin prone to injury and bruising

1.7.8 Hand Rejuvenation

Hand rejuvenation encompasses a variety of cosmetic procedures aimed at restoring the youthful appearance of the hands by addressing common signs of aging, including volume loss, prominent veins, wrinkles, and skin discoloration. These procedures involve the use of dermal fillers, fat grafting, laser treatments, chemical peels, and other skin resurfacing techniques. The primary objective of hand rejuvenation is to enhance skin texture, tone, and overall hand appearance, resulting in fuller, smoother, and more evenly pigmented hands. This transformation aligns the hands' appearance with the more youthful look of other treated areas, such as the face (Kühne & Imhof, 2012).

CHAPTER 2

LITERATURE REVIEW

2.1 Anatomy of the Hand

2.1.1 Bones of the Hand

The human hand comprises 27 bones categorized into three groups: the carpal bones, the metacarpal bones, and the phalanges.

1. Carpal Bones: The wrist contains eight carpal bones arranged in two rows. The proximal row includes the scaphoid, lunate, triquetrum, and pisiform, while the distal row consists of the trapezium, trapezoid, capitate, and hamate (Standring, 2015).

2. Metacarpal Bones: Five metacarpal bones form the palm, each corresponding to one of the five digits. (Standring, 2015)

3. Phalanges: The fingers are composed of phalanges. Each finger has three phalanges (proximal, middle, and distal) except for the thumb, which has two (proximal and distal) (Drake et al., 2015).

2.1.2 Joints of the Hand

1. Carpometacarpal Joints (CMC): These joints enable the thumb's opposition and contribute to the hand's gripping ability.

2. Metacarpophalangeal Joints (MCP): These joints allow for flexion, extension, abduction, and adduction of the fingers.

3. Proximal Interphalangeal Joints (PIP) and Distal Interphalangeal Joints (DIP): These hinge joints enable bending and straightening of the fingers.

2.1.3 Muscles and Tendons of the Hand

1. Extrinsic Muscles: Originate in the forearm and insert into the hand. Key extrinsic muscles include the flexor and extensor groups, which facilitate gross motor movements (Standring, 2015).

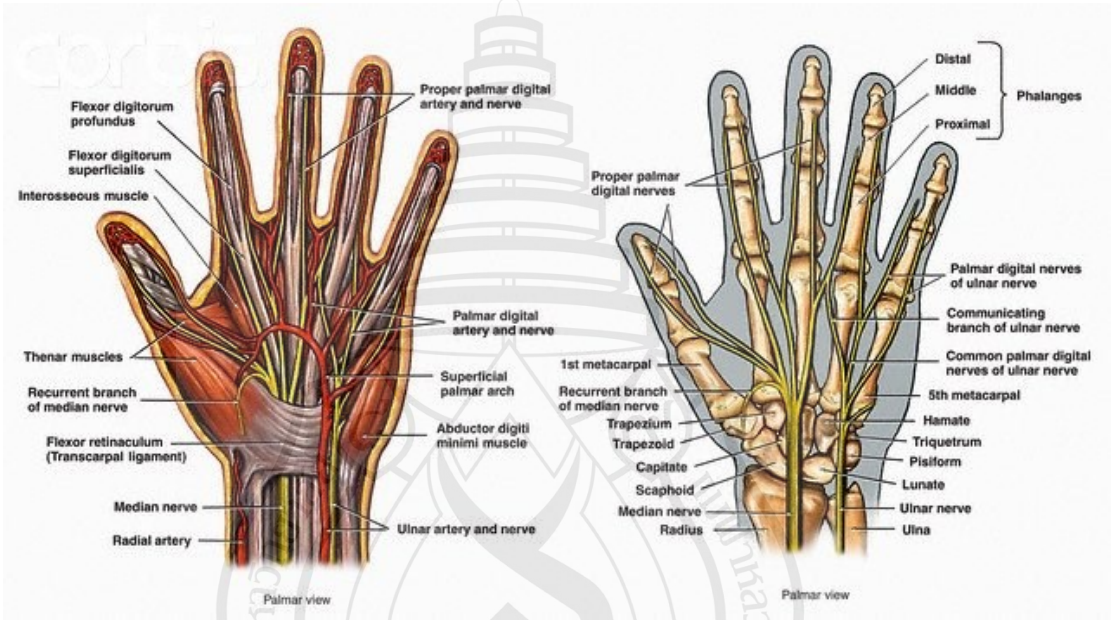
2. Intrinsic Muscles: Originate and insert within the hand, allowing for fine motor control. These include the thenar, hypothenar, interossei, and lumbrical muscles (Drake et al., 2015).

2.1.4 Nerves of the Hand

1. The median nerve supplies the thenar muscles and provides sensation to the thumb, index, middle, and half of the ring finger.

2. The ulnar nerve innervates the hypothenar muscles and provides sensation to the little finger and half of the ring finger.

3. The radial nerve provides sensory innervation to the dorsal aspect of the hand and supplies the extensor muscles (Standring, 2015).



Source Doctor Stock (2012)

Figure 2.1 Anatomy of Hand

2.1.5 Vascular Supply of the Hand

1. The radial artery supplies the thumb and lateral side of the index finger through the deep palmar arch and contributes to the superficial palmar arch.

2. The ulnar artery supplies the medial side of the hand and fingers through the superficial palmar arch and contributes to the deep palmar arch.

2.1.6 Fat Distribution in the Dorsum of the Hand

The dorsum of the hand features a complex fat distribution divided into three laminae, each separated by fascial planes.

1. The superficial lamina is located less than 1 mm beneath the skin surface and contains no significant structures. It exhibits uneven fat distribution and comprises

8 to 12 spanning fascial septae containing small vessels, providing minimal structural support and volume.

2. The intermediate lamina houses veins and sensory nerves, which are crucial for both vascular and neural function. Dorsal veins in this layer average 1.27 mm in diameter, necessitating careful handling during surgical procedures to avoid damage.

3. The deep lamina contains fat and connective tissue.

The hand comprises four compartments housing extensor tendons, crucial for hand movements and dexterity. The fascial planes between these compartments provide structural support and facilitate tendon movement.

2.2 Aging of Hand

2.2.1 Pathophysiology of Hand Aging

2.2.1.1 Cellular and Molecular Changes

1. Collagen and Elastin Dynamics

Collagen, the primary structural protein in the dermis, provides tensile strength and support to the skin. However, with aging, there's a significant decrease in the number and activity of fibroblasts, the cells responsible for collagen production. This leads to reduced collagen synthesis, exacerbated by increased activity of matrix metalloproteinases (MMPs), enzymes that degrade collagen. As a result, collagen fibers become fragmented and disorganized, contributing to skin thinning and reduced structural integrity.

Elastin fibers, crucial for skin elasticity, allow the skin to stretch and return to its original shape. Over time, elastin fibers undergo fragmentation and lose their organized structure, resulting in decreased skin elasticity and the formation of wrinkles. The reduction in both collagen and elastin is a key factor in the aged appearance of the hands.

2. Extracellular Matrix (ECM) Degradation

The extracellular matrix (ECM) provides structural and biochemical support to surrounding cells. Aging disrupts the balance between ECM production and

degradation. Key components of the ECM, such as glycosaminoglycans (e.g., hyaluronic acid), decrease in quantity, leading to reduced skin hydration and volume. This degradation impairs the skin's ability to retain moisture and maintain its plumpness, further contributing to the aged appearance.

3. Cellular Senescence

Cellular senescence is a state where cells permanently stop dividing but remain metabolically active. As we age, factors like DNA damage, oxidative stress, and telomere shortening lead to the accumulation of senescent cells. These cells release a variety of pro-inflammatory cytokines, chemokines, and proteases, collectively known as the senescence-associated secretory phenotype (SASP). The SASP contributes to tissue degradation, chronic inflammation, and disruption of normal cellular functions, accelerating the aging process.

2.2.1.2 Structural and Functional Changes

1. Epidermal Thinning: The epidermis, particularly the stratum corneum, thins with age due to a slower turnover rate of keratinocytes, the primary cells of the epidermis. This thinning reduces the skin's barrier function, making it more susceptible to damage and transepidermal water loss (TEWL). The diminished barrier function increases susceptibility to environmental insults and irritants, further contributing to the aging appearance.

2. Dermal Changes: The dermis undergoes significant alterations with aging. There's a decrease in the number and activity of fibroblasts, leading to reduced synthesis of collagen and elastin. The existing collagen and elastin fibers become fragmented and less organized, resulting in decreased skin strength and elasticity. Additionally, the reduction in glycosaminoglycans and other extracellular matrix (ECM) components diminishes the skin's ability to retain moisture, contributing to dryness and a rough texture.

3. Subcutaneous Fat Loss: The subcutaneous fat layer, which provides cushioning and volume, diminishes with age. This loss of fat leads to a more skeletal appearance of the hands, with prominent veins and tendons. The reduction in subcutaneous fat also decreases the skin's ability to insulate and protect underlying structures, making the hands more vulnerable to mechanical stress and environmental factors.

4. Vascular Changes: Aging affects the microvascular network within the skin, leading to reduced blood flow and capillary density. This results in decreased nutrient and oxygen delivery to the skin, impairing cellular function and slowing the healing process. Reduced microcirculation also contributes to a dull and pallid skin appearance.

5. Pigmentary changes are another hallmark of aging. Melanocytes, the cells responsible for producing melanin, decrease in number with age. However, surviving melanocytes can become hyperactive in response to UV exposure, leading to uneven pigmentation and the formation of age spots (solar lentigines). These hyperpigmented areas are more common on sun-exposed skin, such as the hands.

The distribution of melanin becomes irregular with age, resulting in areas of hyperpigmentation and an uneven skin tone. Prolonged exposure to UV radiation exacerbates this process by stimulating melanocyte activity and increasing melanin production in localized areas.

6. Immune system alterations are also associated with aging. The skin's immune function declines with age, a process known as immunosenescence. Langerhans cells, key players in the skin's immune response, decrease in number and functionality. This reduction weakens the skin's ability to defend against pathogens and repair damage, increasing the risk of infections and skin cancers.

Aging is also associated with a state of low-grade chronic inflammation, referred to as "inflammaging." Pro-inflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) are upregulated. This chronic inflammation contributes to the breakdown of skin structures and accelerates the aging process.

2.3 Clinical Manifestations of Aging Hands

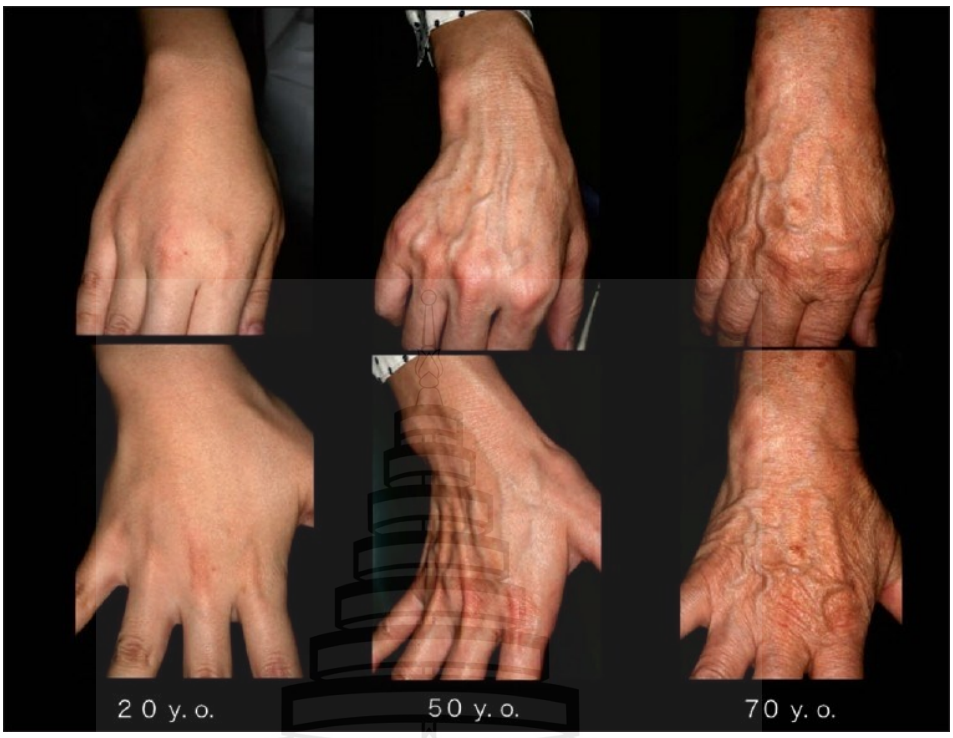
2.3.1 Wrinkles and Fine Lines

Wrinkles and fine lines form as a result of collagen and elastin loss, coupled with repetitive mechanical stress from hand movements. Initially superficial, fine lines can deepen into wrinkles as the skin loses more structural support and elasticity.

Age spots, or solar lentigines, are hyperpigmented areas caused by increased melanin production in response to UV exposure. Uneven pigmentation results from irregular melanocyte activity, leading to a blotchy appearance.Thinning skin and reduced subcutaneous fat make veins more visible, contributing to the aged appearance of hands. Prominent veins are a common sign of hand aging.Decreased sebum production and impaired skin barrier function lead to dry, rough skin. This can be exacerbated by environmental factors such as cold weather and frequent hand washing, which strip the skin of natural oils.

Aging affects the nail matrix, leading to slower nail growth and increased brittleness. Brittle nails are more prone to splitting and breakage and may also develop ridges.

Hand aging is a multifactorial process involving intricate interactions between intrinsic biological changes and extrinsic environmental factors. Understanding these mechanisms highlights the importance of preventive measures, such as sun protection, moisturizing, and maintaining a healthy lifestyle. Therapeutic interventions like retinoids, chemical peels, and laser therapy can also be beneficial. By addressing both intrinsic and extrinsic factors, it is possible to mitigate the signs of aging and maintain hand health. Further research into the molecular pathways and environmental influences on hand aging could lead to more effective anti-aging treatments and preventive strategies.



Source Ono (2011)

Figure 2.2 Hands Aging

2.4 Aesthetics of Hand

Ideal Hand Proportions

The study of hand aesthetics has established normative proportions considered attractive across diverse populations. Key metrics include:

1. Hand Length: Constitutes approximately 11% of total body length, with the middle finger contributing about 49% of this measurement.

2. Hand Width: Typically around 45% of hand length.

3. Dominance and Size: The dominant hand is generally larger, though this difference is less pronounced in left-handed individuals due to greater ambidexterity.

4. Gender Differences: Females possess approximately 25% less hand volume than males of the same height.

5. The Hand Volume Rating Scale (HVRS) is a newly developed 5-grade photonumeric scale designed to objectively assess hand volume changes, particularly in Asian populations. Developed by a group of experienced plastic surgeons, the scale

provides detailed criteria for each grade, ranging from no visible signs of aging (grade 0) to severe soft tissue loss and pronounced anatomical features such as visible tendons and veins (grade 4). The HVRS was meticulously validated through a selection of representative images and morphed illustrations to ensure accurate user comprehension and application in clinical settings. This scale aims to standardize the evaluation of hand aging, thereby enhancing the precision and effectiveness of hand rejuvenation treatments

Figure 2.3 The Hand Volume Rating Scale

2.5 Hand Rejuvenation Treatment

2.5.1 Topical Hand Rejuvenation

Retin-A and hydroquinone are popular topical agents for youthful hands. Retin-A stimulates collagen production, while hydroquinone whitens skin by inhibiting tyrosinase. However, both agents can cause irritation, so physician supervision and sunblock use are recommended.

2.5.2 Fat grafting, a technique used since 1980, involves harvesting and injecting fat into the hands. The distributed injection technique results in smoother outcomes. However, side effects such as graft volume loss, necrosis, and infection can occur. The duration of results varies depending on the technique and fat quality, ranging from months to years. (Coleman, 2002)

2.5.3 Hyaluronic acid, injected using a blunt cannula, provides smooth skin with a low risk of conglomeration. However, its effects last only 3-6 months, requiring frequent reinjections. Raising hands during injection can help reduce swelling. (Kühne & Imhof, 2012)

2.5.4 Biostimulators, including poly-L-Lactic Acid (PLLA), calcium hydroxyapatite (CaHA), and polynucleotides (PN)/polydeoxyribonucleotide (PDRN), are used to enhance skin volume and texture.

1. PLLA, a cosmetic filler since 1999, forms colloidal micelles for injection, promoting cellular activity and tissue regeneration. Biocompatible and degrading within 18 months, PLLA triggers an inflammatory response, leading to new collagen formation and increased dermis thickness. It is effective in volume restoration, skin tightening, and wrinkle reduction, with high patient satisfaction and minimal side effects. (Redaelli, 2006)

2. CaHA, used in aesthetic and reconstructive medicine, offers biocompatibility and biostimulatory properties. It provides immediate volumizing effects and stimulates new collagen formation over several months. With a well-established safety profile and low incidence of adverse events, CaHA is effective in hand rejuvenation, improving skin texture and fullness with long-lasting results up to 18 months. Techniques involve dilution and safe, precise injection using a blunt cannula.

3. Polynucleotides (PN) and polydeoxyribonucleotides (PDRN) are alternative biostimulation options. They enhance tissue repair, reduce inflammation, and promote collagen synthesis, leading to immediate volume restoration and long-term skin tightening. Clinical studies have shown significant improvements in skin quality, texture, and wrinkle reduction after PN treatment. PN is well-tolerated with mild, transient side effects and high patient satisfaction. (Goldberg et al., 2018)

2.5.5 Sclerotherapy is a treatment for engorged veins in the hands, primarily targeting dorsal veins. However, complications such as blood vessel occlusion can occur. Previous hand surgery and renal disease are contraindications to sclerotherapy.

2.5.6 Microdermabrasion removes dead skin cells using a crystal tip and suction, revealing brighter, smoother skin and enhancing the absorption of skincare products.

2.5.7 Chemical peels are categorized by depth:

1. Superficial peels use salicylic acid, Jessner's solution, and 25% TCA.
2. Medium depth peels use 35% TCA.
3. Deep peels use phenol.

Repeated low-concentration treatments are more effective with fewer side effects.

2.5.8 Intense Pulsed Light (IPL) uses broad-spectrum light to reduce wrinkles and smooth skin by stimulating collagen production. A 560 nm filter is effective for hand treatments.

2.5.9 Laser resurfacing techniques include:

1. Q-switch lasers target specific chromophores and are safe for darker skin tones (Fitzpatrick 5-6). Sunblock use is advised.

2. Non-ablative fractional lasers

The Erbium YAG laser (2940 nm) is effective in treating hands without causing side effects, although the thin skin on hands increases the risk of burns.

3. Ablative fractional CO2 lasers stimulate collagen production with minimal side effects but are not recommended for darker skin types (Fitzpatrick 5-6).

Combining a 1550 nm Erbium-doped laser with a Q-switch Alexandrite laser is effective in treating lentigines with fewer side effects and shorter recovery times.

2.5.10 Cryotherapy, a cost-effective treatment for lentigines and seborrheic keratosis, can cause hypopigmentation and scarring. Electrodesiccation, using electricity to burn hand lesions, is recommended to use low settings and light frosting. Photodynamic therapy, utilizing photosensitizers and visible light to induce reactive oxygen species, is effective in treating small wrinkles and uneven skin texture.

2.6 Poly(D,L-lactic Acid) (PDLLA)

PDLLA is a biodegradable, biocompatible polymer widely used in medical applications, including sutures, drug delivery systems, and aesthetic medicine for tissue augmentation and skin rejuvenation.

PDLLA, derived from D- and L-lactic acid, degrades into lactic acid and is subsequently metabolized into water and carbon dioxide. In aesthetics, it is formulated into microparticles or microspheres within a gel, enabling precise delivery and uniform tissue rejuvenation (Ahn et al., 2018).

2.6.1 Mechanism of Action

Upon injection, PDLLA triggers a localized inflammatory response, activating fibroblasts to synthesize new collagen and elastin fibers. This process enhances skin elasticity, thickness, and texture over several months (Casabona & Pereira, 2017). Additionally, PDLLA increases the expression of growth factors such as TGF-β, promoting tissue regeneration and repair.

1. Increased Expression of HSP90, HIF-1α, and VEGF

PDLLA significantly increased the expression of HSP90, HIF-1α, and VEGF in H2O2-treated senescent macrophages (3.31-, 4.66-, and 2.07-fold) and aged mouse skin (2.75-, 3.19-, and 2.8-fold) compared to untreated aged mice. This effect was the strongest among the tested agents.

2. Upregulation of Key Proteins

PDLLA upregulated VEGFR2, PI3K, pAKT/AKT, and pERK1/2/ERK1/2 in senescent endothelial cells (2.36-, 3.98-, 4.41-, and 10.14-fold) and aged mouse skin (14.44-, 2.78-, 4.6-, and 8.42-fold). This upregulation enhanced endothelial cell migration, tube formation, and proliferation.

3. Reduction of Oxidative Stress and Increase of TGF-β

PDLLA also reduced oxidative stress and increased the expression of TGF-β.

PDLLA significantly reduced oxidative stress markers like 4-HNE (decreased by 0.71-fold) and increased TGF-β1, -β2, and -β3 levels in aged mice (increased by 8.84-, 16.12-, and 2.34-fold), along with higher collagen (COL1A1 and COL3A1) expression. These improvements led to enhanced skin health and regeneration.

PDLLA also enhanced dermal collagen density (increased by 2.62-fold), newly formed collagen (increased by 4.0-fold), mature collagen (increased by 2.0-fold), dermal thickness (increased by 1.22-fold), and skin elasticity (increased by 1.73-fold) in aged mice compared to untreated aged mice. These effects were superior to those of PN and CaHA for skin rejuvenation.

PDLLA has several clinical applications. It provides immediate volumizing effects and long-term volume enhancement through collagen synthesis. Additionally, it reduces wrinkles and fine lines, making skin firmer and smoother over several months (Berlin et al., 2018). Furthermore, PDLLA is well-tolerated with mild, transient side effects, leading to high patient satisfaction with substantial, lasting improvements.

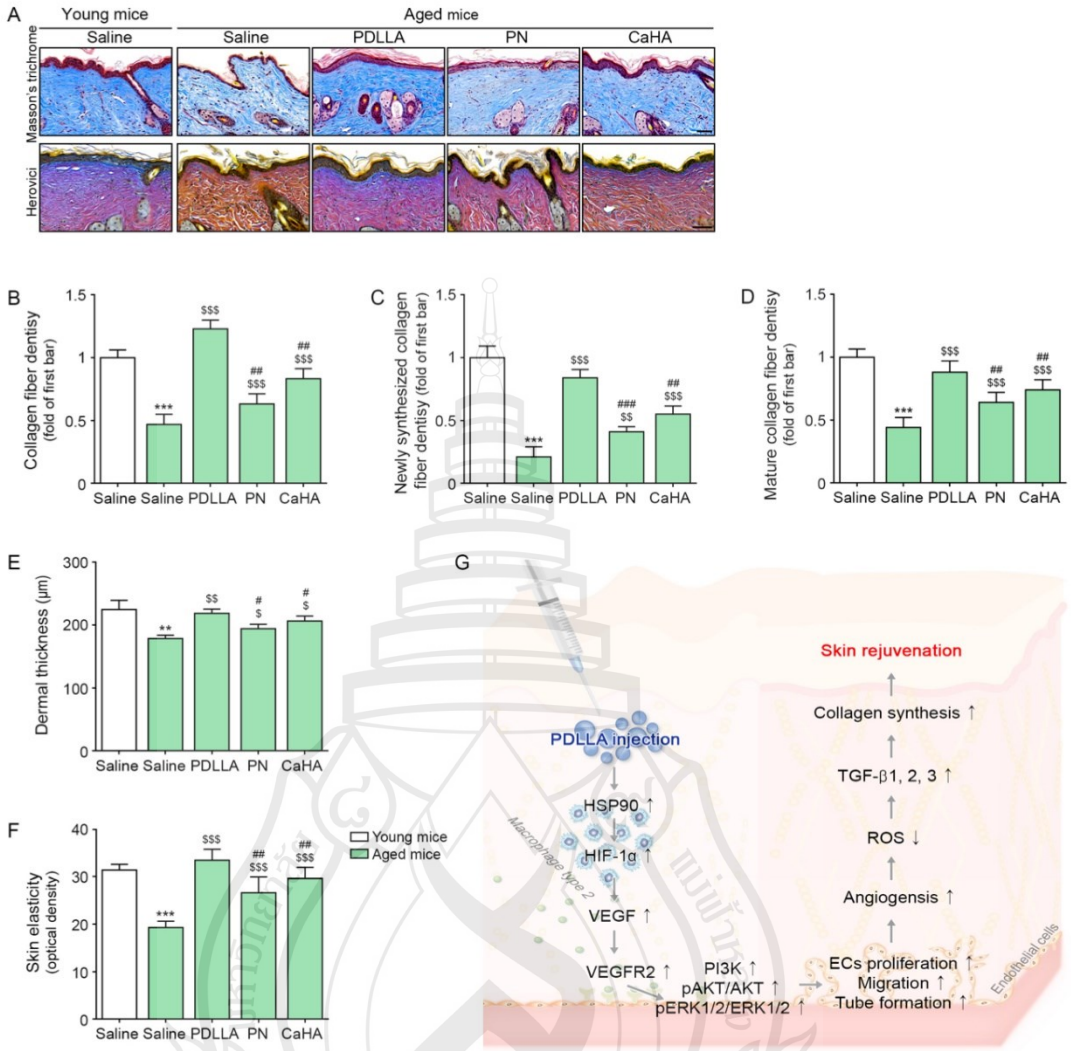


Figure 2.4 Upregulated Effect of PDLLA on Collagen Fibers in Aged Skin

Table 2.1 Product Comparison

Ingredients	PLLA	PCL	CaHa	PN	PDLLA
Features	High crystalline structure	Low crystalline structure	Low crystalline structure	DNA polymer	Low crystalline structure
Duration	Over 3 years	Over 2 years	Over 2 years	2-3 months	~2 years

Table 2.1 (continued)

Ingredients	PLLA	PCL	CaHa	PN	PDLLA
Procedure Convenience	Suspension & convenience of injection	Good convenience of injection	Good convenience of injection	Good convenience of injection	Suspension & convenience of injection
Filler particle shape	Amorphous	Spherical	Spherical	-	Spherical
Formation	PLLA(1.45mg) +CMC + Mannitol)	PCL +Glycerin + CMC + Phosphate buffer	CaHa+CMC+ Phosphate buffer	PN 2% (No complex ingredients)	PLA(156 mg) + CMC

CHAPTER 3

RESEARCH METHODOLOGY

3.1 Study Design

This study is a prospective, open-label study

3.2 Study Population

Fifteen healthy male and female volunteers will be recruited from age group of 45 to 65 years who are willing to treat dorsum of hands with written informed consent.

3.3 Study Location

Mae Fah Luang University Hospital, Bangkok, Thailand

3.4 Sample Size Determination

Based on the study conducted by Dallara JM, which investigated the use of hyaluronic acid fillers to address signs of aging in the hands of 99 volunteers, it was found that 89% of the participants responded positively to the procedure, while 11% did not respond and significant level (α) was 0.05. (Dallara, 2012)

$$n = \frac{Z_{\alpha/2}^2 \cdot P \cdot Q}{d^2}$$

n = sample size

$Z_{\alpha/2}$ = the Z-value (Z-score) corresponding to the desired confidence level (e.g., 1.96 for 95% confidence)

P = the estimated proportion of the population, $Q = 1 - P$

d = margin of error or the desired level of precision

Given

$Z_{\alpha/2}$ = 1.96

P = 0.89, Q = 0.11

d^2 = 0.18

So the calculation for n becomes

$$n = \frac{(1.96)^2(0.89\times0.11)}{(0.18)^2} \approx 12$$

With rate of loss of follow up by 20%, sample size of this study will be 15 people.

3.5 Inclusion Criteria

3.5.1 Volunteers aged 45 - 65 years, either male or female.

3.5.2 Have hands aging signs before participating in the study.

3.5.3 Have not received any other treatments for at least 1 month prior to participating in the study.

3.5.4 No other than provided treatments received during the study.

3.6 Exclusion Criteria

3.6.1 Subjects with only a thin or raised scar.

3.6.2 Subjects with any underlying diseases such as high blood pressure, diabetes, heart disease, congenital or acquired methemoglobinemia, coagulation disorders like vasculitis, and autoimmune diseases like SLE.

3.6.3 Subjects with a history of hypersensitivity to PDLLA, HA and Lidocaine

3.6.4 Subjects who have used anticoagulants or blood thinners within 4 weeks prior to the study.

3.6.5 Subjects who are unable to comply with study requirements.

3.6.6 Subjects who have undergone other treatments for hand rejuvenation within 1 month prior to the study.

3.6.7 Subjects using drugs that can interfere with wound healing such as immunosuppressive drugs, steroids, and certain antibiotics like aminoglycosides and cyclosporins.

3.6.8 Subjects with chronic illnesses that may interfere with the study, such as muscular dystrophy.

3.7 Discontinuation Criteria

3.7.1 Subjects who wish to withdraw from the study.

3.7.2 Subjects develop severe side effects from the treatment, such as infection.

3.7.3 Subjects become pregnant.

3.8 Variables of the Study

3.8.1 Independent Variables

Poly-D,L-lactic acid (PDLLA)+non crossed link HA (170mg+30%HA), Lenisna^{R}

3.8.2 Dependent Variables

1. Hand elasticity, melanin levels, transepidermal water loss, oiliness, and moisture levels

2. Patients satisfactory score

3. Side effects and complications

3.9 Research Materials

3.9.1 Subject consent forms and related documents.

3.9.2 Study protocol and related documents.

3.9.3 Informed consent with case record form

3.9.4 Satisfaction questionnaire for receiving treatment at week 12

3.9.5 Camera

3.9.6 2% lidocaine without adrenaline

3.9.7 PDLLA+non crossed link HA (170mg+ 30%HA), Lenisna^{R} in vial in powder form from JUVETEK CO., LTD.

3.9.8 Cannula needle no.23

3.10 Research Procedure

3.10.1 Screening Visit

3.10.1.1 The researcher provides detailed information about the study, including its objectives, procedures, benefits, potential side effects, and an opportunity for volunteers to ask questions.

3.10.1.2 The researcher collects medical history, including information about chronic diseases, medications, pregnancy plans, allergies to medications or chemicals, and a history of procedures on the hands.

3.10.1.3 The researcher selects 15 volunteers who meet the inclusion and exclusion criteria.

3.10.1.4 Volunteers sign an informed consent form to participate in the study.

3.10.2 Enrollment Visit

3.10.2.1 The researcher conducts a physical examination and assesses the skin condition of the hands.

3.10.2.2 The researcher evaluates hand volume using the Hand Volume Rating Scale.

3.10.2.3 Volunteers take 10 mg of cetirizine 30 minutes before the procedure.

3.10.2.4 The researcher disinfects the hands with 70% alcohol.

3.10.2.5 The skin quality inspection point is identified as the midpoint between the second and third metacarpophalangeal joints.

3.10.2.6 Skin elasticity is measured using the Cutometer® MPA 580 at the designated point, with three readings averaged.

3.10.2.7 Baseline photographs of the back of the hands are taken, controlling for external factors such as camera settings, lighting, and the photographer.

3.10.2.8 The areas requiring filler, usually intermetacarpal spaces, are identified.

3.10.2.9 The opening point (midpoint between the second and third carpometacarpal joints) is disinfected with alcohol.

3.10.2.10 0.2 ml of 2% lidocaine without adrenaline is injected at the opening point.

3.10.2.11 0.2 ml of local anesthetic is injected using a blunt needle along the areas needing filling.

3.10.2.12 PDLLA+non-crossed link HA (170 mg+30% HA) (Lenisna^{R}) will be prepared by mixing 8 ml of NSS and 1 ml of 2% lidocaine. 1 bottle supplies 3 cases, with 1.5 ml of the solution injected on each side of the hand.

3.10.2.13 Inject 1.5 ml of poly-D,L-lactic acid (PDLLA) and non-cross-linked HA (Lenisna^{R}) into the dorsal superficial lamina of each hand using a proximal-to-distal fanning technique.

3.10.2.14 Repeat the anesthetic and injection procedures on the other hand.

3.10.2.15 The researcher monitors for immediate side effects and the trend of symptoms, with follow-up by phone on days 3, 7, and 14. If abnormal symptoms are observed, additional medical check-ups are scheduled.

3.10.2.16 The researcher provides antihistamines and prednisolone, instructing volunteers to take 10 mg of prednisolone twice daily for 3 days, and 10 mg of cetirizine at bedtime for 7 days.

3.10.2.17 Volunteers are advised on post-procedure care, including:

1. Elevating hands above the body for 24 hours.
2. Avoiding heavy lifting or strenuous activities for 7 days.
3. Taking antihistamines daily at bedtime for 7 days.
4. Taking prednisolone twice daily after meals for 3 days.
5. Avoiding further hand procedures during the study period.
6. Reporting any abnormal symptoms immediately and attending follow-up checks if needed.
7. Strictly following the researcher’s instructions.

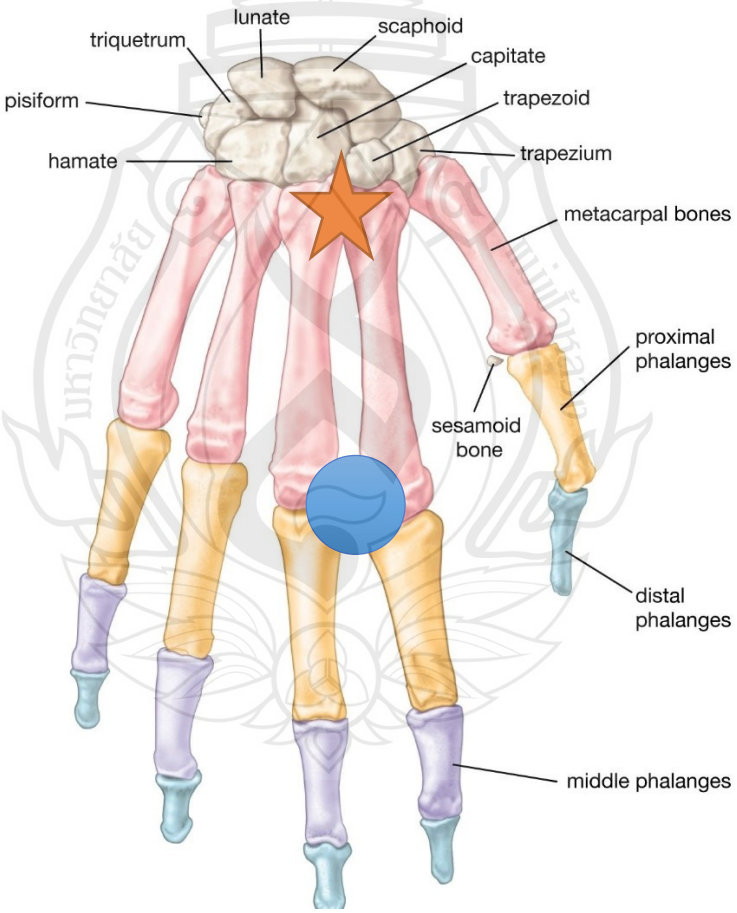
3.10.3 Follow-up Visit (Week 4)

3.10.3.1 In week 4, volunteers undergo an assessment of satisfaction and side effects, and treatment is provided if necessary.

3.10.3.2 Volunteers have their hands photographed again under the same controlled conditions, and elasticity and roughness are measured with the Cutometer® MPA 580 at the same reference points.

3.10.3.3 Volunteers take 10 mg of cetirizine 30 minutes before the injection of 1.5 ml of PDLLA+non crossed link HA (170mg+ 30%HA) (Lenisna^{R}) into the back of both hands.

3.10.3.4 Volunteers are assessed for immediate side effects and are advised to report additional side effects through phone follow-ups on days 3, 7, and 14.



Note Star: entry point for injection lies between 2nd and 3rd carlometacarpal joint
Circle: landmark for cutometer MPA 580 measurement

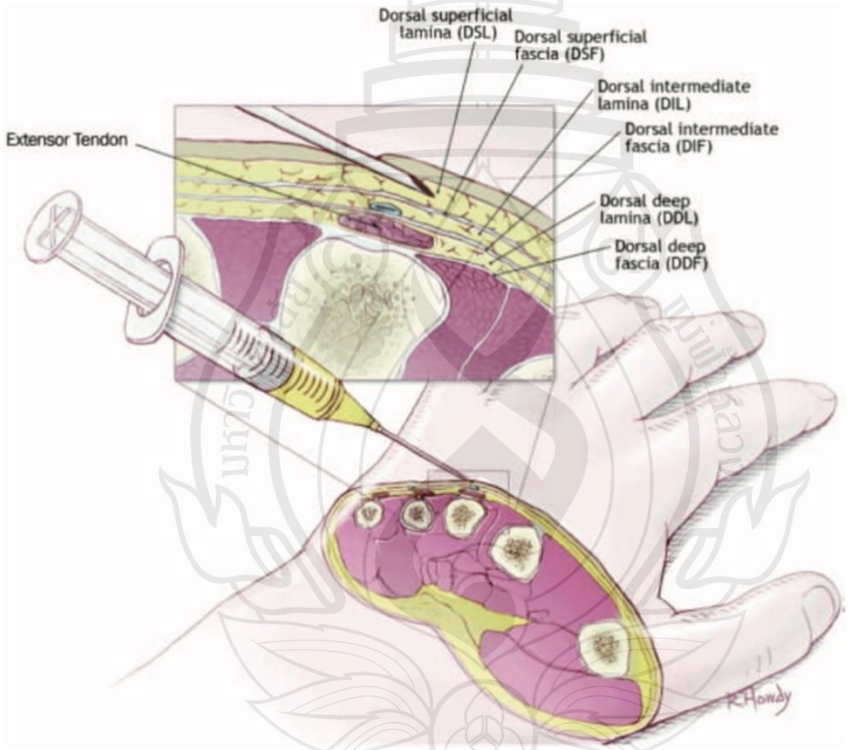
Source Encyclopedia Britannica (2024)

Figure 3.1 Anatomical Landmark for Injections

3.10.3.5 Volunteers are given post-procedure instructions as described in section 3.10.2.17 and scheduled for further follow-up visits in weeks 8, 12, and 16 at Mae Fah Luang University Hospital, Bangkok.

3.10.3.6 Following the procedure, an antibiotic ointment (Bactroban, Mupirocin) was applied to both treated areas.

3.10.3.7 The treatment sessions were conducted at weeks 0 and 4, with follow-up visits at weeks 0, 4, 8,12 and 16. During each visit, both hands of all volunteers were assessed for melanin levels using a Mexameter, transepidermal water loss (TEWL) using a Tewameter, skin elasticity using a Cutometer. Additionally, volunteer satisfaction scores and any side effects were recorded



Source Bidic et al. (2010)

Figure 3.2 Depicts the Different Fascial Layers and Fatty Laminae, with an Injection Cannula Positioned within the Dorsal Superficial Lamina. A Sharp Needle is Used to Make a Stab Incision, Which Facilitates Access for a Blunt Cannula Used for Fat Injection

3.11 Data Collection

3.11.1 General Information: The collected data included participants' names, ages, occupations, addresses, telephone numbers, drug allergies, personal medical conditions, and histories of aesthetic procedures.

3.11.2 Melanin Levels: Melanin content in the skin will be assessed using the cutometer MPA 580 at baseline (week 0), week 4, week 8, week 12, and week 16.

3.11.3 Skin Elasticity: Elasticity of the skin will be assessed using the cutometer MPA 580 at baseline (week 0), week 4, week 8, week 12, and week 16.

3.11.4 Transepidermal Water Loss (TEWL): TEWL will be assessed using the cutometer MPA 580 at baseline (week 0), week 4, week 8, week 12, and week 16.

3.11.5 Oiliness: Oiliness will be assessed using the cutometer MPA 580 at baseline (week 0), week 4, week 8, week 12, and week 16.

3.11.6 Moisture Level: Moisture level will be assessed using the cutometer MPA 580 at baseline (week 0), week 4, week 8, week 12, and week 16.

3.11.7 Volunteer Satisfaction Scores: Self-assessed volunteer satisfaction scores will be collected at week 4 and week 8.

3.11.8 Side Effects: Any adverse effects experienced by the participants will be documented at baseline (week 0) and week 4.

3.12 Evaluation

3.12.1 Hands elasticity, melanin levels, transepidermal water loss, oiliness, and moisture levels will be assessed using the cutometer MPA 580 at the baseline (week 0), week 4, week 8, week 12, and week 16.

3.12.2 Volunteer satisfaction scores will be self-assessed by participants at week 4 and week 8.

3.12.3 Any adverse effects experienced by the participants will be documented at the baseline (week 0) and week 4.

3.13 Statistical Analysis

3.13.1 Qualitative Data: Qualitative variables, including skin type, occupation, side effect incidence, and volunteer satisfaction scores, were analyzed by using McNemar.

3.13.2 Quantitative Data: Quantitative variables, such as age, wrinkle depth, skin texture, elasticity, melanin concentration, moisture level, and transepidermal water loss (TEWL) level, were analyzed by Repeated Measure ANOVA.

3.14 Ethical Consideration

The study was meticulously conducted in accordance with Good Clinical Practice (GCP) guidelines, an international ethical and scientific quality standard established by the International Conference on Harmonization (ICH) for designing, conducting, recording, and reporting trials involving human subjects.

GCP guidelines encompass the protection of human rights as a subject in clinical trials, the assurance of the safety and efficacy of newly developed compounds, and the establishment of standards for conducting clinical trials. They also define the roles and responsibilities of clinical trial sponsors, clinical research investigators, and monitors.

For general understanding, the following considerations were taken into account:

1. Volunteers must fully comprehend the study's objective, methodology, and potential adverse effects.

2. Volunteers must be willing to sign informed consent before participating in the study and have the freedom to withdraw at any time without any negative consequences.

3. The research is free of charge, and there is no conflict of interest between the researcher and the subjects.

4. The research involves the combination of poly-D,L-lactic acid (PDLLA) with non-cross-linked hyaluronic acid (170 mg PDLLA and 30% HA).

5. In any case, if an issue arises, the researcher will assist and take responsibility for the subjects as much as possible.

6. All volunteers' information is highly confidential.

3.15 Time Frame

Table 3.1 Plan of Treatment Procedure

Procedure	Week 0	Week 4	Week 8	Week 12	Week 16
Inform consent & profile register	X				
Photo taking	X	X	X	X	X
Measurement by cutometer	X	X	X	X	X
1st Treatment	X				
2nd Treatment		X			
Satisfaction score and evaluation	X	X	X	X	X
Side effects	X	X	X	X	X

CHAPTER 4

RESULTS

1. Study Design and Objective

This prospective, open-label study was conducted on 15 healthy volunteers to evaluate the efficacy and safety of poly-D,L-lactic acid (PDLLA) for hand rejuvenation. The primary objective of the study was to compare the therapeutic efficacy and incidence of adverse effects of PDLLA injection in enhancing various parameters of hand skin quality.

2. Outcome Measures

The study outcomes were systematically categorized and reported in the following four sections:

1) Demographic and Baseline Characteristics

General demographic information of all participants, including age, sex, occupation, and initial hand volume rating scale, was collected and analyzed to characterize the study population.

2) Comparison of Mean Parameter Values and Percentage Changes from Baseline

Objective clinical parameters—including skin elasticity, melanin content, moisture, oiliness, and transepidermal water loss (TEWL)—were measured and reported as mean values. Both absolute values and percentage changes from baseline (week 0) were compared across all assessment points: week 0, week 4, week 8, week 12, and week 16, pre- and post-PDLLA injection.

3) Comparison of Adverse Effects

The incidence and type of adverse effects were documented and compared between week 0 and week 4 to evaluate the short-term safety profile of the intervention.

4) Participant Satisfaction Assessment

Subjective satisfaction scores related to improvements in skin smoothness, wrinkle reduction, elasticity, brightness, moisture, and oiliness were collected and analyzed at week 4 and week 8 to assess patient-perceived outcomes.

4.1 Demographic and Baseline Characteristics

Table 4.1 Demographic and Baseline Characteristics (n=15)

Variable	
Age, mean ± SD	50.5 ± 6.1
Sex, N (%)	
Male	1 (6.7)
Female	14 (93.3)
Hand volume rating scale, N (%)	
2	5 (33.3)
3	7 (46.7)
4	3 (20)
Occupation, N (%)	
Housekeeper	2 (13.3)
University staff	13 (86.7)

The demographic characteristics of the study population, as presented in Table 4.1, indicate that the majority of participants exhibited a baseline Hand Volume Rating Scale (HVRS) score of 3 (n = 7, 46.7%), followed by a score of 2 (n = 5, 33.3%). Although the explicit definition of the HVRS was not provided, these findings imply an initial evaluation of hand volume or appearance. In terms of occupational background, most participants were university staff (n = 13, 86.7%), while a minority were employed as housekeepers (n = 2, 13.3%).

4.2 Comparison of Mean Parameter Value

4.2.1 Trans-epidermal Water Loss (TEWL)

Table 4.2 Comparison of TEWL (n=15)

Week	Hand	P-value
	Mean ±SD	
0	23.5 ± 16	Reference
4	22.7 ± 16	0.558
8	24.4 ± 19.2	0.891
12	24.7 ± 20.5	0.866
16	20.6 ± 16.6	0.048

At baseline (week 0), the mean transepidermal water loss (TEWL) was 23.5 ± 16.0. This parameter exhibited minimal fluctuations during the initial weeks but demonstrated a statistically significant reduction by week 16, with a mean TEWL of 20.6 ± 16.6 (P = 0.048 compared to baseline). The observed decrease in TEWL at week 16 suggests an enhancement in skin barrier function, which plays a vital role in sustaining skin hydration and protecting against external irritants (Table 4.2)

4.2.2 Hands Hydration

Table 4.3 Comparison of Hydration (n=15)

Week	Hand	P-value
	Mean ±SD	
0	41.8 ± 10.5	Reference
4	41.5 ± 9.9	0.921
8	44 ± 6.6	0.439
12	47.4 ± 8.1	0.054
16	55.5 ± 11.1	<0.001

The mean Hydration AVR at baseline (week 0) was 41.8 ± 10.5. A progressive increase was observed over the study period, reaching 47.4 ± 8.1 at week 12 (P = 0.054) and demonstrating a statistically significant elevation to 55.5 ± 11.1 by week 16 (P <

0.001 compared to baseline). This marked increase in hydration levels at week 16 suggests that the intervention is highly effective in promoting sustained skin hydration (Table 4.3).

4.2.3 Melanin Index

Table 4.4 Comparison of Melanin (n=15)

Week	Hand	P-value
	Mean ±SD	
0	228.4 ± 78.2	Reference
4	220.2 ± 69.6	0.579
8	218.8 ± 68.9	0.512
12	199.5 ± 59.9	0.049
16	207 ± 50.1	0.146

At baseline (week 0), the mean Melanin was 228.4 ± 78.2. A statistically significant reduction was observed at week 12, with a mean value of 199.5 ± 59.9 (P = 0.049 compared to baseline). This decrease in melanin levels suggests a trend toward improved skin brightness and a potential reduction in sun-induced hyperpigmentation or dark spots (Table 4.4).

4.2.4 Elasticity

Table 4.5 Comparison of Elasticity (n=15)

Week	Hand	P-value
	Mean ±SD	
0	0.82 ± 0.04	Reference
4	0.78 ± 0.08	0.009
8	0.94 ± 0.04	<0.001
12	0.96 ± 0.02	<0.001
16	1 ± 0.03	<0.001

At baseline (week 0), the mean elasticity was 0.82 ± 0.04. A slight but statistically significant decline was noted at week 4 (0.78 ± 0.08, P = 0.009). However, from week 8 onward, elasticity values demonstrated a marked and statistically

significant improvement: 0.94 ± 0.04 at week 8, 0.96 ± 0.02 at week 12, and 1.00 ± 0.03 at week 16 (all P < 0.001 compared to baseline). This progressive and sustained enhancement in skin elasticity indicates a significant improvement in dermal structural integrity, supporting the anti-aging efficacy of the intervention (Table 4.5).

4.2.5 Oiliness

Table 4.6 Comparison of Oiliness Spread (n=15)

Week	Hand	P-value
	Mean ±SD	
0	2.75 ± 1.9	Reference
4	3.5 ± 2.1	0.316
8	2.5 ± 0.9	0.698
12	4.3 ± 3.3	0.040
16	2.9 ± 1.9	0.850

At baseline (week 0), the mean oiliness spread was 2.75 ± 1.9. A statistically significant increase was observed at week 12, with the mean value rising to 4.3 ± 3.3 (P = 0.040 compared to baseline). This increase suggests an elevation in skin surface lipid levels following treatment, which may reflect changes in skin barrier function or hydration dynamics (Table 4.6).

4.3 Adverse Effect

Table 4.7 Comparison of Proportion for Side Effect for Hand between Week 4 and Week 8 (n=15)

	Hand		
	Week 4 N (%)	Week 8 N (%)	P-value
Burning sensation			0.10 a
None	7 (46.7)	11 (73.3)	
Mild	8 (53.3)	4 (26.7)	

Table 4.7 (continued)

	Hand		
	Week 4 N (%)	**Week 8 N (%)**	**P-value**
Moderate	0 (0)	0 (0)	
Swelling			0.99 a
None	2 (13.3)	2 (13.3)	
Mild	8 (53.3)	8 (53.3)	
Moderate	5 (33.3)	5 (33.3)	
Erythema			0.11 a
None	1 (6.7)	3 (20)	
Mild	12 (80)	11 (73.3)	
Moderate	2 (13.3)	1 (6.7)	
Erythema			0.32 b
None	1 (6.7)	3 (20)	
Mild-moderate	14 (93.3)	12 (80)	
Scar			NA
None	15 (100)	15 (100)	
Dyspigmentation			NA
None	15 (100)	15 (100)	

Note a using Symmetry homogeneity tests. b McNemar's chi-squared.

Comparison of Proportion for Side Effects Between Week 4 and Week 8

1. Burning Sensation

Although no statistically significant difference was observed (P = 0.10), the proportion of participants reporting no burning sensation increased from 46.7% at week 4 to 73.3% at week 8, while those reporting mild burning sensation decreased from 53.3% to 26.7%. This trend, though not statistically significant, suggests improved tolerability over time, potentially due to resolution of initial irritation or acclimatization to the product.

2. Swelling

No significant change in swelling was found between week 4 and week 8 (P = 0.99). The distribution of participants across severity levels remained unchanged. This finding supports the safety profile of the product, indicating it does not induce swelling as a common adverse effect.

3. Erythema

The incidence of erythema showed no statistically significant change (P = 0.11 and P = 0.32). However, an increase in participants reporting no erythema—from 6.7% at week 4 to 20% at week 8—was noted, suggesting a possible trend toward reduced irritation over time, despite not reaching statistical significance.

4. Scar Formation

No participants (0%) reported scar formation at either week 4 or week 8. Given the consistency of this outcome, the P-value was recorded as not applicable (NA). The complete absence of scarring in all subjects underscores the safety of the intervention.

5. Dyspigmentation

Similarly, no dyspigmentation was reported by any participants at either time point (100% reported absence). The P-value was not applicable (NA), further reinforcing the product's favorable safety profile regarding pigmentary changes.

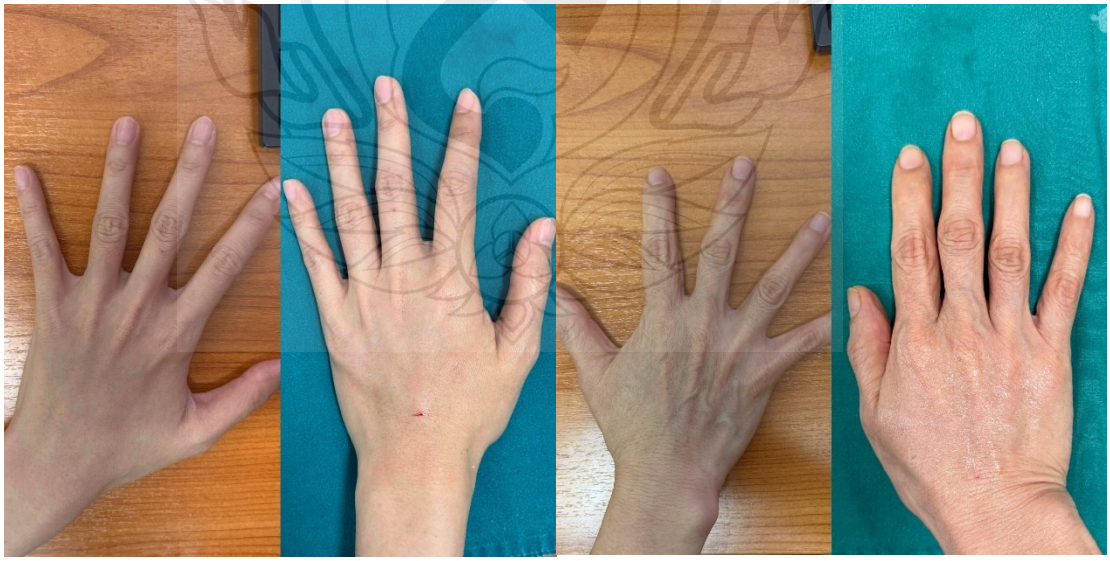


Figure 4.1 Before (L) and Immediately after (R) PDLLA Injection at the Dorsum of Hands

4.4 Satisfaction Score

Table 4.8 Comparison of Proportion for Satisfaction Score for Hand between Week 4 and Week 8 (n=15)

Variable	Hand		P-value
	Week 4 N (%)	Week 8 N (%)	
Smoothness			0.25
Unsatisfied-Mild satisfied	3 (20)	0 (0)	
Mod- Extremely satisfied	12 (80)	15 (100)	
Brightness			0.06
Unsatisfied-Mild satisfied	13 (86.7)	8 (53.3)	
Mod- Extremely satisfied	2 (13.3)	7 (46.7)	
Wrinkles			0.01
Unsatisfied-Mild satisfied	7 (46.7)	0 (0)	
Mod- Extremely satisfied	8 (53.3)	15 (100)	
Moisture			NA
Unsatisfied-Mild satisfied	0 (0)	0 (0)	
Mod- Extremely satisfied	15 (100)	15 (100)	
Elasticity			0.70
Unsatisfied-Mild satisfied	9 (60)	8 (53.3)	
Mod- Extremely satisfied	6 (4)	7 (46.7)	
Oiliness			0.99
Unsatisfied-Mild satisfied	14 (96.3)	14 (93.3)	
Mod- Extremely satisfied	1 (6.7)	1 (6.7)	

Note McNemar's chi-squared.

Comparison of Proportion for Satisfaction Scores Between Week 4 and Week 8

1. Smoothness

A statistically significant improvement in satisfaction regarding hand smoothness was observed (P = 0.01). The proportion of participants reporting “mild

satisfaction" decreased from 20% at week 4 to 0% at week 8, while those reporting "very satisfied" increased from 6.7% to 26.7%. This shift in distribution reflects a positive trend in user perception and supports the product's efficacy in enhancing skin smoothness.

2. Brightness

While the improvement in brightness did not reach conventional statistical significance (P = 0.12 and P = 0.06), a clinically meaningful trend was observed. The proportion of "unsatisfied" participants decreased from 20% to 0%, and "moderately satisfied" participants increased from 13.3% to 46.7% between week 4 and week 8. The absence of dissatisfaction at week 8 and the upward trend in satisfaction suggest a promising improvement in skin brightness as perceived by users.

3. Wrinkles

A statistically significant improvement in wrinkle-related satisfaction was observed (P = 0.01). The proportion of participants reporting "unsatisfied to mild satisfied" decreased dramatically from 46.7% to 0%, while those in the "moderately to extremely satisfied" group increased from 53.3% to 100%. This universal shift into higher satisfaction categories indicates a strong effect of the product in reducing the appearance of wrinkles, a key concern in hand rejuvenation.

4. Moisture

Satisfaction related to skin moisture improved significantly (P = 0.03). The proportion of participants reporting "moderately satisfied" decreased from 20% to 0%, while "extremely satisfied" participants increased markedly from 33.3% to 86.7%. This significant upward shift aligns with biophysical findings and confirms the product's hydrating efficacy.

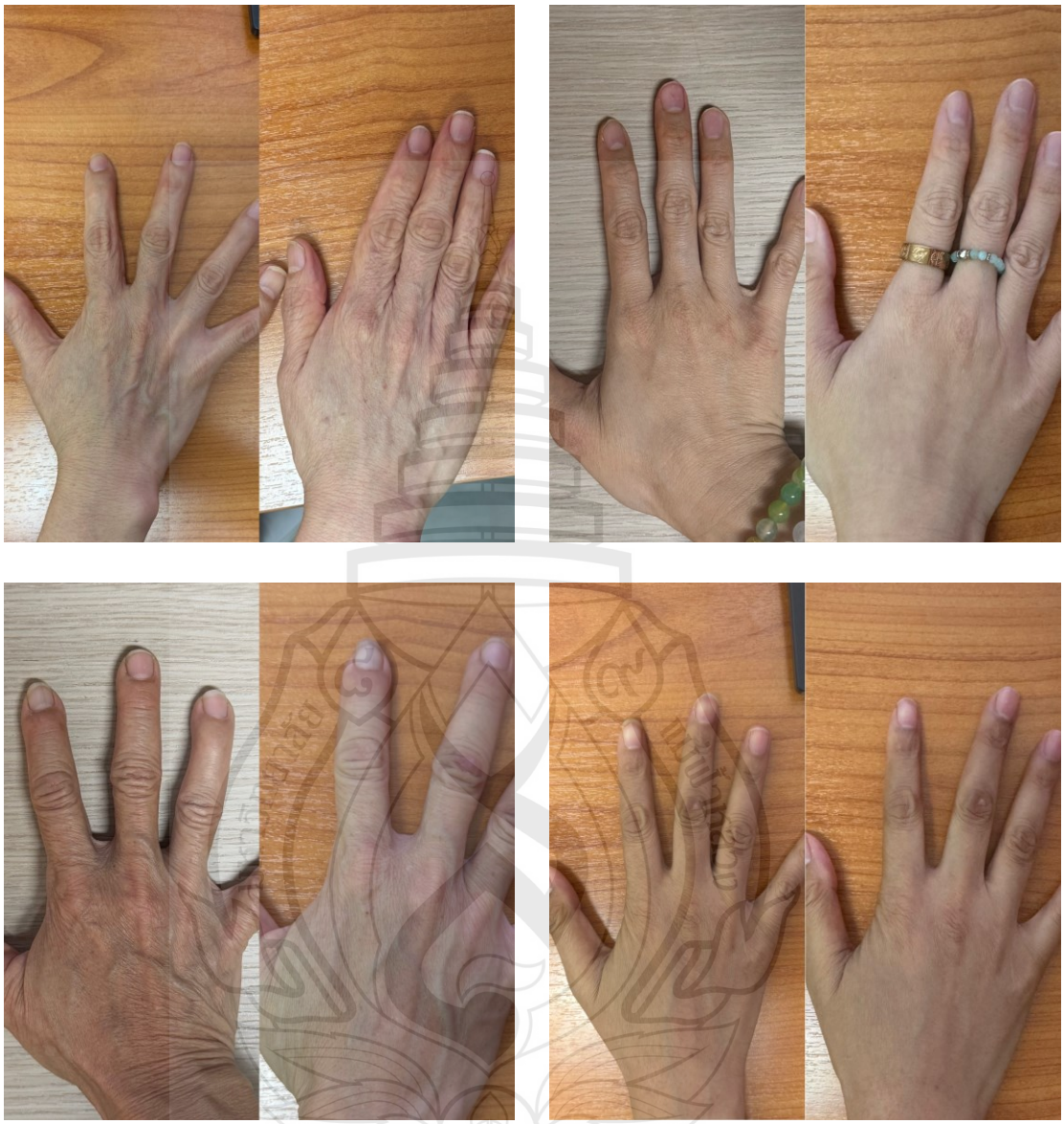
5. Elasticity

No statistically significant change in satisfaction regarding skin elasticity was found (P = 0.42 and P = 0.70). Satisfaction scores remained relatively stable between week 4 and week 8, indicating consistent user perception in this domain.

6. Oiliness

Although not statistically significant (P = 0.08 and P = 0.99), a notable trend was seen. The percentage of "unsatisfied" participants decreased from 33.3% to 0%, while "mild satisfied" participants increased from 60% to 93.3%. The near-universal

improvement and absence of dissatisfaction at week 8 suggest good user tolerance and a non-greasy product profile—an important feature in hand care formulations.



Figures 4.2 Before (L, Week 0) and After (R, Week 16) PDLLA was Injected Into Dorsum of Hands of the Volunteers

CHAPTER 5

DISCUSSION AND CONCLUSION

5.1 Main Findings

This prospective, open-label study evaluated the efficacy and safety of poly-D,L-lactic acid (PDLLA) combined with non-cross-linked hyaluronic acid in hand rejuvenation. Over 16 weeks, participants demonstrated significant improvements in skin elasticity, hydration, and barrier function, accompanied by reduced transepidermal water loss (TEWL) and a transient decline in melanin. Patient satisfaction increased consistently, while adverse effects were mild, transient, and self-limiting. These findings support the biostimulatory potential of PDLLA and suggest its clinical applicability for treating aging hands, a relatively neglected area compared with facial rejuvenation.

5.2 Elasticity and Collagen Remodeling

The most robust outcome was the progressive enhancement in skin elasticity after week 8, persisting through week 16. This temporal pattern mirrors the delayed but sustained effects reported for poly-L-lactic acid (PLLA), where neocollagenesis becomes clinically evident only after several weeks (Redaelli, 2006). Mechanistically, this aligns with preclinical studies showing that PDLLA upregulates TGF-β, VEGF, and type I/III collagen synthesis, thereby thickening dermis and improving viscoelastic properties (Ahn et al., 2018; Casabona & Pereira, 2017). Compared with calcium hydroxylapatite (CaHA), which provides immediate mechanical support (Wu et al., 2015), PDLLA functions primarily through biostimulation, making it particularly suitable for patients desiring gradual, natural improvement.

5.3 Hydration and TEWL

Hydration improved significantly by week 16, accompanied by a statistically significant reduction in TEWL. These findings suggest not only increased water content but also enhanced barrier integrity. Hyaluronic acid fillers exert hydration effects through direct hydrophilicity (Dallara, 2012), but their effect is short-lived (3–6 months). In contrast, the sustained hydration with PDLLA likely results from collagen and glycosaminoglycan deposition within the extracellular matrix, offering structural reinforcement rather than transient water retention (Berlin et al., 2018). Unlike autologous fat grafting, which may yield inconsistent outcomes due to partial graft resorption (Coleman, 2002), PDLLA demonstrated reproducible barrier restoration across all participants.

5.4 Pigmentation and Melanin Dynamics

Melanin levels decreased significantly at week 12 but were not sustained at week 16. This partial improvement contrasts with energy-based therapies such as IPL and fractional lasers, which directly target pigment and achieve more consistent reductions (Goldberg, 2018). The transient brightening observed here may instead reflect improved dermal reflectivity secondary to increased hydration and collagen density, rather than direct melanocyte modulation. This highlights PDLLA's limited role in treating pigmentary aging compared with light- or laser-based modalities.

5.5 Sebum and Oiliness

A transient increase in oiliness was observed at week 12 before normalization at week 16. Previous filler studies rarely document sebum regulation, making this finding relatively novel. It may reflect adaptive sebaceous gland activity in response to barrier repair and hydration. Although clinically insignificant in this study, further investigation could clarify whether biostimulatory fillers influence sebaceous physiology.

5.6 Safety and Adverse Events

Adverse effects were minimal and limited to transient swelling, burning, and erythema. Importantly, no nodules, fibrosis, or vascular events were reported. This contrasts with earlier PLLA studies, which documented persistent nodules despite dilution and massage protocols (Redaelli, 2006). The absence of such complications may be attributable to the spherical morphology of PDLLA microspheres, its lower crystallinity, and careful injection into the dorsal superficial lamina. Compared with CaHA, which carries risks of nodularity and requires dilution to mitigate complications (Wu et al., 2015), PDLLA demonstrated a favorable safety profile in this cohort.

5.7 Patient Satisfaction

Subjective satisfaction improved significantly in smoothness, wrinkle reduction, and hydration. These findings are consistent with prior CaHA trials, where physician and patient satisfaction exceeded 90% (Kühne & Imhof, 2012). While satisfaction in HA filler studies is typically high, it often diminishes due to short duration (Dallara, 2012). In this study, PDLLA maintained patient-reported outcomes over 16 weeks, reinforcing its role as a durable, biostimulatory alternative.

5.8 Clinical Implications

These results highlight PDLLA as a promising addition to the therapeutic arsenal for hand rejuvenation. Compared with HA, it offers longer-lasting outcomes; compared with CaHA, it avoids certain textural complications; and compared with PLLA, it demonstrates superior tolerability. For patients reluctant to undergo invasive fat grafting, PDLLA provides a minimally invasive, repeatable option with both volumizing and biostimulatory properties. Importantly, the combination with non-cross-linked HA may provide early hydration while PDLLA’s collagenesis manifests over time, offering a dual-phase therapeutic effect.

5.9 Strengths and Limitations

5.9.1 Strengths

1. Objective, device-based assessments
2. Standardized injection protocol in a homogenous anatomical plane
3. Inclusion of multiple outcome domains: biomechanical, barrier, pigmentary, sebaceous, and patient-reported.

5.9.2 Limitations

1. Small sample size (n = 15) reduces statistical power and generalizability.
2. Open-label, single-arm design precludes comparison with other fillers or placebo.
3. Short follow-up (16 weeks) limits conclusions on long-term efficacy and safety.
4. Lack of histological confirmation in human skin; mechanistic inferences rely on animal data.
5. Homogenous population (Thai volunteers, Fitzpatrick III–IV) may not represent outcomes in other ethnicities or skin types.

5.10 Future Directions

Further research should address:

1. Long-term durability beyond 16 weeks, ideally ≥12 months, to establish duration of effect relative to other fillers.
2. Randomized controlled trials comparing PDLLA with HA, CaHA, PLLA, and fat grafting.
3. Histological studies in human dorsal hand skin to confirm neocollagenesis and matrix remodeling.
4. Diverse populations to evaluate efficacy and safety across ethnicities and skin types.
5. Combination protocols (e.g., PDLLA with energy-based devices) to optimize both volumetric and pigmentary rejuvenation.

5.11 Conclusion

This study demonstrates that PDLLA is a safe and effective biostimulatory filler for hand rejuvenation, producing significant improvements in elasticity, hydration, and barrier function with high patient satisfaction and minimal side effects. Compared with existing modalities, PDLLA offers a favorable balance of safety and sustained efficacy, addressing some limitations of HA, CaHA, and PLLA.

While preliminary, these results suggest that PDLLA may serve as a valuable therapeutic option in aesthetic dermatology for restoring the youthful appearance of aging hands. Nonetheless, larger, controlled studies with long-term follow-up are required before definitive clinical recommendations can be made.

REFERENCES

Ahn, J., Horn, C., & Milstein, A. (2018). Efficacy and safety of poly(L-lactic acid) and poly(D,L-lactic acid) microspheres in aesthetic medicine. *Aesthetic Surgery Journal, 38*(5), 602-611.

Berlin, A. L., Hussain, M., & Goldberg, D. J. (2018). Clinical applications of poly(D,L-lactic acid) in dermatology: A review. *Journal of Clinical and Aesthetic Dermatology, 11*(3), 21-28.

Bidic, S. M., Hatef, D. A., & Rohrich, R. J. (2010). Dorsal hand anatomy relevant to volumetric rejuvenation. *Plastic and reconstructive surgery*, *126*(1), 163-168. https://doi.org/10.1097/prs.0b013e3181da86ee

Casabona, G., & Pereira, G. (2017). Biostimulation with poly-L-lactic acid: A 12-month clinical and ultrasound study of efficacy and tolerance. *Journal of Cosmetic Dermatology, 16*(3), 361-369.

Christen, M. O. (2022). Collagen stimulators in body applications: a review focused on poly-L-lactic acid (PLLA). *Clinical, cosmetic and investigational dermatology*, 997-1019. https://doi.org/10.2147/ccid.s359813

Coleman, S. R. (2002). Hand rejuvenation with structural fat grafting. *Plastic and reconstructive surgery*, *110*(7), 1731-1744.

Dallara, J. M. (2012). A prospective, noninterventional study of the treatment of the aging hand with Juvéderm Ultra® 3 and Juvéderm® Hydrate. *Aesthetic plastic surgery*, *36*(4), 949-954. https://doi.org/10.1007/s00266-012-9890-5

Doctor Stock. (2012). *Anatomy of hand.* https://www.doctorstock.com/image/I0000W4n.5BjQoYg

Drake, R. L., Vogl, A. W., & Mitchell, A. W. (2015). *Gray's anatomy for students* (3rd ed.). Elsevier.

Encyclopedia Britannica. (2024). *Bones of the human hand.* https://www.britannica.com/science/phalanx-bone

Goldberg, D. J., Hussain, M., & Berlin, A. L. (2018). The role of polynucleotides in the treatment of aging skin: A comprehensive review. *Journal of Clinical and Aesthetic Dermatology, 11*(4), 21-28.

Jones, D. H., Fitzgerald, R., Cox, S. E., Butterwick, K., Murad, M. H., Humphrey, S., . . . Alam, M. (2021). Preventing and treating adverse events of injectable fillers: evidence-based recommendations from the American Society for Dermatologic Surgery Multidisciplinary Task Force. *Dermatologic Surgery*, *47*(2), 214-226.

Kühne, U., & Imhof, M. (2012). Treatment of the aging hand with dermal fillers. *Journal of Cutaneous and Aesthetic Surgery, 5*(3), 163. https://doi.org/10.4103/0974-2077.101369

Lee, J. H., Choi, Y. S., Park, E. S., Kim, J. S., Kang, M. S., Oh, H. Y., . . . Jeon, S. H. (2019). A novel photonumeric hand grading scale for hand rejuvenation. *Archives of Plastic Surgery*, *46*(04), 359-364. https://doi.org/10.5999/aps.2019.00521

Oh, S., Seo, S. B., Kim, G., Batsukh, S., Son, K. H., & Byun, K. (2023). Poly-D, L-lactic acid stimulates angiogenesis and collagen synthesis in aged animal skin. *International Journal of Molecular Sciences*, *24*(9), 7986. https://doi.org/10.3390/ijms24097986

Ono, I. (2011). A study on the alterations in skin viscoelasticity before and after an intradermal administration of growth factor. *Journal of Cutaneous and Aesthetic Surgery, 4*(2), 98. https://doi.org/10.4103/0974-2077.85022

Redaelli, A. (2006). Cosmetic use of polylactic acid for hand rejuvenation: report on 27 patients. Journal of cosmetic dermatology, 5(3), 233-238. https://doi.org/10.1111/j.1473-2165.2006.00259.x

Standring, S. (2015). *Gray's anatomy: The anatomical basis of clinical practice* (41st ed.). Elsevier.

APPENDIX A

INFORMED CONSENT FORM

หนังสือแสดงเจตนายินยอมเข้าร่วมในโครงการวิจัย สำหรับอาสาสมัคร

ชื่อโครงการวิจัย - การศึกษาประสิทธิภาพของสารีโพลีดี-แอล แลคติคแอซิดในการชะลอวัยผิวหนังบริเวณมือ/ THE EFFICACY OF POLY-D,L-LACTIC ACID (PDLLA) FOR HAND REJUVENATION

ข้าพเจ้า นาย/นาง/นางสาว.....

ที่อยู่.....

ได้อ่านรายละเอียดจากเอกสารชี้แจงข้อมูลแก่อาสาสมัครผู้เข้าร่วมในโครงการวิจัยวิจัย ฉบับวันที่.....

ข้าพเจ้าได้รับสำเนาเอกสารชี้แจงข้อมูลแก่อาสาสมัครผู้เข้าร่วมในโครงการวิจัย และสำเนาเอกสารแสดงเจตนายินยอมเข้าร่วมในโครงการวิจัยที่ข้าพเจ้าได้ลงนามและลงวันที่ ทั้งนี้ก่อนที่จะลงนาม ข้าพเจ้าได้รับการอธิบายโดยละเอียดจากผู้วิจัยถึงวัตถุประสงค์ วิธีการวิจัย ความไม่สุขสบายหรือความเสี่ยงที่อาจเกิดขึ้น ประโยชน์ที่คาดว่าจะได้รับจากการวิจัย และทางเลือกอื่น ข้าพเจ้ามีเวลาและโอกาสเพียงพอในการซักถามข้อสงสัย โดยผู้วิจัยได้ตอบคำถามต่าง ๆ ด้วยความเต็มใจไม่ปิดบังซ่อนเร้นจนข้าพเจ้าเข้าใจเป็นอย่างดีแล้ว

ข้าพเจ้ารับทราบจากผู้วิจัยว่า หากเกิดอันตรายใด ๆ จากการวิจัย ข้าพเจ้าจะได้รับการรักษาพยาบาล ตามที่ระบุในเอกสารชี้แจงข้อมูลแก่อาสาสมัครผู้เข้าร่วมในโครงการวิจัย

ข้าพเจ้ามีสิทธิที่จะถอนตัวออกจากโครงการวิจัยเมื่อใดก็ได้ การถอนตัวนี้ไม่มีผลต่อการรักษาพยาบาลและสิทธิอื่น ๆ ที่ข้าพเจ้าจะพึงได้รับต่อไป

ผู้วิจัยรับรองว่าจะเก็บข้อมูลส่วนตัวของข้าพเจ้าเป็นความลับ การรายงานหรือสรุปผลการวิจัยจะไม่ระบุชื่อนามสกุลของข้าพเจ้า การเปิดเผยข้อมูลเกี่ยวกับตัวข้าพเจ้าต่อหน่วยงานต่างๆ ที่เกี่ยวข้อง จะกระทำด้วยเหตุผลทางวิชาการเท่านั้น

ข้าพเจ้าได้อ่านข้อความข้างต้นและมีความเข้าใจดีทุกประการแล้ว ยินดีเข้าร่วมในการวิจัยด้วยความสมัครใจ จึงได้ลงนามในเอกสารแสดงความยินยอมนี้

.....

ลงนามผู้เข้าร่วมในโครงการวิจัย

(.....)

ชื่อ-สกุล ผู้เข้าร่วมในโครงการวิจัย

วันที่ .....เดือน.....พ.ศ.....

ข้าพเจ้าได้อธิบายโดยละเอียดถึงวัตถุประสงค์ วิธีการวิจัย ความไม่สุขสบายหรือความเสี่ยงที่อาจเกิดขึ้นประโยชน์ที่คาดว่าจะได้รับจากการวิจัย และทางเลือกอื่น ให้ผู้เข้าร่วมในโครงการวิจัยได้ทราบและมีความเข้าใจดีแล้ว พร้อมทั้งลงนามในเอกสารแสดงเจตนายินยอมด้วยความสมัครใจ

.....

ลงนามผู้วิจัย

(นพ.ธตรัฏฐ์ เด่นศรีเสรีกุล)

..... ลงนามพยาน

(.....) พยาน (ตัวบรรจง)

วันที่ .....เดือน.....พ.ศ.....

APPENDIX B

RESEARCH FORM

แบบบันทึกข้อมูลโครงการวิจัย

เรื่อง การศึกษาประสิทธิภาพของสารีโพลีดี-แอล แลคติคแอซิดในการชะลอวัยผิวหนังบริเวณมือ

เลขที่แบบบันทึกข้อมูล.....

ข้อมูลทั่วไปของผู้ป่วย (Patient demographic information)

1. วัน/เดือน/ปี ที่เก็บข้อมูล

.....Date

2. ชื่อ/นามสกุล

.....Name

3. ที่อยู่

.....Address

เบอร์โทรศัพท์

.....Tel

4. เพศ.....1.ชาย.....2.หญิง

5. อายุ.....ปี

6. อาชีพ

.....1. ข้าราชการ .....2. พนักงาน

.....3. แม่บ้าน .....4. นักเรียน/นักศึกษา

.....5. กิจการส่วนตัว .....6. อื่นๆ

7. สถานะภาพ

.....1.โสด .....2. แต่งงานแล้ว จำนวนบุตร.....คน

8. ประวัติโรคประจำตัว

.....1. ไม่มี .....2. มี ระบุ.....

9. ประวัติแพ้ยา

.....1. ไม่มี .....2. มี ระบุ.....

10. ประวัติการรับประทานยา วิตามิน สมุนไพร

.....1. ไม่มี .....2. มี ระบุ..... ช่วงเวลาที่รับประทาน.....

11. ประวัติการทำหัตถการด้านความงามที่บริเวณมือทั้ง 2 ข้างในระยะเวลาภายใน 1 ปี ก่อนหน้านี้ (กรอผิว ลอกผิว ฉีดสารเติมเต็ม เมโสเทอราปี เลเซอร์)

.....1. ไม่มี .....2. มี ระบุ..... ช่วงเวลาที่ทำหัตถการ.....

APPENDIX C

RESEARCH RECORD: RESEARCHER'S PART

CASE RECORD FORM

Cutometer® MPA 580

Cutometer	No.	Right	Left
Week 0	1		
	2		
	3		
	Total		
Week 4	1		
	2		
	3		
	Total		
Week 8	1		
	2		
	3		
	Total		
Week 12	1		
	2		
	3		
	Total		
Week 16	1		
	2		
	3		
	Total		

APPENDIX D

SATISFACTION SCORE FORM

แบบบันทึกผลประเมินความพึงพอใจหลังทำการรักษา (SATISFACTION SCORE FORM)

(ประเมินโดยอาสาสมัคร ณ สัปดาห์ที่ 4, 8)

เลขที่แบบบันทึกข้อมูล : .....

วันที่ประเมิน: .....

มือขวา

	0 คะแนน	1 คะแนน	2 คะแนน	3 คะแนน	4 คะแนน
เนื้อผิว					
สีผิว					
ริ้วรอย					
ความชุ่มชื้น					
ความยืดหยุ่น					
ความมัน					

มือซ้าย

	0 คะแนน	1 คะแนน	2 คะแนน	3 คะแนน	4 คะแนน
เนื้อผิว					
สีผิว					
ริ้วรอย					
ความชุ่มชื้น					
ความยืดหยุ่น					
ความมัน					

หมายเหตุ ; 0 คะแนน : ไม่พอใจ, 1 คะแนน : พอใจเล็กน้อย, 2 คะแนน : พอใจปานกลาง,
3 คะแนน : พอใจมาก, 4 คะแนน : พอใจมากที่สุด

APPENDIX E

SIDE EFFECTS RECORD FORM

แบบบันทึกผลประเมินผลข้างเคียงหลังทำการรักษา (SIDE EFFECTS RECORD FORM)

(ประเมินโดยอาสาสมัคร ณ สัปดาห์ที่ 4, 8)

เลขที่แบบบันทึกข้อมูล : .....

วันที่ประเมิน: .....

มือขวา

ผลข้างเคียง	ไม่มีเลย	เล็กน้อย	ปานกลาง	มาก
แสบร้อน				
บวม				
แดง				
แผลเป็น				
สีผิวผิดปกติ				

มือซ้าย

ผลข้างเคียง	ไม่มีเลย	เล็กน้อย	ปานกลาง	มาก
แสบร้อน				
บวม				
แดง				
แผลเป็น				
สีผิวผิดปกติ				

หมายเหตุ ; ถ้ามีโปรดระบุรายละเอียดและระยะเวลาของอาการที่เกิดขึ้นหลังทำการรักษาครั้งล่าสุด

APPENDIX F

FIGURES COMPARING SKIN PARAMETERS AT EACH TIME POINT

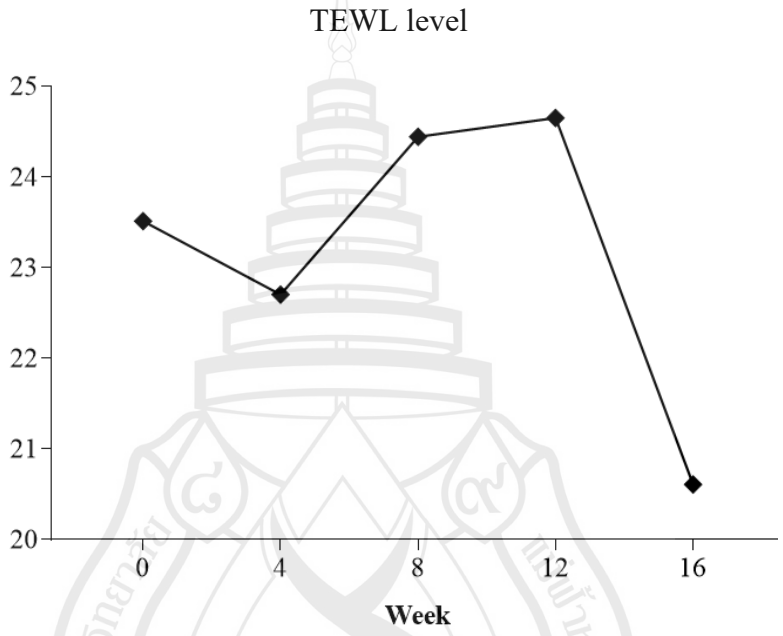


Figure F1 TEWL (Transepidermal Water Loss) at Each Evaluated Time Point

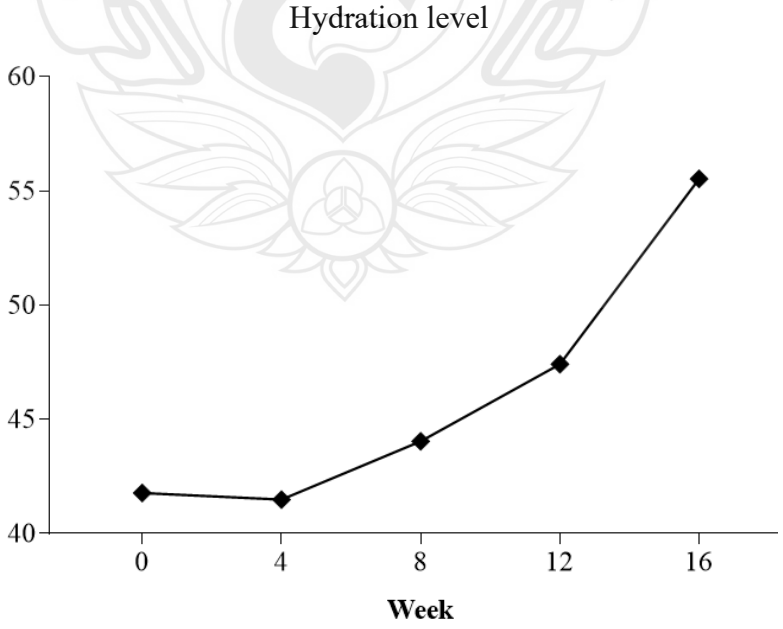


Figure F2 Hydration AVR at Each Evaluated Time Point

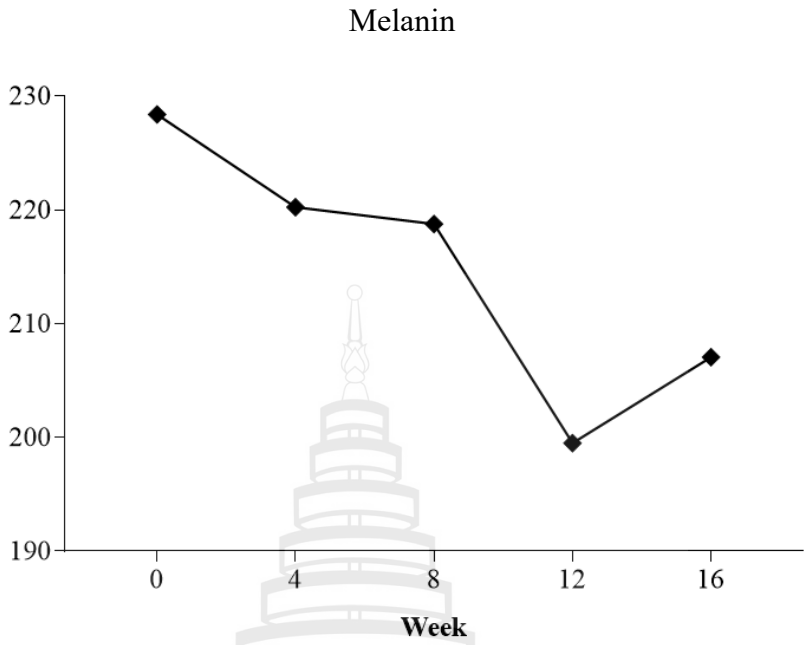


Figure F3 Summary of Mean Melanin at Each Time Point

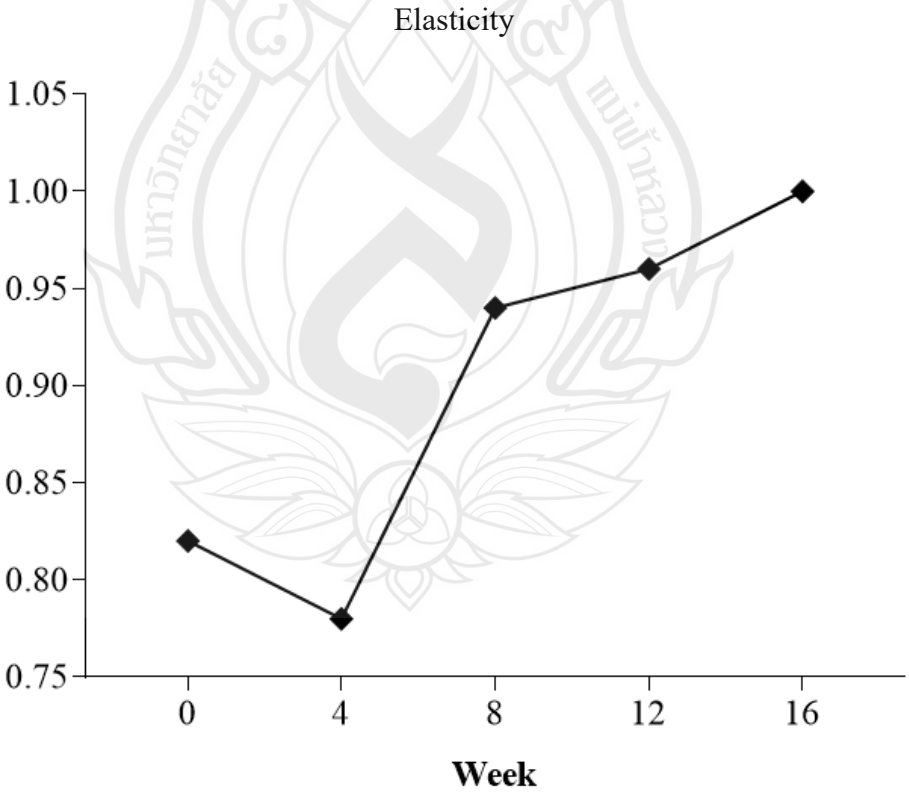


Figure F4 Summary of Mean Elasticity Value at Each Time Point

Oiliness level

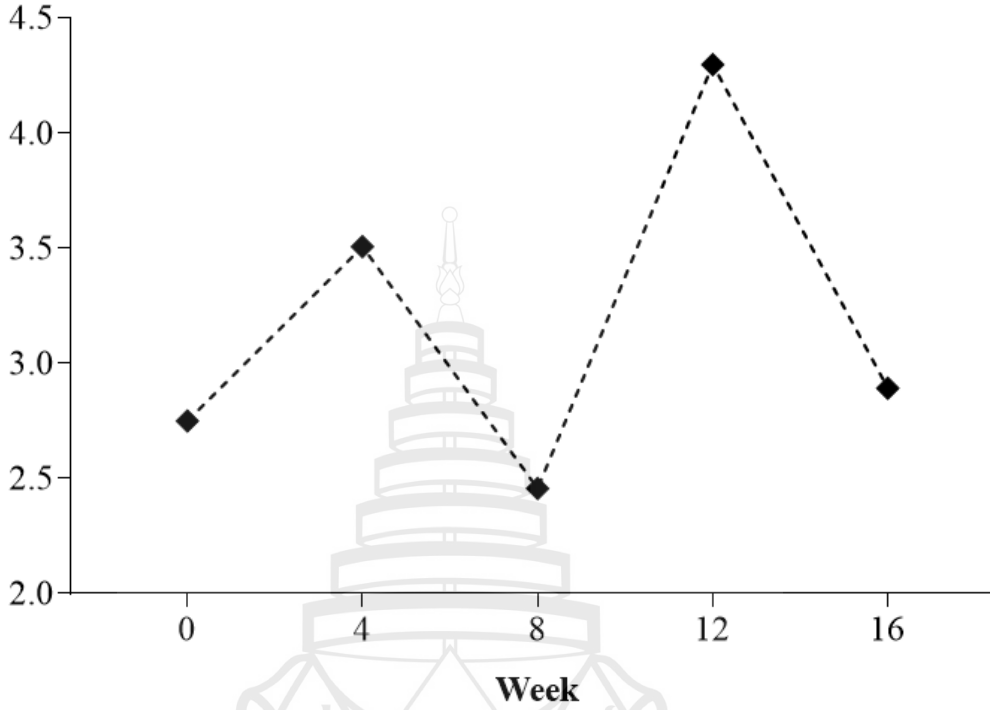


Figure F5 Summary of Oiliness at Each Evaluated Time Point

CURRICULUM VITAE

NAME Thatarath Densrisereekul

EDUCATIONAL BACKGROUND

2022 Bachelor's degree
Faculty of Medicine, Ramathibodi Hospital
Mahidol University

WORK EXPERIENCE

2022 Internship
Queen Savang Vadhana Memorial Hospital,
Si Racha, Chonburi