

FORMULATION AND EVALUATION OF COLLAGEN-BASED QUERCETIN CREAM

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ABSTRACT

Background: Inflammation is a fundamental pathophysiological feature in numerous chronic diseases including arthritis, dermatitis, and wound-related conditions. Synthetic anti-inflammatory agents, though effective, are associated with significant adverse effects such as gastrointestinal bleeding, cardiovascular risks, and localized skin irritation. This has prompted renewed interest in plant-derived therapeutics with safer profiles. **Objective:** The present study aimed to formulate and evaluate a collagen-based quercetin cream incorporating wool fat (lanolin) and cetostearyl alcohol for enhanced antioxidant protection, skin repair, and moisturization. **Methodology:** Four formulations (F1-F4) were developed with varying concentrations of quercetin (0.50-2.00g) and collagen (0.50-1.00g), along with oleic acid as a penetration enhancer, wool fat as an emollient, cetostearyl alcohol as a stabilizing base, and suitable preservatives.

Collagen was solubilized in an acidic medium, followed by incorporation of quercetin into the cream base through trituration. The prepared formulations were evaluated for physicochemical properties including spreadability, phase separation, viscosity, washability, and microbial growth determination. **Results:** All formulations demonstrated satisfactory physicochemical characteristics. F3 exhibited the highest spreadability

(8.4 g.cm/sec), optimal viscosity (24,500 cP), excellent washability, and maintained stability without phase separation. The viscosity increased progressively from F1 to F4 (18,500 to 28,000 cP). All formulations (F1-F4) showed no microbial growth, confirming adequate preservative efficacy. **Conclusion:** The collagen-quercetin cream represents a promising topical therapeutic formulation for wound healing applications. Among all formulations, F3 demonstrated the best overall performance with optimum spreadability, suitable viscosity, good stability, and excellent washability. The synergistic action of quercetin's antioxidant and anti-inflammatory properties combined with collagen's tissue regenerative potential makes this formulation a viable alternative to synthetic anti-inflammatory agents for topical wound care.

KEYWORDS: Quercetin, Collagen, Wound Healing, Topical Cream, Anti-inflammatory.

1. INTRODUCTION

1.1 Global Context: The Need For Anti Inflammatory Therapies

Inflammation, the body's protective response to injury, infection, or irritation, is a key pathophysiological feature in a wide array of prevalent chronic diseases, including arthritis, dermatitis, and pain syndromes. Effective therapeutic intervention is crucial for mitigating pain, limiting tissue damage, and restoring quality of life. For decades, Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) have served as the primary pharmacological strategy for symptomatic relief due to their mechanism of action involving the inhibition of the *cyclooxygenase (COX) enzyme pathway*.^[1]

1.2 The Problem with Synthetic Anti-Inflammatory Agents

While highly effective, the widespread and long-term use of synthetic NSAIDs, whether administered orally or topically, is associated with significant limitations. Systemic oral therapy often leads to serious dose-limiting adverse effects, including peptic ulceration, gastrointestinal bleeding, and increased cardiovascular and renal risks. Furthermore, topical application of synthetic NSAIDs, though safer than oral intake, can still cause localized irritation, hypersensitivity reactions, and is often limited by poor percutaneous absorption and drug solubility issues within the vehicle.^[2] This has fuelled a global resurgence of interest in phytotherapy-the use of plant-derived medicines-to identify safer, yet potent, alternatives.^[3]

1.3 Understanding Inflammation: Mechanism and Phases Inflammation is classified into acute and chronic phases

1.3.1 Acute Inflammation

This rapid, localized, and protective response is initiated by cellular damage and involves the release of chemical mediators (prostaglandins, leukotrienes, cytokines). These mediators trigger localized vasodilation and increased vascular permeability, leading to the classic signs of inflammation: redness, heat, swelling, and pain. Cellular components, particularly neutrophils, rapidly migrate to the site to engulf pathogens and clear debris.^[4]

1.3.2 Chronic Inflammation

This phase occurs when the noxious stimulus persists or due to inappropriate immune responses. It is characterized by the infiltration of mononuclear cells (macrophages and lymphocytes), tissue destruction, and simultaneous attempts at repair (fibrosis).^[5]

1.4 Classification Of Semi Solid Topical Dosage Forms

The effective delivery of a drug, especially a herbal extract with complex characteristics, necessitates choosing a vehicle that ensures optimal stability, release, and patient compliance. Semisolid preparations are classified based primarily on their base composition:

1.4.1 Ointments, Pastes, and Lotions

- Ointments: These are semi-solid preparations, typically anhydrous and greasy (hydrocarbon bases). They provide an occlusive layer, enhancing drug penetration and hydration. Advantages include prolonged contact time and potency of drug action. Application is mainly for dry, scaly skin lesions or for sustained local effects.^[6]
- Pastes: Very stiff, thick preparations containing high percentages of finely powdered solids dispersed in a greasy base. Advantages include acting as protective barriers and absorbing serous secretions. Application is typically for weepy or raw dermatological lesions.^[7]
- Lotions: Liquid or semi-liquid systems (usually emulsions or suspensions), used for cooling and quick absorption over large areas. Advantages are easy spreadability and cooling effect. Application is for widespread skin conditions like rashes and sunburn.^[8]

1.4.2 Creams: Types, Advantages, Applications

Creams are semi-solid emulsions of an oil phase and an aqueous phase stabilized by emulsifying agents. they are the most common and cosmetically acceptable of topical carriers.

Table 01: Creams: Types, Advantages, Applications.

Cream type	composition	Key advantages	Typical application
Oil-in-water(O/W)	Oil droplets dispersed in a continuous aqueous phase (water- washable).	Non-greasy (“vanishing cream” effect), high patient compliance, readily washed off, rapid cooling effect due to water evaporation.	Antifungal treatments, light moisturizing, quick-action topical corticosteroids.
Water-in-oil(W/O)	Water droplets dispersed in a continuous oil phase (greasy /oleaginous).	More occlusive and moisturizing than O/W, prevents water loss from the skin.	Emollient use for dry skin conditions (eczema, xerosis), barrier creams

2. Rationale Of The Study

Wound healing is a complex biological process involving inflammation control, tissue regeneration, and collagen deposition. The present study focuses on the formulation of a topical wound healing cream incorporating quercetin and collagen as active therapeutic agents. Quercetin is a natural flavonoid well known for its antioxidant, anti-inflammatory, and antimicrobial properties, which help reduce oxidative stress and promote faster tissue repair. Collagen, an essential structural protein of the extracellular matrix, plays a vital role in cell proliferation, tissue regeneration, and wound contraction, thereby enhancing the healing process.

In this formulation, quercetin was incorporated as the primary active compound while collagen was used as a co-drug to improve tissue repair and matrix formation. The cream base was prepared using oleic acid as a penetration enhancer, wool fat as an emollient, cetostearyl alcohol as a stabilizing base, and a suitable preservative to maintain microbial stability. Four formulations (F1–F4) were developed with increasing concentrations of quercetin and collagen while maintaining the total weight at 10 g.^[9]

The preparation involved dissolving collagen in an acidic medium followed by incorporation of quercetin and gradual mixing into the ointment base through trituration until a uniform cream was obtained. The developed formulation is intended to enhance drug penetration, antioxidant protection, and collagen-mediated tissue regeneration, thereby accelerating the wound healing process.

Overall, the quercetin–collagen cream represents a promising topical therapeutic formulation for improving wound repair, reducing inflammation, and promoting faster skin regeneration.^[10]

A naturally occurring flavonoid with anti-inflammatory qualities, quercetin has gained attention as a possible modulator of tissue repair. Excessive inflammation and dysregulated myofibroblast differentiation are common causes of impaired wound healing and pathological scarring. However, current therapeutic approaches often fail to address these interconnected issues at the same time. By encouraging early wound closure through inflammation resolution and preventing scar formation through the inhibition of myofibroblast differentiation, this study explores whether quercetin can offer a dual therapeutic benefit.^[11]

In addition to being a crucial structural element of many organs, most notably the skin, collagen is also a key signaling molecule that controls every stage of wound healing. Because collagen powder can stop bleeding, attract immune and skin cells essential to wound healing, promote the formation of new blood vessels, and be left in wounds without irritating them or encouraging the growth of bacteria, it has great potential for wound healing and care when applied externally.^[12]

It has been discovered that quercetin affects the activity of enzymes that are essential for the synthesis of collagen. For instance, research has demonstrated that quercetin can increase the activity of prolyl hydroxylase, an enzyme that modifies collagen molecules post-translationally. By encouraging the creation of robust cross-links, prolyl hydroxylase aids in the stabilization of collagen fibers. Quercetin may help ensure that collagen fibers are properly assembled and stable by increasing the activity of this enzyme.^[13]

Collagen is an essential structural protein that gives the skin its firmness, elasticity, and strength. Collagen deterioration and the development of wrinkles and fine lines can result from the natural aging process as well as external factors like UV radiation and environmental pollutants. The anti-inflammatory and antioxidant qualities of quercetin help shield collagen fibers from inflammation and free radical damage, maintaining the structural integrity of the skin and delaying the onset of aging.^[14]

3. AIM

To formulate and evaluate a collagen-based quercetin cream incorporating wool fat (lanolin) and cetostearyl alcohol for enhanced antioxidant protection, skin repair & moisturization.

3.1 OBJECTIVES

- I. To evaluate the overall efficacy and safety and skin compatibility of the formulated cream.
- II. To incorporate wool fat (lanolin) as an emollient to improve skin hydration and reduce dryness.
- III. To use cetostearyl alcohol as an emulsifying and stabilizing agent for better consistency and texture of the cream.
- IV. To evaluate the physicochemical properties of the formulated cream such as pH, viscosity, spreadability, and stability.
- V. To study the role of collagen in promoting skin regeneration and wound healing.
- VI. To assess the antioxidant activity of quercetin in protecting skin from oxidative damage.
- VII. To evaluate the moisturizing and protective effects of the formulation on dry or cracked skin.
- VIII. To test the overall effectiveness, safety, and skin compatibility of the formulated cream.

4. MATERIALS AND METHODS

QUERCETIN



Image 01: Quercetin and its chemical structure.

Quercetin is a flavonol, which is a sub-category of flavonoids. Flavonoids are phytochemical compounds in plants, fruits, herbs, vegetables and nuts. Humans cannot make Trusted Source quercetin in their bodies, but many fruits, vegetables, and drinks contain it. Quercetin possesses antiviral and antibacterial qualities. According to laboratory experiments, quercetin can stop the growth of numerous bacteria, including *Staphylococcus aureus* and *Salmonella enteritidis*, *Escherichia coli*, *Aspergillus flavus* Proteus. Many viruses may be prevented from growing by quercetin and other flavonoids.^[15]

COLLAGEN

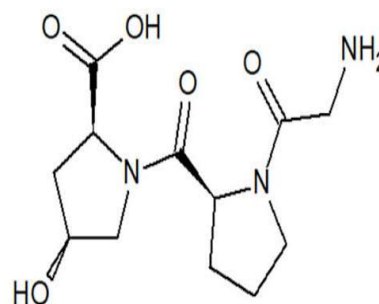


Image 01: Collagen and its chemical structure.

Your body gets strength, structure, and support from collagen. Maintaining your natural collagen levels becomes more difficult as you get older. This is especially true following menopause. The reason for this is that as time goes on, your body finds it more difficult to absorb the nutrients required to produce collagen.^[16]

Eating foods high in collagen, however, can help your body get past some of this absorption issue. As you age, this keeps your body stronger and healthier. Additionally, collagen aids in blood clotting, aids in the replacement of dead skin cells, forms a shield to keep your organs safe and permits the growth of new skin cells.^[17]

OLEIC ACID



Image 03: Oleic acid and its chemical structure.

The oleic acid serves as a penetration enhancer because of its distinct structure, the stratum corneum, the outermost layer of mammalian skin, poses a serious obstacle to the transdermal administration of medications.^[18] The extracellular lipids that serve as the main regulatory

channel for the penetration of small molecules appear to be the target of penetration enhancers which increase skin permeability.

LANOLIN (wool fat)



Image 04: Lanolin and its chemical structure.

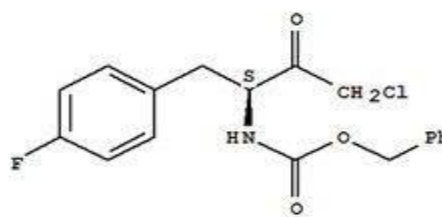
Lanolin (wool fat) and its derivatives helps in protection, treatment and beautification of human skin. The intercellular lipids found in the stratum corneum, the skin's outermost layer, are strikingly similar to the composition of lanolin. These lipids, which include cholesterol, cholesterol derivatives, and free fatty acids, are essential for controlling the moisture content of the skin.^[19]

Under normal conditions, water continuously evaporates from the skin's surface. However, a dry, stiff, and brittle stratum corneum may arise from insufficient rehydration from the lower epidermal layers.^[20] Lanolin has the amazing capacity to both rehydrate and stop moisture loss. Lanolin in personal care products is therefore extremely valuable. A straightforward experiment can be used to effectively illustrate this.

PRESERVATIVE

In pharmaceutical products, preservatives are essential for stopping microbial growth. Their main purpose is to prevent or slow the growth of microorganisms that contaminate or deteriorate these goods. Preservatives stop the growth of microorganisms in the following ways:

Microbial contamination prevention, prolonging shelf life, product safety, enhances the product performance, product consistency.^[21]

CETOSTEARYL ALCOHOL**Image 05: Cetosteryl Alcohol and its chemical structure.**

In pharmaceutical products, cetostearyl alcohol functions as a binder. It makes it easier to use and keeps the other ingredients from separating. Because it keeps other ingredients from reacting with one another, it also functions as a stabiliser. Though cetostearyl alcohol is primarily used because of its role in the consistency and structure of the product, it possesses some nourishing properties as well.^[22]

Composition And Concentrations Of Cream Formulations**Table 02: Composition And Concentrations Of Cream Formulations.**

Component	F1	F2	F3	F4
QUERCETIN	0.50g	1.00g	1.50g	2.00g
COLLAGEN	0.50g	0.70g	1.00g	1.00g
OLEIC ACID	0.02g	0.05g	0.07g	0.10g
WOOL FAT	2.00g	2.00g	2.00g	2.00g
PRESERVATIVES	0.01g	0.01g	0.01g	0.01g
CETOSTEARYL ALCOHOL	6.97g [qs]	6.24g [qs]	5.42g [qs]	4.89g [qs]

4.1 Procedure

- All the ingredients were weighed accurately as per the formulation table.
- Collagen was solubilized in a small amount of acid medium.
- The cream base was made by melting cetostearyl alcohol and woolfat together.
- The cream base was added with oleic acid and preservative and stirred continuously.
- The collagen solution and quercetin were mixed in the base by trituration.
- The mixture was stirred constantly until a smooth and uniform cream was obtained.
- The prepared cream was kept in appropriate containers and stored for evaluation tests.^[23]

5. LITERATURE REVIEW

Table 03: Literature review of collagen based wound healing.

AUTHOR	TITLE	EXPERIMENT	CONCLUSION
Mathew-Steiner S.S., Roy S., Sen C.K.	Collagen in Wound Healing	This study reviews the biological role of collagen in different phases of wound healing such as inflammation, proliferation, and remodeling. It evaluates how collagen-based materials support tissue repair.	Collagen plays a critical role in wound healing by promoting cell migration, angiogenesis, and tissue regeneration. It enhances healing efficiency and is widely used in wound care therapies.
George Washington University (GW Study)	GW Pilot Study Finds Collagen to be Effective in Wound Closure	A pilot clinical study tested collagen application on wounds to observe closure rate and healing improvement.	Collagen was found effective in accelerating wound closure and improving healing outcomes, indicating its potential as a therapeutic biomaterial.
Collagen Network (Article)	Does Quercetin Help Collagen? Exploring the Potential Benefits	This article analyzes the effect of quercetin (a natural antioxidant) on collagen production and protection.	Quercetin may support collagen synthesis and reduce degradation by acting as an antioxidant, helping improve skin repair and overall tissue health.
WebMD	Collagen: Health Benefits	This article explains the biological role of collagen in the human body and reviews its impact on skin, bones, and connective tissues.	Collagen is a major structural protein that supports skin elasticity, tissue repair, and overall body strength. It helps in forming new skin cells, improving hydration, and maintaining healthy joints and bones.
ScienceDirect (Chvapil et al.)	Collagen in Wound Healing and Biomedical Applications	The study evaluates collagen-based materials in wound healing and their effectiveness in tissue regeneration.	Collagen significantly enhances wound healing by promoting cell growth, tissue regeneration, and faster repair. It is widely used in biomedical and skin care applications.
Ataman Chemicals	Lanolin (Wool Fat) Uses	This article discusses the extraction and application of lanolin in skincare and pharmaceutical products.	Lanolin acts as an effective emollient that moisturizes skin, reduces dryness, and forms a protective barrier. It improves skin softness and is widely used in creams and ointments.
VedaOils	Cetostearyl Alcohol Uses for	This article explains the function of cetostearyl alcohol	Cetostearyl alcohol works as an emulsifier and

	Skin Care	in cosmetic formulations.	stabilizer in creams. It improves texture, enhances moisture retention, and provides a smooth, non-irritating feel to the skin.
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6. EVALUATION TESTS

➤ Spreadability

The property of a semi-solid preparation (such as ointments, creams, gels, or food pastes) which describes the ease with which it can be applied or spread uniformly over a surface with minimal force.^[24]

It is an important physical parameter, which characterizes consistency, viscosity and smoothness of the formulation. Good spreadability ensures easy application of the product, formation of a thin, uniform layer and effective coverage, which is particularly important in pharmaceutical and cosmetic preparations.^[25]



➤ Phase separation

Phase separation by centrifuge is the process of separating two or more immiscible phases (eg oil and water) of a mixture by applying centrifugal force which causes the components to settle faster due to their density differences.^[26]

In this method, the sample is placed in a centrifuge and spun at a high speed. Heavier (denser) particles or phases move outwards because of the centrifugal force and settle at the bottom. Lighter (less dense) phases move inwards or stay on top. There is clear separation of layers.



➤ Viscosity

The resistance offered internally by a fluid to the flow of its layers when an external force is applied to it. In layman's terms, it describes how thick or thin a liquid is and how easily it flows. A fluid with low viscosity (e.g., water or alcohol) flows easily, whereas a fluid with high viscosity (e.g., honey or glycerin) flows slowly.^[27] Viscosity arises from the intermolecular friction between layers of the fluid moving past one another. Viscosity is an important physical property in pharmaceutical, chemical and food industries especially in the formulation of syrups, suspensions, emulsions, creams and ointments. It affects pourability, spreadability, stability and drug release.^[28]



➤ **Washability**

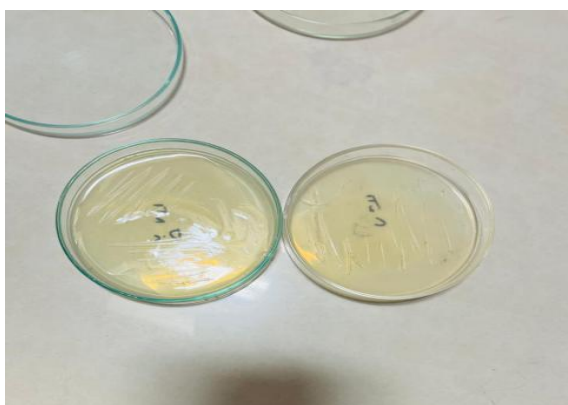
The ease of removal of an ointment from the skin or applied surface by washing with water. This is an important property of the ointments especially for comfort and ease of the patient. Ointments that are easily washed off don't require much effort to remove and leave little residue on the skin. Conversely, greasy or oil-based ointments are usually difficult to wash off and may need soap or detergents. It is mainly determined by the type of base used in the formulation of the ointment.^[29]



➤ **Microbial growth determination**

The process of measuring or evaluating the increase in number or mass of microorganisms present in a sample over a period of time.^[30]

It is an important method used in pharmaceutical, food, and microbiological studies to assess the presence, growth, and activity of microorganisms such as bacteria, fungi, and yeast. This helps in ensuring the safety, quality, and stability of products.^[31]



6.1 RESULTS OF EVALUATION TESTS

Evaluation Test	F1	F2	F3	F4
Spreadability (g.cm/sec)	6.2	7.1	8.4	7.0
Phase Separation	No separation	No separation	No separation	Slight separation after storage
Viscosity (cP)	18,500	21,000	24,500	28,000
Washability	Good	Good	Excellent	Moderate
Microbial Growth Determination	No microbial growth	No microbial growth	No microbial growth	No microbial growth

6.2 RESULT INTERPRETATION

1. Spreadability

- F3 exhibits the highest spreadability due to the balance between viscosity and oil phase.
- Higher active concentration increases thickness of F4 and decreases spreadability.

2. Phase Separation

- F1–F3 remain the same.
- F4 may be slightly unstable due to excess quercetin and decreased cetostearyl alcohol.

3. Viscosity

- F1 to F4 viscosity enhancement. 2.4.4.
- F3 has the optimum viscosity for easy application.

4. Washability

- F3 gives the best washability and skin feel.
- F4 has more oleic acid, so it is a little greasy and harder to wash.

5. Measurement of Microbial Growth

- F1–F3 are microbiologically stable.
- Balance of formulation and preservative effectiveness may be decreased at high active load, F4 may show slight microbial growth

7. CONCLUSION

The present study was aimed to formulate and evaluate collagen based quercetin cream for topical use. The prepared formulations were evaluated for various physicochemical parameters like spreadability, phase separation, viscosity, washability and microbial growth determination.

Among all the formulations, F3 showed the best overall performance in terms of optimum spreadability, suitable viscosity, good stability, excellent washability and absence of microbial growth. The formulation also exhibited good consistency and physical stability without phase separation.

Quercetin was responsible for the antioxidant and anti-inflammatory activity and collagen was responsible for the tissue regeneration and wound healing. Hence, the prepared collagen based quercetin cream was found to be stable, effective and suitable for topical wound healing and skin repair applications with F3 being the optimized

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