CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

SJIF Impact Factor: 7.187

https://doi.org/10.5281/zenodo.15500736

https://www.iajps.com/volumes/volume12-may-2025/28-issue-05-may-25/

Available online at: http://www.iajps.com *Research Article*

FORMULATION AND EVALUATION OF HERBAL CREAM CONTAINING *ANNONA SQAUMOSA* LEAF EXTRACT

Rutuja Dhobale[1]*, Snehal D. Lad[2], Gaffar Sayyed[3], Sanjay Garje [4]

[1*]Student, SAJVPM, College of Pharmaceutical Science and Research Centre, Kada-414202

[2]Assistant Professor, SAJVPM, College of Pharmaceutical Science and Research Centre, Kada-414202

[3]Principal, SAJVPM, College of Pharmaceutical Science and Research Centre, Kada-414202

[4]Associate Professor, SAJVPM, College of Pharmaceutical Science and Research Centre, Kada-414202

Abstract:

The current study focusses on developing and evaluating a herbal anti-aging cream that contains leaf extract from Annona squamosa, sometimes known as custard apple, which is known for its collagen-boosting and antioxidant qualities. The goal of this research is to develop a skin-friendly, potent herbal cream with scientifically proven ingredients like green tea extract and aloe vera, which are both known for their anti-inflammatory and rejuvenating properties, in response to consumers' growing desire for safe and natural alternatives to synthetic cosmetics.

Herbal extracts were blended with appropriate excipients to make the cream, which was made using the slab technique and oil-in-water emulsion process. Following established protocols, the formulation was thoroughly assessed using tests for stability, greasiness, skin irritation, phase separation, spreadability, viscosity, pH, physical appearance, and washability. The end product had a pH of 6.0, was stable, smooth, non-greasy, and had good spreadability. There were also no indications of phase separation or discomfort.

According to this study, a herbal cream made from Annona squamosa is a potential natural anti-aging product that provides safe, efficient skin benefits without hazardous side effects. In the expanding global market for herbal skincare products, the results validate its potential for further development, standardization, and commercialization.

Keywords: *Annona squamosa, Anti-aging cream, Herbal cosmetics, Antioxidant, Collagen booster, Natural skincare, Oil-in-water emulsion, Skin compatibility, Stability study, Phytochemicals*

Corresponding author:

Rutuja Dhobale,

SAJVPM, College of Pharmaceutical Science and Research Centre, Kada-414202

Email: dhobalerutuja2003@gmail.com

QR code

Please cite this article in press Rutuja Dhobale et al., ***Formulation And Evaluation Of Herbal Cream Containing Annona Sqaumosa Leaf Extract.,*** *Indo Am. J. P. Sci, 2025; 12(05).*

INTRODUCTION:

- **Physiology of Human Skin**

Skin is the largest exposed organ, constituting 15% of total adult body weight. Penetration of molecules through skin primarily takes place by three routes, i.e., through intact stratum corneum, sebaceous follicle, and sweat ducts.

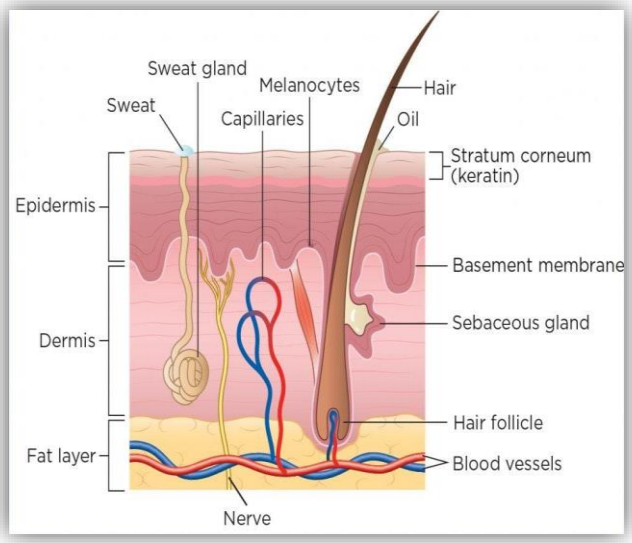

Fig. 1: Structure of skin

Taxonomical classification OF Skin

The skin is taxonomically classified into three scales:
1. Micro scale: It consists of cells and layers of skin.
2. Meso scale: It consists of skin features, hair, freckles, moles pores, skin surface, and wrinkles.
3. Macro scale: It consists of body regions and body parts.

- **Functions Of Skin**:

Primary function of skin is protection of organs. However, it has many other important functions also.

1) **Protective Function:**
All of the body's organs are covered by skin, which shields them from the following elements:
   i. Toxic chemicals and bacteria.
   ii. Forceful blow ultraviolet radiation.
   iii. Defense against bacteria and hazardous materials.

2) **The Sensory Function:**
The biggest sensory organ in the body is thought to be the skin. The specialized cutaneous receptors are formed by its many nerve ends. Touch, pain, pressure, and temperature sensations all activate these receptors, which then send the signals to the brain by afferent neurons. Different sensations are perceived at the brain level.

3) **Function of Storage:**
Sugar, water, chloride, and fat are all stored in the skin. By causing the cutaneous blood arteries to dilate, it can also store blood.

4) **Synthetic Function:**
Sunlight's UV rays react with cholesterol in the skin to produce vitamin D3.

5) **Body Temperature Regulation:**
The control of body temperature is significantly influenced by the skin. Through evaporation, convection, conduction, and radiation, excess heat is expelled from the body through the skin. By secreting perspiration, the skin's sweat glands actively contribute to heat dissipation. Sebum's lipid content keeps the body from losing heat in cold weather.

6) **Water And Electrolyte Balance Regulation:**
By sweating off salts and water, the skin maintains electrolyte and water balance.

7) **Excretory Function:**
Small amounts of waste products, such as urea, salts, and fatty substances, are expelled by the skin.

8) **Absorptive Function:**
Certain ointments and fat-soluble compounds are absorbed by the skin.

Topical Drug Delivery System

Topical drug delivery systems are specialized drug delivery methods used to treat cutaneous disorders by locally delivering therapeutic agents through the skin. Local skin infections are typically treated with these systems. The formulations are offered in a variety of forms, including liquid, semisolid, and solid.

Drug absorption is improved through the skin if the drug substance in the solution has a favorable lipid/water partition coefficient and is a non-electrolyte. Although the most widely used derma products are semisolid dosage forms such as creams, lotion , dermatological products come in a variety of formulations and consistency levels.

Fig. 2: Topical Drug Delivery System

Skin Aging:
We use a range of cosmetics to tone up our skin and reduce wrinkles, acne, pimples, skin tan, blackheads, and other ageing symptoms since we all want to seem young and appealing. First, Damage to proteins and cellular DNA is the source of the ongoing deterioration process that is the result of skin ageing.

(i) Sequential skin ageing
(ii) Photoaging skin ageing.

They alter the physiological characteristics and function of the skin, making sequential skin ageing a universal and predictable process. The stratum corneum reduces the production of neutral lipids throughout the ageing process, leading to dry, pale skin and wrinkles, as a result of inadequate keratinocyte synthesis in the skin layer. On the other side, too much UV exposure results in photoaging.

In addition to enhancing skin's beauty and appeal, cosmetics shield the skin against both endogenous and external pollutants. Cosmetics are used to cure a range of skin diseases and to give us a beautiful exterior appearance in addition to being utilized for development. By reducing type I collagen and offering UV protection, natural chemicals in skin formulations improve the skin's elasticity while also improving its health, texture, and moisture content. Longer durations of skin protection are made possible by the natural ingredients in cosmetic preparations, which help to stop the skin's production of free radicals. Using cosmetic products with natural components is the best option for minimizing skin problems including wrinkles, acne, rough skin texture, hyperpigmentation, ageing, and skin tanning.

As we grow older, our skin naturally loses elasticity, becomes thinner, and develops wrinkles. Skin aging happens in two main ways.

Wrinkles are the part of aging. Wrinkles are folds of skin that are formed through the process of skin deformation. They can be classified into two types:

1. Shallow wrinkles
2. Deep wrinkles.

- **Shallow wrinkles** are usually the end result of the distortion of the epidermis caused by water loss.
- **Deep wrinkles** are mainly formed by the distortion of the dermis due to loss of elasticity induced by decrease of collagen and elastin fibers.

Natural aging occurs due to internal factors such as genetics, gravity, hormonal changes, and immune system function things we cannot control.
Environmental aging, is caused by external factors like UV radiation, pollution, and harsh weather, which speed up the aging process. Wrinkles are the part of aging. Wrinkles are folds of skin that are formed through the process of skin deformation.

Herbal Cream
Herbal cream is a type of cosmetic that is made using a basis of different synthetic components and one or more natural ingredients to give skin care advantages. Because herbal components contain anti-aging, antioxidants, and other qualities, herbal creams are beauty treatments with a variety of activities including healing, smoothing, conditioning, and attractiveness enhancement. Several cosmetic goods contain herbs that have a greater impact than those made by other producers. Demand for herbal cosmetics is high. Using herbal cosmetics is part of a personal care regimen. Cosmetics may be used to promote appearance, beautify, and cleanse without impairing bodily processes. However, synthetic cosmetics, which include chemicals, synthetic compounds, and dyes that are bad for the body over time, might provide different.

- **Advantages of herbal cream**

1. No harsh chemicals are used.
2. Fewer adverse effects and inflammation.
3. Help in the fight against free radicals.
4. Maintains supple and moisturized skin.
5. decreases fine lines and wrinkles.
6. Delays the onset of sagging.
7. There is little chance of injury.
8. Sustainable and biodegradable.

9. Evens and brightens the complexion.
10. Promotes General Health by nourishing the body from the inside out.

- **Preparation of Herbal Antiaging Cream from custard apple leaves:**

The health advantages of custard apple plant leaves, which are assigned to a significant variety of phytochemicals, have been investigated. These substances include phenol-based substances, such as the substances, which are composed of 18 distinct phenolic substances, primarily flavonoids and alkaloids. The biological activity of Annona squamosa leaf extracts, such as their hepatoprotective, lipid-lowering, antioxidant, antibacterial, anticancer, and antidiabetic properties,

Fig.3: Annona Squamosa Leaves

have been investigated. In the current article, we discussed the antiaging property of Annona Squamosa Leaves.

Uses:

- Anticancer

The leaf extract of Annona squamosa, which is abundant in bioactive chemicals, has demonstrated the ability to cause cancer cells to undergo apoptosis and die by causing damage to their DNA, producing toxic reactive oxygen species, and activating proteins linked to apoptosis.

- Antidiabetic

Significant antidiabetic benefits are demonstrated by Annona squamosa leaf extracts (ASLs), which also improve lipid profiles, raise glucose absorption, and reduce blood glucose levels, indicating a possible natural option for diabetes treatment.

- Antioxidant

ASLs (Annona squamosa leaf extracts) have demonstrated strong antioxidant activity because of their diverse phytochemical makeup. They have the ability to decrease oxidative stress, which is connected to degenerative illnesses including cancer, diabetes, and neurodegeneration. The maximum antioxidant activity was found in methanolic extracts, but water extracts had good antioxidant activity.

- Antimicrobial

The antimicrobial qualities of Annona squamosa leaf extracts (ASLs) make them a promising substitute for synthetic antimicrobials. These extracts have antibacterial and antifungal properties against pathogens such as Escherichia coli and Staphylococcus aureus. They are made from secondary metabolites such as phenols, flavonoids, and acetogenins.

- Hepatoprotective

Leaf extracts from Annona squamosa (ASL's) have been shown to have strong hepatoprotective qualities, preventing oxidative stress and drug-induced injury from damaging the liver. These extracts lower bilirubin levels, lipid peroxidation, liver enzymes, and flavonoids, glycosides, saponins, alkaloids, and phenolic compounds.

- **Advantages:**

A. Natural cure:
By providing a natural medicine for several conditions, such as diabetes, inflammation, and infections, custard apple leaves help people become less reliant on artificial drugs.
B. Economical:
Due to their accessibility and low cost, these leaves are a cost-effective choice for wellness and medical treatment.
C. Versatility:
These substances may be used in a variety of ways, including teas, extracts, poultices, and essential oils, providing many kinds of applications according to specific requirements.
D. Health advantages:
The antibacterial, anti-inflammatory, antioxidant, and anticancer activities of custard apple leaves are potent chemicals that promote general health.

MATERIAL AND METHODS:

List of material used:

Sr. No.	Ingredients	F1	Function
1.	Annona squamosa leaf extract	2.0 g	Anti-aging, antioxidant, collagen booster
2.	Aloe Vera	3.0 g	Hydration, soothing, skin healing
3.	Green tea extract	1.0 g	Antioxidant, reduces wrinkles
4.	Stearic acid	1.5 g	Emulsifier, gives creamy texture
5.	Ethanol	1.0` g	Preservative, helps dissolve herbal extracts
6.	Polyethylene glycol (PEG)	1.0 g	Enhances absorption, moisturizing
7.	Glycerin	2.5 g	Moisturizer, retains skin hydration
8.	Triethanolamine	0.5 g	pH balancer, emulsifying agent
9.	Methyl Paraben	0.2 g	Antimicrobial preservative
10.	Rose Water	3.0 g	Fragrance, refreshing, skin toner
11.	Distilled Water	Q.s	Base solvent
	Total	25 gm	

Drug Profile:

1) Annona Squamosa

A Annona squamosa leave high in vitamins and antioxidants, custard apples have several advantages for the skin, such as increased collagen synthesis, decreased pigmentation, and alleviation of irritated skin. Additionally, it may remove dead skin cells for a smoother complexion by acting as a natural exfoliator**.**

Fig.4: Annona Squamosa Leaves

- **Botanical Classification**

Kingdom: Plantae
Clade: Tracheophytes
Order: Magnoliales
Family: Annonaceae
Genus: Annona
Species: A. squamosa
Binomial name: *Annona squamosa*
Synonym: Sugar apple, Sitaphal, Custard apple.
Biological source: Annona squamosa is a small and well-branched tree belonging to Annonaceae that gives edible fruits known as sugar apple

- **Macroscopical studies of leaf:**

Size-10-15 cm long , 3-5cm width
Shape-Alternate, Bilateral, Petiolate, Ovate to Lanceolate
Taste - Bitter
Base- Asymmetric
Margin- Simple
Color - Dark Green Surface Glossy Smooth
Odor- Aromatic

- **Morphological character**

The tree, standing 6 meters tall, has oblong-lanceolate leaves, pubescent sepals, and globose

fruits with a glaucous bloom. Its fruits are yellowish-green and easily breakable.

- **Chemical Constituents:**

Annona squamosa consist of alkaloids, phenolic compounds, flavonoids, saponins, tannins, phytosterols, carbohydrates, proteins and amino acids. It also contains fixed oils, fats, gum and mucilage. Leaves contain anonaine, borneol, camphene, carvone, eugenol, geraniol, menthone, rutin and β- sitosterol. Fruits consist of 28% of sugar, iron, calcium, carotene, thiamine, ascorbic acid. Root and stem give Borneol, Car-3-ene, Farnesol, Geraniol and Limonene

- **Microscopical character**

The internal structure of Annona squamosa leaves is well-organized, with a top surface covered in protective thick-walled cells and a bottom surface with microscopic apertures for gas exchange. They have distinct cells for mucilage and calcium oxalate crystals, two main layers for air movement and photosynthesis, and a robust support system in the middle vein.

Fig 5 : Aloe Vera

2) Aloe vera

Aloe Vera is a kind of plant belonging to the Aloe genus. It is grown for agricultural and medicinal purposes and grows wild in tropical regions all over the world. Aloe is a plant that grows well in pots inside and is often used as decoration.

- **Botanical Classification**

Kingdom: Plantae
Clade: Tracheophytes
Order: Asparagales
Family: Asphodelaceae
Subfamily: Asphodeloideae
Genus: Aloe
Species: A. vera
Binomial name: *Aloe vera (L.) Burm.f.*
Synonyms:

- ✓ *Aloe barbadensis Mill.*
- ✓ *Aloe barbadensis var. chinensis Haw.*
- ✓ *Aloe chinensis (Haw.) Baker*
- ✓ *Aloe elongata Murray*

- **Biological Source:**

Aloe is the dried latex of leaves of various species of Albes, namely: Aloe barbadensis Miller (or Curacao Aloe).

- **Chemical Constituents:**

- Phytochemicals: Anthraquinones, chromones, anthrones, phenolic compounds, flavonoids, tannins, steroids, and alkaloids
- Polysaccharides: Stimulate skin growth and repair
- Glycoproteins: Speed up the healing process by reducing pain and inflammation
- Vitamins: A (beta-carotene), C, E, B12, folic acid, and choline
- Minerals: 27 elements, including P, K, Mg, Na, Ca, Cr, Mn, Fe, Co, Ni, Cu, Zn, Mo, B, As, Ga, In, Ag, Cd, Pb, Hg, V, Bi, Se, Sn, Ba, and Rh
- Other constituents: Sugars, organic acids, lignins, lipids, saponins, phytosterols, protein, and amino acids.

- **Microscopical character**

The thick-walled epidermis of aloe vera contains a vascular system, mesophyll, mucilage cells, waxy cuticle, and paracytic stomata. Its properties, such as calcium oxalate crystals and latex cells, help with authenticity and identification in pharmacognosy.

- **Morphological character**

A succulent perennial herb, aloe vera has a short stem, thick, lance-shaped leaves, yellow to orange blossoms, and a triangular capsule that contains flat seeds. With its shallow, fibrous root structure that is appropriate for arid conditions, its morphology assists in botany and pharmacognosy.

- **Uses**

1) Due to its anti-inflammatory, antibacterial, and wound-healing qualities, aloe vera has long been used to treat digestive issues as well as skin injuries (burns, cuts, insect bites, and eczemas).
2) Aloe Vera may help with blood sugar regulation, wrinkle prevention, wound healing, and dental plaque reduction.

3) For thousands of years, people have utilized the aloe vera plant to treat a range of ailments, including burns, wounds, skin irritations, and constipation.
4) Aloe Vera is frequently used to treat burns because of its cooling, moisturizing, and calming qualities.
5) Aloe Vera helps soothe skin that is sensitive or inflamed.
6) Even the most delicate wounds can be healed with aloe vera.
7) Aloe Vera aids in hastening the healing of burns and other injuries.

3) Green tea

Green tea offers several benefits for the skin due to its rich antioxidant content, particularly catechins, and anti-inflammatory properties. These properties can help reduce inflammation, treat acne, protect against sun damage, and improve overall skin health.

Fig 6 : Green tea

- **Botanical Classification**

Scientific name: *Camellia sinensis*
Family: Theaceae
Common name: green tea
Subkingdom: Tracheobionta
Super division: Spermatophyta
Division: Magnoliophyta
Class: Magnoliopsida
Subclass: Dilleniide
Family: Theaceae
Genus: Camellia L.
Species: Camellia sinensis

- **Chemical constituents:**

Polyphenols, including catechins like epigallocatechin gallate (EGCG), as well as amino acids, carbohydrates, minerals, and trace amounts of lipids and vitamins.

- **Uses:**

1) Rich in antioxidants like catechins that help fight free radicals and reduce cell damage.
2) Can aid in weight loss by increasing fat burning and improving metabolic rate.
3) Contains caffeine and L-theanine, which can enhance focus, alertness, and cognitive function.
4) Helps lower bad cholesterol (LDL) and improves blood vessel function.
5) Some studies suggest green tea's antioxidants may reduce the risk of certain cancers.
6) Its anti-inflammatory properties help reduce acne and protect against sun damage.

❖ **Plant Collection:**

Fresh Annona squamosa leaves weighing 1 kg were collected and carefully cleaned twice with running water and once with sterile distilled water. Shade drying was the next step. Materials from plants were routinely inspected for rotting or fungal development. They ground up the dry leaves.

Fig 7: Extraction of Annona squamosa leaves

❖ **Extraction of the selected plants:**

1) Extraction of Annona squamosa leaves:

Annona squamosa leaves were collected, cleaned with distilled water, and allowed to dry in the shade. Leaves were ground into a powder after being properly dried. Next, a beaker was filled with powdered Annona squamosa leaves. After that, the solution was concentrated and heated to 80–100 °C . To get rid of contaminants, it was filtered through muslin cloth. Next, a clear solution or extract of Annona squamosa leaves the filtrate was utilized in the process.

Fig 7: Extraction of Aloe Vera Gel

2) Extraction of Aloe Vera Gel:

Aloe Vera leaves that were fresh, mature, and in good health collected and cleaned with distilled water. The outer portion of the leaf was then longitudinally dissected using a sterile knife following the appropriate drying of the leaves in a hot air oven. The sterile knife was then used to cut away the colorless parenchymatous tissue, which is aloe vera gel. The fibers and contaminants are then eliminated by filtering it through muslin fabric. The preparation was then done using the filtrate, which is a transparent aloe vera gel.

Formulation of herbal antiaging cream:

The cream was made using a cream base of Stearic acid, triethanolamine, methyl paraben, distilled water, Annona squamosa leaves, and aloe vera gel extracts. The slab technique/extemporaneous approach was used to geometrically and homogeneously blend all of the excipients and aloe extracts in the cream. Using the slab approach, we developed herbal cream. They were tested for appearance, pH, viscosity, and phase separation.

- **Procedure:**
  - ✓ This cream is formulated by oil in water type of emulsion.

In a beaker heat stearic acid, polyethylene glycol and triethanolamine to 70-75°c.

↓

In another beaker heat Distilled Water, Methyl Paraben, Rose Water, glycerin, aloe vera gel to 70-75°c.

↓

Slowly add the aqueous phase to the oil phase under continuous stirring to form a smooth cream.

↓

Allow the mixture to cool to about 40°C, then add Annona squamosa extract, green tea extract, and ethanol while stirring.

↓

Stir until the cream becomes uniform and reaches room temperature. Store in sterile containers.

Fig 18: Prepared Cream

Evaluation of herbal antiaging cream:

1) Physical evaluation:

The formulation was examined visually for their appearance, color, and odor.

2) pH

pH of the formulation were measured by using pH meter. 50 ml of distilled water were used to dissolve 0.5 gram of cream. Next, use a digital pH meter to determine its pH .

3) Skin Irritation Test:

A small patch of skin (about 1cm^2)on the back of left hand was cleaned and marked. The cream was gently applied in this area, and time was noted. Over the next 24hrs the skin was checked regularly to see if there were any sign of reported irritating effects, erythema, and oedema. All the changes observed and recorded.

4) Phase Separation:

The prepared cream was stored in a closed container at a temperature range of 25 to 100°C, kept away from light. It was monitor for 1day to check for any separation of its components. Any visible changes were carefully observed and recorded.

5) Spreadability:

To test how easily the cream spreads, a small amount was placed between two glass slides. A set amount of weight (70 grams) was placed on top to press the slides evenly. The time it took for the top slide to move or slip due to the cream's texture was measured. This time helped

calculate how spreadable the cream is, using the formula:

Formula:

$$S = M \times L / T$$

Where:
S = Spreadability
M = Weight applied
L = Distance moved
T = Time taken

6) Viscosity:
The thickness (viscosity) of the cream was measured using a Brookfield viscometer, set at 2.5 RPM with spindle number 63, at a controlled temperature of 25°C.

7) Wash Ability:
A small amount of cream was applied to the hand and then rinsed with tap water to see how easily it could be washed off. The test also checked whether the cream left any residue behind.

8) Stability Study:
Stability testing of drug products is done from the early stages of drug development until the end of its shelf life. To check how stable the cream and its ingredients are over time, the study followed ICH guidelines. The cream was stored in bottles and placed in a humidity chamber set at 40 ± 2°C and 75 ± 5% relative humidity for three months. After the testing period, the samples were examined for changes in their physical appearance, pH, and thickness (viscosity).

9) Greasiness:
To check for greasiness, the cream was applied to the skin in a thin layer and observed to see whether it left behind an oily or greasy feel.

RESULTS:

Sr. No.	Test	Observation
1.	**Visual Appearance :**	
	a) Appearance	Semi-solid
	b) Color	Faint Yellow
	c) Odor	Pleasant
	d) Texture	Smooth
2.	pH	6.0
3.	**Irritancy**	
	a) Irritant Effect	No
	b) Erythema	No
	c) Edema	No
4.	Wash Ability	Easily Washable
5.	Phase Separation	No Phase Separation
6.	Spread Ability(gm×cm/sec)	2.14
7.	Greasiness	Non-Greasy

SUMMARY:
Natural botanicals like Annona squamosa leaf extract are included in herbal anti-aging creams, which are a safe and natural substitute for synthetic skin care procedures. These products increase collagen formation, lessen oxidative stress, and enhance skin texture. They shield the skin from damage caused by free radicals and other environmental causes. The cream was compatible with the skin's natural balance since its pH stayed near 6. Additional investigation is required to evaluate long-term advantages and enhanced anti-aging effectiveness.

CONCLUSION:

The goal of the study was to develop a herbal anti-aging cream with organic components and leaf extract from Annona squamosa. The cream's homogeneity, stability, pH, spreadability, and appearance were all evaluated. The findings revealed no evidence of deterioration, microbial contamination, or phase separation. Superior antioxidant activity and skin feel were demonstrated by the cream with the greatest concentration of Annona squamosa extract. Future advancements in topical anti-aging medicines and herbal cosmetics may be possible with this plant-based approach.

REFERENCES:

1. Alexiades-Armenakas MR, et al. J Am Acad Dermatol. 2008 May;58(5):719.
2. Anaya-Esparza, L.M.; de Lourdes García-Magaña, M.; Abraham Domínguez-Ávila, J.; Yahia, E.M.; Salazar-López, N.J.; González-Aguilar, G.A.; Montalvo-González, E. Annonas: Underutilized species as a potential source of bioactive compounds. Food Res. Int. 2020, 138.
3. Ansel HC, Popovich NG, Allen LV. Pharmaceutical dosage forms and drug delivery systems. Lippincott Williams & Wilkins; 1995.
4. Babu Marahatta, A.; Aryal, A.; Chandra Basnyat, R.; Anant Babu Marahatta, C. The phytochemical and nutritional analysis and biological activity of Annona squamosa Linn. Int. J. Herb. Med. 2019, 7, 19–28.
5. Chandra, H.; Bishnoi, P.; Yadav, A.; Patni, B.; Prakash Mishra, A.; Nautiyal, A.R.; Mishra, A.P.; Nautiyal, A.R.; Prakash Mishra, A.; Nautiyal, A.R. Antimicrobial resistance and the alternative resources with special emphasis on plant-based antimicrobials—A review. Plants 2017.
6. Chauhan lalita, Gupta Shalini et al, Journal of Drug Delivery and Therapeutics,2020:10[5-s]:281-289.
7. Chen, S. (2016). The external treatment theory and Application about "Yellow Emperor's Inner Canon" bachelor's degree. China: Liaoning University of Traditional Chinese Medicine.
8. Davis, J.A.; Sharma, S.; Mittra, S.; Sujatha, S.; Kanaujia, A.; Shukla, G.; Katiyar, C.; Lakshmi, B.S.; Bansal, V.S.; Bhatnagar, P.K. Antihyperglycemic effect of Annona squamosa hexane extract in type 2 diabetes animal model: PTP1B inhibition, a possible mechanism of action. Indian J. Pharmacol. 2012, 44, 326–332.
9. Dholvitayakhun, A.; Trachoo, N.; Sakee, U.; Cushnie, T.P.T.T. Potential applications for Annona squamosa leaf extract in the treatment and prevention of foodborne bacterial disease. Nat. Prod. Commun. 2013, 8, 1934–1948.
10. El-baz, D.M.; Hssan, A.K. Effects of Egyptian Annona squamosa leaves extracts against alloxan induced hyperglycemia in rats. World J. Pharm. Pharm. Sci. 2019, 8, 145–163.
11. El-Chaghaby, G.A.; Ahmad, A.F.; Ramis, E.S. Evaluation of the antioxidant and antibacterial properties of various solvents extracts of Annona squamosa L. leaves. Arab. J. Chem. 2014, 7, 227–233.
12. Elshafie, H. S., and Camele, I. (2017). An overview of the biological effects of some mediterranean essential oils on human health.
13. Fadholly, A.; Proboningrat, A.; Dewi Iskandar, R.; Rantam, F.; Sudjarwo, S. In vitro anticancer activity Annona squamosa extract nanoparticle on WiDr cells. J. Adv. Pharm. Technol. Res. 2019.
14. Fang-nan, K.O.; Wen-yan, L.I.; You, W.E.; Jing, Z.H.; Jing, Z.H.; Zhi-qiang, Y.A.; Xiu-fen, Z. Optimization of Extraction Process of Polyphenols from Annona squamosa Leaves and Its Antioxidant Activity in Vitro. Sci. Technol. Food Ind. 2020, 41, 162–168.
15. Fischer Josef E, Bland Kirby I, Callery Mark P. Mastery of Surgery. Lippincott Williams & Wilkins, 2006, 482
16. Gajalakshmi, S.; Vijayalakshmi, S.; Devi Rajeswari, V. Phytochemical and pharmacological properties of Annona muricata: A review. Int. J. Pharm. Pharm. Sci. 2012, 4, 3–6.
17. Grzybowski, A. (2008). Cocaine and the eye: a historical overview. Ophthalmol. J. Int. d'ophtalmologie. Int. J. Ophthalmol. Zeitschrift fur Augenheilkunde. 222 (5), 296–301. doi:10.1159/000140625
18. Gupta MA, Gupta AK. Photodamaged skin and quality of life: reasons for therapy. J Dermatol Treat 1996;7:261–264.
19. Halliwell, B.; Gutteridge, J.M.C. Role of free radicals and catalytic metal ions in human

disease: An overview. Methods Enzymol. 1990, 186, 1–85.
20. Hicklin R. Austin. "Anatomy of Friction Ridge Skin". Encyclopedia of Biometrics. Springer US, 2009, 23 28.
21. Ibrahim, F.; Jaber, A.; Ibrahim, G.; Cheble, E. Antioxidant activity and total phenol content of different plant parts of Lebanese Annona Squamosa Linn. Int. J. Pharm. Pharm. Sci. 2020, 100–105.
22. James William, Berger Timothy, Elston Dirk. Andrews' Diseases of the Skin: Clinical Dermatology (10th ed.). Saunders,2005:1:11-12.
23. James WD, Berger TG, Elston DM. Andrews' diseases of the skin: Clinical dermatology (10th edition.). Philadelphia: Elsevier Saunders, 2006.
24. Kaleem, M.; Asif, M.; Ahmed, Q.U.; Bano, B. Antidiabetic and antioxidant activity of Annona squamosa extract in streptozotocin induced diabetic rats. Singapore Med. J. 2006, 47, 670–675.
25. Kalidindi, N.; Thimmaiah, N.V.; Jagadeesh, N.V.; Nandeep, R.; Swetha, S.; Kalidindi, B. Antifungal and antioxidant activities of organic and aqueous extracts of Annona squamosa Linn. leaves. J. Food Drug Anal. 2015, 23, 795–802.
26. Kumar KK. Importance of Critical Quality Attributes in Biopharmaceuticals Development. Research Journal of Topical and Cosmetic Sciences,2019
27. Lin Chang-min et al. "Microencapsulated human hair dermal papilla cells: a substitute for dermal papilla?. Archives of Dermatological Research. Springer,2008:300(9):531–535.
28. malvi. "The Ageing Skin - Part 1 - Structure of Skin and Introduction - Articles". PharmaXChange.info, 2011.
29. Marks James G, Miller Jeffery. Lookingbill and Marks' Principles of Dermatology (4th ed.). Elsevier Inc, 2006, 8-9.
30. Metwaly, A. M., Ghoneim, M. M., Eissa, I. H., Elsehemy, I. A., Mostafa, A. E., Hegazy, M. M., et al. (2021). Traditional ancient Egyptian medicine: a review. Saudi J. Biol. Sci. 28 (10), 5823–5832. doi:10.1016/j.sjbs.2021.06.044
31. Navindgikar N, Kamalapurkar KA, Chavan PS. Formulation and evaluation of multipurpose herbal cream. Int J Curr Pharm Res. 2020; 12(3): 25-30.
32. Neethu, S.K.; Santhoshkumar, R.; Kumar, N.S. Phytochemical analysis and antimicrobial activities of Annona squamosa (L) leaf extracts. J. Pharmacogn. Phytochem. 2016, 5, 128–131.
33. Pastore, M. N., Kalia, Y. N., Horstmann, M., and Roberts, M. S. (2015). Transdermal patches: history, development and pharmacology. Br. J. Pharmacol. 172 (9), 2179–2209. doi:10.1111/bph.13059.
34. Quílez, A.M.; Fernández-Arche, M.A.; García-Giménez, M.D.; De la Puerta, R. Potential therapeutic applications of the genus Annona: Local and traditional uses and pharmacology. J. Ethnopharmacol. 2018, 225, 244–270.
35. Rai R, Poudyl AP, Das S, Pharmaceutical Creams and their use in wound healing: A Review, Journal of Drug Delivery and Therapeutics, 2019; http://dx.doi.org/10.22270/jddt.v9i3-s.3042 9(3-s): 907-912
36. Ross and Wilson. Anatomy and Physiology in Health and Illness, 11eth.
37. Ruddaraju, L.K.; Pallela, P.N.V.K.; Pammi, S.V.N.; Padavala, V.S.; Kolapalli, V.R.M. Synergetic antibacterial and anticarcinogenic effects of Annona squamosa leaf extract mediated silver nano particles. Mater. Sci. Semicond. Process. 2019, 100, 301–309.
38. Sahu T, Patel T, Sahu S, Gidwani B, "Skin cream as Topical Drug Delivery System: A Review" Journal of Pharmaceutical and Biological Sciences, 2016; 4(5):149-154
39. Shanker, K.S.; Kanjilal, S.; Rao, B.V.S.K.; Kishore, K.H.; Misra, S.; Prasad, R.B.N. Isolation and antimicrobial evaluation of isomeric hydroxy ketones in leaf cuticular waxes of Annona squamosa. Phytochem. Anal. 2007, 18, 7–12
40. Shirwaikar, A.; Rajendran, K.; Kumar, C.D.; Bodla, R. Antidiabetic activity of aqueous leaf extract of Annona squamosa in streptozotocin-nicotinamide type 2 diabetic rats. J. Ethnopharmacol. 2004, 91, 171–175.
41. "Wrinkle creams - Consumer Reports Health". Consumerreports.org. 2011 07-28.
42. Young, Barbara. Wheater's functional histology a text and color atlas. Elsevier, 2014, 160-175.
43. Zahid, M.; Mujahid, M.; Singh, P.K.; Farooqui, S.; Singh, K.; Parveen, S.; Arif, M. Annona squamosa linn. (Custard apple): Anaromatic medicinal plant fruit with immense nutraceutical and therapeutic potentials (Review). Int. J. Pharm. Sci. Res. 2018, 9, 1745–1759.
44. Zheng, H. L., and Zhang, Y. C.(2017). Elementary analysis on external treatment in Li Yue pian wen. J. Clin. Acupunct. Moxibustion 33 (5), 78–80.
45. Zhu, L. (2007). Examination and interpretation of the formulas for fifty-two diseases. J. Chin. Med. Mater., 1613–1615.