

Formulation and Development of Aloe vera gel for Wound healing

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ABSTRACT :

Purpose - Create and refined an herbal gel of Aloe vera extract with Carbopol 934 as a gelling agent. Examine how topical application of Carbopol 934 gel with Aloe vera extract affects the healing of surgically inflicted skin wounds in Wistar rats.

Materials and Methods - An excision wound model was used for the study, and various concentrations of the viscosity enhancer Carbopol 934 were tried before a gel with good spread ability and consistency was chosen for the herbal gel of Aloe vera's wound healing property.

A number of clinical trials are being conducted to further evaluate the use of aloe vera gel for the variety of disorders, as well as to further confirm traditional uses of the plant extract. The main limitation of the current knowledge about the Aloe vera gel is small clinical studies that often lack rigorous methodology.

Clinical trials have demonstrated the efficacy of aloe vera gel in treating burns wounds, genital herpes, and seborrheic dermatitis, however, other indications such as psoriasis or internal application for the treatment of type 2 diabetes remain inconclusive.

Result - The optimized gel was assessed for its various physicochemical properties and its ability to promote wound healing. When compared to the control group, the wound healing properties showed differences. Tissue hyperplasia was lower in the control group than in the other treated groups. In the gel-treated animal group, 80.14% of the wounds were observed to be healed up to the 14th day, whereas in the untreated group (control) the healing rate was 52.68%. In addition, the animals in the control group showed signs of inflammation and pus formation up to the fifth day of the study, whereas the treated animals did not exhibit any discernible inflammation and pus formation.

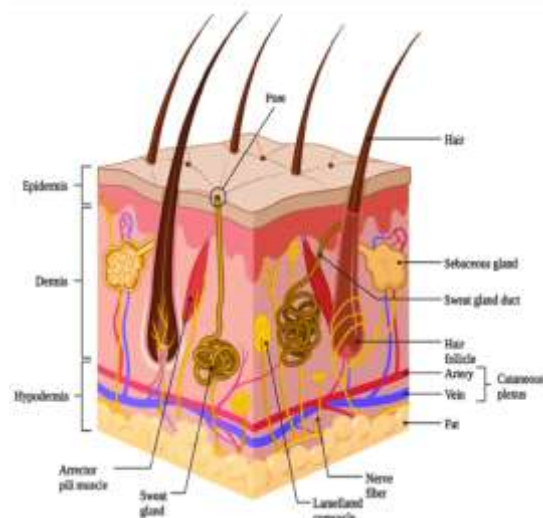
KEYWORDS: skin, wound healing, burns, gel

variety of essential purposes, such as providing against external agents that are biological, physical, and chemical (1)

Skin serves a number of purposes, including regulating body temperature enhancing metabolic process, and synthesizing vitamin D. Skin also serves as barrier against pathogens and water loss and protects against various types of traumata, including thermal, chemical and ultraviolet radiation. (2)

Enhancing skin health in the elderly will help maintain its integrity and, as such, should be the first step in any wound prevention program.

The skin is the most visible and vulnerable organ of the human body, and it is anatomically and functionally affected by aging. Maintaining skin integrity starts with understanding skin anatomy, physiology, and function and recognizing conditions as well as aspects of care that may affect structure and function. Research suggests that appropriate skin cleansing procedures and protection, as well as nutritional and (environmental interventions, may help reduce some of the effects of aging and have positive psychological and health outcomes.(3)



SCHEMATIC REPRESENTATION OF SKIN

I. INTRODUCTION

The skin is the body's largest organ, making up 15% of the adult body weight, and it serves a

Pathology of burns - Many models are available for evaluating burn wounds. Jackson's model is one of the most widely used models; it allows for the detection of three concentric areas based on the degree of tissue damage and changes in blood flow of a burn wound. In short, the primary goal of burn resuscitation is to increase tissue perfusion here and prevent any further damage.

The outermost layer is the zone of hyperaemia; tissue perfusion is increased and the tissue is necrotic. Surrounding the coagulation zone is the zone of stasis, which is characterized by decreased (perfusion. If the ischemia is not reversed, this ischemic zone could progress to full necrosis.(4)

The Aloe vera plant has been used for centuries for its medicinal, cosmetic, and health benefits. The Arabic word "Aloe" means shining bitter substance, and the Latin word "vera" means true. Greek scientists considered Aloe vera to be a universal panacea 2000 years ago, and the Egyptians referred to it as "the plant of immortality." Today, dermatologists use Aloe vera for a variety of purposes(5)

More than 250 species of aloe are known to exist worldwide. However, only two species are currently grown artificially, Aloe barbadense Mill. Specialists: operator and Aloe arborescent are the most common. Aloe Vera grows to a height of 0.8 m by 1 m at a moderate rate and is an evergreen that never stops growing. It is xerophytic, meaning that it prefers light (sandy) and medium (loamy) soil and needs well-drained soil to grow. The plant leans toward destructive, nonpartisan, and fundamental (fundamental) soil; it cannot grow in shade; it needs dry or clammy soil and can withstand periods of drought(6)Antioxidant activity - The literature reported on the in vitro antioxidant activity of A. arborescent, A. ferox, Aloe greenhead var. Divyana, A. Harlan, A. Saponaria, A. maloti, and A. Melan acantha leaf extracts. Sahana et al. reported that leaf extracts from 15 Aloe species exhibited high antioxidant activity. A. ferox's antioxidant capacity was determined using ORAC and FRAP analyses (7)



ALOE VERA PLANT

The tubes containing the reaction solution were then covered and incubated for 90 min at 95 °C. After the samples had cooled to room temperature, the absorbance of the solution was measured at 695 nm against a blank, which consisted of 1 mL of methanol rather than extract(8)

The analysis was conducted periodically (once a week) during the storage and included analysis of moisture content and antioxidant activity with the DPPH method based on the percentage of RSA (Radical Scavenging Activity) and the ferric cyanate (FTC) method to determine the percent inhibition of lipid peroxidation.(9)

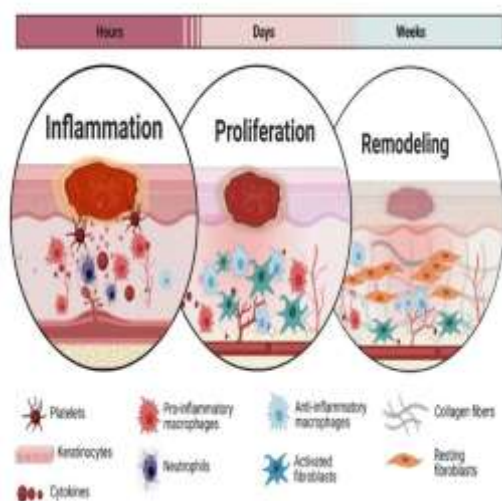
Phases of wound healing - The three main intersecting phases of the healing process are inflammatory, proliferative, and tissue remodelling. The mechanism underlying the healing process consists of cellular, subcellular, physiological, and biochemical events that work together to repair injuries (10)

The term "gel" is derived from "gelatine," and both "gel" and "jelly" can be traced back to the Latin Gelu for "frost," and gel are meaning- Ing "freeze" or "congeal." This origin indicates the essential idea of a liquid setting to a solid-like material that does not flow: but is elastic and retains some liquid characteristics (11) The nature of the product and the type of oil responsible for the coupling determines the network structure of the gel and product (12)

Topical application of aloe vera gel is generally considered safe.7 If applied topically, aloe gel may improve the ability of hydrocortisone to reduce swelling.107 If ingested, aloe vera gel may increase hypoglycaemia when combined with oral antidiabetics or insulin.97 The American

Pharmaceutical Association rates aloe vera gel in category 2, which indicates that “according to a number of well-designed studies and common use, this substance appears to be relatively effective and safe when used in recommended amounts (13)

The lack of clinical data on aloe vera gel may be partly attributed to the wide range of possible indications for the gel. The table lists 18 clinical trials with a total of 7,297 subjects, conducted for different types of aloe gel-derived preparations on numerous indications. (13)



PHASES OF WOUND HEALING

Drug interactions

Topical application of aloe vera gel is generally considered safe.⁷ If applied topically, aloe gel may improve the ability of hydrocortisone to reduce swelling.¹⁰⁷ If ingested, aloe vera gel may increase hypoglycaemia when combined with oral antidiabetics or insulin.⁹⁷ The American Pharmaceutical Association rates aloe vera gel in category 2, which indicates that “according to a number of well-designed studies and common use, this substance appears to be relatively effective and safe when used in recommended amounts.”³⁹ Aloe vera inner gel may significantly increase the absorption of vitamins C and E following oral application.¹⁰⁸ Aloe vera gel for systemic application is not recommended in combination with antidiabetic, diuretic, or laxative drugs; sevoflurane; or digoxin.⁽¹⁴⁾

Gel information :

The term "gel" is derived from "gelatine," and both "gel" and "jelly" can be traced back to the

Latin *Gelu* for "frost," and gel are meaning- Ing "freeze" or "congeal." This origin indicates the essential idea of a liquid setting to a solid-like material that does not flow: but is elastic and retains some liquid characteristics. The use of the term "gel" as a classification originated during the late 1800s as chemists attempted to classify semisolid substances based on their phenomenological characteristics rather than their molecular compositions. (15)

II. MATERIALS AND METHODOLOGY

Materials

- 1) Aloe vera Extract
- 2) Methyl paraben
- 3) Propylparaben
- 4) Triethanolamine
- 5) Potassium Hydroxide pellets
- 6) Carbopol
- 7) Vitamin E

1) Aloe Vera extract :

Taxonomical profile

Kingdom - Plantae

Clade - Monocots

Order - Asparaguses

Subfamily - Aphidoidea

Genus - Aloe

Species - Avera

Binomial name - Aloe vera

Synonyms - Aloe barbadense Mil.

Cultivation of Aloe vera plant :

Aloe plants can become red from sunburn under too much direct sun, though gradual acclimation may help. Terracotta pots are preferred because they are porous.

Potted plants should be allowed to completely dry before rewatering. When potted, aloes can become crowded with "pups" growing from the sides of the "mother plant".

Plants that have become crowded can be divided and reported to allow room for further growth, or the pups can be left with the mother plant.

Aloe vera may become dormant during winter, during which little moisture is required.⁽⁵⁾ Aloe vera's 75 potentially active constituents include vitamins, enzymes, minerals, sugars, lignin, saponins, salicylic acids, and amino acids. Among the vitamins are antioxidants A (beta-carotene), C, and E, as well as folic acid, choline, and vitamin B12.⁽¹⁶⁾



ALOE VERA PLANT

Use of aloe vera :

1)Aloe vera is produced on a large scale in the following countries: Australia, Cuba, the Dominican Republic, China, Mexico, India, Jamaica, Kenya, Tanzania, South Africa, Spain, and the United States. The majority of the crop is used in the cosmetics sector.

2)Aloe vera is used to make two substances that are used in commercial products: a clear gel and its yellow latex. Aloe gel is usually used in topical medications for skin conditions like burns, wounds, frostbite, rashes, psoriasis, cold sores, or dry skin.

3)Aloe latex is used either on its own or in a product that is made with other ingredients and consumed to relieve constipation. Aloe latex can be purchased as "aloe dried juice" or in a dried form called resin.

2) Methyl Paraben

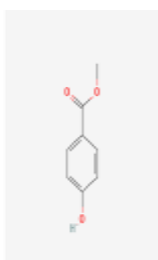
Taxonomical profile -

Molecular formula - C₈H₈O₃

Synonyms - Methyl 4-hydroxybenzoate

Molecular Weight - 152.15 g/Mol

Structure -



Methyl Paraben

3) Propyl Paraben

Taxonomical profile -

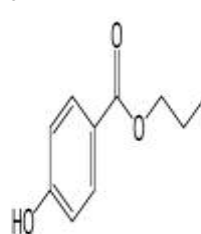
Chemical Formula - C₁₀H₁₂O₃

Molar mass - 180.2 g/Mol

Melting point - 96 to 99 degree Celsius

Synonyms - 4- Hydroxybenzoic acid

Structure -



PROPYL PARABEN

4) Triethanolamine:

Taxonomical profile -

Chemical Formula - C₆H₁₅NO₃

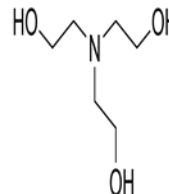
Molar mass - 149.188 g/mol

Boiling point - 335.4 degree Celsius

Synonyms - Triethanolamine, 2,2',2''-

Nitrioltriethanol, Tris(2-hydroxyethyl)amine

Structure -



Triethanolamine

5)Potassium Hydroxide pellets

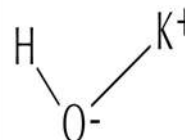
Taxonomical profile -

Molecular formula- KOH

Molecular weight - 56.11 g/Mol

Synonyms - Caustic Potash

Structure -



POTASSIUM HYDROXIDE

6)Carbopol

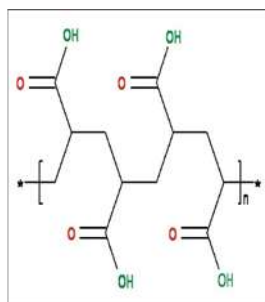
Taxonomical profile -

Molecular formula - C₅H₁₀O₂

Molecular weight - 102.13 g/Mol

Synonyms - Polyacrylic acid

Structure -



Carbapol

7) Vitamin E

Taxonomical profile -

Molecular formula - C₂₉H₅₀O₂

Molecular Weight - 430.717 g/Mol

Synonyms - Tocopherol

III. METHODOLOGY

Preparation of extract :

1) Using thick, succulent Aloe vera (Aloe barbadense) leaves from the campus Herbal Garden, the mucilaginous jelly from the leaf's centre (the parenchyma) was extracted to make Aloe vera extract.

2) The leaves were first dissolved in water, then rinsed with water and a mild chlorine solution, and finally cut into transverse pieces.

3) The thick outer layer was removed using a vegetable peeler, and the inner pulp, which resembled gel in the centre of the leaf, was then separated with a spoon, minced, and continuously stirred in a mixer (17)

By the Centrifugation method :

In order to obtain greater gel recovery and high-quality gel, the centrifugation process for extracting gel from aloe vera should be performed at a speed of 10,000 rpm for 30 minutes at a temperature of 5°C.

Effects of the centrifuge temperature on gel extraction process:

One of the main factors that ultimately influences the viscosity, optical density, refractive index, and TSS content of gel extracted from Aloe vera leaves is temperature. Figures 3 and 4 show the effect of centrifuge temperature on various quality parameters, including crude and pure gel recovery, viscosity, refractive index, optical density, and TSS content on gel extraction from Aloe vera leaves at different temperatures. The

percent recovery of gel remains relatively constant in both cases as the temperature increases, and the extracted gel's viscosity is greatly influenced by these changes.

It was also observed that the optical density of the Aloe vera gel increases with the increase of temperature: the maximum value was found to be 0.244 at 32% process was studied and standardised. The effect and minimum at 5 °C temperatures. The increase of process parameters on different quality in the value of optical density may be due to enzymatic degradation of Aloe vera gel at higher temperatures. The refractive index and TSS increase with the increase of temperature. The minimum and maximum refractive index was found to 1.33603 and 1.33610, while TSS was found to be 1.31 and 1.40 Brix, respectively. The refractive index of the pure gel is found to be closer to distilled water at all the temperatures.

Effect of the centrifuge speed on gel extraction process :

To obtain gel recovery, the centrifuge process was used to separate solid particles from pulp. As centrifuge speed increased, so did viscosity and TSS content in both the crude and pure gel recoveries.

Effect of the centrifuge duration on gel extraction process

Higher recovery of the gel at 30 min duration may be due to the fact that all the particles are getting sufficient residual time during the extraction process. In the gel extraction process, the duration of the centrifuge plays a significant role in the separation of solid particles from the crude pulp. The recovery of both crude and pure gel was found to increase with the extension of the centrifuge, while the recovery of optical density decreased.

Selection and optimization of gelling agents :

Different gel formers, such as Carbomer 934, were used to prepare the gel formulations in order to optimize the concentration of the gelling agent and achieve the desired consistency. Various concentrations of viscosity enhancer, viz 1.0, 2.0, 3.0, and 4.0%, were tried, and the gel that demonstrated good spread ability and consistency was ultimately chosen. (18)

Preparation of Gel :

1) Firstly, take the ingredients for preparation of the gel.

- 2) Weigh all the ingredients in the proper manner.
- 3) Take the mortar and pestle and wash it.
- 4) Take the Vitamin E , Methyl paraben , Propylparaben and dissolved in the water
- 5) After that add the gelling agent and stir continuously until the mixture swelled completely.
- 6) Then Triethanolamine added slowly to dispersion .
- 7) Stir continuously and selectively to get the stiff gel.
- 8) After that add the Aloe vera Extract and stir for the 15 minutes.
- 9) A volume was created with water.
- 10) Stirring continuously until a homogenous gel was formed.

IV. FORMULATION TABLE

SR.NO	INGREDIENTS (Gram)	F1	F2	F3	F4
1	Aloe vera Extract	75	75	75	75
2	Methyl Paraben	0.020	0.020	0.020	0.020
3	Propyl Paraben	0.002	0.002	0.002	0.002
4	Vitamin E	0.200	0.200	0.200	0.200
5	Carbopol	2	3	4	5
6	Potassium Hydroxide Pellets	1	2	3	4
7	Triethanolamine	1.2	1.3	1.5	1.6
8	Purified Water	QS to 100	QS to 100	QS to 100	QS to 100

V. EVALUATION TEST

- 1) Spread ability – The therapeutic efficacy of a formulation is also dependent upon its spreading value. To assess the formulation's spread ability, 0.5 g of gel was placed within a pre-marked circle with a diameter of 1 cm on a 20 × 20 cm glass plate, over which another glass plate was placed. A weight of 500 g was allowed to rest on the upper glass plate for five minutes, during which time the diameter increased due to gel spreading.
- 2) PH - After precisely weighing the gel and dispersing it in 100 millilitres of purified water, the pH of the mixture was measured using a digital pH meter that had been calibrated at 4.0, 7.0, and 9.0 using standard buffer solution prior to use. The pH measurements were made in triplicate, and the average values were computed.
- 3) Viscosity - The R/S CPS Plus Rheometer was used to measure the viscosity of the formulations without diluting them. The spindle 50-1, which has a 50 mm diameter, was used for this purpose.
- 4) Physical Appearance – The physical appearance of the gel can be observed by its colour, roughness and graded.
- 5) Removal : The ease of the removal of the gel applied was examined by washing the applied part with the water.
- 6) Skin irritation – The prepared formation is assessed for primary skin irritation test on our hand little amount of F1 F2 F3 F4 were applied on test site and observed .

VI. RESULT AND DISCUSSION

Sr.no	Evaluation test	F1	F2	F3	F4
1	Colour	Light green	Light green	Green	Green
2	Odour	Characteristics	Characteristics	Characteristics	Characteristics
3	Viscosity				
4	PH	6.3	6.2	6.2	6.1
5	Removal				
6	Skin irritation	No	No	No	No
7	Consistency	Semi-solid	Semi-solid	Semi-Solid	Semi-solid
8	Spread ability	9	10	9	11

VII. CONCLUSION

In order to create cost-effective products based on effective traditional natural medicines for wound healing and to enhance their therapeutic effect, it is crucial to employ contemporary delivery techniques. Chemotherapy treatments for cancer are associated with the presence of ulcers in the oral mucosa that cause pain, bleeding, and difficulty swallowing or speaking; there is no effective standard treatment, and few published studies have been conducted on the therapeutic effects of natural products like AV to improve the local retention period. Therefore, more research is necessary to ensure that these formulations reach the pharmaceutical market. Future research should be conducted to identify new natural bioactive compounds related to their usage in the wound-healing process. Medicinal plants may provide future treatments that have fewer side effects and improved bioavailability for the wound-healing process. Additionally, in the future, a great challenge will be the development of an intelligent treatment that presents anti-inflammatory, antimicrobial, and antioxidant cumulative properties for the treatment of all types of wounds. Moreover, the commercialization and use in preclinical research and clinical practice of natural products used in wound healing must be significantly increased in order to uncover the potential of these products, considered natural bioactive molecules.

The development of multifunctional biomaterials that offer sustained release of agents, facilitate wound healing, decrease inflammation, and prevent or treat microbial infections can be achieved by combining therapeutic agents with AV-based hydrogels; however, it is crucial to remember that the precise formulation and effectiveness of these hydrogels may differ based on the therapeutic agents selected, their concentration, crosslinking technique, and other variables. Consequently, extensive research and testing (rheological analysis, drug release profiles, permeability, and stability studies) are necessary to optimize the formulation, guarantee its safety and efficacy for clinical use, and advance human welfare globally.

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