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Development and evaluation of *Aloe vera* (L.) Burm. based topical cream formulation

Narayan Prasad Yadav, Shruti Srivastava, Priyam Sinha, Debabrata Chanda*, Suaib Luqman* and Sudeep Tandon**

Botany and Pharmacognosy Department, CSIR-Central Institute of Medicinal and Aromatic Plants (CIMAP), P.O. CIMAP, Lucknow-226015, Uttar Pradesh, India

**Molecular Bioprospection Department, CSIR-Central Institute of Medicinal and Aromatic Plants (CIMAP), P.O. CIMAP, Lucknow-226015, Uttar Pradesh, India*

***Process Chemistry and Chemical Engineering Department, CSIR-Central Institute of Medicinal and Aromatic Plants (CIMAP), P.O. CIMAP, Lucknow-226015, Uttar Pradesh, India*

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Abstract

Aloe vera (L.) Burm. is known for its skin care and medicinal properties since time immemorial. The plant is extensively recognized as a remedy for burns, rashes, allergic irritation, skin aging, wounds, infections, sunburns, eczema, psoriasis, dermatitis and inflammation. It is also used as a moisturizer for dry skin, for lightening blemishes and scars as well as a hair growth promoter. Therefore, the present study is aimed to formulate and evaluate *Aloe vera* cream (AVC) containing sap (10%). The formulation was optimized on the basis of textural parameters by varying the concentration of emulsifiers. The sap was incorporated in oil-in-water (o/w) cream base prepared by phase inversion temperature technique. The major components of the cream were mineral oil, petroleum jelly, olive oil, paraffin wax, glycerol monostearate, fragrance and distilled water. The optimized cream formulation was characterized by pH, rheological and textural measurements. The texture of the optimized formulation was compared with a marketed cosmetic formulation (MCF) using Brookfield CT3 Texture analyzer. AVC was found to be much softer and by far spreadable with better extrusion than MCF. AVC was also found to be stable for a period of 90 days and non-irritant in skin irritancy test. Conclusively, a stable, non-irritant and cosmetically elegant *Aloe vera* cream formulation was developed with good aesthetic appearance.

Key words: *Aloe vera* (L.) Burm., cream formulation, texture analysis

1. Introduction

Skin, as an external biological barrier, is involved in the regulation of body temperature, water and lipid stores and becomes a potential target for oxidative stress, UV radiations, toxic chemicals, air and humidity, resulting in dry and damaged skin. Under these conditions, effective cosmetic products are being used to improve skin hydration to maintain the normal texture of skin and to prevent dryness (Mambro *et al*., 2005; Bouftira, 2008; Rasul, 2011). Natural remedies have been used for centuries for treating skin conditions and dermatological disorder such as inflammation, phototoxicity, psoriasis, atopic dermatitis and *Alopecia areata* (Aburjai, 2003, Yadav, 2009). In view of the cosmetic potential of herbal botanicals, products are being made with raw materials of natural origin possessing varied biological responses, *viz.*, antioxidant, anti-inflammatory, antiseptic, emollient, antiseborrhatic, antikerolytic activity, antibacterial and other activities (Isaac *et al*., 2012).

Author for correspondence: Dr. Narayan Prasad Yadav
Botany and Pharmacognosy Department, CSIR - Central Institute of Medicinal and Aromatic Plants (CIMAP), P.O. CIMAP, Lucknow-226015, Uttar Pradesh, India
E-mail: npyadav@gmail.com
Tel.: +91-522-2718657, Mob: +91-9451244418

Aloe vera (L.) Burm. is an imperative functional ingredient exhibiting remarkable biological efficacy display great attention in cosmetic, pharmaceutical and food industries. For centuries, this plant has been used for its medicinal and therapeutic utility without thorough scientific analysis for its health, beauty and skin care properties. It was depicted as the *Plant of Immortality* in stone carvings of Egypt somewhere 6000 year ago and was a traditional funerary gift to the pharaohs (Ulbricht *et al*., 2007). The ancient Egyptian book of remedies reveal its use to cure infections, treat the skin, and prepare laxatives whereas, Greek scientists regarded *Aloe vera* as the universal panacea. *Aloe barbadensis* Miller (Asphodelaceae/ Liliaceae) grows mainly in the regions of Africa, Asia, Europe, America China, India, West Indies, and Japan (Surjushe *et al*., 2008; Eshun, 2010). The leaf consists of the pericyclic cells and the inner central area of the leaf (*i.e*., the gel) along with the leaf extract, juice and polysaccharides. They are widely used for cosmetic products primarily as skin conditioning agents and as a base material for skin moisturizers, soaps, shampoos, sunscreen lotions, perfumes, bath aids and many other products (Anderson, 2007; Foster, 2011). Traditionally, the plant has been reported for the treatment of seborrheic dermatitis, genital herpes, ulcerative colitis, mucositis, radiation dermatitis, acne vulgaris, lichen planus, frostbite, aphthous stomatitis, alopecia, bacterial and fungal skin infections, chronic leg wounds, parasitic infections, systemic lupus erythematosus, arthritis and tic douloureux (Surjushe *et al*., 2008; Reynolds *et al*.,

1999). The plant is also known to possess few significant biological activities, *viz*., wound healing, anti-inflammatory, anticancer, hypoglycemic, gastrointestinal disorders, antibacterial, antiviral, antipsoriatic, antiarthritic and for burn treatment (Reynolds *et al*., 1999).

Oil-in-water (O/W) and water-in-oil (W/O) emulsions are widely used for the treatment of dry skin and emollient applications. A cosmetic formulation, including active principles of strictly natural origin, is designed to protect the skin against exogenous or endogenous harmful agents, as well as to balance again the dermal homeostasis lipids altered by dermatosis and ageing. Besides, the countless skin care benefits of *Aloe vera*, the present study is destined to develop and evaluate a pharmaceutically elegant topical Aloe vera cream (AVC) formulation.

2. Material and Methods

2.1 Materials

Fresh *Aloe vera* (L.) Burm. sap was procured from Process Chemistry and Chemical Engineering Department, CSIR-Central Institute of Medicinal and Aromatic Plants (CSIR-CIMAP), Lucknow, India. Light liquid paraffin was purchased from HiMedia Laboratories Pvt. Ltd., Mumbai, India. Soft white paraffin and paraffin wax were procured from SD Fine Chemicals Ltd., Mumbai, India. Olive oil, cetyl alcohol, stearyl alcohol, glycerol monostereate and sodium lauryl sulphate were supplied from CDH Ltd., New Delhi, India. All the chemicals used in the study were of analytical grade or higher and double distilled water was used throughout the study.

2.2 Processing of *Aloe vera* (L.) Burm. sap

Aloe vera (L.) Burm. leaves were cut, washed and then sliced an inch both on upper and lower sides. The leaves were further cut and the pulp was removed thereafter. The obtained pulp was further crushed in a mechanical crusher. After crushing of the pulp it was filtered in order to remove the attached fibres. The *Aloe vera* juice, thus prepared was heated at 50 - 60°C and then treated with 2% charcoal by continuous stirring. Finally *Aloe vera* sap was prepared by filtering the treated juice through celite bed. The obtained sap was collected and stored at 4°C for further use.

2.3 Preparation of AVC formulation

Phase inversion temperature technique was employed to formulate the AVC with the excipients listed in Table 1. In this study, W/O emulsions were prepared by adding the aqueous phase to the oily phase under continuous agitation. The oily phase consisted of light liquid paraffin, white petroleum jelly, olive oil, paraffin wax, cetyl alcohol, stearyl alcohol and glyceryl monostearate. The components of the water phase were sodium lauryl sulphate, *Aloe vera* sap, and distilled water. The ingredients of oil phase (Phase A) and aqueous phase (Phase B) were heated (50-60 °C) in separate beakers and stirred on magnetic stirrer (IKA, India) at 400 rpm. Then, aqueous phase was added slowly to the oil phase and both the phases were mixed thoroughly with constant stirring in order to ensure proper emulsification. After 40-45 min, heating was stopped and when the system attained a temperature of 40°C, a few drops of fragrance was added with continued stirring to give the formulation a pleasant fragrance and finally a white coloured smooth AVC was obtained. The cream formulations were optimized on the basis of organoleptic characteristics and textural parameters by varying the concentration of the emulsifiers. The optimized formulation was stored in properly labelled collapsible tubes and kept at room temperature for further evaluation.

Table 1: Composition of AVC formulation

Ingredients	Percent Concentration
Phase A	
Light liquid paraffin	6.0
White petroleum jelly	2.0
Olive oil	1.0
Paraffin wax	0.5
Cetyl alcohol	2.0
Stearyl alcohol	2.0
Glycerol monostereate	3.15
Methyl paraben	0.1
Phase B	
Propyl paraben	0.05
Sodium lauryl sulphate	0.85
Purified water	q. s.
Aloe vera sap	10.0
Fragrance	q. s.

2.4 Pharmaceutical evaluation of AVC formulations

2.4.1 pH Measurement

About 10% (w/v) solution of AVC in distilled water was prepared to measure the pH using a digital pH meter (Mettler Toledo, Model LE-438) at 25 ± 1° C. Experiments were performed in triplicate.

2.4.2 Viscosity measurement

Viscosity of AVC was measured using Brookfield Viscometer DVLV-II + Pro Model at 25 ±1°C and 0.5 rpm speed by Spindle No. 96. Measurements were performed in triplicate.

2.4.3 Texture analysis

The developed AVC was also assessed for different texture parameters, parameters that mimic human sensory perceptions namely, firmness, spreadability, extrudability, adhesiveness and cohesiveness by using CT3 Texture Analyzer (Brookfield Engineering Laboratories, USA) and was compared with a popular marketed skin cream. All the graphs and data were generated using Texture Pro CT V1.3 Software, and formulations were evaluated in triplicate.

2.4.4 Stability studies

Stability studies of the optimized formulation were carried out for a period of 90 days to ensure the absence of any sort of degradation or deterioration in the formulation. The optimized cream formulation (AVC) was stored in well closed containers for a period of 90 days at room temperature. At predetermined intervals: 0, 30, 60 and 90 days, samples were collected and their physicochemical evaluation parameters such as colour, consistency, phase separation, texture analysis and pH evaluated (Rai *et al*., 2014). The

centrifugation test was also performed, which is of major interest to determine the stability profile, where the occurrence of phase separation was recorded (Nuno *et al*., 2012).

2.4.5 Skin irritation study

Skin irritation studies were also performed for AVC formulation in six healthy New Zealand white rabbits (1500 ± 500g b.w.) in accordance with the Federal Hazardous Substances Act (FHSA) guidelines. The experimental protocol has been approved by the Institutional Animal Ethical Committee of CSIR-CIMAP, Lucknow, India. As per the procedure, AVC, placebo cream, standard irritant and marketed antiseptic cream (500 mg) were smoothly applied over the previously shaved rabbit's skin on one inch square area. Normal saline (1%) was also applied as positive control on the opposite side of the skin. Observations were made at 4, 24, 48, and 72h to assess individual erythema and edema using the FHSA recommended Draize scoring criteria (Yadav *et al*., 2013). The primary irritation index (PII) was determined using the following formula:

PII = Test Score-Control Score

3. Results and Discussion

Aloe vera cream (AVC) was formulated without any considerable changes in organoleptic characters like colour, odour, consistency, homogeneity and there was no phase separation observed during the course of the study. The prepared formulation was evaluated for pH, viscosity and textural sensory parameters which depicted the human sensorial parameters like hardness, spreadability, extrudability, adhesiveness and cohesiveness. The formulation was also evaluated for stability studies and skin irritation study.

3.1 pH measurement

The pH value of 10 % solution of the developed AVC was found to be 6.6 ± 0.2 which lies within the range of human skin pH (4.5 to 7.0). The result depicted that the pH of the cream formulation implies with its compatibility with the human skin on topical application without any risk of allergy or irritation.

3.2 Viscosity measurement

The viscosity of AVC was measured by a Brookfield viscometer using Spindle No. 96 at 0.5 rpm at room temperature and was found to be 352000 ± 2.65 cps. In topical cream formulations, viscosity is a useful process indicator of emulsion quality, as it is highly sensitive to changes in the emulsion due to variations in process and formulation parameters. It also influences the overall consumer's acceptance via regulation of the spreadability factor. Stoke's law also justifies this fact as according to this law, viscosity is inversely proportional to sedimentation/creaming, thereby, affecting the stability of the formulation (Yadav *et al.,* 2013). As creaming is allied with the size and homogeneity of the particles as well as the viscosity of the system, its rate will be reduced when the particles are homogeneous, small, and the system is having desired viscosity.

3.3 Texture analysis

Firmness, spreadability, extrudability, adhesiveness and cohesiveness, these parameters depicting the human sensorial perception are collectively called texture parameters. This evaluation is performed by using particular probes through CT3 Texture Analyzer (Brookfield Engineering Laboratories, USA; Yadav *et al*., 2013; Rai *et al*., 2014). Without having any fixed selection criteria or official standards (pharmacopoeial/regulatory), these parameters are characterized on the basis of product specific requirement (Meher *et al.,* 2013). The cream formulation (AVC) was assessed on the basis of values obtained for each parameter in comparison to a popular marketed skin cream formulation (MCF) as recorded in Table 2.

Table 2: Texture profile of AVC formulation

Parameter	AVC	MCF
Firmness (g)	53 ± 0.16	57 ± 0.12
Spreadability (mJ)	5.0 ± 0.21	5.6 ± 0.17
Adhesiveness (g)	23.2 ± 0.13	21.52 ± 0.20
Cohesiveness	0.96 ± 0.01	0.79 ± 0.10
Extrudability (mJ)	183.6 ± 0.69	250.7 ± 0.12

The values are expressed as Mean ± SEM, n=3, AVC- *Aloe vera* Cream, MCF-Marketed cream formulation

Firmness of a sample is the maximum positive force required to deform the sample, *i.e*. the formulation with the finger as imitated by the probe. As clear from the values, MCF required more force (57 ± 0.12g), thus showing MCF is harder than the AVC (53 ± 0.16). The overall elegance and consumer's acceptance of the topical formulation is attributed towards the parameter of spreadability, which is known as the amount of work required for spreading the sample over a surface. The value of spreadability of AVC was found to be (5.0 ± 0.21mJ) which was lesser than that of MCF (5.6 ± 0.17), depicting better spreadability of the developed formulation. Likewise, extrudability is the force required to uniformly extrude the sample out of its container. The work done to extrude AVC from its tube was found to be (183.6 ± 0.69mJ) and that of MCF was found to be higher revealing its lesser extrudability properties (250.7 ± 0.12mJ). Poor and non-uniform extrudability is indicative of deterioration or instability of any particular formulation as well as any sort of incompatibity if persists, between sample and its container. Adhesiveness is considered as the maximum force required for overcoming the attractive forces between any surface and sample (cream). It is a measure of the stickiness of the sample (23.2 ± 0.13 g). Cohesiveness signifies the strength of internal bonds that is responsible for overall elegance of the formulation. Mathematically it is the ratio of hardness work done at two cycles (Meher *et al*., 2013).

3.4 Stability studies

Colour, consistency, viscosity, texture profile and pH of AVC were found to be consistent and no signs of separation and deterioration were observed over a period of 90 days. This revealed the reproducibility of the physical and chemical parameters which ensures a consistent quality of the developed AVC over a longer duration. In this test, the formulation showed stability during the 90 days of study. Regarding the organoleptic characteristics, it was observed that no significant changes in colour, odour and consistency occurred ensuring the stability of the cream over a period of 90 days under storage at room temperature. The pH value is a significant parameter as far as the effectiveness of the

Table 3: Primary Irritation Index of different samples in skin irritation test

Sample		Reaction	6h	24 h	48 h	72 h	PII	Results
Saline	Test site	Erythema	0	0	0	0	0.0	Non irritant
		Edema	0	0	0	0		
	Control site	Erythema	0	0	0	0		
		Edema	0	0	0	0		
Base	Test site	Erythema	0	0	0	0	0.0	Non irritant
		Edema	0	0	0	0		
	Control site	Erythema	0	0	0	0		
		Edema	0	0	0	0		
Standard irritant	Test site	Erythema	2	2	2	1	3.8333	Moderate irritant
		Edema	4	3	2	1		
	Control site	Erythema	0	0	1	0		
		Edema	0	0	1	0		
Aloe vera cream (AVC)	Test site	Erythema	0	0	0	0	0.0	Non irritant
		Edema	0	0	0	0		
	Control site	Erythema	0	0	0	0		
		Edema	0	0	0	0		

Table 4: Classification of response categories based on Primary Irritation Index

Primary Irritation Index(PII)	Category
00	No irritation
0.04 - 0.99	Irritation barely perceptible
1.00 - 1.99	Slight irritation
2.00 - 2.99	Mild irritation
3.00 - 5.99	Moderate irritation
6.00 - 8.00	Severe irritation

cream is concerned and it can be used as an indicator of the formulation stability. The pH values of the developed formulation showed minimal changes (between 5.9 and 6.8), without displaying any remarkable alterations. In the centrifugation test, phase separation was not observed in the sample which is an indicative of the proper emulsification and mixing of all the components.

3.5 Skin irritation study

Assessment of skin irritancy of topical cosmetic and pharmaceutical products with natural compounds is a significant step in the evaluation of their biocompatibility (More *et al*., 2013). Skin irritation studies in rabbits ensured that the developed cream formulation (AVC) was non-irritant in nature. According to FHSA regulations, a material with PII less than 1.0 is generally not considered as irritant to the skin. Developed cream formulation exhibited no irritancy with nil PII hence was considered to be non-irritant to skin at the applied dose (500 mg). Erythema and edema, both the reactions were used as indicators to keenly observe any sort of irritation for every treatment in all the rabbits.

Aloe vera is known to contain numerous potentially active constituents, *viz.* vitamins (A, C, E, B_{12}), enzymes aliiase, alkaline phosphatase, amylase, bradykinase, carboxypeptidase, catalase, cellulase, lipase, and peroxidise among which, bradykinase helps to reduce excessive inflammation when applied to the skin topically, minerals, calcium, chromium, copper, selenium, magnesium, manganese, potassium, sodium and zinc, monosaccharides like mannose-6-phosphate and glucomannans as polysaccharides. Alprogen is a recently discovered glycoprotein with anti-allergic properties isolated from this plant. It also possesses traditionally known anthraquinones as laxatives, whereas, compounds aloin and emodin present in this plant act as analgesics, antibacterials and antivirals. Also, a novel anti-inflammatory compound, C-glucosyl chromone, has been identified in *Aloe vera* gel along with other compounds cholesterol, campesterol and β-sisosterol having similar effects. Lupeol present in this plant possess anti-inflammatory, analgesic and antiseptic properties. Hormones, auxins and gibberellins are known to be responsible for its wound healing effects. Lignin, an inert substance, when included in topical preparations, enhances penetrative effect of the other ingredients into the skin. Saponins are also present about 3% of the gel and have cleansing and antiseptic properties (Anderson, 2007; Foster *et al*., 2011). Numerous clinical trials of *Aloe vera* have been conducted worldwide for its use in burn and wound healing, gastrointestinal disorders, constipation, diabetes mellitus, and other skin conditions. The pharmacological actions include anti-inflammatory, antiarthritic activity, antibacterial, antiviral, anticancer, immunomodulatory and hypoglycaemic effects (Vogler

et al., 1999). Numerous subsequent reports have explored the role of topical use of *Aloe vera* in diseased skin conditions including psoriasis, acne vulgaris, dermatitis, oral mucositis, against radiation damage, burn injuries and surgical wounds management (Syed *et al*., 2006; Anderson, 2007; Foster *et al*., 2011).

In view of the widespread skin care uses of *Aloe vera*, it is evident that, mucopolysaccharides present in the gel help in binding moisture into the skin. Aloe stimulates fibroblast which produces the collagen and elastin fibers increasing the elasticity of the skin. Its cohesive effect on the superficial epidermal cells increased capillary perfusion and presence of amino acids softens the skin, moreover zinc acts as an astringent to tighten pores. It is a well-known house hold remedy for its moisturizing effects in treatment of dry skin with improved skin integrity, decreased appearance of wrinkles and erythema (Surjushe *et al*., 2008; Reynolds *et al*., 1999). It could also expedite the healing of chronic skin ulcers on the basis of its occlusive properties (Shelton, 1991). Aloe gel is also noted as a cleanser, anaesthetic, antiseptic, antipyretic, antipruritic, nutrient, and is said to promote cell proliferation. Aloenin is responsible for promoting hair growth and is used as a treatment for brittle hair. It is also recognized to have a marked effect in the prevention and treatment of scar tissue due to the stimulation of cell production, and also, due to the ability to promote regeneration at the deepest layers of the skin. It is suggested that lectin may be responsible for the therapeutic effect of the gel on burns. *Aloe vera* can be used successfully in the general treatment of skin ulcers, including mouth ulcers, cold sores (herpes simplex), and leg ulcers (Eshun, 2010). The moisturizers may act by an occlusive mechanism, impairing evaporation of skin moisture by forming an epicutaneous greasy film that prevents water loss, as is the case with oils and lipids, or as humectants, which act by attracting water from the other layers of the epidermis to the stratum corneum. Moreover, *Aloe vera* not only possesses good moisture retention capability but also has a definite nutritional effect on human skin (Khan *et al*., 2010). It soothes, cools and seals in moisture, due to its high water and mineral content which make it ideally suited for use as a skin cream, and it can be incorporated in a number of commercial cosmetic products. In a report, it is confirmed that *Aloe vera* extract is a natural effective ingredient for improving skin hydration, which can be used in moisturizing cosmetic formulations and also to complement the treatment of dry skin (Daalbelo, 2006).

4. Conclusion

In a nut shell, we conclude that a non-irritant, stable and cosmetically elegant, skin care cream containing *Aloe vera* (L.) Burm. sap has been developed and optimized on the basis of textural parameters. Texture parameters articulated that the overall elegance and aesthetic appearance of the formulation was more appealing compared to the marketed formulation. Thus, the developed AVC formulation has a potential for further application as safe topical preparation to treat various skin conditions and retain skin moisture without any irritation.

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Conflict of interest

We declare that we have no conflict of interest.

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