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Development and Assessment of Polyherbal Face Cream for Skin Whitening

Nithyapriya Karuppusamy[1], Sutha Ponnusamy[2], Sangameswaran Balakrishnan[3], Gayathri.K[4], Gokulnath.D[5], Gowtham.D[6], Gowtham.R[7]

Associate Professor, Department of Pharmaceutics. Principal and Professor, SSM College of pharmacy, Erode-638312, TN, India. The Tamil Nadu Dr. M. G. R Medical University, Guindy, Chennai-600032, TN, India.

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ABSTRACT

To improve their complexion, most people use whitening creams. The primary component of skin pigmentation and color is melanin. Tyrosinase inhibitors are crucial for cosmetic skin whitening because tyrosinase catalyzes the synthesis of melanin. The current study's goal is to create and assess a polyherbal face cream made with extracts of licorice (Glycyrrhiza glabra), aloe vera, turmeric (Curcuma longa), and neem (Azadirachta indica) selected for their reported skin-brightening, antioxidant, and anti-inflammatory properties. The prepared formulation was evaluated for microbial load, stability under accelerated conditions, organoleptic properties, and physicochemical parameters (pH, viscosity, spreadability, and washability). Tyrosinase inhibition and antioxidant activity (DPPH method) were two in vitro tests used to assess the formulation's whitening potential. The results indicated that the cream possessed acceptable physicochemical characteristics, remained stable under different storage conditions, and exhibited significant antioxidant and depigmenting activity compared to the control. The results imply that the created polyherbal face cream is a natural, safe, and efficient substitute for artificial skin-whitening agents, with potential advantages for dermatological and cosmetic uses.

Keywords: Polyherbal formulation, face cream, skin whitening, antioxidant, tyrosinase inhibition, herbal extracts.

INTRODUCTION

"Skin pigmentation" is the term used to describe the coloring of the skin. Melanin, a pigment produced by specialized cells called melanocytes, is deposited in certain areas or patches of the skin, making them darker.

Melanocytes:

Melanocytes are specialized cells that produce melanin and are located in the epidermis' basal layer. The epidermal melanin unit is an ordered structure made up of about 30 to 40 keratinocytes that are functionally connected to each melanocyte. The number of melanocytes is nearly similar among all humans irrespective of skin color; differences arise due to the activity of melanocytes rather than quantity.

Melanocyte

Melanin granules are found in melanosomes, which are produced by melanocytes.

Melanosomes transferred to Keratinocytes.

UV light and melanocyte-stimulating hormone, which the anterior pituitary gland secretes, both promote the production of melanin pigment.

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Melanin types:

Melanin comes in two varieties:

Eumelanin

Pheomelanin

Eumelanin

A brown-to-black pigment. It offers substantial protection from the sun's UV rays and is primarily responsible for darker skin, hair, and eye colors.

Pheomelanin

A reddish-yellow pigment. It adds a reddish or yellowish hue to skin and hair. It is less protective and contributes to photosensitivity.

Melanogenesis or the synthesis of melanin:

Melanosomes are specialized intracellular organelles that produce melanin. Tyrosinase, a crucial enzyme in the biosynthesis of melanin, catalyzes:

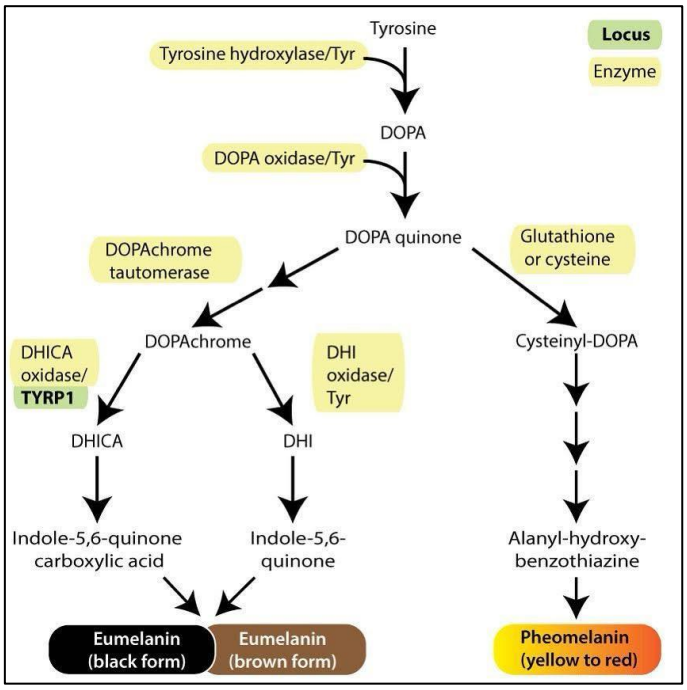

Figure 01: Sequence of reaction involved in the conversion of tyrosine to melanin

Factors influencing the pigmentation of skin:

Genetics, sun exposure, hormonal fluctuations, and skin trauma such as injuries or inflammation are all factors that impact pigmentation. Other influences are age, certain medications, and skin disorders.

- **Genetic factors:**

Because genetics regulates melanin production, it is a major factor in determining an individual's natural skin, hair, and eye color.

A person's sensitivity to sun exposure and melanin production are influenced by variations in genes such as MC1R.

➢ **Environmental aspects:**

Sun exposure: It is the most frequent cause of pigmentation because UV light causes melanocytes to produce more melanin as a defense.

Pollution: Air pollutants can penetrate the skin and contribute to pigment spots, with studies showing a link between exposure to certain pollutants and an increase in pigment spots on the face, notes Dermatology Times.

Skin trauma: Burns, cuts, and even acne can result in post-inflammatory hyperpigmentation because the skin may not properly replace the pigment in those areas after healing.

➢ **Hormonal aspects:**

Fluctuations in hormones like estrogen and progesterone can alter melanocyte activity and trigger pigmentation issues such as melasma, according to Eucerin.

➢ **Age:**

The quantity of melanocytes gradually decreases with age.

This can result in uneven melanin distribution and the development of age spots when combined with lifetime exposure to the sun and other factors.

➢ **Additional factors:**

Medication: Pigmentation can be brought on by or made worse by certain medications.

Skin disorders: Various skin conditions can affect melanin production and lead to pigmentation changes.

Medical conditions: Pigment availability and overall pigmentation can be impacted by health issues that adversely affect digestion and absorption, such as gut dysbiosis.

OVERVIEW OF THE SKIN

The integumentary system includes the skin, hair, nails, and glands. The integument is the body's largest organ and accounts for 15% of body weight. Made up of several layers of ectodermal tissue, skin is the soft outer layer of our body's integumentary system that shields the internal organs, muscles, bones, and ligaments beneath. The skin serves as the body's first line of defense and is crucial in preventing infections, external trauma, and excessive water loss. The skin serves a variety of purposes, such as insulation, protecting vitamin D and folates, controlling body temperature, fluid and electrolyte balance, and providing receptors for touch, pain, and pressure. In an attempt to heal, severely damaged skin formed scar tissue. This is frequently depigmented and discolored. To exert these vital functions, skin has evolved an elaborate structure comprised of tissues of various origins.

Skin functions include:

- Thermoregulation – Sweat evaporation and blood flow control to the dermis.
- Touch, pressure, vibration, pain, warmth, and coolness are examples of cutaneous sensations.
- Vitamin D protection: Skin precursor molecules and UV sunlight produce vitamin D.
- Protection: The layers serve as a physical barrier to stop infectious hazards and organism invasion.
- Absorption and secretion - Water-soluble molecules are absorbed by the skin, and sweat and water are expelled.
- Wound healing: Basal cells of the epidermis separate from the basement membrane, move across the wound, and heal it after a small burn or abrasion.

AIM AND OBJECTIVES

The creation of a polyherbal face cream associated with skin whitening is the aim of this research. The work was divided into several major sections, including collection and authentication of the plant materials, extract preparation, and biological assessment, followed by formulation of cream.

Objectives:

- Plants are chosen based on their ethnomedical uses.
- Extraction of the plant materials by using ethanol as solvent depending on the literature review and condition of the raw material.
- Using certain medicinal plants, topical skin-whitening formulas are created.
- Physical, chemical, microbiological, and functional evaluation of the formulation. Analysis, storage, and stability of prepared formulations.
- Measure antioxidant capacity of extracts and formulations using assays such as DPPH (1,1-diphenyl-2-picryl hydrazyl radical) solution.

MATERIALS AND METHODS

Table no:1 List of Excipients used and their sources

S. No	MATERIALS	USES	MANUFACTURER
1.	Bees Wax	Oil phase	Research labs, Mumbai
2.	Almond oil	Oil phase	Dabur India ltd.,
3.	Borax	Surfactant	Research labs, Mumbai
4.	Methyl paraben	Preservatives	Lepid life science Private ltd., Bangalore
5.	Distilled water	Vehicle	Scientific suppliers, Salem
6.	Liquid paraffin	Moisturizing	Sisco Research Laboratories Pvt Ltd, Mumbai
7.	Stearic acid	Emulsifier	Sisco Research Laboratories Pvt Ltd, Mumbai
8.	Ethanol	Solvent	Loba chemie Pvt Ltd., Mumbai

Table no:2 List of Equipments used

S. No	EQUIPMENTS	MANUFACTURE MODEL/APPLIANCE
1.	Weighing balance	Satorious 21.00(Max 220g)
2.	Water bath	Esel international, Ambla
3.	Blender (mixer grinder)	Preeti wet grinder
4.	Magnetic stirrer	Adarsh Magnetic stirrer
5.	Siever (mesh no:100, 120)	Sethi standard test sieves, Delhi
6.	UV Spectroscopy	UV 1800 Series, Shimadzu
7.	pH Meter	Digital pH Meter

SELECTED PLANT MATERIAL EXTRACTION

Making an ethanolic extract from turmeric (curcuma longa) rhizomes:

The fresh turmeric rhizomes were taken and washed with water to remove the soil, then sliced thinly. Dry in shade or in a hot-air oven at 40-50°C. Grind the dried rhizomes to a coarse powder. A conical flask containing 20 grams of powder is filled with 200 millilitres of 96% ethanol, sealed, and macerated at room temperature for 48 to 72 hours with sporadic shaking. After that, a Büchner funnel was used to filter the maceration. Re-macerate the marc (residue) with fresh solvent for 24 hours and combine filtrates to maximize yield. A dried extract was produced by combining and concentrating the extract filtrations using an evaporator.

Preparation of ethanolic extract of neem leaves (Azadirachta indica):

The fresh neem leaves were taken, and the leaves were washed under running water to remove the dust and then dried in the shade. Grind the dried leaves to a coarse powder. A total of 20 gm of powder is taken in a conical flask, and 200 ml of 96% ethanol is added, then sealed and macerated for 48-72 hours with occasional shaking at room temperature. The maceration was then filtered with a Büchner funnel. Re-macerate the marc (residue) with fresh solvent for 24 hours and combine filtrates to maximize yield. A dried extract was produced by combining and concentrating the extract filtrations using an evaporator.

Preparation of ethanolic extract of licorice root (Glycyrrhiza glabra):

The liquorice root was taken and dried under the shade. The dried root should be ground into a coarse powder. After adding 100 ml of 96% ethanol to a conical flask containing 10 grams of powder, the flask is sealed and allowed to macerate for 48 to 72 hours at room temperature with sporadic shaking. After that, a Büchner funnel was used to filter the maceration. Re-macerate the marc (residue) with fresh solvent for 24 hours and combine filtrates to maximize yield. A dried extract was produced by combining and concentrating the extract filtrations using an evaporator.

Figure 02: Extraction of Turmeric rhizomes, Neem leaves, Liquorice root

Preparation of ethanolic extract of aloe vera:

The fresh aloe vera leaves were cleaned, the base and tip removed, and the inner gel was scraped with a sterile spoon while avoiding the yellow rind and latex. A total of 20 gm of fresh gel was taken and 200ml of 70% ethanol in a conical flask. Transfer to a flask after briefly homogenizing the gel and ethanol in a blender for two to five minutes to increase contact. Sealed and stirred for 24-48 hrs at room temperature. Re-macerate the marc (residue) with fresh solvent for 24 hours and combine filtrates to maximum yield. Because fresh gel contains water, concentrate the combined filtrates on a rotary evaporator under low pressure to remove ethanol to a small volume. Finally, it is dried in an oven at 40-45°C to a constant weight.

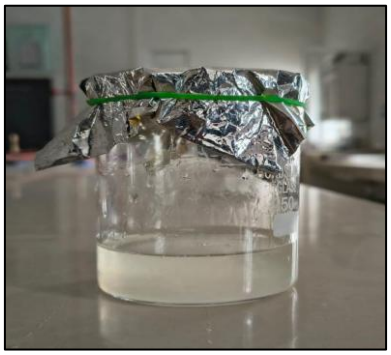

Figure 03: Extraction by maceration

METHODS

Preliminary phytochemical screening of curcuma longa:

Curcuma longa's ethanol extract was subjected to a phytochemical analysis to determine whether alkaloids, carbohydrates, phenols, flavonoids, tannins, saponins, and steroids were present.

Preliminary phytochemical screening of Azadirachta indica:

To identify phytochemicals like alkaloids and flavonoids, an extract of neem leaves (Azadirachta indica) was put through a number of qualitative tests. Glycosides, Anthraquinones, Terpenoids, Tannins, Phenols, and Saponin.

Preliminary phytochemical screening of Glycyrrhiza glabra:

The Glycyrrhiza glabra extract samples were screened for their qualitative phytochemicals screening using qualitative analysis of many constituents, including alkaloids, flavonoids, tannins, saponins, terpenoids, proteins, phenols, and anthraquinones.

Preliminary phytochemical screening of Aloe vera:

To identify phytochemicals like alkaloids, flavonoids, tannins, steroids, anthraquinones, phenols, and terpenoids, the aloe vera extract was put through a number of qualitative tests.

DEVELOPMENT OF FORMULATIONS

Step I: oil phase was prepared by heating beeswax, Cetyl alcohol, liquid paraffin, and almond oil at 70°C and was incorporated separately into each cream.

Step II: The water phase was prepared by adding Curcuma longa, Azadirachta indica, Glycyrrhiza glabra, and Aloe vera gel, which were mixed uniformly. Meanwhile, sodium benzoate and borax were dissolved in water and added to the water phase, and it was allowed to heat up to 70°C.

Step III: After adding the oil phase to the water phase at 70°C and stirring continuously for 20 to 25 minutes, the mixture was homogenized until a homogenous emulsion was formed. The final product is semisolid and has a light yellowish hue. After that, it was transferred into the wide-mouth container and kept at a temperature of no more than 37°C.the various concentration of the polyherbal cream is interpreted in the table no:03.

Table no. 3: Composition of polyherbal cream

S. NO	INGREDIENTS	F1	F2	F3	F4
1.	Stearic Acid	15gm	12gm	12gm	10gm
2.	Cetyl Alcohol	2gm	3gm	4gm	4gm
3.	Bees Wax	2gm	2gm	3gm	3gm
4.	Curcuma longa extract	1ml	1ml	1ml	1ml
5.	Azadirachta indica extract	1ml	1ml	1ml	1ml
6.	Aloe vera extract	1ml	1ml	1ml	1ml
7.	Glycyrrhiza glabra extract	1ml	1ml	1ml	1ml
8.	Borax	2gm	1gm	3gm	2gm
9.	Rose Water	Q. S	Q. S	Q. S	Q. S
10.	Distilled Water	100ml	100ml	100ml	100ml
11.	Liquid Paraffin	2ml	2ml	1ml	2ml
12.	Glycerin	1ml	1.5ml	1ml	2ml
13.	Methyl Paraben	0.1gm	0.1gm	0.1gm	0.1gm
14.	Almond oil	4ml	4ml	4ml	4ml

Figure 04: Prepared Polyherbal face cream for Skin Whitening

PHYSICOCHEMICAL EVALUATION

a) Clarity

Each formulation's clarity was visually assessed, and categorized as turbid, clear, or extremely clear against a black-and-white backdrop.

b) pH

2.5 g of cream was carefully weighed before being dissolved in 25 ml of distilled water. The mixture's pH was determined using a digital pH meter.

c) Smear type, homogeneity, and removal test

All the prepared formulations were tested for homogeneity by their visual appearance and by touch. The kind of film or smear that developed on the skin after the cream was applied was examined. By washing the area where the cream was applied under running water, the ease of removal of the cream was assessed.

d) Acidity level

In a flask, 50 milliliters of a solution of equal parts alcohol and solvent ether were used to dissolve 10 grams of the cream. One milliliter of phenolphthalein is added, and the mixture is titrated with 0.1N NaOH until a faint pink color appears after shaking for thirty seconds. The flask is then connected to a reflux condenser and heated gradually until the sample dissolves completely.

$$\text{Acid value} = n * 5.61/w$$

Where n = The number of ml of NaOH required and w = the weight of the cream

e) Value of saponification

After refluxing 2 g of the cream with 25 ml of 0.5 N alcoholic KOH for 30 minutes, 1 ml of phenolphthalein was added, and 0.5 N HCl was titrated right away.

$$\text{Value of saponification} = (b - a) * 28.05 / w$$

where a is the titrant volume, b is the titrate volume, and w is the cream weight.

f) Viscosity Measurement

The viscosity is measured using a Brookfield viscometer of the F1 through F4 cream formulations. (Model no. LVDV) with measurements were performed using spindle n. LV-62,2 which was rotated at 100rpm, and the temperature was maintained at 25±1°C.

g) Spreadability test

The formulations were placed on the glass slide, and then the empty glass slide was placed on top of the cream-containing slide. The herbal cream placed between slides was pressed to form a thin, uniform layer. A weight of 10 ± 0.5 g was fastened to the upper glass slide after the two slides were fixed. The amount of time needed to divide the two slides that is, the amount of time it took for the upper glass slide to pass over the lower plate was used as a gauge of spreadability because the two slides were separated due to weight. The formula was used to determine the spreadability.

$$S = m \times l/t$$

where m is the weight attached to the upper slide, t is the duration, and l is the distance traveled on the glass slide.

h) Extrudability

This method involved filling a standard collapsible aluminum tube with a cap and sealing it by crimping the end. The tubes' weights were noted. The tubes were clamped between two glass slides. After covering the slide with 500 g, the cap was taken off. The extruded gel's volume was gathered and weighed. The percentage of extruded gel (> 80% extrudability satisfactory, > 90% extrudability excellent) was calculated.

i) Determination of thermal stability

Using a spatula, the cream was moved into the Petri plate, where it was tapped to settle down to the bottom. The petri plate is filled to two thirds of its capacity, and the lid is shut. The filled for 48 hours, the Petri plate was incubated at 45°C.

j) Anti- oxidant activity

To determine the antioxidant activity, 10 mg of the sample was dissolved in 100 ml of methanol, yielding a concentration of 1 µg/ml. Similarly, different concentrations were made at 20, 30, and 40 µg/ml. 3.8 ml of 50 µM DPPH (1,1-diphenyl-2-picryl hydrazyl radical) solution was added after 0.2 ml of the sample solution. After homogenizing the solution mixture, it was allowed to sit at room temperature (25°C) in the dark for half an hour. A UV spectrophotometer operating at a wavelength of 517 nm was used to measure absorption. The following formula was used to determine the scavenging ability, which was represented as the inhibition percentage:

$$\% \text{ inhibition} = [(\text{Control-Test})/\text{control}] \times 100.$$

RESULTS AND DISCUSSION

Studies on phytochemicals

Curcuma longa, Azadirachta indica, Glycyrrhiza glabra, and Aloe vera were studied phytochemically. Table No. 4 displayed whether the ethanolic extract of the aforementioned sample was present or not.

Table no 4: Phytochemical studies

S. No	Phytoconstituents	C.longa extract	Azadirachta indica extract	Glycyrrhiza glabra extract	Aloe vera extract
1.	Alkaloids	+	+	+	-
2.	Phenols	+	+		+
3.	Flavanoids	+	+	+	+
4.	Tannin	+	+	+	+
5.	Saponin	-	+	+	
6.	Terpenoids		+	+	
7.	Proteins			-	
8.	Steroids	+			+
9.	Glycosides		+		
10.	Anthraquinones		-	-	+

Organoleptic properties

The color, odour, consistence, texture of the formulations was reported in the table no:5.

Table no 5: Organoleptic properties.

S.no	Properties	F1	F2	F3	F4
1.	Color	Light yellow	Light yellow	Light yellow	Light yellow
2.	Odour	Pleasant	Pleasant	Pleasant	Pleasant
3.	Consistence	Semisolid	Semisolid	Semisolid	Semisolid
4.	Texture	Soft	Soft	Soft	Soft

pH test

The pH range of the four different formulations' results is 6.4–7.0. This demonstrates that the pH of the four formulations is safe and compliant with the standards based on the specifications, which fall between 3.5 and 8. Thus, it is anticipated that the prepared cream will not irritate the skin. Additionally, the following table no: 6, provides an interpretation of the values.

Viscosity

The viscosity of the different formulations was recorded and the values are interpreted in table no: 6.

Acid value and saponification value

The acid value and saponification value of the different formulations were carried out by and table no: 6 displays the results, which demonstrate satisfactory values**.**

Determination of Spreadability

The formula and the outcomes are used to determine the spreadability of the creams are explained in table no: 7 that follows.

Thermal stability determination

After the incubation period of 48 hours at 45°C, the Petri plates that contain the formulated cream was examined for phase separation and the results are shown in table no: 7.

Table no:6 Evaluation parameters

Formulation	pH	Viscosity	Acid value (mgKOH/gram)	Saponification value(mgKOH/gram)
F1	7.0	4900	4.5	155.10
F2	6.8	4900	5.2	157.08
F3	6.5	4900	6.5	173.5
F4	6.4	4900	6.7	187.03

Table no:7 Evaluation parameters

Formulation	Homogeneity	Type of smear	Removal test	Spreadability (seconds)	Thermal stability
F1	Homogenous	NG	ER	7	NPS
F2	Homogenous	NG	ER	10	NPS
F3	Homogenous	NG	ER	8	NPS
F4	Homogenous	NG	ER	5	NPS

NG-Non greasy, ER- easy removal, NPS- No phase separation

Extrudability

The extrudability of different formulations were recorded and the values are listed in the table no:8.

Table no:8 Extrudability of Formulations

S. No	Formulations	Extrudability
1.	F1	+
2.	F2	++
3.	F3	+
4.	F4	++

Anti-oxidant activity

The stable free radical DPPH, which has a deep violet hue, reacts with the antioxidants to produce 1,1-diphenyl-2-picryl hydrazine with decolorization. The formulation's percentage inhibitions are 78.9%, 80.6%, 83.8%, and 86.5%, respectively. There was an increase in the scavenging of DPPH radicals because various herbal extracts had higher levels of radical-scavenging capacity than ascorbic acid, which had a scavenging effect of 89.6%. The percentage inhibition of the test sample is compared with the standard ascorbic acid percentage inhibition, and results are interpreted in the following table no. 9.

Table no:9 Anti-oxidant activity

S. No	Formulation	Percentage inhibition
1.	F1	75.9%
2.	F2	81.5%
3.	F3	82.8%
4.	F4	86.5%
5.	Ascorbic acid (Standard)	89.6%

CONCLUSION

The study states that, in the preparation of four formulations, F1, F2, F3, and F4, while performing evaluation tests Regarding the F1, F2, F3, and F4 formulations, the formulation F4 shows good results in pH, viscosity, homogeneity, type of smear, removal test, spreadability, thermal stability, and the antioxidant of 86.5%, and the phytochemical analysis confirmed the presence of bioactive components linked to skin-brightening and melanin-regulating effects, such as flavonoids, phenols, and glycosides, which are associated with skin-brightening and melanin-regulating effects. So, from the above result, it was concluded that F4 is the best formulation. As everyone knows, it is impossible to increase the level of efficacy of a single plant extract's therapeutic and cosmetic qualities, but it might be possible to do so by combining a variety of different plant extracts. In this regard, we combined the extracts of Curcuma longa, Azadirachta indica, Glycyrrhiza glabra, and aloe vera to improve and complement the product's aesthetic characteristics in comparison to the extracts used alone. However, further research is needed to make this a useful formulation.

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