FORMULATION AND EVALUATION OF HERBAL HYPERPIGMENTATION CREAM FOR ITS TYROSINASE INHIBITOR ACTIVITY

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ABSTRACT-

The present study was point out with the object of development, formulation and evaluation of a herbal hyperpigmentation cream that improve uneven skin tone , reduce the appearance of dark spots , hyper pigmentation and promote the breakdown of melanin or restrict its creation, so preventing it from reaching the skin's surface. Herbal hyperpigmentation cream was formulated with the juice of *Sweet potato* and aqueous extract of *Glycyrrhiza glabra* that are commonly used for skin hyperpigmentation because of their tyrosinase inhibitor and antioxidant property. Tyrosinase inhibitor and antioxidant are crucial in treatment skin pigmentation disorders because they target the key enzyme, tyrosinase, responsible for melanin production, reducing the photo-oxidation of existing melanin, thereby reducing hyper pigmentation and promoting skin lightening. In present study our aim is to develop an Herbal Hyperpigmentation cream which would be natural. The Herbal Hyperpigmentation cream was prepared by Trituration method and further Evaluated for various evaluation parameters such as Physical properties, Determination of pH, Spreadability, Viscosity, Washability, after feel test, Greasiness, Phase separation, Irritancy test, Stability test. The Results demonstrated that the formulated Herbal Hyperpigmentation creams show the good physical appearance with faint pink Color, Smooth consistency, pleasant odor, and Semi-solid state. In conclusion, herbal Hyperpigmentation cream represent a significant contribution to skincare research. Through meticulous formulation processes and rigorous evaluation methods, the herbal Hyperpigmentation cream has been crafted to address the specific needs for reducing pigmentation and uneven skin tone of the face.

KEYWORD- Hyperpigmentation, Melanocytes, Skin lightening, antioxidant, Sweet potato, tyrosinase activity.

INTRODUCTION-

The term melasma is derived from the Greek word ‘melas’ meaning black . It is a disorder of pigmentary system characterized by irregular brown or greyish-brown, acquired hypermelanosis of sun-exposed areas especially the face. Melanin largely decides our skin color and is an essential defense mechanism against the sun for us. Melanin also overproduces with acne and this is what causes the dark skin spots to remain long after the red acne spots have gone . Hyperpigmentation of the skin is a common dermatological condition in which the color of the skin generally becomes darker. These changes in skin coloration can be a result of various internal and external factors including hormonal changes, inflammation, injury, acne, eczema, certain medication, UV exposure, etc. Herbal anti-pigmentation creams are skincare products formulated with natural ingredients derived from plants, herbs, and botanical extracts. These creams aim to address skin discoloration issues, offering an alternative to synthetic or chemical-based treatments. Topical polyherbal formulations are the latest additions to the dermatologists repertoire of treatment. Scientists have known for decades that some plants are amazingly good at reducing and diverting the production of Melanin .Common herbal ingredients include sweet potato, liquorice extract, orange peel extract, beet root extract, vitamin E are known for their skin-brightening and anti-inflammatory properties. Sweet potato is rich in vitamin C, enzymes,and antioxidant which are known to inhibit tryrosinase activity which is key enzyme in melanin synthesis. Liquorice extract, containing glabridin, which also has demonstrated tyrosinase inhibition, effectively reducing melanin production. Orange peel extract contain hesperidin ,vitamin C and flavonoids that show antioxidant and skin-brighting property. Beet root extract and vitamin E also rich in Vitamin C and antioxidant respectively since they also help in hyperpigmentation of skin. The creams are applied topically, targeting specific areas with dark spots or uneven pigmentation. While herbal anti-pigmentation creams are generally considered safer due to their natural origins.

Pigmentation-

pigmentation" refers to the natural coloring of the skin, determined by the pigment melanin produced by specialized cells called melanocytes.

Causes of Skin Pigmentation –

Skin pigmentation is a common condition that can be triggered by various factors. The three leading causes of skin pigmentation are genetics, sun exposure, and particular medications.

Types of Pigmentation-

The two main types of melanin, eumelanin, and pheomelanin, are produced by melanocytes in the epidermal layer of the skin.

a. Pheomelanin- causes lighter skin tones
b. Eumelanin- responsible for darker skin tones

Skin pigmentation disorder-

Changes in melanin production can lead to various skin conditions, including

- **Hyperpigmentation:** Darker patches of skin due to excessive melanin production.
- **Hypopigmentation:** Lighter patches of skin due to reduced melanin production.
- **Depigmentation:** Complete loss of pigment, resulting in white patches.

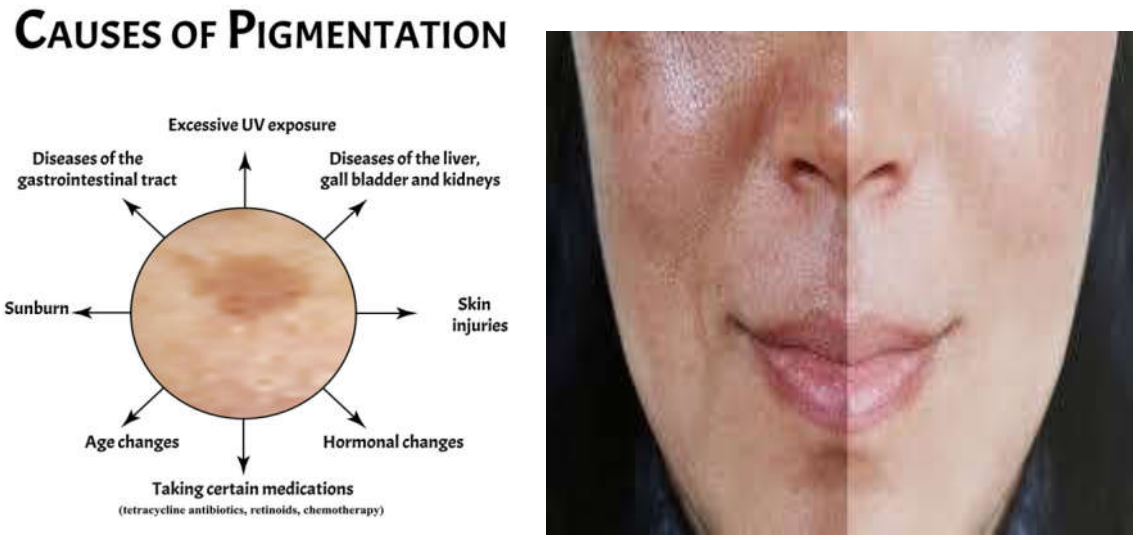


Fig 1-Hyperpigmntation on face

Mechanism-

Skin pigmentation is a complex biological process primarily governed by the synthesis of and distribution of the pigment melanin. This pigment is produced by specialized dendritic cells known as melanocytes, which are located in the basal layer of the epidermis.

1. **Melanogenesis-**
The synthesis of melanin occurs in organelles called melanosomes within melanocytes. Melanogenesis is initiated by the enzyme tyrosinase, which catalyzes the conversion of the amino acid L-tyrosine to L-dopa, and subsequently to dopaquinone.Though a series of enzymatic and non –enzymatic reaction, dopaquinone is then converted to either eumelanin or phenomelanin.

2. **Regulation of melanin Production-**

- UV radiation from sunlight stimulates melanocytes to produces more melanin more melanin as a protective response.
- Hormonal signals, such as melanocytes-stimulating hormones(MSH)bind to MC1R receptors on melanocytes, increasing melanin production.
- Genetics plays amajor role in baseline skin color and how skin reacts to sunlight.

3. **Transfer to keratinocytes-**

Melanosomes are transferred from melanocytes to Keratinocytes, the main cells in the epidermis.
The melanin forms a cap over the nuclei of keratinocytes to protect DNA from UV –induced damage.

4. **Skin color Variation -**

The number of melanocytes is similar across all skin types, but:

- Lighter skin produces less melanin and smaller, less persistent melanosomes.
- Darker skin produces more melanin and larger, more stable melanosomes.

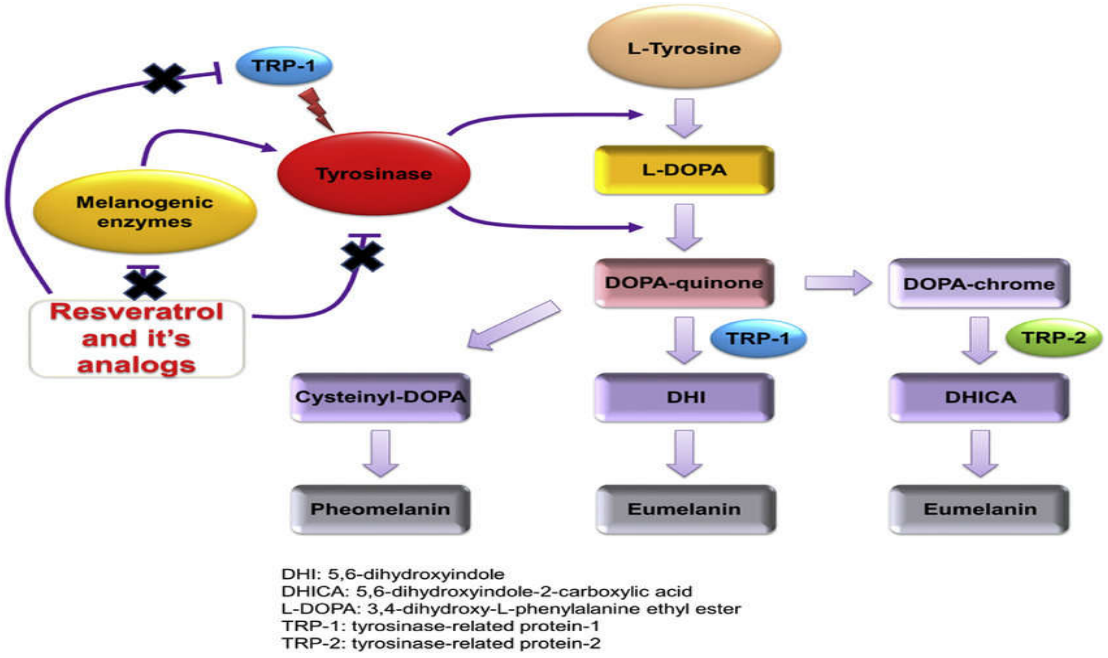


Fig 2 - Mechanism of skin pigmentation

MATERIAL & METHODS-

Pigmentation cream

Skin lightening or brightening creams, often referred to as pigmentation creams, are topical cream intended to treat dark patches, uneven skin tone, and hyper pigmentation. The active components in these creams target the synthesis of melanin, block tyrosinase activity, and encourage skin rejuvenation.

Treatment of skin pigmentation by herbs

In addition to photo safety, there are number of drugs and therapies to treat hyper pigmentation of the skin of darken skin patients can safely and effectively treat with some adverse reaction .Therefore, using herbs and phytoconstituents to treat skin conditions is a superior option excessive pigmentation.

The possible mechanisms of actions of the herbs used for the treatment of hyper pigmentation are namely tyrosinase inhibitor, anti-oxidants and skin whitening effects.

Ingredients used in Hyperpigmentation cream

Sr.no	Ingredients	Uses
1	Sweet potato juice	Anti-pigmentation
2	Liquorice extract	Reduce hyperpigmentation
3	Beet root juice	Antioxidant
4	Orange peel extract	Vitamin C
5	Vitamin E	Soothing agent.
6	Glycerine	Moisturizer, Humectants
7	Bees wax	Emulsifier, Thickener.
8	Cetostearyl alcohol	Moisturizing agent, emollient.
9	Liquid paraffin	Prevent dryness
10	Triethanolamine	pH adjuster
11	Propyl paraben	Preservative,anti-bacterial.
12	Rose oil	Perfuming agent, improve complexaion.

Table 1- Ingredients Used in Hyperpigmentation Cream

INGREDIENTS

1. SWEET POTATO

Synonyms – Batata, sakarkand

Biological source – It is obtained from the under ground tubers of plant *Ipomoea batata*

Family – Convolvulaceae

Chemical constituents – anthocyanins ,beta- carotinine





Fig 3- Sweet Potato Juice

Mechanism:

Sweet potato contain anthocyanins and other antioxidant that may help combat hyperpigmentation by reducing oxidative stress and inflammation, and potantially inhibiting melanin production. Generally, tyrosinase is an enzyme that play a key role in melanin production. some research suggests that certain compound in sweet potatoes may have the ability to inhibit tyrosinase activity, potentially reducing melanin production.

2. **LIQUORICE ROOT**

Synonyms: mulethi, sweet root

Biological source: It is obtain from the dried roots and stolons of *Glycyrrhiza glabra*

Family: Leguminosae

Chemical constituent: Glycyrrhizin, Glabridin, Isoliquiritigenin, Licochalcone A.



Fig 4 - Liquorice Root

Mechanism:

Liquorice root contains several chemicals constituent including glabridin, liquiritin , isoliquiritigenin and licochalcone A, which have antioxidant and anti-melanogenic properties, that

inhibit melanine production and help to lighten dark spots and even out skin tone. The primary reasons glycyrrhiza glabra extract are important for skin health is because of their potent antioxidants, particularly glycyrrhizin, titerpene saponins, and flavonoids . the principle characteristics are skin lighitning, skin whitening skin depigmentation , anti-aging, antiarrythmic, emollient , anti-acne and photo protective properties.

Method of Extraction –

Dried *liquorice root* is cleaned and cut into small pieces to increase the surface area.



The crushed or cut root is soaked into a solvent, typically ethanol, though sometimes a hydroalcoholic solution is used depending on the desired extract. The ratio is around 1 part of root to 5 part of solvent .The mixture is kept in a closed container to avoid contamination .



Maceration typically for 24 to 72 hours. It is done at room temperature. With occasional stirring helps to improve extraction.



After thr soaking period, the mixture is filtered to separate the liquid extract from the plant material.



The extract may be concentrated under evaporation to produce the *liquorice* extract in syrup form.

3. ORANGE PEEL EXTRACT:

Synonym: santra

Biological source: orange peel is consisting fresh and dried outer part of the pericarp of ripe or nearly ripe fruit of *Citrus aurantium Linn.*

Family: Rutaceae

Chemical constituent: Hesperidin (flavonoids) limonoids, and carotenoids



Fig 5 - Orange peel extract

Mechanism:

Orange peel extract is rich in antioxidant which helps to protect the skin from damage caused by free redicals and prevent from hyperpigmentation. The hesperidin compound in orange peel extract that can inhibit activity of tyrosinase and can also block melanosome transport, the process by which melanin is moved from melanocytes to transport keratinocytes . By inhibiting this transport, melanin is prevented from accumulating in the upper layer of the skin, resulting in a reduction of dark spots and an improvement in skin tone.

4. Beet root juice:

Biological source: Beet root juice is obtained from the root of the *Beta vulgaris* plant

Family: Chenopodiaceae

Chemical constituent: Betalains, phenols, carotenoids, vitamin B



Fig 6 –Beet root juice

Mechanism: Beet root juice is rich in antioxidant and vitamin c can help to reduce the appearance of dark spots and pigmentation by inhibiting melanin production.

PREPARATION OF BASE AND FORMULATION

Water in oil (W/O) cream was prepared by the addition of aqueous phase to the oily phase with continuous agitation. To prepare base oily phase that consisted of paraffin oil, beeswax,Vitamin E and cetosteatyl alcohol, are heated up to 75°C±1°C. Aqueous phase consisting of sweet potato juice, licorice extract, beet root juice, glycerin and water is heated to the same temperature. Each formulation consists of preserved water (propyl paraben 0.02% w/w and methyl paraben 0.1% w/w) to 100g. The formulations were neutralized by Triethanolamine to pH=5.5 at 25°C.



Fig 7- Preparation of oil and aqueous phase



Fig 8- Hyperpigmentation cream

Sr.no	Ingredient	F1	F2	F3	F4
1	sweet potato juice	10ml	7ml	7ml	7ml
2	Liquorice extract	1ml	2ml	1ml	1ml
3	Beet root extract	4ml	2ml	2ml	2ml
4	Orange peel extract	1ml	1ml	1ml	1ml
5	Gycerine	7ml	7ml	5ml	5ml
6	Vitamin E	1-capsule	1-2capsule	1-2capsule	1-2capsule
7	Bees wax	5gm	5gm	5gm	5gm
8	Cetostearyl Alcohol	5gm	5gm	5gm	5gm
9	Liquid Paraffin	10ml	5ml	10ml	10ml
10	Triethanolamine	2ml	2ml	2ml	2ml
11	Propyl paraben	0.02ml	0.02ml	0.02ml	0.02ml
13	Rose Oil	q.s	q.s	q.s	q.s
14	Distilled water	q.s	q.s	q.s	q.s

Table 2 –Composition of depigmentation cream

EVALUATION OF CREAM

Evaluation of herbal cream was following.

1) **Physical Evaluation**-

Formulated herbal creams was further Evaluated by using the following physical parameter physical parameter colour, odour, consistency, and state of the formulation.

a) **Colour**: White

The colour of the cream was observed by visual examination. It is presumed that there is no change in color of any sample of base and formulation at different storage condition i.e. 8 C, 25C, 40C the observation period of 28 days.

b) **Odour:** The odour of cream was found to be characteristics.

c) **State:** The state was cream was examined visually. The cream was semi solid in state.

d) **Consistency:** The formulation was examined by rubbing cream on hand manually. The cream having smooth consistency.

2) **Determination of PH**: pH of prepared herbal cream was measured by using digital pH meter. All the samples have a pH close to the skin pH with range 5.5 for the formulation and decreased in case of base to 4.9 during the observation of study period.

3) **Speadability**- Speadability is carried out for all formulation. The less time take for the separation of both slide better the speadability. The F2C had better speadiability.

4) **Stability Tests-** Stability tests were performed at different conditions for cream to note the effect of these conditions on the storage of creams. These tests on samples were kept at 8°C ± 0.1°C (in refrigerator), 25°C ± 0.1°C (R.T), 30°C(in oven), 40°C ± 0.1°C (in oven) and

40°C ± 0.1°C (in oven) with 75% relative humidity (RH).The result was shown that all Samples are stable at different conditions.

5) **Washability**: formulation was applied on the skin and then ease extends of washing with water was checked. All formulations are easily washable.

6) **Non- irritancy test**: Herbal cream formulation was evaluated for the non-irritancy test. Preparation shown no redness and irritancy. Observation of the state was done for 24 h 28 days.

7) **Phase separation-**Phase separation was not observed in any of samples of base and formulation kept at 8°C, 25°C and 30°C, but there was a little bit of separation in samples kept at 40°C and 40°C + 75% RH from the 21 day of observation.

8) **Greasiness-** This test is basically used to check nature of cream either oily or greased. According to result we can say that all formulation were non greasy.

9) **Viscosity-** Viscosity of formulation was done by using brookefield viscometer at the temp of 25 C using spindle no.63 at 200 rpm the viscosity was shown to be 1450 Cps.

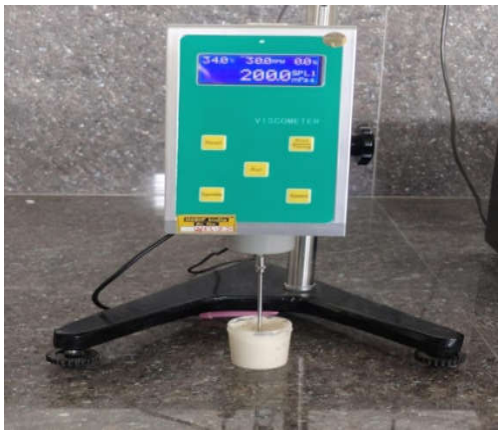


Fig 9 - Viscosity measurement

RESULT AND DISCUSSION-

1) **Physical Evaluation**- Cream was evaluated for organoleptic parameters showed in the following table.

Sr.no	Parameter	F1	F2	F3	F4
1	Color	Faint Pink	White	White	White
2	Odor	Pleasant	Pleasant	Pleasant	Pleasant
3	Consistency	Smooth	Smooth	Smooth	Smooth
4	State	Semisolid	Semisolid	Semisolid	Semisolid

2) **Washability, pH and Irritancy results**

Sr.no	Parameter	F1	F2	F3	F4
1	Washability	Not easily washable	easily washable	easily washable	easily washable
2	pH	5.9	5.9	6	5.7
3	Irritancy	Non-irritancy	Non-irritancy	Non-irritancy	Non-irritancy

3) **Phase separation and Greasiness results**

Sr.no	Parameter	F1	F2	F3	F4
1	Phase Separation	Slightly Phase separation	No phase separation	No phase separation	No phase separation
2	Greasiness	Non-greasy	Non-greasy	Non-greasy	Non-greasy

4) **Spreadability and stability tesr result**

Sr.No	Parameter	F1	F2	F3	F4
1	Speadability	21.8gcm/s	28.68gcm/s	35.58gcm/s	16.58gcm/s
2	Sability	Stable	Stable	Stable	Stable

5) **Viscosity result-**

Sr.no	Formulation	Viscosity(Cps)
1	F1	21837
2	F2	33771
3	F3	31856
4	F4	28552

CONCLUSION:

In this present study are conclude that the prepared formulation of anti-hyperpigmentation cream complies all the evaluation parameters which are tested. It proved that the cream was prepared is effective for reducing hyperpigmentation, cleansing, moisturizing, smoothing effect on the skin. The formulation is beneficial for easy application and no side effects and are mostly preferred by the peoples. Due to antibacterial, anti tyrosinase and anti-inflammatory properties of sweet potato and liquorice it prevents skin related disorders also improves skin tone, protects from damaging UV rays. By this study, using sweet potato and liquorice achieved more effective and quality product to improve skin tone, and beautifying skin. After the evaluation of prepared formulation it suggested that the prepared formulation was physico-chemically stable and possessed characteristics of standard topical formulation.

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