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FORMULATION AND EVALUATION OF POLYHERBAL EYE PATCH

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ABSTRACT

The purpose of present study is to formulate and evaluate Polyherbal eye patch. Dark circles under the eyes are bilateral, homogeneous pigment macules on the infraorbital regions. Due to their ability to precisely administer active ingredients to the sensitive under eye region, under-eye gel patches are utilized as both cosmetics and cosmeceutical. The Polyherbal under eye patch is prepared by using natural ingredients like Aloe Vera, Honey, Neem, and Coconut Oil with gelling agents like Carbopol 934, PVA, and Gelatin. Gel base is prepared by using Carbopol 934, PVA, and Gelatin. By changing the ingredients and their concentration we formulated 4 different formulations namely F1 to F4. The herbal under eye patch was evaluated by different parameters such as Organoleptic evaluation, pH test, homogeneity, DPPH test, spreadability, thickness, peel test, stability study, viscosity, swelling index and phase separation were observed. After the evaluation, we found good properties for the eye patch (Formulation1, F1) and maintained its consistency even after stability storage conditions. The DPPH study result also a supporting document for the antioxidant activity of our extract, the activity increases as the quantity of extract increases. The eye patches were to be stable during stability studies according to ICH guidelines. It can be concluded that herbal eye patch without side effects having anti-oxidant property having enough potential to give a barrier to protect the skin and avoid aging of skin. The overall study is useful to substantiate product claims due to its useful benefits on anti-wrinkling activity.

KEYWORDS: Polyherbal under eye patch; Dark Circles; Aloe Vera; Honey; Neem; Carbopol934; PVA; Gelatine; Coconut Oil And Anti-Wrinkling Activity.

1. INTRODUCTION

As per Indian and E.U regulation, cosmetics is defined as the means "any article intended to be rubbed, poured, sprinkled or sprayed on or introduced into or otherwise applied to the human body or any part thereof for cleaning, beautifying, promoting attractiveness or altering the appearance and includes any article intended for use as a component of cosmetic".

"Cosmeceutical are defined as those cosmetic products that elicit pharmaceutical therapeutic benefits, but not biological therapeutic benefits. It indicates those skincare products with active ingredients beneficial for improving the appearance of the skin as well as nourishment of the skin.".[1]

1.1 INFRAORBITAL DARK CIRCLES

Conditions that cause the infraorbital eyelids to appear relatively dark are referred to as infraorbital dark circles. Dark circles beneath the eyes are worsening by general exhaustion, particularly sleep deprivation. Because the skin on the eyelids is the thinnest in the body, blood vessels can easily protrude through it, giving puffy eyes their swollen, black appearance. Numerous variables, including fluid retention from excessive alcohol or salt consumption, emotions, particularly crying, allergies, hormonal fluctuations, lack of sleep, and other conditions, can contribute to puffy eyes.[2] Periorbital hyperpigmentation is a common dermatological disorder that typically affects females between the ages of 16 and 45. It manifests as a dark periorbital area under the lower eyelids. Another issue that can have a number of reasons, including stress, lack of sleep, aging, and genetics, is dark circles under the lower eyelids.[3] Dark circles have two primary causes:

1. Vessel fragility
2. Poor blood flow beneath the eyes.[4]

Antioxidant skin care products help improve skin health and lessen dark circles and aging symptoms. These items frequently contain important antioxidants like caffeine and vitamins E and C, aloe Vera. Caffeine stimulates blood flow in the capillaries surrounding the eyes and enhances blood circulation in the surrounding area. Due to its qualities, caffeine may help prevent wrinkles and shield the skin from harm. Blood circulation and coagulation are enhanced by Vitamin K. Aloe Vera reduces inflammation and help in wound healing. The accumulation of blood pigments, particularly haemoglobin, and the by-products of its breakdown in the skin, such as hemosiderin (a protein that accumulates iron), biliverdin, bilirubin, and methaemoglobin, cause pigmented dark circles. Melanin accumulation in the

skin may be a contributing factor in these pigmented circles, often referred to as hyperpigmentation, which are typically associated with chronic inflammation.[5]

1.2 TYPES OF DARK CIRCLES

There are four types of dark circles

1. Bluish, purple Tone / Vascular Dark Circles
2. Mixed Dark Circles
3. Structural Dark Circles
4. Brownish Tone / Pigmented Dark Circles.

1. Bluish, Purple Tone / Vascular Dark Circles: Enlarged veins and thin skin under the eyes can lead to bluish dark circles. Stimulants like caffeine, energy drinks, and certain medications can cause these veins to dilate, making the under-eye area appear bluish. Purplish dark circles are caused by factors such as allergies, poor blood circulation, insufficient sleep, and the use of certain medications.

2. Mixed Dark Circles: combination of two or three types of dark circles, such as pigmented structural, pigmented vascular, and pigmented vascular-structural dark circles etc.

3. Structural Dark Circle: These dark circles are shadows that are caused by sagging skin, fat loss under the skin, and eye bags.

4. Brownish Tone / pigmented Dark Circles: These circles are formed by the accumulation of brown pigments under the eyes caused by post-inflammatory pigmentation and may also result from exposure to the sun, heredity or constant eye rubbing. It gives rise to a brownish black colour. This category of dark circles is mostly observed among medium to dark skin toned individuals, who most likely experience overproduction of melanin and deposition of pigments unevenly over the skin.[6]

1.3 CAUSES OF DARK CIRCLE ON SKIN

Dark circles (DC) under the eyes are defined as bilateral, round, homogeneous pigment macules on the infraorbital regions. It is caused by multiple etiologic factors, dermal melanin deposition, post inflammatory hyperpigmentation due to atopic or allergic contact dermatitis, periorbital edema, superficial location of vasculature, and shadowing due to skin laxity.

Despite being a phenomenon within the limit of physiology, patients, especially women, frequently associate them as a notable impact on their quality of life.

Dark circles interfere with the face appearance, giving the patient an exhausted, sad, or hangover look. They are worsened by general fatigue, especially lack of sleep.

Dermal melanin deposition

The thickening of the dermis due to edema increases incidence of diffused light reflection from the pigments thereby enhancing darkness of the skin. The efficacy of the CO2 laser depended on the tightening of dermal tissues and improvement on the skin surface texture, which caused the Tyndall effect.

Post inflammatory hyperpigmentation secondary to atopic or allergic contact dermatitis

Dark circles are common in allergic individuals. In these people it is caused by rubbing and scratching the skin around the eyes and by accumulation of fluid due to facial allergy.

Superficial location of vasculature

As patients grow older, loss of the subcutaneous periorbital fat and skin atrophy leads to unveiling of the orbital vasculature. The bluish colour is due to the visible dermal capillary network.

Tear trough depression

The tear trough is a depression centered over the medial inferior orbital rim. Due to anterior displacement of infraorbital fat with aging, it gets deeper creating shadow below it depending on the lighting conditions. The condition aggravates with the eyelid and midface aging because of the loss of subcutaneous fat with thinning of the skin over the orbital rim ligaments that, combined with cheek descent, making orbital rim area appear hollow.[7]

1.4 AETIOLOGY OF INFRAORBITAL DARK CIRCLES

Various features can play a role in the development of dark circles around the eyes.

These include the layout of facial ligaments, the shape of the skull, the soft tissues in the middle of the face, orbicularis oculi muscle, blood vessels, and delicate eyelid skin with minimal fat underneath.[8]

1.5 CONTRIBUTIONS FROM THE SKIN

The condition of the skin around the eyes greatly affects the look of dark circles. The skin under the lower eyelid is the thinnest on the body, making the structures beneath it more noticeable. With very little fat under the skin, it is closely connected to the muscle around the eye, leading to changes as we age. Aging and environmental factors cause the skin to lose its elasticity and firmness due to the reduction of collagen and elastin. Also, the thinning of the skin, along with problems like uneven colour, visible blood vessels, oily changes, and sun damage, all contribute to the aged appearance of the skin. Several things can cause darker skin around the eyes, either from birth or later in life. These include conditions like melasma, moles, dermal melanocytosis, too much sun exposure, hemosiderin build up, hormonal changes, or a mix of these factors. Inflammation from problems like atopy and contact dermatitis can also lead to darker skin. Additionally, some medicines, such as oral contraceptives and ophthalmic prostaglandin F2alpha, have been linked to increased skin pigmentation.[8]

1.6 WRINKLING OF SKIN

Wrinkles are an important sign of skin aging. It is developed due to a number of factors arising from the internal and external aging process. This includes a thinning of the epidermis due to a lack of laminin 511 loss of collagen. Glycosaminoglycans (GAGs) and subcutaneous fat. Movement of joints also causes wrinkles. Internal factors such as hormones, genetics, oxidative stress, systemic conditions, as well as external influences such as temperature, pollution, smoking and alcohol, contribute to premature skin aging. Although there are many anti-aging products available in the cosmetic market, even in facial cleansing products but the short contact time between cleansing is often not enough to provide a significant anti-aging effect. But cleansing can still act as a preventative measure or healing time, depending on the type of cosmetics used, for example, oil-based or cream-based cleanser. Helps protect the skin's natural defence mechanisms. Another important aspect of an effective wrinkle treatment strategy is photo protection. UV-A/B should be part of your daily routine. Excipients also play an important role in these products, including carriers such as liposomes, nanosomes, cyclodextrins, phytosomes, oleosomes, besides providing a controlled release mechanism that guarantees a direct action. Anti-aging supplements have recently entered the market, providing additional support for prevent wrinkles.[9]

1.8 HYDROGEL UNDER EYE PATCH

Hydrogels are three-dimensional networks of cross-linked polymers that can absorb water in dry form, swell without dissolving or altering their chemical structure. The hydrogel maintains its three-dimensional shape as it swells with the help of cross linking points or junctions. These cross-links are physical or chemical and they form a mesh structure that prevents the polymer matrix from fully dissolving. When hydrated, hydrogels become soft and highly flexible.[10]

1.9 TYPES OF HYDROGEL

I. SOURCES OF POLYMER

1. Natural
2. Synthetic
3. Hybrid

II. BASED ON CROSS LINKING

1. Covalent
2. Non-Covalent

III. BASED ON POLYMERIC COMPOSITION

1. Homo polymer
2. Co Polymer
3. Block Copolymer
4. Interpenetrating Network

IV. BASED ON DEGRADATION

1. Biodegradable
2. Non-Biodegradable

V. BASED ON RESPONSE

1. Non-Responsive
2. Stimuli Responsive.[10]

1.10 UNDERSTANDING HYDROGEL TREATMENT FOR EYE CONDITON

A basic perception of the anatomy and functions of the eye is necessary for the effective use of hydrogel in the treatment of eye diseases. The anterior segment and the posterior segment are the two primary compartments of the eye. The cornea, tear film, and eyelids protect the

eye. The cornea, a clear layer covering the front of the eye, including the iris, is very sensitive even though it doesn't have its own blood supply. The cornea acts as a barrier to prevent medicines from being absorbed and it is made of three tissue layers separated by a membrane. The sclera, the strong, white part of the eye that helps keep its shape, is mostly made of collagen fibers. The conjunctiva, a mucous membrane covers it. Rich in blood and lymphatic veins that support the ocular tissues, this thin, translucent tissue covers the front of the eye, except the cornea. Mucus is applied to its exterior, improving the wettability of the optical surfaces and lubricating the eyeball while it moves. The colourful portion of the eye is called the iris, and the ciliary body, which is situated behind the iris, is in charge of creating aqueous humor and controlling vision by modifying the lens.

The vitreous fluid, retina, choroid, and optic nerve are the primary constituents of the posterior portion of the eye. Located between the lens and the retina in the posterior cavity of the eye, the vitreous humor is a transparent, gel-like material. It aids in preserving the structure of the eye. The choroid is a vascularised layer that creates the blood-retinal barrier, which divides the retina from the sclera. The retina is a complex tissue situated between the vitreous humor and the sclera.[11]

1.11 DARK CIRCLE PATCH

Dark circle eye patches are a type of under-eye mask that can help reduce the appearance of dark circles under the eyes. Dark circle eye patches are mini sheet masks that are made of hydrogel material and curve to fit the contours of the face. The hydrogel material in the patches helps maximize nutrient absorption and provide fast-acting results. Dark circle patch is used to reduce hyperpigmentation, puffiness. Reduces fine lines & wrinkles, Cools & refreshes skin, Lightens dark circles, Hydrates & soothes skin.[12]

2. MATERIALS AND METHOD

2.1 FORMULATION

The ingredients used in the formulation of dark circle hydrogel patch are as follows:

- Aloe Vera
- Carbopol 934
- PVA (Poly vinyl alcohol)
- Honey
- Neem

- Triethanolamine
- Gelatin
- Coconut oil
- Methyl Paraben
- Distilled water

2.2 ROLE OF INGREDIENTS

1. **Aloe Vera:** Dehydration is one of the reasons for dark circles. As Aloe Vera is hydrating, it helps in improving skin moisture. Due to ageing, structure of skin changes and loss of volume on face may increase the appearance of dark circles; Aloe Vera supports mature skin and reduces inflammation.[13]
2. **Neem:** helps reduce puffiness and dark circles as it nourishes and soothes the delicate skin around the eye.[14]
3. **Carbopol 934:** It acts as a gelling agent which provides stable gel like consistency that helps the under eye active ingredients to stay in place. It is one of the natural eye cream ingredients that hydrates the skin for longer periods and helps in erasing the puffiness and dark circles.[15]
4. **Polyvinyl Alcohol (PVA):** PVA has hydrating and gel forming functions by providing moisture under the eyes which decreases the dark patches on the skin that forms during menstruation through better moisture delivery and the use of cooling agents.[16]
5. **Honey:** It is an organic moisturizer and possesses anti-inflammatory effects, so it protects the skin underneath the eyeball, caused puffiness of the eyes to soothe and lightens the look of dark circles by stimulating collagen production and adequate neutralization against free radicals. It helps to hydrate the skin. [17]
6. **Gelatin:** It is a key ingredient in under eye patches for dark circles because it helps bind other ingredients together and contains collagen, which can help with skin elasticity.[18]
7. **Coconut oil:** Coconut oil can be used as a natural remedy to reduce the appearance of dark circles under the eyes by gently massaging a small amount onto the area, as it can help improve blood circulation and moisturize the delicate skin around the eyes. It provides anti -oxidant activity, promote cell turnover and strengthen the skin.[19]
8. **Triethanolamine**: Act as pH adjuster in gel preparation.[20]
9. **Methyl Paraben:** The paraben (methyl, ethyl, propyl, and butyl) were the most widely used preservatives in cosmetics.[21]
10. **Distilled Water:** The common solvent used in the preparation.

2.3 FORMULA

Table 1: Ingredients for poly herbal eye patch.

INGREDIENTS	F1	F2	F3	F4
CARBOPOL 934	5g	3g	-	5g
PVA	4ml	2ml	4ml	4ml
ALOE VERA	4g	3g	4g	4g
HONEY	1ml	1ml	1ml	1ml
NEEM	1g	1g	1g	1g
GELATIN	-	-	1g	-
COCONUT OIL	-	-	-	1ml
TRIETHANOLAMINE	0.25ml	0.25ml	-	0.25ml
METHYL PARABEN	0.25ml	0.25ml	0.25ml	0.25ml
DISTILLED WATER	70ml	70ml	70ml	70ml

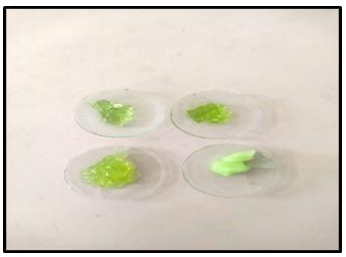

Fig 1: Formulations.

2.4 INSTRUMENTS USED

- Shimadzu Digital Electronic Balance BL220H
- KEMI Homogenizer
- KEMI Magnetic stirrer
- ALCO Laboratory stirrer
- pH meter

2.5 METHOD OF PREPARATION

Preparation of gel

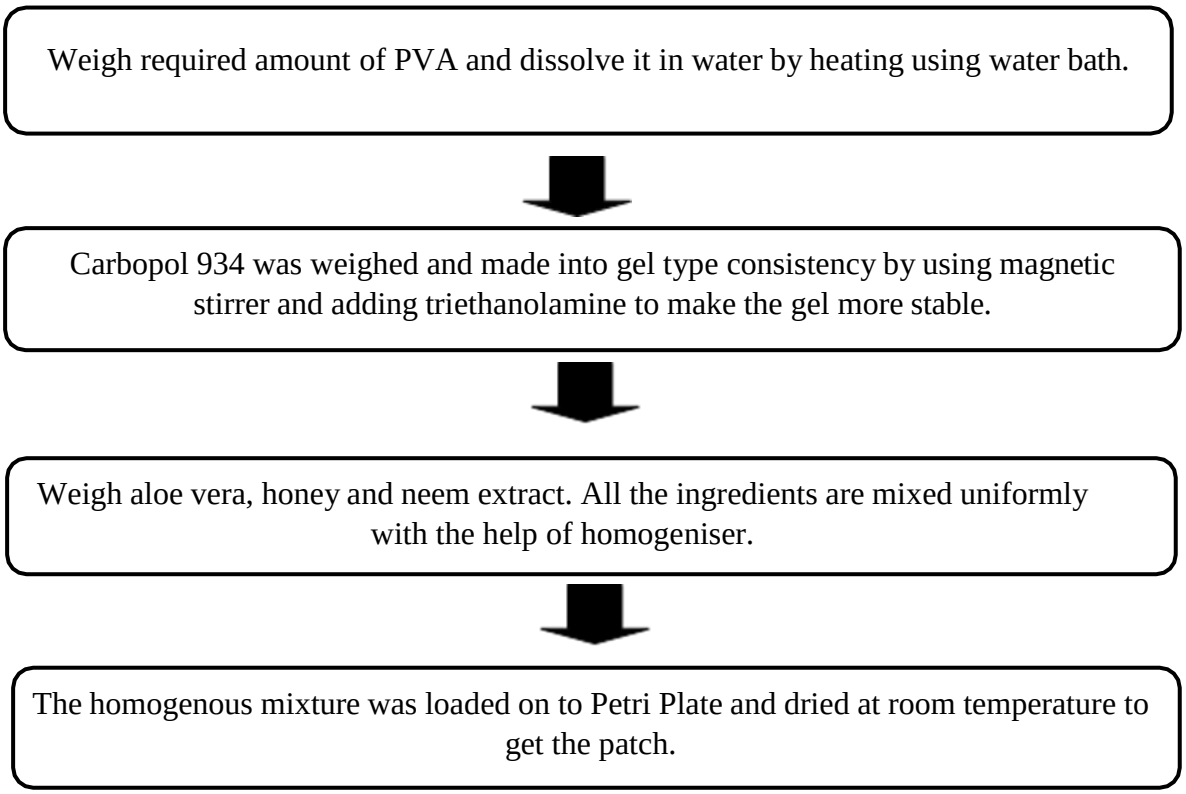

Fig 2: Method of preparation.

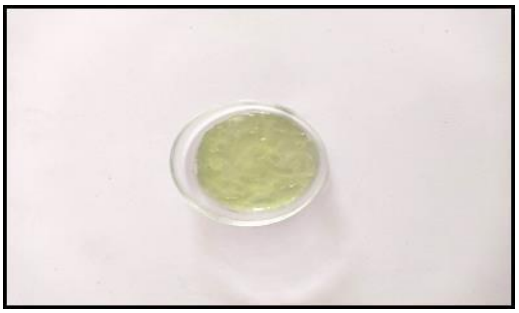

Fig 3: Patch.

3. EVALUATION

3.1 Organoleptic evaluation

The prepared hydrogels were visually inspected for colour, appearance, consistency, uniformity, viscosity, and adhesion.[22]

3.2 pH

Take 5±0.01g in 100ml beaker with 45ml of water and disperse at 27ºC.[23]

3.3 DPPH Scavenging assay test

A DPPH scavenging assay involves preparing a solution of the test sample, mixing it with a DPPH (2, 2-diphenyl-1-picrylhydrazyl) solution, incubating in the dark, and then measuring the decrease in absorbance at 517nm on a spectrophotometer, which indicates the antioxidant activity of the sample by how much it scavenges the DPPH free radical; the higher the decrease in absorbance, the greater the antioxidant activity.

3.4 Swelling index

The hydrogel eyelid swelling index is a measure of the amount of water or other fluid that the hydrogel can absorb in relation to its initial dry weight. This is an important property to evaluate the performance of hydrogel-based products. This is particularly relevant for products like moisturizing eye patches. There is an initial burden. If desired, the hydrogel eyelids were weighed in their dry state, then the dried hydrogel was immersed in distilled water at room temperature for two hours to ensure full swelling. After the swelling period, carefully remove the hydrogel from the water bath and gently absorb with filter paper. To remove excess surface water, avoid any pressure. That might change its weight. The swollen hydrogel was then weighed to determine the final weight.[23]

Swelling Index= (WA-WB)/WB ×100%

a. WA = hydrogel patch weight after hydration
b. WB = hydrogel patch weight before hydration

3.5 Thickness

The thickness of the formulated patches was measured using vernier calipers, and the average thickness was then calculated.[24]

3.6 Spreadability

1gm of sample is placed between two glass slides.50gm of weight was placed on the upper slide so that the gel was pressed uniformly between two slides to form thinlayer. The time required for spreading before and after the application of weight was noted.[25]

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

Where,

S= Spreadability

m= Weight tied to the upper slide L= length of the glass

t= time taken in seconds

3.7 Homogeneity test

All herbal preparation developed were tested for their homogeneity visually. The homogeneity test as carried out by applying the herbal gel eye patch formula on the object glass. The herbal was placed on a slide then covered with a glass to see the clarity and presence of aggregate in the herbal patch.[26]

3.8 Viscosity

Prepared gels with different concentration of Carbopol or Gelatin. Setup the base level of the instrument using level indicator. The spindle was cleaned and attached to the instrument. Then the spindle was rotated in the gel until a constant reading displaced on the viscometer. Repeat the method for three times and find out the average value. The Brookfield viscometer was used to measure the viscosity of the gel. The viscosity value was expressed in units of cps.[27]

3.9 Phytochemical screening

Phytochemical screening is performed to determine the presence of alkaloids, tannins, Flavanoids, phenol, sterol, glucose, Anthraquinone, protein, quinine, Saponins and carbohydrates.

3.10 Stability test

All five formulations were stored in polyethylene boxes at room temperature for 2 days. After this time, the formulation profiles of the hydrogel samples were visually evaluated for chemical stability (pH) and physical stability (colour, spreadability).[28]

4. RESULT AND DISCUSSION

4.1 ORGANOLEPTIC CHARACTERS

The formulations were found to maintain elegance during the entire course of observation.

Table 2: Organoleptic evaluation.

FORMULATION	F1	F2	F3	F4
COLOUR	Pale green	Pale green	Pale green	Pale green
ODOUR	Pleasant smell	Pleasant smell	Skinny smell	Pleasant smell
APPEARANCE	Gel	Gel	Gel	Gel

4.2 pH

The pH of the formulations were found to be in the range of 5.0 – 5.65, equivalent to the pH of skin.

Table 3: pH of the poly herbal eye patch.

SL.NO.	FORMULATION	pH
1.	F1	5.12
2.	F2	5.23
3.	F3	5.35
4.	F4	5.61

4.3 DPPH SCAVENCHING ASSAY

Among the solvents tested, the highest scavenging activity was detected as 68%.

Table 4: DPPH Assay table.

SOLVENT	EXTRACTION YIELD	%RSA-DPPH%
HEXANE	3.58	26 ± 08
DICHLOROMETHANE	6.83	36 ± 58
METHANOL	19.44	66 ± 48

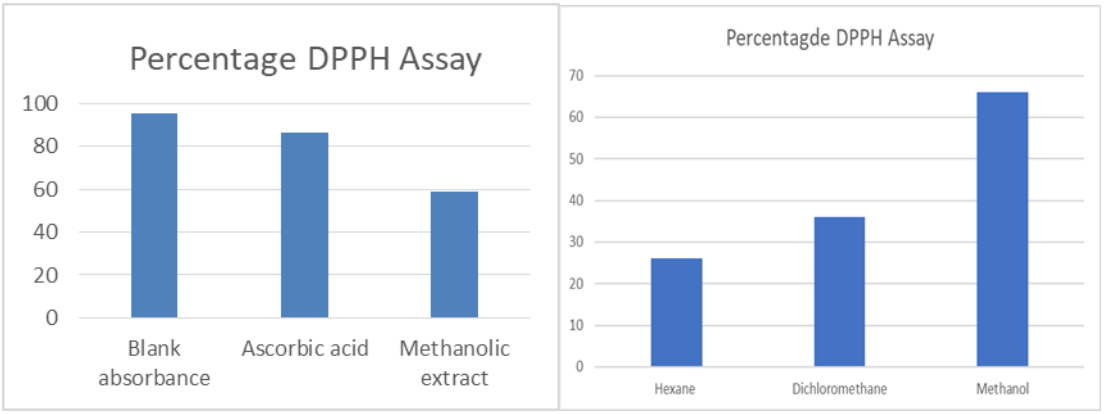

Fig 4: DPPH Graph.

Table 5: DPPH Absorbance Assay.

EXTRACT	ABSORBANCE	%DPPH ASSAY
Blank Absorbance	0.92	95.23 ± 1.34
Ascorbic acid	0.16	86.56 ± 1.78
Methanolic Extract	0.33	59.01 ± 2.65

6.4 SWELLING INDEX

The swelling index of the patch was observed.

Table 6: Swelling index of poly herbal eye patch.

SI NO	FORMULATION	SWELLING INDEX
1	F1	0.7831 ± 0.112
2	F2	1.113 ± 0.0015
3	F3	1.763 ± 0.0026
4	F4	1.759 ± 0.0028

Fig 5: Swelling index.

6.5 THICKNESS

The thickness of the patch was observed using vernier callipers.

Table 7: Thickness of poly herbal eye patch.

SI.NO	FORMULATION	THICKNESS(mm)
1	F1	0.143 ± 0.015
2	F2	0.167 ± 0.027
3	F3	0.179 ± 0.039
4	F4	0.0179 ± 0.0384

6.6 SPREADABILITY TEST

The spreadability of the prepared gel was evaluated by parallel plate method. A good spreadability indicates high therapeutic efficacy of gel and uniform application to the skin.

Fig 6: Spreadability Graph.

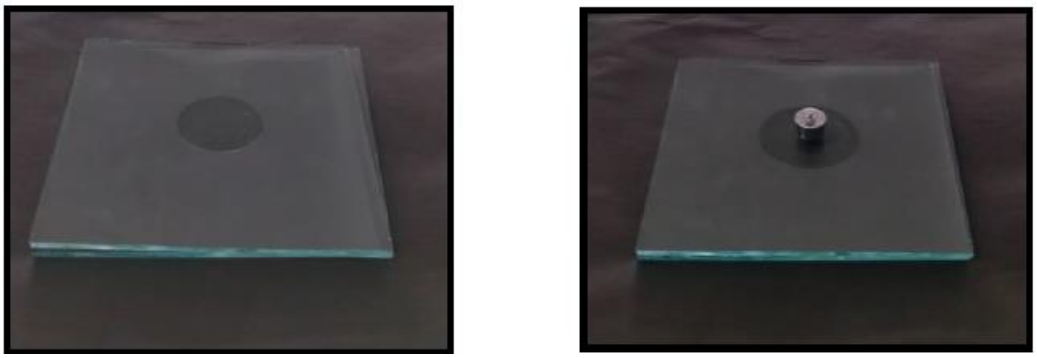

Fig 7: Spreadability without weight and with weight.

Table 8: Spreadability of poly herbal eye patch.

SI.NO	FORMULATION	SPREADABILITY(cm)
1	F1	5.9
2	F2	7.53
3	F3	7.3
4	F4	7.6

6.7 VISCOSITY

Viscosity of gel was found to be in the range 200-500 cps. F1 shows good spreadability than other formulations.

Table 9: Viscosity of poly herbal eye patch.

SI.NO	FORMULATION	VISCOSITY(cps)
1	F1	309
2	F2	315
3	F3	389
4	F4	284

6.8 HOMOGENEITY TEST

The formulated gels were found to be homogenous (evenly distributed).

Table 10: Homogeneity of poly herbal eye patch.

SI.NO.	FORMULATION	DESCRIPTION
1	F1	Excellent
2	F2	Good
3	F3	Good
4	F4	Good

6.9 PHYTOCHEMICAL SCREEENING

Phytochemical analysis of the extract has shown the presence of different secondary plant metabolites such as Alkaloids, Tannins, and Flavanoids etc.

Table 11: Phytochemical screening of extract.

TEST	EXTRACT METHANOL	AQUEOUS EXTRACT
Alkaloid	+++	+
Tannins	+++	+++
Phenol	+++	-
Sterol	-	-
Flavanoids	+++	+++
Glucose	+++	-
Anthraquinone	+++	-
Protein	+	++
Quinine	++	+
Saponins	+++	+++
Carbohydrates	+++	+++

6.10 STABILITY TESTING

Stability testing provides evidence on how the quality of a drug substance or drug product changes with time under the influence of environmental factors (temperature, humidity, and light) and to establish a re-test period for the drug substance or a shelf life for the drug product and recommended storage conditions.

Stability studies are done according to ICH guideline Q 1 A (R2). The gel is kept in the humidity chamber maintained at 40°C ± 2°C/75% RH ± 5% RH. After the study, the formulations were observed for any changes.

Table 12: Stability testing table.

FORMULATION	COLOUR	pH	VISCOSITY(cps)
F1	PALE GREEN	5.12	309
F2	PALE GREEN	5.23	315
F3	PALE GREEN	5.35	389
F4	PALE GREEN	5.61	284

SUMMARY AND CONCLUSION

Nowadays, dark circle has become one of the main obstacles among people. On account of this, we started a study to formulate Polyherbal eye patch. Since people believe that natural products are safer, our goal of the current study was to formulate “Polyherbal eye patch” of natural origin with minimal use of synthetic agents.

Aloe Vera, Neem, Honey etc were used as main ingredients of our Eye patch. Aloe Vera, Neem, Honey etc have an anti-oxidant activity. Carbopol 934 and PVA are used as gel bases for formulation of the under eye patch. To establish the efficacy of the prepared poly herbal eye patch evaluation tests such as pH, viscosity, spreadability, thickness, and homogeneity were performed. Additionally, DPPH (2, 2-diphenyl – picrylhydrazyl) supported the anti oxidant activity of the patch. Phytochemical screening was done to detect the presence of secondary metabolites in the extract.

By changing the concentrations of ingredients four different formulation were developed. These studies suggest that the composition of the extracts and base of F1 (Carbopol, PVA, aloe vera, honey, and neem) is more stable and safe.

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