DESIGN AND DEVELOPMENT OF MULTI-EFFECT UNDEREYE CREAM USING NANOSPONGE TECHNOLOGY

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A B S T R A C T
Nanosponge technology offers entrapment of ingredients and is believed to contribute towards reduced side effect by controlling the release, improved stability, increased elegance and enhanced formulation flexibility. This technology is being used currently in speciality skin care products like under eye cream, anti-wrinkle cream, sunscreen lotion etc.The nanosponge technology is advanced drug delivery system which helps to deliver drug to the targeted location. The goal of present study is to formulate and evaluate the multi-effect under eye cream using nanosponge technology which would help to reduce the dark shadows, puffiness and crow's feet wrinkles near the eyes
Keywords:Nanosponge Technology, Advanced Drug Delivery System, Under Eye Cream Evaluation Parameters.

1. INTRODUCTION

Dark circles under the eyes are defined as bilateral, round, homogeneous pigment macules on the infraorbital regions. It is an ill-defined entity and a common cosmetic concern popularly known as "infraorbital skin discoloration", "infraorbital darkening", "infraorbital hyperchromia", "darkening of the skin around the eyes" and "periorbital hyperchromic macules and patches" [22,23]. Although dark circle is the most commonly used term for the condition, it is not a formal medical term.

As regard to distribution, the skin below lower eye lid is first involved and with age pigmentation progress to the area of the upper eyelid [24]. The hyperpigmentation may also include the eyebrow, malar bone and half sides of the base of the nose. While there are no statistics giving the frequency of its occurrence, dark circles under the eyelid are definitely a cosmetic concern for a large number of individuals [25]. Dark circles under the eyes are one of the main aesthetic facial concerns that affect individuals of any age, both genders and all races[26]. These dark circles interfere with the face appearance, giving the patient a tired, sad, or hangover look. Disguising the lesions is almost mandatory for some individuals who depend on a well-cared and positive appearance for their work or social activities [27].

The causes for under eye dark circles include hereditary/ genetic factors, stress, allergies and lack of sleep. It has been stated to result from a variety of reasons including dermal melanin deposition, post inflammatory hyperpigmentation from atopic or contact allergic dermatitis as well as shadowing from lax skin and infraorbital swelling [22]. Excessive pseudoherniation of orbital fat is also intimately related to the presence of infraorbital dark circles. Importantly, under eye dark circles is a consequence of poor microcirculation, namely due to increased permeability of the capillaries wherein hemoglobin leaks out and accumulate as hemosiderin in the surrounding tissue. This gives a dark hue to the skin, especially in the under eye area, where the skin is very thin. These visible effects on the skin are sometimes accompanied by skin irritation or a feeling of tension or local warmth, particularly in the case of sensitive skin. There is no doubt that the dark rings are worsened by general fatigue, especially lack of sleep. Management of under eye dark circles includes topical treatment (eg.

chemical peels, sunscreens, demelanizing agents, moisturizers, anti-aging lotions and gels) and surgical treatment (eg. laser surgery, dermabrasion, face lifts and dermal fillers).

1.1 Nanosponge: New Colloidal Drug Delivery System for Topical Delivery

Nanosponges are novel class of hyper-crosslinked polymer based colloidal structures consisting of solid nanoparticles with colloidal sizes and nanosized cavities. They enhance stability, reduce side effects and modify drug release. The outer surface is typically porous, allowing sustain release of drug. They are mostly use for topical drug delivery. Size range of nanosponge is 50nm-100nm [15].This technology is being used in cosmetics, over-the-counter skin care, sunscreens and prescribed drugs. Conventional formulation of topical drugs accumulate excessively in epidermis and dermis. Nanosponge prevent the accumulation of active ingredient in dermis and epidermis.

It is possible to control the size of nanosponge. To varying the portion of cross-linkers and polymers, the nanosponge particles can be made larger or smaller [10]. These particles are capable of carrying both lipophilic and hydrophilic substances and of improving the solubility of poorly water soluble molecules [28]. Nanosponge technology offers entrapment of ingredients and is believed to contribute towards reduced side effects, improved stability, increased elegance and enhanced formulation flexibility [29]. Nanosponges are non-irritating, non-mutagenic, nonallergenic and non-toxic [30].The nanosponges are solid in nature and can be formulated as oral, parenteral, topical or inhalational dosage forms. For topical administration, they can be effectively incorporated into topical hydrogen [l8]. Topical nanosponge can be more patient compliant and provide sufficient patient benefits by reducing repeated doses and side effects [31].

1.2 Advantages of nanosponges [32,33]

- This technology offers entrapment of ingredients and reduces side effects
- Improved stability, increased elegance and enhanced formulation flexibility.
- These formulations are stable over range of pH 1 to 11.
- These formulations are stable at the temperature up to 1300C.
- These formulations are compatible with most vehicles and ingredients.
- These are self sterilizing as their average pore size is 0.25μm where bacteria cannot penetrate.
- These formulations are free flowing and can be cost effective. These modify the release of drug. They increase the solubility of poorly soluble drug.

2 .EXPERIMENTAL WORK

2.1 Preparation of nanosponge (loaded) [30]

Procedure:

To prepare inner phase 1.5 g of ethyl cellulose was taken. Then ethylcellulose was dissolved in 50ml dichloromethane and shadownyl active under ultrasonication for 45 mins until it was complete solution. 1.5 ml polyvinylalcohol was taken in 100ml hot water and solution was made to prepare outer phase. after the outer phase w was prepared, now the solution of ethyl cellulose and dichloromethane was poured into 50ml of PVA solution by means of syringe needle drop by drop, following 1 and half hour stirring. After that stirring was stop and the mixture was filtered by whattman filters paper. The powder thus obtained was air dried and stored for analysis.

Although, the general procedure for the preparation of nanosaponge was same, but some variation in formulation condition have been observed. The different parameters under study were,

- Concentration of stabilizer
- Mode of mixing
- Time of ultrasonication
- Concentration of ethyl cellulose

Various batches of nanosponges of ethyl cellulose were prepared by varying the parameter under study, keeping the outer parameter constant. The batches were evaluated for particle size; yield and other characteristics. The variation done and result

obtained are tabulated below.

Table No.1 - OPTIMIZATION OF NANOSPONGE (loaded)

Batch no	name	parameter	level	Remark
1	LOADED-1	Time of stirring	60 mins	Large size
2	LOADED-2		1 hour 30 mins	Optimum size
3	LOADED-3	Concentration of stabilizer	3%	Large size
4	LOADED-4		1.5%	Optimum size
5	LOADED-5	Speed of stirring	1500 rpm	Large size
6	LOADED-6		2500 rpm	Optimum size
7	LOADED-7	Time of ultrasonication	Without	Large size
8	LOADED-8		With	Optimum size
9	LOADED-9	Concentration of ethyl cellulose	3%	Rubbery nanosponge
10	LOADED-10		1.5%	Soft nanosponge

2.2 ACTIVE USED[34] :

SHADOWNYL

Description: Aqueous extract of a marine algae(focus vesiculasus)

Inci : water, algae extract, hexylene glycol, xanthan gum

Specifications :

- Dry weight – 1-3 %
- Color – reddish brown
- Odour – characteristic
- Ph – 4-7

Properties:

- Stimulates the expression of heme oxygenase type 1-novel pathway
- Boosts elimination of pigments such as heme responsible for dark circles
- Rejuvenates the eye contour area

2.3 Formulation of cream containing active loaded nanosponge

In cream 3, the nanosponge was incorporated as 0.5%, 1% and 1.5%

Table No. 2 - FORMULATION

SR. NO	INGREDIENTS	QUANTITY IN 100 GRAMS		
		CREAM 1	CREAM 2	CREAM 3
	WATER PHASE			
1	Water	Upto 100	Upto 100	Upto 100
2	Edta	0.05	0.05	0.05
3	Aqupec HVHC	0.2	0.2	0.2
4	Glycerin	2	2	2
5	Propylene glycol	1	1	1
6	Methyl paraben	0.2	0.2	0.2
7	TEA	0.4	0.4	0.4
	OIL PHASE			
8	Stearic acid	4	5	6
9	GMS	1	1.5	2
10	Mineral oil	5	4.5	4.6
11	Iso propyl myristate	3	3	3
12	Cetyl alcohol	1.5	2	2.5
13	Petrolactum	1	1.25	1.50
14	Almond oil	0.25	0.25	0.25
15	Vitamin E	0.2	0.2	0.2
16	Propyl paraben	0.1	0.1	0.1
17	Silicone oil	0.5	0.5	0.5
18	Loaded nanosponge with active shadownyl	0.5	1.0	1.5
19	Perfume	q.s	q.s	q.s

Procedure

- Wash the apparatus clean
- Weigh oil phase and water phase separately

- Heat both the phases upto 75-80
- After heating add oil phase into water phase and stir continuously with the help of mechanical stirrer in one direction upto 45
- Add loaded nanosponge and perfume and stir until it gets cool
- Fill into suitable container

After optimization of above formulations, cream 3 was found to have the most desirable characteristics and hence was selected as the best formulation.

2.4 Evaluation [35]

IN-VITRO TESTS

- Determination of physical parameters
- Determination of ph of the cream
- Determination of viscosity
- Determination of thermal stability
- Determination of total fatty matter
- Determination of stability under centrifuge test
- Determination of total mircrobial count

2.4.1)Determination of physical parameters

In physical parameters, appearance,consistency,color, odour and spreadability was taken into consideration.

2.4.2)Determination of ph of cream

As ph of cream shoukd be directly measured, 10% dilutions was made with distilled water and then resultant Ph was determined by ph meter.

2.4.3)Determination of viscosity

The viscosity was determined by spindle no 6 using Brookfield viscometer.

2.4.4)Determination of thermal stability

Keep the beaker(100ml capacity) containing material to be tested spreaded on inner wall as 20mm broad and 5mm thick strip for 8 hours in the humidity chamber at 60-70% relative humidity and temperature 37 ± 1 °C

2.4.3)Determination of total microbial count

Microbial growth may occur in cosmetics and toiletry products like creams, lotions and gels and many more preparations and thus they come in direct contact with the skin. Thus it is very important that the cosmetic product must be free from microbial contamination, safe and adequately preserved.

2.4.4) Centrifuge test

The cream is subjected to centrifugation to test to study creaming or separation.

2.4.5)Determination of total fatty matter

The total fatty matter is determined by breaking down the cream with dilute mineral acid and fatty matter is extracted with petroleum ether. It is weighed after removal of solvent.

IN-VIVO TEST [8,9]

- Patch test
- Mexameter evaluation

2.4.6) Patch test

This test is performed to see whether it causes some reaction or irritation.

2.4.7) Mexamater

In this the probe of mexameter is touched on the face to note the initial reading of melanin.then after application of cream,the reading is taken by touching the probe on the part of application for analysis of melanin.

3 .RESULT

Table No. – 3 Mexameter Evaluation

DURATION	APPEARANCE	SPREADABILITY	COLOUR	SHINE	FEEL	VISCOSITY	ODOUR	pH
INITIAL	O	VG	W	VG	VG	38000	P	6.8
AFTER 8 DAYS	T	VG	W	VG	VG	37500	P	6.8
AFTER 16 DAYS	T	VG	W	VG	VG	37600	P	6.8

VG: Very good W-White P-Pleasant T-Transparent O-opaque

Table No. 4 IN-VITRO TESTS

SR NO	PARAMETERS	CREAM 3
1	THERMAL STABILITY	Passes the test
2	TOTAL FATTY MATTER	19.3
3	TOTAL MICROBIAL COUNT	Passes the test
4	CENTRIFUGE	Passes the test

IN VIVO TEST

Table No. 5 - PATCH TEST

SR NO	PARAMETERS	PATCH TEST FOR CREAM CONTAINING LOADED NANOSPONGE
1	Immediately after removal of products	No reaction
2	After 24 hours	No reaction
3	After 48 hours	No reaction

Table No 6 - MEXAMETER EVALUATION

SR NO	DAYS	% MELANIN CONTENT
1	Before application	310
2	After application	270
3	After 8 days	230
4	After 15 days	19
5		

4. CONCLUSION

It was concluded that nanosponge acts as carrier for study active ingredients in order to reduce under eye dark circles, puffy bags and crow feets wrinkles. The product formulated for this is cream. The cream was formulated with nanosponge technology which helps to release active ingredients at slow rate. In the cream the use of shadownyl helps to remove dark circle and crow feets wrinkles at the same time.

Of the three formulations, active concentration of was satisfied with all desired characteristics and the formulation containing this concentration of active was evaluated on all parameters and was selected to possess all desirable characteristics.

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