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Research article

Development and evaluation of novel skin lightening preparation

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Abstract

Skin lightening creams are the products which work on skin by reducing a pigment called melanin in the skin. It also lightens naturally dark skin. In this research article various In-Vitro and In-Vivo studies are conducted for the preparation of skin lightening cream. Base is formulated and various evaluation testing's of base formulation is done that include pH, Consistency, appearance, spreadability, viscosity and according to these testing's the one base formulation is selected optimized. Further active ingredients are incorporated in optimized base and five formulations are made, and evaluation testing's of formulations is done that included In-Vitro study: pH, Consistency, appearance, spreadability, viscosity, total fatty substance content &water content, thermal stability. The one formulation is selected that have very satisfactory results and its further study is done that include Anti-microbial study and Stability study. In-Vivo study is also done that includes: skin irritation test and photographic evaluation. Very satisfactory and desirable results are obtained after all the evaluation studies. Finally a novel skin lightening Preparation was developed.

Keywords: Cream base Formulation, skin lightening cream, In-Vitro study, In-vivo study, thermal stability.

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1. Introduction

Skin lightening creams are the products which work on skin by reducing a pigment called melanin in the skin. It also lightens naturally dark skin. Skin lightening products are also known as, whiteners, skin brighteners, etc [1].As skin is daily exposed to sunlight which causes skin pigmentation disorders such as melasma, Hyperpigmentation, skin problems such as freckles, age spots, acne scars, or discoloration related to hormones. Thus most people who use skin lightening creams do so to treat skin problems such as hyperpigmentation, age spots, freckles, dark skin etc [1,2]. The aim of present study was to develop a novel skin lightening preparation that gave an effective skin lightening effect. Literature survey reveals that, author Marike Ganz *et al*, used fatty phase and aqueous phase with surface active agent as an emulsifier, while Lakshmi Prakash, *et al*, used fatty phase and aqueous phase with addition of emollients and thickening agent and an emulsifier [2].In this research article the formulation is made without adding any alkali substance which is used for formation of emulsifying base, rather, various emulsifying agents are added to formulate an emulsion base.

1. Methodology:

2.1 Materials: Niacinamide, and Bearberry (*Arctostaphylosuva-ursi*) Extract was selected after referring various articles for their skin lightening effect. Niacinamide and Bearberry (*Arctostaphylosuva-ursi*) Extract was obtained from kingVish extracts company, Mumbai as a

gift sample. Other chemicals were used of analytical grade.

2.2 Preparation of cream base:

The preparation of base is important before incorporating the active ingredients, to obtain a stable cosmetic formulation. The effectiveness and stability of product depends on the compatibility of active ingredients. Ingredients were used in preparation of various base formulations are mentioned in table no. 1[4-6]

Table no. 1. Formulation of base preparation

SN	Ingredients	Formulations			
		BF1	BF2	BF3	BF4
1	Isopropyl Myristate	1.0	1.0	1.1	1.0
2	Cetosteryl alcohol	3.0	1.0	1.5	1.5
3	Stearic acid	20.0	8.0	12.0	12.0
4	Light liquid paraffin	3.0	1.1	1.0	1.0
5	Glycerine	2.0	1.0	1.0	1.0
6	Dimethacone-200cps	1.0	1.0	1.0	1.0
7	Propylene glycol	2.0	1.4	1.0	1.0
8	Sodium Methyl paraben	0.1	0.1	0.1	0.1
9	Sodium Propyl paraben	0.02	0.02	0.02	0.02
10	Cetamacrogol-1000	1.0	0.5	1.0	1.5
11	Simugel SMS 88	2.5	0.5	1.6	1.5
12	Simusol 165	2.0	1.5	1.5	1.5
13	SA-TR 10	0.5	0.5	0.5	0.5
14	Demineralized water	Up to 100	Up to 100	Up to 100	Up to 100
15	Di-sodium EDTA	0.08	0.08	0.08	0.08
16	Butyl hydroxyl toluene	0.05	0.05	0.05	0.05
17	Vitamin-E	0.1	0.1	0.1	0.1
18	Perfume	0.8	0.8	0.8	0.8

2.1 Evaluation of cream base: Various evaluation testing's of base formulations were done that include pH, Consistency, appearance, spreadability etc [7,8] and according to these testing's the one base formulation was selected as an optimized formulation.

2.2 Preparation of skin lightening preparation: Five formulations of skin lightening preparation were prepared by emulsification method. All ingredients were incorporated in various concentration ranges in the selected Base Formulation (Table 2) [9,10].

2.3 Evaluation of skin lightening cream:

2.5.1 Determination of physical parameters:

In physical parameters, appearance, consistency, transparency, odour and spreadability and pH were taken into consideration according to the procedures given in Indian Standards (IS) [11].

2.5.2 Determination of thermal stability:

Phase separation study of skin lightening cream was tested by thermal stability in humidity chamber controlled at 60 to 70% RH and 37± 1ºc according to the procedure given in the Indian Standards (IS) [11,12].

2.5.3 Determination of total fatty substance content and water content:

The emulsion is broken with diluted mineral acid and the fatty matter is extracted with petroleum ether. It is weighed after removal of the solvent. Water content was carried out by Karl Fischer method according to the procedure given in the Indian Standards (IS) [3].

2.5.4 Determination of viscosity:

The viscosity of formulated creams was measured by brook field viscometer (DV-II) at room temperature. [3]

2.5.5 Determination of microbial contamination:

The microbial content present in the skin lightening preparation was determined by using the pour plate method and serial dilution technique according to the procedure given by the author Kokare R. C. [13].

2.5.6 Determination of stability study:

The stability studies carried out to assess physical and chemical stability of the product, stability with respect to the product referred to maintain protection against microbial contamination. A general methodology predicting stability was accelerated analysis, which subjects the material to elevated temperatures. So stability studies were carried

Table no 2: Formulation of skin lightening cream

SN	Ingredients	Formulations				
		PF1	PF2	PF3	PF4	PF5
1	Bearberry extract	2.0	3.0	1.0	3.0	1.0
2	Niacinamide	4.0	4.0	3.0	2.0	1.0
3	Isopropyl Myristate	1.1	1.1	1.1	1.1	1.1
4	Cetosteryl alcohol	1.5	1.5	1.5	1.5	1.5
5	Stearic acid	12.0	12.0	12.0	12.0	12.0
6	Light liquid paraffin	1.0	1.0	1.0	1.0	1.0
7	Glycerine	1.0	1.0	1.0	1.0	1.0
8	Dimethacone-200cps	1.0	1.0	1.0	1.0	1.0
9	Propylene glycol	1.0	1.0	1.0	1.0	1.0
10	Methyl paraben	0.1	0.1	0.1	0.1	0.1
11	Propyl paraben	0.02	0.02	0.02	0.02	0.02
12	Cetamacrogol-1000	1.0	1.0	1.0	1.0	1.0
13	Simugel SMS 88	1.6	1.6	1.6	1.6	1.6
14	Simusol 165	1.5	1.5	1.5	1.5	1.5
15	SA-TR 10	0.5	0.5	0.5	0.5	0.5
16	Demineralized water	Up to 100				
17	Di-sodium EDTA	0.08	0.08	0.08	0.08	0.08
18	Butyl hydroxyl toluene	0.05	0.05	0.05	0.05	0.05
19	Vitamin-E	0.1	0.1	0.1	0.1	0.1
20	Perfume	0.8	0.8	0.8	0.8	0.8

out for product. The products were kept in the room temperature and at 45ºc. The formulation was checked for every week. [3]

2.4 In-vivo Evaluation Testing of skin lightening cream(PF3):

2.6.1 Skin Irritation Test:

This test was carried out according to the procedure given in Indian Standards (IS) [3].The patches are applied on upper arm for 48 hrs. After 48 hrs the patches are removed and inspected.

2.6.2 Photographic Evaluation:

Photographic evaluation test was conducted on four human volunteers, among them two male and two female, was used. During long term study upto 30 days, all the volunteers were well examined and precaution was taken for any inconvenient. The results were shown in photographic form.

2. Results and discussion:

Among four base formulations, formulation BF3 showed satisfactory results in terms of pH, consistency, appearance, and viscosity over the period of one week. Hence, formulation BF3

was continued for preparation of skin lightening cream.

Table no.3. Evaluation data of skin lightening cream

Product Formulation	PF1	PF2	PF3	PF4	PF5
Consistency	Satisfactory	Satisfactory	Good	Satisfactory	Good
Appearance	Satisfactory	Satisfactory	Good	Satisfactory	Good
Skin Irritation	No Irritation	No Irritation	No Irritation	No Irritation	No Irritation
pH	6.4	6.5	6.1	6.4	6.3
Thermal Stability	Fail	Fail	Pass	Fail	Pass
Total fatty matter	6.7	8.9	7.5	8.6	7.1
Water content	81.77±0.5	82.51±0.5	85.89±1.3	83.33±0.5	84.45±0.7
Viscosity (Cps)	61520	63390	51300	59350	53330

Various physical parameters of skin lightening creams were studied. The results of Consistency, Appearance, Skin Irritation, pH, Thermal Stability, Total fatty matter, Water content and Viscosity (Cps) of various formulation was shown in table no.3, indicating. From the observation it was found that all the formulation had desirable properties. Among all formulations, formulation PF3 showed excellent results, hence selected for further studies.

3.1 Antimicrobial study:

Data shown in table no. 4 indicated that, the formulation PF3 completely passes the antimicrobial test. It might be due to presence of sodium methyl paraben and sodium propyl paraben.

3.2 Stability study:

The formulation PF3 was subjected to stability performance for the period of 30 days at room temperature and at 45ºc. The appearance, Consistency, Spreadability, pH, viscosity and odour were studied. pH of all the formulation up to 30 days was constant with desired viscosity, that made preparation stable. No appreciable changes were found for the respective parameters. The results were shown in table no. 5 and from the observations PF3 showed satisfactory results and hence it was selected as final product. It might be due to proper and appropriate concentration of active that helped to maintain proper viscosity of the preparation.

Table no 4: Microbial content present in skin lightening cream

Test	PF3	Limit
Total viable aerobic count	10 cfu/gm	≤1000cfu/gm
Total combined yeast and moulds count	≤10 cfu/gm	≤100cfu/gm
Escherichia coli	Absent	Absent/gm
Pseudomonas aeruginosa	Absent	Absent/gm
Staphylococcus aures	Absent	Absent/gm

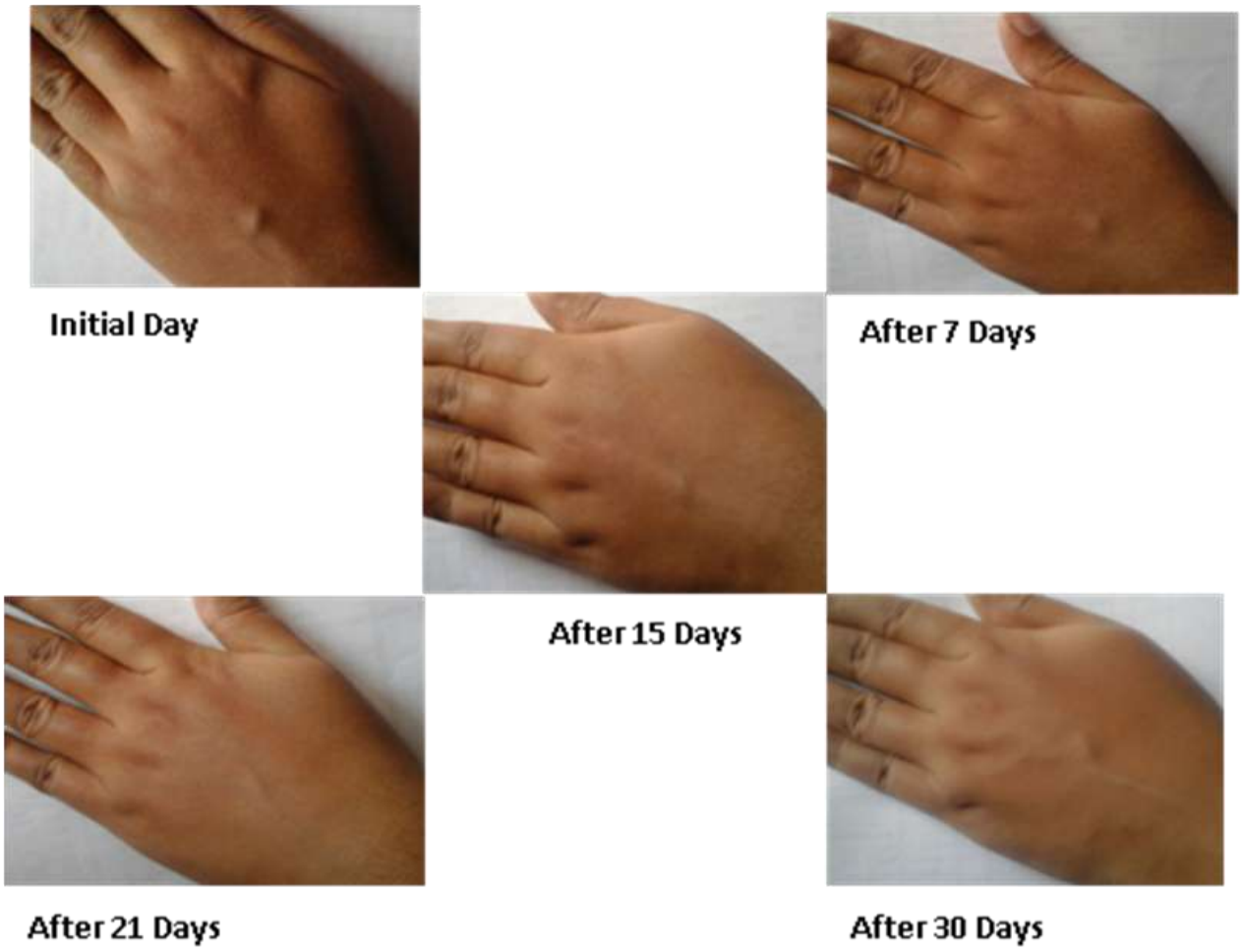
3.3 In-vivo testing of skin lightening cream

3.3.1 Skin irritation test:

A very satisfactory result was obtained for all the formulation. Data from table no.3 indicated that, no irritation to human skin was obtained over 48 hour study.

Table no.5: Stability data of skin lightening

SN	Parameters	Stability Study of skin lightening cream at room temperature and at 45ºc temperature				
		Initial Day	7 Days	15 days	21 Days	30 Days
1	Appearance	Milky White	No Change	No Change	No Change	No Change
2	Consistency	Semi-Solid	No Change	No Change	No Change	No Change
3	Odour	Good	No Change	No Change	No Change	No Change
4	pH	6.1	6.1	6.1	6.1	6.1
5	Viscosity	51300	51300	51300	51300	51300



3.3.2 Photographic evaluation of skin lightening cream:

Long term photographic evaluation of optimized formulation (PF3) was conducted over a period of 30 days. The figure no.1 indicated that, gradually the lightening effect was obtained from initial day to last day of evaluation period. It was observed that skin was so hydrated and its tone was maintained. It may be due to presence of niacinamide and bearberry extract.

Conclusion

The skin lightening cream prepared by conventional procedure is very simple formulation with no toxicity or skin irritancy. All the desired properties were found in these conventional cream formulations. After studying the *in-vitro* and *in-vivo* evaluation, it is concluded that the product has the best capacity to lighten the skin colour and also it has an appropriate stability. And according to the in-vivo study, the product had no skin irritation or redness after application on skin. Therefore this skin lightening cream should be used as an effective formulation for lightening the skin colour tone.

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