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Research Article

FORMULATION AND EVALUATION OF SUN PROTECTIVE TOPICAL PREPARATION

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ABSTRACT

In recent days, many people are facing problem of sun tanning and darkening of skin. Sun tanning causes erythema (sunburn inflammation), reddening of skin, local or systemic immunosuppression, photoaging and photocarcinogenesis. Skin is a delicate organ of body, thus by considering the facts related to this attempt are made to develop cream having Sunprotective as well as Fairness activity with improved user compliance and avoidance of undesirable effect. It is reported that Oxybenzone gives protection against UV B rays. Hence the present work is a humble attempt to evaluate sunscreen activity of oxybenzone along with the fairness activity of Arbutin. The procured sample of the chemical material was first evaluated for their quality by determining colour, odour, pH, melting point, residue on ignition, loss on drying and % purity. Proper cream base was formulated by taking different trials. Three different base trials were then evaluated. On the basis of evaluation results of pH, viscosity and appearance the base trial 2 (B2) was selected for incorporation of active ingredients into the base. Cream containing 6 % of Oxybenzone and 1.5 % of Arbutin was selected for the evaluation of fairness activity and from the observation, it was concluded that the cream improves complexion, makes the skin soft and ensure ease of application. Hence it is concluded that it may be used as Sunscreen and Fairness cream.

Keywords: Oxybenzone, Arbutin, Sun protective, Fairness cream

INTRODUCTION

Skin is the outermost and the largest part of the body and it is most sensitive to photodamage because it directly exposed to solar radiation and other environmental factors. The harmful effects of solar radiation are usually caused by the ultraviolet (UV) region of the electromagnetic spectrum. It may cause several harmful effects to the eye, skin and immune system. Prolong exposure of UV radiations may initiate the production of reactive oxygen species, which causes oxidative injury and impairment of the antioxidant system. These injuries impaired the metabolic pathways of the skin, which leads to photoaging, erythema, edema, sunburn, lines and wrinkles, photosensitivity, immunosuppression, DNA damage as well as skin cancer in most severe conditions. Therefore, sunscreen compounds are generally incorporated in many cosmetic formulations such as creams, lotions, moisturizers and other skin care products. The main purpose of sunscreen is to protect the skin against UVA and UVB rays and to conserve the moisture content of skin and its own natural oils, which may be lost during the exposure of solar radiation. The sunscreen should be protective, chemically inert, non-irritating, non-toxic and photo stable. The skin's natural sunscreens such as squalane, proteins, absorbing lipids and nucleotides have been used from several years [1, 2].

The photo protection against UV radiation can be determined *in-vivo* or *in-vitro*. The *in-vivo* determined by photo testing in human volunteers has been used from several years. It is complicated, time consuming as well as costly technique. Due to this, scientists have developed an *in-vitro* technique to measure the efficiency of sunscreen. The *in-vitro* test is quick, inexpensive screening methodology. The sunscreen protection factor (SPF) is defined, as the UV energy required producing a minimal erythema dose (MED) on protecting skin, divided by the UV energy required to produce a MED on unprotected skin. The MED is defined as the lowest time interval or dosage of UV light irradiation sufficient to produce a minimal, perceptible erythema on unprotected skin [3].

Fairness creams are intended to lighten the colouration of the skin and are desired to remove the dark spots on the skin. Since they are designed to work by penetrating the skin and interfering with the pigment production by the skin cells thus have a little effect on the normal structure and function of the skin[3].

Reduction of skin pigmentation is responsible for fairness of the skin. Interference with the melanin formation can be achieved by reducing the number of Melanocytes in the skin or by interfering with the oxidation of tyrosine. An abnormal increase in the amount of melanin in the epidermis is the main causes of hyper pigmentation such as cholasma, or freckles, spots, etc. Some of the principle causes are exposure to UV-light, female hormones and genetic reasons. Consequently, the pharmaceutical and cosmetic agents which control melanin production or melanin metabolism are used as a whitening agent. Whitening agent is believed to act on the production and metabolism of melanin of the skin by inhibiting melanin production in Melanocytes, reducing extent melanin [4,5].

In present study, the cream formulation containing oxybenzone along with the fairness activity of Arbutin. The proper cream base was formulated by taking different trials. The active materials were then incorporated into the selected cream base in different concentrations. Then various parameters were evaluated such as

pH, viscosity, determination of thermal stability, determination of total fatty content, determination of in vitro SPF, determination of in vitro sunscreen activity and evaluation of fairness activity.

CHEMICALS

Arbutin and oxybenzone (Beijing Brilliance Biochemical, Co. Ltd)
Other chemicals used were of analytical grade of LOBA Chemie Pvt. Ltd. India.

INSTRUMENTS

UV visible spectrophotometer (Model No. UV2401 PC Shimadzu Corporation, Koyto, Japan)
FTIR (Model-8400 S, Shimadzu Corporation, Koyto, Japan)
Viscometer (Brookfield Engeeniring laboratories, INC. USA)
Incubator (Cas lab. Co. India)

METHOD

Preparation of base for cream

A cream formulation was prepared and its ingredients are shown in Table 1. A small quantity of water was taken in processing vessel, heating up-to 85^{0}C and carbopol 940 was added slowly with constant stirring till it completely dispersed. Heating was removed and added propylene glycol, glycerine and methyl paraben at 70-75^{0}C. Side by side in another vessel given quantity of oil phase were melted at 70-75^{0}C. At same temperature (70-75^{0}C) both phases water and oil were mixed slowly till homogeneous mass obtained [5, 6].

Table 1: Formula of Cream Base

Sl. No.	Ingredient	Formulation (For 100 g)			
		B1	B2	B3	
1	Carbopol-940	0.165g	0.2g	0.3g	Part A
2	Propylene glycol	2.0ml	2.0ml	2.0ml	
3	Methyl paraben	0.25g	0.25g	0.25g	
4	Glycerine	2.0ml	2.0ml	2.0ml	
5	Propyl paraben	0.15g	0.15g	0.15g	Part B
6	Triethanolamine	1.15ml	1.15ml	1.15ml	
7	Light liquid paraffin	16.0ml	16.0ml	16.0ml	
8	Steric acid	4.0g	4.0g	4.0g	
9	Glyceryl monostearate	3.36g	3.36g	3.36g	
10	Cetosteryl alcohol	2.29g	2.29g	2.29g	
11	Paraffin wax	0.9g	0.9g	0.9g	
12	Water	Make up volume	Make up volume	Make up volume	

Preparation of cream

For formulating the cream, oxybenzone was selected as sunscreen agent and Arbutin is selected as whitening agent. The different concentrations of oxybenzone (F1-2g, F2- 4g and F3- 6g) and Arbutin (F1-0.5g, F2-1.0g and F3- 1.5g) were incorporated finally in the cream base (B2) at 40-45^{0}C with continuous stirring and were evaluated for various physicochemical parameters [6].

Evaluation of cream

The physicochemical properties such as color, odor, pH, viscosity, spreadability and thermal stability of the cream were evaluated [7].

pH measurement

1 g of cream was dispersed in 9 ml of distilled water to determine the pH at 27°C using the pH meter[7].

Determination of viscosity

Procedure: Viscosity of the formulation was determined by Brookfield Viscometer at 25 rpm, using spindle no. 64[7].

Spreadability

The parallel plate method is most widely used method for determining the spreadability of semisolid preparations. A modified laboratory apparatus was used to evaluate spreadability. The setup consists of two glass slides placed on a tripod stand on which excess of cream (3g) was applied in between two glass slides. The upper slide is movable and the lower slide was firmly fixed to the stand. 100 g weight was placed on them for 5 minutes to compress the cream to uniform thickness and the excess cream was scrapped off from the edges. Then 50 g weight was added to one side of the slide and the slide is pulled till it covers a distance of 10 cm. The time in seconds required to separate two glass slides by 10 cm was taken as a measure of spreadability. A shorter interval indicates better spreadability. The spreadability was calculated by using the formula[8].

$$S=m.l/t$$

Where, S=Spreadability, m=Weight tied to upper glass slide, l=Length of glass slide, t=Time taken to separate them.

Determination of thermal stability

The cream was transferred into glass bottle with the help of spatula and tapped it to settle to the bottom. Filled up to two third capacity of bottle, plug was inserted and tightened the cap. The filled bottle was kept in the incubator at 45^{0}C for 48 hr [8, 9].

Determination of *in vitro* SPF

1.0 g of cream formulation and commercial cream was weighed, transferred to 100 ml volumetric flask, diluted to volume with ethanol and water (40:60) then ultrasonication for 5 minutes after that filtered through Whatman No. 1 filter paper and collect the filtrate by rejecting the first 10 ml of filtrate. 5.0 ml of aliquot was taken in 50 ml volumetric flask and diluted to volume with ethanol and water (40:60). Subsequently 5.0 ml of aliquot was transferred to 25 ml volumetric flask and the volume completed with ethanol and water (40:60). The absorbance values of each aliquot prepared were determined from 290 nm to 320 nm at 5 nm interval, using ethanol and distilled water (40:60) solution as a blank. The readings were taken in triplicate and the

determinations were made at each point. The obtained absorbance values between 290 and 320 nm were multiplied with the respective EE (λ) values. Their summation was taken and multiplied with the correction factor (10) to obtain the SPF values. Data were expressed as ± standard error mean [8,9,10].

Photo stability determination

2 mg/cm^2 of each sunscreen cream was weighed and spread evenly between two plates of polished fused quartz silica (thickness 5 mm and diameter 25 mm). To avoid absorption distortion, thinner layer was applied. The AUC for UVA, UVA1 (340–400 nm), UVA2 (320–340 nm) and UVB was measured for each spectrum before (AUC before) and after (AUC after) UV artificial (980 kJ/m^2 UVA and 12 kJ/m^2 of UV radiation (UVB included) and before and after UV natural. If the AUCI (AUCI = AUC after/AUC before) was >0.80, the sunscreen was considered photostable. The AUC was calculated with the following equation[10,11, 12].

$$\sum_{\lambda\,\min}^{\lambda\,\max} A(\lambda)\,\Delta\lambda$$

where A is absorption and λ is wavelength. It was measured in steps of 1 nm.
For UVA λmax = 400 nm and λmin = 320 nm. The same measurement was done for every UV range respectively, before and after UVartificial and before and after UV natural.

Determination of total fatty substance content

Weighed 2 g of the material with 25 ml of dilute hydrochloric acid and reflux until the solution perfectly cleared. The contents of the flask were cooled to room temperature. Add 50 ml of petroleum ether in portions of 10 ml and poured it into the separating funnel. The separating funnel was shake well and leave until the layers separated. Separated the aqueous phase and shaked it with 50 ml portions of petroleum ether twice. Combined all the ether extracts and washed them with water until free of acid (when tested with methyl orange indicator solution). The petroleum ether extract was filtered through a filter paper containing sodium sulphate into a conical flask which has been previously dried at a temperature of 90 °C and then weighed. Washed the sodium sulphate on the filter with petroleum ether and combined the washings with filtrate. Distilled the petroleum ether and dried the material remaining in the flask at a temperature 90 °C up to constant mass [11, 12].

Total fatty substance % By mass = M_1/M_2
M_1= Mass in g of the residue.
M_2 = Mass in g of the material taken for the test.

Determination of fairness activity

This study was an open prospective, non-comparative phase III clinical trial. Cream was given to Ten subjects (5 male and 5 female), aged between 18 to 45 years for 4 weeks to carry out the subjective evaluation on the basis of their feedback. All the volunteers were followed –up at weekly intervals for a period of 4 weeks and the symptoms score evaluation was done during each follow-up visit. Response to fairness cream was evaluated on a 5-point visual analogue scale (0-Nil, 1-Mild, 2-Moderate, 3-Good, 4-Excellent)[13].

Stability studies

Stability by centrifugation

During the centrifugation studies, sunscreens were centrifuged at 3500- 13,500 rpm at interval of 500 rpm for 10 min. The formulations were observed for the phase separation. The results are shown in the Table 4.

Stability studies as per ICH guidelines

For assessing the stability of formulated creams, the following parameters were taken into consideration like color, phase separation, viscosity; Spreadability,pH and SPF of formulation. These studies are essential to ensure that the product is stable throughout its designated shelf life. The stability was carried out for thirty days at temperatures 40 ± 2°C and relative humidity at 75 ± 5% using stability chamber [12,13,14].

RESULT AND DISCUSSION

Physicochemical parameters

The results of physicochemical analysis of cream formulation are shown in Table 2.

Table 2: Physicochemical parameter of cream

Parameters	BASE	F1	F2	F3
Colour	White	White	White	White
Consistency	Good	Good	Good	Good
Texture	Fine	Fine	Fine	Fine
pH	7.11	6.95	7.11	7.10
Viscosity	16032	15780	17202	16640
Spreadability	17.09	17.85	17.04	18.52
Thermal stability	No separation of phases	No separation of phases	No separation of phases	No separation of phases

Monitoring the pH value is important for determining the stability of pharmaceuticals and cosmeceuticals. Any change in pH of the product indicates a possible interaction or occurrence of chemical reactions which may provide an idea on the quality of the final product. The pH of human skin normally ranges from 4.5 to 6.0. Due to frequent washing and used of soap, the acidity of the skin is lost. Therefore, moisturizer has an acidic range should be used to normalize the skin. Acceptable pH range of moisturizers should be 5-8 range. The cream formulation had a pH value of 6.5-7.5 range (Table 2), which is an acceptable and non-skin irritating pH value. The therapeutic efficacy of the formulation depends on its spreading value. The spreadability showed that formulation F3 have better spreadability when compared with F1 and F2. The nature of cream formulation was homogenous, uniformly spreadable and emollient.

Determination of In vitro SPF

The SPF is a quantitative measurement of the effectiveness of a sunscreen formulation. In this study the cream formulation containing oxybenzone and arbutine was evaluated for sunscreen activity using in-vitro SPF method. The SPF values obtained is shown in Tables 3 and Spectrum of all formulations were taken from 290nm-400nm and depicted in Figure 1 and 2.

Table 3: Sun protection factor (SPF) values for cream

Sample	wavelength	290	295	300	305	310	315	320	SPF
	EE(λ)XI(λ)	0.0150	0.0817	0.2874	0.3278	0.1864	0.0839	0.0180	
F1	A	0.532	0.455	0.373	0.324	0.306	0.310	0.319	3.4 ±
	EE X I X A	0.0079	0.0371	0.1072	0.1062	0.0570	0.0260	0.0057	0.03
F2	A	0.555	0.456	0.366	0.312	0.291	0.292	0.300	3.36 ±
	EE X I X A	0.0083	0.0372	0.1051	0.1022	0.0542	0.0244	0.0054	0.03
F3	A	0.912	0.787	0.652	0.570	0.543	0.550	0.564	6.09 ±
	EE X I X A	0.0136	0.0642	0.1873	0.1868	0.1012	0.0461	0.0101	0.06

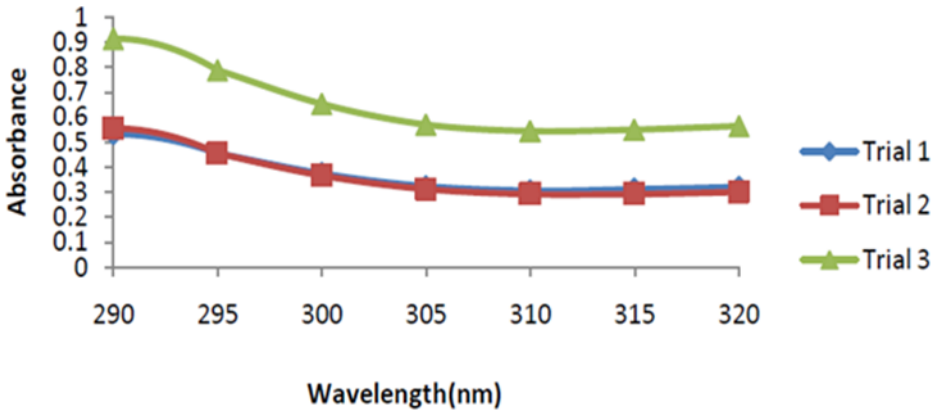

Figure 1: Absorbance of cream for SPF

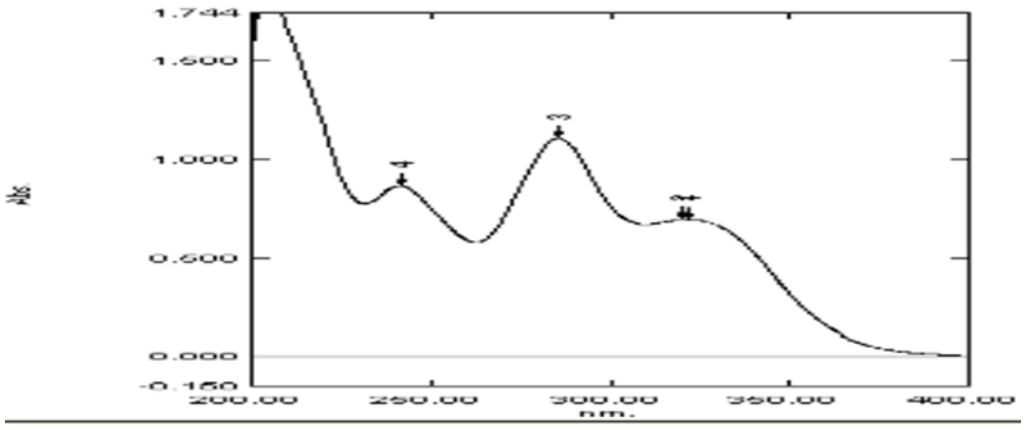

Figure 2: Absorbance spectrum of F3 for SPF

Photo stability determination

The photo stability of the all formulation of sunscreen showed considerable stability of ingredients. Samples on plate showed similar spectrum before and after heating for 20 min at 50°C. The photo unstable sunscreens begin to degrade rapidly when exposed to the sun. After 120 min of UV natural, AUCI found to be <0.70 for sunscreen F1and F2 which indicate that these are unstable shown in table 4. While exposure F3 showed shift in wavelength to shorter range and found stable by both UV artificial and UV natural. Thus it can be said that F3 can give consumer satisfaction for photo stable sunscreen product. All cream showed relatively good photo stability and it can be consider that antioxidant nature.

Table 4: Results of photo stability evaluation of sunscreen cream batches

AUCI (AUCI before/ AUCI after)						
			After UV natural exposure		After UV artificial exposure	
Formulation	Exposure time	UVA radiation (kJ/m2)	UVA	UVB	UVA	UVB
F1	30	55	0.65	0.68	0.72	0.72
	90	165	0.68	0.63	0.65	0.69
	120	235	0.59	0.61	0.71	0.77
F2	30	58	0.45	0.59	0.65	0.73
	90	160	0.85	0.88	0.78	0.81
	120	230	0.65	0.69	0.82	0.87
F3	30	62	0.75	0.70	0.60	0.81
	90	155	0.79	0.72	0.65	0.80
	120	242	0.84	0.87	0.90	0.82

Determination of Total Fatty Content

Table 5: Determination of TFC

Parameter	Base	F1	F2	F3
Total fatty content (% by mass)	3	3.5	3	4

Determination of Fairness Activity

From the results of subjective evaluation of fairness activity, it was observed that cream with 1.5% Arbutin was well appreciated. It caused no irritation on regular application. It also showed Skin whiting effect along with excellence in terms of appearance, spreadability along with softness and glowing effect. It reduced the intensity of hyperpigmentation spot.

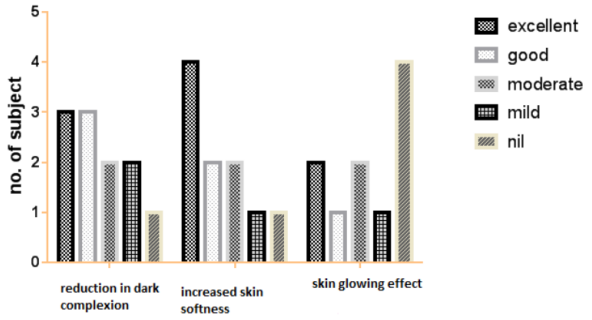

Figure 3: Effect of fairness cream at the end of study.

Stability studies

The stability studies of varies parameters like visual appearance, pH, spreadability, viscosity showed that there were no significant changes after 1 month of study period and result are summarised in table 6. During centrifugation studies, it was observed that there was no phase separation in F3 formulation, confirming that formulation was stable at accelerated speed. All formulations had increasing viscosity values after storage in freeze-thaw condition. All samples were oil-in-water creams; hence, their water content might lose at fluctuated temperatures. Therefore, the suggested storage condition for these products should be at constant temperature. No phase separation and changing in colour as well as odour were observed in all samples after stability test. From the results it was observed the given formulation was relatively stable at accelerated temperature and humidity.

Table 6: Stability parameters for cream

Parameters	Values
Colour	White
Consistency	Good
Phase separation	No phase separation
pH	7.10
Viscosity	17392
Spreadability	18.13
SPF	6.11 ± 0.03

CONCLUSION

The values obtained after the analysis of oxybenzone and Arbutin were within the standard limits (table 9 and 11) and hence it was concluded that the procured material was pure and can be used for the further experimentation. From the results of pH, viscosity, *in vitro* SPF, sunscreen activity and other evaluated parameter for the cream it was concluded that the cream containing 6 % of oxybenzone and 1.5 % of Arbutin was good for prevention of harmful effects caused by sun rays. From the results of percent protection of cream (table 16) it can be concluded that the cream gives protection against UVA and UVB rays. The SPF of trial 3 was found to be good as compared to the rest of the cream trials.

The cream containing 6 % of Oxybenzone and 1.5 % of Arbutin (trial 3) was selected for the evaluation of fairness activity and from the observation it was concluded that the cream improves complexion, makes the skin soft and ensure ease of application. Hence it is concluded that it may be used as Sunscreen and Fairness cream.

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