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A Review on Marketed Formulations of Anti-Wrinkle Cream and Make an Effective Anti-Wrinkle Cream and Their Standardization

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Abstract **Review Article**

Herbal formulations have growing demand in the world market and the plants have been reported in the literature having good anti-microbial, anti-oxidant and anti-inflammatory activity. In this study cream was formulated based on the anti-oxidant potential of herbal extracts and its evaluation. The cream was formulated with Licorice oil, Cinnamon oil, of different concentrations namely F1, F2, F3. The cream was stable during stability studies according to ICH guidelines 30±2 0C/50±5% RH and 40±2 0C/75±5% RH for two months. The evaluations of all formulations were done on different parameters like pH, spreadability, stability etc. Formulations F2 and F3 showed good spreadability, good consistency, and homogeneity with good appearance, pH, and no evidence of phase separation and ease of removal. The formulation F2 and F3 shows no redness, edema, inflammation and irritation to the skin during irritancy studies. These studies suggest that the composition of extracts and base of cream of F3 is more stable and safe, it may produce synergistic action. It can be concluded that herbal cream without side effects having anti-oxidant property can be used as provision of a barrier to protect the skin and avoid aging of the skin.
Keywords: Herbal cream, anti-aging, Licorice oil, antioxidant and Cinnamon oil.

INTRODUCTION

WHO defines traditional medicine "the health practices, approaches, knowledge and beliefs incorporating plant, animal and mineral-based medicines, spiritual therapies, manual techniques and exercises, applied singularly or in combination to treat, diagnose and prevent illnesses or maintain well-being". In some Asian and African countries, 80% of the population depends on traditional medicine for primary health care [1]. In many developed countries, 70% to 80% of the population has used some form of alternative or complementary medicine (e.g. acupuncture). Herbal treatments are the most popular form of traditional medicine, and are highly lucrative in the international marketplace. Annual revenues in Western Europe reached US$ 5 billion in 2003-2004.In China sales of products totaled US$ 14 billion in 2005. Herbal medicine revenue in Brazil was US$ 160 million in 2007. Over one-third of the population in developing countries lack access to essential medicines. The provision of safe and effective TM/CAM therapies could become a critical tool to increase access to health care. While China, the Democratic People's Republic of Korea, the Republic of Korea and Vietnam have fully integrated traditional medicine into their health care systems, many countries are yet to collect and integrate standardized evidence on this type of health care. 70 countries have a national regulation on herbal medicines but the legislative control of medicinal plants has not evolved around a structured model. This is because medicinal products or herbs are defined differently in different countries and diverse approaches have been adopted with regard to licensing, dispensing, manufacturing and trading [2].

Review of Litleture

Marketed formulation used as anti-aging

1. Amara Organics Retinol Cream [3].
   Composition: hyaluronic acid, aloe vera, Vitamins E and B5.
2. Baebody Eye Gel for Dark Circles
   Composition: hyaluronic acid, Matrixyl 3000, Vitamin E, and plant stem cells.
3. Cardea Luxe
   Composition: retinol, hyaluronic acid, and cardea luxe.
4. Eucerin Sensitive Skin Experts Q10 Anti-Wrinkle Face Cream
   Composition: Coenzyme Q10, Vitamin E, and beta-carotene.
5. Illustra Skin Care

Composition: retinol with hyaluronic acid, sheabutter, jojoba oil, and Vitamin E.

6. Khali Beauty Retinol Moisturizer Gel Cream for Face and Eye Area – Anti-Wrinkle Facial Night Cream
   Composition: retinol & Vitamins C and E.
7. Kriama 2.5% Retinol Cream
   Composition: hyaluronic acid, Vitamins C, A, and E, and retinol.
8. Kriama Night Repair Cream
   Composition: jojoba oil, avocado oil, and retinyl palmitate.
9. L'Occitane Anti-Aging Divine Cream
   Composition: immortelle flower essential oil.
10. L'Oréal Paris Collagen Moisture Filler Night Cream
    Composition: collagen, sheabutter.
11. L'Oreal Paris Wrinkle cream.
    Composition: L'Oreal's unique Stimuplex formula with 8 natural lifters such as elastin, collagen, chondroitin sulfate.
12. My little beauty Anti-Aging Wrinkle Firming Moisturizing Skin Face Cream, 30ml
    Composition: jojoba oil, ginseng extract, collagen, and 24k gold.
13. Neutrogena Rapid Wrinkle Repair Moisturizer with SPF 30
    Composition: SPF 15, retinol, glucose complex, and hyaluronic acid.
14. Olyphan
    Composition Hyaluronic acid, she butter, jojoba oil, Vitamins D, K, and E, blue green algae,
15. Pond's Rejuveness Anti-Wrinkle Cream
    Composition: alpha hydroxy acids and collagen.
16. Progenix Profesional Skin Care Retinol Anti-Wrinkle Night cream for fine lines, deep wrinkles, sun damaged skin
    Composition: aloe, Vitamin E, retinol, and hyaluronic acid.
17. Pure Biology Anti-Aging Night Cream
    Composition: retinol, Hyaluronic acid
18. Radha Beauty Retinol Moisturizer Cream for Face and Eye Area, 1.7 Oz
    Composition: retinol, Vitamin E, hyaluronic acid, and green tea.
19. Lily Ana Naturals Retinol Cream Moisturizer
    Composition: retinol, aloe vera, hyaluronic acid.
20. Vena Beauty
    Composition: hyaluronic acid, retinol, Vitamin E.
21. TULA Probiotic Skin Care Advanced Neck Cream
    Composition: probiotic formula, jojoba oil, cocoa butter.
22. Yeouth Composition: hyaluronic acid, aloe vera, Vitamins C, E, and Beta Carotene
23. St. Ives Timeless Skin Facial Moisturizer
    Composition: collagen and elastin

METERIALS AND METHODS

Collection and identification of plant material

The oil of *Glycyrrhiza glabra* were collected from Greenwood Essential 1st Floor or, A2/92, Janakpuri New Delhi India. The oil of *Cinamomum zeylanicum* was collected from the local shop Vaidh Prakashi Lala Town Fatehganj (w), Bareilly (U.P) India. The plant *Glycyrrhiza glabra and Cinamomum zeylanicum* collected during the months of April 2019. The species was identified by the local people during the time of collection and later on authentication was made by department of Pharmacognosy, Invertis University, bareilly (U.P) India.

Preparation of Cream base

The six formulations of cream bases were prepared. Various ingredients were weighed accurately. Oil in water (O/W) emulsion-based cream (semisolid formulation) was formulated. The emulsifier and other oil soluble components were melted in a beaker (Part A) and heated to 75° C. The methyl paraban and glycerol was dissolved in required amount of water and heated to 75° C. When the temperature of both the phases was 75°C.The aqueous phase was added gradually into oily phase with continuous stirring until cooling of emulsifier took place, and left at room temperature to obtain the required product. The flavoring agent was added when it is hot to obtain cream base [4-8]. The compositions of the cream base are given in table.

List of ingredients used to formulate base for herbal cream

S.No.	Ingredients	Used as
1.	Sodium Lauryl Sulphate (SLS)	Surfactant
2.	Cetyl alcohol	Emulsifying and solubilizing agent
3.	Sheabutter	Thickening agent
4.	Methyl paraban	Preservatives
5.	Triethanolamine	Emulsifying agent

Composition of herbal cream

Ingredients	Formula % w/w		
	F1	F2	F3
Cetyl alcohol	0.5gm	0.5gm	0.5gm
Sodium Lauryl Sulphate	0.5gm	0.5gm	0.5gm
Methyl paraban	0.025 gm	0.025 gm	0.025 gm
Triethanolamine	0.5gm	0.5gm	0.5gm
Sheabutter	25gm	25gm	25gm
Glycyrrhiza glabra	1ml	1.5ml	2ml
Cinamomum zeylanicum	1ml	1.5ml	2ml

Qualitative chemical tests

Qualitative chemical tests were performed to determine the presence of alkaloids, Carbohydrates, cardiac glycosides, polyphenols, Saponins, tannins and terpenoids [4-6].

Test for alkaloids

- **Dragendorff's test:** To 1 ml of the extract, add 1 ml of Dragendorff's reagent (Potassium Bismuth iodide solution). An orange-red precipitate indicates the presence of alkaloids.
- **Mayer's test:** To 1 ml of the extract, add 1 ml of Mayer's reagent (Potassium mercuric iodide solution). Whitish yellow or cream colored precipitate indicates the presence of alkaloids.
    - **Hager's test:** To 1 ml of the extract, add 3ml of Hager's reagent (Saturated aqueous solution of picric acid), yellow colored precipitate indicates the presence of alkaloids.
        - **Wagner's test:** To 1 ml of the extract, add 2 ml of Wagner's reagent (Iodine in Potassium Iodide), Formation of reddish brown precipitate indicates the presence of alkaloids.

1. **Test for Saponins:** Take small quantity of alcoholic and aqueous extract separately and add 20 ml of distilled water and shake in a graduated cylinder for 15 minutes lengthwise. A 1cm layer of foam indicates the presence of Saponins.

2. **Test for Glycosides**

- **Legal test:** Dissolve the extract in pyridine and add sodium nitroprusside solution to make it alkaline. The formation of pink red to red colour shows the presence of glycosides.
    - **Baljet test:** To 1ml of the test extract, add 1ml of sodium picrate solution and the yellow to orange colour reveals the presence of glycosides.
- **Keller-Killiani test:** 1gm of powdered drug is extracted with 10ml of 70% alcohol for 2 minutes, filtered, add to the filtrate, 10ml of water and 0.5ml of strong solution of lead acetate and filtered and the filtrate is shaken with 5ml of chloroform. The chloroform layer is separated in a porcelein dish and removes the solvent by gentle evaporation. Dissolve the cooled residue in 3ml of glacial acetic acid containing 2 drops of 5% ferric chloride solution. Carefully transfer this solution to the surface of 2ml of concentrated sulphuric acid. A reddish brown layer forms at the junction of the two liquids and the upper layer slowly becomes bluish green, darkening with standing.

3. **Test for carbohydrates and sugars**

- **Molisch's test:** To 2ml of the extract, add 1ml of a-napthol solution, add concentrated sulphuric acid through the side of the test tube. Purple or reddish violet colour at the junction of the two liquids reveals the presence of Carbohydrates.
- **Fehling's test:** To 1ml of the extract, add equal quantities of Fehling solution A and B, upon heating formation of a brick red precipitate indicates the presence of sugars.

4. **Test for flavonoid**

- **Shinoda's test:** The alcoholic extract of powder treated with magnesium foil and concentrated HCl give intense cherry red colour indicates the presence of flavonones or orange red colour indicates the presence of flavonols.

5. **Test for steroids**

- **Libermann-Burchard test:** 1gm of the test substance was dissolved in a few drops of chloroform, 3ml of acetic anhydride, 3ml of glacial acetic acid were added, warmed and cooled under the tap and drops of concentrated sulphuric acid were added along the sides of the test tube. Appearance of bluish-green colour shows the presence of sterols.

Evaluation of Cream

1. **PH Measurement:** To measure the pH, 1 g of each herbal cream was diluted with 9 ml of distilled water and then pH was checked using pH meter [12, 13].
2. **Viscosity:** The viscosity of each herbal cream was measured and compared before and after accelerated test by Brookfield Viscometer at 100 rpm, using spindle no7[12].
3. **Dye solubility test:** The scarlet red dye is mixed with the cream. Place a drop of the cream on a microscopic slide covers it with a cover slip, and

examines it under a microscope. If the disperse globules appear red the ground colourless. The cream is o/w type. The reverse condition occurs in w/o type cream i.e. the disperse globules appear colourless in the red ground [12].

4. **Spreadability:** Spreadability and layer thickness are the measure of consistency of the product. The lower plate holds the sample, while the upper plate, which weighs 42 g, exerts forces to the sample in the lower plate. One gram of moisturizer formulation was placed on the lower plate and the upper plate was place on the top of the sample. A constant force was generated by adding known weight on the upper plate. Each sample was tested at least three times at constant temperature and exerted weight and the mean values of spread surface area on the lower plate were calculate [13, 14-18].
5. **Homogeneity:** The formulations were tested for the homogeneity by visual appearance and by touch.
6. **Appearance:** The appearance of the cream was judged by its color, pearlscence and roughness and graded.
7. **After Feel:** Emolliency, slipperiness and amount of residue left after the application of fixed amount of cream was checked.
8. **Types of smear:** After application of cream, the type of film or smear formed on the skin were checked.
9. **Removal:** The ease of removal of the cream applied was examined by washing the applied part with tap water.
10. **Saponification value:** Saponification value, acid value and nonvolatile % are determined as per Indian Pharmacopoeia (I.P.) [13]. Higher the saponification value and acid value, lesser is thermal stability and more is the microbial count. Saponification values are highly significant in the making of soap. It is important that the saponification value is just right. If it is too high, the soap might contain too much alkali even though there is sufficient soapiness; so, it would react with skin. If the saponification value is too small, the fatty acid salts will not be sufficient enough to remove or saponify the fat or oil, leading to less soapiness. The saponification value is the number of milligrams of potassium hydroxide necessary to neutralize the free acids and to saponify the esters present in 1 g of the substance. Two grams of each formulation was accurately weighed and introduced into a 200 ml flask of borosilicate glass fitted with a reflux condenser. Then 25 ml of 0.5 M ethanolic potassium hydroxide and a little pumice powder were added to it and boiled under reflux on a water bath for 30 minutes. This is followed by the addition of 1 ml of phenolphthalein solution and the solution is titrated immediately with 0.5 M hydrochloric acid ("*an*" ml). The operation was repeated by omitting the substance being examined ("b" ml) [13, 19-25]. The saponification value was calculated from the expression:

Saponification value = 28.05 (b − a)/w, where w is the weight of the substance in grams.

11. **Acid value:** The acid value is the number which gives in milligrams the amount of potassium hydroxide necessary to neutralize the free acids present in 1 g of the substance. Five grams of the formulation being examined was accurately weighed and dissolved in 50 ml of a mixture of equal volumes of ethanol (95%) and ether, previously neutralized with 0.1 M potassium hydroxide to phenolphthalein solution. Then 1 ml of phenolphthalein solution was added and titrated with 0.1 M potassium hydroxide until the solution remains faintly pink after shaking for 30 seconds. The acid value was calculated from the expression [13, 19-25].

Acid value = 5.61 *n*/*w*

Where *n* = the number of ml of 0.1 M potassium hydroxide required and
w = the weight in grams of the substance.

RESULT

S. No	Chemical tests	Aqueous Extract
1.	Tests for carbohydrates	
	a) Molisch's test (general test)	Positive
	a) Fehling's test	Positive
2.	Tests for alkaloids	
	a) Dragendorff's test	Positive
	b) Wagner's test	Positive
	c) Mayer's test	Negative
	d) Hager's test	Positive
3.	Tests for flavonoids	
	Shinoda test	Positive
4.	Tests for glycosides	
	a) Keller Killani test	Negative
	b) Legal's test	Positive
	c) Baljet's test	Positive
5.	Tests for saponins	
	a) Foam test	Positive

6.	Tests for sterols and triterpenoids a) Libermann buchard test	Positive

Evaluation of Cream

1. **PH of the Cream:** The pH of the cream was found to be in between 5.6-6.8 which is good for skin pH. All the formulations of cream were shown pH nearer to skin required.

S. No.	Formulation	PH
1.	F1	5.8
2.	F2	6.0
3.	F3	6.5

2. **Viscosity:** The viscosity of cream was in between 500-1000 cps which indicates that the cream is easily spreadable by small amounts of shear. F2 and F3 show good spreadable property than other formulations.
3. **Dye test:** This dye confirms that all formulations were o/w type emulsion cream. But formulation (F2) shows more stable in o/w type emulsion.
4. **Spreadability Studies:** When formulation was subjected to spreadability studies, it was found that the cream takes less time to spread as shown in Table.

Formulation	Time in Seconds	Spreadability(g cm/sec)
F1	11	13.63
F2	11	13.63
F3	10	15

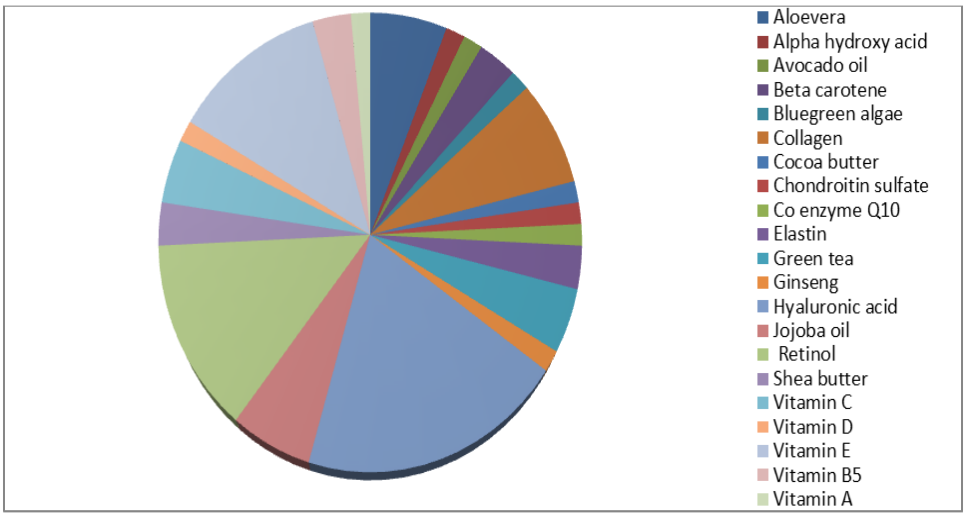
5. **Type of smear:** After application of cream, the type of smear formed on the skin were non greasy.
6. **Homogeneity:** All formulations produce a uniform distribution of extracts in cream. This was confirmed by visual appearance and by touch.
7. **After feel:** Emolliency, slipperiness and amount of residue left after the application of fixed amounts of cream was found good.
8. **Removal:** The cream of F2 and F3 applied on the skin was easily removed by washing with tap water.
9. **Appearance:** When formulation was kept for a long time, it was found that there is no change in organoleptic properties of cream as shown in Table.

S.NO.	Specifications	Limits
1.	State	Semi-solid
2.	Colour	Pale brown-white
3.	Odor	Characteristic
4.	Texture	Smooth

10. **Acid value and Saponification value:** The results of acid value and Saponification value of all formulation were presented in table and showed satisfactorily values.

S.NO	Parameter	F1	F2	F3
1.	Acid value	6.1	5.7	5.3
2.	Saponification value	27.1	27.3	26.3

Review of marketed formulation



DISCUSSION

Glycyrrhiza glabra and *Cinamomum zeylanicum* are well known for its medicinal value in Indian traditional system of medicine and in ayurvedic preparations. In the present work, it was decided to extract and formulate herbal face cream. The herbal face cream was O/W type emulsion, hence can be easily washed with plane water that gives better customer compliance. There is a growing demand for herbal cosmetics in the world market and they are invaluable gifts of nature. Therefore, we tried to make an herbal face cream containing the extract of *Glycyrrhiza glabra* and *Cinamomum zeylanicum* in different concentration along with almond oil. Our study indicated that the formulation F1 and F2 found to be more stable, while remaining formulations were not stable and resulted in breakdown of the emulsion when stored for long time. These formulations F1 and F2 had almost constant pH, homogeneous, emollient, non-greasy and easily removed after the application. The stable formulations were safe in respect to skin irritation and allergic sensitization. The prepared herbal face cream is intended for cosmeceutical use rather than as other cosmetic. The extracts of *Cucumis sativus* produces whitening of skin as well removing marks, healing and soothing to irritated skin. The extractof *Glycyrrhiza glabra* has antibacterial activity, anti-inflammatory activity, and also increases whitening of skin. The almond oil increases the glow on skin and has emollient properties Hence all these properties are beneficial to normal human keratinocytes and it is safe and stable too. These studies suggest that composition of extracts and base of cream of F1 and F2 are more stable and also it may produce synergistic action.

CONCLUSION

From which are mentioned all the above results, it is concluded that on combining the Licorice oil and Cinnamon oil different components in different ratio to get multipurpose effect such as whitening, anti-wrinkle, antiaging and sunscreen effect on skin and suggesting that composition of oil and base of cream of F2 and F3 are more stable up to 12 months and safe, it may produce synergistic action without side effects as this cream comprising of much natural substances.

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