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A Dermal Cream of Coenzyme Q10 and Kojic Acid

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Abstract---*UV radiation is responsible for up to 80% of premature skin aging. Oxidative stress is the major factor in skin aging caused by UV radiation. Therefore, there is a necessity to produce a safe and effective topical antioxidant method, which would not only reduce the likelihood of skin aging but will also have whitening benefits in addition to skin rejuvenation. Coenzyme Q10, a fat-soluble vitamin like substance, is a strong antioxidant present in almost every cell of the human body. The antioxidant properties of Coenzyme Q10 help to significantly reduce oxidative tissue damage. Kojic acid is an antibiotic produced by many species of Aspergillus and Penicillum in an aerobic process from a wide range of carbon sources. Kojic acid has been extensively used as a cosmetic agent with an excellent whitening effect because it inhibits tyrosinase. In this paper pharmaceutical composition of a dermal cream having combination of Coenzyme Q10 and Kojic acid for treating, preventing, minimizing, and/or diminishing signs of aging and exerting skin whitening effect. Therefore, in the present innovation, a new and revolutionary prescription dermal cream has been developed for the prevention of ageing and to exert skin whitening effect.*

Keywords--- *Skin Ageing, Coenzyme Q10, Kojic acid, dermal cream, Topical drug delivery, Anti-oxidant, Anti-ageing, Skin Whitening/Glowing effect*

I. INTRODUCTION

As theskinages, it gets thinner and easier to damage. The decreasing ability of skin to heal itself as an individual ages is an intensifying effect. Among others, a decrease in volume and elasticity is observed in skin aging. An example of the effects of aging are for example: laxity (sagging), rhytids (wrinkles), and the various categories of photo aging, including erythema (redness), dyspigmentation (brown discolorations), solar elastosis (yellowing), keratosis (abnormal growths), and poor[1]. The effects of aging can have an effect on multiple different layers of a person's skin. There are five different layers to a person's skin: Stratum corneum; Stratum basale; Stratum lucidum; Stratum granulosum; Stratum germinativum and Stratum spinosum. Stratum basale is the innermost layer whereas Stratum corneum is outermost layer. Keratinocytes are located in different layers of the skin. Melanocytes are located in the bottom layer or the stratum basale layer of a person's skin. Skinaging is a complex process affecting skin function and appearance. The common signs and symptoms of skin aging are wrinkles, volume loss and elasticity loss. Structural integrity during ageing is lost due to both internal and external factors[2]. The natural consequence of physiological changes in the course of time is the inner aging of the skin[3]–[6]. External factors can be monitored to varying degrees and include UV exposure, ionizing radiation, psychological stress and severe physical, alcohol intake, over-eating of poor nutrition and environmental pollution[1], [7]–[13]. In addition, up to 80 per cent of premature skin ageing are caused by UV radiation. Studies show that Coenzyme Q10, a powerful

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antioxidant, is effective in skin aging prevention and treatment. Coenzyme Q10 is effective agent against skin aging. It is also known as ubiquinone on the basis that it occurs ubiquitously in biological systems. Coenzyme Q10 is a quinone derivative with a long isoprenoid tail. The number of 5-carbon isoprene units in the coenzyme is variable. The most common form in mammals contains 10 isoprene units (Coenzyme Q10, or CoQ10), but other forms contain up to 15 isoprene units (CoQ15). Coenzyme Q10 is the coenzyme for at least three mitochondrial enzymes (Complexes I, II, and III) as well as enzymes in other parts of the cell. These mitochondrial enzymes, which function in the oxidative phosphorylation pathway, are essential for the production of ATP, the energy source upon which all cellular functions depend. The biosynthesis of Coenzyme Q is known to be a multi-stage process requiring at least eight vitamins and several trace elements.Kojic acid is an antibiotic produced by many species of Aspergillus and Penicillum in an aerobic process from a wide range of carbon sources. Kojic acid has been extensively used as a cosmetic agent with an excellent whitening effect because it inhibits tyrosinase. Avocado butter has excellent absorption properties which allow for superior skin moisturizing and protection for up to 24 hours. 100% pure avocado butter is an all-natural vegetable extract that is rich in vitamins A, D, G (Riboflavine or Vitamin B2), and E for total skin moisturizing treatment. This butter is naturally resistant against UV rays. Applying the smooth avocado butter as a natural sunscreen moisturizes and nourishes skin while providing complete protection. Rich in vitamin A, B, G and E, avocado butter is the ideal moisturizer for all skin types. The butter rejuvenates skin by improving elasticity, provides relief to dehydrated and sensitive skin, and prevents sun damage. The vitamin rich butter promotes maximum cell regeneration to help skin elasticity and smoothness. Avocado butter is perfect for massage butter, body balm, sunscreen, dry and damage skin repair

Coenzyme q10

Coenzyme Q10 is a crystalline powder which is insoluble in water. It acts as an antioxidant, but only 2-3% of the Coenzyme Q10 absorbs orally. The ideal properties of a molecule to be absorbed through the skin must have molecular weight less than 500 Da and *log P* value in the range of 1-3[8]–[10], [12], [14]–[19]. Hence, Coenzyme Q10 needs to penetrate the skin to exert its antiaging and antioxidant effect. However, the topical bioavailability of Coenzyme Q10 is limited owing to its lipophilic (log P>10) and thermo-labile properties, as well as a relatively high molecular weight (863 Da). Furthermore, the bioavailabilty of pure topical Coenzyme Q10 depends on the formulation design, extent of absorption, as well as interaction with other factors or excipients. For instance, Coenzyme Q10 (in ethanol as a vehicle) is able to penetrate into the stratum corneum of porcine skin. On the other hand, coenzyme Q10 either alone or in combination with other antioxidants or therapeutic agents is administered through topical route in the form of dermal cosmetic cream or lotion or serum to exert its antiaging and antioxidant activity.

II. MATERIALS AND METHODOLOGY

- **Materials**

Coenzyme Q10, Kojic Acid, Avocado Butter, Ascorbic acid, Glycerine, Cetyl alcohol, Peppermint oil, Tocopheryl acetate, Methyl paraben, Jojoba Oil and Polysorbate 60.

- **Formulation Design and Preparation of Dermal Cream of Coenzyme Q10 and Kojic Acid**

The novel Coenzyme Q10 and kojic acid combination dermal cream was prepared by oil in water emulsion method for improving the anti-aging and skin whitening effect. The ingredients were mixed together along with Avocado Butter, Ascorbic acid, Glycerine, Cetyl alcohol, Peppermint oil, Tocopheryl acetate, Methyl paraben, Jojoba Oil and Polysorbate 60 that allows direct compression of the cream mixture. The Optimized composition of pharmaceutical dermal cream containing combination of Coenzyme Q10 and Kojic acid as Active Pharmaceutical Ingredients with role of other excipients is shown below in table 1.

Name of ingredient	Quantity (gm)	% Composition (W/w)	Use
Coenzyme Q10	0.070	0.79%	Antioxidant and API
Kojic acid	0.060	0.68%	Antioxidant and skin-whitening agent
Avocado butter	1.00	11.37%	Antioxidant and cream base
Ascorbic acid	2.00	22.74%	Strong Antioxidant
Glycerin	1.20	13.64%	Emulsifier and humectant
Cetyl alcohol	1.20	13.64%	Emollient, emulsifier
Peppermint oil	2.00	22.74%	Flavoring agent
Tocopheryl acetate	1.00	11.37%	Antioxidant
Methyl paraben	0.004	0.045%	Preservative agent
Jojoba oil	0.060	0.68%	Skin softener, moisturizer
Polysorbate 60	0.20	2.27%	Emulsifier

Table 1:- Optimized composition of pharmaceutical dermal cream containing combination of Coenzyme Q10 and Kojic acid as Active Pharmaceutical Ingredients with role of other excipients

III. RESULT

Dermal novel Cream of Coenzyme Q10 and kojic acid was prepared by oil in water emulsion method for improving the anti-aging and skin whitening effect. The dermal cream was characterized for physical appearance, viscosity, drug content, and protective effect. The colour, state, texture and homogeneity were recognized by visual appearance and observed to be yellowish, semisolid, smooth and uniform, respectively. Here, we can observe characterization of Coenzyme Q10 and Kojic acid combination loaded cream in Table 2.

Table 2: Characterization of Coenzyme Q10 and Kojic acid combination loaded cream

Sample	Colour	State	Texture	Homogeneity	pH	Spreadability (g cm/sec)	Drug content (CQ10)
CQ10 cream	Yellowish	Semisolid	Smooth	Homogenous	5.23±0.424	84.07±3.147	54.2%
CQ10 and Kojic acid combination loaded cream	Yellowish	Semisolid	Smooth	Homogenous	4.15±0.107	158.9±22.75	55.6%

Note: All experiments were carried out in triplicate (n=3)

- *Viscosity*, as function of shear rate the viscosity of combination of CoQ10 and kojoic acid cream is higher than CoQ10 cream. As well as, the viscosity of dermal cream was determined using Brookfield viscometer at 100 rpm, using spindle 75 and it was observed to be 500-1000 cps. Measurement of viscosity of Coenzyme Q10 cream and Coenzyme Q10 and Kojic acid combination loaded cream is shown in figure 1.

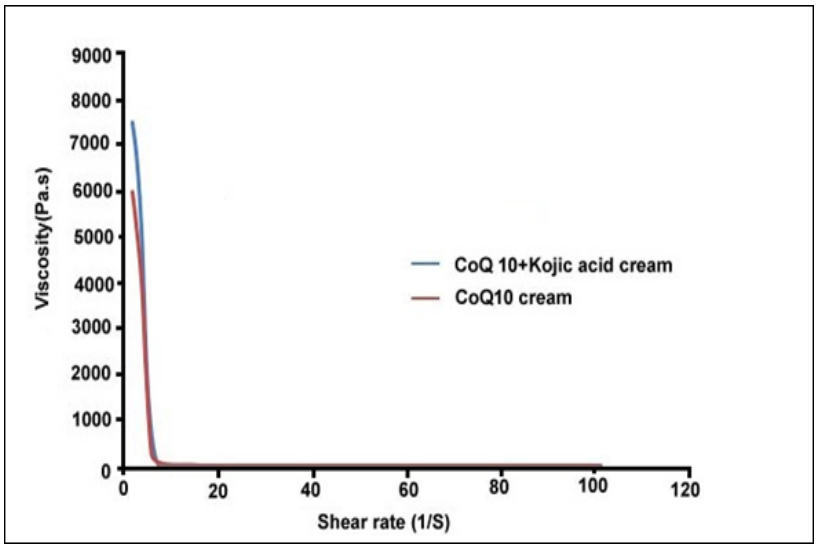

Figure 1: Measurement of viscosity of Coenzyme Q10 cream and Coenzyme Q10 and Kojic acid combination loaded cream as function of shear rate

- The spread ability of the cream was measured to be 84.07±3.147 g cm/sec.
- The pH of the dermal cream was measured using pH meter and noticed to be 4.153±0.1073 (n=3).
- Drug content was determined using HPLC method and calculated to be 698.69 µg/ 1 gm of cream.
- *Scavenging activity*, Hydrogen peroxide scavenging activity of Ascorbic acid was determined to 100 µg/ml, Coenzyme Q10 is 20 µg/ml, Coenzyme Q10 cream is 0.2µg/ml CQ10 and CQ10 and Kojic acid cream is 0.2µg/mlCQ10+0.232 µg/ml Kojic acid). The statistical data is shown below in figure 2.

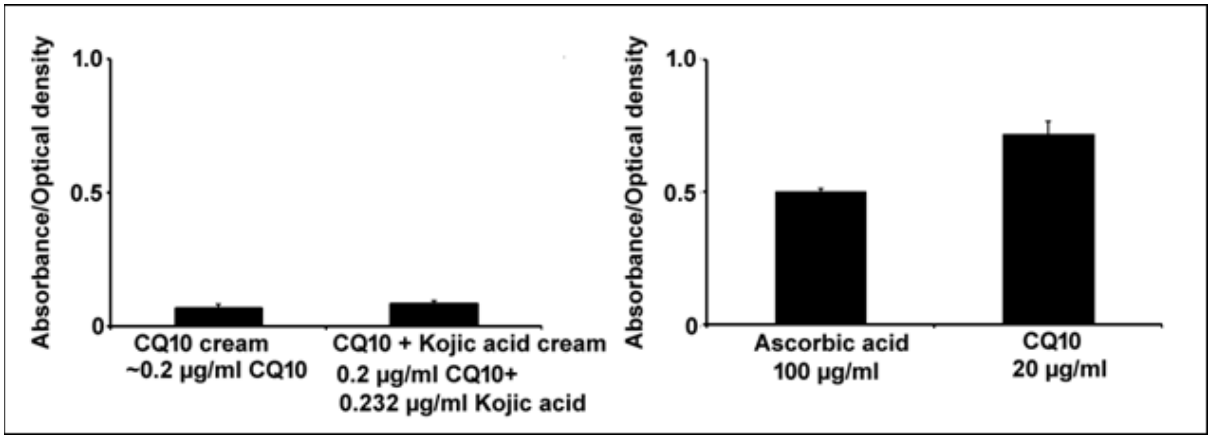

Figure 2: Hydrogen peroxide scavenging activity of Ascorbic acid (100 µg/ml), Coenzyme Q10 (20 µg/ml),

Coenzyme Q10 cream (0.2µg/ml CQ10) and CQ10 and Kojic acid cream (0.2µg/mlCQ10+0.232 µg/ml Kojic acid)

- *Absorbance or optical density*, given below in figure 3, it shows the reducing power activity of ascorbic acid with the combination of Coenzyme Cq10 cream and kojic acid.

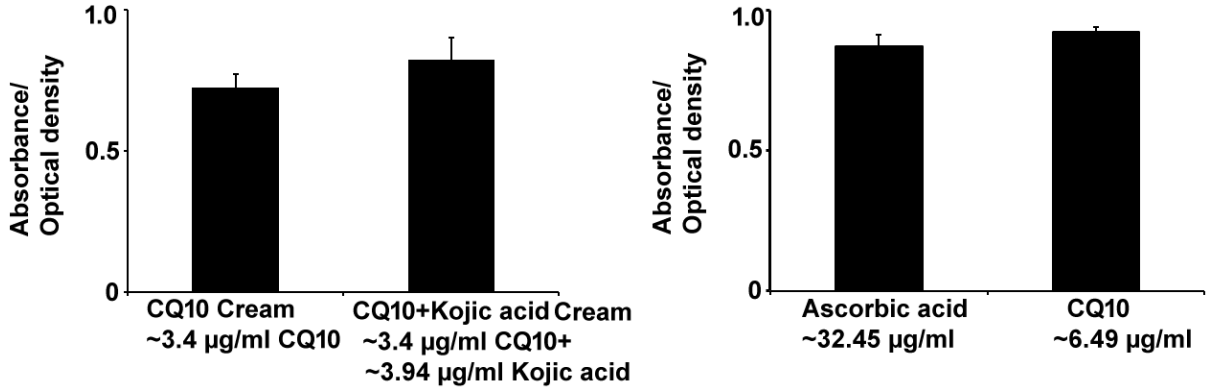

Figure 3: Reducing power activity of ascorbic acid (32.45 µg/ml), Coenzyme Q10 (6.49 µg/ml), Coenzyme Q10 cream (3.4 µg/ml CQ10) and Coenzyme Q10 (3.4 µg/ml CQ10) and Kojic acid (3.94 µg/ml) combination loaded cream

- The protective effect of optimized dermal cream was established by measuring antioxidant potential in terms of hydrogen peroxide assay, glutathione content, TBARS level, and skin whitening effect was measured using in-vitro tyrosinase inhibition assay, and histological alterations, respectively.

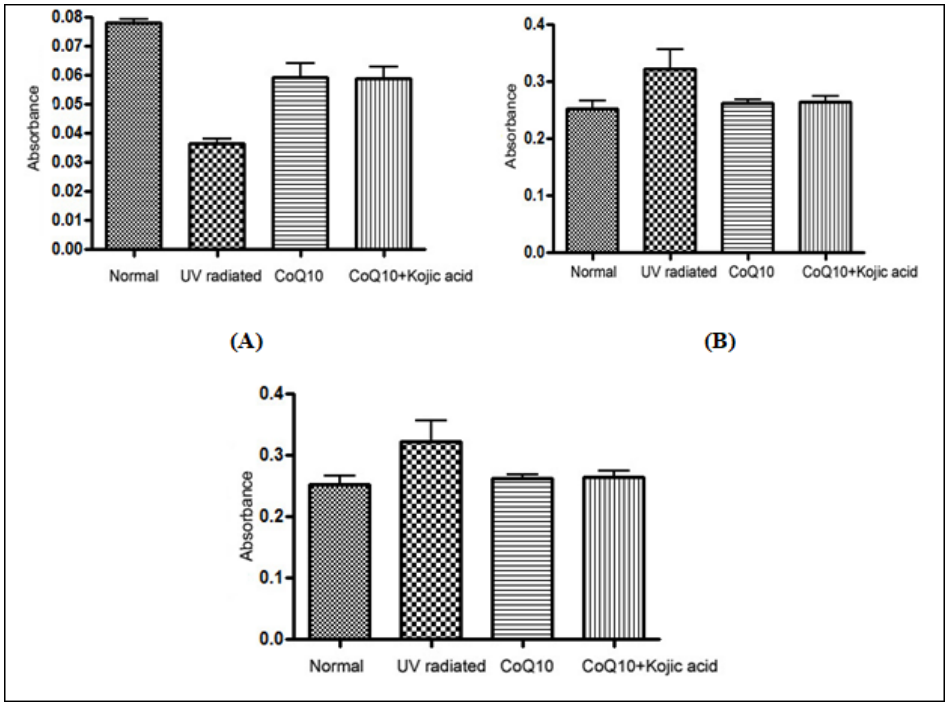

Figure 5: Measurement of GSH (Glutathione) level of skin (**A**), H_2O_2scavanging activity (**B**), and TBARS (Thiobarbituric acid reactive species) level (**C**).

- *Skin Sample*, Several studies on rat skin have been performed with different chemicals. First of all, Histopathological analysis has been performed on normal rat skin. In second experiment, UV radiated rat skin for 5 minutes twice a day and 10 times/week for 4 weeks induced erythema. In third experiment, Pre-treatment with 0.3-0.5% of Coenzyme Q10 standard cream has been done for twice a day for one week protected the skin from the formation of erythema upon simultaneous exposure of UV radiation for 5 min twice a day and 10 times/week for 4 weeks. In fourth experiment,pre-treatment with 0.3-0.5% of Coenzyme Q10 and Kojic acid combination loaded test cream has been done for twice a day for one week displayed identical results and protected the skin from the formation of erythema upon simultaneous exposure of UV radiation for 5 min twice a day and 10 times/week for 4 weeks. We can easily observe the results in Figure 6.

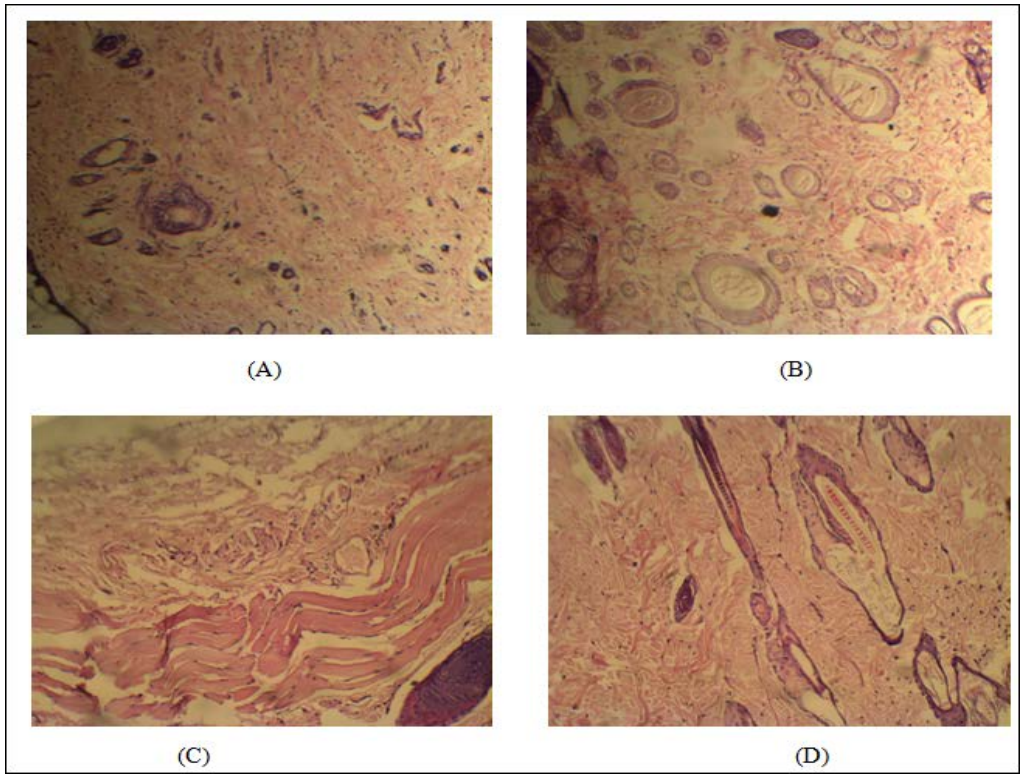

Figure 6: Histopathological analysis of normal rat skin (**A**), UV radiated ratskin for 5 min. twice a day and 10 times/week for 4 weeks induced erythema) (**B**), Pretreatment with 0.3-0.5% of Coenzyme Q10 standard cream for twice a day for one week protected the skin from the formation of erythema upon simultaneous exposure of UV radiation for 5 min twice a day and 10 times/week for 4 weeks (**C**) and pretreatment with 0.3-0.5% of Coenzyme Q10 and Kojic acid combination loaded test cream for twice a day for one week displayed identical results and protected the skin from the formation of erythema upon simultaneous exposure of UV radiation for 5 min twice a day and 10 times/week for 4 weeks (**D**).

IV. CONCLUSION

A pharmaceutical dermal cream is formulated for the prevention of skin aging and to exert skin whitening effect.

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The optimized composition of the tailored anti-aging cream include Combination of Coenzyme Q10 and Kojic Acid having antioxidant properties to prevent skin aging and have skin whitening effects respectively and Other ingredients include Avocado Butter (antioxidant and cream base), Ascorbic acid (strong antioxidant), Glycerine (emulsifier and humectant), Cetyl alcohol (emollient and emulsifier), Peppermint oil (flavouring agent), Tocopheryl acetate (antioxidant), Methyl paraben (preservative agent), Jojoba Oil (skin softener and moisturizer) and Polysorbate 60 (emulsifier).The dermal cream was characterized for physical appearance, viscosity, drug content, and protective effect. The color, state, texture and homogeneity were recognized by visual appearance and observed to be yellowish, semisolid, smooth and uniform, respectively.

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