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FORMULATION AND EVALUATION OF FACE SERUM CONTAIN PHYTOSOME OF GINGEROL OIL, CARICA PAPAYA PULP EXTRACT AND *ALOE VERA* GEL

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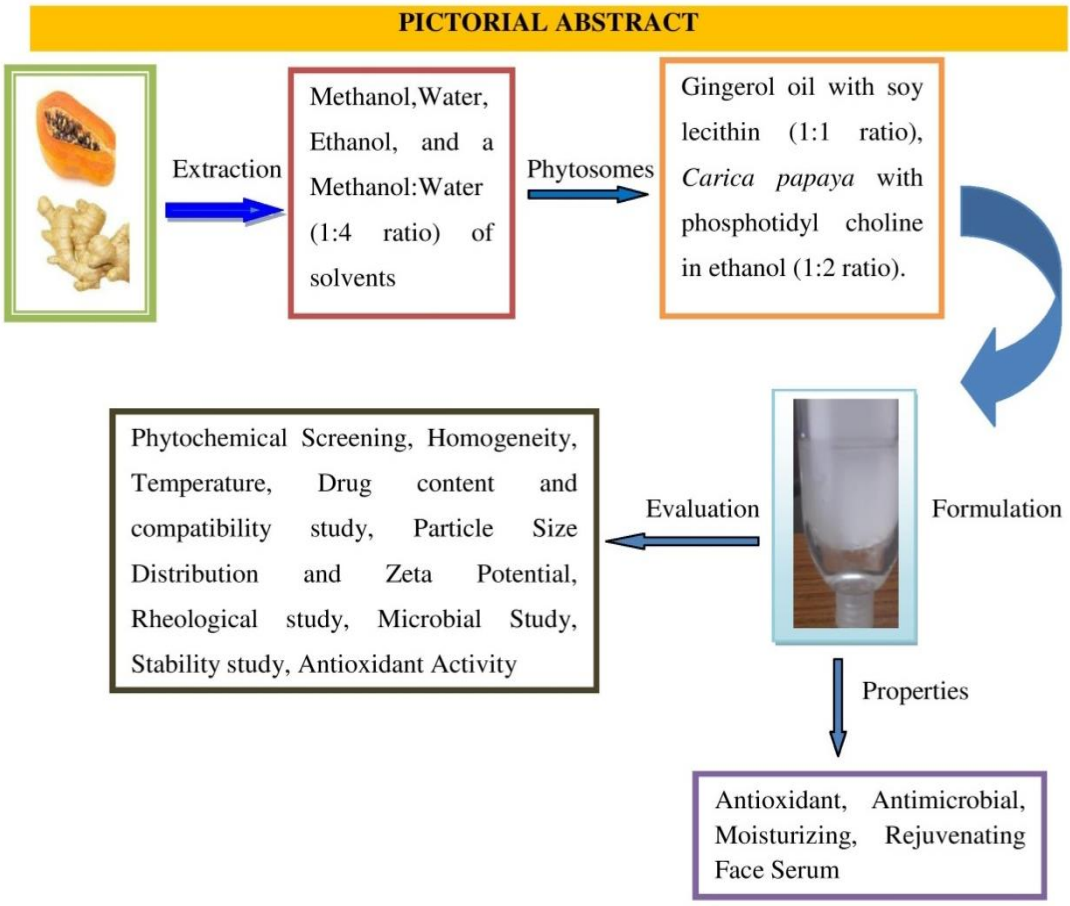
ABSTRACT

The aim of the current study is to development, evaluation and application of phytosomes of gingerol oil, Carica papaya pulp extract, and aloe vera gel extracts in face serum formulations. The freshly cut ginger rhizome was meticulously extracted with water using the distillation technique and Carica papaya pulp with methanol:water (1:4) ratio through maceration method. Qualitative phytochemical screening detects the presence of flavonoids, terpenoids, phenol, phytosterol, and ascorbic acid in both the herbal plant extract. The phytosomes of Gingerol oil and Cariya papaya were made by mixing it in a 1:1 molar ratio with soy lecithin, and in a 1:2 molar ratio with phosphatidyl choline in ethanol respectively. Face serum composition formula includes aloe vera gel, Carica papaya phytosome, Gingerol phytosome carbomer 934, honey, isopropyl palmitate, EDTA and other ingredients. All of the formulated products were non-greasy and non-oily, homogeneously dispersed with a milky white finish and pH was discovered to be 5.6. Cariya papaya phytosomes had an average diameter of 198.09±0.04 nm while gingerol phytosomes had a diameter of 245.21±0.06 nm as determined by DLS with a negative zeta potential surface charge of -27.8 mV. The viscosity, transition temperature and absorbance time were found to be 2687cps, 25-35^{0}C and 1-2 min respectively. The activity of antioxidants rises as reaction time increases. When compared to rutin (standard), the formulation demonstrated (42.26%) strong total antioxidant and hydrogen peroxide scavenging properties. The microbiology test and stability tests indicated that the formulation was free of microorganisms and had good stability throughout the 3 months stability testing period, with no notable changes in physicochemical properties.

KEYWORD: Carica papaya phytosome, Gingerol phytosome, Aloe Vera, Face serum, Antioxidant, Antimicrobial, Moisturizing, Instant glow face serum.



INTRODUCTION

Natural ingredients have been used for centuries for skin care purposes. Nowadays, they are becoming more prevalent in formulations, due to consumers' concerns about synthetic ingredients/chemical substances. Skin care has evolved into an essential practice for everyone, including celebrities and common individual. A good skin care regimen may also improve the structure and functionality of your skin in addition to maintaining its health. Examples of skincare cosmetics that can be used to wash, exfoliate, protect, and regenerate the skin include cleansers, toners, serums, moisturisers, and balms. In contrast to earlier times, when beauty products were made using natural processes, skin care is today frequently made with synthetic materials, chemicals, and colours. On the other hand, overusing these products harms the skin's smoothness and natural shine. The majority of them suffered from skin incompatibility, skin damage, and other negative effects.[1]

Customers are educated on the benefits of using natural colours, neutraceuticals, cosmetics, and herbal medications. Due to the market's rapid growth and potential, more focus is being placed on herbal-based cosmetics in the personal care sector.[2]

Generally, botanical products are a rich source of vitamins, antioxidants, essential oils and oils, hydrocolloids, proteins, terpenoids and other bioactive compounds.[1] The ability of these ingredients to enhance skin's brightness, texture, and luminosity while reducing wrinkles and hyperpigmentation and lightening the skin's general tone gave rise to the development of herbal skin fairness solutions.[3]

A face serum, a cosmetic item with a non-greasy finish and intensive nutrition for the deeper layers of the skin, has one of the highest concentrations of active ingredients of any cosmetic product. A face serum has an anti-aging, anti-wrinkle, antioxidants and moisturizer's consistency, gel or a light lotion that can penetrate further to deliver active ingredients to the skin. Your skin may become smoother and firmer and have more hydration thanks to a good face serum. Face serum with plant extracts has been shown to have antioxidant, tyrosinase-inhibiting, and antibacterial properties. The listed examples concern plant extracts that can be found naturally and have potential use in skin care. Utilizing these plants' extracts could be beneficial for creating effective face serum.

Ghikanwar liliaceae for smoothness, healing controller, sun burn; *Azadirachta indica* as an antiseptic; *Zingiber officinale* for lightening scars; Carica papaya contains carotenoids, ascorbic acid, potassium, flavonoids, and other phytonutrients that instantly hydrate the skin and give it a healthy glow; Saffron for reducing pigmentation, brown spots and other skin blemishes; Antioxidant and skin rejuvenation vitamins C and E.[4]

Ginger (Zingiber officinale) contains a bioactive moiety; gingerol that has antipyretic and anti-inflammatory properties. It stops the synthesis of melanin in murine B16F10 melanoma cells by reducing MITF and inhibiting tyrosinase activity.[5]

The polysaccharides in aloe vera are incredibly hydrating, and when they are combined with essential oils, they make fantastic lotions for sun protection and skin smoothing. Due to its relaxing and cooling qualities, Aloe Vera is suggested by Ayurveda for a variety of skin ailments. Aloe vera extract's antibacterial and antifungal properties may also be helpful in treating minor skin infections.[6]

Recent developments in herbal medicine have led to the development of phytosomes, which are more readily absorbed, have better bioavailability, and have more advantageous effects than conventional phyto-molecules or plant extracts. A plant's biologically active components are primarily made up of polar or water-soluble substances. Flavonoids, tannins, and glycosidic aglycones are examples of water-soluble phytoconstituents that are poorly absorbed either due to their large molecular size, which prevents passive diffusion, or due to their poor lipid solubility, which severely limits their ability to cross lipid-rich biological membranes and results in poor bioavailability.[7]

The current study makes reference to a few plant species whose extracts have been scrutinised. The scientific studies aiming at the development, evaluation and application of phytosomes of extracts in face serum formulations and that simultaneously meet consumer concerns are a challenge.

MATERIALS AND METHODS

Instrumentation

UV-1800 shimadzu with UV probe software system were utilized for qualitative determination of extract.

Crude Sample purchase

Carica papaya dry pulp powder and ginger powder was purchased from (sigma Aldrich) and Aloe vera gel from Patanjali's. Each of the additional ingredients was of an analytical grade. They were procured from the GRY Institute of Pharmacy's laboratory in Borawan, India.

Extraction of *Carica papaya* pulp: Carica papaya dry powder pulp weighing 200gm was macerated in different solvents (500ml) for two days, including methanol, water, ethanol, and methanol: water (1:4), before being filtered and condensed under low pressure and placed in the refrigerator for later use.[8]

Extraction of gingerol from ginger rhizome: The Soxhlet extractors received the extraction solvent, 500 ml of different solvents including methanol, water, ethanol, and methanol: water (1:4), along with 50 gm of dried ginger rhizome powder, which was ground until the extraction solvent was evaporated. The extract is filtered, compressed under low pressure, and refrigerated for use later.[9]

Preliminary phytochemical testing of gingerol oil and Cariya papaya extracts: Preliminary phytochemical experiments were conducted to examine different chemical groups present in methanol, hydro-methanol, ethanol, and water extracts for the stigmas of both the extract.[10]

Phytosome of gingerol: The anti-solvent precipitation technique was used to mix gingerol oil with soy lecithin in a molar ratio to produce phytosomes of gingerol (2:2). A 100 ml round bottom flask was filled with the exact proportions of gingerol and soy lecithin, and it was refluxed for two hours with 30 ml of dichloromethane at a temperature of no greater than 60^0C. To make the precipitate, 20 ml of n-hexane were added to the mixture after it had been carefully concentrated to 5 ml, while being constantly stirred. Following filtering, collection, and overnight storage in vacuum desiccators, the precipitate was then prepared. Phytosomes are packaged in a glass bottle with an amber colour and kept at ambient temperature (3-40^0C).[11]

Phytosome of *Carica papaya* pulp: The extract and phosphatidyl choline were mixed in ethanol at a 1:2 molar ratio, and the mixture was then refluxed for two hours at 30°C and 120 rpm in a vacuum rotary evaporator to create the phytosomes. Aquadest is used to hydrate the residue in order to create phytosome suspension.[12]

Formulation of phytosomal gel: Different composition formulas were optimized as a primary face serum for the former formulation [Table 2]. As a primary face serum for the earlier formulation, various composition formulas were improved. The gel was created using carbomer 934, which was then dispersed in distilled water while being continuously stirred. After this, an aqueous solution of EDTA was added, and the gel was then left overnight to ensure complete hydration. In 10ml of distilled water, aloe vera gel, vitamin E and C, and honey were dissolved with constant stirring to create a uniform solution. Then trituration was added along with span 80 and tween 20. The prepared phytosomes of Casica papaya and gingerol were then added to the mixture while it was being continuously stirred. The gel was then allowed to sit for two hours to allow the air bubbles to be removed, resulting in a phytosomal gel.[10-13]

EVALUATION PARAMETERS OF FACE SERUM

Color and Appearance

Face serum appearances were assessed visually using terms like transparent, semi-transparent, and fuzzy.

Homogeneity

The homogeneity of the serum was checked both visually (for the absence of any particle matter) and physically (by contacting the product). By examining the serum under a microscope, it was possible to verify the homogeneity (size, shape, and coalescence of the droplets).[12]

pH of the serum: In order to check for any potential adverse effects in vivo, the serum's pH was measured. The skin may get irritated by an acidic or alkaline pH. Therefore, maintain the serum pH in a range of 4-6, which is as close to neutral as feasible. In order to do this, the serum was dissolved in 10 ml of pure water, and the pH was assessed using a pH meter. The process was carried out three times, and the standard deviation was reported.[13]

Zeta potential and particle size determination: Dynamic light scattering (DLS) was utilised to determine the average diameter and surface charge of Carica papaya phytosomes and Gingerol oil phytosomes using a particle size analyzer. The analysis was performed three times, and the average hydrodynamic particle size was expressed using the value of z-average size SD.[11]

Transition temperature: The transition temperature of the phytosome systems was observed by using a melting point apparatus.[7]

Determination of UV Spectrum

A 100µg/ml stock solution of each extract was prepared by dissolving 10 mg of the extract in 100 ml of pH 5.4 buffer solutions solution. The λ_{max} of each extract was determined by scanning suitable dilutions under UV Spectrophotometer.[14]

Ash Value

The extract was taken in a platinum dish with a flat bottom, and aching was carried out at 600^0C in a muffle furnace.

Rheological study: A spindle-type model 63 Brookfield viscometer (DV2T model) is used with 100 rpm, 100 ml of serum, to measure the viscosity of the formulation. Putting the spindle dipped in the big mouth container with the serum for about 3 minutes before to the measurement.[15]

Test for product spreadability

Indicating the extent of the region to which it was administered, the serum spreads over the filter paper. For each of the chosen filter paper sizes, the total area of each filter paper (A1) and its weight are measured (W1). Choose the test formulation, pour a few millilitres to a B-D 5 mL syringe, and inject 20 drops into the filter paper's centre. As soon as the final drip strikes the filter paper, start a stopwatch or timer to count down until precisely 10 minutes have passed. Throughout the 10-minute test, a mostly consistent circular pattern of liquid will cover the filter paper. Ten minutes later, cut precisely on the line between the soaked spread.

Additionally, dry the filter paper using scissors. Weigh the remaining dry filter paper (unsaturated). This weight should be noted as W2. It is necessary to gauge the diameter of the saturated filter paper. If the spread was not a complete circle, take many diameter readings in the spread zone to get the average diameter. The appropriate entry for this measurement is A2.[12]

$$\% \text{ Spread by Area} = (A2/A1)100$$

Absorbance time

Apply the serum to the skin, use a stopwatch to record the time, and then assess how quickly it absorbs.[16]

Washability

Apply the product to your face, and then personally test how easily and thoroughly it can be washed off with water.[5]

Microbial study

The antibacterial activity of natural products was assessed against Staphylococcus aureus bacteria species. Cultures were kept for 24 h at 38ºC ± 2ºC and the purity of cultures was checked after 8 h of incubation. After 24 h of incubation, bacterial suspension (inoculum) was diluted with sterile physiological solution, for the diffusion tests, to 100 CFU/mL. Screening the natural products antimicrobial activity, agar diffusion test is followed. The

bacterial inoculum was uniformly spread using sterile cotton swab on a sterile Petri dish agar. Five serial dilutions yielded concentrations of 100, 80, 60, 40, 20, 10mg/mL for extracts and fractions and four serial dilutions yielded concentrations of 40, 20, 10 mg/mL for pure substances. 50 µL of natural products were added to each of the 5 wells. The systems were incubated for 24 h at 38ºC ± 2ºC, under aerobic conditions. After incubation, confluent bacterial growth was observed. Inhibition of the bacterial growth was measured in mm. Chloramphenicol used as reference discs.[6]

Stability analysis

The formulation and development of a pharmaceutical product cannot be finished without a careful examination of the product's physical and chemical stability, which shows the product's safety. The process of accelerated stability analysis, which involves heating the material to a high temperature, is frequently used to predict stability. ICH guidelines were followed when conducting the stability investigations. A three-month accelerated short-term stability study was carried out for the formulation. The samples were stored in a range of temperatures and relative humidity levels, including at 25^0C RH=60% and 40^0C±2% RH=75% for 3 month. Every month, samples were obtained and assessed.[15]

Antioxidant activity

The measurement of antioxidant activity was performed using the H_2O_2 scavenging method. In three test tubes, a 400 µl H_2O_2 solution was made (Blank, Sample, Standard). In the sample test tube and standard test tube, 100µL of the sample formulation and rutin, respectively, are introduced. In each test tube, add phosphate buffer (pH 7.4) to bring the volume to 4 ml. All test tubes should be incubated for 10 minutes at room temperature. Compare the H_2O_2 solution's absorbance at 230 nm to a blank solution.[16]

H_2O_2 scavenging activity is calculated by the formula:

$$\% H_2O_2 \text{ Scavenged} = [(A_C - A_S)/A_C] \times 100$$

RESULT AND DISCUSSION

Phytochemicals screening of different extracts

Phytochemical components primarily control the pharmacological and toxicological characteristics of plants. These metabolites are advantageous to plants, but dangerous to animals, including people. These chemical elements are present in this plant, which implies

that, if thoroughly screened, it could be able to produce pharmaceutically significant drugs. The results of phytochemicals screening summarizes in [Tablet 1].

Color & Appearance

The texture, colour, and aroma of the serum were directly examined in order to gauge its physical characteristics. All formulas resulted in products that had a milky white finish and were non-greasy and non-oily. Compared to the classic damask rose scent, the rose smells pleasant. It seemed like it was transparent white in hue [Figure 1].

Homogeneity

Products with a higher concentration of active ingredients than other types of skin care may offer more obvious advantages. Some serum drops will be applied to a hand, and the homogeneity will be checked by seeing it. The formulation requires that the serum be applied evenly. Under a microscope, the serum was analysed. It was discovered that the phytosomes from both extracts are uniform in size and shape and are dispersed with a gelling agent.

pH of the serum

The formulation's pH was found to be 5.6, which is close to the expected value. The medicine is still unionised, helping it to be compatible with skin pH, and there are no heavy metals in the formulation. The formulation is not responsible for irritation or allergic reactions [Tablet 3].

Particle Size Distribution and Zeta Potential

The phytosomes come in a variety of shapes, including spherical and oval. *Cariya papaya* phytosomes had an average diameter of 198.09±0.04 nm while gingerol phytosomes had a diameter of 245.21±0.06 nm as determined by DLS with a negative zeta potential surface charge of -27.8 mV [Tablet 3].

Transition Temperature

The transition temperature of the phytosome systems was determined by using a melting point apparatus. The average Tm measurement was found to range in between 32-35^{0}C.

Drug content & compatibility study

The samples were prepared by dissolving 10 mg percent w/v concentration into 100 ml of pH 5.6 buffer solutions (10 mg/100ml). The extract's UV absorption spectra were measured using a Shimadzu-1800 double beam UV-Vis Spectrophotometer in the 200-800 nm range.

The highest absorbance of *Cariya papaya* pure extract was 378 nm, while gingerol pure extract was 265 nm. The same procedure should be used for the compatibility study. Both the medication extract phytosome and the control phytosome produced results in the same range **[**Figure 2].

Rheological study

The viscosity of the formulation was assessed using a Brookfield Viscometer, and it was found to be 2687cps.

Ash Value

The ash value of the extract was determined to be less than 1%.

Spreadability test

It was anticipated that the formulation would have good spreadability. There is a Viscosity and spreadability has a linear relationship in rheological studies; the lower the viscosity, the lower the surface tension, and the higher the spreadability.

Absorbance time

The serum starts to absorb as soon as it is applied to the skin and is fully absorbed in 1-2 minutes.

Washability

The washability of the formula was evaluated on the face. The skin was left fresh, luminous, and moist after its simple removal.

Microbial Study

The results of antimicrobial studies indicate that agar plate of test inoculums show similar microbial growth as compared to standard from 24 h grown culture. The result indicating that the formulation was free of microorganisms and safe to use.

Stability study

Stability studies for physical and chemical change were conducted on the formulation. There were no discernible differences in the formularization's attributes. Throughout the stability study, the product's quality, safety, and efficacy are maintained.

Antioxidant Activity

Blank, sample, and standard solution were tested after 10 minutes of incubation. The activity of antioxidants rises as reaction time increases. When compared to rutin, the standard, the formulation demonstrated (42.26%) strong total antioxidant and hydrogen peroxide scavenging properties [Figure 3].

DISCUSSION

Qualitative phytochemical screening detects the presence of flavonoids, terpenoids, phenol, phytesterol, and ascorbic acid in both the herbal plant extracts. The exhausted phytochemicals show antioxidant and antimicrobial activity. The phytosomes of gingerol was prepared by anti-solvent precipitation technique by mix gingerol oil with soy lecithin in a molar ratio of (2:2) and gingerol phytosomes had a diameter of 245.21±0.06 nm. The extract of *Carica papaya* pulp and phosphatidyl choline were mixed in ethanol at a 1:2 molar ratio, and the mixture was then refluxed for two hours at 30^0C and 120 rpm in a vacuum rotary evaporator to create the phytosomes and it had an average diameter of 198.09±0.04 nm. The negative zeta potential surface charge of found to be -27.8 mV. The viscosity of the formulation was determined by using a Brookfield Viscometer, and it was 2687cps.The formulation has 42.26% antioxidant and hydrogen peroxide scavenging properties. The stability study indicated that the product has good quality, efficacy, and safe to use (Table 4).

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Without the assistance of Dr. Sujit Pillai, Mr. Prakash and family, this research would not have been feasible. I'd like to take this initiative to thank GRY Institute of Pharmacy for providing the required equipment and materials to enable me to conduct the research project.

Table 1: Phytochemical Screening Result.

Plant Constituents	Carica papaya Extract				Ginger Extract			
	Aq.	M	HM	E	Aq.	M	HM	E
Carbohydrate	+	+	+	+`	-	-	-	-
Protein & Amino Acid	+	+	+	+	-	-	-	-
Fate & Oil	-	+	-	+	-	+	+	+
Alkaloids	-	+	+	+	-	-	-	-
Flavonoids	+	-	-	-	+	+	++	+
Terpenoids	-	-	+	-	+	+	++	+
Steroids	-	+	-	+	-	++	+	+
Saponins	-	-	-	-	+	+	+	+
Tannins	+	++	+	+	-	-	-	-
Phenolics	+	++	+	+	+	+	+	+

Phytesterol	+	+	+	+	+	+	+	+
Ascorbic acid	+	+	+	+	+	+	+++	+
Cardiac glycoside	-	-	-	+	+	+	+	+

Table 2: Composition Formula.

Composition	Formulation code (100 ml)			Purpose
	F_1	F_2	F_3	
Aloe Vera gel	10 mg	15 mg	1o mg	Botanical
Carica papaya extract	15 mg	10 mg	10 mg	Botanical
Ginger extract	10 mg	10 mg	15 mg	Botanical
Carbomer 934	5%	4%	5%	Gelling agent
Honey	10%	8%	12%	Emollient
Milk cream	5%	5%	5%	Emollient
Isopropyl palmitate	3%	4%	5%	Emollient
Glyceryl sterate	5%	5%	5%	Emollient
Vit. E & C	2%	2%	3%	Antioxidant
Speen 80	2%	1%	1%	Emulsifier
Tween 20	1%	2%	1%	Emulsifier
EDTA	0.02%	0.03%	0.02%	Preservative
Rose water	qs	qs	Qs	Fragrance
Distilled water	qs	qs	Qs	Vehicle

Table 3: Evaluation Parameters Result.

Formulation Code	pH	Particle size (Phytosome)		Rheological study	Absorbance time
		Carica papaya	Gingerol oil		
F_1	5.62 ± 0.047	198.09±0.04 nm	245.21±0.06 nm	2687 cps	1min 35 sec
F_2	5.79 ± 0.085	197.12±0.32 nm	245.32±0.12nm	2654 cps	1min 42 sec
F_3	5.60 ± 0.111	198.34±0.16 nm	244.28±0.20nm	2678 cps	1min 38 sec

Table 4: Result Summary.

Parameters	Result
Colour & Appearance	Translucent white in color
Homogeneity	Homogenous mixture
pH of the serum	Between 5.6
Particle Size Distribution and Zeta Potential	198.09±0.04 nm, 245.21±0.06 nm, -27.8 mV
Transition Temperature	Between 32-35^{0}C
Drug content & compatibility study	*Carica papaya* pure extract was 378 nm, gingerol pure extract was 265 nm,
Rheological study	2687cps
Ash Value	Less than 1%
Spreadability test	Higher the spreadability
Absorbance time	Completely absorbed within 1-2 minutes
Washability	Easy to remove and left the skin moist, luminous, and fresh
Microbial Study	Free of microbial growth
Stability study	No change in physical & chemical properties

Figure 1: Serum formulation.

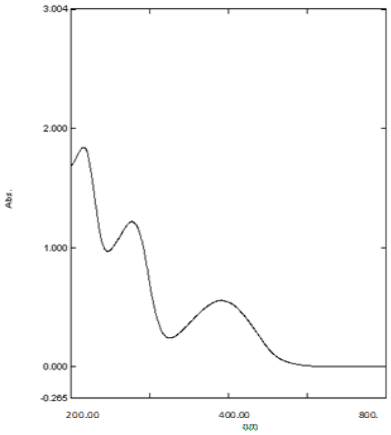

Figure 2: UV Spectrum Carica of papaya Extract and gingerol oil.

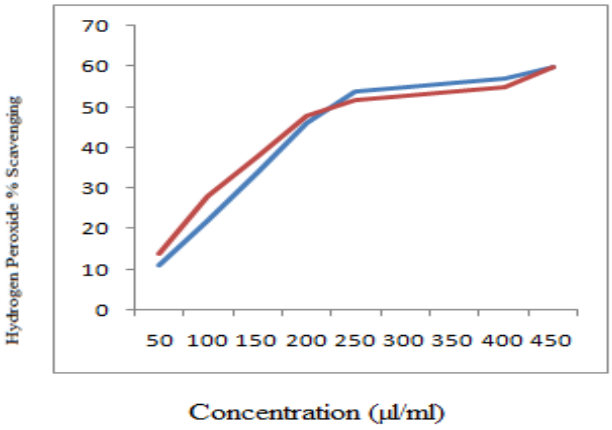

Figure 3: Antioxidant Study.

ABBREVIATION

UV: Ultra Violet, **DLS:** Dynamic light scattering, **EDTA:** Ethylene diamine tetra acetic acid, **ICH:** International Council of Harmonisation, **MITF:** Melanocyte Inducing Transcription Factor, **RH:** Relative Humidity.

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