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Original Article

QbD-Driven Development of PACE-GC: A Synergistic Polyherbal Anti-Ageing Cream with Extracts of Grape and Carrot

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ABSTRACT

Background: Skin ageing is a multifactorial biological process influenced by extrinsic factors like UV radiation and intrinsic factors like genetics. Oxidative stress mediated by ROS plays a pivotal role in premature ageing, manifesting as wrinkles and loss of elasticity. **Objectives:** This study aims to develop and characterise a polyherbal anti-ageing cream (PACE-GC) incorporating *Daucus carota* and *Vitis vinifera* extracts, focusing on antioxidant properties and safety. **Materials and Methods:** Aqueous *Vitis vinifera* and acetone *Daucus carota* extracts were incorporated into a vanishing cream base using Quality by Design (QbD) methodology. Formulations were evaluated for pH, viscosity, and spreadability. Antioxidant activity was assessed using DPPH and hydrogen peroxide scavenging assays. **Results and Discussion:** *Vitis vinifera* and *Daucus carota* extracts showed notable antioxidant activity (IC_{50} of 14.10±0.68 µg/mL and 11.90±0.55 µg/mL, respectively). The polyherbal cream (PACE-GC) displayed acceptable physicochemical properties and skin-compatible pH. **Conclusion:** The PACE-GC formulation effectively increases antioxidant capacity and demonstrates a favourable profile for mitigating oxidative stress-induced skin ageing.

Keywords: Anti-ageing cream, Antioxidant activity, *Daucus carota*, Herbal cosmeceuticals, Oxidative stress, *Vitis vinifera*.

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INTRODUCTION

The U.S. Food and Drug Administration (FDA) defines cosmetics as topical preparations applied to the human body to cleanse, beautify, and improve appearance without interfering with physiological processes. By enhancing psychological well-being, maintaining skin and hair health, and boosting aesthetic appeal, cosmetics have traditionally served both protective and ornamental roles. As knowledge of skin biology and ageing has expanded, cosmetic products have evolved to provide functional benefits (Pimentel *et al*., 2017; S, 2015; Sriram and Gopal, 2023). This has led to the development of cosmeceuticals containing physiologically active chemicals. Common ingredients in cosmeceuticals that improve skin elasticity, reduce wrinkles, protect against UV rays, and preserve collagen include retinoic acid, alpha-hydroxy acids, vitamins C and E, coenzyme Q10, and plant-derived compounds. The safety, biocompatibility, and multifunctional properties of herbal cosmetics have attracted increasing attention. Numerous medicinal plants, such as *Curcuma longa, Emblica officinalis, Withania somnifera, Camellia sinensis*, and *Vitis vinifera*, have demonstrated anti-ageing, anti-inflammatory, and antioxidant effects in traditional systems like Ayurveda (Crous *et al*., 2024; Monteiro *et al*., 2026; Sarswat, 2025). Oxidative stress caused by reactive oxygen species plays a significant role in the complex process of skin ageing, involving both intrinsic and extrinsic factors. Despite the availability of synthetic anti-ageing products, consumers are increasingly favouring natural alternatives due to safety concerns. By reviewing the cosmetic and therapeutic importance of herbal antioxidants, understanding intrinsic and extrinsic skin-ageing mechanisms, evaluating the formulation aspects of herbal anti-ageing creams-particularly vanishing creams—and connecting Ayurvedic anti-ageing concepts with modern cosmeceutical approaches, this study aims to provide an objective assessment of the role of herbal ingredients in anti-ageing cosmeceutical formulations (Datta and Paramesh,

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2010; Papaccio *et al.*, 2022; Poljšak and Dahmane, 2012; Sriram and Gopal, 2025).

MATERIALS AND METHODS

Collection and Authentication of Plant Material

The plant specimens of carrot (*Daucus carota*) and grapes (*Vitis vinifera*) used in the present study were obtained from the local market in Dharmaj, Gujarat, India. All samples were examined and confirmed to be authentic. The procured plant materials were thoroughly washed with tap water, followed by distilled water, to remove adhering dirt and impurities. The samples were then processed further according to experimental requirements.

Preparation of the Plant Extracts

Vitis vinifera

Grape residues, such as skins and seeds, were used to prepare the aqueous extract of *Vitis vinifera* at room temperature. To remove particulate debris, the extract was centrifuged at 9000 rpm for 15 min at 20ºC. After concentrating it in a water bath, the supernatant was filtered. The concentrated extract was then stored at -20ºC before further examination (Al-Mousawi *et al.*, 2019; Baldi *et al.*, 1995; Braidot *et al.*, 2008; Djemaa-Landri *et al.*, 2020a; Felhi *et al.*, 2016; Nirmala *et al.*, 2017; Karageçili *et al.*, 2023; Loupit *et al.*, 2020; Martin *et al.*, 2020; Pepi *et al.*, 2016; Oliveira, *et al.*, 2017a; Sreemantula *et al.*, 2005; Staniszewska and Kula 2001; Trošt *et al.*, 2016; Wang and Li 2006; Zannella *et al.*, 2021).

Daucus carota

Fresh *Daucus carota* samples (200 g) were homogenised in 300 mL of acetone and extracted for 60 min. After centrifuging the homogenate for 20 min, the supernatant was collected. The residue was extracted twice more using 400 mL of 60% acetone, and the resulting supernatant was combined. At 35ºC, acetone was extracted at low pressure. Two consecutive extractions using petroleum ether (2:1, v/v) were performed to remove the pigments and fatty acids. The crude extract was prepared from the residual aqueous phase (Bas-Bellver *et al.*, 2023; Luque *et al.*, 2018; Miękus *et al.*, 2019; Oliveira *et al.*, 2017b; Shebaby *et al.*, 2012; Yahyaa *et al.*, 2015, 2016).

Development of Polyherbal formulation

White beeswax (4.4 g), liquid paraffin (13.2 mL), borax (0.22 g), rose oil (0.044 mL), and filtered water (4.4 mL) were used to prepare the cream. The oil phase was created by grating white beeswax into tiny bits and melting it with liquid paraffin in a China dish over a water bath at 70ºC. To prepare the aqueous phase, borax was separately dissolved in water and heated to the same temperature as the oil phase. To ensure even emulsification, the hot aqueous phase was gradually added to the molten oil phase while continuously stirring. Rose oil was added and thoroughly blended to create a uniform semisolid cream after the mixture was stirred until it cooled to 40-45ºC.

Quality by Design (QbD) Strategy

A systematic methodology was employed to identify pH, viscosity, and spreadability as Critical Quality Attributes (CQAs), with the *Vitis vinifera* to *Daucus carota* extract ratio designated as the independent variable (factor) in the formulation studies.

Incorporation of Herbal Extracts (DoE Factorial Design)

Rose oil was added to the mixture when it cooled to 40-45ºC, followed by the addition of plant extracts. Four formulations (E1-E4) were used to optimise the extract composition using a methodical Design of Experiments (DoE) methodology. To assess their impact on formulation performance, different ratios of *Vitis vinifera* to *Daucus carota* extracts were used: 1:2 (E1), 2:3 (E2), 3:2 (E3), and 3:1 (E4) (Ahmad *et al.*, 2011; Ahshawat and Saraf, 2008; Arshad *et al.*, 2024; Atalar *et al.*, 2021; Cronin and Draelos, 2010; Djemaa-Landri *et al.*, 2020b; Jadoon *et al.*, 2015; Jannah and Aznam, 2022; Vaishali *et al.*, 2022).

Evaluation of Cream Formulation

pH measurement

To determine the pH of the cream formulation, 5 g of the sample was dispersed in 45 mL of distilled water to create a homogeneous suspension. A calibrated digital pH meter was used to measure the pH at 27ºC (Shamsuddin *et al.*, 2018).

Viscosity

A Brookfield viscometer with spindle number 64 was used to measure the viscosity of the prepared vanishing creams. To assess viscosity at different shear rates, measurements were performed at various rotational speeds (Shamsuddin *et al.*, 2018).

Appearance

The colour, texture, and surface homogeneity of the cream were visually assessed, and the formulation was rated accordingly (Shamsuddin *et al.*, 2018).

Spreadability

By sandwiching three grams of the sample between two sterile glass slides. To achieve a consistent thickness of the cream layer, a weight of 1000 g was applied for 5 min. The upper slide was then equipped with a 50 g weight that was permitted to move in response to the applied force. The time taken for the upper slide to move 10 cm over the lower slide was noted. A shorter time interval indicated better spreadability of the formulation (Shamsuddin *et al.*, 2018).

DPPH Free Radical Scavenging Activity

The DPPH (2,2-diphenyl-1-picrylhydrazyl) test was used to assess the extracts' ability to scavenge free radicals. Briefly, 4.0 mL of a freshly prepared 6×10^{-1} M DPPH solution in methanol was mixed with 0.1 mL of the test extract at various concentrations. The maximum absorbance of DPPH was measured using a control solution containing the same volume of solvent instead of the extract. The benchmark antioxidant for comparison was ascorbic acid. The reaction mixtures were left to stand at room temperature for 30 min in the dark. A UV-visible spectrophotometer was used to measure the absorbance at 517 nm after incubation. The extract's ability to scavenge DPPH radicals was indicated by a decrease in absorbance (Baliyan *et al.*, 2022; Singha and Das, 2015).

The percentage inhibition of DPPH free radicals was calculated using the following formula:

$$\% \text{ DPPH Scavenging Activity} = \frac{A_0 - A_1}{(A_0)} \times 100$$

Where,

A_0=absorbance of the control.

A_1=absorbance of the sample or standard.

Hydrogen Peroxide Scavenging Activity

The ability of the extracts to scavenge hydrogen peroxide was assessed using a conventional spectrophotometric technique. A 40 mM hydrogen peroxide solution was prepared in phosphate buffer (pH 7.4). A UV-visible spectrophotometer was used to measure the absorbance of hydrogen peroxide at 230 nm to confirm its content. The hydrogen peroxide solution (0.6 mL) was mixed with the test extracts produced in distilled water at concentrations ranging from 0.1 to 1 mg/mL. The reaction mixtures were incubated at room temperature. Following incubation, the absorbance was measured at 230 nm and compared to a blank solution that included hydrogen peroxide-free phosphate buffer. For comparison, a common antioxidant was used. The percentage of hydrogen peroxide scavenging activity was calculated relative to the control (Al-Amiery *et al.*, 2015; Fernando and Soysa, 2015; Stanojević *et al.*, 2009).

The percentage scavenging activity of hydrogen peroxide was calculated using the following formula:

$$\% \text{ Scavenging Activity} = \frac{A_0 - A_1}{(A_0)} \times 100$$

Where,

A_0=absorbance of the control (hydrogen peroxide solution without extract).

Table 1: Effect of *Vitis vinifera* Extract in DPPH Antioxidant Method.

Concentration (µg/mL)	% Inhibition (Ascorbic Acid)	% Inhibition (*Vitis vinifera*)
1	14.20±0.85	4.10±0.52
2	21.85±1.12	13.40±0.95
4	29.10±1.45	24.85±1.28
6	34.75±1.68	31.20±1.55
8	39.60±1.89	35.90±1.72
10	50.10±2.15	41.80±1.98
25	62.40±2.45	56.30±2.28
IC_{50} (µg/mL)	9.80±0.42	14.10±0.68

Data presented as Mean±SD (*n*=3). The antioxidant activity of *Vitis vinifera* extract was statistically significant ($p<0.05$) compared to the control, but lower than that of ascorbic acid standard.

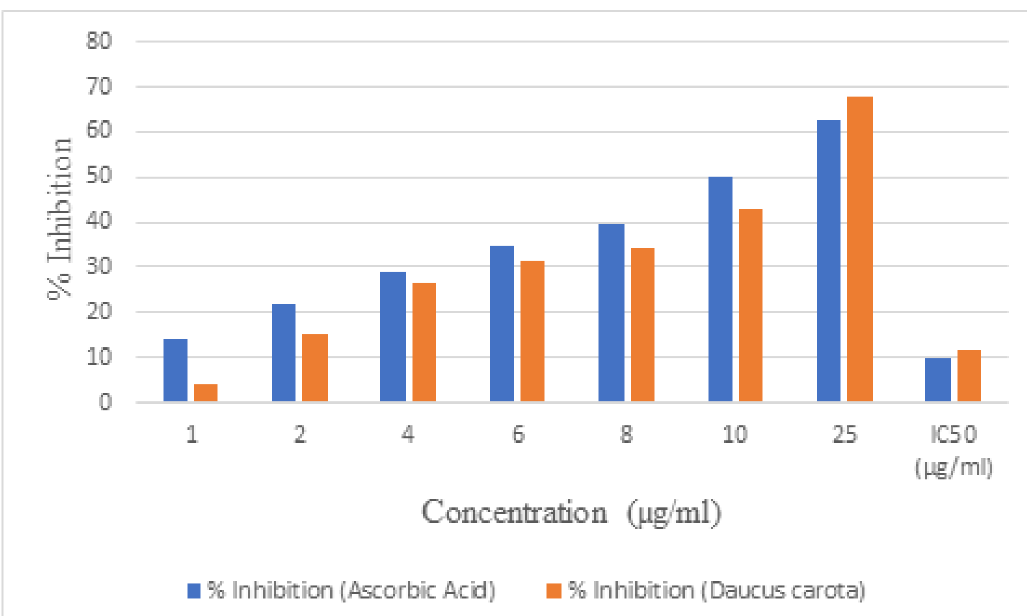


Figure 2: Comparative effect of *Daucus carota* extract & Ascorbic acid on DPPH method.

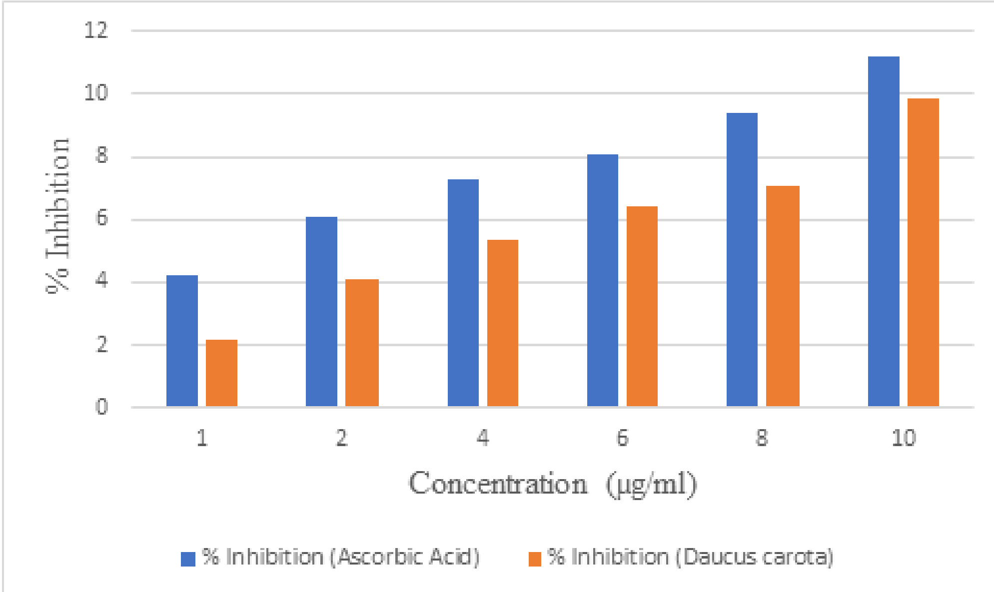


Figure 3: Effect of aqueous extract of *Vitis vinifera* in hydrogen peroxide scavenging activity.

Table 2: Effect of *Daucus carota* Extract in DPPH antioxidant method.

Concentration (µg/mL)	S	% Inhibition (*Daucus carota*)
1	14.20±0.85	3.95±0.48
2	21.85±1.12	14.90±0.98
4	29.10±1.45	26.40±1.35
6	34.75±1.68	31.60±1.58
8	39.60±1.89	34.10±1.65
10	50.10±2.15	42.75±2.05
25	62.40±2.45	67.80±2.65
IC_{50} (µg/mL)	9.80±0.42	11.90±0.55

Data presented as mean±SD (n=3). *Daucus carota* extract showed potent antioxidant activity with IC_{50} comparable to ascorbic acid (p>0.05).

A_1=absorbance of the sample or standard.

Ethical Statement

Ethical Approval: No human or animal subjects were used in this study; no ethical approval was required. Materials and Methods: This study evaluated the *in vitro* antioxidant activity and physicochemical properties. Standard safety guidelines for topically administered formulations were adhered to. Additional studies are needed to confirm safety and efficacy.

Statistical Analysis

All experiments were performed in triplicate and results are expressed as mean±Standard Deviation (SD). The IC_{50} values (concentration required for 50% inhibition) were calculated by non-linear regression analysis using GraphPad Prism software. Physicochemical parameters of cream formulations (pH, viscosity, and spreadability) were statistically analyzed using one-way Analysis of Variance (ANOVA) followed by Tukey's *post hoc* test for multiple comparisons. Statistical significance was set at $p<0.05$. All graphs were plotted using Microsoft Excel.

RESULTS

Antioxidant activity of individual extracts

DPPH Free radical Scavenging activity

The antioxidant activity of the DPPH free radical-scavenging method revealed that there was concentration-dependent activity by the *Vitis vinifera* extract, where 56.30% inhibition occurs at 25 µg/mL with an IC_{50} of 14.10±0.68 µg/mL. Greater activity was observed for ascorbic acid, where 62.40% inhibition occurs at 25 µg/mL with an IC_{50} of 9.80±0.42 µg (as shown in Figure 1 and Table 1).

From the study of the DPPH method, it was found that the extract from *Daucus carota* showed a dose-dependent rise in its ability to scavenge free radicals up to 67.80% at a concentration of 25 µg/mL, higher than that for ascorbic acid (62.40%). The IC_{50} for *Daucus carota* extract was statistically comparable to ascorbic acid at 11.90±0.55 and 9.80±0.42 µg/mL, respectively (as shown in Figure 2 and Table 2).

Hydrogen Peroxide Scavenging Activity

The hydrogen peroxide scavenging activity of the water extract of *Vitis vinifera* increased significantly ($p<0.05$) with increasing concentration from 1 µg/mL (1.45%) to 10 µg/mL (9.05%). Ascorbic acid showed greater scavenging (11.20% at 10 µg/mL). Although absolute inhibition can be lower than in DPPH assay, the effect of the extract was statistically significant ($p<0.05$) (as shown in Figure 3 and Table 3).

The extract from *Daucus carota* exhibited highly significant scavenging action for hydrogen peroxide in a dose-dependent manner ($p<0.05$), where at 10 µg/mL, 9.85% inhibition was observed, which is nearly equal to that observed for ascorbic acid, i.e., 11.20%. However, its scavenging action remained significantly higher than that of *Vitis vinifera* extract (as shown in Figure 4 and Table 4).

Table 5 and Figure 5 present the physicochemical analysis of the polyherbal anti-ageing cream formulations (E1-E4). The consistency and stability of the manufactured creams are demonstrated by the semi-solid nature of all formulations, as well as their acceptable colour and appearance. The pH values of the formulations, which range from 6.1 to 6.7, are within the skin-compatible and nearly neutral range, indicating that they can be applied topically without causing skin irritation. The viscosities of the compositions range from 3825 to 4120 cps, suggesting high consistency and ease of application. The spreadability results show acceptable spreading properties, ranging from 11.85-15.95 g·cm/sec.

DISCUSSION

The DPPH free radical scavenging experiment was used to assess the antioxidant capacity of the aqueous extracts of *Daucus carota* and *Vitis vinifera*. For *Daucus carota* and *Vitis vinifera*, the IC_{50} values were 11.90±0.55 µg/mL and 14.10±0.68 µg/mL, respectively, indicating high free radical scavenging activity equivalent to that of ascorbic acid, a standard antioxidant. Statistical analysis confirmed that both *Daucus carota* (IC_{50}=11.90±0.55 µg/mL) and *Vitis vinifera* (IC_{50}=14.10±0.68 µg/mL) extracts exhibited potent antioxidant activity. The IC_{50} value of *Daucus carota* was not significantly different from ascorbic acid (IC_{50}=9.80±0.42 µg/mL; $p>0.05$), demonstrating comparable radical scavenging efficacy. The DPPH free radical scavenging experiment was used to assess the antioxidant capacity of the aqueous extracts of *Daucus carota* and *Vitis vinifera*. For *Daucus carota* and *Vitis vinifera*, the IC_{50} values were 11.90±0.55 µg/mL and 14.10±0.68 µg/mL, respectively, indicating high free radical scavenging activity equivalent to that of ascorbic acid, a standard antioxidant. The

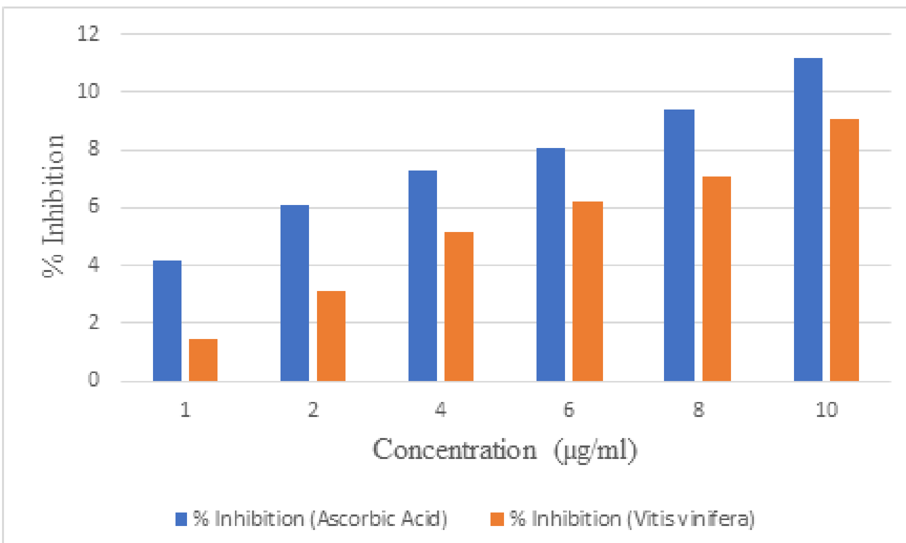


Figure 4: Effect of aqueous extract of *Daucus carota* in hydrogen peroxide scavenging activity.

Table 3: Effect of aqueous extract of *Vitis vinifera* in Hydrogen peroxide scavenging activity.

Concentration (µg/mL)	% Inhibition (Ascorbic Acid)	% Inhibition (*Vitis vinifera*)
1	4.20±0.25	1.45±0.18
2	6.10±0.32	3.15±0.24
4	7.30±0.38	5.20±0.32
6	8.10±0.42	6.25±0.36
8	9.40±0.48	7.10±0.41
10	11.20±0.55	9.05±0.52

Data presented as mean±SD (n=3). Hydrogen peroxide scavenging activity was concentration-dependent and statistically significant ($p<0.05$).

Table 4: Effect of aqueous extract of *Daucus carota* in Hydrogen peroxide scavenging activity.

Concentration (µg/mL)	% Inhibition (Ascorbic Acid)	% Inhibition (*Daucus carota*)
1	4.20±0.25	2.20±0.20
2	6.10±0.32	4.10±0.28
4	7.30±0.38	5.35±0.34
6	8.10±0.42	6.40±0.38
8	9.40±0.48	7.05±0.42
10	11.20±0.55	9.85±0.56

Data presented as mean±SD (n=3). *Daucus carota* exhibited significant H_2O_2 scavenging potential in a dose-dependent manner ($p<0.05$).

Table 5: Physical evaluation of different Cream Formulation.

Formulation no.	E1	E2	E3	E4
Semi-solid	Semi-solid	Semi-solid	Semi-solid	
Colour	Yellow	Yellow	Yellowish brown	Yellowish brown
Appearance	Good	Good	Very good	Good
pH	6.1	6.3	6.5	6.7
Viscosity (cps)	3825	3985	4050	4120
Spreadability (g·cm/sec)	11.85	13.10	14.40	15.95

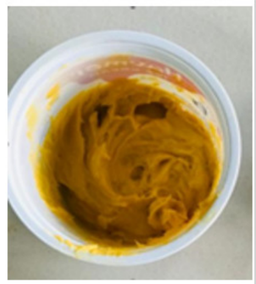
E1	E2	E3	E4
1:2	2:3	3:2	3:1
			

Figure 5: Creams with extracts in different proportions.

findings indicate that all formulations were physicochemically acceptable in terms of state, colour, and appearance, suggesting appropriate ingredient distribution and formulation stability. The ratio of *Vitis vinifera* to *Daucus carota* extracts was identified as the Critical Material Attribute (CMA) in the formulation, which was developed following Quality by Design (QbD) principles. As the percentage of *Vitis vinifera* extract increased, the viscosity rose from 3825 cps (E1) to 4120 cps (E4), and the spreadability improved from 11.85 to 15.95, demonstrating a linear relationship between extract composition and cream properties. All formulations exhibited no signs of irritation and maintained a skin-compatible pH range (6.1-6.7), confirming their safety and suitability for topical application. Formulation E3 was identified as the optimal design among the four batches. It exhibited a Very Good appearance rating and demonstrated an ideal balance between spreadability (14.40) and viscosity (4050 cps), indicating favourable physicochemical properties for topical application.

CONCLUSION

Using a QbD technique, the PACE-GC polyherbal cream was effectively optimized. Oxidative stress is the primary mediator of the complex and progressive process of skin ageing, which is influenced by both internal and external factors. To obtain multipurpose cosmetic benefits, such as skin whitening, anti-wrinkle, and anti-ageing effects, *Vitis vinifera* and *Daucus carota* were chosen for their antioxidant potential and combined in various ratios in the current study. Compared to the individual extracts, the combined herbal anti-ageing cream exhibited good antioxidant activity, suggesting a synergistic effect. These results indicate that combining plant extracts may enhance cosmetic efficacy and potentially protect the skin from UV-induced oxidative damage, a key contributor to skin ageing. The aqueous extracts of *Daucus carota* and *Vitis vinifera* demonstrated strong antioxidant activity, as indicated by low IC_{50} values comparable to those of ascorbic acid. All creams had acceptable physicochemical characteristics, a pH suitable for the skin, and did not irritate. This study employed a Quality by Design (QbD) approach to develop a stable polyherbal cream. Design of Experiments (DoE) analysis revealed that precise adjustment of herbal extract ratios enables control over key physicochemical properties. Among the formulations, E3 demonstrated superior physical and aesthetic characteristics, making it the most suitable candidate for further therapeutic evaluation.

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ABBREVIATIONS

FDA: U.S. Food and Drug Administration; **UV:** Ultraviolet; **ROS:** Reactive Oxygen Species; **DPPH:** 2,2-diphenyl-1-picrylhydrazyl; **PACE-GC:** Polyherbal Anti-Ageing Cream with Extracts of Grape and Carrot; **QbD:** Quality by Design; **CQA:** Critical Quality Attributes; **DoE:** Design of Experiments; **IC_{50}:** Half Maximal Inhibitory Concentration; **CMA:** Critical Material Attribute. **SD:** Standard Deviation; **ANOVA:** Analysis of Variance; **CI:** Confidence Interval

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

FUNDING

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AUTHOR CONTRIBUTIONS

Mehul Bhatt planned the study, oversaw the investigation, analysed the data, and wrote the report. Maneesha Parmar offered technical assistance and contributed to methodology, Quality by Design (QbD), and Design of Experiments (DoE) planning. Divyang Patel developed the cream's recipe and assessed its physicochemical properties. Smit Agrawal researched antioxidants, processed data, and interpreted findings. Ankit Yadav assisted with statistical analysis, manuscript editing, and literature review.

SUMMARY

This study successfully utilised a QbD approach to develop a polyherbal cream containing *Daucus carota* and *Vitis vinifera*. The optimised Formulation (E3) showed significant synergistic antioxidant activity and ideal skin-compatibility.

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