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PHARMACEUTICAL CREAM WITH *CARTHAMUS TINCTORIUS* L. EXTRACT: FORMULATION AND EVALUATION

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The aim. *The aim of this study was to develop and evaluate a pharmaceutical cream formulation containing a liquid extract of Carthamus tinctorius L. flowers. The research focused on characterizing the extract using instrumental analytical methods (IR spectroscopy, spectrophotometry with rutin standard, HPLC, and UV spectroscopy for β-carotene) and on designing cream bases with different hydrophilic, hydrophobic, and emulsion components. The study further sought to assess the quality parameters of the developed formulations, including appearance, homogeneity, thermostability, colloidal stability, and pH, in order to identify the most stable and pharmaceutically promising compositions.*

Methods*. A liquid extract of Carthamus tinctorius L. flowers was used as the active pharmaceutical ingredient. Its composition and properties were analyzed using IR spectroscopy, spectrophotometry (λmax = 410 nm, rutin standard), HPLC (comparison with rutin), and UV spectroscopy for β-carotene (λmax ≈ 450 nm). Based on the extract, eight cream samples were formulated with different hydrophilic, hydrophobic, and emulsion bases. The quality of the samples was evaluated according to the following parameters: appearance, homogeneity, thermostability, colloidal stability, and pH.*

Results*. IR spectroscopy confirmed the presence of polyphenols, flavonoids, and organic acids. The total flavonoid content was 2.2% (calculated as rutin). HPLC analysis revealed multiple peaks, including rutin (Rt = 18.17 min), coinciding with the standard (Rt = 18.20 min). The UV spectrum showed a high level of β-carotene (A = 4.35 compared to A = 0.60 in the standard). Out of the 8 cream samples, only formulations No. 3, No. 5, and No. 7 demonstrated stability.*

Discussion*. Instrumental analysis confirmed the presence of a complex of biologically active substances in the extract, ensuring its anti-inflammatory and antioxidant properties. The high content of flavonoids and β-carotene substantiates the therapeutic potential of the product. Selection of the cream base showed that a rational combination of hydrophilic and hydrophobic components ensures stability and preservation of active ingredients.*

Conclusions*. A therapeutic-cosmetic cream with a liquid extract of Carthamus tinctorius L. has been developed. Out of 8 tested formulations, samples No. 3, No. 5, and No. 7 demonstrated the best quality parameters and are recommended for further investigation. The obtained data confirm the prospects of using safflower extract in the creation of modern phytopharmaceuticals with pronounced anti-inflammatory and antioxidant activity*

Keywords*: Carthamus tinctorius L., safflower extract, flavonoids, β-carotene, IR spectroscopy, spectrophotometry, HPLC, pharmaceutical cream, soft dosage form, formulation development, rheology, microscopy*

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1. Introduction

In recent years, there has been a steady global increase in interest toward herbal medicines. This is primarily due to their rich and balanced content of biologically active compounds, which usually demonstrate anti-inflammatory and antioxidant properties and are relatively safe compared to synthetic drugs, as they rarely cause pronounced toxic, allergic, or irritant reactions and show high therapeutic efficacy in a wide range of diseases [1, 2]. Unlike synthetic analogs, phytopharmaceuticals seldom cause adverse effects and do not contribute to the development of resistant microbial strains, which is particularly important in the treatment of chronic and hard-to-heal wounds with inflammatory complications [3, 4].

An important aspect in the development of herbal dosage forms is the rational combination of plant extracts with excipients and the optimal selection of a base. The cream base not only determines the consistency, volume, and viscosity of the formulation, but also regulates the release rate of active components, thereby increasing their bioavailability and enhancing pharmacological activity [5, 6].

Among promising medicinal plants, *Carthamus tinctorius* L. (safflower) has attracted attention due to its long history of traditional use and its proven pharmacological effects. Historically, safflower flowers were used as powders and ointments to treat skin itching, vitiligo, allergic manifestations, and inflammatory skin conditions. Modern studies have confirmed its wide spectrum

of activities, including anticoagulant, vasodilatory, antihypertensive, antioxidant, neuroprotective, immunosuppressive, and antitumor effects, as well as inhibition of melanin synthesis and anti-allergic properties [7, 8].

The use of safflower extracts in combination with properly selected excipients opens up opportunities for creating effective phytopharmaceuticals in dermatology, gynecology, dentistry, and cosmetology. For example, ointments with chamomile flower polyextracts, containing essential oils, flavonoids, sterols, tannins, and polysaccharides, have shown pronounced anti-inflammatory and antimicrobial activity and are used in the treatment of eczema and dermatitis, including infected forms [9, 10].

Thus, the development of new pharmaceutical soft dosage forms based on *Carthamus tinctorius* L. extract is a relevant task of modern pharmaceutical science aimed at creating safe, effective, and stable preparations for the treatment and prevention of dermatological diseases.

The aim of the research. The aim of this study was to develop the technology and select the optimal base concentration for creating a soft pharmaceutical dosage form containing *Carthamus tinctorius* L. flower extract, demonstrating the highest therapeutic efficacy.

2. Planning (methodology) of research

1. Selection of a suitable base for a therapeutic-cosmetic cream with *Carthamus tinctorius* L. extract.

2. Development of formulation and technology with evaluation of quality parameters.

3. Design of a technological scheme for cream preparation.

3. Materials and methods

This work was carried out at the Departments of Dosage Form Technology and Pharmaceutical Chemistry, Tashkent Pharmaceutical Institute. As the active pharmaceutical ingredient, a liquid extract of *Carthamus tinctorius* L. flowers was selected, known for its pronounced anti-inflammatory and regenerative effects [2, 3].

The liquid extract of *Carthamus tinctorius* L. (safflower) flowers was prepared using the maceration method with a hydroalcoholic solvent. Dried and powdered safflower flowers, meeting the pharmacopeial quality requirements, were used as the raw material.

For extraction, 100 g of the plant material was placed in a glass vessel and mixed with 70% ethanol at a 1:10 (w/v) ratio. The mixture was macerated at (25 ± 2)°C for 48 hours in a dark place, with intermittent stirring every 6 hours to facilitate mass transfer of biologically active substances such as flavonoids, carotenoids, and organic acids into the solvent.

After maceration, the mixture was filtered through double-layer filter paper to separate the solid residues. The obtained filtrate was then concentrated under reduced pressure using a rotary evaporator (Büchi R-210, Switzerland) at 40°C to remove most of the solvent. A thick, orange-colored liquid extract with a characteristic odor was obtained. The average extraction yield was 16.8 ± 0.9%.

The obtained liquid extract was stored in amber glass bottles at 4°C to protect it from light and oxidation. Under these conditions, the extract remained physically and chemically stable for up to 3 months.

IR spectroscopy of the liquid extract. Infrared Fourier spectroscopy (FTIR) was applied to identify the main functional groups of biologically active compounds. The analysis was performed in the range of 4000–400 cm^{-1} using a Shimadzu IRTracer-100 spectrometer. The liquid extract was placed in a KBr cuvette. The obtained spectrum allowed the identification of characteristic absorption bands corresponding to functional groups of flavonoids, phenolic compounds, and fatty acids [11, 12].

Determination of flavonoids in the liquid extract by spectrophotometry. The quantitative determination of the total flavonoid content was carried out spectrophotometrically using rutin (Sigma-Aldrich (Germany)) as a standard. Optical density was measured with a UV-Visible spectrophotometer (Shimadzu UV-1800, Japan) at λmax = 410 nm. A 70% ethanol solution was used as the solvent. The concentration of flavonoids, expressed as rutin equivalents, was calculated according to a calibr tion curve in the concentration range of 5–50 μg/mL [13, 14]. A calibration curve was prepared using rutin standard solutions in the range of 5–50 μg/mL, showing good linearity ($R^2 \geq 0.998$). The limit of detection (LOD) and limit of quantification (LOQ) were calculated based on the standard deviation of the blank and the slope of the calibration curve. The resulting values were LOD ≈ 0.13 μg/mL and LOQ ≈ 0.4 μg/mL.

HPLC analysis of the liquid extract. High-performance liquid chromatography (HPLC) was used for qualitative and quantitative analysis of individual biologically active compounds. The analysis was performed on an Agilent 1200 Series chromatograph equipped with a UV detector. Chromatographic conditions: C18 column (250 × 4.6 mm, 5 μm), column temperature 25°C, flow rate 1.0 mL/min, injection volume 20 μL. The mobile phase consisted of a gradient mixture of acetonitrile and 0.1% aqueous phosphoric acid.

Repeatability was confirmed with three replicate injections, showing a relative standard deviation (RSD) ≤ 2%, indicating good precision. The limit of detection (LOD) and limit of quantification (LOQ) for rutin were calculated based on the standard deviation of the blank and the slope of the calibration curve, resulting in LOD ≈ 0.12 μg/mL and LOQ ≈ 0.36 μg/mL.

Table 1

Gradient program for HPLC analysis of the *Carthamus tinctorius* L. extract

Time (min)	% of solvent A (acetonitrile)	% of Solvent B (0.1% phosphoric acid in water)
0–5	10	90
5–20	10 → 40	90 → 60
20–30	40 → 60	60 → 40
30–40	60 → 80	40 → 20
40–45	80	20

Detection was performed at λ = 280 nm. The main flavonoid and phenolic components of the extract were

identified by retention time and spectral characteristics. Quantification was carried out using the external standard method with rutin and quercetin (Sigma-Aldrich (Germany)) [15, 16].

UV spectroscopy for β-carotene. For this study, β-carotene standard (purity ≥98%) and ethanolic extract of *Carthamus tinctorius* L. petals were used. Standard β-carotene solutions were prepared freshly in 96% ethanol prior to measurements. The extract was obtained by maceration of dried plant material (safflower flowers) in 70% ethanol at room temperature for 48 hours, followed by filtration [17, 18]. UV spectra were recorded on a spectrophotometer in the range of 200–600 nm with a step of 1 nm. Ethanol was used as the solvent and blank control. All measurements were performed at (25 ± 1)°C in quartz cuvettes of 1 cm path length. The calibration curve was constructed using β-carotene standard solutions in the concentration range of 5–50 μg/mL, showing good linearity ($R^2 \geq 0.998$). The limit of detection (LOD) was approximately 0.10 μg/mL, and the limit of quantification (LOQ) was about 0.30 μg/mL.

The cream was prepared through the following steps:

1. Oil phase preparation. The oil phase included the active ingredients (e.g., amaranth oil, safflower extract) and oil-soluble excipients (e.g., petrolatum, lanolin, fatty alcohols), which were gradually heated to ensure complete dissolution and homogeneity.

2. Aqueous phase preparation. The aqueous phase consisted of water-soluble excipients (e.g., Na-CMC, glycerin) and emulsifiers (both primary and co-emulsifiers), which were mixed thoroughly.

3. Emulsion formation. The aqueous phase was gradually added to the oil phase under high-speed stirring to form a homogeneous emulsion. This ensured even distribution of the droplets and overall cream stability.

4. Stability optimization. The main emulsifier (e.g., Tween-80) was combined with a co-emulsifier (e.g., fatty alcohol or glyceryl stearate) in an optimized ratio. The HLB values were calculated to match the desired O/W (oil-in-water) emulsion type, ensuring uniform distribution of active ingredients and oil phase within the aqueous medium and minimizing droplet aggregation.

Microscopy. The microstructure of the creams was studied using optical microscopy (magnification ×400) with a Leica DM500 microscope. A thin layer of cream evenly spread on a glass slide was used for sample preparation [19].

*Rheological analysis***.** Rheological properties of the creams were studied using a rotational viscometer (Brookfield DV-III Ultra). Measurements were performed at (25 ± 1)°C, registering shear stress versus shear rate to determine thixotropic characteristics [20].

All experiments were conducted in triplicate ($n = 3$). Results are expressed as mean ± SD. One-way ANOVA (GraphPad Prism 9) was used; $p < 0.05$ considered significant.

4. Results

For the development of a therapeutic-cosmetic cream, a liquid extract of *Carthamus tinctorius* L. flowers was selected as the active pharmaceutical ingredient. The extract possesses pronounced anti-inflammatory and moisturizing effects, contributing to skin regeneration and wound healing.

At the first stage, the physicochemical properties of the extract were evaluated using IR spectroscopy, spectrophotometry, and HPLC analysis. The obtained data confirmed the presence of flavonoids, phenolic compounds, and organic acids, which determine the pharmacological activity of the extract.

In the IR spectrum of the liquid extract of *Carthamus tinctorius* L. (Fig. 1), characteristic absorption bands were observed at several key regions.

A broad, intense band centered at 3380–3410 cm^{-1} corresponds to the stretching vibrations of hydroxyl (–OH) groups, confirming the presence of phenolic and alcoholic constituents.

The C–H stretching vibrations of aliphatic and aromatic structures appear near 2920 cm^{-1} and 2850 cm^{-1}, respectively.

A distinct band at 1654 cm^{-1} is attributed to the C=O stretching of flavonoid carbonyl and organic acid groups.

Strong peaks in the 1510–1600 cm^{-1} region correspond to C=C vibrations in aromatic rings typical of polyphenols.

The absorption at 1108 cm^{-1} indicates C–O–C glycosidic linkages, suggesting the presence of flavonoid glycosides, while the bands between 600–800 cm^{-1} represent out-of-plane C–H bending vibrations of substituted aromatic nuclei.

These spectral features confirm the presence of a complex mixture of polyphenolic compounds, flavonoids, and organic acids, which are known to contribute to the anti-inflammatory and antioxidant properties of *Carthamus tinctorius* L. extract [20].

The total flavonoid content in the liquid extract of *Carthamus tinctorius* L. was determined using spectrophotometric analysis.

For sample preparation, the liquid extract was diluted in 70% ethanol to fall within the linear range of the calibration curve. Absorbance was measured at λmax = 410 nm against a 70% ethanol blank. The optical density of the extract was 0.665, while the rutin standard showed 0.485. Using the calibration curve, the total flavonoid content, expressed as rutin equivalents, was found to be 2.2% (Fig. 2).

The precision of the method was confirmed by analyzing three replicates of the extract solution. The relative standard deviation (RSD) was ≤ 2%, indicating good repeatability and reliability of the method.

The liquid extract of *Carthamus tinctorius* L. was analyzed using high-performance liquid chromatography (HPLC) to identify and quantify flavonoids. A calibration curve was prepared using rutin standard solutions in the range of 5–50 μg/mL, showing good linearity ($R^2 \geq 0.999$).

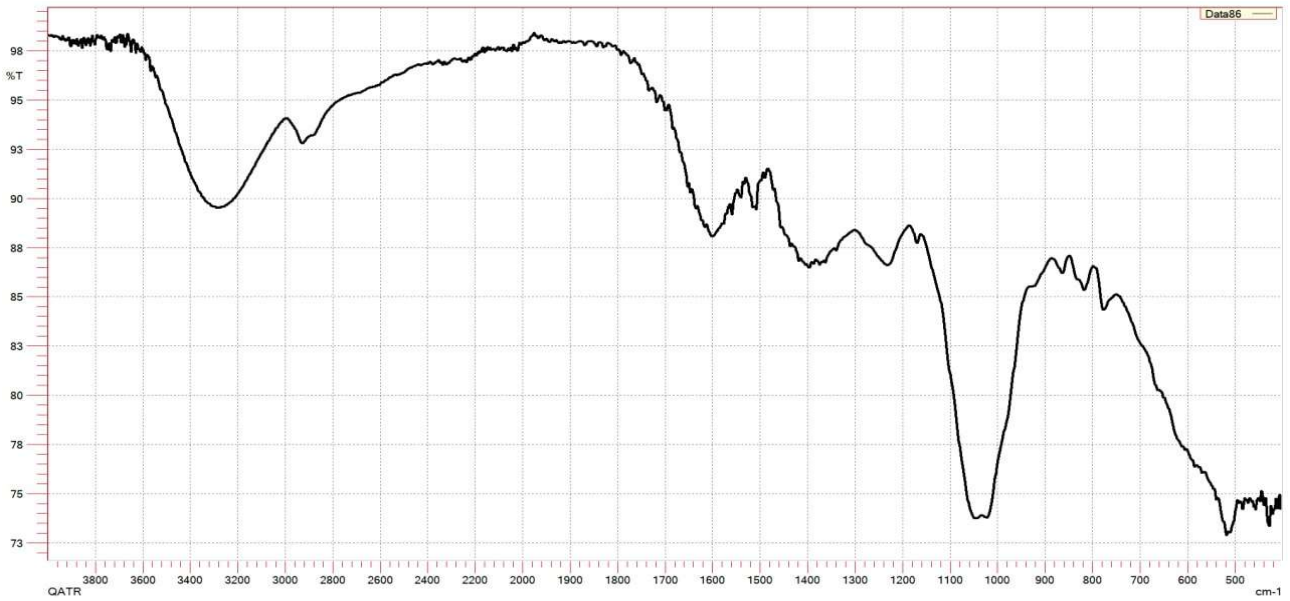
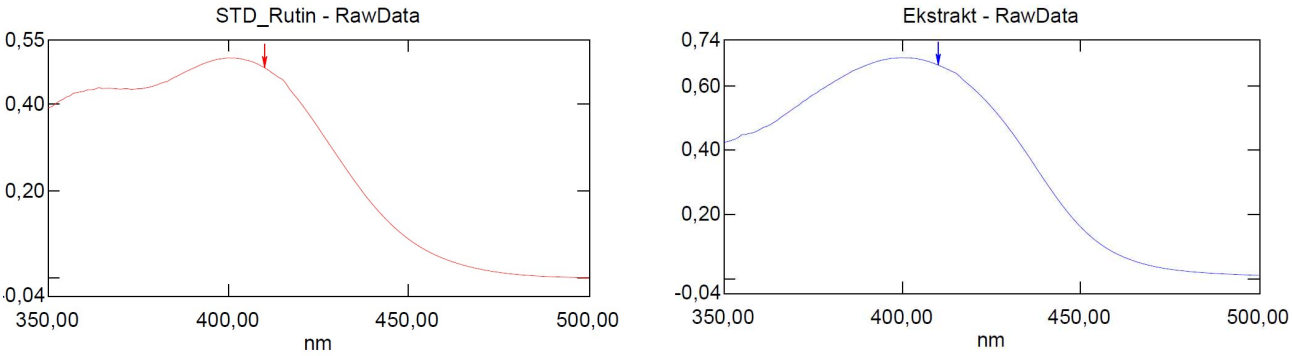


Fig. 1. IR spectrum of the liquid extract of *Carthamus tinctorius* L. flowers



a *b*

Fig. 2. UV spectrum of the liquid extract of *Carthamus tinctorius* L: *a* – standard of rutin; *b* – liquid extract of *Carthamus tinctorius* L.

Sample preparation. The liquid extract was filtered through a 0.45 µm membrane and diluted with the mobile phase (acetonitrile:0.1% phosphoric acid in water) to achieve a concentration within the linear range of the calibration curve. A 20 µL aliquot was injected into the HPLC system.

Chromatographic analysis (Fig. 3) revealed the presence of multiple peaks, indicating the complex composition of the extract. The main peaks were recorded in the retention time range of 13.2–19.9 min. Among them, the most pronounced peak at 18.17 min coincided with the retention time of the rutin standard (18.20 min), confirming the presence of this flavonoid in the extract.

In addition to rutin, additional peaks were observed at 15.75, 16.64, 17.43, and 17.62 min, which are likely to correspond to other flavonoids (e.g., quercetin, isorhamnetin) and phenolic compounds.

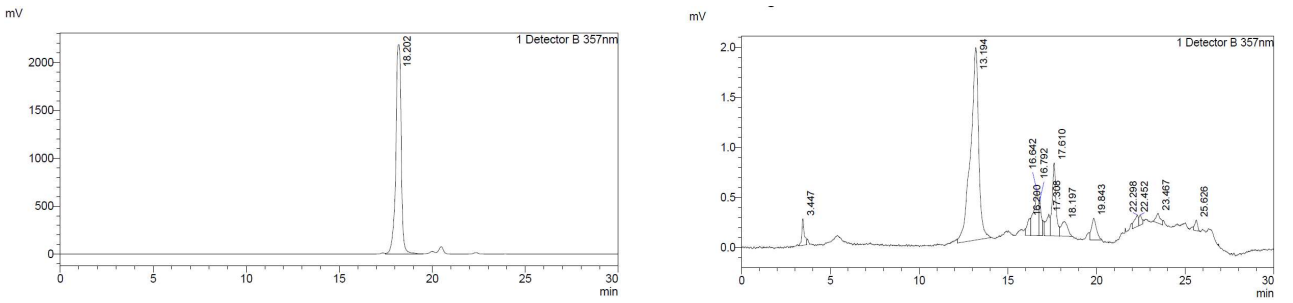
Thus, the HPLC analysis demonstrated that the liquid extract of *Carthamus tinctorius* L. contains rutin and several other biologically active components, which determine its pharmacological activity.

The HPLC analysis demonstrated that the liquid extract contains rutin and several other biologically active compounds, which contribute to its pharmacological activity.

The UV spectrophotometric analysis was performed to compare the absorption profiles of the β-carotene standard and the ethanolic extract of *Carthamus tinctorius* L.

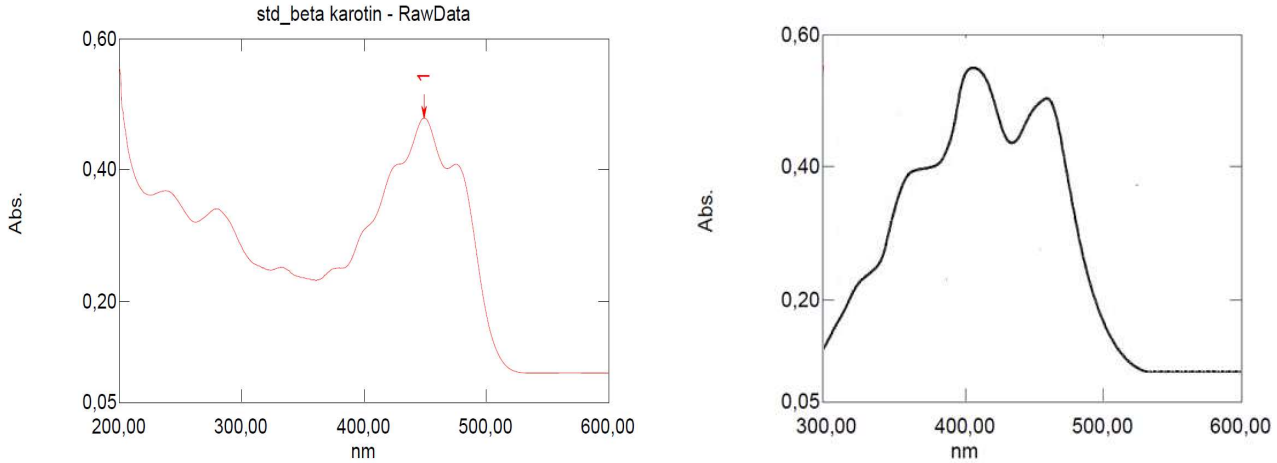
The extract was diluted in 96% ethanol to match the linear range of the calibration curve.

The β-carotene standard showed a single absorption maximum at λmax ≈ 465 nm with an optical density of ~0.45, which corresponds to literature data [21, 22]. The *Carthamus tinctorius* L. extract exhibited a more complex spectrum with two distinct maxima: at λmax ≈ 410 nm (Abs ~0.55) and λmax ≈ 465 nm (Abs ~0.50). Based on the relative peak intensities, the contribution of the 410 nm band was estimated at ~52%, while the 465 nm band accounted for ~48% of total absorption. Additionally, weak absorption in the range of 300–350 nm was observed, indicating the presence of phenolic compounds (Fig. 4).



a *b*

Fig. 3. Chromatogram of liquid extract of *Carthamus tinctorius* L: *a* – standard of rutin; *b* – liquid extract of *Carthamus tinctorius* L.



a *b*

Fig. 4. UV spectrum of the liquid extract of *Carthamus tinctorius* L: *a* – standard of *β*-carotene; *b* – liquid extract of *Carthamus tinctorius* L.

The results demonstrate that the extract possesses a multicomponent absorption profile containing both carotenoid and flavonoid structures, which contribute comparably to the overall UV spectrum. Repeatability was confirmed by triplicate measurements, showing a relative standard deviation (RSD) ≤ 2%, indicating good precision.

Further experiments were carried out to select the optimal cream base and auxiliary components. The following excipients were used: petrolatum repels water, which helps prevent moisture loss from the skin; petrolatum oil serves as an emollient and protective agent; anhydrous lanolin makes the skin soft and elastic, which makes it a popular ingredient in creams; yellow wax is used in creams, lip balms, and other cosmetic products due to its moisturizing and protective properties; solid paraffin is included in many cosmetic products, such as lip balms and creams, because of its moisturizing properties; aerosil helps achieve the desired consistency, which is especially important for creams and gels; glycerin is often used in creams, lotions, and other skin products because of its ability to retain moisture, thereby maintaining skin hydration; sunflower oil is included in many cosmetic products due to its moisturizing and nourishing properties; peach oil is used in facial and body care products; sodium carboxymethylcellulose (Na-CMC) provides good texture and improves product distribution on the skin; Tween-80 helps mix immiscible liquids, increases product stability, and prevents separation; nipagin–nipazol are effective preservatives that help extend the shelf life of various products by preventing microbial growth. Their use is widespread in pharmaceuticals and cosmetics.

Biopharmaceutical research indicates that for water-soluble pharmaceutical substances, ointment bases with hydrophilic properties are the best choice, especially when applied to wounds and mucous membranes [6]. From the biopharmaceutical perspective, hydrophobic ointment bases are the most preferable for the diffusion of fat-soluble substances. This is due to the fact that such substances dissolve in hydrophobic ointment components, providing a high degree of dispersion and, consequently, higher activity [7].

The effectiveness of soft dosage forms is largely determined by the choice of an appropriate ointment base, since it regulates the rate and completeness of active substance release. In the course of the study, 8 ointment models were created, differing in hydrophilic, hydrophobic, and emulsion properties (Table 1).

To determine effectiveness and stability, it was decided to add the active ingredient in an equal amount up to 10.0 g. The experimental results are presented in Table 2.

The components listed in Table 1 are distributed across technological stages according to their physicochemical properties and functional purpose. Proper organization of the production stages (Fig. 1) makes it possible to preserve the effectiveness of the active substances and to obtain a stable cream formulation.

Table 2

Composition of creams with *Carthamus tinctorius* L. flower extract.

Formula No.	Safflower flower extract (%)	Amaranth oil (%)	Petrolatum (%)	Petrolatum oil (%)	Anhydrous lanolin (%)	Yellow wax (%)	Paraffin (%)	Aerosil (%)	Sunflower oil (%)	Peach oil (%)	Na-CMC (%)	Glycerin (%)	Tween-80 (%)	Nipagin–Nipazol (%)	Purified water (%)	Total mass (%)	Dispers system type*	Dosage form
1	10.00	10.00	40.00	25.00	–	–	–	–	–	–	–	–	6.70	–	8.30	100.00	W/O	Ointment
2	10.00	10.00	–	–	–	–	–	–	5.50	–	10.00	25.00	–	1.25	38.25	100.00	O/W	Cream
3	10.00	10.00	25.00	10.00	35.00	–	–	–	–	–	–	–	–	–	10.00	100.00	W/O	Cream
4	10.00	10.00	–	–	–	–	–	2.00	–	51.00	–	–	2.00	–	25.00	100.00	O/W	Emulsion cream
5	10.00	10.00	–	–	–	22.50	–	–	28.75	–	18.75	–	3.00	–	7.00	100.00	O/W	Cream
6	10.00	10.00	–	–	–	–	22.50	–	28.75	18.75	–	–	3.00	–	7.00	100.00	W/O	Ointment
7	10.00	10.00	–	–	–	–	–	9.00	38.85	28.85	–	–	3.00	6.30	–	100.00	Anhydrous gel	Gel (anidrogel)
8	10.00	10.00	–	–	–	–	–	–	5.00	–	7.50	25.00	–	1.25	41.25	100.00	O/W	Cream-gel

Note: W/O – Water-in-Oil; O/W – Oil-in-Water.

Subsequently, studies were carried out on the primary quality indicators: appearance, homogeneity, thermostability, colloidal stability, and pH, which must comply with the requirements for soft dosage forms established by the State Pharmacopoeia of the Republic of Uzbekistan [9]. The experimental results are presented in Table 3.

Although microbiological assays (total aerobic microbial count, yeast and mold) and oxidative indicators (peroxide value and acid value) performed on representative samples did not reveal significant contamination or advanced lipid oxidation, several formulations (No. 1, 2, 4, 6, 7 and 8) displayed markedly acidic pH values (2.13–3.69). To elucidate the origin of low pH, pH measurements were repeated using a flat-surface electrode with multipoint calibration (pH 4.01, 7.00), and pH of the separated aqueous phase was determined after gentle centrifugation. The repeated measurements confirmed the initial observations: the aqueous phase pH of the acidic samples remained low, indicating that the acidity was associated with the water-soluble fraction or with intrinsic acidic constituents of the plant extracts rather than with gross microbial spoilage or advanced oxidative degradation.

As a result of the preliminary visual evaluation, only samples No. 3, 5, 7 out of the eight tested formulations were selected, as they demonstrated favorable physicochemical characteristics: appearance, homogeneity, thermostability, colloidal stability (no phase separation), and appropriate pH values.

The remaining samples exhibited heterogeneity, phase separation, and the appearance of mold or clumps, indicating poor quality and instability of the formulations.

Microscopic analysis revealed that in samples No. 3, 5, 7 the active substance particles were uniformly distributed, with fat globule sizes ranging from 5–15 μm, and no signs of aggregation were observed. In contrast, the other samples showed enlarged globules and phase heterogeneity, which correlated with low stability.

Microscopic examination of creams containing *Carthamus tinctorius* L. extract demonstrated that samples No. 3, 5, 7 had a uniform dispersed structure without signs of coalescence (Fig. 5):

– in sample No. 3, fat globules were evenly distributed with diameters predominantly in the range of 5–12 μm; the structure was stable and no aggregation was detected;

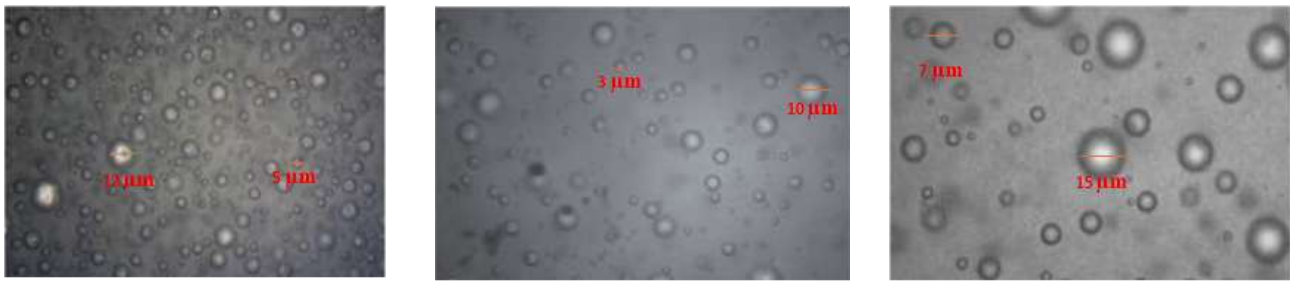
– in sample No. 5, the particles were smaller (3–10 μm) and exhibited high uniformity, indicating good colloidal stability.

Thus, microscopic analysis confirmed that samples No. 3 and No. 5 possessed the optimal microstructure, ensuring stability and uniform release of active substances.

Table 3

Results of the study of quality indicators of the therapeutic-cosmetic cream based on *Carthamus tinctorius* L. flower extract (after 12 months of storage)

Sample	Appearance	Homogeneity	Thermostability	Colloidal stability	pH
1	Light yellow cream, soft fatty consistency, mold formation	Non-homogeneous	Separated	Separated	3.25
2	Dark yellow cream, turbid aqueous consistency, mold film formation	Non-homogeneous	Not thermostable	Separated	2.70
3	Light yellow cream, soft fatty consistency, no foreign inclusions	Homogeneous	Thermostable	Not separated	6.40
4	Bright yellow cream, viscous oily consistency, mold formation	Non-homogeneous	Not thermostable	Separated	3.38
5	Light yellow cream, dense fatty consistency, no foreign inclusions	Homogeneous	Thermostable	Not separated	5.98
6	Light yellow cream, soft fatty consistency, partial rancidity	Non-homogeneous	Not thermostable	Separated	2.13
7	Intensely yellow cream, transparent jelly-like soft consistency, no foreign inclusions	Homogeneous	Thermostable	Not separated	3.69
8	Turbid yellow cream, dense gel-like consistency, formation of lumps in the mass	Non-homogeneous	Not thermostable	Separated	2.44

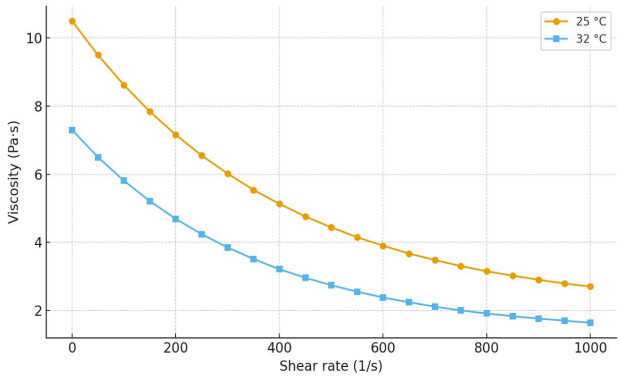


a *b* *c*

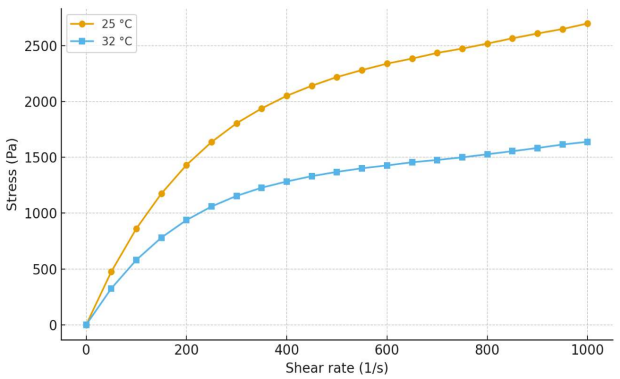
Fig. 5. Microstructure of creams with *Carthamus tinctorius* L. extract: *a* – sample No. 3 (5–12 µm); *b* – sample No. 5 (3–10 µm); *c* – sample No. 7 (7–15 µm)

Rheological studies showed that all cream samples exhibited a nonlinear "shear stress–shear rate" relationship, characteristic of pseudoplastic systems. The most pronounced thixotropic properties were observed in samples No. 3, and No. 5 which indicates their high stability and ease of application.

Rheological testing of cream samples containing *Carthamus tinctorius* L. extract demonstrated pseudoplastic behavior typical of emulsion systems. On the "viscosity–shear rate" curves (Fig. 6, *a*), a decrease in viscosity with increasing shear rate was observed, indicating the thixotropic properties of the product. At 25°C, viscosity values ranged from 10.5 Pa·s (at 0 s^{-1}) to 2.7 Pa·s (at 1000 s^{-1}), while at 32°C they decreased from 7.3 Pa·s to 1.64 Pa·s, respectively. This shows that increasing temperature leads to a reduction in the structural viscosity of the cream.



a



b

Fig. 6. Rheological characteristics of the cream with *Carthamus tinctorius* L. extract: *a* – viscosity curve; *b* – shear stress curve

On the "shear stress–shear rate" curves (Fig. 6, *b*), a nonlinear relationship was also observed. At 25°C, the maximum shear stress reached approximately 2600 Pa, while at 32°C it reached about 1650 Pa. This behavior indicates a stable emulsion structure with good plasticity and thixotropy.

Thus, the rheological results confirmed that the developed cream possesses optimal structural and mechanical properties: high stability during storage, ease of application, and uniform distribution of active substances upon contact with the skin.

5. Discussion

The study provided a comprehensive characterization of the composition and physicochemical properties of the liquid extract of *Carthamus tinctorius* L., substantiating its potential use as an active pharmaceutical ingredient for the development of a therapeutic-cosmetic cream. The results demonstrated that the extract contains a wide spectrum of biologically active compounds–flavonoids, phenolic compounds, organic acids, and carotenoids–that determine its pharmacological activity.

IR spectroscopy confirmed the presence of functional groups (–OH, C=O, C=C, C–O–C) characteristic of polyphenolic and flavonoid compounds, explaining the pronounced antioxidant and anti-inflammatory properties of the extract. Spectrophotometric analysis showed that the total flavonoid content, expressed as rutin equivalents, was 2.2%, which correlates with literature data indicating that safflower flowers are rich in flavonoids and polyphenols responsible for strong antioxidant activity [2, 4].

HPLC analysis revealed the complex composition of the extract: multiple peaks were detected, with the most prominent at 18.17 min, coinciding with the retention time of the rutin standard (18.20 min). This provides strong evidence for the presence of rutin and confirms that safflower cultivated under local conditions contains the same major flavonoid markers reported by other researchers [3, 4]. [3] reported that safflower extracts are characterized by the presence of hydroxysafflor yellow A, carthamin, and rutin derivatives with significant antioxidant and wound-healing activities, which is consistent with our findings. Similarly, [4] identified antioxidative flavonoids such as quercetin and luteolin derivatives in safflower leaves, supporting our results indicating a flavonoid-rich profile contributing to anti-inflammatory activity.

The UV spectral analysis further highlighted differences between the β-carotene standard and the plant extract. For β-carotene, a single strong maximum was recorded at 460–470 nm, typical of carotenoids due to their conjugated double-bond system. In contrast, the ethanol extract of Carthamus tinctorius L. showed a more complex profile with an additional maximum at 400–420 nm, indicative of flavonoid chromophores (quercetin glycosides and chalcones). The presence of two pronounced maxima suggests that both carotenoids and flavonoids contribute significantly to the extract's absorption profile, supporting its multicomponent nature and confirming the data presented by [2], who also noted the synergistic antioxidant effects of these compound groups.

The optimization of cream base composition confirmed that the type and ratio of excipients significantly affect formulation quality. Among eight tested samples, only No. 3, 5, 7 showed desirable characteristics – homogeneity, thermostability, absence of phase separation, and pharmacopoeially acceptable pH values.

The observed acidity in several samples, despite negative microbiological and oxidative results, is most likely related to the intrinsic properties of plant extracts rather than formulation spoilage. Safflower and amaranth extracts naturally contain organic and phenolic acids that can lower the pH of the aqueous phase. Moreover, pH measurement in semi-solid emulsions may vary depending on electrode type and sampling technique. Our repeated tests using a flat-surface electrode confirmed that the acidity was confined to the water phase, indicating the presence of natural acidic constituents rather than degradation.

This finding aligns with [1], who emphasized that a balanced combination of hydrophilic and lipophilic bases is essential for the stability and controlled release of active compounds in topical formulations [1].

Microscopic and rheological analyses confirmed that No. 3, 5, 7 possessed stable dispersed structures and thixotropic behavior, with uniformly distributed globules of 3–15 μm. This finding aligns with the observations of [4] that particle size and uniformity are critical for enhancing bioavailability and ensuring consistent pharmacological response in semisolid preparations.

Overall, the present results are in agreement with previously published data [1–4], confirming the high pharmacological value of *Carthamus tinctorius* L. extract and its relevance for developing modern therapeutic-cosmetic products with antioxidant and anti-inflammatory effects.

Practical relevance. The results of this study can be applied in the development of phytotherapeutic creams and gels intended for the prevention and treatment of inflammatory and oxidative skin conditions such as eczema, dermatitis, and minor wounds. The optimized formulations (No. 3, 5, 7) demonstrated stable physicochemical parameters and are suitable for further pharmacological evaluation and potential cosmetic use.

Research limitations. The main limitation of this study is that the pharmacological activity of the developed formulations was not assessed through comprehensive *in-vitro* or *in-vivo* biological testing. The present research focused primarily on physicochemical characterization, formulation optimization, and stability evaluation. Therefore, further *in-vivo* pharmacological and clinical investigations are required to substantiate the therapeutic efficacy, bioavailability, and safety of the proposed creams.

Prospects for further research. Future research will focus on detailed bioavailability studies, antioxidant and anti-inflammatory activity assessment in animal models, and the incorporation of other synergistic plant extracts to enhance the therapeutic potential of *Carthamus tinctorius* L.-based formulations.

6. Conclusions

1. A technology for producing a therapeutic-cosmetic cream with liquid *Carthamus tinctorius* L. flower extract, exhibiting pronounced anti-inflammatory and antioxidant activity, was developed.

2. Instrumental analyses (IR spectroscopy, spectrophotometry, and HPLC) confirmed the presence of a wide spectrum of biologically active substances in the extract: polyphenolic compounds, flavonoids (including rutin, content equivalent to 2.2%), and carotenoids (β-carotene), which account for its pharmacological activity.

3. HPLC analysis revealed characteristic peaks, including one at 18.17 min, coinciding with the retention time of rutin (18.20 min), confirming its presence in the extract.

4. Spectrophotometric analysis at ~450 nm confirmed the presence of β-carotene, with an optical density (A = 4.35) significantly exceeding that of the standard (A = 0.60), indicating a high carotenoid content.

5. Of the eight developed cream formulations, only samples No. 3, 5, 7 demonstrated satisfactory quality indicators (homogeneity, thermostability, colloidal stability, pH) and can be recommended for further pharmacological evaluation and practical application.

Conflict of Interest

The authors declare that they have no conflict of interest in relation to this research, whether financial, personal, authorship, or otherwise, that could affect the research and its results presented in this article.

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Data availability

Data will be made available on reasonable request from the corresponding author.

Use of artificial intelligence

The authors declare the use of generative AI in the research and preparation of the manuscript. Tasks dele-

gated to generative AI tools under full human supervision: language editing and grammar correction; improvement of academic style and formatting;

Generative AI tool used: ChatGPT (OpenAI GPT-5, 2025 version).

The authors bear full responsibility for the content and final version of the manuscript.

Generative AI tools are not credited as authors and are not responsible for the research outcomes.

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Authors' contributions

Nilufar Rizaeva: Conceptualization, Supervision, Methodology, Validation; **Gulrano Akhmadova:** Investigation, Data curation, Writing – original draft, Visualization; **Dilnoza Bakhriddinova:** Formal analysis, Experimental work, Data processing; **Munojat Akhmedova:** Methodology, Visualization, Literature review; **Nozima Aripova:** Validation, Review and Editing; **Irodakhon Sharipova:** Resources, Technical supervision; **Nigora Azlarova:** Experimental support, Data verification; **Umida Anarmetova:** Literature search, Data interpretation.

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