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A.D. Moldashi[1], Y. Sailaukhanuly[2], S. Azat[2], K. Toshtay[3], N. Nurgaliyev[4]*
[1]GEMS International School Al Khail, 246587, Dubai, UAE, Exit 18 Al Khail Road
[2]Satbayev University, 050013, Almaty, Kazakhstan, Satbayev str. 20
[3]Al-Farabi Kazakh National University, Almaty, Kazakhstan, Al-Farabi 97
[4]Shakarim University, 071412, Semey, Kazakhstan, Glinki str. 20
e-mail: adilyamoldash7@gmail.com

DEVELOPMENT AND STANDARDIZATION OF A CARAMEL DOSAGE FORM BASED ON *ARTEMISIA ANNUA L.* MEDICINAL PLANT RAW MATERIALS

Abstract: *Acute respiratory viral infections (ARVIs) represent one of the most prevalent infectious diseases worldwide, with the COVID-19 pandemic further highlighting the critical need for novel therapeutic alternatives. Recent in vitro studies demonstrated inhibitory activity of Artemisia annua L. ethanolic extracts against SARS-CoV-2 through synergistic multi-component mechanisms. This study aimed to develop a standardized medicated caramel lozenge based on bioactive extracts of Artemisia annua L. using isomalt as the pharmaceutical base, in compliance with the State Pharmacopoeia of the Republic of Kazakhstan (SP RK). Raw material was collected during peak flowering in July-August 2025 at the Ile Alatau foothills, Almaty region, Kazakhstan. Physicochemical characterization confirmed mass loss on drying of 6.5%, extractive substance content of 40.2%, and complete absence of heavy metals by atomic absorption spectrometry. Essential oil yield was 0.4% (v/w, dry basis), with 1,8-cineole constituting 8.6% by gas chromatography-mass spectrometry (GC-MS). GC-MS profiling of the ethanolic extract identified more than 50 bioactive compounds, with Camphor (9.35%) and 1,8-cineole (8.60%) as predominant constituents. The detection of Squalene, a triterpene hydrocarbon with antimicrobial, antifungal, and immunostimulatory properties, is of particular significance. The optimal 1:2 extract-to-isomalt ratio produced a thermally stable, ethanol-free, diabetic-compatible dosage form meeting all five SP RK standardization parameters: organoleptic properties, mass uniformity (average mass 1.7084 g; maximum deviation <0.05%), disintegration (<10 min), and water content (<2.0%). The developed formulation represents a stable and accessible alternative to tincture-based delivery, suitable for pediatric, elderly, and diabetic populations.*

Key words: *Artemisia annua L., Annual Wormwood, medicated caramel, lozenge, isomalt, 1,8-cineole, phytopreparation, SARS-CoV-2.*

1. Introduction

Acute respiratory viral infections (ARVIs) represent one of the most prevalent and socioeconomically significant groups of infectious diseases worldwide, recording millions of new cases annually and accounting for billions of lost working days each year. Despite decades of pharmaceutical advancement, the range of targeted antiviral treatments for respiratory infections remains narrow, with current approaches largely relying on symptomatic relief. The COVID-19 pandemic, caused by the SARS-CoV-2 coronavirus, brought the limitations of existing antiviral therapies into sharp focus on a global scale.

In this context, medicinal plants have attracted renewed scientific interest as potential sources of novel therapeutic agents. Kazakhstan possesses exceptional reserves of medicinal plant raw materials, with more than 1,300 species documented across its territory, among them 81 species of the genus *Artemisia L.*, characterized by a wide geographical distribution and a substantial raw material base [1]. Among these, *Artemisia annua L.*, or Annual Wormwood, has emerged as a subject of particular scientific interest, valued for its antipyretic, anthelmintic, anti-inflammatory, antifungal, antiparasitic, and cytotoxic properties [2-3]. Its principal bioactive constituents include essential oils, organic acids, fatty acids, and tannins, with an essential oil yield ranging from 0.1 to 0.64% [4]. The variability of the chemical composition of its essential oils has been shown to depend on geographical origin and the developmental stage of the plant at the time of harvest [6-9]. The biological activity of *Artemisia annua L.* essential oils and extracts is well documented in the literature.

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Of particular relevance, research published in *Scientific Reports* demonstrated that both hot water and ethanol extracts of *Artemisia annua L*. are active against SARS-CoV-2 in vitro, across seven varieties sourced from four continents [10]. Antiviral effectiveness correlated inversely with artemisinin content, suggesting that viral inhibition results from synergistic action among multiple phytochemical constituents rather than a single compound [10].

Despite this therapeutic potential, the most common delivery form – the alcohol water tincture – presents significant practical limitations, including the requirement for precise dosing, dilution, and special storage conditions [11]. Caramel medicinal forms represent a promising alternative, offering gradual release of active substances directly at the site of action, inherent stability without preservatives, and significantly greater convenience of use, particularly for pediatric and elderly patient populations [11-12].

This study aimed to develop a standardized medicated caramel lozenge based on bioactive extracts of *Artemisia annua L.,* using isomalt as the pharmaceutical base. The study encompasses: identification and physicochemical characterization of the raw material; determination of extractive substance content and essential oil yield; quantitative analysis of 1,8-cineole (1); chromatographic profiling by GC-MS; development of the caramel formulation technology; and standardization of the finished dosage form in accordance with the requirements of the State Pharmacopoeia of the Republic of Kazakhstan (SP RK).

2. Experiment

All physicochemical characteristics were recorded using the following instrumentation: a drying oven (Memmert UF55, Germany) for mass loss determination; an atomic absorption spectrometer (AADuo55B/240Z, Analytik Jena, Germany) for heavy metal analysis; and an Agilent Technologies 6890 gas chromatograph equipped with a 5973 mass spectrometric detector (Agilent Technologies, USA) for chromatographic analysis. All reagents were of analytical grade and obtained from commercial suppliers. The SP RK Vol. 1 served as the primary regulatory reference for all analytical procedures [13].

2.1 Collection and Identification of medicinal plant raw materials

Artemisia annua L. raw material was collected during mass flowering in July-August 2025 at the foothills of the Ile Alatau, Almaty region, Republic of Kazakhstan, in accordance with Good Agricultural and Collection Practice (GACP). Above-ground parts were harvested before 10:00 AM by cutting at 10-15 cm from the ground, dried in the shade at 30 ± 5°C in uniform layers of 10-15 cm, and turned periodically. Verification was performed through macroscopic and microscopic analysis in accordance with SP RK Vol. 1, «Herbs» monograph [13].

2.2 Determination of mass loss on drying

Five portions of 1.0 g of crushed raw material (particle size ~10 mm) were placed into pre-dried tared weighing bottles and dried in a drying oven (Memmert UF55) at 100–105°C to constant mass in accordance with SP RK Vol. 1 [13]. Mass loss on drying (X, %) was calculated as:

$$X = \frac{(m_{before} - m_{after}) \times 100}{m_{before}}$$

where m $before$ and m $after$ are the masses of raw material before and after drying (g), respectively. The average mass loss on drying was 6.5%.

2.3 Determination of heavy metals

Heavy metal content was determined by atomic absorption spectrometry (AAS; AADuo55B/240Z, Analytik Jena) in accordance with SP RK Vol. 1, Article 2.2.23 [13]. Test solutions were prepared by microwave digestion of 0.50 g of crushed raw material in 6.0 mL of heavy metal-free HNO_3 and 4.0 mL of heavy metal-free HCl (80% power, 15 min; 100% power, 5 min; 80% power, 20 min), followed by addition of 4.0 mL of heavy metal-free H_2SO_4. Each digest was transferred quantitatively to a 50.0 mL volumetric flask with 1.0 mL of $Mg(NO_3)_2$ solution (10 g/L) and 1.0 mL of $NH_4H_2PO_4$ solution (100 g/L), diluted to volume with deionized water. Seven parallel test solutions were prepared. Calibration curves were constructed from a minimum of three reference solutions per target element; each solution was measured in triplicate. No heavy metals were detected in any analyzed sample.

2.4 Determination of extractive substances in the medicinal plant raw material

Approximately 3.0 g of crushed raw material (passed through a 1 mm sieve) was refluxed with 50.0 mL of 70% EtOH (ethanol; CAS No. 64-17-5; analytical grade, commercial preparation) in

a 250 mL ground-glass flask for 2 hours. Following filtration, 25.0 mL of filtrate was evaporated to dryness in a tared porcelain dish, dried at 102.5 ± 2.5°C to constant mass, and cooled in a desiccator for 30 min. Extractive substance content (X, %) on a dry basis was calculated as:

$$\mathrm{X} = \frac{m \text{ x } 200 \text{ x } 100}{m_1(100 - \mathrm{W})}$$

where m is the mass of the dry residue (g); m_1 is the sample mass (g); and W is the mass loss on drying (%). The average extractive substance content was 40.2%.

2.5 Determination of essential oils

Essential oil content was determined by steam distillation using a Clevenger-type apparatus in accordance with SP RK Vol. 1 [13]. A sample of crushed raw material was placed in a 1000 mL round-bottom flask with 300 mL of deionized water and refluxed for 30 minutes. Xylene (analytical grade, commercial preparation) was used in the graduated receiving tube (graduation scale 0.025 mL) to absorb the distilled oil, with the aqueous phase returned automatically to the flask. Essential oil content (X, %) on a dry basis was calculated as:

$$\mathrm{X} = \frac{V \text{ x } 100 \text{ x } 100}{\mathrm{m}(100 - \mathrm{W})}$$

where V is the volume of essential oil (mL); m is the sample mass (g); W is the mass loss on drying (%). The essential oil yield was determined to be 0.4%, which falls within the documented literature range of 0.1-0.64% for this species [4].

2.6 Quantitative determination of 1,8-cineole in essential oils

1,8-Cineole (1) (eucalyptol; 1,3,3-trimethyl-2-oxabicyclo [2.2.2]octane; CAS No. 470-82-6) was quantified by GC-MS on an Agilent Technologies 6890 gas chromatograph with a 5973 mass spectrometric detector in accordance with SP RK Vol. 1, Article 2.8.11 [13]. Sample preparation: 2.5 mL of essential oil was dissolved in $CHCl_3$ and adjusted to 50.0 mL. Chromatographic conditions: column DB-5 (30 m × 0.25 mm × 0.25 μm); carrier gas He (purity ≥ 99.999%), flow rate 1.2 mL/min; injector temperature 250°C; column temperature program 50→320°C at 4°C/min; splitless mode; Scan detection. Compound identification was performed against the NIST 05 and WILEY libraries (>470,000 spectra) using AMDIS and NIST programs. Content of (1) (X, %) was calculated as:

$$x = \frac{S_x \text{ x } 100}{\sum S_x}$$

where S_x is the peak area value of (**1**); $\sum S_x$ is the sum of the areas of all major peaks in the chromatogram. The content of (**1**) in the essential oil was 8.6%.

2.7 Preparation of extracts from *Artemisia annua L*. herb

Ethanolic extracts were prepared by maceration of raw material (particle size 3-5 mm) in 70% EtOH (ethanol; CAS No. 64-17-5; analytical grade, commercial preparation) at ambient temperature. Following maceration, the extract was decanted, the marc pressed, and the combined extract allowed to settle for 24 hours at ≤ 25 ± 5°C. The clarified extract was filtered through «blue ribbon» filter paper (analytical grade, commercial preparation) and stored at 4°C.

The chemical composition of the extract was determined by GC-MS on an Agilent 7890 gas chromatograph with a 5977 mass spectrometric detector and flame ionization detector (Agilent Technologies, USA) [13-14]. Chromatographic conditions: column HP-5 (30 m × 0.25 mm × 0.25 μm); carrier gas He (purity ≥ 99.999%), flow rate 1.2 mL/min; sample injection heater temperature 250°C; column thermostat temperature program – from 50°C to 320°C at a rate of 4°C/min; splitless injection mode; Scan detection. Compound identification was performed against the NIST 05 and WILEY libraries (>470,000 spectra) using AMDIS and NIST programs [13-14]. Results are presented in Figure 1 and Table 1.

2.8 Caramel formulation development

The optimal formulation ratio of *Artemisia annua L*. extract to isomalt (2) ((3R,4R,5R)-6-[(2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxyhexane-1,2,3,4,5-pentol; CAS No. 64519-82-0; E953) was established as 1:2 (v/w) – 10.0 mL extract and 20.0 g of 2 per batch – following preparative experiments evaluating crystallization behavior, texture, and organoleptic properties. Isomalt (2) was selected over sucrose due to its reduced crystallization tendency, moisture resistance, low glycemic index, and approval by JECFA, WHO, and the EEC Scientific Committee on Food [15]. Safe daily doses are up to 50 g for adults and 25 g for children [15].

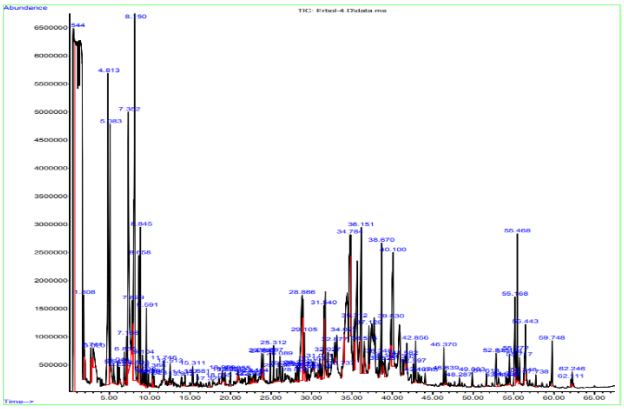


Figure 1 – Chromatogram of the *Artemisia annua* L. annual wormwood extract

Table 1 – Component composition of the annual wormwood extract

№	Retention Time, min	Composition, %	Compound Name	№	Retention Time, min	Composition, %	Compound Name
1	1.8	1.53	Pyrrolidine	24	30.1	0.11	Aromadendrene
2	3.0	0.63	α-Pinene	25	30.8	0.14	Isovelleral
3	4.8	8.6	1,8-Cineole	26	31.0	0.22	Camphene
4	5.5	0.33	Sabinene hydrate	27	31.5	1.77	Hexadecanoic acid
5	6.2	0.22	Terpineol	28	32.0	0.38	Falcarinol
6	6.8	0.29	4-Thujanol	29	35.3	1.22	Longifolene
7	7.1	0.81	Sabinol	30	36.1	3.21	Achillin
8	8.1	9.35	Camphor	31	38.6	1.87	Patchoulane
9	8.5	0.13	Pinocarvone	32	39.1	0.36	α-Cadinol
10	9.1	0.33	terpinen-4-ol	33	41.5	0.48	α-Bisabolene
11	9.3	0.20	Carveol	34	42.5	0.23	1-Heptacosanol
12	9.6	0.89	Fenchol	35	44.0	0.16	Docosanoic Acid
13	10.3	0.25	Dihydrocoumarin	36	48.2	0.11	Squalene
14	10.5	0.15	2,3-Pinanediol	37	51.6	0.16	Brucine
15	11.7	0.24	3,5-dimethylphenol	38	53.1	0.26	α-Tocopherol
16	12.5	0.29	Fumaric acid	39	54.2	0.13	Cirsimaritin
17	13.9	0.20	Citral	40	54.4	0.46	Stigmasterol
18	14.3	0.15	Eugenol	41	55.1	1.86	4,5-dihydroxy-3,6,7-trimethoxyflavone
19	15.3	0.33	Verbenol	42	55.2	0.41	Eriostemin
20	22.4	0.14	α-Selinene	43	55.4	2.12	γ-Sitosterol
21	23.8	0.36	Caryophyllene	44	56.4	1.04	Taraxasterol
22	24.0	0.32	Bisabolol	45	59.7	0.67	Neophytadiene
23	24.8	0.38	Chamazulene				

Silicone molds were cleaned with 70% EtOH and treated with silicone oil. Isomalt (2) (20.0 g) was dissolved in deionized water and heated to 140°C until caramelization, verified by cold water drop test. The mass was cooled to 90°C under running water to prevent crystallization. The *Artemisia annua L*. extract (10.0 mL), pre-heated to 80°C in a water bath to ensure complete evaporation of the ethanol vehicle, was added and stirred until homogeneous. The caramel mass was poured into molds, cooled at ambient temperature until solidification, and demoulded. Although 1,8-cineole and camphor are unstable, they do not completely evaporate and their composition is determined after the dosage form has been obtained. The technological scheme for caramel production is presented in Figure 2.

2.9 Standardization of caramels

Finished caramel medicinal products were standardized in accordance with SP RK Vol. 1 [13], EP, and USP across five quality parameters.

Organoleptic properties were assessed by visual inspection and sensory evaluation. Products presented as round lozenges (~1 cm diameter), brown to dark caramel in color, with a smooth surface and pleasant sweet taste. All characteristics were within acceptable limits.

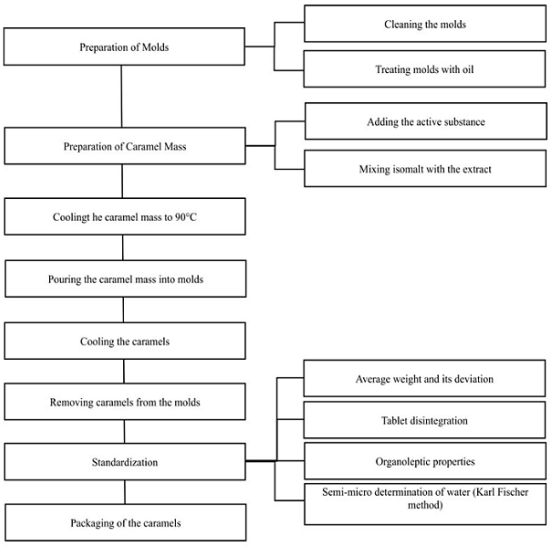


Figure 2 – Technological scheme for obtaining caramels

Mass uniformity was determined using a calibrated analytical balance (±0.0001 g) on 20 individually weighed units in accordance with SP RK Article 2.9.5 [16]. The average mass (M_{avg}) and deviations of minimum (M_{min}) and maximum (M_{max}) individual masses were calculated as:

$$M_{avg} = \frac{M_1 + M_2 + \cdots + M_{20}}{20} \;;\; M_{min} = \frac{M_{min} - M_{avg}}{M_{min}} \text{ x } 100 \;;$$

$$M_{max} = \frac{M_{max} - M_{avg}}{M_{max}} \text{ x } 100$$

Individual masses are presented in Table 2. The average mass was 1.7084 g; no unit deviated by more than 0.05% from the average, well within the 5% acceptance limit of SP RK Article 2.9.5 [13].

Table 2 – Individual masses of 20 units of the caramel dosage form

1	2	3	4	5	6	7	8	9	10
1.7083	1.7082	1.7081	1.7085	1.7087	1.7081	1.7086	1.7088	1.7085	1.7082
11	12	13	14	15	16	17	18	19	20
1.7083	1.7084	1.7081	1.7082	1.7087	1.7086	1.7088	1.7083	1.7085	1.7083

Disintegration was tested using an Erweka disintegration tester (Erweka GmbH, Germany) in deionized water at 37 ± 0.5°C in accordance with SP RK Article 2.9.1 [16]. All six units disintegrated completely within 10 minutes, within the 15-minute acceptance limit.

Water content was determined by semi-micro Karl Fischer titration in accordance with SP RK Vol. 1 [13], using Karl Fischer reagent and anhydrous MeOH (CAS No. 67-56-1), with amperometric endpoint detection under dry N_2 atmosphere, based on the following reactions:

$$SO_2 + I_2 + H_2O \leftrightarrow SO_3 + 2HI \quad (1)$$

$$C_5H_5N + SO_3 \rightarrow [C_5H_5N]^+[SO_3]^- \quad (2)$$

$$[C_5H_5N]^+[SO_3]^- + MeOH \rightarrow [C_5H_5NH]^+[MeOSO_3]^- \quad (3)$$

Water content was below 2.0% in all samples, confirming compliance with SP RK requirements [13]. The water content of all analyzed caramel samples was determined to be below 2.0%, meeting the acceptance criterion for moisture content in solid dosage forms as specified by SP RK requirements [16]. This result confirms the long-term stability of the formulation with respect to moisture-induced degradation.

Packaging: Hard caramel dosage forms are inherently hygroscopic and highly susceptible to absorption of atmospheric moisture, which can compromise both the physical integrity and chemical

stability of the finished product. To preserve product quality throughout storage, the caramel medicinal products were individually wrapped in cellophane film and subsequently sealed in plastic bags, providing a dual moisture barrier. The finished medicinal products are recommended to be stored in a dry, dark location at ambient temperature, out of reach of children. A mandatory warning statement, «Keep out of reach of children», is required on the packaging, in accordance with pharmaceutical labeling requirements for caramel dosage forms [11].

3. Results and Discussion

Artemisia annua L. raw material collected at the Ile Alatau foothills was verified against SP RK Vol. 1 macroscopic and microscopic standards, conforming fully to the «Herbs» monograph requirements [11], consistent with previously published morphological data [4]. Mass loss on drying was 6.5%, within the acceptable range for dried herbal materials per SP RK Vol. 1 [13] and consistent with previously reported values for *Artemisia annua L*. harvested under analogous conditions [5]. Heavy metal analysis by AAS confirmed complete absence of heavy metals across all seven analyzed samples, consistent with heavy metal screening data for *Artemisia* species from mountainous Central Asian regions [1], confirming the pharmaceutical suitability of the Ile Alatau collection site. Extractive substance content was 40.2% (w/w, dry basis) – notably higher than the 20-35% typically reported for *Artemisia* species [6-9], likely attributable to collection during peak flowering and controlled drying conditions. This suggests the Ile Alatau population of *Artemisia annua L.* represents a particularly rich source of extractable bioactive material. Essential oil yield was 0.4% (v/w, dry basis), consistent with values reported by Ćavar et al. [8] and Li et al. [5] for flowering-phase material, and falling within the upper-middle range of documented literature values of 0.1-0.64% [4]. Essential oil yield variability due to altitude, soil composition, and climate is acknowledged [6-9]. 1,8-Cineole (1) constituted 8.6% of the essential oil fraction, consistent with previously published data for *Artemisia annua L*. across multiple geographical populations [5, 8]. As a monocyclic monoterpene oxide with well-documented expectorant, antiseptic, and bronchodilatory properties [6], (1) is an active ingredient in several approved respiratory pharmaceutical preparations, confirming its direct therapeutic relevance to this formulation. Absolute quantification using an external standard is recommended in future studies to establish precise pharmacopoeial specification limits for *Artemisia annua L*. raw material of Kazakhstani origin.

GC-MS analysis identified 45 quantifiable compounds (Table 1); additional low-abundance peaks of insufficient identification confidence brought the total to more than 50, consistent with the chemically complex profile previously reported for this species [6-10]. The predominant constituents were Camphor (9.35%) and 1,8-Cineole (8.60%), followed by Achillin (3.21%), γ-Sitosterol (2.12%), and Patchoulane (1.87%), consistent with previously published GC-MS profiles of ethanolic *Artemisia annua L.* extracts [5,8]. The detection of Chamazulene (0.38%) is noteworthy, since this sesquiterpene is absent in the intact plant and forms during extraction through thermal decomposition of its precursor matricin [6], confirming correct extraction conditions. Its well-documented anti-inflammatory activity through inhibition of leukotriene biosynthesis further supports the anti-inflammatory therapeutic profile of this extract [6]. Of particular significance is the detection of Squalene (3) ((6E,10E,14E,18E)-2,6,10,15,19,23-hexamethyltetracosa-2,6,10,14,18,22-hexaene; CAS No. 111-02-4; 0.11%; retention time 48.2 min), a triterpene hydrocarbon with documented antimicrobial, antifungal, anticarcinogenic, and immunostimulatory properties, already utilized as an adjuvant in approved vaccine formulations [10]. Its presence opens compelling directions for future antiviral pharmacological investigation.

The diverse chemical profile – spanning terpenoids, sterols, flavonoids, organic acids, and fatty acids – is consistent with the hypothesis of synergistic multi-component antiviral activity proposed by Zhou et al. [10], who demonstrated that *Artemisia annua L.* antiviral effectiveness against SARS-CoV-2 correlated inversely with artemisinin content. The absence of artemisinin (CAS No. 63968-64-9) from the chromatographic profile may reflect its low concentration in the Kazakhstani population or limitations of the GC-MS method; targeted quantification by HPLC is recommended in future studies.

The optimal formulation ratio of *Artemisia annua L*. ethanolic extract to isomalt was established as 1:2 (v/w), corresponding to 10.0 mL of extract and 20.0 g of isomalt per batch. This ratio was selected on the basis of a series of preparative experiments evaluating crystallization behavior, physical texture, and organoleptic properties. Higher extract concentrations resulted in unacceptable viscosity and impaired mold filling, while lower concentrations produced a product with

insufficient therapeutic content. The 1:2 ratio produced a caramel mass of optimal viscosity at 90°C, amenable to clean mold filling and complete solidification at ambient temperature. The selection of isomalt over sucrose was justified by its lower crystallization tendency, critical for maintaining the amorphous glassy structure of hard caramel dosage forms [11-12], and its poor gastrointestinal absorption, rendering the formulation suitable for diabetic patients – clinically important given that respiratory infections disproportionately affect metabolically vulnerable populations [15]. These advantages are consistent with previously published evaluations of isomalt-based lozenge formulations [12]. Complete evaporation of the 70% EtOH vehicle was ensured by sequential thermal treatment – heating the extract to 80°C prior to incorporation, followed by addition to the 90°C caramel mass – confirming that the finished dosage form is ethanol-free. The absence of post-formulation GC-MS analysis to confirm retention of volatile terpenoids, particularly Camphor and 1,8-Cineole, following thermal processing is acknowledged as a limitation; post-formulation characterization is proposed as a future research priority.

All five standardization parameters met SP RK Vol. 1 acceptance criteria [13]. Mass uniformity across 20 units yielded an average mass of 1.7084 g with a maximum deviation of less than 0.05%, substantially below the 5% SP RK limit [13] comparing favorably with analogous isomalt-based lozenge formulations [12] and confirming manufacturing reproducibility. Complete disintegration within 10 minutes, well within the 15-minute SP RK limit, is consistent with the high aqueous solubility of (2), and is pharmacokinetically advantageous for maximizing contact of active constituents with the oral and pharyngeal mucosa. Water content below 2.0% confirmed by Karl Fischer titration is consistent with the known hygroscopic resistance of (2) relative to sucrose-based systems [15], validating the dual cellophane-and-plastic packaging strategy.

4. Conclusion

This study successfully developed a standardized medicated caramel lozenge based on bioactive extracts of *Artemisia annua L*. – a medicinally significant plant species abundantly distributed across Kazakhstan – in compliance with SP RK requirements, addressing the need for accessible therapeutic alternatives in the context of respiratory viral infections including COVID-19.

Physicochemical characterization of the raw material confirmed a mass loss on drying of 6.5%, an extractive substance content of 40.2%, notably higher than values typically reported for *Artemisia* species, and complete absence of heavy metals. Essential oil yield was 0.4% (v/w, dry basis), with 1,8-cineole constituting 8.6% of the essential oil fraction. GC-MS profiling identified more than 50 bioactive compounds in the ethanolic extract, with Camphor (9.35%) and 1,8-cineole (8.60%) as predominant constituents. The detection of Squalene, a triterpene hydrocarbon with antimicrobial, antifungal, and immunostimulatory properties, is of particular significance for future antiviral therapeutic development.

The optimal 1:2 (v/w) extract-to-isomalt formulation produced a thermally stable, ethanol-free, diabetic-compatible dosage form that met all five standardization parameters — organoleptic properties, mass uniformity (average mass 1.7084 g; maximum deviation <0.05%), disintegration (<10 min), and water content (<2.0%) – confirming full pharmacopoeial compliance and manufacturing reproducibility.

The developed formulation represents a practically accessible and stable alternative to conventional tincture-based delivery, with particular suitability for pediatric, elderly, and diabetic patient populations. The comprehensive chemical profile established for *Artemisia annua L*. of Kazakhstani origin contributes to the broader understanding of the phytochemical diversity of this species and provides a basis for future investigation of synergistic multi-component antiviral mechanisms. Future research should prioritize post-formulation GC-MS characterization, accelerated stability studies, artemisinin quantification by HPLC, toxicological evaluation, and clinical trials to establish therapeutic efficacy and dosage recommendations.

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А.Д. Молдаши[1], Е. Сайлауханулы[2], С. Азат[2], К. Тоштай[3], Н. Нургалиев[4]*
[1]GEMS International School Al Khail, 246587, Дубай, ОАЭ, ул. .Al Khail 18
[2]Satbayev University, 050013, Алматы, Казахстан, ул.Сатпаева 20
[3]Казахский национальный университет,
050040, Алматы, Казахстан, Аль-Фараби проспект 71
[4]Шәкәрім университет, 071412, Семей, Казахстан, ул. Глинки, 20
e-mail: adilyamoldash7@gmail.com

РАЗРАБОТКА И СТАНДАРТИЗАЦИЯ ЛЕКАРСТВЕННОЙ ФОРМЫ КАРАМЕЛИ НА ОСНОВЕ ЛЕКАРСТВЕННОГО РАСТИТЕЛЬНОГО СЫРЬЯ *ARTEMISIA ANNUA L.*

Острые респираторные вирусные инфекции (ОРВИ) являются одними из наиболее распространённых инфекционных заболеваний в мире, а пандемия COVID-19 дополнительно подчеркнула острую необходимость в разработке новых терапевтических альтернатив. Недавние исследования in vitro продемонстрировали ингибирующую активность этанольных экстрактов

Artemisia annua L. в отношении SARS-CoV-2 посредством синергетических многокомпонентных механизмов. Целью настоящего исследования являлась разработка стандартизированной лекарственной карамели на основе биоактивных экстрактов Artemisia annua L. с использованием изомальта в качестве фармацевтической основы, в соответствии с требованиями Государственной фармакопеи Республики Казахстан (ГФ РК), Европейской фармакопеи и Фармакопеи США. Лекарственное растительное сырьё было собрано в период массового цветения в июле-августе 2025 года у подножия хребта Иле Алатау, Алматинская область, Казахстан. Физико-химическая характеристика подтвердила потерю массы при высушивании 6,5%, содержание экстрактивных веществ 40,2% и полное отсутствие тяжёлых металлов по данным атомно-абсорбционной спектрометрии. Выход эфирного масла составил 0,4% (об./м., в пересчёте на абсолютно сухое сырьё), при этом содержание 1,8-цинеола составило 8,6% по данным газовой хроматографии-масс-спектрометрии (ГХ-МС). Профилирование этанольного экстракта методом ГХ-МС позволило идентифицировать более 50 биологически активных соединений, среди которых преобладали камфора (9,35%) и 1,8-цинеол (8,60%). Особое значение имеет обнаружение сквалена, тритерпенового углеводорода, обладающего антимикробными, противогрибковыми и иммуностимулирующими свойствами. Оптимальное соотношение экстракта и изомальта 1:2 позволило получить термически стабильную, не содержащую этанола, совместимую с диабетом лекарственную форму, отвечающую всем пяти параметрам стандартизации ГФ РК: органолептическим свойствам, однородности массы (средняя масса 1,7084 г; максимальное отклонение <0,05%), распадаемости (<10 мин) и содержанию воды (<2,0%). Разработанная лекарственная форма представляет собой стабильную и доступную альтернативу настойкам, пригодную для применения в педиатрической практике, у пожилых пациентов и больных сахарным диабетом.

***Ключевые слова**: Artemisia annua L., однолетняя полынь, лекарственная карамель, пастилка, изомальт, 1,8-цинеол, фитопрепарат, SARS-CoV-2.*

А.Д. Молдаши[1], Е. Сайлауханұлы[2], С. Азат[2], К. Тоштай[3] , Н. Нургалиев[4]*
[1]GEMS International School Al Khail, 246587, Дубай, ОАЭ, Al Khail көшесі 18
[2]Сәтбаев Университеті, 050013, Алматы, Қазақстан, Сатпаева көшесі 20
[3]Әл-Фараби атындағы Каз¥У, 050040, Алматы, Қазақстан, Әл-Фараби даңғылы 71
[4]Шәкәрім университеті, 071412, Қазақстан Республикасы, Семей, Глинки көшесі, 20
e-mail: adilyamoldash7@gmail.com

ARTEMISIA ANNUA L. ДӘРІЛІК ӨСІМДІК ШИКІЗАТЫ НЕГІЗІНДЕ КАРАМЕЛЬ ДӘРІЛІК ФОРМАСЫН ӘЗІРЛЕУ ЖӘНЕ СТАНДАРТТАУ

Жіті респираторлық вирустық инфекциялар (ЖРВИ) әлем бойынша ең кең таралған жұқпалы аурулардың бірі болып табылады, ал COVID-19 пандемиясы жаңа терапевтік баламаларды әзірлеудің өзекті қажеттілігін одан әрі айқындады. Соңғы in vitro зерттеулер Artemisia annua L. этанолдық экстрактларының SARS-CoV-2-ге қарсы синергетикалық көпкомпонентті механизмдер арқылы тежеуші белсенділігін көрсетті. Осы зерттеудің мақсаты Қазақстан Республикасының Мемлекеттік фармакопеясының (ҚР МФ), Еуропалық фармакопея мен АҚШ фармакопеясының талаптарына сәйкес изомальтты фармацевтикалық негіз ретінде пайдалана отырып, Artemisia annua L. биоактивті экстракттары негізінде стандартталған дәрілік карамель пастилкасын әзірлеу болды. Шикізат 2025 жылғы шілде–тамыз айларында жаппай гүлдеу кезеңінде Алматы облысы, Қазақстан, Іле Алатауының етегінде жиналды. Физика-химиялық сипаттама кептіру кезіндегі массасының жоғалуы 6,5%, экстрактивті заттардың мөлшері 40,2% және атомдық-абсорбциялық спектрометрия бойынша ауыр металдардың толық болмауын растады. Эфир майының шығымы 0,4% (к./м., абсолютті құрғақ шикізатқа қайта есептегенде) құрады, бұл ретте 1,8-цинеолдың мөлшері газды хроматография–масс-спектрометрия (ГХ-МС) әдісімен 8,6% құрады. Этанолдық экстрактты ГХ-МС әдісімен профильдеу 50-ден астам биологиялық белсенді қосылысты анықтауға мүмкіндік берді, олардың ішінде камфора (9,35%) және 1,8-цинеол (8,60%) басым болды. Антимикробтық, саңырауқұлаққа қарсы және иммуностимуляциялық қасиеттері бар тритерпен көмірсутегі, сквален анықталуы ерекше маңызға ие. Экстракт пен изомальттың оңтайлы 1:2 қатынасы ҚР МФ стандарттау параметрлерінің барлық бесеуіне сәйкес келетін термиялық тұрақты, этанолсыз, диабетпен үйлесімді дәрілік форманы алуға мүмкіндік берді: органолептикалық қасиеттер, масса біркелкілігі (орташа масса 1,7084 г; ең жоғары ауытқу <0,05%), ыдырау (<10 мин) және су мөлшері (<2,0%). Әзірленген дәрілік форма педиатриялық, егде жастағы және қант диабеті бар науқастарға қолдануға жарамды, тұрақты және қолжетімді балама болып табылады.

***Түйін сөздер:** Artemisia annua L., жылдық жусан, дәрілік карамель, пастилка, изомальт, 1,8-цинеол, фитопрепарат, SARS-CoV-2.*

Information about authors

Adiliya Dinmuhamedkyzy Moldashi – Student, GEMS International School Al Khail; e-mail: adilyamoldash7@gmail.com. ORCID: https://orcid.org/0009-0008-5258-4737.

Yerbolat Sailaukhanuly – PhD, Satpayev University, Senior researcher of the Laboratory of Engineering Profile; e-mail: s.erbolat@mail.ru. ORCID: https://orcid.org/0000-0001-8417-4136.

Azat Seitkhan – PhD, Professor, Satpayev University, Head of the Laboratory of Engineering Profile; e-mail: seytkhan.azat@gmail.com. ORCID: https://orcid.org/0000-0002-9705-7438.

Kainaubek Toshtay – PhD, Associate professor, KazNU named after Al-Farabi, Department of Physical Chemistry, Catalysis, and Petrochemistry; e-mail: kainaubek.toshtay@gmail.com. ORCID: https://orcid.org/0000-0003-1182-7460.

Nurzhan Nurlybekovich Nurgaliyev* – PhD, associate professor-researcher, Shakarim University, Department of Chemistry and Ecology; e-mail: n.nurgaliyev@shakarim.kz. ORCID: https://orcid.org/0000-0003-1216-7150.

Сведения об авторах

Адилия Динмухамедовна Молдаши – студент, Международная школа GEMS Al Khail; e-mail: adilyamoldash7@gmail.com. ORCID: https://orcid.org/0009-0008-5258-4737.

Ерболат Сайлауханулы – PhD, научный сотрудник лаборатории инженерного профиля, Сатпаев университет; e-mail: s.erbolat@mail.ru. ORCID: https://orcid.org/0000-0001-8417-4136

Азат Сейтхан – PhD, Профессор, Директор лаборатории инженерного профиля, Сатпаев университет; e-mail: seytkhan.azat@gmail.com. ORCID: https://orcid.org/0000-0002-9705-7438.

Кайнаубек Тоштай – PhD, Ассоц. профессор, кафедра физической химии, катализа и нефтехимии; e-mail: kainaubek.toshtay@gmail.com. ORCID: https://orcid.org/0000-0003-1182-7460.

Нуржан Нурлыбекович Нургалиев* – PhD, доцент-исследователь, кафедра химии и экологии, Шәкәрім университет, кафедры химии и экологии; e-mail: n.nurgaliyev@shakarim.kz. ORCID: https://orcid.org/0000-0003 1216-7150.

Авторлар туралы мәліметтер

Адилия Дінмұхамедқызы Молдаши – оқушы, GEMS International School Al Khail; e-mail: adilyamoldash7@gmail.com. ORCID: https://orcid.org/0009-0008-5258-4737.

Ерболат Сайлауханулы – PhD, аға ғылыми қызметкер, инженерлік бейінді зертханы, Сатпаев университеті; e-mail: s.erbolat@mail.ru. ORCID: https://orcid.org/0000-0001-8417-4136.

Сейтхан Азат – PhD, профессор, Инженерлік бейінді зертханы басшысы, Сатпаев университеті; e-mail: seytkhan.azat@gmail.com. ORCID: https://orcid.org/0000-0002-9705-7438.

Кайнаубек Тоштай – PhD, Қауымдастырылған профессор, физикалық химия, катализ және мұнайхимия кафедрасы, Әл-Фараби атындағы Қазақ Ұлттық университеті; e-mail: kainaubek.toshtay@gmail.com. ORCID: https://orcid.org/0000-0003-1182-7460.

Нұржан Нұрлыбекұлы Нұрғалиев* – PhD, доцент-зерттеуші, Шәкәрім университеті, Химия және экология кафедрасы; e-mail: n.nurgaliyev@shakarim.kz. ORCID: https://orcid.org/0000-0003 1216-7150.

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Н.К. Ахмадиева[1]*, Е.Б. Абикак[1], Н.М. Бурабаева[2], Т.К. Сагынтаева[1], Н. Оракбай[2]

[1]Институт металлургии и обогащения, 050010, Республика Казахстан, г. Алматы, ул. Шевченко 29

[2]Восточно-Казахстанский технический университет им. Д. Серикбаева,
070004, Республика Казахстан, г. Усть -Каменогорск, ул. Серикбаева, 19

*e-mail: akhmadiyeva141@gmail.com

КАРБОНАТНО-ГИДРОТЕРМАЛЬНАЯ АКТИВАЦИЯ АЛЮМОСИЛИКАТНОГО СЫРЬЯ ДЛЯ ИНТЕНСИФИКАЦИИ ИЗВЛЕЧЕНИЯ ГЛИНОЗЁМА

Аннотация: *В статье приведены результаты исследования карбонатно-гидротермальной активации смеси нефелиновой руды и красного шлама как эффективного способа предварительной активации алюмосиликатного сырья перед щелочным выщелачиванием. Актуальность работы*

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