UDC 615.451.232+615.322:616.348-002
DOI: 10.15587/2519-4852.2024.302941

DEVELOPMENT OF AN EMULSION COMPOSITION WITH FENNEL AND CARAWAY ESSENTIAL OILS FOR USE IN THE COMBINED THERAPY OF ULCERATIVE COLITIS

Oleksandr Shmalko, Tetiana Kovalova, Liubov Bodnar, Volodymyr Kovalov, Volodymyr Iakovenko, Liliia Vyshnevska

The aim *of the study is to develop the composition of an emulsion containing essential oils of Fennel and Caraway seeds for use in the symptomatic complex therapy of ulcerative colitis with the aim of eliminating functional intestinal disorders.*

Materials and methods. *The objects of the study were samples of emulsions containing active pharmaceutical ingredients (essential oils of Fennel and Caraway), purified water, oils (refined sunflower oil, refined olive oil, refined sesame oil), emulsifiers (polyethylene glycol 40 hydrogenated castor oil, polysorbate 80, polyethylene glycol 100 stearate, acacia gum, guar gum, xanthan gum, soya lecithin), viscosity regulator – apple pectin and flavouring agents (food additives with cherry and tarragon flavour).*

Organoleptic properties, stability, rheological parameters, pH, particle size determination by microscopy, and a taste test were carried out with model emulsion samples. Research to establish the optimal technological parameters was carried out in parallel.

Results. *The main parameters of the technological process have been established, which allow to obtain an emulsion with evenly distributed particles: 15 minutes at maximum speed. The concentration of emulsifiers at which the emulsions are stable was selected. It was found that the samples containing polyethylene glycol 100 stearate, gums, and soy lecithin have satisfactory organoleptic properties.*

The sample with soy lecithin emulsifier differs from the others in its ability to form microemulsions, but it has low viscosity. To improve the rheological properties, apple pectin was added to the emulsion.

The taste test showed that among vegetable oils, refined sesame oil has a more neutral taste, and the flavouring additive "Tarkhun" balances the taste better.

The release of active pharmaceutical ingredients (APIs) from the emulsion base was confirmed by thin-layer chromatography.

Conclusions. *A microemulsion with essential oils based on refined sesame oil, soy lecithin, with the addition of viscosity and flavour correctors was developed. The obtained emulsion has satisfactory organoleptic properties and conforms to the requirements for emulsion quality indicators*

Keywords: *ulcerative colitis, intestinal disorders, oral microemulsion, Fennel and Caraway essential oil*

How to cite:
Shmalko, O., Kovalova, T., Bodnar, L., Kovalov, V., Iakovenko, V., Vyshnevska, L. (2024). Development of an emulsion composition with fennel and caraway essential oils for use in the combined therapy of ulcerative colitis. ScienceRise: Pharmaceutical Science, 2 (48), 74–82. doi: http://doi.org/10.15587/2519-4852.2024.302941

1. Introduction

Chronic non-specific ulcerative colitis (UC) is a chronic inflammatory disease of the large intestine, which is characterized by the appearance of ulcers, hemorrhages, and sometimes purulent exudate. Epidemiological data indicate an increase in the incidence rate in urbanized countries. UC is most common among people aged 20 to 40 years, and cases of the disease are also increasing in children [1].

UC has an unknown etiology, a rather wide range of pathogenetic factors. It is characterized by specific intestinal (liquid stools with impurities of mucus, blood, sometimes pus; pain, which is more often localized in the left lower quadrant of the abdomen) and many extraintestinal manifestations. UC often leads to life-threatening complications, including bleeding, stenoses, perforation, or cancer [2].

With a conservative approach, therapy is reduced to pathogenetic and symptomatic. The increase in morbidity, the lack of etiological therapy and the chronic course make it necessary to find new approaches to alleviating the symptoms of the disease, in particular, the development of new drugs [3].

One of the pathological conditions that deserve attention are functional intestinal disorders (FID), because they lead to discomfort, significant pain and complicate the course of the disease. To eliminate FID, medicines in form of suspensions, emulsions and soft gelatin capsules are used, which include simethicone (A03 AX13), and dietary supplements that improve digestion and the functional state of the gastrointestinal tract. Previous studies have confirmed the feasibility of developing a new drug for the treatment of FID based on the essential oil of common fennel [4].

Common fennel essential oil contains anethole, linalool, fenchone, limonene, methylhavicon. Due to the presence of anethole, it has a carminative, anti-inflammatory and bactericidal effect. It is widely used for the symptomatic treatment of functional intestinal disorders. It is part of dill water, which is used to relieve colic in babies [5, 6].

In addition, to ensure the strengthening of the effect, the essential oil of cumin was chosen. Its composition includes carvone, carveol, limonene, dihydrocarvone. In addition to antimicrobial, carminative and anti-inflammatory effects, cumin essential oil has antispasmodic activity [7, 8]. Preparations with the medicinal raw material of cumin and its products are widely used for the treatment of diseases of the gastrointestinal tract, including in medicinal teas in combination with fennel fruits [9].

Considering the convenience of use, the uniform distribution of the active substance in the entire volume of the drug, the possibility of introducing both water-soluble and fat-soluble active pharmaceutical ingredients (API) or auxiliary substances into the composition, an emulsion was chosen as the dosage form.

The SPhU does not list oral emulsions in the Finished Drug section, instead, USP Compounding includes one oral emulsion that uses mineral oil as an emulsifier – gum acacia, flavouring agents – vanillin and syrup, preservative – ethanol, water cleaned [10].

Modern research on the creation of emulsions for internal use is directed to the study of methods of obtaining micro- and nanoemulsions, as well as the introduction into their composition of substances that are difficult to dissolve in the aqueous environment to increase their bioavailability and effectiveness when taken orally [11]. Research aimed at the creation of preparations for the treatment of FID concerns the development of the composition of herbal teas on the one hand [12] and enzymatic preparations in the form of solutions for internal use or syrups – on the other [13]. In an oral emulsion [14], it was possible to combine enzymes with carminative oils, but the development required additional studies to improve stability.

The aim of the study. The development of an emulsion composition, which includes essential oils of common fennel and common caraway, for use in the symptomatic block of UC complex therapy to eliminate FID.

2. Research planning (methodology)

Conducting research on the development of emulsion composition can be divided into three stages. At the first stage, the selection of auxiliary substances was carried out, at the second stage, the optimal parameters of the technological process were established, at the third stage, the quality control of the studied samples was carried out (Fig. 1). The parallel conduct of certain studies is characteristic of the second and third stages.

When planning an experimental study, it is important to establish the reliability of the forecast. Statistical methods of research planning make it possible to determine the level of approximation with 95 % probability [15]. The constructed model of the experiment indicates that the initial parameters of the studied samples depend on several qualitative and quantitative factors (Table 1).

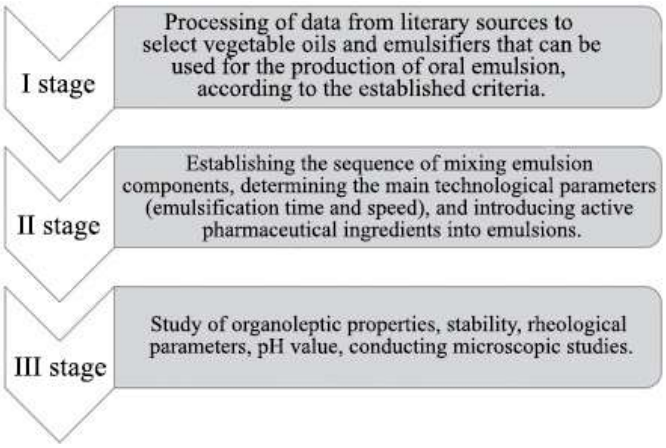


Fig. 1. Characteristics of research stages

Table 1

Model of experimental research

Input parameters ↓						
Quantitative factors (x_{qv})				Qualitative factors (x_{qu})		
Amount of excipients[1]	Emulsification speed[2] (1000–2000 r/min)	Emulsification time[3] (5–15 min)	Temperature[4] (x<40<x °C)	Equipment[1]	The nature of API[2]	The nature of excipients[3]
Equation No. 1	$y^1 \Rightarrow x^1_{qv} \cdot x^3_{qv} \cdot x^1_{qv} \cdot x^2_{qv}$					
Equation No. 2	$y^2 \Rightarrow x^2_{qv} \cdot x^3_{qv} \cdot x^1_{qu} \cdot x^3_{qu}$					
Equation No. 3	$y^3 \Rightarrow x^1_{qv} \cdot x^2_{qu} \cdot x^3_{qu}$					
Equation No. 4	$y^4 \Rightarrow x^1_{qv} \cdot x^3_{qu}$					
Equation No. 5	$x^2_{qv} \cdot x^3_{qv} \Rightarrow x^1_{qu}$					
Equation No. 6	$x^4_{qv} \Rightarrow x^2_{qu}$					
Stability[1]	Particle size[2]		Taste[3]	Viscosity[4]		
Output parameters (y) ↑						

The first four equations traditionally reflect the dependence of each output parameter on the input. In addition, the dependence of some input parameters on each other is observed, in equation No. 5 the dependence of the speed and time of emulsification on the equipment, and in equation No. 6 the dependence of the temperature of the technological process on the nature of the API. Equation No. 6 cannot be neglected, since the selected APIs are essential oils, the temperature of the technological process directly affects the future pharmacological effect of the drug. Instead, equation No. 5 can be reduced

by minimizing the impact of the equipment by choosing a technology using means of small mechanization. Production of emulsions with the help of a homogenizer allows you to speed up the process, increase productivity, compared to manual production, update, and bring the technology closer to the parameters of industrial production, which will further facilitate its scaling.

For equations No. 1–4, considering the quantitative input data, based on the predicted output data, regression models were built using the methods of classical regression analysis, the software is MS Excel 2021 (Fig. 2), and it was established that the level of approximation (R^2) in each of them exceeds the reliability limit (70 %). The experimental research model is reproducible and with a 95 % probability (α=0.05) guarantees reliable results.

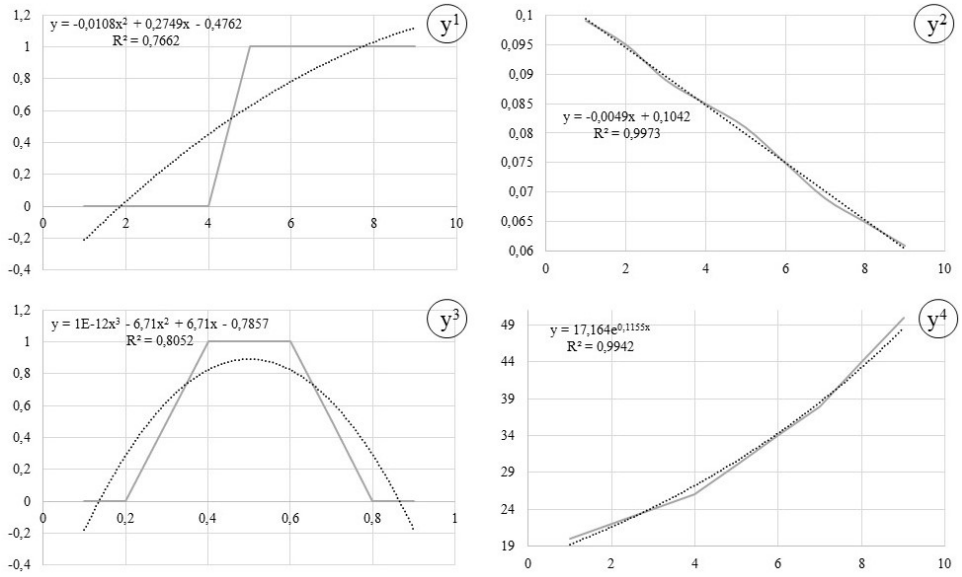


Fig. 2. Regression models of the planned experiment

3. Materials and methods

The study was conducted based on the Department of Pharmacy Technology of Medicines of the National Pharmaceutical University from May to November 2023.

The objects of the study were samples of emulsions, which included active pharmaceutical ingredients: essential oils of common fennel, sweet form of Styx (Austria) and common cumin Vivasan (Switzerland). A well-known drug for the treatment of FID is dill water, which includes API, as in our case, in the form of an essential oil. The drug is recommended for babies and contains 0.05 g of essential oil per 1000 ml of the finished drug. Recalculation of the amount of AFI in the preparation for adults was carried out according to the inverse Clark formula, which takes into account the average body weight of a person to determine the AFI dose: $D=d*70/m$, where D is the dose for adults, d is the dose for children, 70 is the average body weight of an adult, m is the body weight of the child (the average weight of an infant aged 0 to 4 months was taken into account) [16].

It was established that 0.33 g of essential oils should be used to make 50.0 g of emulsion.

Excipients: purified water, vegetable oils, emulsifiers, flavor correctors, viscosity regulator. Among vegetable oils, refined sunflower oil (Ukraine), refined olive oil (Italy) and refined sesame oil (Ukraine) were considered for inclusion in the emulsions being developed [17]. Emulsifiers of the first kind, nonionic surfactants were used: polyethylene glycol 40 hydrogenated castor oil (PEG40GRO), polysorbate 80, polyethylene glycol 100 stearate (PEG100C) [17, 18]; plant-based gelling stabilizers: acacia gum, guar gum, xanthan gum [19, 18]; vegetable phospholipid emulsifier – soy lecithin [19, 20]. Flavor correctors: liquid flavoring food additives "Cherry" (JAR, Poland) and "Tarhun" (Ukraine), which are characterized by a sweet and sour taste. Viscosity regulator – apple pectin (Poland).

Since emulsions for internal and external use have identical quality indicators, methods were used to determine organoleptic properties and stability given in DSTU 4765:2007 "Cosmetic creams. General technical conditions". Thermal stability tests were carried out by thermostating the emulsions at a temperature of 40–42 °C for 24 hours. To study the colloidal stability, after keeping the test samples in a thermostat at a temperature of 42–45 °C for 20 minutes, centrifugation was performed. Device: clinical centrifuge DM 0412, rotation frequency 100 s-1 for 5 min [21].

The size of emulsion particles was determined using a Granum laboratory microscope with a Toupcam UCMOS video camera. Magnification is ×10. Photomicrograph software – ToupView 4.10 from ToupTek. Determination of pH was carried out potentiometrically using a pH-150 MI pH meter [21, 22].

The study of rheological parameters was carried out according to the standard pharmacopeial method on a rotary viscometer with Reotest-2 coaxial cylinders at temperatures of 20±2 °C and 37±2 °C. The study of rheological indicators at a temperature of 37 °C was carried out to study the properties of the emulsion at body temperature and to confirm that these properties do not change when using the emulsion [22].

The taste test was conducted by interviewing 20 volunteer respondents who rated emulsions on a scale from 0 to 5 points, where 0 is no pronounced taste, 5 is rich taste, according to the following criteria:

– "greasy" aftertaste of oil;

– the characteristic taste of the emulsifier;

– characteristic taste of essential oils;

– the characteristic flavour of flavouring additives, cherry or tarragon;

– sweet taste;

– sour taste.

Since the drug under development is intended for oral use, the API release study was conducted in 0.1 M hydrochloric acid at a temperature of 37±0.5 °C. Qualitative analysis of the obtained dialysate was carried out by the method of thin-layer chromatography (TLC) in accordance with the methodology given in the European Pharmacopoeia 8.0 [18]. Conditions for detecting biologically active substances of essential oils: mobile phase – ethyl acetate with toluene 5:95, drying was carried out in air at room temperature, reagents and development conditions were used in accordance with the data given in the pharmacopeial methodology for each of the essential oils.

Statistical processing of the conducted studies was carried out in accordance with the requirements of the Federal State of Ukraine [22]. Software: Excel 2021, StatisticKingdom.

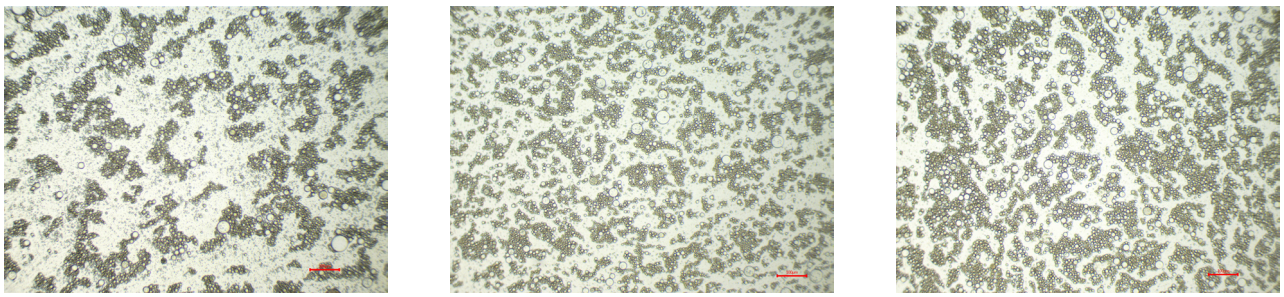
4. Research results

To establish the optimal concentration of the emulsifier, initial studies were carried out with the samples of sunflower oil emulsions in the standard concentration (10 %) shown in Table 2.

Each of the emulsifiers provides characteristic features to technological processes. PEG100C is characterized by heating the oil in a water bath, melting the emulsifier and adding hot purified water to the mixture. A decrease in the temperature of the process leads to the formation of a heterogeneous mixture with white flakes. Emulsions with both PEG40GRO and polysorbate 80 are easily formed at room temperature. Emulsions with gums are characterized by first making an aqueous solution of gums (guar gum at room temperature, acacia and xanthan gum – when heated), then adding oil at room temperature, emulsifying and homogenizing. Soy lecithin has a thick, viscous consistency, so it is important to first prepare a homogeneous oily solution of it, then gradually add purified water to emulsify.

At the same time, on the example of an emulsion with PEG40GRO (sample No. 1), it was established that emulsification for 15 minutes is optimal at a maximum speed of 2000 rpm (homogenizer Eprus U200). The data were confirmed by photomicrographs obtained after 5, 10 and 15 min of emulsification (Fig. 3).

The results of organoleptic studies and the stability of the emulsions formed are shown in Table 3.



a *b* *c*

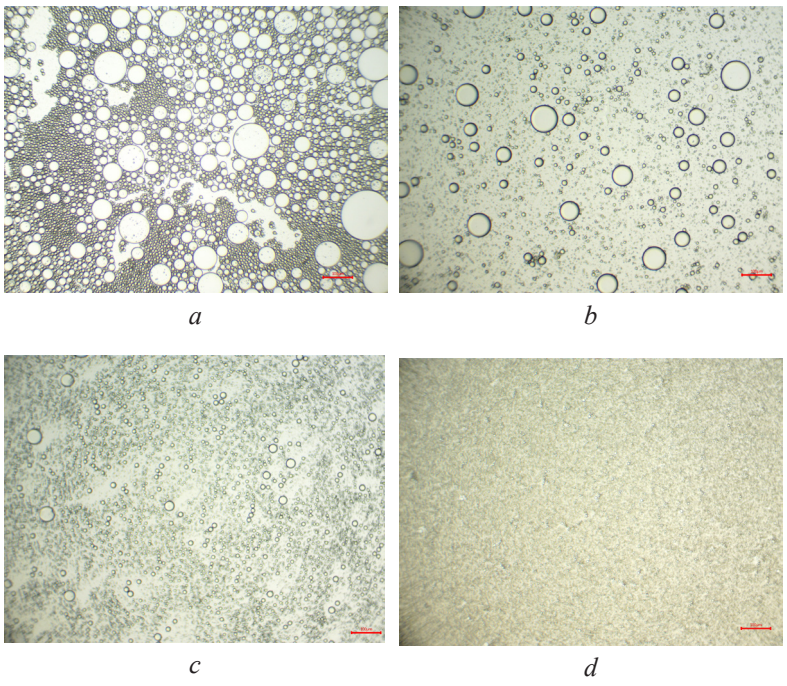
Fig. 3. Photomicrographs of sample #1: *a* – after 5 min; *b* – after 10 min; *c* – after 15 min of emulsification, ×10

Table 2

Compositions of the studied samples of sunflower oil emulsions, g

Composition	Oil	PEG40GRO	Polysorbate 80	PEG100C	Acacia gum	Guar gum	Xanthan gum	Soy lecithin	Purified water
1	5.0	1.0	–	–	–	–	–	–	to 50.0
2	5.0	2.0	–	–	–	–	–	–	to 50.0
3	5.0	4.0	–	–	–	–	–	–	to 50.0
4	5.0	–	0.5	–	–	–	–	–	to 50.0
5	5.0	–	1.0	–	–	–	–	–	to 50.0
6	5.0	–	2.0	–	–	–	–	–	to 50.0
7	5.0	–	–	1.5	–	–	–	–	to 50.0
8	5.0	–	–	2.25	–	–	–	–	to 50.0
9	5.0	–	–	3.0	–	–	–	–	to 50.0
10	5.0	–	–	–	1.0	–	–	–	to 50.0
11	5.0	–	–	–	1.75	–	–	–	to 50.0
12	5.0	–	–	–	2.5	–	–	–	to 50.0
13	5.0	–	–	–	–	0.25	–	–	to 50.0
14	5.0	–	–	–	–	0.375	–	–	to 50.0
15	5.0	–	–	–	–	0.5	–	–	to 50.0
16	5.0	–	–	–	–	–	0.25	–	to 50.0
17	5.0	–	–	–	–	–	0.375	–	to 50.0
18	5.0	–	–	–	–	–	0.5	–	to 50.0
19	5.0	–	–	–	–	–	–	2.5	to 50.0
20	5.0	–	–	–	–	–	–	3.75	to 50.0
21	5.0	–	–	–	–	–	–	5.0	to 50.0

Therefore, samples No. 9, which includes PEG100C (6 %), went to the next stage of research (determining the size of emulsion particles), No. 15, which includes guar gum (1 %), No. 18, which includes xanthan gum (1 %), No. 21, which includes soy lecithin (10 %) (Fig. 4).



a *b* *c* *d*

Fig. 4. Photomicrographs of samples: *a* – No. 9; *b* – No. 15; *c* – No. 18; *d* – No. 21, ×10

Graphs of the dependence of the average size of emulsion particles on emulsification time (Fig. 5) indicate a gradual decrease in particle size with increasing emulsification time.

Compared to other samples, the sample containing soy lecithin (No. 21) has a significantly smaller particle size. In the field of view, which is wide enough, more than 50 % of the particles are smaller than 200 nm, so sample No. 21 is a microemulsion [23].

The conducted comparative study of rheological indicators shows that the consistency of the sample under study is too thin and the need to add a viscosity regulator (Table 4) [24]. For this purpose, apple pectin was used, which was introduced into the aqueous phase before the start of emulsification (samples No. 21.1 with 0.1 % pectin, No. 21.2 with 0.2 % pectin, No. 21.3 with 0.3 % pectin).

For further research (taste test), samples No. 21.2c, No. 21.2m, and No. 21.3k were prepared, which included 10 % of sunflower oil, olive oil, and sesame oil, respectively. At this stage of the research, API (0.33 g of essential oils each) was added to the emulsions, as well as flavouring additives that are water-soluble and are introduced into the aqueous phase before the start of emulsification (in the code of the samples, cherry – v, tarragon – t).

Table 3

Results of primary research

Composition	Organoleptic properties	Thermal stability	Colloidal stability
No. 1–3	Homogeneous liquid of white color, has an unpleasant taste	All samples are stable	All samples are stable
No. 4–6	Homogeneous liquid of white color, has an unpleasant taste	All samples are stable	All samples are stable
No. 7–9	Homogeneous liquid of white color, has a neutral taste	Only sample #9 is stable	All samples are stable
No. 10–12	Homogeneous liquid, grayish-white in color, has a neutral taste	All samples are stable	Only sample #12 is stable
No. 13–15	Homogeneous, slightly thick mass of white color, has a neutral taste	Only sample #15 is stable	All samples are stable
No. 16–18	Homogeneous, slightly thick mass of white color, has a neutral taste	Only sample #18 is stable	Only samples #17, 18 are stable
No. 19–21	Homogeneous liquid, cream-colored, has a neutral taste with a slight aftertaste of soy lecithin	Only sample #21 is stable	All samples are stable

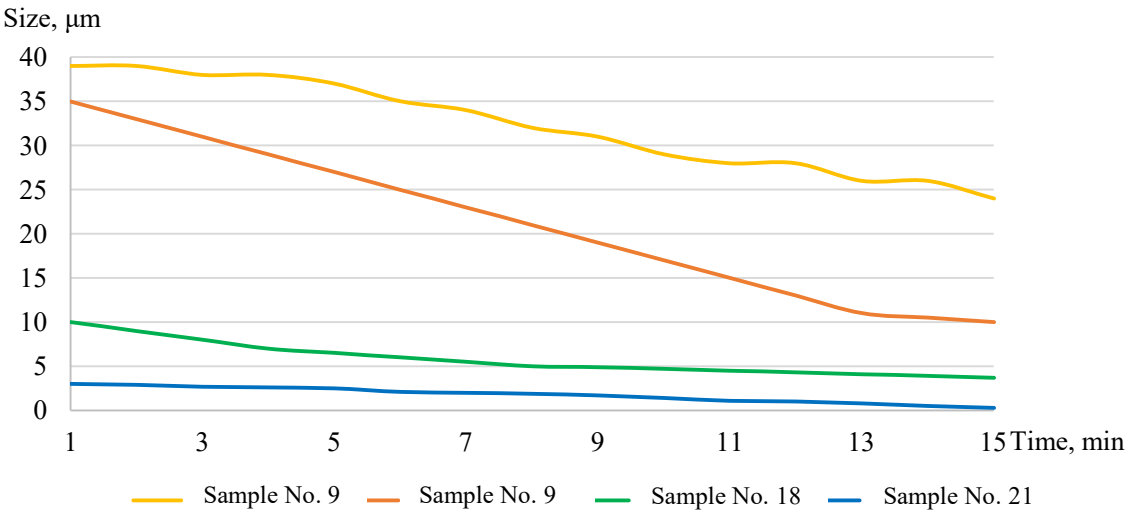


Fig. 5. Graphs of the dependence of the average size of emulsion particles on the emulsification time

Based on the average results of the survey, diagrams were constructed to visualize the taste characteristics of each of the samples (Fig. 6–11).

Table 4

The results of the study of rheological parameters

Sample	mPa·s, t=(20±2) °C	mPa·s, t=(37±2) °C
Reference drug	362±33.9	360±32.9
No. 21	40±3.9	40±3.9
No. 21.1	188±14.4	188±14.4
No. 21.2	354±28.4	350±27.2
No. 21.3	482±34.4	478±28.6

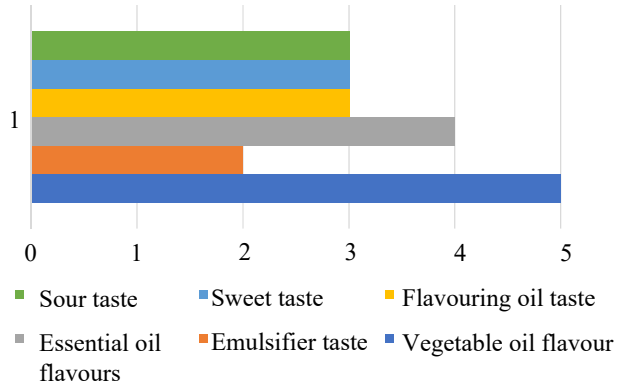


Fig. 6. Taste characteristics of the sample No. 21.2s/t

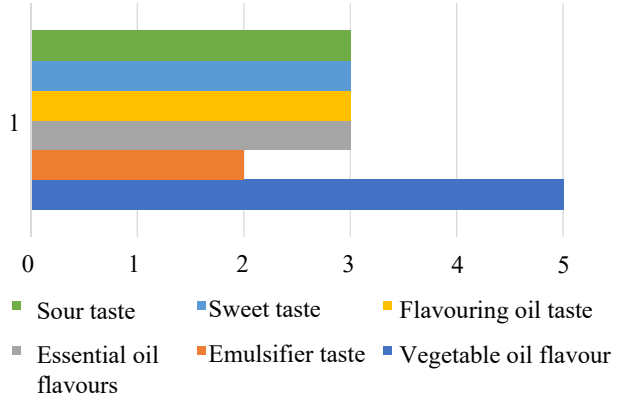


Fig. 7. Taste characteristics of the sample No. 21.2m/t

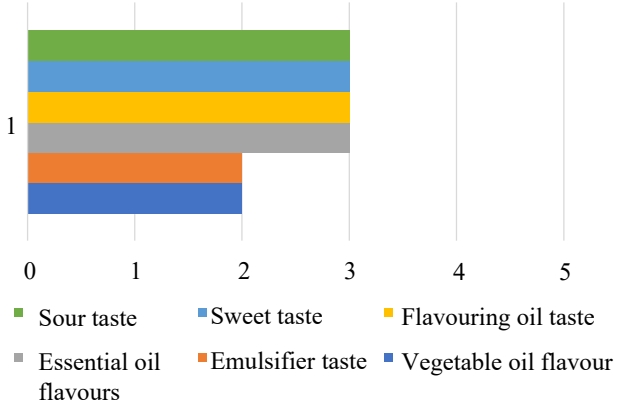


Fig. 8. Taste characteristics of the sample No. 21.2k/t

According to the taste characteristics, the most balanced taste is the sample, which includes sesame oil and flavouring additive “Tarhun”. For the sample obtained as a result of the conducted research (Table 5), the main quality indicators were controlled immediately after production and after 3 months of storage at room temperature in order to establish the stability of the developed emulsion during a long period of storage (Table 6), and a study of the release of API in medium of 0.1 M hydrochloric acid (qualitative analysis by TLC method) (Fig. 12).

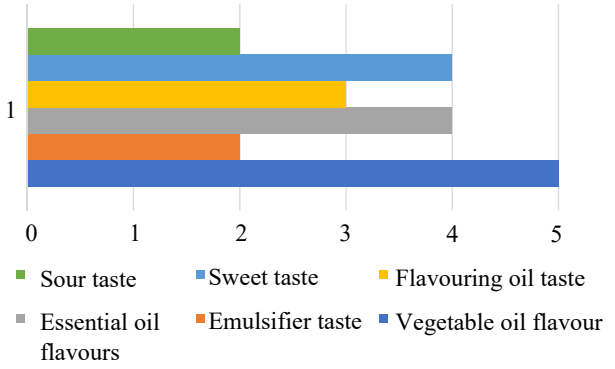


Fig. 9. Taste characteristics of the sample No. 21.2s/v

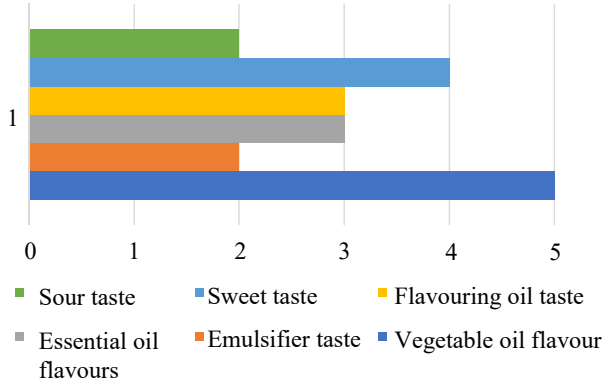


Fig. 10. Taste characteristics of the sample No. 21.2m/v

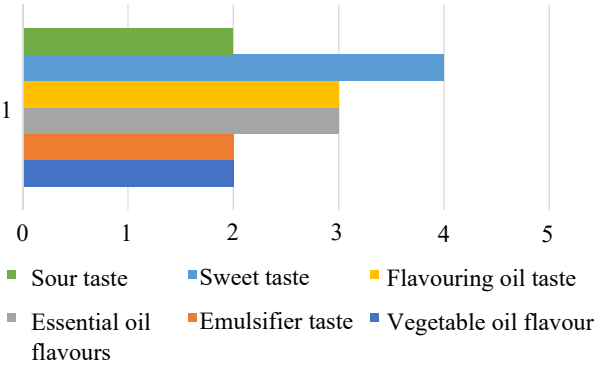


Fig. 11. Taste characteristics of the sample No. 21.2k/v

Table 5

The composition of the developed emulsion

Component	Quantity, g	Purpose
Common fennel essential oil	0.33	API
Cumin essential oil	0.33	API
Refined sesame oil	5.0	Solvent, oil phase
Soy lecithin	5.0	Emulsifier
Apple pectin	0.5	Viscosity regulator
Flavouring additive «Tarhun»	0.005	Corrector of taste
Purified water	to 50.0	Solvent, aqueous phase

Table 6

The main indicators of the quality of the developed emulsion

Characteristics	Immediately after production	After 3 months
Organoleptic properties	Homogeneous, cream-colored liquid with a pleasant sweet-sour taste of tarragon and essential oils	
Thermal stability	Stable	Stable
Colloidal stability	Stable	Stable
pH	6.5±0.1	6.4±0.1
Viscosity, mPa·s	352±30.2 at *t*=20±2 °C; 350±26.4 at *t*=37±2 °C	351±31.2 at *t*=20±2 °C; 350±25.1 at *t*=37±2 °C
Particle size	the base of the dispersed phase consists of particles <200 nm	the base of the dispersed phase consists of particles <200 nm

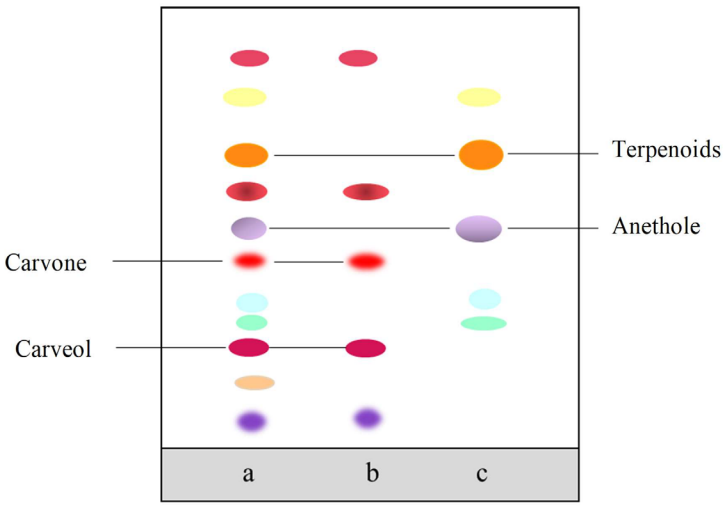


Fig. 12. Schematic representation of the chromatogram of: a – the investigated emulsion; b – Cumin essential oil; c – Fennel essential oil

5. Discussion of research results

The obtained results testify to the ability of all selected emulsifiers in one or another concentration to form stable emulsions, however, the specific sharp taste that PEG40GRO and polysorbate 80 impart to emulsions makes their use in emulsions for oral use undesirable. The ability of soy lecithin to form microemulsions distinguishes it from other emulsifiers, but the rheological properties of such an emulsion require correction. Viscosity indicators were increased by adding 0.2 % of the total weight of the emulsion of apple pectin, which made it possible to obtain an emulsion that has viscosity indicators close to the reference drug and is convenient for use.

Each of the considered vegetable oils has an optimal fatty acid composition, is safe for oral use, does not have a negative effect on the stability of emulsions and does not change their rheological properties. Therefore, the choice was made according to their taste characteristics. Refined sesame oil has the most neutral taste, sunflower and olive oils give emulsions an unpleasant "greasy" taste. Flavour correctors generally improve the taste, somewhat masking the pronounced essential oil taste of API. The most balanced is the taste of tarragon, which, unlike cherry, has a less pronounced sweet taste, which is advantageously combined with the characteristic taste of essential oils.

It was established that the addition of AFI and additional auxiliary substances to the composition of the emulsion does not have a negative effect on its quality indicators. The developed emulsion is a microemulsion, has the optimal viscosity for convenient dosing and use, pleasant taste, almost neutral pH, remains stable and has the proper quality indicators after three months of storage.

The study of the release of API into the medium of 0.1 M hydrochloric acid showed the presence of the main components of the essential oil of common fennel (anethole – a purple zone in the center of the chromatogram, terpenoids – a red-brown zone above the zone of anethole) and essential oil of common cumin (carvone – a bright the red zone in the center of the chromatogram and carveol – the red-violet zone closer to the bottom of the chromatogram).

Study limitations. The study we planned was fully implemented, the obtained results are predictable and reproducible. The chosen methods within the framework of the planned research have no limitations. However, we did not conduct additional studies on the choice of preservative, which should be carried out by means of microbiological tests.

Prospects for further research. At the next stages of the research, it is advisable to study the biopharmaceutical profile *in vitro* and the pharmacological activity and effectiveness of the application in UC *in vivo* for the developed microemulsion.

6. Conclusions

An oil-in-water microemulsion was developed, which includes about 100 % natural substances: essential oils of ordinary fennel and ordinary cumin, refined sesame oil, soy lecithin, apple pectin, food flavouring additive "Tarragon" (0.01 %) and water cleaned. The resulting microemulsion has satisfactory organoleptic, rheological properties, pH, stability and is convenient for use.

The technological parameters that ensure the formation of an emulsion with the most uniform distribution of particles of the dispersed phase in the dispersion medium, 2000 rpm for 15 minutes, have been established.

Conflict of interests

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

Funding

The study was conducted without financial support.

Data availability

The manuscript has data included as electronic supplementary material.

Use of artificial intelligence

The authors confirm that they did not use artificial intelligence technologies when creating the presented work.

References

1. Horobets, A. O. (2015). Unspecific ulcerative colitis in children. Perinatologiya i pediatriya, 1 (61), 74–80. https://doi.org/10.15574/pp.2015.61.74

2. Tomasik, M., Warzyszak, P., Małek, R., Milczek, M., Żołyniak, W., Hawranik, I. et al. (2023). Ulcerative colitis – recent and potential methods of treatment – review. Journal of Education, Health and Sport, 13 (3), 65–73. https://doi.org/10.12775/jehs.2023.13.03.009

3. Unifikovanyi klinichnyi protokol pervynnoi, vtorynnoi (spetsializovanoi) ta tretynnoi (vysokospetsializovanoi) medychnoi dopomohy. Zapalni zakhvoriuvannia kyshechnyka (khvoroba krona, vyrazkovyi kolit) (2015). Nakaz Ministerstva okhorony zdorovia Ukrainy No. 90. 11.02.2016. Available at: https://ips.ligazakon.net/document/MOZ26054

4. Fylypiuk, O. M., Shmalko, O. O., Vyshnevska, L. I. (2021). Analysis of the assortment of drugs used in functional gastrointestinal disorders at the pharmaceutical market of Ukraine. Social Pharmacy in Health Care, 7 (4), 70–78. https://doi.org/10.24959/sphhcj.21.238

5. Abdellaoui, M., Bouhlali, E. dine T., Derouich, M., El-Rhaffari, L. (2020). Essential oil and chemical composition of wild and cultivated fennel (Foeniculum vulgare Mill.): A comparative study. South African Journal of Botany, 135, 93–100. https://doi.org/10.1016/j.sajb.2020.09.004

6. Nastanova. Vymohy do vyhotovlennia nesterylnykh likarskykh zasobiv v umovakh aptek. ST-N MOZU 42-4.5:2015. (2015). Kyiv: MOZU. Available at: https://atl.nuph.edu.ua/wp-content/uploads/2022/09/vimogi-do-vigotovlennja-nesterilnih-likarskih-zasobiv-umovah-aptek.pdf

7. El-Rady, Mohamed F. A., Rasmy, Nagwa M. H., Yasin, N., Fahmy, H., Amer, A. (2023). Phytochemicals and biological activities of caraway (Carumcarvi L.) essential oil. Egyptian Pharmaceutical Journal, 22 (2), 285–293. https://doi.org/10.4103/epj.epj_154_22

8. Aly, A., Maraei, R., Rezk, A., Diab, A. (2022). Phytochemical constitutes and biological activities of essential oil extracted from irradiated caraway seeds (Carum carviL.). International Journal of Radiation Biology, 99 (2), 318–328. https://doi.org/10.1080/09553002.2022.2078004

9. Sompendium. Dovidnyk likarskykh preparativ. Available at: https://compendium.com.ua/uk/

10. USP Compounding Compendium. The National formulary (2020). Rockville: United States Pharmacopeial Convention, Inc.,

11. Sonawane, A., Deshmukh, A., Sonawane, S. (2021). A Review on Self Micro Emulsifying Drug Delivery System (SMEDDS). Ijsrm.Human, 19 (1), 25–33.

12. Verma, R. (2023). Development and Evaluation of Polyherbal Formulation with Carminative Effect. Internationale Pharmaceutica Sciencia, 16 (1), 1–8. https://doi.org/10.31531/2231-5896.1000131

13. Kabiraj, A., Garai, S., Banerjee, S., Chatterjee, S., Bose, S., Adhikari, A. (2023). A Study of Perception of Safety and Functional Efficacy of a Medicated Digestive Syrup in Gastrointestinal Disorders. The Antiseptic, 120, 23–26.

14. Kabiraj, A., Deshmukh, R. (2024). Formulation, Analytical Method Development and Validation of an Emulsion of Multi-enzyme with Carminative Oils. Current Pharmaceutical Analysis, 20 (1), 46–60. https://doi.org/10.2174/0115734129286029240106123114

15. Çetin, I., Aydin, M., Bilgiç, Ş. (2024). Matematiksel Modelleme Araştırmalarının İncelenmesi: Betimleyici Bir İçerik Analizi Çalışması. Necatibey Eğitim Fakültesi Elektronik Fen ve Matematik Eğitimi Dergisi, 17 (2), 994–1025. https://doi.org/10.17522/balikesirnef.1321365

16. Guidelines for medicine donations (2011). World health organization.

17. Derzhavna farmakopeia Ukrainy. Vol. 2 (2015). Kharkiv: DP «Ukrainskyi naukovyi tsentr yakosti likarskykh zasobiv», 723.

18. European Pharmacopoeia (2013). European Department for the Quality of Medicines. Strasbourg, 3655.

19. The National formulary (2012). Rockville: United States Pharmacopeial Convention, Inc.

20. Council of Experts, United States Pharmacopeial Convention (2012). Food Chemicals Codex. Rockville: United States Pharmacopeia (USP).

21. DSTU 4765:2007 «Kremy kosmetychni. Zahalni tekhnichni umovy» (2008). Kyiv: Derzhspozhyvstandart Ukrainy.

22. Derzhavna farmakopeia Ukrainy. Vol. 1 (2015). Kharkiv: DP «Ukrainskyi naukovyi tsentr yakosti likarskykh zasobiv», 1126.

23. Shah, N., Patel, K., Singhvi, I. (2023). Topical Delivery of Eberconazole Nitrate Loaded Microemulsion: Formulation, Design and Evaluation. International Journal of Pharmaceutical Sciences and Drug Research, 15 (4), 478–487. https://doi.org/10.25004/ijpsdr.2023.150412

24. Kukhtenko, H., Gladukh, I., Kukhtenko, O., Soldatov, D. (2017). Influence of excipients on the structural and mechanical properties of semisolid dosage forms. Asian Journal of Pharmaceutics, 11 (3), 575–578.

Received date 05.02.2024
Accepted date 26.04.2024
Published date 30.04.2024

Oleksandr Shmalko, Associate Professor, Department of Pharmacy, Pharmacology, Medical, Bioorganic and Biological Chemistry, Medical Institute, Petro Mohyla Black Sea National University, Desantnykiv str., 10, Mykolaiv, Ukraine, 54000

Tetiana Kovalova, PhD, Associate Professor, Department of Pharmaceutical Technology of Drugs, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002

Liubov Bodnar*, Postgraduate Student, Department of Pharmaceutical Technology of Drugs, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002

Volodymyr Kovalov, PhD, Philosophy Doctor, Associate Professor, Department of Pharmaceutical Technology of Drugs, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002

Volodymyr Yakovenko, Doctor of Pharmaceutical Science, Professor, Department of Industrial Pharmacy and Economics, National University of Pharmacy, Pushkinska str., 53, Kharkov, Ukraine, 61002

Liliia Vyshnevska, Doctor of Pharmaceutical Science, Professor, Head of Department, Department of Pharmaceutical Technology of Drugs, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002

***Corresponding author:** *Liubov Bodnar, e-mail: bodnar_la@ukr.net*