Prospects for the use of complex medicines from Petroleum and Peppermint

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RESUME

Objective. To obtain a series of complex pharmaceuticals based on petroleum, where is used effectively not only as an extractant, but also as a pharmacologically active principle, and to explore its physical and chemical properties.

Authors were first to obtain preparation made of combination of petroleum plus peppermint. Newly created homeopathic medicine "MenthaU", the non-toxicity of which was studied in the experiment on 60 broiler chickens, proved to be of the high biological activity. With the use of modern medicalbiological and chemical methods we studied petroleum and petroleum products with peppermint. Female patients with Paecilomyces toxicosis were successfully treated with "Mentha" preparation.

Keywords: petroleum, peppermint, Paecilomyces toxicosis during pregnancy, homeopathic treatment, gas chromatography – mass spectrometry.

SUMMARY

Purpose of work. To obtain a number of complex medicinal preparations based on petroleum, where it is effectively used not only as an extractant, but also as a pharmacologically active principle, and also to study its physicochemical properties.

For the first time, the authors obtained the preparations of Petroleum plus peppermint. For the first time a homeopathic preparation "MentaU" was obtained, the toxicity of which was excluded in an experiment on 60 broiler chickens and a high biological activity was proved. Petroleum and preparations based on petroleum plus peppermint have been studied using modern medicobiological and chemical methods. Patients with pesilomycosis toxicosis of women with the drug "Menta" have been successfully treated.

Key words: petroleum, peppermint, pesilomycosis toxicosis of pregnant women,homeopathic treatment, chromatography-mass spectrometry.

One of the urgent tasks of public health is the search and study of new drugs for the treatment of diseases of the musculoskeletal system, such as: neuralgia, sciatica, sciatica, etc. Along with significant success in the production and use of synthetic drugs, plants remain one of the best and most promising sources obtaining medicinal products.

Peppermint (Mentha piperita L., sem. Lamiaceae) is an official medicinal plant that is widely used, among other things, for the treatment of inflammatory

processes [1]. On the modern pharmaceutical market, there are a large number of drugs used both externally and internally as anti-inflammatory drugs, which include peppermint essential oil or menthol. Well-known drugs, such as: "Menovazin", ointments "Boromenthol", inhaler "Ingakamf" and balm "Golden Star" [2].

Petroleum is a pharmacologically active substance and is used abroad for the treatment of inflammatory diseases both in homeopathy therapy and in academic medicine. Well known is the Weleda drug, Petroleum, for the treatment of sciatica, as well as having a positive irritating and expectorant effect on coughs and severe bronchitis (including in children) [3]. Unfortunately, in Russia, despite the availability of a large number of sources of raw materials for the production of petroleum, this drug is not produced.

purpose of work

To obtain a number of complex medicinal preparations based on petroleum, where it is effectively used not only as an extractant, but also as a pharmacologically active principle, and also to study its physicochemical properties.

Materials and research methods

To carry out the work, the following methods were used:

1. Chromato-mass spectrometry. The analysis was carried out on an Agilent Technologies ", consisting of: 1) a 7890 gas chromatograph (HP-5 column, 50 mx 320 μ m x 1.05 μ m) and 2) a mass-selective detector 5975 C with a quadrupole mass analyzer. Temperature chromatography program: at 40 ° C - isotherm 2 min; then programmed heating up to 250 ° C at a rate of 5 ° C / min., at 250 ° C - isotherm for 15 min .; then programmed heating up to 320 ° C at a rate of 25 ° C / min., at 320 ° C - isotherm 5 min. Injection 1 μ L. Split injector 1:50. Injector temperature 250 ° C. Interface temperature 280 ° C. Carrier gas - helium; flow rate - 1 ml / min. The chromatogram of the samples is based on the total ionic current. Software - ChemStationE 02.00. Conditions for mass spectrometric analysis: energy of ionizing electrons 70 eV; registration of mass spectra in positive ions in the range (m / z) from 20 to 450 at a rate of 2, 5 scan / sec. The identification of the component composition was carried out using the NIST-05 complete mass spectra library and the corresponding values of the Kovach chromatographic indices. The relative content of the mixture components (%) was calculated by the simple normalization method.

2. Spectrophotometry. Optical absorption spectra were obtained on a single-beam spectrophotometer Hitachi U 1900 at room temperature and atmospheric pressure. The optical path length of the quartz cell is 10 mm. Data was recorded and recorded at 2 nm intervals and a scan rate of 1200 nm / min. in the range from 1100 to 200 nm.

3. Making homeopathic granules [4]. Based on the methodology outlined in a private In the pharmacopoeial monograph in the German State Pharmacopoeia and in the general monograph "Homeopathic granules" OFS 42-0023-04 RF, we obtained homeopathic granules "Petroleum" C3 and homeopathic granules of a complex preparation based on C3 hydrocarbon extract and analyzed some quality indicators.

To obtain the dosage form "granules", it is first necessary to obtain homeopathic dilutions (potencies) according to the Hahnemann method - production in many containers. In this case, the technique specified in the general pharmacopoeial monograph of OFS 42-0023-04 was used.

4. The toxicity and healing properties of the created drug were studied on the basis of methods and recommendations of the Pharmacological Committee of Russia [5].

Results and discussion

Petroleum is obtained from oil from Russian fields by distillation in the range

temperatures 80–280 ° C. According to its physicochemical properties, petroleum is a colorless transparent liquid with a pungent characteristic odor, practically insoluble in water, poorly soluble in ethanol and highly soluble in organic solvents (benzene, toluene, chloroform, ethyl acetate).

We obtained a hydrocarbon extract from air-dry raw materials (leaves) of peppermint, where petroleum was used as an extractant.

Dried standard crushed raw materials and petroleum were taken in a ratio of 1:10 by weight. An exact weighed portion of the medicinal plant material (50 g) was placed in a dark glass jar with a tight-fitting lid, and petroleum (500 g) was added. The hydrocarbon extract was obtained by maceration for 2 weeks with periodic stirring every 3 days. The resulting hydrocarbon extract of peppermint leaves was filtered through a double layer of gauze. Hydrocarbon extraction is a clear, dark green liquid with a pungent specific odor, readily soluble in ethyl acetate, diethyl ether, toluene, methylene chloride and chloroform. The extract is slightly soluble in ethanol and practically insoluble in water.

In the study of solubility, the method of GF 12 edition was used.

We have determined the density of the extractant (petroleum) and the hydrocarbon extract of mint according to the GF 11 edition: 0.789 and 0.807 g / ml, respectively.

We have studied a solution containing 10% (by volume) mint essential oil (NV-74, GBS) in petroleum. The aforementioned essential oil of mint was obtained from the leaves of a plant of the 2nd year of vegetation by means of hydrodistillation (with a yield of 3.37%) and is an introduced variety cultivated on the basis of the experimental plot of the GBS im. N.V. Tsitsin RAS. More than 80 components were identified in the essential oil, studied by gas chromatography-mass spectrometry, for which their relative (%) content was calculated. For the investigated essential oil, selective control of 18 most representative components was carried out: α -pinene (0.13%), β -pinene (0.13%), 1,8-cineole (0.12%), limonene (0, 29%), linalool (0.04%), menthone (18.60%), menthol and menthyl acetate (74.90%), pulegon (0.15%), piperitone (0.92%), β -bourbonene (0.16%), β -caryophyllene (1.00%), β -cubeben (0,

Comparative gas chromatography-mass spectrometric analysis of the obtained samples was carried out. - 1) petroleum; 2) a hydrocarbon extract of mint from air-dry raw materials; and 3) a combined essential oil substance with petroleum (in a ratio of 10:90 by volume).

More than 100 individual components have been identified in petroleum. The relative percentage of both individual compounds and the total composition of components belonging to different classes of hydrocarbons has been estimated (Table 1).

Table 1

Component composition of Petroleum

АЛКАНЫ	СОЕДИНЕНИЯ	50
н-Алканы	Гептан, октан, нонан, декан, ундекан, додекан, тридекан, тетрадекан, пентадекан, гексадекан	35,90
Pasner- naemuse	2,3,5-Триметилгексан; 2,2,3,3-тетраметилгексан; 2- и 3-метилгептаны; 2,3-, 2,5- и 2,6-диметилгептаны; 3-этил- 2-метилгептан; 3- и 4-метилоктаны; 2,3-, 2,6- и 3,5-диметилоктаны; 2-, 3-, 4- и 5-метилнонаны; 2,5-, 2,6- и 3,7- диметилнонаны; 2-, 3-, 4- и 5-метилдеканы; 3,7-диметилдекан; 5-этил-5-метилдекан; 2-, 3- и 4-метилундеканы; 2,6-диметилундекан; 4,6-диметилдодекан; 2,6,10-триметилдодекан, 2-метилтетрадекан	25,80
Циклические	1-Бутил-2-метилциклопропан; 1-бутил-1-метил-2-пропилциклопропан; 1-метил-2-пентилциклопропан; этил- и пропилциклопентаны; 1-этил-3-метилциклопентан и 1-метил-2-пропилциклопентан; 2-этил-1,1- диметилциклопентан; метил-, этил-, пропил-, втор-бутилциклогексаны и и-амилциклопексан; 1,1-, 1,2-, 1,3- и 1,4-диметилциклогексаны; 1,2-диэтилциклогексан, 1-этил-2-метилциклогексаны, 1-этил-4-метилциклогексан, 1-метил-2-пропилциклогексан и п-ментан; 1,1,2- и 1,1,3-триметилциклогексаны; 1,1,2,3-тетраметилциклогек- сан; 2-бутил-1,1,3-триметилциклогексан	10,20
АЛКЕНЫ	1-фенил-1-бутен; децен (один из изомеров по двойной связи)	2,10
АРЕНЫ	Толуол; о- и п-ксилолы; кумол, пропил-, бутил-, втор-бутил- и н-амилбензолы; п-цимол и о-, м-, п-этил-, п-пропил-, п-изо-бутил-, п-втор-бутилтолуолы; 1,2-диэтилбензол; 2-фенилпентан; 1-этил-1-метилиндан; ге- меллитол, ψ-кумол и мезитилен; 3-этил-о-ксилол и 4-этил-м-ксилол; пренитол и изодурол; пентаметилбензол; нафталин, 1- и 2-метилнафталины, 2- и 1-этилнафталины, диметилнафталины	26,00

Among the major components, the most significant were n-alkanes (35.90%). In total, branched alkanes (25.80%) and arenes (26.00%) were present in equal amounts.

Elemental analysis of a Petroleum sample was carried out on a EuroEA 3000 analyzer from EuroVector. It is shown that the relative content of C - 85.81%, H - 14.24%; S and N - in trace amounts.

In hydrocarbon (petroleum) extract fromair dry raw materials mint identified (and estimated the quantitative ratio from the calculation of the entire set of components, both extracted from the air-dry mass, and included in the composition of the extractant petroleum): menthone (the sum of stereoisomers, no more than 0.20%), pulegon (no more than 0.25%) and piperitone (no more than 0.15%).

As a result of the analysis of the combined substance of essential oil with petroleum (in a ratio of 10:90 by volume), the possibility of a clear chromatographic separation for a number of major components of essential oil and petroleum, for example, menthol (one of the stereoisomers, KI = 1199) and dodecane (KI = 1200); menthyl acetate (one of the stereoisomers, KI = 1312) and tridecane (KI = 1300), which can later be used to standardize the proposed drug.

A comparative spectrophotometric analysis of three samples: 1) petroleum; 2) a hydrocarbon extract of mint from air-dry raw materials; and 3) a combined essential oil substance with petroleum (in a ratio of 10:90 by volume). The spectra of petroleum (Fig. 1) recorded absorption maxima at 266 and 216 nm with absorption absorption 3.40 and 1.14, respectively (at a dilution of petroleum-EtOH 1: 500). In the hydrocarbon extract of mint (Fig. 2) in the measurement range from 1100 to 200 nm (when the hydrocarbon extract is diluted with EtOH 1:50), additional peaks are recorded (in addition to the peaks of the extractant) with absorption maxima at 667, 609, 560, 534, 505, 471 and 408 nm with absorbance of 0.54, 0.12, 0.09, 0.13, 0.18, 0.27 and 1.01, respectively, in the hydrocarbon extract of mint, these additional peaks correspond to pheophytin a.



Rice. 2. Absorption spectrum of mint hydrocarbon extract.

The combined substance of essential oil with petroleum (in a ratio of 10:90 by volume) was investigated spectrophotometrically in order to realize the possibility of indirect standardization of this mixture by the absorption maximum (266 nm), typical for the extractant-petroleum.

Based on the hydrocarbon extract of mint, a homeopathic preparation "MentaU" was obtained using centesimal dilutions.

For Hahnemann dilutions, a separate pot is required for each potency, although intermediate potencies are generally not used. Prepare a sequential number of vials with the required amount (99.0 g) of solvent (62% ethanol by weight or 70% by volume). The concentration of ethanol diluted according to table GF XI is determined by density (with a densimeter). The dilution must be indicated on the bottle cap and on the bottle itself. The volume of the bottle should be 1 / 2–1 / 3 more than the volume of the diluted liquid.



Rice. 3. Dependence of optical density on petroleum dilutions.

In the first bottle with 99.0 g of alcohol, 1.0 g of the previously obtained hydrocarbon extraction is introduced. Shake each dilution for at least 10 minutes vertically. Then, 1.0 g of the previous solution (dilution C1) is transferred to the second vessel with the designation C2 with a clean pipette. Shake the bottle vigorously again. This continues until the desired C2 dilution is obtained. Clean pipettes are used each time and each dilution is shaken.

Then, using the obtained third and sixth centesimal dilutions, we obtain homeopathic granules according to the method described in the General Pharmacopoeia Monograph on homeopathic granules. Granules are a dosage form for sublingual administration. They are made from pure cane sugar and must be completely soluble in purified water. Granules differ in size, which is indicated by a number (Table 2).

table 2

		197	
Номер гранул	Масса одной гранулы	Число гранул в 1г	Средний диа- метр, мм
4	12,5 мг	80 ± 10	2,5
5	22 мг	45 ± 5	3,0
6	40 мг	25 ± 3	3,7

Sizes of the most commonly used granules

Method for preparing homeopathic granules

Only 70% ethanol (62% by weight) is used, which ensures the opening of the pores of the sugar grains and their saturation with a medicinal substance. The volume of the mixer should be 1.5–2 times the mass of the original granules. We weigh 100 g of granules No. 5, place them in a 200 ml glass bottle, add 1.0 g of the previously obtained C2 dilution and the same amount by weight of 70% ethanol to wet the granules. Close the bottle with a lid wrapped in parchment paper and immediately begin stirring. Shaking is carried out for 10 minutes

manually with vigorous circular movements or for 3-4 minutes by machine in mechanical mixers.

At the end of shaking, the granules are poured for drying on wooden boards with holes covered with parchment paper. Air dry at room temperature until dry. Dried granules are packed in paper bags of 10.0 g, indicating the raw material, extraction, dilution, weight.

Analysis of the quality of homeopathic granules

When analyzing the quality of homeopathic granules, the appearance of the granules was assessed; disintegration, the number of granules in 1 g were determined.

Appearance of granules

Three weighed portions of granules of homeopathic hydrocarbon extract of yarrow were weighed with an accuracy of 0.01 g. Assessment of the appearance of the granules was carried out visually with the naked eye.

Disintegration

10 granules were placed in a conical flask with a capacity of 100 ml, 50 ml of purified water having a temperature of 37 ° C \pm 2 ° C was added. The flask is slowly shaken 1–2 times per second, at least 3 determinations were carried out.

Homeopathic granules should disintegrate within no more than 5 minutes. (Table 3).

Table 3

№ пробы	Количество гранул	Время распадаемости
1	10	4 мин. 30 сек.
2	10	4 мин. 50сек.
3	10	4 мин. 50сек.

Analysis of disintegration of homeopathic granules

Estimation of the number of granules in one gram

The tests were carried out by the gravimetric method. To do this, in the sample of the preparation (the weight of the sample for each size of sugar granules is given in Table 15 in the General Pharmacopoeia Monograph "Homeopathic Granules"), weighed with an accuracy of 0.01 g, count the number of granules (Table 4). The determination is carried out in two parallel samples.

Table 4

№ гра- нул	Количество гранул в 1 г	Масса навески гранул для подсче- та их количества	Средний диаметр гранул, мм
1	45	1,01	$3,0\pm0.1$
2	48	1,01	3.1 ± 0.1
3	50	0,99	2.9 ± 0.1

Characteristics of the auxiliary component - sugar granules

The chronic toxicity of the drug "MentaU" was studied in a laboratory model in vivo - chickens.

Sixty chickens of one month old were selected for the experiment, divided into 6 groups according to the analogy principle. To test the homeopathic preparation "MentaU" with the participation of poultry farmers, veterinarians, laboratory doctors, animal examinations were carried out. There is no statistically significant difference in the six groups of chickens before the administration of the drug according to the data of the general blood test.

Poultry farmers call one-month-old chickens reared chickens. Each group of reared young chickens was kept in a special metal cage, in which

there were 5 females and 5 cockerels together. The homeopathic "MentaU" was tested in dilutions of C3. Before giving the drug was dissolved in distilled water, dynamization was carried out according to the generally accepted homeopathic technique, then the drugs were administered to the animals inside, each individually in 4 ml of distilled water 20–40 minutes before feeding, at the rate of four crumbs for each bird in the morning, afternoon and evening.

Group 1 for 30 days daily (each animal) received orally three times 4 ml of distilled water, group 2 three times a day 4 grains of homeopathic "MentaU" in 4 ml of distilled water, group 3 - placebo, which is 4 grains milk sugar dissolved in 4 ml of distilled water, not containing a homeopathic agent, group 4 - 1 ml of hydrocarbon extract from mint, group 5 - intact, received nothing, group 6 - 1 ml of hydrocarbon extract. Throughout the experiment, the bird felt good, grew and developed normally, had good appetite, was active, feathers were shiny, visible mucous membranes of pale pink color, growing scallops were bright red. However, the group receiving the mint hydrocarbon extract and the group receiving the hydrocarbon extractant, i. E. groups 4 and 6 were different from the rest of the bird. Almost all animals suffered from diarrhea. The bird consumed much more water.

We have studied the blood parameters of experimental chickens. The digital material of blood tests, which belongs to us, shows that after daily administration of the homeopathic preparation "MentaU" for 30 consecutive days, there was a statistically significant increase in the hemoglobin content and the number of erythrocytes in the blood, which is statistically significant (p <0.05). The highest live weight, good biochemical and immunological parameters of blood were found in the bird that received the homeopathic preparation "MentaU".

Currently, the medical and national economic problem is petsilomycosis, a new fungal disease accompanied by severe damage to vital organs in children and adults with the transition of the disease to sepsis with a fatal outcome [6–9]. At the last stage of pregnancy, women often develop pecilomycosis toxicosis and children are born with intrauterine pecilomycotic pneumonia with the transition to lethal sepsis [10–12].

69 patients with pecilomycosis toxicosis of mothers were observed before childbirth, were treated with homeopathic preparations, and also before pregnancy were treated by homeopaths for various concomitant diseases, since they had an intolerance to antibiotics and modern fungicides. The age of the patients is from 22 to 29 years old.

During the last 5 years they suffered from chronic and acute bronchitis. A thorough examination of therapists concluded that all patients suffer from COPD (chronic obstructive pulmonary disease). None of these women had been screened for pesilomycosis prior to pregnancy. Only upon admission to the obstetric-gynecological department of the clinical hospital, they were thoroughly examined for the presence of pecilomycosis, the number of spherules of pecilomyces fungi in 1 μ l of blood was: 21.75 ± 5.70 thousand (with n = 69, M ± m). These women in labor were diagnosed with gestosis of pecilomycotic etiology. Two weeks before giving birth, 69 women in labor had an increased body temperature: from 37.7 to 38.5 ° C. All patients in this group had an increased amount of sugar in the blood, it fluctuated from 9.5 to 14.5: 11.50 ± 4.50 (with n = 69, M ± m).

Our biochemical studies have shown that an increase in the amount of glucose in the blood of patients contributes to the intensive reproduction of fungal spherules and leads to a generalization of the process. The diet of these women was dominated by cakes, pastries, ice cream, chocolate, sweet jam, sweet fruits: grapes, apricots, persimmons, unabi, melons, and there was less protein food. With the help of nutritionists, the diet was changed. A full-fledged protein diet was introduced: beef alternated with fish and chicken, every day greens, tomatoes, fresh sauerkraut, from fruits: sweet and sour apples, pears, plums, currants, raspberries (no more than 300 g per day), bread rye, such as Borodinsky. Drinking coffee, tea is excluded. Every day the patients received 0.5 l of Mechnikov's curdled milk. For the first three days, all patients received Aconit 3,

water cooled to room temperature. In graduated sterile bottles, 150 ml of boiled water cooled at room temperature were poured, 4 grains of Aconite x3 were immersed, the bottle was closed with a polyethylene cognac stopper, dynamization was carried out according to S.A. Nikitin, rotating 50 times to the right, 50 times to the left. The drug was prepared every day and was used on the same day. In the morning after 10 shakes for 20-30 minutes. one sip was taken before breakfast. Approximately 2 hours after breakfast, a second sip was taken in the same way; the third sip - in 20-30 minutes. before lunch, the fourth - 2 hours after lunch, the fifth - 20-30 minutes. before dinner, the sixth - 20-30 minutes. before bedtime. On the 4th day of treatment, the fever subsided: in 37 patients the temperature was from 36.2 to 36.8 ° C, in 32 patients it was 37.3–37.6 ° C. The neuropathologist found that common to all 69 patients is a nighttime headache, manifested after a short sleep, then insomnia, fear of the forthcoming birth. Arsenicum C6 was appointed from the 4th day. The method of application is the same as Aconita.

On the 7-9th day of homeopathic treatment, a total of 5 patients with fever showed exacerbation of COPD, accompanied by dry irritable cough, gastrointestinal tract disorders, and nervous facial pain. Pain in the teeth. Dentists ruled out tooth damage. Early prescribed homeopathic remedies were canceled for these patients. For the treatment, the drugstore "Menta" C6 was used. The method of application is similar to the treatment with aconite. After three days of using the Menta drugstore, the cough stopped, the pain in the face and teeth disappeared, and the stool was restored. Temperature - from 37.2 to 37.8 ° C. In the future, the delivery went well. Mothers and newborns recovered after homeopathic treatment.

Based on the studies carried out, we come to the following conclusions:

1. More than 100 individual components have been identified in petroleum. Evaluated the relative percentage of both individual compounds and the total composition of components belonging to different classes of hydrocarbons. Among the major components, the most significant were n-alkanes (35.95%). In total, branched alkanes (25.80%) and arenes (25.95%) were present in equal amounts.

2. In hydrocarbon (petroleum) extract from air-dry raw mint identified (and estimated the quantitative ratio from the calculation of the entire set of components, both extracted from the air-dry mass, and included in the composition of the extractant petroleum): menthone (the sum of stereoisomers, no more than 0.20%), pulegon (no more than 0.25 %) and piperitone (no more than 0.15%).

3. In the spectra of petroleum, absorption maxima were recorded at 266 and 216 nm s absorption absorption 3.40 and 1.14, respectively (at dilution of petroleum-EtOH1: 500). In the hydrocarbon extract of mint in the measurement range from 1100 to 200 nm (at dilution of the hydrocarbon extract-EtOH 1:50), additional peaks are recorded (in addition to the peaks of the extractant) with absorption maxima at 667, 609, 560, 534, 505, 471 and 408 nm with an absorbance of 0.54, 0.12, 0.09, 0.13, 0.18, 0.27 and 1.01, respectively.

4. In the hydrocarbon extract of mint additional peaks correspond to pheophytin a. The absorption bands of terpene compounds in mint extract (for example, menthone, with absorption maxima at 276 and 228 nm, menthone-EtOH 1: 1500 and absorption adsorption of 0.20 and 0.71, respectively) coincide with the region of intense absorption of the extractant components.

5. Based on the hydrocarbon extract of mint, a homeopathic preparation was obtained "MentaU" using centesimal dilutions. In therapeutic doses, the drug was found to be non-toxic to broiler chickens. Clinicians have tested the drug Menta (pharmacy) in the treatment of pregnant women with pecilomycosis toxicosis, having received a positive result.

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