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## PHARMACOLOGICAL ACTIVITIES AN OINTMENT OF SAFFLOWER *CARTHAMUS TINCTORIUS L.* FLOWERS GROWN IN KAZAKHSTAN

### SUMMARY

The objects of study were samples of CO<sub>2</sub>- extract, obtained from the flowers of safflower (*Carthamustinctorius L.*), and collected in the flowering stage. Dried plant material (safflower flowers) collected in the summer, subjected to treatment and disposal of mechanical impurities, drying and then grinding to hyperfine state. Harvesting plants was made on the territory of Almaty region. Theoretical and experimental composition was developed and ointments technology conforming to the Pharmacopeia Republic of Kazakhstan. The composition of ointments presented ingredients: sunflower oil, T-2 and peppermint oil, purified water. From the obtained sample CO<sub>2</sub>-extract ointment developed. The resulting samples of CO<sub>2</sub>-extract were moving, volatile Cinnamon, with a pleasant characteristic odor. From the obtained sample CO<sub>2</sub>-extract ointment developed. Developed laboratory regulations antimicrobial, anti-inflammatory phytopreparation based on medicinal plants.

**Key words:** CO<sub>2</sub>-extract, safflower flowers, ointment.

### INTRODUCTION

Safflower (*Carthamustinctorius L.*), a member of the Compositae or Asteraceae family has long been cultivated mainly for its seed (source of an edible oil), colorful petals (valued as a food coloring and flavoring agent), and also as a source of red and yellow dyes for clothing and food in the Far East, Central and North Asia, America, North Africa, Europa, and Caucasia. India, U.S.A. and Mexico are the principle producers of safflower however; the crop has also been cultivated in many other countries, such as Kazakhstan, Ethiopia, Argentina, China, Uzbekistan, Australia, Russian Federation, Pakistan, and Spain. Traditionally, the crop was grown for its flowers, used for coloring and flavoring foods and making dyes, especially before cheaper aniline dyes became available and in medicines. It is considered one of the alternative oil crops, particularly in the dry and semi dry lands due to its tolerance to drought, salinity and cold stress. Safflower oil quality is high due to its fatty acids composition. Standard safflower oil contains about 6-8 % palmitic acid, 2-3 % stearic acid, 16-20 % oleic acid and 71-75 % linoleic acid. In addition, very low levels of

myristic (0.24 %) and behenic (0.43 %) acids were recorded in its oil.

Annually seeds are harvested for oil (30 to 45 %) used in human food (low cholesterol) or for industrial uses and meal for livestock protein supplement (24 % protein) which is high in fibre. Planted in April/May (early spring) in areas, which have at least 120 days of frost-free periods, and hot summers. The crop is frost-tolerant in the seedling stage and can withstand temperatures of -7 °C. Typically grown at less than 1100 m altitude and sowing rates is 17-28 kg/ha for dry land and 28-39 kg/ha for irrigated conditions (pure live seed), at depths of 2.5-4 cm, after soil temperature has reached 4 °C. Row spacing may be kept up to 35 cm [1-3].

### Marketing analysis of drugs.

Currently in the Republic of Kazakhstan population's need for drugs completely satisfied but the share of domestic production of medicines in the total consumption is only 15 %. This situation can not but worry the government of the Republic of Kazakhstan and pharmaceutical manufacturers because drugs are the national security of any state. Measures have been taken to resolve the situation.

The first step was the adoption of the State Program of development of pharmaceutical and medical industry where the most was assigned to drug products, whose share in the market of drugs currently exceeds 90 %. In addition, the government adopted other sectoral laws and regulations for the orderly development of the industry, which ultimately led to an increase in the share of domestic producers so far only 15 %.

In order to the measures brought the desired results, a set of measures must be done, including research and development: marketing research of drugs, forms, both domestic and foreign competitors, research production efficiency, quality and competitiveness of products.

Among the drugs of applicator exposure rational drug form in which it is possible to realize multi-factorial effect on damaged texture is soft dosage forms which are presented by ointments, pastes, creams, gels, liniments.

Modern range of medicines for external use in the Republic of Kazakhstan is quite extensive, it can be divided into two groups: medicines containing as an active pharmaceutical ingredient synthetic drugs and medicines with the active ingredients of medicinal plant.

Herbal preparations for external use are presented on the market mainly by ointments, oil extract, suppositories, drops, gels, films. The most widely represented among them are ointments, which constitute more than 65 %; suppositories – constitute 15 %; vegetable oil extracts – 12 %; pastes, drops in the general population is about 5 %, gels, plasters, films, pencils – 3 %.

Drugs in the soft medical forms are imported from more than 100 countries, including Germany, Austria, Portugal, Belgium, Switzerland, Poland, Hungary, Slovenia, Italy, Estonia, Lithuania, India, Iran, etc., products of the neighboring countries are presented by manufacturers from Russia, Belarus and Ukraine.

The largest assortment of soft medical forms on the market of the Republic of Kazakhstan are supplied from: «Nizhpharm» (Russia), «Schering», «Bayer», «Schering – Ploug» (Germany), «Ranbaxy, Lupin, Microlabs, Glenmark, Agio» (India), Poland, ZMP Borisov (Belarus), Borshchahivskiy HFZ, FF «Darnitsa» (Ukraine), «Schering» (Italy), Tallinsky Plant JSC (Estonia), «Gedeon Richter» (Hungary), «Lek, KRKA» (Slovenia). Other companies supply from 1 to 4 items. Nomenclative analysis of drugs found that 94 % of the total number of registered

the soft medical forms are imported from countries near and far abroad.

In Kazakhstan, the production of soft medicinal forms are mainly represented by the names of even the Soviet era and technology. This ointment such as streptocidal, zinc, ihtiolovaya, sulfuric, methyluracil, furatsilinovoy, balsamic liniment, etc. Virtually no modern high-tech soft medicinal forms of new generation. Leading positions occupied by factories: «Santo», «Romat», LLP «Shansharov», «Rauan», JSC «Pharmacy» (Karaganda). Other companies produce 1-2 titles, table 1.

Table 1

**Domestic manufacturers of soft dosage forms on the market of the Republic of Kazakhstan**

Company name	Number of items	Relative value%
Santo	7	1,6
Romat	5	1,13
LTT «Shansharov»	4	0,9
Rauan	3	0,67
JST «Pharmacy» (Karaganda)	7	1,6

It is found that the market is mainly represented by herbal anti-inflammatory activity, they are – 34 %. This is followed by a group of antimicrobial action of herbal remedies, their share is – 21 %. The drugs, which increases the regeneration – 16 %, less represented groups of phytopreparations of painkillers action – 11 %, antburn – 9 %, irritating – 7 %. The collection of hemostatic, capillaries strengthen, toning and anti-fungal herbal remedies account for only 2 %.

Arose interest in and research of herbal remedies on the market, depending on the systematic position of plant species. The analysis found that the most widely available herbal legumes and Asteraceae, myrtle, they make up about 48 %. What follows is the nightshade family, poppy and pine – 21 %. Families of cereals, valerian, nut are about – 31 %.

Produced by the pharmaceutical industry phytotherapy divided: 1) containing the amount of biologically active substances; 2) containing a purified amount of biologically active substances; 3) containing the individual substances. It was found that the leading position occupied by the plant essential oil, their share is – 33 %, followed by alkaloids medicinal plants – their share is 18 %. Third place is oc-

cupied flavanoids medicinal plants, their share is 13 %. The group includes all the other different herbs containing coumarins, resins, fatty oils, etc. Their share of about 6 % each.

From the table it follows that the domestic soft dosage forms approximately 6 % of the total number of titles.

The analysis found that a special group of ointments containing the active compounds of medicinal plants, the active ingredients which are available in various pharmacological groups, such as anti-inflammatory, antimicrobial, reinforcing the body's regeneration, painkillers, antitumor, irritating and antifungal.

### Materials and Methods

#### Plant material

The plant material was collected from the Southern Kazakhstan region during the flowering stage in the summer of 2013. The plant was identified by Konyrbekov M., taxonomist of the station. A voucher specimen was deposited at the herbarium Krasnovodopadskaya Breeding Experimental Station, Ministry of Agriculture, Republic of Kazakhstan. Dry plant material (seeds and petals) are collected in the summer of 2013, and was subject to treatment and disposal of solids, drying, and then grinding before the experiments.

#### Extraction of essential oils

The objects of the study were samples of CO<sub>2</sub>-extract obtained in critical conditions of the flowers of safflower (*Carthamus tinctorius L.*), collected in the flowering stage. Dried plant raw material (flowers safflower) harvested in the summer, are processed and removal of mechanical impurities, drying and then grinding in a ball mill to a hyperfine state (flowers – to a particle size of 4-6 mm, seeds – 0.3-0.5 mm). Procurement the plants was made on the territory of Almaty region. From the 1 kg of the crushed material – safflower flowers grown in Kazakhstan crushed to 4-6 mm. CO<sub>2</sub>-extraction on a laboratory extractor at a pressure of 60 atm. and 22 °C in carbon dioxide produced light – yellow extract. The extract was analyzed by gas-liquid chromatography using mass spectrometry [4-5].

### Results and Discussion

Thus, the development of ointments with biologically active substances of aromatic plants with antimicrobial activity is relevant to the pharmaceutical industry of the Republic of Kazakhstan.

An ointment of essential oil the from safflower flowers grown Kazakhstan: for creating ointment

of flowers safflower (*Carthamus tinctorius L.*) optimum composition of the excipients. So several models were created ointment bases – emulsion, a slurry, combined with application of various the excipients – sunflower oil, glycerol, paraffin oil, lanolin, etc., Emulsifiers – Tween-80, T-2 and others. The most efficient composition of the technological parameters was ointment base with the following composition:

Table 2

#### The rational an ointment consisting to 100.0 grams:

The active substance essential oil obtained from the flowers of safflower	9.0
The auxiliary substances sunflower oil	40.0
T-2	5.0
Purified Water	46.8
<i>Oleum Menthaepiperitae</i>	0.2
Total weight	100.0

By its consistency suitable for application of ointment and a prolonged exposure to lesion focus. Other compositions were not suitable for their consistency of, as were liquefaction or thick, which was inconvenient terms of application, and distinguished by the fact that the system was subjected to separation and was losing their structural and mechanical properties.

At the stage of carried out preparation and auxiliary of drugs and materials. At the initial stage emulsion base was prepared of the following composition: 40 parts of sunflower oil, 5 parts of emulsifier T-2 ad 100.0 parts of purified water. Emulsion base was prepared in the following way: an emulsifier T-2 was melted in a water bath, and added to overheated oil in the last turn slowly added in a thin stream hot water (40 °C). Then, medicinal substances were injected into the finished emulsion base. The addition of essential oil obtained from safflower flowers to the base was carried out at preliminary maximum dispersing them before molecular state, which was carried out with constant stirring to forming a stable system. In the next step was carried out homogenization ointment to obtain homogeneous mass. Ointment from almost white to slightly yellowish color with a weak a characteristic smell of *Oleum Menthaepiperitae*. The proposed method allows obtaining means of wound healing, regenerating and anti-inflammatory activity.

#### Characteristics of the final product production

##### 1. Name of product:

Ointment, «AkMai», 30 g

2. *The main purpose of production:* anti-inflammatory, antimicrobial and wound healing agent

3. *Description:* Ointment from almost white to slightly yellowish color, with a characteristic smell.

In appearance must meet the requirements DPh RK

4. *Packing:* 30 g aluminum tubes with a sealed mouth, varnished with a screw cap of high density polyethylene.

Each tube with instruction on medical use at the national and Russian languages put in a cardboard box.

5. *Identification:* Approved comp image package.

6. *Storage:* At temperatures below 25 °C in tightly closed internal packaging to avoid moisture.

7. *Storage life:* 3 years

#### **Studying the security local irritating and allergenic effect of the ointments.**

Before the experiment, the animals were two-week quarantine on a standard ration the vivarium.

To study the local irritating action used the method of skin applications. Experiments were used the guinea pigs weighing 300-400 g (15 animals, 3 groups). On clipped and depilate area of skin side surface of the trunk of guinea pigs, closer to the middle of the trunk was applied 500 mg. The ointment was applied for 2 weeks to 5 times a week. We take into account the reaction of the skin on a daily basis on the scale of evaluation of the skin tests. The reaction was observed on the outer surface of the skin or by means line calorimeter. Suvorov after 24 hours and evaluation in points on the following scale:

- 0 – no visible reaction;
- 1 – pale pink erythema around the area or its periphery;
- 2 – bright pink erythema around the portion or its periphery;
- 3 – red erythema throughout the site;
- 4 – infiltration and skin edema (thickening of the skin folds) in the presence or absence of erythema.

During the whole experience of research on local irritating effect showed that the application of ointments on the clipped and depilate area of skin of guinea pigs does not irritate the skin and does not affect the general condition of the animals (body temperature, the dynamics of body weight).

#### **The study allergenic effect**

The study allergenic effect ointment carried out by the conjunctival samples of 6 rabbits (weight

3.0-4.0 kg). For this using a syringe in the transition zone mucosal century and globe eye rabbits were injected with 1000 mg of ointment into the other eye (control) were administered placebo ointment. The reactions take account after 15 minutes (fast reactions) and 24-48 hours (hypersensitivity) and delayed type evaluated on the following scale (in points):

- 1 – slight reddening tear duct;
- 2 – redness and sclera tear duct in a direction towards the cornea;
- 3 – redness of the conjunctiva and sclera whole.

No signs of allergenic effect (hyperemia, swelling, and others.) From the skin and mucous membranes showed no sensitization to components of ointment.

#### **The study acute toxicity study ointment**

Acute toxicity study ointment were studied in experimental animals for their skin-resorptive effect. Experiments were put on 24 rats weighing 200-260 g (6 animals in each group – separate males and females). They used the method of application of the tail. For the one half of the animals used ointment anticipated therapeutic dose (1.36 g to 100.0 drug concentrate), and for the other – agents containing concentrate 2-fold greater (2.72 g 100.0 concentrate preparation), lubricants daily once, for 2 weeks. Pay attention to the presence of local reactions at the application site means (in the form of redness, swelling) of the outer cover of the tail of rats.

Results of the experiments showed the absence of pathological changes in the nature of general and specific indicators over the entire study period. Animals in all groups remained active, there was no case of death or poisoning.

So topical application of an effective and maximum doses of means did not have toxic effect, both common and local character. For the organism of experimental animals developed ointment is harmless.

#### **Conclusions**

From the result of the study, it could be concluded that the safflower collected from the Southern region of Kazakhstan is one of the best genotype available. *Carthamustinctorius* regarded as a valuable plant in Kazakh system of medicine, Chinese medicine and modern drug development areas for its versatile medicinal uses. The aim was designed to study the biological activity and chemical composition of volatile oil of *Carthamustinctorius L.* The experimental data on high antimicrobial, anti-inflammatory and other prop-

erties of safflower determines its prospects of further study as a therapeutic and prophylactic agent in a variety of dosage forms. In comparison with other studies in this area, since the flowers of safflower grown in Kazakhstan, with a large stock of raw materials in Kazakhstan are used as ornamen-

tal plants, have not previously been studied in the territory Republic of Kazakhstan. Also topical application of an effective and maximum doses of means did not have toxic effect, both common and local character. For the organism of experimental animals developed ointment is harmless.

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## АННОТАЦИЯ

Объектами исследования послужили образцы CO<sub>2</sub>-экстракта, полученные из цветков сафлоры (*Carthamustinctorius L.*), собранных в фазу цветения. Сухое растительное сырье (цветки сафлоры) собранные летом, подвергнутые обработке и удалены механические примеси, просушены и измельчены до сверхтонкого состояния. Заготовка растения производилась на территории Алматинской области. Полученные образцы CO<sub>2</sub>-экстракта представляли собой подвижную, легколетучую смесь коричневого цвета, с приятным специфическим запахом. Теоретически и экспериментально был разработан состав и технология масел соответствующий требованиям ГФ РК. Состав масел представлен ингредиентами: масло подсолнечное, Т-2 и мятное масло, вода очищенная. Разработан лабораторный регламент антимикробных, противовоспалительных фитопрепарата на основе лекарственного растительного сырья. Исследованиями на животных показана безвредность, хорошая переносимость.

**Ключевые слова:** CO<sub>2</sub>-экстракт, цветки сафлоры, мазь.

## ТҮЙІН

Ғылыми зерттеу аймағы гүлденген кезеңінде жиналған мақсары (*Carthamus tinctorius L.*) гүлі өсімдігінен алынған CO<sub>2</sub>-экстракт болып табылады. Кептірілген дәрілік өсімдік шикізаты жаз айында жиналып, бөгде заттардан толығымен тазартылды, талапқа сай кептірілген, майда бөлшектерге майдаланды. Дәрілік өсімдік шикізатын дайындау Алматы обласында жүзеге асырылды. Мақсары өсімдік шикізаты негізінде алынған CO<sub>2</sub>-экстракт ұшқыш, өзіне тән исі бар, қоңыр түсті зат. Теориялық және тәжірбиелік зерттеулердің нәтижесінде ҚР МФ талаптарына жауап беретін жақпа майының технологиясы мен құрамы жасалды. Жақпа майының оңтайлы құрамы келесідей: күнбағыс май, Т-2 және жалбыз майы, тазартылған су. Дәрілік өсімдік шикізаты негізінде микробқа, қабынуға қарсы фитопрепараттың лабораторлық регламент құрастырылды. Алынған CO<sub>2</sub>-экстракт негізінде жақпа майы жасалынды. Алынған жақпа майының қауіпсіздігі, дәрілік құралдың әсер ету жоғары.

**Түйінді сөздер:** CO<sub>2</sub>-экстракты, Мақсары гүлдері, май.