RESULTS OF STUDYING OF THE KINETICS AND RELEASE OF ACTIVE SUBSTANCES FROM OINTMENTS WITH ESSENTIAL OIL OF ARTEMISIA ANNUA L.

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Abstract: *In order to develop a dosage form in the form of an ointment based on the essential oil of the herb Artemisia annua, studies were conducted to comparatively study the kinetics of release of active substances from various ointment bases. The studies were carried out in in vitro experiments using the diffusion method in agar gel. Conducted studies to study the kinetics of essential oil release confirmed the feasibility of using a polyethylene oxide base as a carrier in the developed ointment, consisting of an alloy of polyethylene oxides with a molecular weight of 400 and 1500 in a 1:1 ratio. Currently, the study of the physicochemical properties, biological safety, pharmacological and antibacterial properties of the resulting ointment, as well as its effectiveness in the treatment of burns and purulent wounds, continues.*
Keywords: *Artemisia annua L., essential oil, ointment, ointment bases, biologically active substances, flora of Turkmenistan.*

РЕЗУЛЬТАТЫ ИЗУЧЕНИЕ КИНЕТИКИ ВЫСВОБОЖДЕНИЯ ДЕЙСТВУЮЩИХ ВЕЩЕСТВ ИЗ МАЗЕЙ С ЭФИРНЫМ МАСЛОМ ПОЛЫНИ

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Аннотация: *с целью разработки лекарственной формы в виде мази на основе эфирного масла травы полыни однолетней проведены исследования по сравнительному изучению кинетики высвобождения действующих веществ из различных мазевых основ. Исследования проводился в опытах «in vitro» методом диффузии в агаровый гелью. Проведенные исследования по изучению кинетики высвобождения эфирного масла подтвердили целесообразность использования в качестве носителя в разработанной мази полиэтиленоксидной основы, состоящей из сплава полиэтиленоксидов с молекулярной массой 400 и 1500 в соотношении 1:1. В настоящее время продолжается изучение физико-химических свойств, биологической безвредности, фармакологических и антибактериальных свойств полученной мази, а также ее эффективности при лечении ожоговых и гнойных ран.*
Ключевые слова: *Artemisia annua L., эфирное масло, мазь, мазевые основы, биологически активные вещества, флора Туркменистана.*

The study of medicinal plant raw materials as a source of drugs is an urgent problem of modern pharmaceutical science. The most widespread plant as a weed in the flora of Turkmenistan is - *Artemisia annua L.*

Artemisia annua L. is an ancient herbaceous plant that has been used by traditional medicine practitioners for more than 5,000 years [1].

In Mongolian folk medicine, the inflorescences and leaves were used for anthrax and as an antipyretic. In Tibetan medicine, the inflorescences are used for throat and lung diseases. In Chinese and Indian medicine decoction of the above-ground part is used to stimulate appetite, leaves - for the preparation of juice and ointment, externally for skin diseases. The above-ground part is used as a diuretic and for jaundice in Indian medicine. Extracts from plants have bacteriostatic property [6].

Artemisia herb has been widely used in the folk medicine of Turkmenistan since ancient times for the treatment of many diseases [1. 2].

Researchers' interest in Artemisia is due to its wide therapeutic activity, its use in the traditional medicine of many peoples as an antipyretic, expectorant, anthelmintic, styptic, stimulating blood clotting, for wound healing. In African folk medicine, the herb of Artemisia is used as an antimalarial and anticancer agent [11].

In modern folk medicine of Tajikistan and Uzbekistan, the juice of fresh leaves of Artemisia is used to treat skin diseases. Decoction of the herb (1 tablespoon of herb to 1 glass of boiling water) drink 1 tablespoon before meals as an appetite stimulant. Infusion of the herb is drunk with rheumatism and lichen [6].

The herb has antioxidant activity [8]. Experimental studies have shown that extracts of the plant prevent the development of oxidative stress in the ingestion of galactose [9]. Artemisinum has a pronounced anti-inflammatory effect [12]. The flavonoids cathicin and chrysosplenol D - also possess anti-inflammatory properties. [10]. Extracts of Artemisia are potent inhibitors of tumour necrosis factor TNF-α and inhibitor of prostaglandin E2 production in activated neutrophils. Sesquiterpene lactones of the plant have a pronounced anti-pain effect [13].

Experimental studies have revealed pronounced sedative properties of Artemisia [7].

In the development of dosage forms in the form of ointment for topical treatment of purulent-inflammatory diseases of soft tissues, a special place is occupied by studies on the selection of an optimal carrier [3, 4, 5].

Essential oil obtained from Artemisia has a pronounced wound-healing effect in the treatment of experimental burn wounds and antimicrobial activity.

In order to develop a dosage form in the form of ointment based on the essential oil of Artemisia, we conducted studies on the comparative study of the kinetics of the release of active substances from different ointment bases. The studies were carried out in ‘in vitro’ experiments by the method of diffusion into agar gel [5].

For this purpose, ointments with 2% content of essential oil of annual Artemisia on different bases were prepared (Table 1).

Table 1. Composition of ointment bases used for preparation of ointment with wormwood essential oil.

№	Ointment base	Base components and their concentrations in g.
1.	Emulsion	Polyethylene oxide - 400 (PEO-400) - 18,0 Vaseline - 30,0 Lanolin - 30,0 Emulsifier 1 - 10,0 Purified water - 10,0
2.	Polyethylene oxide №1	Polyethylene oxide - 400 - 50,0 Polyethylene oxide-1500 - 50,0
3.	Cellulose gel	Cellulose - 6,0 Glycerine - 20,0 Purified water - 74,0
4.	Starch-glycerine	Starch - 7,0 Glycerine - 93,0 Purified water - 7,0
5.	Gelatin-glycerine	Gelatin - 10,0 Glycerine - 40,0 Purified water - 40,0
6.	Vaseline-lanolinic №1	Vaseline - 60,0 Lanolin - 30,0 Purified water - 10,0
7.	Vaseline-lanolinic №2	Vaseline - 50,0 Lanolin b/w - 35,0 Purified water - 15,0
8	Vaseline	Vaseline - 100,0

The diffusion rate of essential oil was determined by the diameter of the stained zone, which was formed by the interaction of Artemisia essential oil and sudan III. The diameter of the stained zones was measured every

hour for 6 hours, as well as after 12 and 24 hours from the beginning of the experiment. The essential oil of Artemisia was used as a control.

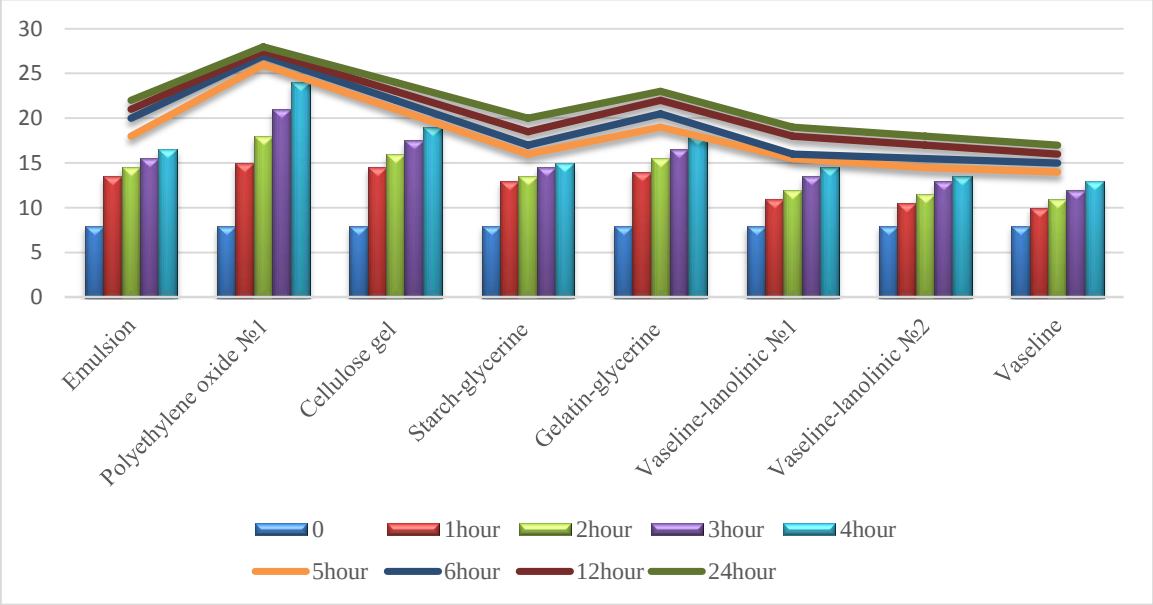

Fig. 1. Kinetics of essential oil release from ointment bases.

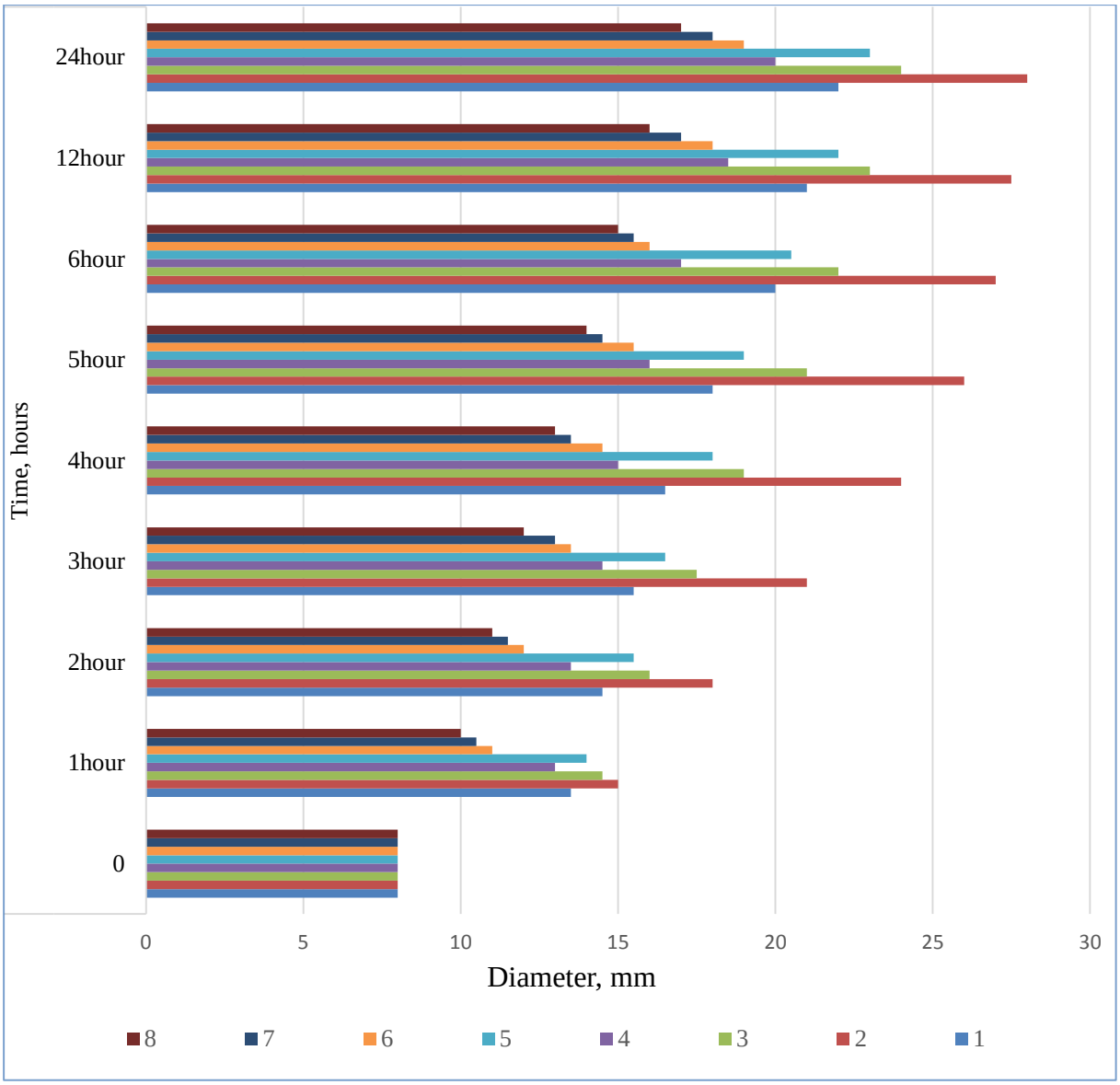

Fig. 2. Diagram of dependence of essential oil release kinetics on the nature of ointment base.

The results of studies presented in Figures 1 and 2 clearly show that the nature of ointment base significantly affects the rate of essential oil release. The highest diffusion rate was observed from bases No. 2, 3, 1, 5.

The results of the conducted studies allow all the studied ointment bases, depending on the rate of reduction of essential oil release, to be arranged in the following order:

Base No. 2 - base No. 3 - base No. 5 - base No. 1 - base No. 4 - base No. 7 - base No. 6 - base No. 8.

The conducted studies on the kinetics of essential oil release confirmed the expediency of using polyethylene oxide base consisting of an alloy of polyethylene oxides with molecular weights of 400 and 1500 in the ratio of 1:1 as a carrier in the developed ointment.

At present, the study of physicochemical properties, biological harmlessness, pharmacological and antibacterial properties of the obtained ointment, as well as its effectiveness in the treatment of burn and purulent wounds continues.

Список литературы / References

1. *Berdimuhamedow G.* Türkmenistanyň dermanlyk ösümlikleri, 1t – A.: TDNG, 2010. 141-142 sah.
2. Abu Aly Ibn Sina. Lukmançylyk ylmynyň kanunlary. – Aşgabat, 2004
3. *Грецкий В.М.* Основы для медицинских мазей. –М., 1975. -56с.
4. *Грецкий В.М., Цагарейгвили Г.В.* Носители лекарственных веществ в мазях. –Тбилиси. Мецниереба, 1979г. – 203с.

5. Методические рекомендации по экспериментальному (фактическому) изучению лекарственных препаратов для местного лечения гнойных ран /Б.М. Доценко; С.В. Бирюкова; Т.И. Тамм и др. – М., 1989г. -45с.
6. *Ходжиматов М.* Дикорастущие лекарственные растения Таджикистана. – Душанбе, 1989.
7. *Emadi F., Yassa N., Hadjiakhoondi A., Beyer C., Sharifzadeh M.* Sedative effects of Iranian Artemisia annua in mice: possible benzodiazepine receptors involvement – Pharm. Biol. 2011, Aug., 49(8), 784-788.
8. *Iqbal S., Younas U., Chan K.W., Zia-Ul-Haq M., Ismail M.* Chemical composition of Artemisia annua L. leaves and antioxidant potential of extracts as a function of extraction solvents – Molecules. 2012, May 21, 17(5), 6020-6032.
9. *Kim M.H., Seo J.Y., Liu K.H., Kim J.S.* Protective effect of Artemisia annua L. extract against galactose-induced oxidative stress in mice – PLoS One. 2014, Jul 2, 9(7), e101486.
10. *Melillo de Magalhгes P., Dupont I., Hendrickx A., Joly A., Raas T., Dessy S., Sergent T., Schneider Y.J.* Anti-inflammatory effect and modulation of cytochrome P450 activities by Artemisia annua tea infusions in human intestinal Caco-2 cells – Food Chem. 2012, Sep 15, 134(2), 864-871.
11. *Suberu J.O., Romero-Canelyn I., Sullivan N., Lapkin A.A., Barker G.C.* Comparative cytotoxicity of artemisinin and cisplatin and their interactions with chlorogenic acids in MCF7 breast cancer cells – Chem.Med.Chem. 2014, Dec., 9(12), 2791-2797.
12. *Wang K.S., Li J., Wang Z., Mi C., Ma J., Piao L.X., Xu G.H., Li X., Jin X.* Artemisinin inhibits inflammatory response via regulating NF-κB and MAPK signaling pathways – Immunopharmacol. Immunotoxicol. 2017, Feb., 39(1), 28-36.
13. *Favero F. de F., Grando R., Nonato F.R., Sousa I.M., Queiroz N.C., Longato G.B., Zafred R.R., Carvalho J.E., Spindola H.M., Foglio M.A.* Artemisia annua L.: evidence of sesquiterpene lactones' fraction antinociceptive activity – BMC Complement. Altern. Med. 2014, Jul 28, 14, 266.
14. *Hunt S., Yoshida M., Davis C.E., Greenhill N.S., Davis P.F.* An extract of the medicinal plant Artemisia annua modulates production of inflammatory markers in activated neutrophils – J. Inflamm. Res. 2015, Jan 14, 8, 9-14.