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Chromagraphic Research Of Liniment, Which Active Substance Belongs To New Derivatives Of 1, 2, 4-Triazole.

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ABSTRACT

Scientific fact is the relevance of search of new biologically active compounds among derivatives of 1,2,4-triazole [1, 2]. Researchers from different countries demonstrate the efficiency of such exploratory research. The feature of heterocycle system 1,2,4-triazole is not only high reactivity [3], but also low toxicity and biological activity [4]. We should also note the presence of antimicrobial action of some derivatives of 1,2,4-triazole-3-thiols [5].

Keywords: (4-((5-decylthio)-4-methyl-4H-1,2,4-triazole-3-yl)methyl)morpholine, chromatographic studies, physico-chemical properties.

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INTRODUCTION

Introduction in medical practice of antifungal drugs with new pharmacological properties is achieved by optimization of the treatment of animals through the use of appropriate dosage forms. In this case, their effectiveness depends on both the substance included in its composition, and on the solvent or basis. Under conditions of external use, ointments and liniments are the most widely used in veterinary medicine practice. The advantage of these is that they have better bioavailability due to light absorption of the skin and no traumatic granulation tissue [6, 7].

However, it should be remembered that the liniments are characterized by low stability of the components, both at the stage of preparation and storage [8, 9]. Scientists synthesized a new compound, which has antimicrobial properties and is promising for creation of new original veterinary medicinal product [10].

When you create a new veterinary drug in the suspension liniment we investigated this active ingredient – (4-((5-decylthio)-4-methyl-4H-1,2,4-triazole-3-yl)methyl)morpholine [10]. Solvent (base) for liniment has been used standardized oil of Silybum marianum (DSTU – copy with a sticker), which according to the literature and our own research is not only a good dispersion medium for the active substances, but also independently (Per se) manifests expressed anti-inflammatory, membrane-stimulating and wound healing properties [11, 12, 13].

However, one of the requirements for dosage forms of new drugs is that they must have a high stability when preparing and a sufficiently long shelf life. The presence of even slight impurities can lead to negative consequences, because they are, at least, indifferent, and often have a harmful effect. Especially undesirable is the presence of such substances in long-term preservatives and applications, which are ointments and liniments [7-9].

Therefore, **the aim** of our study was to identify the active substance in a soft medicinal form and to deny the existence of conglomerates (impurities) that could be formed by chemical interactions between the active substance and oil.

MATERIALS AND METHODS

The study of samples in the oils was carried out at the laboratory of gas chromatography-mass spectrometry Zaporozhye state medical University, which are designated by numbers 1, 2, 3, 4, of which:

- solution 1 – oil corn;
- a solution of 2 – (4-((5-decylthio)-4-methyl-4H-1,2,4-triazole-3-yl)methyl)morpholine butter corn;
- a solution of 3 – (4-((5-decylthio)-4-methyl-4H-1,2,4-triazole-3-yl)methyl)morpholine in the Thistle oil;
- a solution of 4 – Thistle oil.

For analysis the samples were diluted with hexane (1:10) and placed in a chromatographic Viali volume of 1.5 m. The substances were analyzed using a gas chromatograph Agilent 7890B with mass spectrometry detector 5977B. Separation of substances was performed on a column DB-5ms of length 30 m, internal diameter 250 µm and thickness phase 0.25 µm. The speed of the carrier gas (helium) – 1.6 ml/min injection Volume – 0.5 µl. The division of the flow – 1:30. The temperature of the input block of samples, 275 OS.

Temperature of thermostat: programmable – 80 OS (1 min delay), rising to 240 OS with the Swiss. About 40/min, then to 280 OS with the Swiss. 10 o/min, then to 302 OS with the Swiss. 2 o/min. Peak (4-((5-decylthio)-4-methyl-4H-1,2,4-triazole-3-yl)methyl)morpholine was identified by mass molecular ion, as reflected in the mass spectrum. The library of mass spectra NIST14 was used to identify background components of the oils.

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RESULTS AND THEIR DISCUSSION

Chromatogram demonstrated the presence of the peak of the active substance (4-((5-decylthio)-4-methyl-4H-1,2,4-triazole-3-yl)methyl)morpholine in solutions 2 and 3 (retention time of approximately 12.7 min) and its absence in solutions 1 and 4 (solutions of pure oils in hexane).

The obtained mass spectrum for peak compounds in solutions 2 and 3 indicates the presence of the molecular ion, characteristic for this compound (mass number 354,3), which confirms its presence in the oil solutions 2 and 3. Chromatogram solutions are reproduced in figures 1-4. Figure 1.5 reflects the mass spectrum obtained for peak (4-((5-decylthio)-4-methyl-4H-1,2,4-triazole-3-yl)methyl)morpholine.

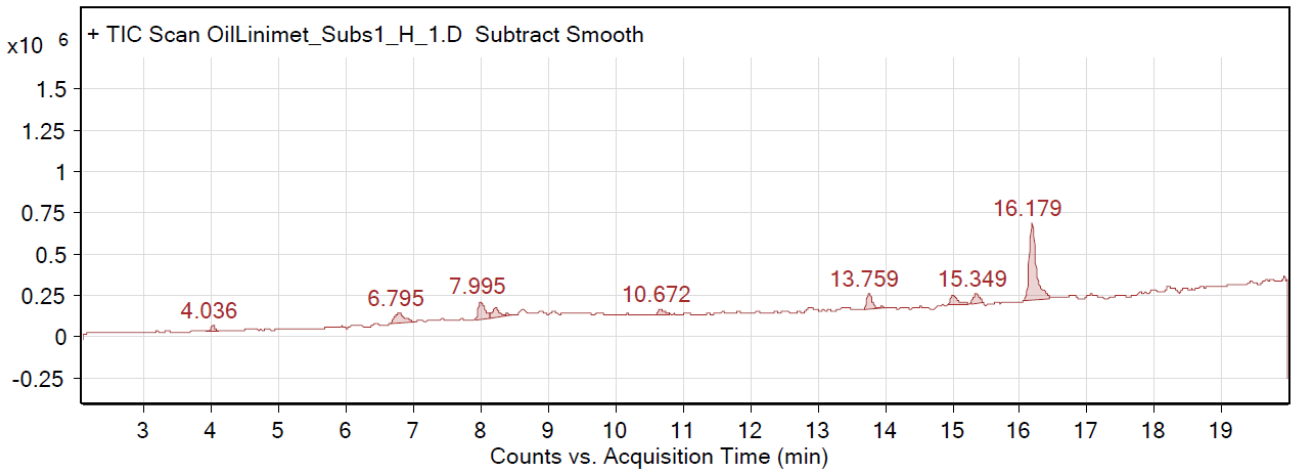

Fig 1: The chromatogram of solution 1 (oil corn).

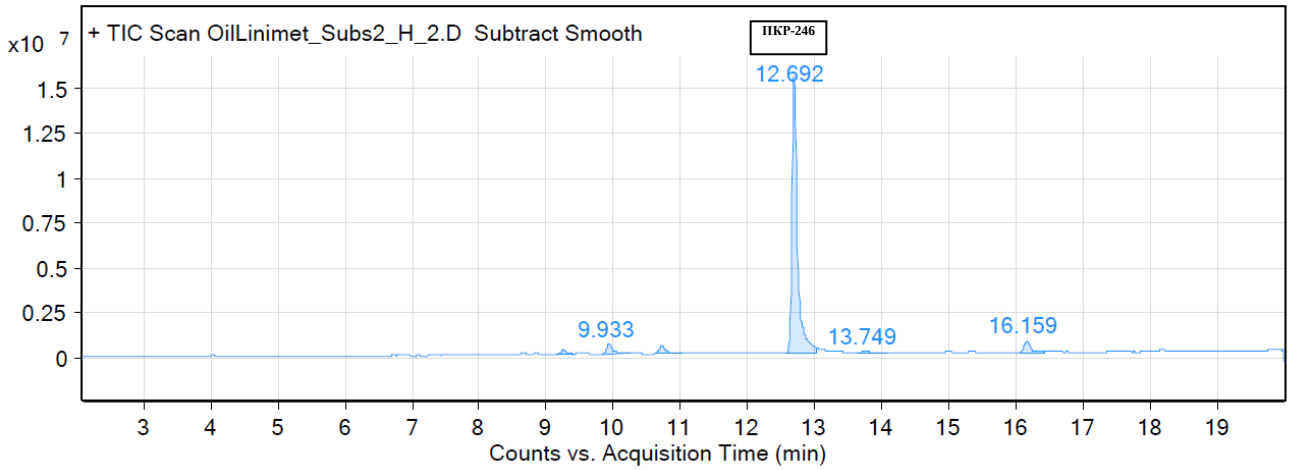

Fig 2: Chromatogram of a solution of 2 ((4-((5-decylthio)-4-methyl-4H-1,2,4-triazole-3-yl)methyl)morpholine in corn oil).

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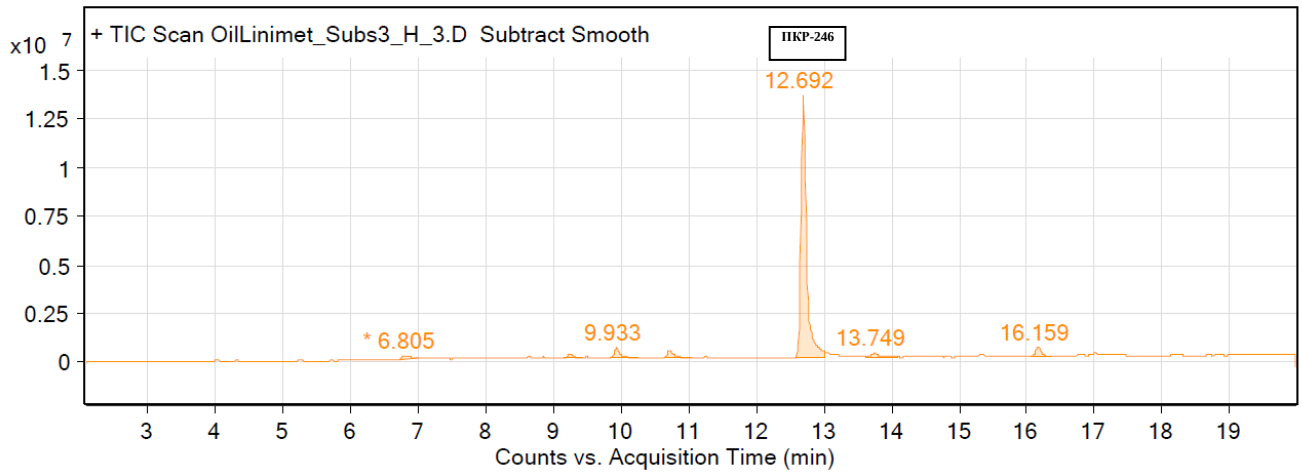

Fig 3: Chromatogram of a solution of 3 ((4-((5-decylthio)-4-methyl-4H-1,2,4-triazole-3-yl)methyl)morpholine in the Thistle oil).

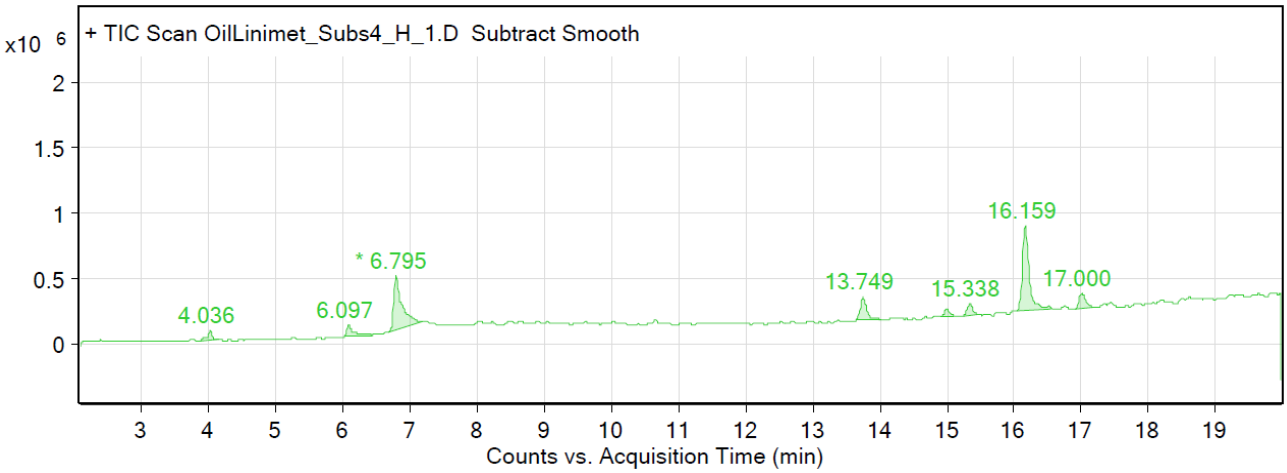

Fig 4: Chromatogram of a solution of 4 (Thistle oil).

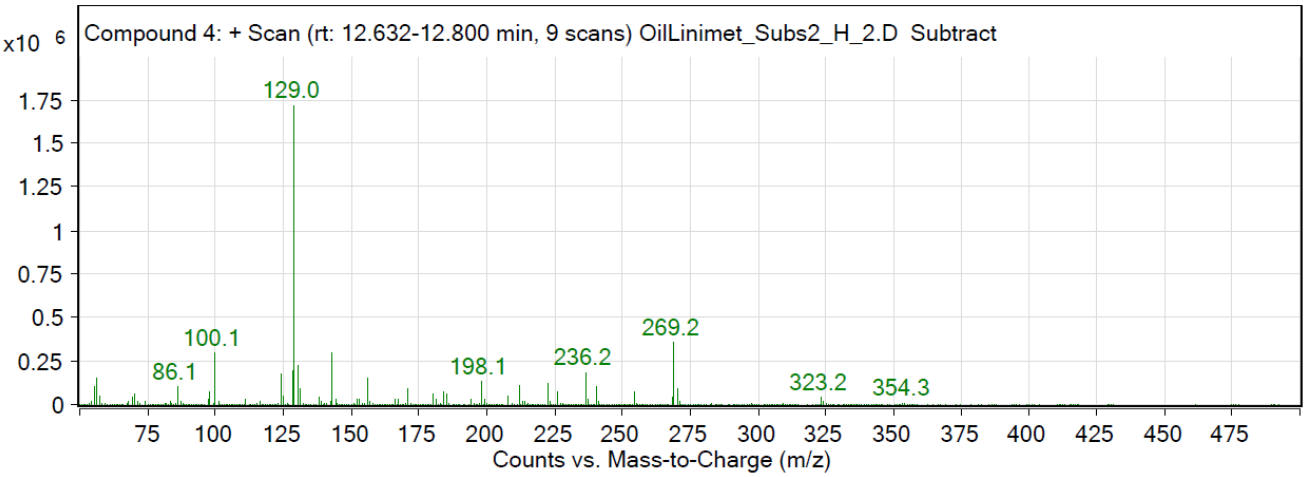

Fig 5: The mass spectrum obtained for peak (4-((5-decylthio)-4-methyl-4H-1,2,4-triazole-3-yl)methyl)morpholine (retention time 12,692 minutes).

In this case, it is possible to observe a separate peak (4-((5-decylthio)-4-methyl-4H-1,2,4-triazole-3-yl)methyl)morpholine on chromatograms 2 and 3, and the peaks of substances that are characteristic of corn

oil and milk Thistle which have the same substances found in pure oils without the addition of the compounds on chromatogram 1 and 4, respectively. A separate peak (4-((5-decylthio)-4-methyl-4H-1,2,4-triazole-3-yl)methyl)morpholine on chromatograms with solutions 2 and 3 shows that the active substance does not form stable bonds with molecules characteristic of corn oil and milk Thistle, respectively. Otherwise, chromatograms 2 and 3 would be available impurities with a high molecular weight, while a separate peak PKR-246 would be absent. This can be explained by the fact that the pharmaceutical form for substances 2 and 3 ((4-((5-decylthio)-4-methyl-4H-1,2,4-triazole-3-yl)methyl)morpholine in corn oil and milk Thistle, respectively) is a suspension in which the dispersion medium is one of the oils (liquid state), and the dispersed phase acts as the active substance (substance (4-((5-decylthio)-4-methyl-4H-1,2,4-triazole-3-yl)methyl)morpholine). In this system the active substance is practically not mixed and does not show chemical interactions with corn oil or milk Thistle. Thus, we can conclude that when using this drug in the form of soft medicinal forms there are no obstacles for the action of the active pharmaceutical ingredient, i.e. the substance (4-((5-decylthio)-4-methyl-4H-1,2,4-triazole-3-yl)methyl)morpholine.

CONCLUSIONS

1. Using gas chromatography-mass spectrometry samples of soft medicinal form with an active pharmaceutical ingredient – (4-((5-decylthio)-4-methyl-4H-1,2,4-triazole-3-yl)methyl)morpholino was examined for the first time.
2. Analyzing the results of the chromatographic mass spectrometry studies, the active ingredient of this formulation - (4 - ((5-decylthio) -4-methyl-4H-1,2,4-triazol-3-yl) methyl) morpholine and auxiliary components of a soft dosage form were identificated.
3. It is established that in this system the active substance is practically not mixed and does not show chemical interactions with corn oil or milk Thistle.

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