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RECEIVING SUSPENSION FORM OF 3(H)-6-NITROQUINAZOLIN-4-ONE

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ПОЛУЧЕНИЯ СУСПЕНЗИОННАЯ ФОРМА 3(H)-6-НИТРОХИНАЗОЛИН-4-ОНА

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ABSTRACT

The stable 10% suspension form of 3(H)-6-nitroquinazolin-4-one based on quinazolin-4-one was obtained. The anti-fungal activity of the resulting suspension was studied against the phytopathogen Fusarium oxysporum Schrf. Suspension of 3(H)-6-nitroquinazolin-4-one fully complies with the requirements for use in plant protection. It has been established that the resulting suspension form of 3(H)-6-nitroquinazolin-4-one exhibits high activity against 3(H)-6-nitroquinazolin-4-one.

АННОТАЦИЯ

Получена стабильная 10% суспензионная форма 3(H)-6-нитрохиназолин-4-она на основе хиназолин-4-она. Противогрибковую активность полученной суспензии изучали в отношении фитопатогена *Fusarium oxysporum Schrf.* Суспензия 3(H)-6-нитрохиназолин-4-она полностью соответствует требованиям для применения в защите растений. Установлено, что полученная суспензионная форма 3(H)-6-нитрохиназолин-4-она проявляет высокую активность в отношении 3(H)-6-нитрохиназолин-4-она.

Keywords: heterocyclic compounds, biological activity, IR spectroscopy, 3(H)-6-nitroquinazolin-4-one, suspension, particle size, stability, antifungal activity, fungicide.

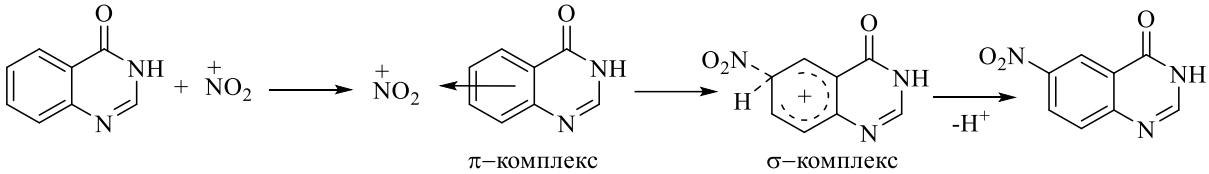
Ключевые слова: гетероциклическая соединения, биологическая активность, ИК-спектроскопия, 3(H)-6-нитрохиназолин-4-он, суспензия, размер частиц, устойчивость.

Introduction. Recently, the production of drugs with high demand is increasing every year, which is associated with the introduction of new innovative technologies for the synthesis of organic substances based on heterocyclic compounds. The use of new catalysts in the synthesis of quinazolin-4-one derivatives from natural raw materials, carrying out technological calculations of process control, development of drug forms, the use of 6-monosubstituted quinazolin-4-one derivatives in the chemical industry, medicine and agriculture in obtaining high-quality drugs is of great importance. obtaining and modification of many new substances by introducing various functional groups into their composition.

The development of new, low-stage, technologically inexpensive and convenient methods of synthesis for obtaining highly biologically active compounds from existing raw materials is one of the urgent tasks facing the science of organic chemistry and chemical technology. Fused heterocyclic compounds known to chemists around the world exhibit various biological activities. Quinazolin-4-one is also a heterocyclic compound. The literature presents methods for the synthesis of quinazolin-4-one derivatives in the presence of various catalysts and their analgesic, antiviral, antituberculosis, antibacterial, anticonvulsant, antifungal, antimicrobial biological activity [1; 87-91 pp., 2; 93-101 pp., 3; 3430-3440 pp., 4; 1-11 pp., 5; 289-296 pp., 6; 1-16 pp., 7; 10-13 pp., 8; 66-613 pp., 9; 25-27 pp., 10; 23-25 pp.].

Preparations for chemical plant protection, in particular fungicides, are often used in the form of aqueous suspensions or emulsions of active ingredients. This is due to the fact that biologically active substances, as a rule, are hydrophobic compounds, slightly soluble in water or completely insoluble in water. The use of powdered preparations causes practical inconvenience. As a result, their activity against bacteria and strains is significantly reduced when used as drugs in agriculture.

In the course of our studies, the factors influencing the synthesis and course of the reaction of the compound 3(H)-6-nitroquinazolin-4-one were studied in detail, and the following reaction mechanism was proposed [11; 48-53 pp.].



3(H)-6-nitroquinazolin-4-one extra reaction

The synthesized 3(H)-6-nitroquinazolin-4-one is a pale yellow, odorless, finely crystalline substance, slightly soluble in 96% ethanol and practically insoluble in water.

When determining the stretching vibrations of 3(H)-6-nitroquinazolin-4-one by the IR spectrum, the stretching vibration of the C=O group, which is in the fourth state of the compound, is in the region of 1668 sm^{-1}, the NH group in the third position in the region of 3417 sm^{-1}, and the C=N group in the region of 1618 cm^{-1}, and the C-N group in the region of 1467 sm^{-1}, and the stretching vibrations of the C-NO_2 bond in the aromatic ring in the fields, the appearance of 1514 sm^{-1} was observed.

The structure of synthesized 3(H)-6-nitroquinazolin-4-one was analyzed using ^1H, NMR spectrum method. In this case, the value of the aromatic H-2 proton in the weak field is 8.45 ppm. in the field, the chemical shift appears in the form of a one-proton singlet. H-5 proton value is 8.98 ppm. chemical shift is shown in the form of one-proton doublet doublet (J_1=0.41, J_2=2.66 Hz) and the H-7 proton value is 8.55 ppm in the field, one-proton doublet is in the form of a doublet (J_1=2.66, J_2=9 Hz), and the value of the H-8 proton is 7.9 ppm chemical shifts in the form of a one-proton doublet (J_1=0.42 Hz) in the fields and the absence of signals of the proton in the H-6 state in the corresponding field confirms that it is 3(H)-6-nitroquinazolin-4-one.

The spectrogram of this compound obtained by the mass spectroscopic analysis method was analyzed. From the obtained spectra (LC/MS), it can be seen that the presence of an intense peak of the molecular ion at m/z 191 and the following fragmentations: 146 $[M-CONH]^+$, 119 $[M-CONHCHN]^+$ prove the given structure. This molecular mass corresponds to the molecular mass of 3(H)-6-nitroquinazolin-4-one. The calculated molecular mass corresponds to the mass obtained from the mass spectrum. ESI-HRMS: calculated $C_8H_5N_3O_3$: 191.0332, found 191.0331. R_f=0,48. The system is acetone: benzene 3:2. Melting temperature 287-289 °C. Molecular mass 191,144.

In this study, a 10% suspension form of 3(H)-6-nitroquinazolin-4-one compound, which showed high biological activity against *Fusarium oxysporum Schrf*, was developed. To create a stable suspension form of the drug, it is necessary to minimize the particle size of the active substance. In addition, the minimum size of the active iingredients helps to ensure the best contact of the drug with the object of exposure. Therefore, the use of drugs in the suspension form in agriculture is widely proven to give positive results.

Experimental part

4.0 g of glycerol, 9.0 g of ethyl alcohol and 14.6 g of 3(H)-6-nitroquinazolin-4-one were stirred with a magnetic stirrer for 60 minutes. until a pale yellow homogeneous mass is obtained. Then, 80.0 g ml of a 2.0% pre-prepared CMC solution was added with continuous stirring. To the resulting suspension was added 3.0 g of a 5% pre-prepared solution of sodium benzoate to obtain a stabilized suspension of 3(H)-6-nitroquinazolin-4-one (10%) with a pH of 5.8.

To determine the particle size of 3(H)-6-nitroquinazolin-4-one in the resulting suspension, we used an

electron microscope brand MOTIC BA 210; manufacturer Motic China Group Co. Ltd., (China).

Determination of antifungal activity was carried out by the method of paper discs *Fusarium oxisporum Schrf* [12; 216-217 pp]. Was isolated from plant material by methods [13; 550 p, 14; 193 pp]. The emulsion was applied to disks (0.6 mm in diameter) and laid out on the surface of the nutrient medium. The cups were placed in a thermostat and incubated at a temperature of 25-28°C for 5 days. The activity of substances was judged by the size of the zone of no growth. Methanol was used as a negative control, and Tebuconazole, a triazole fungicide used in agriculture to protect field and grain crops from pathogenic fungicide, was used as a standard [15; 27-32 pp].

A suspension is a dispersed system that consists of at least two components, one of which is dispersed in the form of small particles in another substance - a dispersion medium. A characteristic property of a dispersed system is the presence of a large interfacial surface; therefore, the surface properties for it are decisive. There are two methods for obtaining suspensions: dispersion and condensation. The condensation method for obtaining suspensions is based on the replacement of the solvent, this method is used mainly in the conditions of a small pharmacy production.

The dispersion method for obtaining suspensions is based on grinding particles of the active substance. Dispersion methods require energy to overcome the forces of intermolecular interaction. Grinding of solid substances of AD is carried out by crushing, abrasion, crushing. splitting mechanically using crushers, mortars and mills of various designs (ball, vibration, jet), ultrasound, as well as electrical methods [13; 64-67 pp.].

In this work, we used a dispersion method for obtaining a stable suspension of 3(H)-6-nitroquinazolin-4-one. For suspensions as a heterogeneous system, sedimentation stability (stability) is very important. It is known that the sedimentation stability of suspensions depends very much on the size of the dispersed particles of the active substance, the smaller the size, the more stable the suspension. Usually, mechanical reduction of the particle size is carried out by grinding in a liquid dispersion medium, in which it is insoluble, is. This approach is more efficient than dry grinding. In this work, the dispersion medium used to reduce the particle size of 3(H)-6-nitroquinazolin-4-one is alcohol-glycerol.

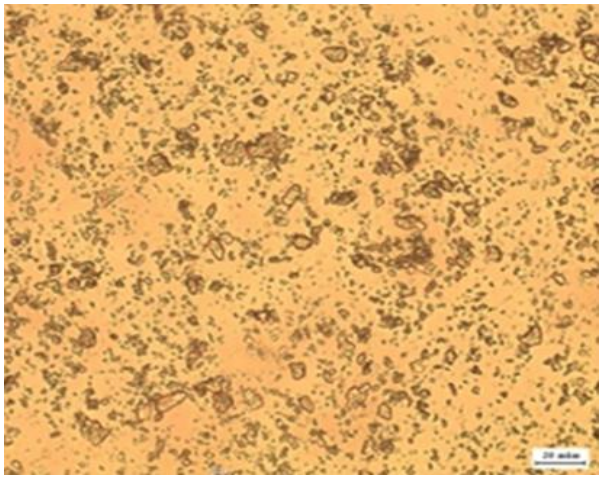


Figure 1.

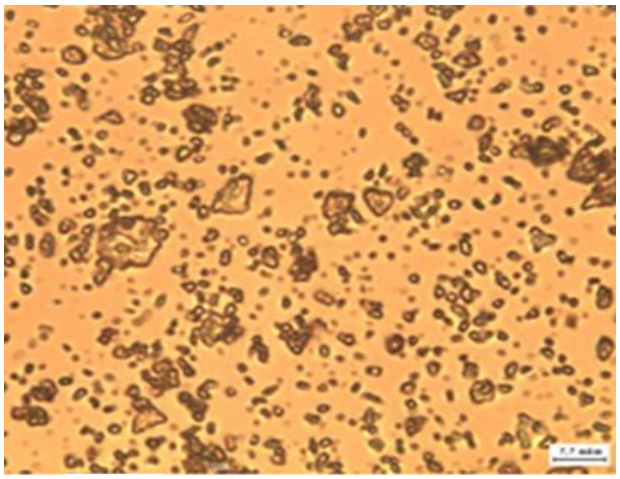


Figure 2.

Figure 1, 2. Images of the suspension under the electron microscope

Surfactants and stabilizers are used to increase sedimentation stability in the preparation of suspensions. In the scientific literature, Tween-80 and xanthan gum, liquid paraffin, agar-agar, propylene glycol, etc. are most often used as stabilizers [14; 29-34 pp].

In this work, as a stabilizer and surfactant, we used sodium carboxymethylcellulose, which is produced in the Republic of Uzbekistan and is quite affordable and inexpensive drug. Figures 1-2 show pictures of a 10% suspension of 3(H)-6-nitroquinazolin-4-one under an electron microscope at various magnifications.

Obviously, the size and shape of particles in suspensions depend on the intensity and duration of mixing of the mixture of components, as well as on the type of stirrers in the device. We used a laboratory magnetic stirrer in our work. Dispersion was carried out by intensive stirring in a dispersive alcohol-glycerol medium until a visually homogeneous dispersion in the form of a white mass was formed. As can be seen from the figures, 3(H)-6-nitroquinazolin-4-one particles in suspension have a generally rounded shape. In addition, the distribution of particles is sufficiently uniform to meet all the requirements for suspension preparations.

Table 1 presents the analytical data of a 10% suspension of 3(H)-6-nitroquinazolin-4-one.

Table 1.

Analytical characterization of 10% suspension of 3(H)-6-nitroquinazolin-4-one

Name of indicator	Analysis results
Appearance, color	Milky white suspension
Density 20°C g/sm^3	1,05-1,10
pH value	5,0-5,5
Particle size, μm	Before 5 μm
Mass share 3(H)-6-nitroquinazolin-4-one, %	10±0,25
Sedimentation resistance, min.	Over 60

As can be seen from Table 1, the 10% suspension of 3(H)-6-nitroquinazolin-4-one we received meets all the requirements for suspension preparations.

The study of the antifungal activity of a 10% suspension of 3(H)-6-nitroquinazolin-4-one was carried out in laboratory tests against the phytopathogen *Fusarium oxisporum Schrf.* in comparison with the original powder 3(H)-6-nitroquinazolin-4-one. The results are presented in table 2.

Table 2.

Comparative fungicidal activity of 3(H)-6-nitroquinazolin-4-one in suspension and powder form

№	Drugs	Concentration, %	No growth zone, mm
1	Powder 3(H)-6-nitroquinazolin-4-one	10	17,6
2	Suspension 3(H)-6-nitroquinazolin-4-one	10	20,1
3	TEBU (control)	0,5	20,2

It can be seen that the zone of no growth of the phytopathogen in the case of the initial 3(H)-6-nitroquinazolin-4-one powder is 17.6 mm, and when using the suspension form we obtained, it is 20.1 mm. The well-known fungicide tebuconazole was used as a control. The results obtained indicate that both forms of 3(H)-6-nitroquinazolin-4-one exhibit fungicidal activity against the phytopathogen *Fusarium oxisporum Schrf.* almost on the same level.

Conclusions

Thus, we obtained an effective stable 10% suspension form of 3(H)-6-nitroquinazolin-4-one, which meets all the requirements for suspension preparations. Biological studies have shown that the resulting suspension has a higher fungicidal activity than the original 3(H)-6-nitroquinazoline-4-one powder.

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