The Austrian Journal of Technical and Natural Sciences, No 1–2
ISSN 2310-5607

PREMIER Publishing
ppublishing.org

DOI:10.29013/AJT-24-1.2-28-35

SYNTHESIS AND BIOLOGICAL ACTIVITY OF HYDROCHLORID QUINAZOLIN-4-ONE

Saitkulov Foziljon Ergashevich [1], Elmuradov Burkhon Zhuraevich [2], Sapaev Bayramdury [3]

[1] Tashkent state agrarian universitet of Uzbekistan, Tashkent

[2] Institute of Chemistry of Plant Substances Academy of Sciences of the Republic of Uzbekistan, Republic of Uzbekistan, Tashkent

[3] Alfraganus University of Uzbekistan, Tashkent

Cite: *Saitkulov F.E., Elmuradov B.Z., Sapaev B. (2024). Synthesis and Biological Activity of Hydrochlorid Quinazolin-4-one. Austrian Journal of Technical and Natural Sciences 2023, No 11-12.* https://doi.org/10.29013/AJT-24-1.2-28-35

Abstract

By the interaction of anthranilic acid with formamide, an almost quantitative yield of quinazoline-4-oh was obtained. Optimal reaction conditions were established: temperature 130–140 °C, duration 2 hours. Quinazoline-4-oh hydrochloride was obtained from quinazoline-4-oh by passing hydrogen chloride with 96% yield. These compounds at a dose of 100–150 mg/kg exhibit 92% anthelmintic activity against fascioles common in cattle, sheep and goats.
Keywords: *Formamide, quinazoline-4-one, quinazoline-4-oh hydrochloride fascioliasis, stability of the drug, medamine, albendazole, cattle, sheep and goats, activity against fascioliasis*

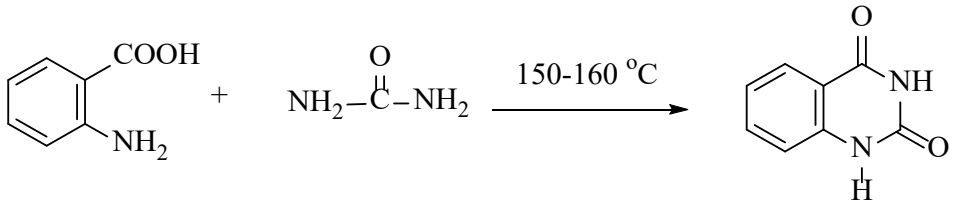
Introduction

The government attaches more importance to the further increase of folk medicine. A significant place in these activities has been removed from the chemicalization of agriculture and animal husbandry. The Government drew attention to the need for extensive development of scientific research on the creation of herbicides, fungicides, anthelmintic drugs and drugs for pest control of agricultural crops, the organization and search for industrial production of new pesticides. A number of biologically active drugs are known from derivatives of quinazoline-4-one and its sulfur analog quinazoline-4-thion (Saitkulov, F.E., Tashniyazov, A.A., Mamadrahimov, A.A., & Shakhidoyatov, K.M., 2014). Recently, scientists from various countries have led to the creation of a large group of highly effective anthelmintic drugs, among the derivatives of quinazoline-4-one (Sapaev, B., Saitkulov, F.E., Tashniyazov, A.A., & Normurodov, O.U., 2021). Infection with various kinds of helminths is a widespread disease among both humans and animals. The main requirements for new anthelmintic drugs should be considered a high therapeutic index, a wide spectrum of action, ease of administration, in particular, single-dose

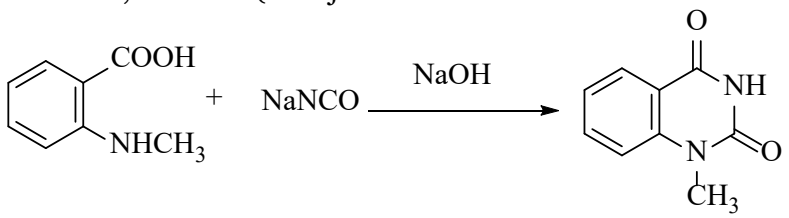
treatment and stability of the drug in dosage forms (Sapaev, B., Sapaev, I. B., Saitkulov, F. E., Tashniyazov, A. A., & Nazaraliev, D., 2022; Baymuratova, G., Nasimov, K., & Saitkulov, F., 2023).

Results

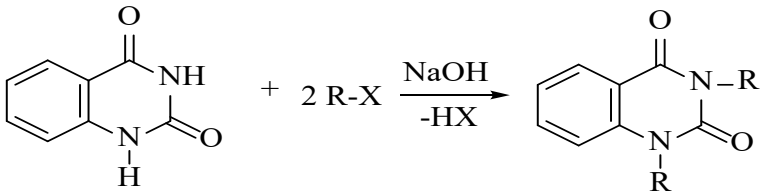
It is known from the literature that quinazoline-2,4-dione is synthesized by heating a mixture of anthranilic acid with mochevina at 150–160 °C (Khatamov, K., Saitqulov, F., Ashurov, J., & Shakhidoyatov, K., 2012).



The cyclization reaction of N-methylanthranilic acid with sodium cyanate under alkaline conditions resulted in the synthesis of 1-Methylqinazoline-2,4-dione (Foziljon Saitkulov, Bairamdurdi Sapaev, Khasan Nasimov, Dilorom Kurbanova and Nargiza Tursunova, 2023).

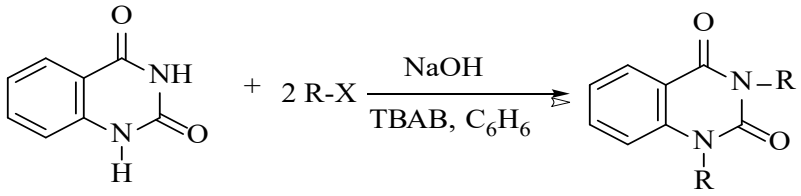


From the reaction of quinazoline-2,4-dione with alkylgalogenides under alkaline conditions, 1,3-dialkylchinazoline-2,4-diones were obtained with high prosent (A-method) (Bairamdurdi Sapaev, Foziljon Saitkulov, Muattar Mamedova, Shahlo Saydaliyeva and Dilafruz Makhmudova, 2023).



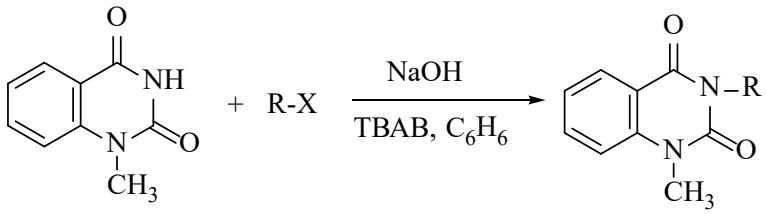
X=Cl, I
R=CH_3, R= н-C_3H_7, R= н-C_4H_9, R= $C_6H_5CH_2$

It should be noted that under the conditions of interphase catalysis (Саиткулов, Ф. Э., Элмурадов, Б. Ж., & Гиясов, К., 2023). 80–95% oxidation of compounds (B) can be observed in these reactions.



X=Cl, I

Quinozoline-2,4-dione is an equivalent alkylating agent and is formed as a result of the reaction of 1,3-dialkylquinazolin – 2,4-dione to form 1- or 3-monoalkyl molecules (Saitkulov, F., Qilichyeva, N., Abdullayev, B., Anvarov, A., & Ergasheva, M., 2022).



R=н-C_3H_7, R=н-C_4H_9, R=$C_6H_5CH_2$
X=Cl, I

Synthesis of 1-methylquinazoline-2,4-dione alkyl iodides and benzyl chloride of Bilan tetrabutylammonium bromide (TBAB) ishtirok by interphase catalysis in sharoitide (Saitkulov, F., Farhodov, O., Olisheva, M., Saparboyeva, S., & Azimova, U., 2022) as a result of alkylation of 1-methyl-3-alkyl(benzyl)quinazoline-2,4-diones not listed in the literature.

There are many works on the synthesis of quinazoline-4-one and its derivatives (Boymuratova, G.O., Saitkulov, F.E., Nasimov, K.M., & Tugalov, M., 2022; Murodillayevich, K.M., Shoyimovich, K.G., & Ergashevich, S.F., 2022; Саиткулов, Ф.Э., 2022; Saitkulov, F., Begimqulov, I., O'ralova, N., Gulimmatova, R., & Rahmonqulova, D., 2022; Saitkulov, F., Elmuradov, B., O'lmasova, K., & Alijonova, A., 2023; Bairamdurdi Sapaev, Foziljon Saitkulov, Muattar Mamedova, Shahlo Saydaliyeva and Dilafruz Makhmudova, 2023). In most cases, synthesis is carried out from anthranilic acid and its derivatives. Known methods of obtaining quinazoline-4-it is not simple and affordable. The most widely used method is based on the use of hard-to-reach substances.

Method and Methodology

Quinazoline-4-one. Method: A

13.7 g (0.1 mol) of anthranilic acid and 16 ml (0.4 mol) of formamide (p = 1.13 g/ sm^3) were placed in a two-neck flask equipped with a reverse refrigerator.

The reaction mixture was heated in a glycerin bath at 130–135 °C for 2 hours. After cooling to room temperature, the reaction mixture was poured into a glass containing crushed ice and left for 6–8 hours at room temperature. The fallen crystals were filtered, dried and recrystallized in water in the presence of activated carbon. Received 10.7 g (73.3%) of quinazoline-4-one**.**

T = 218 ºC, R_f = 0.63.

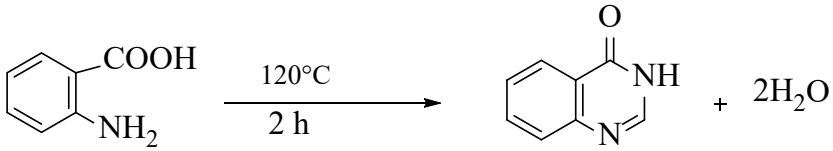
Method B. Similar to Method A, a mixture of 13.7 g (0.1mol) of anthranilic acid and 16 ml (0.4 mol) of formamide (p= 1.13 g/cm^3) heating the Vood alloy at 130–135 °C for 2 hours and received 13.92 g (96%) of quinazoline-4-one, T = 218 ºC R_f = 0.63.

Preparation of quinazoline-4-one hydrochloride

To a mixture of 13.7 g (0.1 mol) of quinazoline-4-one and 50 ml of dry acetone, while stirring, hydrogen chloride gas, obtained from 11.7 g (0.1 mol) of sodium chloride and 9.8 g (0.1 mol) of sulfuric acid, was slowly passed through a gas outlet tube for an hour. After removal of the solvent, quinazoline-4-oh hydrochloride was isolated with almost quantitative yield, T=180–181 °C.

The aim of the work was to obtain quinazoline-4-oh hydrochloride and laboratory tests for anthelmintic activity.

The synthesis of quinazoline-4-one by the Nimentovsky reaction proceeds when anthranilic acid is heated with an excess of formamide with the cleavage of two water molecules. The low yield in this reaction was tried to explain by its dehydration.



Depending on the reaction conditions, we increased the yield of quinazoline-4-one to 96% by two methods (A and B).

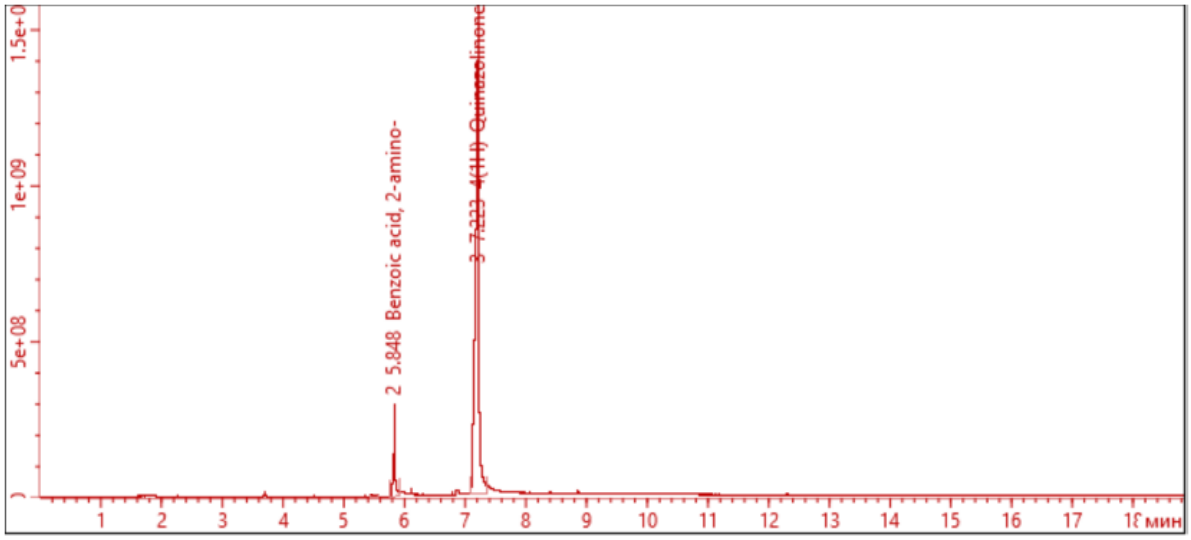
Method A. To obtain the substance quinazoline-4-one, 16 ml (0.4 mol) of formamide (p = 1.13 g/sm^3) was added to

13.7 g (0.1 mol) of anthranilic acid, and the reaction mixture was heated in a glycerin bath at 130–135 °C for 2 hours. Quinazoline-4-oh was obtained at 72% yields.

Conclusion

In the method, a mixture of anthranilic acid and formamide in a ratio of 1:4 was heated into Vood alloy at 130–135°C for 2. The yield of quinazoline-4-one was 96%. Thus, heating plays an important role in the reaction output (Fig. 1).

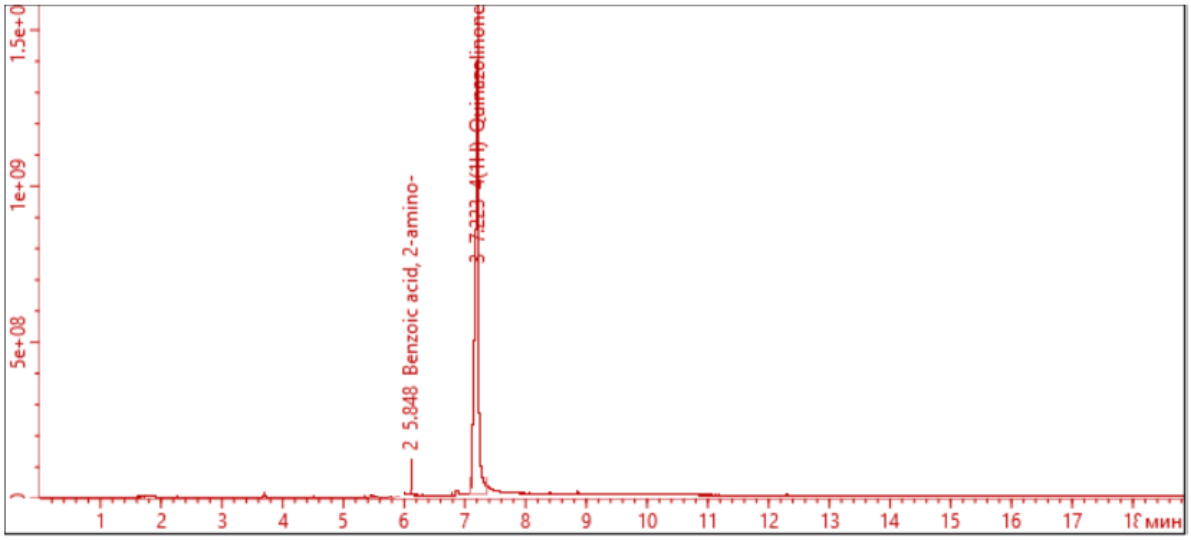
Figure 1.



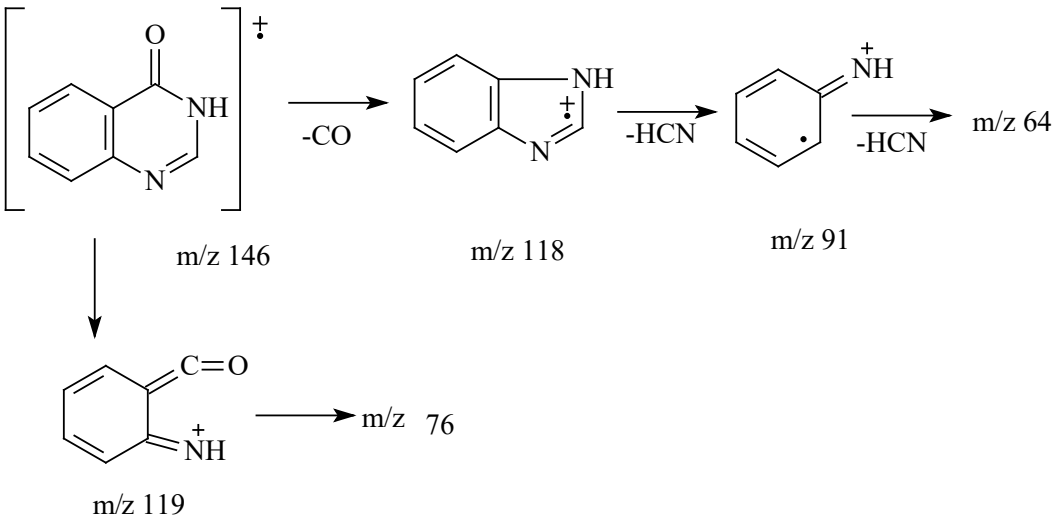
The purity of the product and the course of the reaction were controlled by TLC, Silufol UV-254. (system benzene: acetone 5:3). The melting point of quinazoline-4-oh was determined on the heating table “BOETIUS (Germany)”.

The mass spectrum of quinazolin-4-one was removed by chromatek Crystal with the Chromatek-Crystal 5000 mass spectrometric detector, fully confirm the structure of quinazolin-4-one (Fig-2).

Figure 2.



The mass spectrum of quinazoline-4-one is characterized by the presence of an intense peak of the molecular ion. The decay of the molecular ion quinazoline-4-it proceeds with the elimination of CO and HCN. Further fragmentation of the (M–CO)+ ion occurs with the releaseof two HCN molecules.



The structure of the quinazoline-4-on molecule is fully consistent with valence angles 1HNMR spectra.

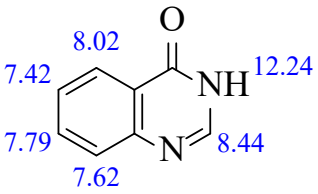


Figure 3.

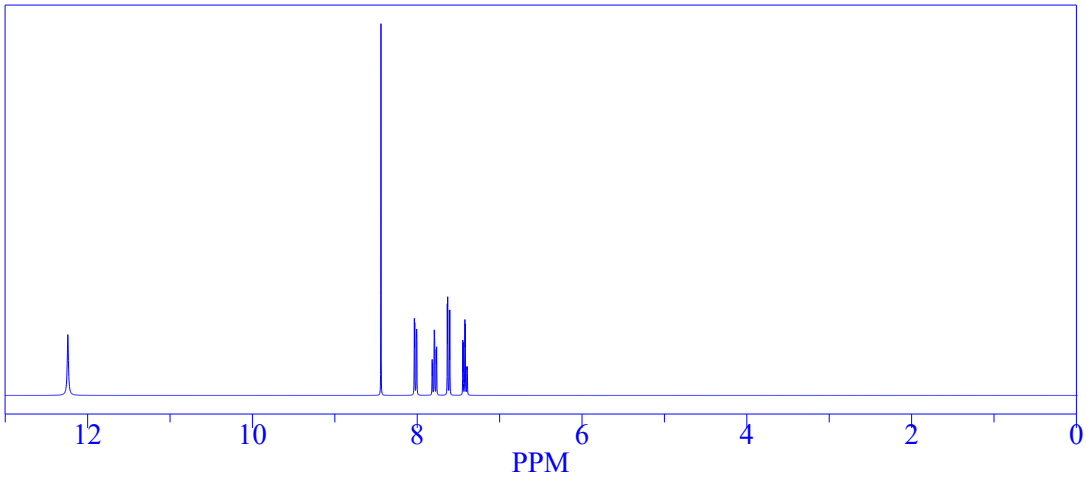
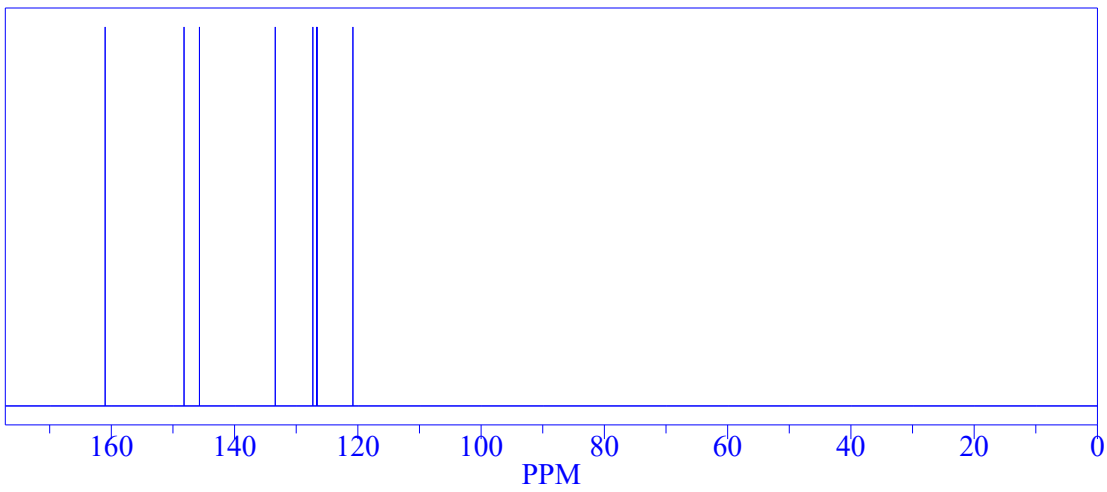


Table 1.

Protocol of the C-13 NMR Prediction: (Lib=S)			
Node	**Shift**	**Base + Inc.**	**Comment (ppm rel. to TMS)**
C	161.0	165.0	1 – amide
		4.7	1–1: C*C*C*C*C*C*1
		?	1 unknown substituent(s) from N-amide
		–8.7	general corrections
CH	145.7	162.8	1–imine
		?	1 unknown substituent(s)
		0.0	1 – C*R from N-imine
		–17.1	general corrections

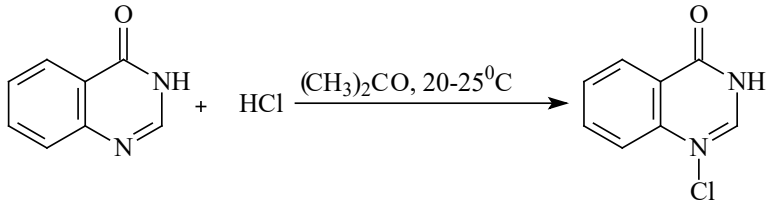
Protocol of the C-13 NMR Prediction: (Lib=S)			
Node	**Shift**	**Base + Inc.**	**Comment (ppm rel. to TMS)**
C	148.2	128.5	1–benzene
		20.5	1 – N=C
		–1.2	1 –C(=O)-N
		0.4	general corrections
C	120.8	128.5	1 – benzene
		–6.5	1 –N=C
		5.0	1 – C(=O)-N
		–6.2	general corrections
CH	126.7	128.5	1–benzene
		–6.5	1 – N=C
		0.1	1 – C(=O)-N
		4.6	general corrections
CH	126.6	128.5	1 – benzene
		1.3	1 – N=C
		–1.2	1 – C(=O)-N
		–2.0	general corrections
CH	133.4	128.5	1 – benzene
		1.3	1 – N=C
		3.4	1 – C(=O)-N
		0.2	general corrections
CH	127.3	128.5	1 – benzene
		–1.5	1 – N=C
		0.1	1 – C(=O)-N
		0.2	general corrections

Figure 4.



The structure of the quinazoline-4-on molecule is fully consistent with valence angles NMR1^{3}C spectra.

By passing hydrogen chloride to the acetone solution of quinazoline-4-one, hydrochlorid quinazoline-4-one was obtained with almost quantitative yield.



Derivatives of quinazoline-4-oh have been studied for anthelmintic activity against gastric-intestinal fascioles of various concentrations in laboratory conditions. According to the test results, the derivative did not exhibit anthelmintic properties. On the other hand, it has been studied that quinazoline-4-oh hydrochloride has anthelmintic properties. Substances that fight certain anthelminths were obtained in the form of Medamine, Albendazole, a confirming (reference) agent in the fight against a wide range of spirals. Good results were achieved in cattle, sheep, goats when using quinazoline-4-one hydrochloride. At a dose of 100–150 mg/ kg, it exhibits 92% anthelmintic activity against fascioliasis.

In the future, it is possible to create drugs from among substances derived from quinazoline-4-oh and quinazoline-4-tion, which may exhibit high anthelmintic activity. Thus, the recommended quinazoline-4-oh hydrochloride can be used as an effective drug against fascioliasis helminthiasis.

1. A one-stage method for obtaining quinazoline-4-oh has been developed by condensation of anthranilic acid and formamide when heated into Wood alloy. The optimal temperature was established – 130–135 °C, duration 2 h

2. It was shown that quinazoline-4-oh hydrochloride in doses of 100–150 mg/kg eliminates up to 100% of helminthiasis of gastrointestinal fascioles.

References

Saitkulov, F. E., Tashniyazov, A. A., Mamadrahimov, A. A., & Shakhidoyatov, K. M. (2014). 2, 3-Dimethylquinazolin-4 (3H)-one. *Acta Crystallographica Section E: Structure Reports Online*,– *70*(7).– o788-o788.

Sapaev, B., Saitkulov, F. E., Tashniyazov, A. A., & Normurodov, O. U. (2021). Study of methylation reactions of 2-phenylquinazoline-4-tion with “soft” and “hard” methylation agents and determination of its biological activity. In *E3S Web of Conferences* (Vol. 258, p. 04023). EDP Sciences.

Sapaev, B., Sapaev, I. B., Saitkulov, F. E., Tashniyazov, A. A., & Nazaraliev, D. (2022, June). Synthesis of 2-methylquinazoline-4-thione with the purpose of alkylation of 3-propyl 2-methylquinazoline-4-thione with alkylating agents. In *AIP Conference Proceedings* (Vol. 2432, No. 1). AIP Publishing.

Baymuratova, G., Nasimov, K., & Saitkulov, F. (2023). Synthesis of 6-benzylaminopurine and the study of biological active properties of cotton C-6424 plants. In *E3S Web of Conferences* (Vol. 389, p. 03032). EDP Sciences.

Khatamov, K., Saitqulov, F., Ashurov, J., & Shakhidoyatov, K. (2012). 3, 5, 6-Trimethylthieno [2, 3-d] pyrimidin-4 (3H)-one. *Acta Crystallographica Section E: Structure Reports Online*, *68*(9), o2740-o2740.

Foziljon Saitkulov, Bairamdurdi Sapaev, Khasan Nasimov, Dilorom Kurbanova and Nargiza Tursunova. Structure, aromatic properties and preparation of the quinazolin-4-one molecule. E3S Web of Conf., – 389. (2023).– 03075 p.

Bairamdurdi Sapaev, Foziljon Saitkulov, Muattar Mamedova, Shahlo Saydaliyeva and Dilafruz Makhmudova. Chromato-mass-spectrometry of the analysis of the sum of the common mushrooms 01006 Published online: 04 September, 2023.

Саиткулов, Ф. Э., Элмурадов, Б. Ж., & Гиясов, К. (2023). Алкилирования хиназолин-4-она «мягким» и «жестким» алкилирующими АГЕНТАМИ. *Universum: химия и биология*, (1–2 (103)), 53–56.

Saitkulov, F., Qilichyeva, N., Abdullayev, B., Anvarov, A., & Ergasheva, M. (2022). Titrimetric analysis of calcium cation in» megaton» variety of cabbage. *International Bulletin of Applied Science and Technology*, – 2(10). – P. 134–135.

Saitkulov, F., Farhodov, O., Olisheva, M., Saparboyeva, S., & Azimova, U. (2022). Chemical feeding method of lemon plant using leaf stomata. *Академические исследования в современной науке*, – 1(17). – P. 274–277.

Boymuratova, G. O., Saitkulov, F. E., Nasimov, K. M., & Tugalov, M. (2022). To Examine the Processes of Biochemical Action Of 6-Benzylaminopurine with Cobalt-II Nitrate Dihydrate on the "Morus Alba" Variety of Moraceae Plant. *Eurasian Journal of Physics, Chemistry and Mathematics*, – 3. – P. 39–42.

Murodillayevich, K. M., Shoyimovich, K. G., & Ergashevich, S. F. (2022). Chromoto-Mass Methods for Detecting Simple Esters in Chromatography-Mass Spectrometry Method. *international journal of biological engineering and agriculture*, – 1(6). – P. 53–56.

Саиткулов, Ф. Э. (2022). Гиясов Кучкар, Элмурадов Бурхон Жураевич Метилирование 2-метилхиназолин-4-она «мягкими» и «жесткими» метилирующими агентами. *Universum: химия и биология*, (11–2), – 101 с.

Saitkulov, F., Begimqulov, I., O ʻralova, N., Gulimmatova, R., & Rahmonqulova, D. (2022). Biochemical effects of the coordination compound of cobalt-II nitrate quinazolin-4-one with 3-indolyl acetic acid in the "amber" plants grades PHASEOLUS AUREUS. *Академические исследования в современной науке*, – 1(17). – P. 263–267.

Saitkulov, F., Elmuradov, B., O'lmasova, K., & Alijonova, A. (2023). preparation of a mixed coordination compound cobalt-ii nitrate hexahydrate with quinazoline-4-one and 3-indolylacetic acid on "amber" plants of the phaseolus aureus variety. *Science and innovation in the education system*, – 2(1). – P. 81–87.

Bairamdurdi Sapaev, Foziljon Saitkulov, Muattar Mamedova, Shahlo Saydaliyeva and Dilafruz Makhmudova. Chromato-mass-spectrometry of the analysis of the sum of the common mushrooms. BIO Web Conf., – 65. (2023). – 01006 p.

submitted 17.01.2024;
accepted for publication 31.01.2024;
published 18.03.2024

Contact: fsaitkulov@bk.ru