# Proteflazid® effectiveness for prevention and treatment of acute viral respiratory infections in the conditions of COVID-19

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*The original antiviral drug Proteflazid® has been used in clinical practice since the early 2000s for the etiotropic treatment of acute respiratory viral diseases, due to its property of blocking viral RNA and DNA polymerases. Considering that at the beginning of the global COVID-19 pandemic, caused by RNA-containing virus of SARS-CoV-2 species in 2020, the ability of the drug active substance to inhibit the activity of 3CL- protease of the SARS-CoV-2 coronavirus was shown by molecular docking and, subsequently, to confirm the property of the active substance to block the reproduction of the SARS-CoV-2 virus in cell cultures in vitro. It was extremely important to test the effectiveness of the drug Proteflazid, drops for the prevention and treatment of COVID-19 disease at „off labell use".*

***The aim** of the study was to provide a statistical assessment of the effectiveness of the drug Proteflazid®, drops in terms of COVID-19 pandemic.*

***Materials and methods.** The analysis has been performed including the letters-references from medical institutions from different regions of Ukraine about the effectiveness of the drug Proteflazid®, drops. Methods of statistical analysis have been focused on dynamics and structure analysis, meta-analysis, generalization, etc.*

***Results.** 90 letters-references about the effectiveness of the drug Proteflazid®, drops, during the prevention and treatment of acute respiratory viral infections, including COVID-19 diseases were analyzed. The study used references that contained the most complete information. The number of deleted letters-references is 11. Letters-references from 79 medical institutions from different cities and regions of Ukraine were analyzed. The period of starting taking the drug by employees and patients of medical institutions began on February 27, 2020. Final information – October 01, 2020. The vast majority of letters from medical institutions indicated that medical staff were in contact with patients potentially suffering from COVID-19. This means a high risk of being infected with Coronavirus infection. Total number of patients who took Proteflazid® for preventive purpose was 8,572, including 7,444 medical workers and 1,128 ordinary patients. Indicator „Number of fatalities" for the medical institutions providing such information was „0". Total number of patients who took Proteflazid® for therapeutic purposes was 433, including 23 medical workers and 410 ordinary patients. Indicator „Number of fatalities" for the medical institutions providing such information was „0". The total number of medical personnel and patients who used Proteflazid drops for preventive and therapeutic purposes was 9005 people.*

***Skuteczność Proteflazidu® w profilaktyce i leczeniu wirusowych ostrych zakażeń oddechowych w czasie COVID-19***

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*Oryginalny preparat przeciwwirusowy Proteflazid® stosowany jest w praktyce klinicznej od początku lat 2000. do etiotropowego leczenia wirusowych ostrych zakażeń oddechowych ze względu na jego właściwości blokujące polimerazę wirusów RNA i DNA. Biorąc pod uwagę fakt, iż na początku ogólnoświatowej pandemii COVID-19, spowodowanej przez SARS-CoV-2 zawierającego RNA w 2020 r. przy pomocy metody dokowania molekularnego udało się udowodnić, iż substancja czynna preparatu wykazuje zdolności do inhibicji aktywności proteazy $3CL^{pro}$, z czasem potwierdzono również, iż substancja czynna jest w stanie zablokować rozmnażanie się SARS-CoV-2 w hodowlach komórek in vitro. Niezwykle ważne było zbadanie skuteczności środka Proteflazid® w kroplach, stosowanego w profilaktyce i leczeniu choroby COVID-19 przy «off labell use».*

***Celem pracy** była prezentacja oceny statystycznej zastosowania środka leczniczego Proteflazid® w kroplach w warunkach pandemii COVID -19.*

***Materiały i metody.** Analizie poddano opinie ośrodków medycznych z różnych regionów Ukrainy dotyczące efektywności stosowania środka Proteflazid® w kroplach. Zastosowano metody analizy statystycznej, a w tym: analizę struktury i dynamiki, metaanalizę, uogólnienie itd.*

***Wyniki.** Przeanalizowano 90 opinii na temat efektywności stosowania środka Proteflazid® w kroplach podczas profilaktyki i leczenia ostrych wirusowych chorób oddechowych, w tym również zachorowań na COVID-19. W badaniu wykorzystano opinie zawierające najpełniejsze informacje. Liczba wybranych opinii wynosiła 11. Przeanalizowano opinie z 79 ośrodków medycznych z różnych miast i regionów Ukrainy. Okres przyjmowania preparatu przez pracowników służby zdrowia i chorych rozpoczeto 27 lutego, a zakończono 1 października 2020 roku. Zdecydowana większość opinii z placówek medycznych zawierała informację, iż personel medyczny ma kontakt z osobami potencjalnie chorymi na COVID-19. Oznacza to wysoki stopień ryzyka zakażenia się koronawirusem. Ogólna liczba przyjmujących Proteflazid® w celach profilaktycznych wynosiła 8572, w tym: 7444 pracowników służby zdrowia i 1128 chorych. Wskaźnik «Ilość wypadków śmiertelnych» w placówkach medycznych, które przekazały takie informacje wynosił „0". Ogólna liczba przyjmujących Proteflazid® w celach leczniczych wynosi 433 osoby, w tym 23 pracowników służby zdrowia i 410 chorych. Wskaźnik «Ilość wypadków śmiertelnych» w placówkach medycznych, które przekazały takie informacje wynosi „0". Ogólna liczba pracowników służby zdrowia oraz chorych zażywających preparat Proteflazid w kroplach w celach profilaktycznych i leczniczych stanowi 9005 osób.*

***Conclusions.*** *The statistical analysis confirmed the effectiveness of the drug Proteflazid® for the prevention and treatment of COVID-19, as, when compared with official actual data, regarding the main indicators of the incidence of COVID-19: there were no fatalities; the average treatment period decreased (1.8 times); the proportion of recovered increased (at least 1.5 times); the proportion of sick medical workers in the total population of sick medical workers decreased (2.2 times); the proportion of patients with a severe course decreased (3.3 times). It can be argued that the drug Proteflazid®, drops has shown high effectiveness in the prevention and treatment of acute respiratory viral infections, including COVID-19, among medical personnel and patients.*

**Key words:** *Proteflazid®, SARS-CoV-2, „off–label use", COVID-19 prevention and treatment*

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***Wnioski.*** *Analiza statystyczna potwierdza efektywność stosowania preparatu Proteflazid® w celu profilaktyki i leczenia ŃOVID-19, ponieważ w porównaniu z oficjalnymi i faktycznymi danymi, dotyczącymi wskaźników zachorowań na COVID-19: brak jest przypadków śmiertelnych; skraca się średni okres leczenia (o 1,8 razy); zwiększa się liczbę ozdrowieńców (co najmniej o 1,5 razy); zmniejsza się liczbę zachorowań u pracowników medycznych na tle ogólnej liczby pracowników medycznych (o 2,2 razy); zmniejsza się liczbę chorych z ciężkim przebiegiem choroby (o 3,3 razy). Można zatem stwierdzić, iż preparat Proteflazid® w kroplach wykazał się wysoką skutecznością w profilaktyce i leczeniu wirusowych ostrych chorób oddechowych w tym również w chorobie ŃOVID-19 u personelu medycznego i chorych.*

**Słowa kluczowe***: Proteflazid®, SARS-CoV-2, «off–label use», profilaktyka i leczenie ŃOVID-19*

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In the early 2000s, the arsenal of antiviral agents was supplemented by the original drug Proteflazid® (Developed by „SMC „Ecopharm" Ltd., Kyiv, Ukraine) having direct antiviral, interferonogenic, immunomodulatory, antioxidant apoptosis – modulating effect, being of great practical importance, and accompanied by evidence-based scientific studies for the assessment of its effectiveness and safety in various pathologies of viral etiology.

Proteflazide® is an ethanol extract from herbal raw materials – green parts of wild cereal plants of Gramineae family, genera Calamagrostis Adans and Deschampsia Beauv, containing biologically active substances with polypharmacological action (PCTWO2004/058285; PCT/UA2015/000101). The active ingredients of Proteflazid API are flavonoid aglycon compounds: tricin, apigenin, luteolin. The active molecules of the PROTEFLAZID The active molecules of API Proteflazid are flavones and flavone glycosides forming complexes of the following composition: [Tricin, Tricin-7-O or 8-C glycoside] : [Luteolin-7-O or 8-C glycoside] : [Apigenin, Apigenin-7-O glycoside or 8-C glycoside] in the „matrix" of excipients: amino acids; carboxylic acids and sugars; polysaccharides, pectins, chlorophyll (a and b) and hemicellulose (A and B).

More than 22 thousand people took part in clinical studies; among them, more than 12 thousand patients of various age, social and other groups took the drug Proteflazid® for etiotropic treatment of viral diseases caused by RNA – or DNA-containing viruses.

In order to confirm and summarize the scientific data obtained clinically, and to form an evidence base confirming the effectiveness and safety of the drug Proteflazid® in the period 2014-2018, a number of thematic meta-analyses and systematic reviews of clinical observations and long-term results of the drug use were carried out, which was reflected in scientific publications (meta-analyses and systematic reviews) [2,7,9, 11,15-16,22,27-28,31-33,35,37-38,41,44].

Clinical studies have established and statistically confirmed that Proteflazid® is therapeutically effective at any stage of infection, and not only at the time of replication of the viral pathogen, unlike, for example, acyclic nucleosides. In addition, repeated and long-term courses of administering the drug did neither cause the development of resistant strains of viruses, nor lead to immunosuppression.

With regard to RNA-containing influenza viruses, Proteflazid® has been found to not only inhibit neuraminidase activity but, unlike other drugs in this class recommended for treatment of influenza, it also inhibited intracellular replication of influenza viruses by inhibiting the synthesis of virus-specific enzymes, namely thymidine kinase and RNA polymerase. Another significant difference between the drug Proteflazid® and influenza virus neuraminidase inhibitors (especially in epidemic periods, as in the structure of influenza morbidity is only 6 to 10% of ARVI patients) is that Proteflazid®, due to its direct antiviral activity against other causative agents of acute respiratory viral infections (adeno-, enteroviruses and others) can inhibit their replication as well.

**Modern preclinical studies were performed to examine the specific antiviral activity of the active substance proteflazid against RNA-containing coronaviruses, including SARS-CoV-2.**

The property of the active ingredient Proteflazid to block the reproduction of RNA and DNA-containing viruses (through inhibition of RNA and DNA polymerase) was established 15 years ago and formed the basis for the theoretical justification of the attempt to investigate the active ingredient of the drug for its possible antiviral activity against coronaviruses in preclinical studies, as scientists worldwide are now actively searching for drugs – RNA polymerase and 3CL protease inhibitors of SARS-CoV-2 virus.

It is known that active targets for antiviral drugs against the SARS-CoV-2 can be RNA polymerase, 3CL Protease and transcription factor Nrf2. Back in early 2020, Chinese, Korean and Ukrainian scientists showed in their works that flavonoids inhibit 3CL protease activity and bind ACE-2, an angiotensin-converting enzyme-2, which acts as a receptor for the coronavirus surface spike glycoprotein, thus promoting the entry of the virus into human cells [1,29].

In preclinical studies, in early 2020, it was found by molecular docking [29] that the active ingredient Proteflazid is well positioned in the catalytic pocket of the 3CL protease of SARS-Cov-2 coronavirus, forming hydrogen bonds with Ser 144, Gly 143 residues, being located between catalytic residues His 163, Asn 142 and Cys 145 and, thus hydrogen bonds with two hydroxyl catechol residues Glu 166, which evidences the inhibition of 3CL protease activity of SARS-Cov-2 coronavirus [29], and during testing the drug based on the active substance Proteflazid, it was established 15 years ago that this substance was an inhibitor of RNA and DNA polymerase of influenza and ARVI viruses.

Materials of research and experimental work of specialists of the SI "L.V. Hromashevskyi IEID of NAMS of Ukraine" showed that the active substance Proteflazid has a high antiviral activity in vitro on a model using transmissible gastroenteritis of swine coronavirus, inhibiting the reproduction of RNA-containing coronavirus (effectiveness was confirmed on two cell cultures) structurally similar to human coronavirus [29].

The Animal Health Research Centre (IRTA-CreSA, Autonomous University of Barcelona, Spain) investigated the specific antiviral activity of Proteflazid against SARS-CoV-2 coronavirus in vitro on Vero E6 cell culture. The drug Proteflazid, drops in a series of successive dilutions in the range 0.0000819 µg – 160 µg was injected into a Vero E6 cell culture with simultaneous infection with SARS-CoV-2 at an infecting tissue dose of

TCID50 /ml 101.8 followed by incubation. Viral infection was assessed microscopically based on the cellular cytotoxic effect. Proteflazid showed antiviral activity against SARS-CoV-2 virus in the concentration range of 1.28 μg – 6.4 μg [10].

US scientists at Galveston National Laboratory focusing on SARS/MERS/COVID-19 (P-3) viruses from the Department of Microbiology and Immunology, Center for Biodefense and Emerging Diseases (Galveston National Laboratory, University of Texas Medical School, Galveston, USA) conducted studies in vitro of African green monkey kidney cell cultures (Vero E6) and human pulmonary adenocarcinoma cells with ACE2 receptor (A549/ACE2) demonstrating the ability of Proteflazid to prevent the virus-induced cytopathic effect caused by SARS-CoV-2 (USA-WA-1/2020 isolate), and provide 100% antiviral protection against cell damage by SARS-CoV-2 virus [4].

Published scientific studies confirm that flavonoids activate the transcription factor Nrf2, thereby reducing the expression of ACE receptors (ACE-2, angiotensin-converting enzyme 2) in respiratory epithelial cells, thus preventing virus penetration into epithelial cells and blocking SARS-CoV-2 virus multiplication, protecting cells from oxidative stress and inflammation, thus reducing the probability of acute respiratory distress syndrome [12,13,17-19,21,23-25].

**Proteflazid, drops is a direct-acting antiviral agent** with the following mechanism of action in acute respiratory viral disease COVID – 19:

a) **blocking the proteolytic activity of 3C-like protease**, which is vital for SARS-CoV-2 virus proliferation [12,18, 20,29];
b) **blocking the RNA polymerase** which is necessary for SARS-CoV-2 virus replication [25,40,42];
c) **activation of the transcription factor Nrf2**, which reduces the expression of ACE (angiotensin-converting enzyme 2) receptors in respiratory epithelial cells, thus preventing virus entry into lung epithelial cells and blocking SARS-CoV-2 multiplication, protecting cells from oxidative stress and inflammation, thus reducing the chance of acute respiratory distress syndrome [12-14,17-18,19-21,23-25, 40,42].

The purpose of the work was to provide a statistical assessment of the effectiveness of the drug Proteflazid®, drops in terms of COVID-19 pandemic.

## MATERIALS AND METHODS

Stages of the study completion were as follows:

1. Forming a database for statistical analysis of the results of the use of humanitarian aid in the form of the drug Proteflazid®, drops in terms of the COVID-19 pandemic. The database contains collected, sorted, and generated data presented in the form of tables.
2. Statistical analysis of the results of the use of humanitarian aid in the form of the drug Proteflazid®, drops in terms of the COVID-19 pandemic.

The database was formed on the basis of 90 letters-references on the effectiveness of the drug Proteflazid®, drops provided by the customer sent by medical institutions from different regions of Ukraine.

Statistical analysis methods were used during the analysis, such as dynamics and structure analysis, meta-analysis, generalization, etc. [39].

**Table 1.** The main indicators of COVID-19 global incidence as of 01.10.2020 incidence as of 01.10.2020
**Tabela 1.** Podstawowe wskaźniki zachorowań na COVID-19 na świecie zgodnie ze stanem na dzień 01.10.2020 r.

| Country | Number of patients | Number of recovered | Number of fatalities | Percentage of recovered | Proportion of fatalities |
|---|---|---|---|---|---|
| The USA | 7484357 | 4725190 | 212393 | 63.1 | 2.8 |
| India | 6391960 | 5348653 | 99804 | 83.7 | 1.6 |
| Brazil | 4820116 | 4180376 | 144103 | 86.7 | 3.0 |
| Russia | 1185231 | 964242 | 20891 | 81.4 | 1.8 |
| Colombia | 829679 | 743653 | 25998 | 89.6 | 3.1 |
| Peru | 814829 | 683815 | 32463 | 83.9 | 4.0 |
| Spain | 778607 | - | 31973 | - | 4.1 |
| Argentina | 751001 | 594645 | 16937 | 79.2 | 2.3 |
| Mexico | 743216 | 533886 | 77646 | 71.8 | 10.4 |
| RSA | 676084 | 609584 | 16866 | 90.2 | 2.5 |
| France | 577505 | 96797 | 32019 | 16.8 | 5.5 |
| Chile | 464750 | 438148 | 12822 | 94.3 | 2.8 |
| Iran | 461044 | 383368 | 26380 | 83.2 | 5.7 |
| United Kingdom | 460178 | - | 42202 | - | 9.2 |
| Iraq | 367474 | 295882 | 9231 | 80.5 | 2.5 |
| Bangladesh | 364987 | 277078 | 5272 | 75.9 | 1.4 |
| Saudi Arabia | 335097 | 319746 | 4794 | 95.4 | 1.4 |
| Turkey | 320070 | 281151 | 8262 | 87.8 | 2.6 |
| Italy | 317409 | 228844 | 35918 | 72.1 | 11.3 |
| Philippines | 314079 | 254223 | 5562 | 80.9 | 1.8 |
| Pakistan | 312806 | 297497 | 6484 | 95.1 | 2.1 |
| Germany | 295530 | 257900 | 9586 | 87.3 | 3.2 |
| Indonesia | 291182 | 218487 | 10856 | 75.0 | 3.7 |
| Israel | 253490 | 179468 | 1622 | 70.8 | 0.6 |
| Ukraine [26] | 217661 | 96591 | 4261 | 44.4 | 2.0 |
| Ukraine [6] | 213028 | 94443 | 4193 | 44.3 | 2.0 |
| Global | 34400568 | 25589531 | 1022512 | 74.4 | 3.0 |

Source: [34]

## RESULTS AND DISCUSSION

Forming a database for statistical analysis of the results of the use of humanitarian aid in the form of the drug Proteflazid®, drops in terms of the COVID-19 pandemic was carried out on the basis of an analysis of letters sent by medical institutions regarding the use of Proteflazid® for preventive purposes, and directly for therapeutic purposes.

90 letters-references about the effectiveness of the drug Proteflazid®, drops (No UA/4220/01/01 as of 21.09.2020) were received from medical institutions and analyzed during the prevention and treatment of acute respiratory viral infections, including COVID-19 disease. Some medical institutions sent several letters in different periods. The study used the letters that contained the most complete information. The number of deleted letters-references is 11.

Letters-references from 79 medical institutions from different cities and regions of Ukraine were analyzed, including Vinnytsia Region – 3; Volyn Region – 5; Dnipropetrovsk Region – 5; Donetsk Region – 2; Zakarpattia Region – 1; Zaporizhzhia Region – 2; Ivano-Frankivsk Region – 2; Kirovohrad Region – 1; Luhansk Region – 5; Lviv Region – 1; Odesa Region – 3; Poltava Region – 2; Rivne Region – 7; Ternopil Region – 1; Kharkiv Region – 13; Kherson Region – 2; Khmelnytskyi Region – 2; Cherkasy Region – 1; Chernivtsi Region – 9; Chernihiv Region – 1 and the city of Kyiv – 11 letters.

The period of the beginning of administering the drug by employees and patients of medical institutions was February 27, 2020 (since the first batch of humanitarian aid, in the form of a direct antiviral drug Proteflazid, drops, was transferred to medical workers in Novi Sanzhary [Poltava Region, Ukraine] directly, after the return of Ukrainian citizens and citizens of other countries from Wuhan city, China, for staying under observation due to the possible occurrence of COVID – 19).

The final information was obtained on October 01, 2020.

The vast majority of letters from medical institutions indicated that medical staff were in contact with patients potentially suffering from COVID-19. This means a high risk of being infected with Coronavirus infection.

I. The following can be noted on the analysis results of the information base regarding medical professionals and patients who were administered the drug Proteflazid® for prevention purposes.

Total number of patients who took Proteflazid® for preventive purpose was 8,572, including 7,444 medical workers and 1,128 ordinary patients.

Indicator „Number of fatalities" for the medical institutions providing such information was „0".

II. The following can be noted on the analysis results of the information base regarding medical professionals and patients who were administered the drug Proteflazid® for therapeutic purposes.

Total number of patients who took Proteflazid® for therapeutic purposes was 433, including 23 medical workers and 410 ordinary patients.

Indicator „Number of fatalities" for the medical institutions providing such information was „0".

The total number of medical personnel and patients who used Proteflazid drops for preventive and therapeutic purposes was 9005 people.

**Statistical analysis** of the results of the use of humanitarian aid in the form of the drug Proteflazid®, drops was performed in terms of the COVID-19 pandemic. For the analysis, actual data as of 01.10.2020 were used, since just in this period the information generated in information databases regarding medical

**Table 2.** The main indicators of COVID-19 incidence in Ukraine as of 01.10.2020
**Tabela 2.** Podstawowe wskaźniki zachorowań na COVID-19 na Ukrainie zgodnie ze stanem na dzień 01.10.2020 r.

| Region | Number of patients | Number of recovered | Number of fatalities | Percentage of recovered | Proportion of fatalities |
|---|---|---|---|---|---|
| Vinnytsia Region | 6308 | 4041 | 116 | 64.1 | 1.8 |
| Volyn Region | 8194 | 5253 | 170 | 64.1 | 2.1 |
| Dnipropetrovsk Region | 6088 | 3221 | 114 | 52.9 | 1.9 |
| Donetsk Region | 3557 | 1117 | 56 | 31.4 | 1.6 |
| Zhytomyr Region | 6088 | 3433 | 111 | 56.4 | 1.8 |
| Zakarpattia Region | 9918 | 4798 | 308 | 48.4 | 3.1 |
| Zaporizhzhia Region | 4128 | 1429 | 64 | 34.6 | 1.6 |
| Ivano-Frankivsk Region | 13837 | 6536 | 318 | 47.2 | 2.3 |
| Kyiv Region | 9279 | 5639 | 178 | 60.8 | 1.9 |
| Kirovohrad Region | 1127 | 877 | 57 | 77.8 | 5.1 |
| Luhansk Region | 1091 | 576 | 14 | 52.8 | 1.3 |
| Lviv Region | 20590 | 7387 | 565 | 35.9 | 2.7 |
| Mykolaiv Region | 3270 | 1086 | 77 | 33.2 | 2.4 |
| Odesa Region | 13789 | 2550 | 208 | 18.5 | 1.5 |
| Poltava Region | 2345 | 1072 | 42 | 45.7 | 1.8 |
| Rivne Region | 12554 | 10064 | 167 | 80.2 | 1.3 |
| Sumy Region | 4435 | 1798 | 75 | 40.5 | 1.7 |
| Ternopil Region | 13767 | 8183 | 170 | 59.4 | 1.2 |
| Kharkiv Region | 19128 | 4363 | 354 | 22.8 | 1.9 |
| Kherson Region | 1168 | 616 | 26 | 52.7 | 2.2 |
| Khmelnytskyi Region | 6188 | 2645 | 120 | 42.7 | 1.9 |
| Cherkasy Region | 4165 | 1740 | 57 | 41.8 | 1.4 |
| Chernivtsi Region | 14605 | 8115 | 364 | 55.6 | 2.5 |
| Chernihiv Region | 4254 | 963 | 71 | 22.6 | 1.7 |
| Kyiv | 23155 | 6941 | 391 | 30.0 | 1.7 |
| Ukraine [26] | 217661 | 96591 | 4261 | 44.4 | 2.0 |
| Ukraine [6] | 213028 | 94443 | 4193 | 44.3 | 2.0 |

Source: [34]

professionals and patients who took Proteflazid® for preventive purposes, and directly for therapeutic purposes. Table 1 presents the summary of the main indicators of COVID-19 global incidence as of 01.10.2020, ranked in descending order by such an indicator as the number of patients.

As of 1.10.2020 Ukraine was among the top 25 in terms of the number of patients. The largest number of cases was observed in the United States. In Ukraine, the proportion of recovered patients has been too small at the level of 44.3% when compared to 74.4% in the whole world. And in some countries (Saudi Arabia, Pakistan and Chile), it even reaches 95%.

The proportion of fatalities in Ukraine is 2% (global value is 3%). The highest number of fatalities was observed in Italy (11.3%) and Mexico (10.4%), and the lowest – in Israel (0.6%). Table 2 presents the main indicators of COVID-19 incidence in Ukraine as of 01.10.2020.

As of 1.10.2020, the largest number of patients falls on the city of Kyiv, and Lviv and Kharkiv Regions. The largest proportion of recovered falls to Rivne Region (80.2%), and the smallest one – to Odesa Region (18.5%). The largest proportion of fatalities is observed in Kirovohrad Region (5.1%), and the smallest one – in Ternopil Region (1.2%). Table 3 presents a comparison of the proportion of recovered patients among those who took Proteflazid® for prevention, and the proportion of recovered patients on a country-by-country basis.

The proportion of recovered among those who took Proteflazid® for the prevention of COVID-19 is 86.1%. It is slightly underestimated, since not all medical institutions provided information on the number of recovered patients. The proportion of those who recovered among those who took Proteflazid® for the prevention of COVID-19 is 1.94 times higher than the proportion of those who recovered in Ukraine as a whole and 1.16 times higher than in the whole world. At the same time, by this indicator, it almost reaches the value of the most effective countries. Table 4 presents a comparison of the proportion of recovered patients among those who took Proteflazid® directly for therapeutic purposes, and the proportion of recovered patients on a country-by-country basis.

The proportion of recovered among those who took Proteflazid® directly for therapeutic purposes against COVID-19 is 90.8%. It is slightly underestimated, since not all medical institutions provided information on the number of recovered patients. The proportion of those who took Proteflazid® directly for therapeutic purposes against COVID-19 is 2.05 times higher than the proportion of those who recovered in Ukraine as a whole and 1.22 times higher than in the whole world. Table 5 presents a comparison of the proportion of those who took Proteflazid® for preventive purposes, and the proportion of recovered patients on a country-by-country basis.

The proportion of recovered among those who took Proteflazid® for preventive purposes against COVID-19 is 1.07 times higher than the highest proportion of those who recovered in Ukraine (Rivne Region) and 4.65 times higher than the lowest proportion of those who recovered in Ukraine (Odesa Region). Table 6 presents a comparison of the proportion of those who took Proteflazid® directly for therapeutic purposes, and the proportion of recovered patients in the regions of Ukraine.

**Table 3.** Comparison of the proportion of recovered patients among those who took Proteflazid® for prevention, and the proportion of recovered patients on a country-by-country basis as of 01.10.2020.
**Tabela 3.** Porównanie liczby ozdrowieńców wśród osób przyjmujących Proteflazid® w celu profilaktyki COVID-19 oraz liczby ozdrowieńców w innych krajach zgodnie ze stanem na dzień 01.10.2020 r.

| Country | Average proportion of the recovered patients among those who took Proteflazid® for preventive purposes (Ukraine), % | Proportion of patients recovered on a country-by-country basis, % | Difference (Ukraine/ country from the list), fold |
|---|---|---|---|
| The USA | 86.1 | 63.1 | 1.36 |
| India | 86.1 | 83.7 | 1.03 |
| Brazil | 86.1 | 86.7 | 0.99 |
| Russia | 86.1 | 81.4 | 1.06 |
| Colombia | 86.1 | 89.6 | 0.96 |
| Peru | 86.1 | 83.9 | 1.03 |
| Spain | 86.1 | - | - |
| Argentina | 86.1 | 79.2 | 1.09 |
| Mexico | 86.1 | 71.8 | 1.20 |
| RSA | 86.1 | 90.2 | 0.95 |
| France | 86.1 | 16.8 | 5.13 |
| Chile | 86.1 | 94.3 | 0.91 |
| Iran | 86.1 | 83.2 | 1.03 |
| United Kingdom | 86.1 | - | - |
| Iraq | 86.1 | 80.5 | 1.07 |
| Bangladesh | 86.1 | 75.9 | 1.13 |
| Saudi Arabia | 86.1 | 95.4 | 0.90 |
| Turkey | 86.1 | 87.8 | 0.98 |
| Italy | 86.1 | 72.1 | 1.19 |
| Philippines | 86.1 | 80.9 | 1.06 |
| Pakistan | 86.1 | 95.1 | 0.91 |
| Germany | 86.1 | 87.3 | 0.99 |
| Indonesia | 86.1 | 75.0 | 1.15 |
| Israel | 86.1 | 70.8 | 1.22 |
| Ukraine | 86.1 | 44.4 | 1.94 |
| Global | 86.1 | 74.4 | 1.16 |

Source: Information database of medical professionals and patients who took Proteflazid® directly for therapeutic purposes [6,26,34]

**Table 4.** Comparison of the proportion of recovered patients among those who took Proteflazid® directly for therapeutic purposes, and the proportion of recovered patients on a country-by-country basis as of 01.10.2020
**Tabela 4.** Porównanie liczby ozdrowieńców wśród osób przyjmujących Proteflazid® bezpośrednio w celu leczenia COVID-19 oraz liczby ozdrowieńców w innych krajach zgodnie ze stanem na dzień 01.10.2020 r.

| Country | Average proportion of the recovered patients among those who took Proteflazid® directly for therapeutic purposes (Ukraine), % | Proportion of patients recovered on a country-by-country basis, % | Difference (Ukraine/ country from the list), fold |
|---|---|---|---|
| The USA | 90.8 | 63.1 | 1.44 |
| India | 90.8 | 83.7 | 1.08 |
| Brazil | 90.8 | 86.7 | 1.05 |
| Russia | 90.8 | 81.4 | 1.12 |
| Colombia | 90.8 | 89.6 | 1.01 |
| Peru | 90.8 | 83.9 | 1.08 |
| Spain | 90.8 | - | - |
| Argentina | 90.8 | 79.2 | 1.15 |
| Mexico | 90.8 | 71.8 | 1.26 |
| RSA | 90.8 | 90.2 | 1.01 |
| France | 90.8 | 16.8 | 5.40 |
| Chile | 90.8 | 94.3 | 0.96 |
| Iran | 90.8 | 83.2 | 1.09 |
| United Kingdom | 90.8 | - | - |
| Iraq | 90.8 | 80.5 | 1.13 |
| Bangladesh | 90.8 | 75.9 | 1.20 |
| Saudi Arabia | 90.8 | 95.4 | 0.95 |
| Turkey | 90.8 | 87.8 | 1.03 |
| Italy | 90.8 | 72.1 | 1.26 |
| Philippines | 90.8 | 80.9 | 1.12 |
| Pakistan | 90.8 | 95.1 | 0.95 |
| Germany | 90.8 | 87.3 | 1.04 |
| Indonesia | 90.8 | 75.0 | 1.21 |
| Israel | 90.8 | 70.8 | 1.28 |
| Ukraine | 90.8 | 44.4 | 2.05 |
| Global | 90.8 | 74.4 | 1.22 |

Source: Information database of medical professionals and patients who took Proteflazid® directly for therapeutic purposes [6,26,34]

**Table 5.** Comparison of the proportion of those who took Proteflazid® for preventive purposes, and the proportion of recovered patients on a country-by-country basis as of 01.10.2020
**Tabela 5.** Porównanie liczby ozdrowieńców spośród osób przyjmujących Proteflazid® w celu profilaktyki COVID-19 oraz liczby ozdrowieńców w poszczególnych obwodach na Ukrainie zgodnie ze stanem na dzień 01.10.2020 r.

| Region | Average proportion of the recovered patients among those who took Proteflazid® for preventive purposes, % | Proportion of patients recovered on a region-by-region basis, % | Difference, fold |
|---|---|---|---|
| Vinnytsia Region | 86.1 | 64.1 | 1.34 |
| Volyn Region | 86.1 | 64.1 | 1.34 |
| Dnipropetrovsk Region | 86.1 | 52.9 | 1.63 |
| Donetsk Region | 86.1 | 31.4 | 2.74 |
| Zhytomyr Region | 86.1 | 56.4 | 1.53 |
| Zakarpattia Region | 86.1 | 48.4 | 1.78 |
| Zaporizhzhia Region | 86.1 | 34.6 | 2.49 |
| Ivano-Frankivsk Region | 86.1 | 47.2 | 1.82 |
| Kyiv Region | 86.1 | 60.8 | 1.42 |
| Kirovohrad Region | 86.1 | 77.8 | 1.11 |
| Luhansk Region | 86.1 | 52.8 | 1.63 |
| Lviv Region | 86.1 | 35.9 | 2.40 |
| Mykolaiv Region | 86.1 | 33.2 | 2.59 |
| Odesa Region | 86.1 | 18.5 | 4.65 |
| Poltava Region | 86.1 | 45.7 | 1.88 |
| Rivne Region | 86.1 | 80.2 | 1.07 |
| Sumy Region | 86.1 | 40.5 | 2.13 |

| | | | |
|---|---|---|---|
| Ternopil Region | 86.1 | 59.4 | 1.45 |
| Kharkiv Region | 86.1 | 22.8 | 3.78 |
| Kherson Region | 86.1 | 52.7 | 1.63 |
| Khmelnytskyi Region | 86.1 | 42.7 | 2.02 |
| Cherkasy Region | 86.1 | 41.8 | 2.06 |
| Chernivtsi Region | 86.1 | 55.6 | 1.55 |
| Chernihiv Region | 86.1 | 22.6 | 3.81 |
| Kyiv | 86.1 | 30.0 | 2.87 |
| Ukraine | 86.1 | 44.4 | 1.94 |

Source: *Information database of medical professionals and patients who took Proteflazid® for preventive purposes* [6,26,34]

The proportion of recovered among those who took Proteflazid® directly for therapeutic purposes against COVID-19 is 1.13 times higher than the highest proportion of those who recovered in Ukraine (Rivne Region) and 4.91 times higher than the lowest proportion of those who recovered in Ukraine (Odesa Region). All these results confirm the effectiveness of using the drug Proteflazid® for the prevention and treatment of COVID-19.

The effectiveness of the drug Proteflazid® for the treatment of COVID-19 is evidenced by the absence of fatalities (information bases of medical workers and patients who took „Proteflazid®" for preventive purposes and directly for therapeutic purposes) when compared to 2% in Ukraine and 3% in the world as a whole (tab. 1,2).

To assess the effectiveness of the drug Proteflazid® in terms of the COVID-19 pandemic, a meta-analysis was used, which in modern studies is used to generalize the effectiveness of the results of various groups of objects. In our case, this method is used for a generalized assessment of the effectiveness of the drug „Proteflazid®" in the regions of Ukraine.

As the main indicator for assessing the effectiveness of the drug Proteflazid®, *RR* (Risk Ratio) was chosen – the risk ratio which demonstrates how many times the proportion of those who recovered differs among those who took „Proteflazid®" for preventive purposes and directly for therapeutic purposes, compared with the general population of patients with COVID-19 in Ukraine on a region-by-region basis. This indicator is calculated separately for each region using the formula:

$$RR = \frac{a \times N}{b \times M} = \frac{a \times 100}{b \times 100} = \frac{a}{b},$$

**Table 6.** Comparison of the proportion of those who took Proteflazid® directly for therapeutic purposes, and the proportion of recovered patients in the regions of Ukraine as of 01.10.2020
**Tabela 6.** Porównanie liczby ozdrowieńców wśród osób przyjmujących Proteflazid® bezpośrednio w celu leczenia COVID-19 oraz liczby ozdrowieńców w poszczególnych obwodach Ukrainy zgodnie ze stanem na dzień 01.10.2020 r.

| Region | Average proportion of the recovered patients among those who took Proteflazid® directly for therapeutic purposes (Ukraine), % | Proportion of patients recovered on a region-by-region basis, % | Difference, fold |
|---|---|---|---|
| Vinnytsia Region | 90.8 | 64.1 | 1.42 |
| Volyn Region | 90.8 | 64.1 | 1.42 |
| Dnipropetrovsk Region | 90.8 | 52.9 | 1.72 |
| Donetsk Region | 90.8 | 31.4 | 2.89 |
| Zhytomyr Region | 90.8 | 56.4 | 1.61 |
| Zakarpattia Region | 90.8 | 48.4 | 1.88 |
| Zaporizhzhia Region | 90.8 | 34.6 | 2.62 |
| Ivano-Frankivsk Region | 90.8 | 47.2 | 1.92 |
| Kyiv Region | 90.8 | 60.8 | 1.49 |
| Kirovohrad Region | 90.8 | 77.8 | 1.17 |
| Luhansk Region | 90.8 | 52.8 | 1.72 |
| Lviv Region | 90.8 | 35.9 | 2.53 |
| Mykolaiv Region | 90.8 | 33.2 | 2.73 |
| Odesa Region | 90.8 | 18.5 | 4.91 |
| Poltava Region | 90.8 | 45.7 | 1.99 |
| Rivne Region | 90.8 | 80.2 | 1.13 |
| Sumy Region | 90.8 | 40.5 | 2.24 |
| Ternopil Region | 90.8 | 59.4 | 1.53 |
| Kharkiv Region | 90.8 | 22.8 | 3.98 |
| Kherson Region | 90.8 | 52.7 | 1.72 |
| Khmelnytskyi Region | 90.8 | 42.7 | 2.13 |
| Cherkasy Region | 90.8 | 41.8 | 2.17 |
| Chernivtsi Region | 90.8 | 55.6 | 1.63 |
| Chernihiv Region | 90.8 | 22.6 | 4.02 |
| Kyiv | 90.8 | 30.0 | 3.03 |
| Ukraine | 90.8 | 44.4 | 2.05 |

Source: Information database of medical professionals and patients who took Proteflazid® directly for therapeutic purposes [6,26,34]

where:

*a* – the proportion of patients who recovered among those who took Proteflazid® for preventive purposes and directly for therapeutic purposes in the corresponding region, %;

*b* – the proportion of those who recovered among the total population of COVID-19 cases in Ukraine in the corresponding region, %;

*N* – the maximum proportion of recovered patients among those who took Proteflazid® for preventive purposes and directly for therapeutic purposes in the corresponding region (*N* = 100), %;

*M* is the maximum proportion of those who recovered from the total population of COVID-19 cases in Ukraine in the corresponding region (*M* = 100), %

The total *RR* value for regions is calculated taking into account the weight coefficients for each region (Weight). If the risk ratio (*RR*) is 1, then there are no differences. The closer to zero and the further away from one, the stronger the differences. If the *RR* exceeds 1, then there is a predominance of the proportion of recovered patients among those who took Proteflazid® for preventive purposes and directly for therapeutic purposes, when compared with the general population of patients with COVID-19 in Ukraine on a region-by-region basis. The difference values in this case will be equal to the *RR* value. If the *RR* is 0 to 1, then there is a decrease in the proportion of recovered patients among those who took Proteflazid® for preventive purposes and directly for therapeutic purposes, when compared with the general population of patients with COVID-19 in Ukraine on a region-by-region basis. The value of the difference, in this case, will be equal to the ratio of 1 to *RR*.

Calculations were performed with the use of the RevMan software.

The main results of meta-analysis, including the value of the risk ratio (*RR*) and the generalized risk value („big rhombus") are shown in the Forest plot graphs (fig. 1 and 2).

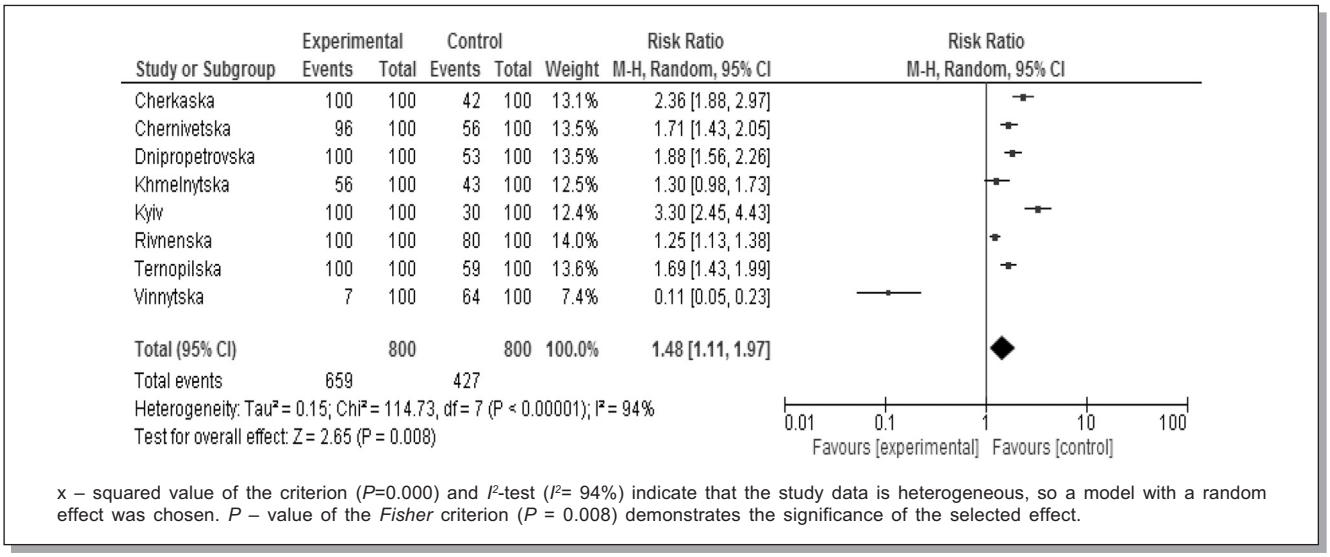
The vertical line in the middle of the graph (*RR* = 1) corresponds to the situation when the proportions of those who recovered among those who took Proteflazid® for preventive or directly for therapeutic purposes do not differ from the proportions of the total population of COVID-19 patients in Ukraine on a region-by region basis. The greater the statistical weight for this region in the general pool, the larger the size of the mark for each specific region. Horizontal lines ("whiskers") near the mark of each region show the 95% confidence interval. The „big rhombus" mark is a generalized total, with the length of the rhombus reflecting the combined estimate of the 95% confidence interval. The lower horizontal scale assesses the difference between the two populations. The area to the left of the vertical „1" corresponds to a decrease in the recovery rate among those who took Proteflazid® for preventive purposes or directly for therapeutic purposes, compared with the total number of COVID – 19 cases in Ukraine on a region-by-region basis. The area to the right of the vertical „1" corresponds to an increase in the recovery rate among those who took „Proteflazid®" for preventive purposes or directly for therapeutic purposes, compared with the total number of COVID – 19 cases in Ukraine on a region-by-region basis.

In the lower-left corner in fig. 1 and 2 generalized values of statistical criteria for checking the uniformity of the recovery rates in the regions of Ukraine for two populations ($Chi^2$ criterion and $I^2$ ), and the statistical significance of differences in populations (*Z*-criterion) are given The main indicators of these criteria are the values *P* and $I^2$. If *P*-value of $Chi^2$ and *Z*-criteria is less than 0.05, this indicates a statistically significant heterogeneity of data and significant differences between the recovery rate among those who took Proteflazid® for prevention or treatment purposes, compared with the total number of COVID-19 cases in Ukraine by regions with COVID-19 in Ukraine on an region-by-region basis. If the result of the $I^2$ test exceeds 50%, this indicates the existence of heterogeneity among the data. In this case, a model with a random effect is selected. Otherwise, a model with a fixed effect is selected.

To assess the effectiveness of treatment with the drug Proteflazid® of COVID-19 patients among those who took the drug for prevention purposes, information from 7 regions of Ukraine (Vinnytsia, Dnipropetrovsk, Rivne, Ternopil, Khmelnytskyi, Cherkasy, Chernivtsi) and the city of Kyiv (fig. 1). In 13 regions of Ukraine (Volyn, Donetsk, Zakarpattia, Zaporizhzhia, Ivano-Frankivsk, Kirovohrad, Luhansk, Lviv, Odesa, Poltava, Kharkiv, Kherson and Chernihiv) as a result of taking the drug Proteflazid® for prevention purposes, not a single person fell ill.

To assess the effectiveness of treatment with the drug Proteflazid® of COVID-19 patients among those who took the drug directly for therapeutic purposes, information from 6 regions of Ukraine (Vinnytsia, Zaporizhzhia, Odesa, Poltava, Chernivtsi, Chernihiv) and the city of Kyiv (fig. 2).

Recovery rates among those who took Proteflazid® for the prevention and treatment of COVID-19 are underestimated in some areas, since not all medical institutions provided information.

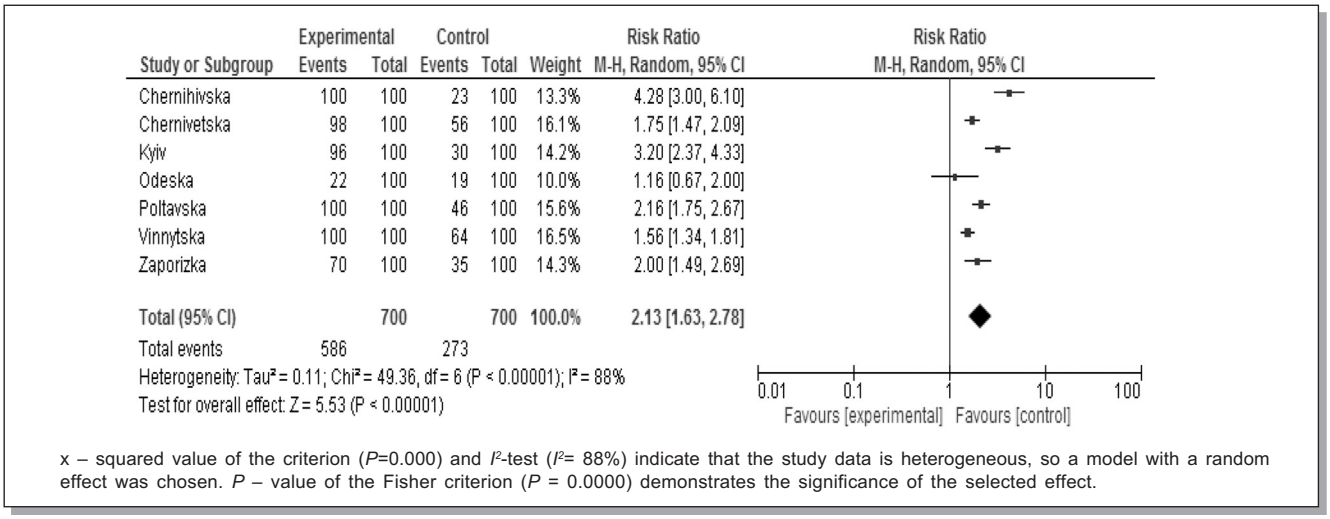



x – squared value of the criterion (*P*=0.000) and $I^2$-test ($I^2$= 94%) indicate that the study data is heterogeneous, so a model with a random effect was chosen. *P* – value of the *Fisher* criterion (*P* = 0.008) demonstrates the significance of the selected effect.

**Figure. 1.** Results of a meta-analysis of comparison of recovery rate among those who took Proteflazid® for the preventive purposes, and in total amount of COVID-19 cases in Ukraine on a region-by-region basis

**Rycina. 1.** Wyniki metaanalizy liczby ozdrowieńców wśród osób przyjmujących Proteflazid® w celu profilaktyki i ogólnej liczby osób, które zachorowały na COVID-19 na Ukrainie w poszczególnych obwodach

Source: Information database of medical professionals and patients who took Proteflazid® for preventive purposes [6,34]




x – squared value of the criterion ($P$=0.000) and $I^2$-test ($I^2$= 88%) indicate that the study data is heterogeneous, so a model with a random effect was chosen. $P$ – value of the Fisher criterion ($P$ = 0.0000) demonstrates the significance of the selected effect.

**Figure. 2.** Results of a meta-analysis of comparison of recovery rate among those who took Proteflazid® for the therapeutic purposes, and in total amount of COVID-19 cases in Ukraine on a region-by-region basis
**Rycina 2.** Wyniki metaanalizy liczby ozdrowieńców wśród osób przyjmujących Proteflazid® bezpośrednio w celu leczenia oraz ogólnej liczby osób, które zachorowały COVID-19 na Ukrainie w poszczególnych obwodach
Source: Information database of medical professionals and patients who took Proteflazid® directly for therapeutic purposes [6,34]

Value of the risk ratio (*RR* = 1.48) indicates that the recovery rate among those who took Proteflazid® directly for the prevention purposes is 1.48 times higher than the proportion in the total amount of COVID-19 cases in Ukraine.

Value of the risk ratio (*RR* = 2.13) indicates that the recovery rate among those who took Proteflazid® directly for the prevention purposes is 2.13 times higher than the proportion in the total amount of COVID-19 cases in Ukraine.

So, the statistical analysis shows in favour of the use of the drug Proteflazid®, since the recovery rate increases as a result of the drug use in comparison with the recovery rate in the total population of patients with COVID-19 in Ukraine. Figure 3 shows a comparison of the proportion of ill medical workers who took Proteflazid® for preventive purposes, with the proportion of medical workers infected with COVID-19 in the total population of medical workers in Ukraine.

The proportion of ill medical workers who took Proteflazid® for preventive purposes was 2.2 times less than the proportion of medical workers infected with COVID-19 in the total population of medical workers in Ukraine. Since equal-probability events were selected as comparison items, the assessment confirms the effectiveness of the use of the drug Proteflazid® for prevention purposes. Figure 4 shows the comparison of the proportion of doctors with severe disease, and patients who took Proteflazid® for the prevention purposes, with the proportion of patients with severe disease in the total population of patients with COVID-19.

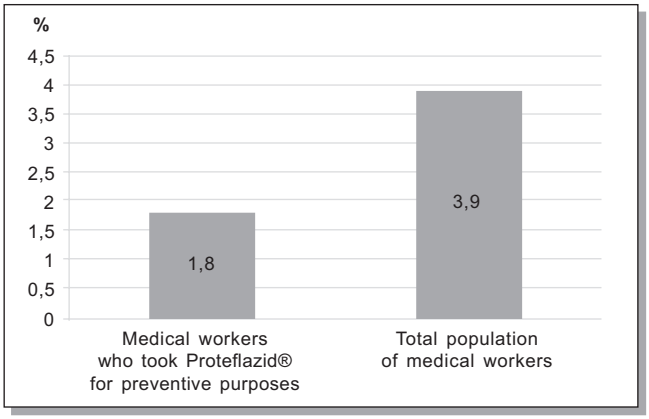



**Figure. 3.** Comparison of the proportion of ill medical workers who took Proteflazid® for preventive purposes, with the proportion of medical workers infected with COVID-19 in the total population of medical workers in Ukraine
**Rycina 3.** Porównanie liczby chorujących pracowników służby zdrowia, którzy zażywali Proteflazid® w celach profilaktycznych z liczbą pracowników medycznych, którzy zachorowali na COVID-19 spośród ogólnej ilości pracowników służby zdrowia Ukrainy
Source: Information database of medical professionals and patients who took Proteflazid® for preventive purposes [30,43]

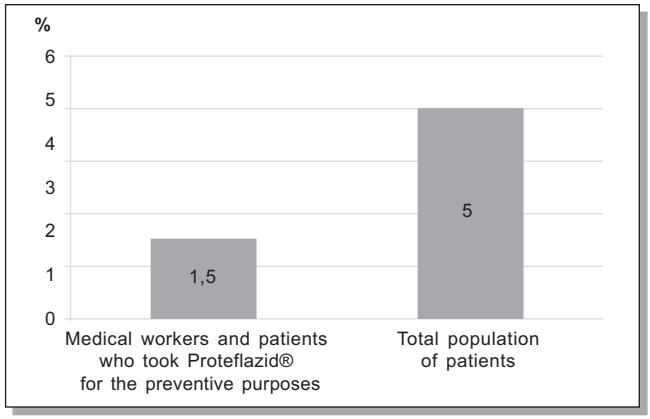



**Figure 4.** The comparison of the proportion of medical workers with severe disease, and patients who took Proteflazid® for the preventive purposes, with the proportion of patients with severe disease in the total population of patients with COVID-19
**Rycina 4.** Porównanie liczby pracowników medycznych oraz chorych z ciężkim przebiegiem choroby, którzy zażywali Proteflazid® w celach profilaktycznych z liczbą chorych z ciężkim przebiegiem choroby w ogólnej liczbie chorujących na COVID-19
Source: Information database of medical professionals and patients who took Proteflazid® for preventive purposes [30]

The proportion of medical workers with severe disease, and patients who took Proteflazid® for the preventive purposes is 3.3 times lower than the proportion of patients with severe disease in the total population of patients. Performed calculations also confirm the effectiveness of the use of the drug Proteflazid® for the preventive purposes. Fig. 5 shows the average duration of treatment of doctors and patients who took Proteflazid® was compared with the average duration of treatment in the total population of COVID-19 patients. The average duration of COVID-19 cases in the total population of cases was calculated using the weighted average formula.

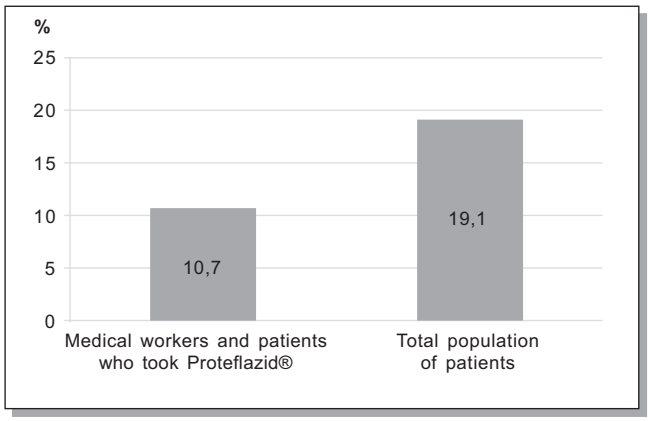



**Figure 5.** Average duration of treatment of doctors and patients who took Proteflazid® was compared with the average duration of treatment in the total population of COVID-19 patients
**Rycina. 5.** Porównanie średniej długości leczenia pracowników służby zdrowia oraz chorych zażywających Proteflazid®, ze średnią długością leczenia ogólnej liczby chorych na COVID-19
Source: Information database of medical professionals and patients who took Proteflazid® for preventive purposes [6,34]

The average duration of treatment of medical workers and patients who took Proteflazid® is 1.8 times lower than the average duration of treatment for COVID-19 patients in the total population of patients. Performed calculations also confirm the effectiveness of the use of the drug Proteflazid® for both preventive and therapeutic purposes.

## CONCLUSIONS

It was found out that as of 01.10.2020 Ukraine was among the top 25 in terms of the number of patients. At the same time, the proportion of recovered patients has been too small at the level of 44.3% when compared to 74.4% in the whole world. And in some countries, it even reaches 95%. During this period, the share of fatalities was 2%. All this requires immediate measures to improve the effectiveness of treatment of COVID-19 patients in Ukraine.

During the period declared a pandemic by WHO due to the spread of the SARS-CoV-2 coronavirus that causes COVID-19 disease worldwide, "SMC "Ecopharm" Ltd. provided charitable assistance in the form of 32,995 packages of the drug Proteflazid®, drops (no. UA/4220/01/01 from 21.09.2020), in order to prevent and treat the diseases caused by acute respiratory viral infection (ARVI), including those caused by COVID-19.

90 reference letters were received from medical institutions. 79 letters-references about the effectiveness of the drug Proteflazid®, drops, during the prevention and treatment of acute respiratory viral infections, including COVID-19 diseases were analyzed. The references indicate the effectiveness of the use of the drug Proteflazid®, drops, for prevention purposes among medical personnel in the number of 7444 persons, patients in the number of 1128 persons; treatment of mild, moderate, severe course of the disease in patients during prevention in the number of 137 persons, who fell ill against the background of preventive use of the drug; and direct treatment of patients with a mild, moderate, or severe course of the disease in the number of 433 persons; under zero mortality under preventive and therapeutic use of the drug Proteflazid®, drops.

Performed statistical analysis confirms the effectiveness of the drug Proteflazid® for the prevention and treatment of COVID-19, as, when compared with official actual data, regarding the main indicators of the incidence of COVID-19: there were no fatalities; the average treatment period decreased (1.8 times); the proportion of recovered increased (at least 1.5 times); the proportion of sick medical workers in the total population of sick medical workers decreased (2.2 times); the proportion of patients with a severe course decreased (3.3 times).

According to the aforementioned statistical data, it can be argued that the drug Proteflazid®, drops has shown high effectiveness in the prevention and treatment of acute respiratory viral infections, including COVID-19, among medical personnel and patients.

From the above information, the main conclusion follows: out of 9005 persons who used the drug Proteflazid, drops for the prevention and treatment of acute respiratory viral diseases (including COVID-19), not a single fatal case was registered.

With this in mind, we can give recommendations regarding the „off-label" use of the drug Proteflazid, drops for the prevention and treatment of COVID-19 disease :

– preventive reception – 15 drops twice daily (for a month, followed by a weekly break);
– preventive treatment – immediately after contact with a COVID-19 patient, when no symptoms of the disease have yet appeared, 30 drops twice daily, for 15 days;
– treatment – from the first hours of the onset of the disease symptoms, 30 drops twice daily, for 15 days.

In some cases, the use of the drug may be continued to prevent complications due to possible infection of the patient with other viral pathogens.

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