

UDC 616.33/.342-002.44-005.1-08-092

**ANALYSIS OF THE MODERN PHARMACEUTICAL MARKET FOR
HERBAL ANTI-ULCER MEDICINES AND PROSPECTS FOR
CREATING A NEW ANTI-ULCER MEDICINE BASED ON GRAPE
SEED POLYPHENOLS**

A. O. Minaieva¹, O. I. Zalyubovska², T. I. Tiupka²

¹V. N. Karazin Kharkiv National University, Kharkiv, Ukraine,

e-mail: 12345alina@gmail.com

²Kharkiv National Medical University, Kharkiv, Ukraine

Summary

Introduction. It is known that peptic ulcer refers to human pathology, which has traditionally been widespread among the population and has a constant upward trend. In addition, the problem of the treatment of peptic ulcer includes not only the clinical, but also the socio-economic component, since the majority of patients (about 60 %) have a young and average, most working age. The high prevalence of peptic ulcer disease and the unsatisfactory results of treatment require the search for new treatment methods that can affect both local and general mechanisms of ulcerogenesis.

The aim of the study was to analyze the modern pharmaceutical market for herbal anti-ulcer medicines and evaluate the prospects for creating a new anti-ulcer medicine based on grape seed polyphenols.

Materials and methods. The study of scientific literature sources.

Results. Phytotherapy of chronic hyperacid gastritis, gastric ulcer and duodenal ulcer plays an important role in the treatment of these diseases, where the anti-ulcer effect is realized with the help of antioxidant, membrane-stabilizing, anti-inflammatory, reparative effects, which are provided by biologically active substances contained in medicinal plant raw materials; mucous, phytoncides, vitamins, essential oils, tannins and flavonoids. *Vitis vinifera* L. (grape) is one of the richest sources of polyphenols. The seeds of the Cabernet-Sauvignon grape variety contain the whole gamma of flavanoid and non-flavanoid groups of polyphenols, as well as microelements. This ensures antioxidant, P-vitamin, antibacterial, antiviral activity, as well as the synergistic effect of total grape polyphenols and antioxidant protection enzymes of the human body. None of the known imported analogues has such a potential of biological activity the antioxidant properties of grape seeds' oligomeric proanthocyanidins are 20 times stronger than vitamin C and 50 times stronger than vitamin E. Phenolic substances from grape seeds, including flavonoids and polyphenols, are of interest because of their ability to absorb free radicals. In addition to the antioxidant effect, polyphenols from grape seeds inhibit certain enzymes that catalyze the release of histamine (which causes inflammation and allergic reactions) into the bloodstream, thus, they also have anti-inflammatory properties. Also they are able to inhibit the growth and development of pathogenic microflora of the gastrointestinal tract, to which *H. pylori* belongs, while they do not affect the beneficial lactobacilli and bifidobacteria.

Conclusions. The analysis of the modern pharmaceutical market for herbal anti-ulcer drugs, the pharmacological properties of grape seed polyphenols, the presence of a sufficient raw material base in Ukraine and its low cost is a theoretical basis for creating new anti-ulcer medicines on their basis.

Keywords: gastric and duodenal ulcers, herbal anti-ulcer medicines,

grape seed polyphenols.

**АНАЛИЗ СОВРЕМЕННОГО ФАРМАЦЕВТИЧЕСКОГО РЫНКА
АНТИ ЯЗВЕННЫХ ЛЕКАРСТВЕННЫХ ПРЕПАРАТОВ НА
РАСТИТЕЛЬНОЙ ОСНОВЕ И ПЕРСПЕКТИВ ДЛЯ СОЗДАНИЯ
НОВОЙ АНТИ ЯЗВЕННОЙ МЕДИЦИНЫ НА ОСНОВЕ
ПОЛИФЕНОЛОВ ВИНОГРАДА**

А. О. Минаева¹, О. І. Залюбовская², Т. І. Тюпка²

**¹Харьковский национальный университет им. В. Н. Каразина,
Украина,**

e-mail: 12345alina@gmail.com

²Харьковский национальный медицинский университет, Украина

Резюме

Введение. Известно, что язвенная болезнь относится к патологии человека, имеющей традиционно широкое распространение среди населения и постоянную тенденцию к росту. Кроме того, проблема лечения язвенной болезни включает не только клиническую, но и социально-экономическую составляющую, поскольку большинство больных (около 60 %) имеет молодой и средний, наиболее трудоспособный возраст. Большая распространенность язвенной болезни и неудовлетворительность результатами лечения требуют поиска новых способов лечения, которые позволяют воздействовать как на местные, так и на общие механизмы ульцерогенеза.

Целью исследования был анализ современного фармацевтического рынка существующих растительных противоязвенных лекарственных

средств и оценка перспективы создания нового — на основе полифенолов виноградных семян.

Результаты исследования. Фитотерапия хронического гиперацидного гастрита, язвенной болезни желудка и двенадцатиперстной кишки играет важную роль в лечении данных заболеваний, где противоязвенное действие реализуется с помощью антиоксидантного, мембраностабилизирующего, противовоспалительного, репаративного действия компонентов. В семенах винограда сорта "Каберне-Совиньон" содержится вся гамма флаваноидной и нефлаваноидной групп полифенолов, благодаря чему обеспечивается антиоксидантная, Р-витаминная, антибактериальная, противовирусная активности, а также синергическое действие суммарных полифенолов винограда и ферментов антиоксидантной защиты организма человека.

Выводы. Проведенный анализ современного фармацевтического рынка растительных противоязвенных лекарственных препаратов, фармакологические свойства полифенолов виноградных семян, наличие достаточной сырьевой базы на территории Украины и её дешевизна являются теоретическим основанием для создания на их основе новых противоязвенных средств.

Ключевые слова: язва желудка и двенадцатиперстной кишки, растительные противоязвенные лекарственные средства, полифенолы виноградных семян.

АНАЛІЗ СУЧАСНОГО ФАРМАЦЕВТИЧНОГО РИНКУ АНТИ ВИРАЗКОВИХ ЛІКАРСЬКИХ ПРЕПАРАТІВ З РОСЛИННОЇ СИРОВИНИ І ПЕРСПЕКТИВ ДЛЯ СТВОРЕННЯ НОВОЇ АНТИ ВИРАЗКОВОЇ МЕДИЦИНИ НА ОСНОВІ ПОЛІФЕНОЛІВ ВИНОГРАДУ

А. О. Мінаєва¹, О. І. Залюбовська², Т. І. Тюпка²

**¹Харківський національний університет ім. В. Н. Каразіна, Україна,
e-mail: 12345alina@gmail.com**

²Харківський національний медичний університет, Україна

Резюме

Вступ. Відомо, що виразкова хвороба відноситься до патології людини, що має традиційно широке розповсюдження серед населення та постійну тенденцію до зростання. Крім того, проблема лікування виразкової хвороби включає не тільки клінічну, але й соціально-економічну складову, оскільки більшість хворих (близько 60 %) має молодий та середній, найбільш працездатний вік. Велика розповсюдженість виразкової хвороби та незадовільність результатами лікування вимагають пошуку нових способів лікування, що дають змогу впливати як на місцеві, так і на загальні механізми ульцерогенезу.

Метою дослідження було проаналізувати сучасний фармацевтичний ринок існуючих рослинних противиразкових лікарських засобів та оцінити перспективи створення нового — на основі поліфенолів виноградного насіння.

Результати дослідження. Фітотерапія хронічного гіперацидного гастриту, виразкової хвороби шлунка та дванадцятипалої кишки відіграє важливу роль в лікуванні даних захворювань, де противиразкову дію, що

реалізується за допомогою антиоксидантної, мембраностабілізуючої, протизапальної, репаративної дії компонентів. У насінні винограду сорту "Каберне-Совіньйон" міститься вся гамма флаваноїдної та нефлаваноїдної груп поліфенолів, завдяки цьому забезпечується антиоксидантна, Р-вітамінна, антибактеріальна, протівірусна активності, а також синергічна дія сумарних поліфенолів винограду та ферментів антиоксидантного захисту організму людини.

Висновки. Проведений аналіз сучасного фармацевтичного ринку рослинних противиразкових лікарських препаратів, фармакологічні властивості поліфенолів виноградного насіння, наявність достатньої сировинної бази на території України та її дешевизна є теоретичним підґрунтям для створення на їх основі нових противиразкових засобів.

Ключові слова: виразка шлунка та дванадцятипалої кишки, рослинні противиразкові лікарські засоби, поліфеноли виноградного насіння.

Today, the problem of the treatment of peptic ulcer remains one of the top priorities not only in gastroenterology, but also for clinical medicine in general [1]. It is known that peptic ulcer refers to human pathology, which has traditionally been widespread among the population and has a constant upward trend [2]. In addition, the problem of the treatment of peptic ulcer includes not only the clinical, but also the socio-economic component, since the majority of patients (about 60 %) have a young and average, most working age [3].

The high prevalence of peptic ulcer disease and the unsatisfactory results of treatment require the search for new treatment methods that can affect both local and general mechanisms of ulcerogenesis [4].

Analyzing the current situation on the pharmaceutical market, it was noted that the domestic pharmaceutical industry for the treatment and prevention of diseases of the gastrointestinal tract produces drugs based on biologically active

substances of medicinal plants, including *Glycyrrhiza glabra* L., *Inula helenium* L., *Hippophae rhamnoides* L., *Berberis vulgaris* L., *Calendula officinalis* L., *Acorus calamus* L., *Atropa belladonna* L., *Vitis vinifera* L. cv. Cabernet Sauvignon, *Valeriana officinalis* L., *Hypericum perforatum* L., *Rosa canina* L., *Cucurbita pepo* L., *Brassica oleracea* L., *Aloe arborescens* L., *Linum usitatissimum* L., *Plantago major* L., *Urtica dioica* L., *Achillea millefolium* L., *Sanguisorba officinalis* L., *Polygonum bistorta* L., *Prunus padus* L., *Vaccinium myrtillus* L.

In general, modern phytotherapy of peptic ulcer cannot be imagined without *Glycyrrhiza glabra* L. (licorice) root medicines, with its biologically active substances in the 60s of the twentieth century such medicines as glycyram, flacarbin, carbenoxolone containing pentacyclic terpenes (produced abroad under the name biogastron and duogastron) were obtained, the effect of which is mainly associated with an increase in the quantity and quality of the protective layer of the gastric mucosa. Biologically active substances of these drugs stimulate the production of a protective gel, increase its resistance to the action of hydrochloric acid, prevent premature destruction of the epithelium, stimulate reproduction and, most importantly, differentiation of epithelial cells, inhibit the synthesis of thromboxane and proinflammatory prostaglandins, while suppressing the pepsinogen transition to pepsin. Like all *Glycyrrhiza glabra* L. medicines, these drugs have the properties of aldosterone, one of the adrenal hormones. It is noteworthy that licorice roots contain two main classes of biologically active substances: triterpene saponins (glycyrrhizic acid dominates) and flavonoids (licurazide, liquiritin, isoliquiritin, etc.), exhibiting gastroprotective effect. Saponins from licorice roots and medicines based on them (glycyram) accelerate regeneration processes and inhibit the formation of free radicals. Licorice root flavonoids are a medicinal substance for the production of antiulcer and choleric drugs: liquiriton, relcer, flacarbin, including the amount of flavonoids that cause the anti-inflammatory,

antispasmodic and antisecretory effects of these drugs [5, 6, 7, 8].

Gastritol (pharmaceutical company Dr. Gustav Klein (Germany)) is an original herbal complex medicine, which includes *Potentilla anserina* L. grass, *Matricaria chamomilla* L. flowers, *Glycyrrhiza glabra* L. roots, *Hypericum perforatum* L. grass, *Artemisia absinthium* L. grass, *Centaurea benedicta* L. grass, *Archangelica officinalis* L. root. Gastritol due to the content of biologically active substances from medicinal plants has local effects in the gastrointestinal tract and has a central effect on the secretory and motor function of the stomach [6, 7].

Alanton is obtained from the *Inula helenium* L. (elecampane) roots, sea buckthorn oil and Terra-plant sea buckthorn are obtained from the *Hippophae rhamnoides* L. (sea buckthorn) fruits. These medicines are actively used for the prevention and treatment of hyperacid gastritis, gastric ulcer and duodenal ulcer. Berberin is obtained from the *Berberis vulgaris* L. (barberry) roots, which is used as an anti-inflammatory agent for gastric ulcers and duodenal ulcers, as a choleric agent for chronic hepatitis, hepatocholecystitis, cholecystitis and gallstone disease. Caleflon, obtained from *Calendula officinalis* L. (pot marigold, calendula) flowers, is used for the prevention and treatment of diseases such as gastritis, gastric ulcer and duodenal ulcer, colitis, enterocolitis, liver disease and biliary tract. Vicair, Vicalin, Ancarcin (from *Acorus calamus* L. (sweet flag, calamus) rhizomes); Besalol, Bellalgin, Bellasthesin, Becarbon (contain an extract of *Atropa belladonna* L. (belladonna) leaves); Vin-vita (concentrated extract of *Vitis vinifera* L. cv. Cabernet Sauvignon (Cabernet type grapes) seeds and skin) is recommended in a special diet for the correction of disorders of the gastrointestinal tract, ulcerative erosive lesions, with hyperacid gastritis, gastric ulcer and duodenal ulcer [9, 10, 11, 12].

Successful treatment of peptic ulcer is promoted by plants that have a sedative effect. In this respect, the undisputed leader is *Valeriana officinalis* L. (valerian), the rhizomes of which are used to produce a variety of medicines

(Infusion, tincture, dry extract in the form of tablets, various collections including carminative and gastric). Medicines from *Hypericum perforatum* L. (Saint John's wort) grass as helarium, deprim forte, relaptan, negrustin, gastroguttal are used due to their antidepressant effect [7, 13, 14, 15].

Stimulation of the processes of regeneration of the gastric mucosa is achieved by the appointment of reparants — agents that affect the processes of regeneration and protein synthesis. This group should include carotenoids (provitamin A), which provide wound healing, epithelizing and antioxidant effects: they are found in *Hippophae rhamnoides* L. fruits (oil), *Calendula officinalis* L. flowers (infusion, caleflon), *Rosa canina* L. fruits (infusion, oil, carotolinum), *Cucurbita pepo* L. seed (oil, tykveol). Other vitamin medicines from medicinal plants that show antioxidant and capillary-strengthening properties also belong to the means that stimulate the regeneration processes: B₁ (thiamine) — *Helianthus annuus* L. and *Pisum sativum* L. seeds; B₂ (riboflavin) and B₆ (pyridoxine) — almost in all medicinal plants; C (ascorbic acid) — *Ribes nigrum* L. and *Petroselinum crispum* Mill. leaves, *Capsicum annuum* L. and *Rosa majalis* L. fruits, citrus fruits, etc.; P (rutin, ascorutin, quercetin, diquertin) — *Sophora japonica* L., *Aronia melanocarpa* Michx. Vitamin U (S-methylmethionine) plays a special role in regulating the regeneration of gastric and duodenal ulcers and has antiallergic effect due to inactivation of histamine. It is contained in freshly squeezed *Brassica oleracea* L. (cabbage) juice, and is also obtained by chemical synthesis as methylmethionine sulfonium chloride [14, 15, 16, 17, 18].

Gastrofit is a medicinal collection of 15 medicinal plants, which stimulates reparative processes. It is used to prevent and optimize the treatment of gastritis (including hypoacidic), duodenitis, enterocolitis, prevention of recurrence of gastric ulcer and duodenal ulcer, colitis, cholecystitis, cholangitis, urinary dyskinesia, regulation of motor function of the stomach and intestines, normalization of stool [16].

Folk herbal medicine experience recommends in the treatment using *Aloe arborescens* L. leaves juice, propolis, *Brassica oleracea* L. leaves and stem juice and medicinal plants containing carotenoids, antioxidants, flavonoids to improve the regeneration of the gastric mucosa. As plants that combine enveloping and anti-inflammatory properties, preparations of *Linum usitatissimum* L. seeds and *Plantago major* L. leaves, as well as *Glycyrrhiza glabra* L. roots can be recommended [19, 20, 21].

With a tendency to bleeding of the gastric mucosa, plants containing vitamin K are recommended (*Urtica dioica* L. leaves, *Achillea millefolium* L. grass, etc.) and tannins (*Sanguisorba officinalis* L. and *Polygonum bistorta* L. rhizomes, *Hypericum perforatum* L. grass, *Prunus padus* L. and *Vaccinium myrtillus* L. fruits) which have hemostatic, astringent and anti-inflammatory effects [13, 22].

Thus, the phytotherapy of chronic hyperacid gastritis, gastric ulcer and duodenal ulcer plays an important role in the treatment of these diseases, where the anti-ulcer effect is realized with the help of antioxidant, membrane-stabilizing, anti-inflammatory, reparative effects, which are provided by biologically active substances contained in medicinal plant raw materials; mucous, phytoncides, vitamins, essential oils, tannins and flavonoids.

Vitis vinifera L. (grape) is one of the richest sources of polyphenols [23]. Polyphenols are the collective name of a whole class of substances, which includes flavonoids, lignins, coumarins and other substances whose formula contains more than one phenolic group [24, 25, 26, 27]. General phenolic substances from grapes, which are subject to extraction, are distributed in the following ratio: 60-70 % — in seeds, 28-35 % — in a skin, the rest — in a pulp [7].

The seeds of the Cabernet-Sauvignon grape variety contain the whole gamma of flavanoid and non-flavanoid groups of polyphenols, as well as microelements: Zn, Cu, Mn, Fe, etc. This ensures antioxidant, P-vitamin,

antibacterial, antiviral activity, as well as the synergistic effect of total grape polyphenols and antioxidant protection enzymes of the human body. None of the known imported analogues has such a potential of biological activity [28, 29, 30].

For many years, scientists conducted research on the biological role of viticulture, including studies of the composition of grape seeds of the variety "Cabernet Sauvignon" (table).

Table

**Concentrate of polyphenols of grape seeds of the variety
"Cabernet Sauvignon" (analysis 12/01/2012)**

<i>Biologically active substances</i>	<i>mg/l</i>
Citric acid	5011
Tartaric acid	880
Saccharose	0
Glucose	7187
Fructose	18350
Gallic acid	1123,8
5-Oxymethylfurfural	0.0
(+)-D- Catechin	1281,6
(-)-Epicatechin	388,6
Syringic acid	60,7
Quercetin	7,6
Oligomeric proanthocyanidins	4455,0
Polymeric proanthocyanidins	149056,4
The amount of phenolic HPLC	156373,8

Note. HPLC — high-performance liquid chromatography.

Grape seed polyphenols are powerful antioxidants, many times stronger

than, for example, vitamins C and E. Clinical trials have confirmed that the antioxidant properties of grape seeds' oligomeric proanthocyanidins are 20 times stronger than vitamin C and 50 times stronger than vitamin E [28]. Phenolic substances from grape seeds, including flavonoids and polyphenols, are of interest because of their ability to absorb free radicals [31].

In addition to the antioxidant effect, polyphenols from grape seeds inhibit certain enzymes that catalyze the release of histamine (which causes inflammation and allergic reactions) into the bloodstream, thus, they also have anti-inflammatory properties [32, 33].

It is also known that polyphenols play the role of prebiotics in the digestive system [34]. They are able to inhibit the growth and development of pathogenic microflora of the gastrointestinal tract, to which *H. pylori* belongs, while they do not affect the beneficial lactobacilli and bifidobacteria [35, 36].

The selling prices for 1 gram of grape polyphenols abroad vary in the range of 8-10 USD, while in Ukraine it is equivalent to 2,5 USD, which is at least 3 times cheaper [28].

Conclusions. The analysis of the modern pharmaceutical market for herbal anti-ulcer drugs, the pharmacological properties of grape seed polyphenols, the presence of a sufficient raw material base in Ukraine and its low cost is a theoretical basis for creating new anti-ulcer medicines on their basis.

References:

1. Tsimmerman Ya. S. Yazvennaya bolezni: aktualnyie problemyi etiologii, patogenez, differentsirovannogo lecheniya // Klinicheskaya meditsina. — 2012. — № 8. — P. 11-18. (in Russian)
2. Minina T. D. Gastrit i yazvennaya bolezni. Sovremennyiy vzglyad na lechenie i profilaktiku / Tatyana Dmitrievna Minina. — M.: Ves', 2014. — 590 p. (in Russian)
3. Perederij V. G. Praktichna gastroenterologiya. Suchasna taktika j

algoritmi vedennya hvorih z osnovnimi gastroenterologichnimi zahvoryuvannyami i sindromami: posibnik dlya likariv / V. G. Perederij, S. M. Tkach. — Vinnicya: Nova Kniga, 2012. — 736 p. (in Ukrainian)

4. Sheptulin A. A. Kak izmenilis podhodyi k lekarstvennoy terapii yazvennoy bolezni za poslednie 30 let // Klinicheskaya meditsina. — 2015. — № 8. — P. 50-54. (in Russian)

5. Gerchikov L. N. Reltser — novyy mnogokomponentnyy lekarstvennyy preparat s rastitelnyim komponentom solodki dlya lecheniya gastro-enterologicheskikh zabolevaniy / L. N. Gerchikov, V. V. Krasnikov // Russkiy med. zhurn. — 2005. — Vol. 7, № 5. — P. 74-76. (in Russian)

6. Cyrempilova A. Ch. Rastitelnye lekarstvennye sredstva v profilaktike yazvennoj bolezni zheludka i dvenadcatiperstnoj kishki / A. Ch. Cyrempilova, S. V. Cyrempilov // Byulleten VSNC RAMN. — 2012. — №4 (86), Ch. 1. — P. 164-165. (in Russian)

7. Farmakognoziya: bazovij pidruch. dlya stud. vish. farmac. navch. zakl. (farmac. f-iv) IV rivnya akreditaciyi / V. S. Kislichenko, I. O. Zhuravel, S. M. Marchishin ta in.; za red. V. S. Kislichenko. — Kharkiv: Zoloti storinki, 2015. — 736 p. (in Ukrainian)

8. Spiridonov S. V. Rozrobka skladu ta tehnologiyi likarskogo preparatu u viglyadi granul dlya likuvannya ta profilaktyky zapalnyh zahvoryuvan' shlunkovo-kyshkovogo traktu / S. V. Spiridonov, D. I. Dmitrievskiy // Visnyk farmatsiyi. — 2007. — № 1 (49). — P. 28-31. (in Ukrainian)

9. Prochazkova D. Antioxidant and prooxidant properties of flavonoids / D. Prochazkova, I. Bousova, N. Wilhelmova // Fitoterapia. — 2011. — Vol. 82. — P. 513–523.

10. Kalugina S. M. Ocinka antiulcerogennoyi diyi kaleflonu pri modelyuvanni subhronichnih erozivno-virazkovih urazhen gastroduodenalnoyi dilyanki / S. M. Kalugina // Liki. — 2001. — № 3-4. — P. 88-91. (in Ukrainian)

11. Chepurnoj I. P. Biohimiya fitoterapii i novye podhody v vosstanovitelnyh processah bolnyh dlya ih polnogo vyzdorovleniya / I. P. Chepurnoj // Tehnologii XXI veka i Fitoterapiya. — 2008. — № 2. — P. 5-14. (in Russian)

12. Shahidi F., Yeo J. Bioactivities of Phenolics by Focusing on Suppression of Chronic Diseases: A Review. *Int. J. Mol. Sci.* 2018; 19 (6): 1573.

13. Yakovleva O. O. Klinichna farmakologiya likarskih zasobiv dlya likuvannya zahvoryuvan organiv travlennya: navch. posibnik / O. O. Yakovleva, K. V. Pivtorak, I. V. Fedzhega. — Vinnicya: Nova Kniga, 2014. — 288 p. (in Ukrainian)

14. Kompendium — lekarstvennyye preparaty / pod red. V. N. Kovalenko — K.: MORION, 2017. — 536 p. (in Russian)

15. Chekman I. S. Klinichna fitoterapiya / I. S. Chekman. — K.: vid-vo A.S.K., 2003. — 552 p. (in Ukrainian)

16. Nikolaev S. M. Farmakoterapevticheskaya effektivnost rastitelnogo sredstva pri hronicheskoy acetatnoj yazve zheludka / S. M. Nikolaev, A. A. Toropova, Ya. G. Razuvaeva, S. V. Cyrempilov // *Vestnik Buryatskogo gosudarstvennogo universiteta.* — 2011. — S. 23-26. (in Russian)

17. Suchasna fitoterapiya: navch. posib. / S. V. Garna, I. M. Vladimirova, N. B. Burda ta in. — Kharkiv: «Drukarnya Madrid», 2016. — 580 p. (in Ukrainian)

18. Mashkovskij M. D. Lekarstvennyye sredstva / M. D. Mashkovskij; [16 izd., pererab., ispr. i dop.]. — M.: «Novaya volna», izd-1 Umerenkov, 2019. — 1120 p. (in Russian)

19. Plant Bioactives and Drug Discovery: Principles, Practice, and Perspectives / Ed. by V. Cechinel-Filho. — Hoboken, New Jersey: John Wiley & Sons Publishing, 2012. — 586 p.

20. Kiosev P. A. Lekarstvennyye rasteniya: samyj polnyj spravochnik /

Plamen Angelov Kiosev. — M.: EKSMO, 2011. — 944 p. (in Russian)

21. Tovstuha Ye. S. Fitoterapiya v narodnij medicini ukrajinciv / Ye. S. Tovstuha // Fitoterapiya. Chasopis. — 2008. — № 4. — P. 64-65. (in Ukrainian)

22. Flavonoidy: biohimiya, biofizika, medicina / Yu. S. Tarahovskij, Yu. A. Kim, B. S. Abdrasilov, E. N. Muzafarov; [otv. red. E. I. Maevskij] — Pushino: Sunchrobook, 2013. — 310 p. (in Russian)

23. Vozmozhnosti fitoterapii pri zabolevaniyah sistemy pishevareniya / A. V. Kurkina, V. R. Galyamova, V. A. Kurkin, E. V. Avdeeva // Farmaciya i farmakologiya. — 2016. — T. 4, № 2 (15). — P. 26-39. (in Russian)

24. Korsun V. F. Fitolektiny. Rukovodstvo po klinicheskoj fitoterapii / V. F. Korsun, V. M. Lahtin, E. V. Korsun, A. Mickonas. — M.: Prakticheskaya medicina, 2007. — 285 p. (in Russian)

25. Rasteniya — donory BAD: za i protiv / G. E. Pronchenko, V. V. Vandyshev. — M.: GEOTAR — Media, 2013. — 216 p. (in Russian)

26. Abdulla M. A. Anti-ulcer activity of Centella asiaticaleaf extract against ethanol-induced gastric mucosal injury in rats / M. A. Abdulla, F. H. Al-Bayaty, L. T. Younis [et al.] // Journal of Medicinal Plants Research. — 2010. — Vol. 4, № 13. — P. 1253-1259.

27. Al-Mofleh I. Antisecretagogue, antiulcer and cytoprotective effects of peppermint mentha piperita L. in laboratory animals / I. Al-Mofleh, A. Abdulqader, J. Mossa [et al.] // J. Med. Sci. — 2006. — Vol. 6, № 6. — P. 930-936.

28. Zagajko A. L. Biodostupnist i antioksidantna aktivnist polifenoliv z nasinnya vinogradu u vilnomu viglyadi ta u skladi fitosom / A. L. Zagajko, V. P. Filimonenko, O. A. Krasilnikova [ta in.] // Med. himiya. — 2011. — Vol. 13, №3 (48). — P. 109-112. (in Ukrainian)

29. Tipikin I. S. Korrekciya flavonoidami funkcionalnoj elastichnosti eritrocitarnyh membran i gemoreologicheskikh narushenij pri okislitel'nom stresse hronicheskogo fizicheskogo perenapryazheniya u myshej / I. S. Tipikin, E. A.

Rozhkova, R. D. Sejfulla [i dr.] // Eksperimentalnaya i klinicheskaya farmakologiya. — 2011. — № 10. — P. 26-30. (in Russian)

30. Fikselova M. Antioxidant (antiradical) and antimicrobial (antifungal) effects of slovak tokaj wines / M. Fikselova, M. Kacaniova, M. Mellen // Acta Alimentaria. — 2010. — T. 39, № 3. — P. 256-264.

31. Chekman I. S. Flavonoyidi: farmakoterapevtichnij aspekt / I. S. Chekman, I. V. Zavalko // Medicina. — 2008. — № 2. — P. 3-7. (in Ukrainian)

32. Zenkov N. K. Antioksidantnye i protivovospalitelnye svojstva novykh vodorastvorimyh serosoderzhashih fenolnyh soedinenij / N. K. Zenkov, E. B. Menshikova, N. V. Kandalinceva // Biohimiya. — 2007. — T. 72, vyp. 6. — P. 790-798. (in Russian)

33. Jovanovic A. Polyphenols extraction from plant sources / A. Jovanovic, P. Petrovic, V. Đorđević [et al.] // Lekovite Sirovine. — 2017. — Vol. 37. — P. 45-49.

34. Menshikova E. B. Okislitelnyj stress. Prooksidanty i antioksidanty / E. B. Menshikova, V. Z. Lankin, N. K. Zenkov [i dr.] // — M.: Firma «Slovo», 2006. — 556 p. (in Russian)

35. Zverev Ya. F. Flavonoidy glazami farmakologa. Antioksidantnaya i protivovospalitel'naya aktivnost // Obzory po klinicheskoy farmakologii i lekarstvennoj terapii. — 2017. — T. 15. — № 4. — P. 5-13. (in Russian)

36. Zenkov N. K. Antioxidant and anti-inflammatory properties of new water-soluble sulfur-containing phenolic compounds / N. K. Zenkov, E. B. Menshchikova, N. V. Kandalintseva // Biochemistry. — 2007. — № 72 (6). — P. 790-798.