Drugs of radiological pharmacology: Quercetin

N.N. Kolotilov

SI "Institute of Nuclear Medicine and Diagnostic Radiology of the National Academy of Medical Sciences of Ukraine", Kiev

Quercetin (C₁₅H₁₀O₇, molar mass – 302.236 g/mol) is a natural biochemical substance of the flavonoid group with P-vitamin activity (figure) [2].

Food sources of Quercetin. Quercetin is found in plants (mainly red, crimson): in lovage, capers, buckwheat, onions (especially red, in large quantities in outer shells and husks), apples, pepper, garlic, golden mustache, red grapes, tea, citrus fruits, dark cherries, lingonberries, tomatoes, broccoli, raspberries, blueberries, cranberries, chokeberries, chokeberry, mountain ash, sea buckthorn, crowberry, some sorts of honey (eucalyptus, tea tree), nuts, cauliflower and cabbage, red wine, olive oil, acorns – in the form of a water-soluble rutin.

Quercetin is best digested in combination with pectin and insoluble oligosaccharides. A diet with high content of simple saccharides (a large quantity of berries, vegetables and fruits in the diet) for 6 weeks doubles plasma levels of quercetin, while a diet with low content results in a 30 % decrease in plasma levels. Studies on the combination of Quercetin with simple saccharides (healthy volunteers, 2 months duration) showed an increase in plasma Quercetin levels by 32–51 %. A diet with the addition of a minimum amount of fat or lecithin also improves the absorption of Quercetin, and its excretion from the body is retarded when a significant amount of fat is included in the diet [11].

The purpose of the article is to draw attention to Quercetin as a means of radiological pharmacology within the framework of medicines' repurposing [5].

Spectrum of pharmacological activity. Quercetin possesses anti-inflammatory (blockade of the lipoxigenase pathway of arachidonic acid metabolism, decreased synthesis of leukotrienes, serotonin and other inflammatory mediators), antioxidant, antispasmodic, diuretic, membrane stabilizing, capillary stabilizing, regenerative, estrogen-like (effect on proline hydroxylase, inhibition of tumor necrosis factor and synthesis of interleukins), immunomodulatory, anticataractogenic, antisclerotic, angioprotective, antiviral (against influenza viruses), antitumor, proosteoclastic, gastroprotective, actoprotective action [1–11].

Quercetin exhibits antiulcer action associated with the anti-inflammatory drugs, and also has a

radioprotective activity (after X-ray and gamma irradiation).

The cardioprotective properties of Quercetin are conditioned by an increase in the energy supply of cardiomyocytes due to its antioxidant effect and an improvement in blood circulation.

Quercetin influences bone remodeling processes. Quercetin is able to normalize blood pressure and stimulate the release of insulin, accelerate platelet aggregation, and inhibit thromboxane synthesis.

Indications: prevention of erosive and ulcerative lesions of the upper alimentary canal caused by the intake of non-steroidal anti-inflammatory drugs. In complex treatment: prevention and treatment of local radiation injuries after X-ray and gamma radiation therapy; treatment of periodontal disease, erosive and ulcerative diseases of the oral mucosa; purulent-inflammatory diseases of soft tissues; climacteric, vertebral pain syndrome, neuroreflex manifestations of the spine osteochondrosis; chronic glomerulonephritis; neurocirculatory dystonia, ischemic heart disease, angina pectoris II–III functional class [2].

Oncology. The in vitro experience clearly shows that Quercetin has a pronounced activity against tumor cells, which is realized through various mechanisms that provide its antiproliferative, antioxidant, proapoptotic effect, suppression of tumor growth factor, as well as due to its synergy with some chemotherapeutic agents [11].

In vitro studies evidence that Quercetin reduces the tumor cells resistance to some standard chemotherapeutic combinations and has a synergistic action with some chemotherapeutic drugs [6, 9].

The combination of Quercetin with the anticancer drug dasatinib gives a greater senolytic effect (selective death initiation of aged cells) compared to the separate application of dasatinib. Quercetin cleanses the human body from aging endothelial cells [10].

The combination of the senolytic drugs dasatinib and Quercetin (D + Q) reduces liver lipid accumulation and alleviates age-related physical dysfunction in mice [8].

Radiobiology [10]. In the experiment, one leg of 4-month-old male mice was irradiated at 10 Gy while

protecting the rest of the body. By 12 weeks, the hair on the irradiated leg had turned gray and the animals had a reduced ability to work on the running path. In 5 days after a single dose of D + Q in mice, exercise time, distance, and total work done to exhaustion on the running path were greater compared to control group. In 7 months after a single treatment, working capacity was significantly better in mice that were irradiated and received a single dose of D + Q, than in control animals. Animals receiving D + Q demonstrated the same endurance as non-irradiated controls. A single dose of D + Q 7 months ago resulted in a sustained improvement in working capacity due to the senolytic effect of D + Q, which provides physical endurance in more mature age.

Quercetin.

Quercetin is a common drug and dietary supplement. If the source of Quercetin is natural products, it poses no danger to the human body. The inclusion of supplements in the diet does not cause any side effects. An exception is taking drugs in the amount of more than 1000 mg per day [2, 11].

Conflict of interest information. The author declares no conflict of interest related to the publication of this article.

Literature

1. Активация сигнального пути интерферона- α ресвератролом, генистеином и кверцетином / О. А. Власова, А. А. Борунова [и др.] // Сибирский онкологический журнал. – 2019. – Т. 18(1). – С. 50-55. <https://doi.org/10.21294/1814-4861-2019-18-1-50-55>.
2. Коваленко В. Н. Компендиум. Лекарственные препараты/ авт.-сост. М. Ю. Титов [и др.]; под ред. В. Н. Коваленко, А. П. Викторов. – К.: Морион, 2007. – 1664 с.
3. Узунжасова А. Б. Сравнительное исследование противовирусной активности кверцетина и его производных / А. Б. Узунжасова, А. С. Турмагамбетова, И. А. Зайцева // European science review. – 2014. – № 3-4. – С. 3-7.
4. Chirumbolo S. Quercetin in cancer prevention and therapy/ S. Chirumbolo // Integr Cancer Ther. – 2013. – Vol. 12 (2). – P. 97-102. <https://doi.org/10.1177/1534735412448215>.
5. Kolotilov N. N. Repurposing of Drugs: Radiological Aspect / N. N. Kolotilov, A. Alekseyenko, I. V. Andrushchenko [et al.] // Radiation Diagnostics, Radiation Therapy. – 2019. – № 3. – P. 70-73. <https://doi.org/10.37336/2707-0700-2019-3-7>.
6. Oh S. J. Inhibition of angiogenesis by quercetin in tamoxifen-resistant breast cancer cells/ S.J. Oh, O. Kim [et al.] // Food Chem Toxicol. – 2010. – Vol. 48. – P. 3227-3234. <https://doi.org/10.1016/j.fct.2010.08.028>.
7. Satué M. Quercitrin and taxifolin stimulate osteoblast differentiation in MC3T3-E1 cells and inhibit osteoclastogenesis in RAW 264.7 cells / M. Satué, M. M. Arriero // Biochem Pharmacol. – 2013. – Vol. 86(10). – P. 1476-1486. [doi:10.1016/j.bcp.2013.09.009](https://doi.org/10.1016/j.bcp.2013.09.009).
8. Senolytic Cocktail Dasatinib+Quercetin (D+Q) Does Not Enhance the Efficacy of Senescence-Inducing Chemotherapy in Liver Cancer / K. Kovacovicova, M. Skolnaja, M. Heinmaa [et al.] // Front. Oncol. – 2018. – Vol. 8. – P. 459. <https://doi.org/10.3389/fonc.2018.00459>.
9. Thangasamy T. Quercetin abrogates chemoresistance in melanoma cells by modulating deltaNp73 / T. Thangasamy, S. Sittadjody, G. C. Mitchell [et al.] // BMC Cancer. – 2010. – Vol. 10. – P. 282. <https://doi.org/10.1186/1471-2407-10-282>.
10. The Achilles' heel of senescent cells: from transcriptome to senolytic drugs / Y. Zhu, T. Tchkonja, T. Pirtskhalava [et al.] // Aging Cell. – 2015. – Vol. 14. – P. 644-658. <https://doi.org/10.1111/acer.12344>.
11. Zhou W. Dietary polyphenol quercetin targets pancreatic cancer stem cells/ W. Zhou, G. Kallifatidis, B. Baumann [et al.] // Int. J Oncol. – 2010. – Vol. 37. – P. 551-561. <https://doi.org/10.3892/ijo-00000704>.

DRUGS OF RADIOLOGICAL PHARMACOLOGY: QUERCETIN

N.N. Kolotilov

The purpose of the article is to draw attention to Quercetin as a means of radiological pharmacology within the framework of medicines' repurposing.

Spectrum of pharmacological activity. Quercetin possesses anti-inflammatory (blockade of the lipoxygenase pathway of arachidonic acid metabolism, decreased synthesis of leukotrienes, serotonin and other inflammatory mediators), antioxidant, antispasmodic, diuretic, membrane stabilizing, capillary stabilizing, regenerative, estrogen-like (effect on proline hydroxylase, inhibition of tumor necrosis factor and synthesis of interleukins), immunomodulatory, anticataractogenic, antisclerotic, angioprotective, antiviral (against influenza viruses), antitumor, proosteoclastic, gastroprotective, actoprotective action [1-11].

Quercetin exhibits antiulcer action associated with the anti-inflammatory drugs, and also **has a radioprotective activity (after X-ray and gamma irradiation).**

The cardioprotective properties of Quercetin are conditioned by an increase in the energy supply of cardiomyocytes due to its antioxidant effect and an improvement in blood circulation.

Quercetin influences bone remodeling processes. Quercetin is able to normalize blood pressure and stimulate the release of insulin, accelerate platelet aggregation, and inhibit thromboxane synthesis.

Key Words: Quercetin, radioprotector, senolytic effect, dietary supplement.

ЛІКАРСЬКІ ЗАСОБИ РАДІОЛОГІЧНОГО ФАРМАКОЛОГІЇ: КВЕРЦЕТИН

М.М. Колотілов

Мета статті – в рамках перепрофілювання лікарських засобів звернути увагу на квертин, як на засіб радіологічної фармакології.

Спектр фармакологічної активності. Кверцетин має протизапальну (блокада ліпооксигеназного шляху метаболізму арахідонової кислоти, зниження синтезу лейкотрієнів, серотоніну та інших медіаторів запалення), антиоксидантну, спазмолітичну, діуретичну, мембраностабілізуючу, капіляростабілізуючу, регенеративну, естрогеноподібну (вплив на пролінгідроксілазу, пригнічення фактора некрозу пухлин і синтез інтерлейкінів), імуномодулюючу, антикатарактогенну, антисклеротичну, ангиопротекторну, протівірусну (по відношенню до вірусів грипу), протипухлинну, проостеокластну, гастропротекторну, актопротекторну дію.

Кверцетин проявляє противиразову дію, пов'язану із застосуванням протизапальних засобів, а також **володіє радіопротекторною активністю (після рентген- та гамма-опроміненнь).**

Кардіопротекторні властивості кверцетину обумовлені підвищенням енергетичного забезпечення

кардіоміоцитів завдяки антиоксидантній дії і поліпшенню кровообігу.

Кверцетин впливає на процеси ремоделювання кісткової тканини. Кверцетин здатний нормалізувати артеріальний тиск і стимулювати вивільнення інсуліну, прискорювати агрегацію тромбоцитів, пригнічувати синтез тромбоксану.

Ключові слова: кверцетин, радіопротектор, сенолітичний ефект, біологічно активна добавка.

ЛЕКАРСТВЕННЫЕ СРЕДСТВА РАДИОЛОГИЧЕСКОЙ ФАРМАКОЛОГИИ: КВЕРЦЕТИН

Н.Н. Колотілов

Цель статьи – в рамках перепрофилирования лекарственных средств обратить внимание на квертин, как на средство радиологической фармакологии.

Спектр фармакологической активности. Кверцетин обладает противовоспалительным (блокада липооксигеназного пути метаболизма арахидоновой кислоты, снижение синтеза лейкотриенов, серотонина и других медиаторов воспаления), антиоксидантным, спазмолитическим, диуретическим, мембраностабилизирующим, капилляростабилизирующим, регенеративным, эстрогеноподобным (влияние на пролингидроксилазу, угнетение фактора некроза опухолей и синтез интерлейкинов), иммуномодулирующим, антикатарактогенным, антисклеротическим, ангиопротекторным, противовирусным (по отношению вирусов гриппа), противоопухолевым, проостеокластным, гастропротекторным, актопротекторным действием.

Кверцетин проявляет противоязвенное действие, связанное с применением противовоспалительных средств, а также **обладает радиопротекторной активностью (после рентген- и гамма-облучений).**

Кардиопротекторные свойства кверцетина обусловлены повышением энергетического обеспечения кардиомиоцитов благодаря антиоксидантному действию и улучшению кровообращения.

Кверцетин влияет на процессы ремоделирования костной ткани. Кверцетин способен нормализовать артериальное давление и стимулировать высвобождение инсулина, ускорять агрегацию тромбоцитов, угнетать синтез тромбоксана.

Ключевые слова: кверцетин, радиопротектор, сенолитический эффект, биологически активная добавка.