PROSPECTS FOR THE DEVELOPMENT OF PHARMACOLOGICAL PREPARATIONS BASED ON THE ANALYSIS OF THE BIOLOGICAL ACTIVITY OF KARACOLINE ALKALOID AND ITS DERIVATIVES

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Abstract: *An overview is presented of the well-established role of alkaloids in drug discovery, the application of more sustainable chemicals, and biological approaches, and the implementation of information systems to address the current challenges faced in meeting global disease needs. The necessity for a new international paradigm for natural product discovery and development for the treatment of multidrug resistant organisms, and rare and neglected tropical diseases in the era of the Fourth Industrial Revolution and the Quintuple Helix is discussed.*

Keywords: *alkaloids, drug discovery, fourth industrial revolution, quintuple helix, neglected tropical diseases, multidrug resistance, genomics, artificial intelligence*

Alkaloids are a paradox and an enigma. Inexplicable, contradictory, mysterious, and yet essential for all forms of life. There are the alkaloids we love as spices (capsaicin, piperine, and the Murraya alkaloids), those we fear as toxins (batrachotoxin, strychnine, and aconitine), those which affect perceptions in the brain (psilocin, N,N-dimethyltryptamine, and ibogaine), and there is caffeine, the global stimulant of coffee, tea, maté, and guarana. There are those alkaloids which can relieve pain and, in another context, elicit pain and enormous disruption in society (morphine and cocaine), and alkaloids whose diverse impacts can strain health care systems (nicotine). There is also a plethora of alkaloids from diverse sources which serve as medicines (paclitaxel, vincristine, the cephalosporins, the penicillins, atropine, pilocarpine, quinine, vincamine, etc.). A recent review has provided a concise introduction to plant alkaloids and their broad biological impact on human health, and some of the biosynthetic aspects of alkaloids have been summarized.

There have been several excellent reports of the role of natural products in drug discovery and the challenges to be faced. The terrestrial and marine biomes are recognized as essential providers of new source opportunities for natural product discovery. This review will examine the need for new medicinal agents, the evolving strategies for natural product drug discovery, and how the various facets of the Fourth Industrial Revolution (4IR), interfacing with the activities embodied in the Quintuple Helix, provide new opportunities for the development of natural products. The focus will be on the role of alkaloids in the complex milieu of the evolving discovery process, particularly for overcoming multiple drug resistance (MDR), and for the treatment of

rare and tropical diseases, including the neglected tropical diseases (NTDs). It will approach the question of how the present and future levels of technological development in the 4IR can enhance the utilization of alkaloids as drugs in new ways to address these global health needs and the welfare of the patient.

Currently, in the domestic pharmaceutical market there are a large number of drugs of various origins - synthetic, semi-synthetic, natural. The most popular of them are drugs produced and / or made from medicinal plant materials. Over 250 species of medicinal plants are used in modern scientific medicine, the most important of which are included in the State Pharmacopoeia of the Russian Federation. They have a different therapeutic effect, which is determined by the biologically active substances contained in the medicinal plant material. The most significant group of such substances are alkaloids.

Alkaloids are a group of nitrogen-containing organic substances of natural origin with pronounced physiological activity. In the plant world, they are most common among the Angiospermae (Magnoliophyta) division, less often among the Gymnospermae division. The families Papaveraceae, Solanaceae, Fabaceae, Campanulaceae, Ranunculaceae, Apocynaceae, Rutaceae, Loganiaceae, Ephedraceae, Malvaceae, Taxaceae and others are rich in them. Alkaloids are able to accumulate in various plant organs, being localized in cells in the form of salts of organic and inorganic acids. Their content as biologically active substances is small - it is hundredths and tenths of a percent. Usually a plant has in its chemical composition not one, but several types of alkaloids located in its different parts. For example, the tubers of Stephania glabra (Roxb.) Miers contain a sum of alkaloids, which include gindarin, rotundine, stefarin and many others. Despite this, only one representative, cycleanin, was found in the leaves and stem. In the herb Thermopsis lanceolata R.Br. there is a high content of alkaloids thermopsin, homothermopsin, pachycarpine, anagirin, but as a medicinal plant material it is used as a source of cytisine accumulated in seeds. In addition to localization, alkaloids also differ in concentration, which is influenced by numerous factors: climatic conditions (temperature, humidity), mineral composition of the soil, time of day and vegetation stage. It is known that under conditions of high humidity, the amount of alkaloids gradually decreases. The synthesis and accumulation of these biologically active substances are favorably affected by soils rich in nitrogen, high temperature and daylight hours.

Caracoline alkaloid and its derivatives have potential applications in pharmacology due to their cognitive enhancement, anti-inflammatory, neuroprotective, antioxidant and antitumor properties. These compounds have been extensively studied for use in the development of new and more effective drugs. For example, studies have shown that the alkaloid caracolin and its derivatives may have beneficial effects in the treatment of Alzheimer's disease by improving cognitive function. In addition, their antioxidant and anti-inflammatory properties help treat diseases such as Parkinson's disease and cancer.

Where, what, and how to source alkaloids are primary questions for any natural product drug discovery program. That source may be a specialized marine or terrestrial location, from a microbe, an extract or compound library based on traditional medicine reports, a specific taxonomic source, or through in silico binding studies of alkaloid libraries at the active sites of specific enzymes or receptors (vide infra). In the past twenty-five years cyanobacteria have become a significant source of new alkaloid metabolites possessing a range of biological activities. Generating and maintaining a meaningful number of pure alkaloids for bioassay, even for a modest in vitro screening program, is a significant challenge. Some alkaloids can be purchased, but source collection and re-isolation would be necessary to truly populate library space. Relief may come from concentrates of alkaloid fractions, but even this approach leads to relatively small (1000–2000) sample numbers. Maintaining the stability of alkaloids, particularly basic alkaloids, requires low temperature storage in an inert atmosphere to avoid transformation to their N-oxides. For such alkaloid-based drug discovery to be successful, a different strategy is necessary, requiring centralization of analyzed samples, including semi-purified alkaloid concentrates, and a distribution network for biological testing.

The major issue in antibiotic drug discovery lies in the consistent emergence of antibiotic resistant strains of microbes due to the production of virulent genes encoding protective mechanisms. These include biofilm formation, beta lactamases, etc. Mitigation of the progression of antibiotic resistance includes more controlled use and stewardship of use, while maintaining access in middle- and low-income countries, coupled with improved local diagnostic testing to target more succinctly an effective antibiotic therapy for the individual patient. In addition to controlling more aggressively the use of 30 different antibiotics as animal and plant growth promoters, chemically based strategies to overcome drug resistance include: (i) seeking new antibiotic scaffolds through in-field or bioinformatics approaches, (ii) combining antibiotics in therapy, (iii) using adjuvants in combination or alternately for treatment, and (iv) structure modifications of existing antibiotics.

Accordingly it can be said that caracolin alkaloid and its derivatives have great potential as pharmacological agents in various diseases. However, more research is needed to fully explore their effects and optimize their use in drug development. Caracoline alkaloid and its derivatives studied in the analysis have potential applications in pharmacology due to their ability to enhance cognitive functions, exhibit anti-inflammatory, neuroprotective, antioxidant and antitumor properties. These compounds have been extensively studied for their potential use in the development of new and more effective drugs. However, the development of drugs based on caracolin alkaloid and its derivatives may face problems such as low bioavailability and the risk of toxic effects at high doses. Therefore, further research is needed to better understand the potential clinical applications of these substances and to overcome the problems associated with them. As we mentioned above,

caracolin alkaloid and its derivatives have great potential as pharmacological agents for various diseases. However, further research is needed to fully understand their effects and optimize their use in drug development.

REFERENCES:

1. Debnath B., Singh W.S., Das M., Goswami S., Singh M.K., Maiti D., Manna K. Role of plant alkaloids on human health: A review of biological activities. Mater. Today Chem. 2018;9:56–72. doi: 10.1016/j.mtchem.2018.05.001.
2. Funayama S., Cordell G.A. Alkaloids—A Treasury of Poisons and Medicines. Academic Press; New York, NY, USA: 2015. p. 284.
3. Butler M.S. The role of natural product chemistry in drug discovery. J. Nat. Prod. 2004;67:2141–2153. doi: 10.1021/np040106y.
4. Carter G.T. Natural products and Pharma 2011: Strategic changes spur new opportunities. Nat. Prod. Rep. 2011;28:1783–1789. doi: 10.1039/c1np00033k.
5. Qiu S., Sun H., Zhang A.-H., Xu H.-Y., Yan G.-L., Han Y., Wang X.-J. Natural alkaloids: Basic aspects, biological roles, and future perspectives. Chin. J. Nat. Med. 2014;12:401–406. doi: 10.1016/S1875-5364(14)60063.
6. Harvey A.L., Edrada-Ebel R., Quinn R.J. The re-emergence of natural products for drug discovery in the genomics era. Nat. Rev. Drug Discov. 2015;14:111–129. doi: 10.1038/nrd4510.
7. Shen B. A new golden age of natural products drug discovery. Cell. 2015;163:1297–1300. doi: 10.1016/j.cell.2015.11.03.
8. Mirzaolimov M. M., Abdullaev G. R., Abdullayev S. S. ROLE OF A CALORIE-RESTRICTED DIET IN PROLONGING THE LIFESPAN OF AN ORGANISM AND ITS MITOCHONDRIAL MECHANISMS //Scientific Bulletin of Namangan State University. – 2019. – Т. 1. – №. 10. – С. 106-112.
9. Soliev N., Mirzaolimov M. ACTION OF CALCIUM ON THE CONTENT OF PHOSPHOTYDYLCHOLIN, PHOSPHATYL ETHANOLAMINE AND THEIR LYSOFORMS IN THE RAT LIVER MITOCHONDRIA //Scientific Bulletin of Namangan State University. – 2019. – Т. 1. – №. 3. – С. 69-71.
10. Mirzaolimov M. M. et al. THE METHOD OF SEPARATION OF MITOCHONDRIAS AND DETERMINATION OF PHYSIOLOGICAL AND BIOCHEMICAL CHANGES IN ORGANISMS IN ONTOGENESIS //Scientific Bulletin of Namangan State University. – 2020. – Т. 2. – №. 3. – С. 175-178.
11. Бохонова Н. С., Мирзаолимов М. М. ВЛИЯНИЕ КАЛОРИЙНО-ОГРАНИЧЕННОЙ ДИЕТЫ НА ПРОДОЛЖИТЕЛЬНОСТЬ ЖИЗНИ ЖИВОТНЫХ //TA'LIM VA RIVOJLANISH TAHLILI ONLAYN ILMIY JURNALI. – 2022. – С. 139-142.
12. Анваров Ф. Р., Мирзаолимов М. М. ГЕРИАТРИЯ (ОПРЕДЕЛЕНИЕ ПОНЯТИЙ; ЗАДАЧИ, СТОЯШИЕ ПЕРЕД ЭТИМ НАУКАМ; РАЗДЕЛЫ И

ДОСТИЖЕНИЯ) //TA'LIM VA RIVOJLANISH TAHLILI ONLAYN ILMIY JURNALI. – 2022. – С. 326-332.

13. Мирзаолимов М. М. и др. ГЕРИАТРИЯ (ОПРЕДЕЛЕНИЕ ПОНЯТИЙ; ЗАДАЧИ, СТОЯШИЕ ПЕРЕД ЭТИМ НАУКАМ; РАЗДЕЛЫ И ДОСТИЖЕНИЯ) //TA'LIM VA RIVOJLANISH TAHLILI ONLAYN ILMIY JURNALI. – 2022. – С. 143-149.

14. Таджибаева Г. И., Мирзаолимов М. М. КАЛАМУШЛАРДА СУРУНКАЛИ ЭМОЦИОНАЛ СТРЕСС МОДЕЛИНИ ЯРАТИШ ВА ОРГАНИЗМДАГИ БИОКИМЁВИЙ ЎЗГАРИШЛАРНИ АНИҚЛАШ //BARQARORLIK VA YETAKCHI TADQIQOTLAR ONLAYN ILMIY JURNALI. – 2022. – С. 166-170.

15. Mirzavalievich M. M., Adashaliyevich N. Q. Soy Protein, Isoflavones, and Cardiovascular Health //International Journal of Scientific Trends. – 2023. – Т. 2. – №. 4. – С. 10-18.

16. Мирзаолимов М. М. и др. ГЕРИАТРИЯ (ОПРЕДЕЛЕНИЕ ПОНЯТИЙ; ЗАДАЧИ, СТОЯШИЕ ПЕРЕД ЭТИМ НАУКАМ; РАЗДЕЛЫ И ДОСТИЖЕНИЯ) //TA'LIM VA RIVOJLANISH TAHLILI ONLAYN ILMIY JURNALI. – 2022. – С. 143-149.

17. Мирзаолимов М. М. и др. КИСЛОРОД ВА АЗОТ ФАОЛ ШАКЛЛАРИ СИНТЕЗИ //PEDAGOGS jurnali. – 2022. – Т. 7. – №. 1. – С. 394-400.