Bone diseases are quite common among the Ukrainian population and occur in most children with leukemia. Therefore, Corectin preparation has been developed on the basis of fundamental research conducted earlier at the Palladin Institute of Biochemistry of the NAS of Ukraine. Corectin has proved itself to be an effective remedy for the treatment of bone lesions of various genesis, including those occurring in hemoblastoses.

The purpose of this research is to assess the prospects for application of Corectin and Glycivit C dietary supplements based on Corectin preparation and to introduce them into production.

As a result, it has shown that these dietary supplements can be used as an additional source of glycine for functional normalization of nervous and immune systems. It increases bone density, cleanses the blood, decreases psycho-emotional tension, speeds up alcoholic detoxification, and, possibly, can be used for the treatment of bone and liver diseases and oncohematological pathologies. The obtained results of marketing research testify that bringing the developed supplements to market will be expedient.

The trial batches of dietary supplements have been made with involvement of Nutrimed LTD (Ukraine). The specifications for production have been approved and listed in the national registry of specifications. The developed supplements have been endorsed by State Research Center for Food Hygiene of the Ministry of Health of Ukraine and the Marzeev Institute of Public Health of NAMS of Ukraine.

Keywords: dietary supplements, glycine, ascorbic acid, osteoporosis, leukemia, and hepatitis.
Ukraine, together with the National Scientific Center of Radiation Medicine of the National Academy of Medical Sciences of Ukraine (NAM-SU), significant changes in the organic component of bones have been revealed for leukemia and the possibility of correction of hemopoiesis processes by low molecular weight metabolites indirectly through extracellular matrix has been proved [2, 3]. As a result, Corectin preparation has developed. It can be used as an independent therapeutic and prophylactic agent for the treatment of various genesis bone lesions, in particular, as part of complex chemotherapy of hemoblastomas accompanied with complications affecting the musculoskeletal system.

The main task of this research is commercialization of cheap and effective dietary supplements Corectin and Glycivit C (modified Corectin with vitamin C added) developed on the basis Corectin preparation. These drugs have a normalizing effect on bone tissue condition and many additional indications for use.

THE RESEARCH RESULTS

Changes in extracellular matrix with collagen structures as main component are believed to be one of causes for blocking hemopoiesis in leukemia. Taking into account the fact that in bone tissue the stromal and hemopoietic lines are interrelated, and leuko-pathogenesis is associated with blocked differentiation of hemopoietic line cells, researchers team of the Palladin Institute of Biochemistry of the NAS of Ukraine led by Full Member of NAS of Ukraine M.F. Gulyi suggested that there were mechanisms of indirect metabolic influence on the hemopoiesis processes through the extracellular matrix. The possibility of treating oncohematological diseases by eliminating the associated pathologies of bone tissue has been studied. The main purpose of these studies was to find out effects of low molecular weight metabolites, among which a special place was given to glycine, on the exchange and the state of extracellular matrix against the background of protein-free diet. One of the key results was observations of glycine blocking the formation of intermolecular joints in the collagen structure, which is an indicator of inhibition of aging processes and a sign of improving the regeneration of connective tissue [4].

This discovery made it possible to assume a positive effect of glycine on the condition of bone and connective tissue in patients undergoing intensive chemotherapy of lymphoblastosis using cytostatics and radiation therapy. In co-authorship with the National Research Center for Radiation Medicine of the NAMS of Ukraine, Corectin preparation has been developed and doses that contributed significantly to improvement of the state of above-mentioned patients have been identified. The drug has been tested by the Pharmacological Center of the Ministry of Healthcare of Ukraine, with a permit for clinical trials obtained. Based on the facilities of the Institute of Clinical Radiology of the National Research Center for Radiation Medicine of the NAMS of Ukraine, the first two phases of clinical trials have been conducted for cancer patients undergoing basic chemotherapy. As a result, an additional hepatoprotective effect of Corectin preparation has been discovered. It has made it particularly promising for use in complex chemotherapy of oncolgical patients [5]. The positive effect of this preparation on complications affecting the bone tissue and hepatitis of various etiologies (viral nature or induced by aggressive chemotherapy) has been concluded.

Medico-biological background of functional properties of Corectin and Glycivit C dietary supplements

Based on Corectin the Palladin Institute of Biochemistry NAS of Ukraine has developed special food products, dietary supplements Corectin and Glycivit C having the following chemical composition:

1 capsule of Corectin contains active ingredients: 400 mg glycine; auxiliary substances: microcrystalline cellulose fillers, calcium stearate,
amorphous silicon dioxide (orisil), maltodextrin; capsule shell (gelatin);

1 capsule of Glycivit C contains: active ingredients: 400 mg glycine, 50 mg vitamin C (ascorbic acid); auxiliary substances: microcrystalline cellulose fillers, calcium stearate, amorphous silicon dioxide (orisil), maltodextrin; capsule shell (gelatin).

Below, the properties of main components of Corectin and Glycivit C dietary supplements, as well as their possible applications are described (Fig. 1).

Glycine (aminoacetic acid) is a neurotransmitter amino acid, which receptors are encoded by the GLRA1, GLRA2, GLRA3, and GLRB genes, and present in many parts of the brain and spinal cord. Bound with receptors glycine causes an inhibitory effect on neurons, reducing the excretion of excitatory glutamic acid from them and increasing the release of inhibiting \( \gamma \)-aminobutyric acid (GABA). It also binds with specific regions of NMDA receptors and stimulates signal transduction from excitatory neurotransmitters of glutamate and aspartate [6]. Glycine leads to inhibition of spinal cord motor neurons, which allows it to be used in neurological practice to eliminate muscle hypertonicity.

The glycine ability to normalize and to activate the protective inhibition processes in the central nervous system (CNS) gives it the following properties: to reduce psycho-emotional stress, aggressiveness, and proneness to conflict; to improve social adaptation; to improve the mood; to ease sleep onset and to normalize sleep; to enhance mental working capacity; to reduce vegetative-vascular disorders (including in the menopause); to reduce manifestations of cerebral disorders caused by ischemic stroke and craniocerebral trauma; to mitigate toxic effects of alcohol and drugs that suppress the CNS function; and to

**Fig. 1.** Biochemical properties of glycine and possible applications of dietary supplements based on it: VVD – vegetative-vascular dystonia; CCT – craniocerebral trauma; CNS – central nervous system
reduce sweet cravings. Glycine shows moderate sedative properties, weak antidepressant effect, reduces anxiety and fear. It is an auxiliary component of treatments to reduce alcohol, opiate and other abstinence [6—8].

Glycine plays an important role in the formation of connective tissue, since it is part of its main proteins, collagen and elastin. Collagen is the most common fibrillar protein in the human body. Its share accounts for 25—33% of all proteins, that is about 6% of the body weight. Each of the three collagen polypeptide chains contains about 1000 amino acid residues, including 33% glycine, about 21% proline and oxyproline, 11% alanine, and only about 35% all other amino acids [9].

Collagen contains two unusual derivatives of amino acids, oxyproline and oxylysine located in certain positions relative to glycine. They are formed as a result of posttranslational modification of collagen polypeptide chains by enzymes requiring the presence of vitamin C as a cofactor [9, 10].

Elastin is main component of elastic fibers that are abundantly present in ligaments, walls of large arteries, and lungs. The molecule of this protein contains about 800 amino acid residues. The spiral areas of elastin rich in the glycine residues are separated by shorter sections containing lysine and alanine residues. As compared with collagen, elastin consists of the same amount of glycine and alanine, a little less proline, and a little more valine; it does not contain such amino acids as oxylysine and cysteine [11, 12].

Glycine has hepatoprotective properties as a result of the fact that it is part of L-glutathione (a tripeptide consisting of glutamine, cysteine, and glycine). The glutathione system is known to provide a protective action in the three directions [13]:

1) antioxidant protection (glutathione is also called the main antioxidant): glutathione binds free radicals and restores other antioxidants such as vitamins C and E, since having neutralized free radicals these antioxidants become unstable molecules;

2) detoxification: the elimination of toxins and chemicals that have already been absorbed and circulating in the body; neutralization of toxins in the gastrointestinal tract before their absorption;

3) immunostimulation: stimulation of natural killers (NK-cells), activation of T-lymphocytes.

Glycine is an active metabolite involved in the synthesis of many vital compounds: glutathione, purine bases, various coenzymes, creatine, creatine phosphate, serine, glycolic acid, etc. It is the main substrate of porphyrins synthesis and therefore plays a significant role in the elimination of anemia. In addition, glycine is involved in the neutralization of toxic compounds and contributes to the removal of benzoic acid that enters the body in significant quantities with food products of vegetable origin [14].

Ascorbic acid is an organic compound with formula C6H8O6 contained in many fruits and vegetables and is also one of the essential substances necessary for the normal functioning of human connective tissue and bone tissue. This substance is an antioxidant that performs biological recovery and a coenzyme necessary for some metabolic processes. Only one its isomer, L-ascorbic acid also called vitamin C, is biologically active [10, 14].

The biological role of vitamin C is as follows: it is involved in the formation of collagen, catecholamines, and corticosteroids, the synthesis of serotonin from tryptophan, and in the transformation of cholesterol into bile acids. Vitamin C is essential for the detoxification with participation of cytochrome P450 in hepatocytes. Vitamin C neutralizes the superoxide radical to hydrogen peroxide, restores ubiquinone and vitamin E, stimulates the synthesis of interferon, and, consequently, participates in immune modulation [15].

Due to the mentioned properties of main components Corectin and Glycivit C dietary supplements have a high physiological activity and can positively influence various processes in the human body. Like their predecessor, the Corectin preparation, they can activate anabolic processes, increase regeneration of bone tissue, help eliminate ostalgia, osteoporosis, anemia, early arthrosis,
chronic hepatitis of various etiologies, improve the adhesion and aggregation properties of platelets and prevent bleeding, mobilize antibacterial protection by blood granulocytes without causing allergic reactions. These supplements can be used for curing various complications affecting the musculoskeletal system, including those associated with cancer. In the last case, they can be used as an additional therapeutic component to basic chemotherapy to reduce the time of remitting, since the removal of structural and functional disorders of the locomotor system promotes the improvement of hematological parameters increasing the effectiveness of hemoblastosis treatment. The components that are part of these dietary supplements are rapidly metabolized, which helps to eliminate acidosis that accompanies hemoblastosis. Bound with acetate acetic acid, they normalize the acid-base balance in the human body preventing the release of bone calcium and the development of osteoporosis [5, 16].

In addition, Corectin and Glycivet C dietary supplements can be recommended as an additional source of glycine and ascorbic acid (vitamin C) for normalizing the functional state of the nervous and immune systems, bone tissue, skin, blood, as well as for the overall human body health promotion. Their use can facilitate the organism adaptation to adverse factors, reduce psychoemotional tension and fatigue, enhance mental capacity, improve sleep, and accelerate alcohol detoxification.

The dietary supplements do not contain any narcotic, psychotropic or potent substances. The prescribed daily intake dose (1—2 capsules for adults) does not exceed the therapeutic dose for adults. The on-treatment period is 1—2 months and can be repeated if necessary.

Given the acute need for domestic medical products for the treatment and prevention of musculoskeletal system pathologies, the availability of industrial capacities and raw materials for the production of Corectin and Glycivet C dietary supplements in Ukraine, their competitive ability and relatively low cost, commercialization of these additives is of paramount importance. Potential manufacturer of these dietary supplements is Nutrimed (Ukraine) having a considerable experience in the manufacture of special foodstuff.

The commercial value of Corectin and Glycivet C dietary supplements is justified by a high incidence of musculoskeletal system diseases among the Ukrainian population. Thus, 30% population has osalogic syndromes associated with osteoporosis, osteochondrosis, osteomalacia, hormonal regulation disorders, and malignant diseases of the hematopoietic organs accompanied with destruction of bone tissue. Medical statistics show a significant increase in the morbidity from the bone and muscular system diseases among the adult population of Ukraine, which rank fourth in the structure of disabilities falling behind cardiovascular and oncological diseases and domestic injuries. Two million adults and more than 300 thousand children are traumatized annually in Ukraine, with traumatic and orthopedic diseases among children accounting for 280—300 cases per 10 thousand children [17].

It should be noted that in 80% of cases there are complications affecting the musculoskeletal system in children with diagnosed acute lymphoblastic and acute myeloblastic leukemia in the phase of full-scale clinical manifestations. In 2015, in Ukraine, the incidence of leukemia was 4.6 per 100,000 (306 cases per year) among children and 8.5 per 100,000 (3075 cases per year) among adults. Out of them about 1250—1300 adults needed the treatment of bone lesions [18].

In addition, thousands cases of various forms of hepatitis are diagnosed every year in Ukraine. It can be assumed that as of today, totally about 23 million people need preventive or therapeutic treatment with the use of Corectin and Glycivet C dietary supplements.
ous socio-psychological and biological factors (socio-economic problems, global information oversaturation, chronic fatigue, deterioration of ecological situation and quality of life). These factors lead to increased fatigue of the body and reduced work capacity, promote manifestations of irritability, tension, anxiety, depressed mood, loss of habitual interests, unmotivated fears, sleep disturbances, etc. [19].

To treat neurotic disorders the sedative drugs (psychotrophic drugs that have a sedative effect on the central nervous system without noticeable violations of its functions) are used. An increased demand for sedative drugs among consumers is explained by the possibility of self-treatment, easy use, minimum contraindications and side effects. Glycine has drowsy, anti-stress and nootropic (those that affect the mental activity) properties and helps to normalize metabolic processes in the brain. The substance quickly penetrates into the nervous system, improves brain nutrition, memory, and mental capacity. In addition, glycine helps to fight stress and improves sleep [7, 20].

The demand for glycine-based drugs is reported among various population groups: glycine can be used by the actively working people as antidepressant, sedative and hypnotic drug; by the students to improve the successful mastering of knowledge, especially during the sessions, when the brain works especially hard; by the adolescents with deviant behavior to calm down; it helps the children to sleep and to cope with hyperactivity and the elderly to improve memory and to prevent the development of sclerosis.

Let us consider the trends in the Ukrainian market for glycine-based medical drugs and di-

![Fig. 2. Dynamics of glycine-based drugs group and average GR in 2010–2015: a — in money terms (UAH); b — in-kind (packs) GR (Growth Rate) is percentage ratio of current sales to past sales.](image)
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The dynamics of growth in the glycine-based drugs in money terms is quite impressive as for the period 2010—2015, the average growth rate (GR) that is current sales to past sales reached over 29% (Fig. 2, a). In absolute terms, the market grew from UAH 22.6 million, in 2010, to UAH 79.3 million, in 2015. The highest growth rates were observed in 2012 (+49%).

The growth rate for the analyzed drugs in terms of packs sold is much lower as the average GR is 7% (Fig. 2, b) for the period 2010—2015. Moreover, starting with 2014, the market has been tending to stagnation as GR has become negative. In absolute terms, the market grew from 1.91 million packs, in 2010, to 2.45 million packs, in 2015, reaching a peak of 2.97 million packs, in 2013. The highest growth rate was observed in 2012 (+31%). The growth rate of glycine-based drugs in money terms is explained basically by a significant rise in prices.

The market segment of glycine-based dietary supplements is quite young: it appeared only in 2011 with sales of UAH 50 thousand; in 2012, it increased more than twice, to UAH 120 thousand (Fig. 3, a). The average GR for the period 2012—2015 was over 100%. Since 2011, the market grew to UAH 0.9 million, in 2015. The highest growth rate was recorded in 2015 (+124%).

The dynamics of glycine-based dietary supplements group in terms of packs sold is slightly lower as the average GR for the period 2010—2015 was 94% (Fig. 3, b). In absolute terms, the market grew from 2.72 thousand packs, in 2011, to 36.89 thousand packs, in 2015, with the highest growth rate observed in 2014 (+133%).
significant difference between the GR for 2015 in money terms, (+124%), vs that in absolute terms, (+55%), is explained by a sharp rise in prices for medical drugs.

In 2013–2016 (Fig. 4), the glycine-based drugs totally dominated over the glycine-based dietary supplements: in the 5 months of 2016, in terms of sales, their market shares were 98.3% and 1.7%, respectively (Fig. 4, d). The share of glycine-based dietary supplements was steadily growing, but the growth pace was insignificant as it did not reach 2% either for the specified period.

The analysis of general group of glycine-based drugs and dietary supplements in stock keeping units (SKU) for May 2016 has enabled to identify the leader of drug market — Glycised 100 mg No. 50 manufactured by Arterium (Ukraine) (62.8%), the second one is Glycine drug 100 mg No. 50 by Biotics (Russia) (33.2%). These two drugs cover 96% of the market (Fig. 5). The third is Glycine Forte 100 mg No. 50 manufactured by Arpimed (Armenia) with a market share of 1.9%.

The leader of dietary supplement market, Glycine 250 mg, No. 40 by Beauty and Health (Ukraine) has only 1% of the total market. Glycine preparation 250 mg No. 40 by Euro Plus (Ukraine) makes up 0.4%; Glycine 250 mg No. 40 by Apteka 283 (Ukraine), Glycine Complex 250 mg No. 40 by Beauty and Health (Ukraine), and Glycine 300 mg No. 20 by Evalar (Russia) have 0.2% of the market each. Other dietary supplements possess a share of less than 0.1% of the market.

The analysis of retail prices in May 2016 for the general group of glycine-based drugs and dietary supplements has shown that the price for the main group of drugs ranges from UAH 0.65 to

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**Fig. 4.** Analysis of market share dynamics for glycine-based dietary supplements (DS) and medical drugs (MD) in packs. The charts show shares in sales: a — in 2013; b — in 2014; c — in 2015; d — the first 5 months in 2016

**Fig. 5.** Share in in-kind sales of glycine-based medical drugs and dietary supplements in stock keeping units (SKU) in May 2016: 1 — Glycised (pills, 100 mg No. 50) manufactured by Arterium (Ukraine); 2 — Glycine drug (pills, 100 mg No. 50) by Biotics (Russia); 3 — Glycine drug (pills, 100 mg No. 50) by Arpimed (Armenia); 4 — Glycine Forte (pills, 600 mg No. 20) by Evalar (Russia); 5 — Glycine Forte (pills, 300 mg No. 20) by Evalar (Russia); 6 — Glycine complex (pills, 250 mg No. 40) by Beauty and Health (Ukraine); 7 — Glycine (pills, 250 mg No. 40) by Beauty and Health (Ukraine); 8 — Glycine Plus (pills, 500 mg No. 30) by Apteka 283 (Ukraine); 9 — Glycine B (pills, 250 mg No. 50) by Apteka 283 (Ukraine); 10 — Glycine preparation (pills, 250 mg No. 40) by Euro Plus (Ukraine); 11 — Glycine Forte (pills, 500 mg No. 40) by Euro Plus (Ukraine).
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UAH 0.85 per pill/capsule. This group includes all glycine-based drugs and glycine-based dietary supplements manufactured by Beauty and Health (Ukraine) and Apteka 283 (Ukraine) (Fig. 6).

The average price is significantly exceeded for dietary supplements Glycine Evalar (Russia) — UAH 1.62 for a 300 mg pill and 1.70 UAH per 600 mg pill. The dietary supplements by Euro Plus (Ukraine) and Apteka 283 (Ukraine) are cheaper than the average price (UAH 0.50 and less).

Consequently, due to a relatively low competition in the group and a significant constantly growing stress on the human body the market for glycine-based preparations is quite promising. Their total market value in 2015 amounted to UAH 80.1 million, UAH 2.49 million of which belonged to 6 companies with leaders, Arterium (Ukraine) and Biotics (Russia). It should be noted that the absolute leader in the group is the drugs having 98.5% of the market. The reason for this is a much more powerful marketing system of drug manufacturers.

CONCLUSIONS

In cooperation with Nutrimed (Ukraine), the technology for obtaining the capsular form of glycine-based dietary supplements Corectin and Glycivit C has been developed. Technical specifications (TS) for the products, package layouts, and instructions for use have been elaborated;
pilot industrial batches of the mentioned dietary supplements with corresponding markings have been manufactured (Fig. 7). The entire process has been implemented in compliance with the requirements of the Law of Ukraine on Basic Principles and Requirements for the Safety and Quality of Food Products and with the Technical Regulations for Labeling of Food Products.

The expert examination of TS for dietary supplements developed by the State Research Center for Problems of Hygiene of the Ministry of Healthcare of Ukraine (MHU) on request of the Palla-din Institute of Biochemistry of the NAS of Ukraine has confirmed the conformity of developed products to the hygienic requirements for dietary supplements as approved by the MHU Order of 19.12.2013, No. 1114, and to the Norms of Physiological Needs of the Population of Ukraine in the Basic Nutrients and Energy as approved by the MHU Order of 18.11.1999, No. 272.

The results of marketing research of the retail pharmaceutical market of Ukraine for the glycine-based drugs and dietary supplements have shown the expediency of market introduction of preparations developed.

If commercialized, the Corectin and Glycivit C dietary supplements can be used to eliminate structural and functional damages of bone tissue, including those accompanying oncological diseases, and as part of therapy, to treat chronic hepatitis of different etiologies. In addition, they can be recommended for use in stressful situations and in the case of psycho-emotional stress, deviant forms of children and adult behavior, neuroses, neurasthenia, vegetative-vascular dystonia, cranio-cerebral traumas, sleep disorders, abstinence, etc.

The research has been carried out within the framework of R&D project of the NAS of Ukraine «Creation and Commercialization of Dietary Supplements with Polyfunctional Biological Effect of Detoxification, Osteogenesis, and Improvement of Metabolism» (2016), state registration number 0116U007076.

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ВНЕДРЕНИЕ ДИЕТИЧЕСКИХ ДОБАВОК С ЭФФЕКТОМ ДЕЗИНТОКСИКАЦИИ, УЛУЧШЕНИЯ ОСТЕОГЕНЕЗА И МЕТАБОЛИЗМА

Заболевания опорно-двигательной системы являются достаточно распространенными среди населения Украины и встречаются у большинства детей, больных лейкемией. На основе фундаментальных исследований, проведенных ранее на базе Института биохимии
им. А.В. Палладина НАН Украины, был разработан препарат «Коректин», который оказался эффективным средством для лечения костных повреждений различного генеза, в том числе, возникающих при гемобластозах.

Целью работы было оценить перспективность применения диетических добавок «Коректин» и «Глицивит С», разработанных на основе препарата «Коректин», и внедрить их в производство.

Полученные результаты показывают целесообразность использования указанных диетических добавок как дополнительного источника глицина с целью нормализации функционального состояния нервной и иммунной систем, укрепления костной ткани, очищения крови, уменьшения психэмоционального напряжения, ускорения алкогольной детоксикации, а также, вероятно, для лечения заболеваний опорно-двигательной системы, печени и онкогематологических патологий. Полученные результаты маркетинговых исследований свидетельствуют о целесообразности поставок на рынок разработанных добавок.

При участии ООО «Нутримед» (Украина) изготовлены опытно-промышленные партии добавок «Коректин» и «Глицивит С». Технические условия их производства утверждены и занесены в государственный реестр ТУ. Разработанные добавки получили одобрение ПП «ГНИЦ по проблемам гигиены питания МОЗ Украины» и Института общественного здоровья им. А.М. Марзеева НАМН Украины.

**Ключевые слова:** диетические добавки, глицин, аскорбиновая кислота, остеопороз, лейкемия, гепатит.