

Healthy Food, Healthy People

FUNCTIONAL FOODS FOR CHRONIC DISEASES



**The Modern Day Cure
without the Side Effects of
Traditional Treatments**

Edited by Danik M. Martirosyan, Ph.D.

FUNCTIONAL FOODS FOR CHRONIC DISEASES

The Modern Day Cure without the Side Effects of Traditional Treatments

D&A Inc.
580 W. Arapaho Rd., Suite 130
Richardson, TX 75080
<http://www.functionalfoodscenter.net>

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Important Notice:

This publication is neither a medical guide nor manual for self-treatment. If you should suspect that you suffer from a medical problem, you should seek competent medical care. The reader should consult his or her health professional before adopting any of the suggestions in this book.

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LEUZEA CARTHAMOIDES DC.: APPLICATION PROSPECTS AS PHARMPREPARATIONS AND BIOLOGICALLY ACTIVE COMPONENTS

N.P. Timofeev

Collective Farm BIO; 165650, Koryazhma, Russia

ABSTRACT

Leuzea carthamoides DC. (synonym: *Rhaponticum carthamoides*) is a rare and threatened plant of unique properties. It contains biostimulators, phytoecdysteroids, and takes a prominent position among other adaptogens by its ability to prevent many diseases and efficiently cure a great number of pathologies.

Pharmpreparations and food components from *Leuzea* are used as antidepressants and immunostimulators, concentrators of psychical energy, physical and sexual strength, anti-shock, -pain and wound-healing remedies. The preparations cause an anabolic effect in vertebrates by stimulating the protein biosynthesis in muscle tissues. The preparations of *Leuzea* do not have any age or seasonal restrictions. Their safety and the absence of side effects have stood a test of usage in East medicine. Moreover, they are excellently combinable with classical drugs.

Till recent time, their inaccessibility for most people lied in absence of a cultivated source of raw materials. At present, there are technologies contributing to stable ecdysteroid biosynthesis in an artificial cenosis; problems with loosing highly active fractions during crop selection and treatment are solved. New highly active pharmpreparations have been developed (daily doses 0.5-10.0 mcg/kg biomass or $10^{-12} \dots 10^{-11}$ M, if 20-hydroxyecdysone).

Keywords: *Leuzea carthamoides*, *Rhaponticum*, medicinal plants, agropopulations, ecdysteroids, 20-hydroxyecdysone

INTRODUCTION

Modern medicine seems to be omnipotent. Information about tens of thousand diseases and hundreds of thousand symptoms, use of last achievements of chemistry and physics making the processes in organism even more differentiated and difficult to understand. Development of new drugs has no end. New preparations seem to have no limit of perfection. We buy the remedies offered without knowing what their real efficiency rate is, but believing that these preparations are even better than those from yesterday.

However, the history of humans counts many millions of years, and their biology does not change every day. It means that the matter lies not in developing new medicines but in imperfection of the old ones. Let us analyze whether there are many remedies appeared five or ten years ago and still retaining their efficiency. They are, but their units. Are there unique matters from pharmacopeia that have been used by people for centuries and even thousands of years? Even if they exist, they are very few in number. One of them is represented by *Leuzea*, an unfading "legend of East medicine", which the scientists propose to be "the future of green medicine of XXI century" [1].

The botanical history of the *Rhaponticum* plants goes back to the ancient times of East medicine where they were used under the name *Lou cao* and *Lou lu* [2]. Among several species of plants from genera, *Rhaponticum* (*Leuzea*, *Stemmacantha*) *Leuzea carthamoides* DC (synonym: *Rhaponticum carthamoides*), a rare, fragile and threatened species, became most

popular [3]. It is a perennial (up to 75-150 living years) herbaceous, semi-rosulate plant growing in the sub alpine meadows [4].

Pharmacological use of *Leuzea* never stopped, beginning with the ancient Chinese, Tibet and Mongolian medicine until our days. In different times and at different places it was known as *Sinops*, *radix Echinopsis*, *radix Rhapontici*, 鹿茸 (chinese)); *Cnicus*, *Stemmacantha*, *Leuzea*, *russian leuzea*, *leuzea rapontica*, *maral root*, *maral koren* (english); *hirschwurzel*, *rhapontikum*, *bergscharte* (german); *maraljuuri* (finnish); *parcha caflorova* (czech); *maralrot*, *rapontik* (slovak), *szczodrak krokoszowy* (polish); *velikogolovnik* (ukranian); *levzeja saflorovidnaja*, *bolshegolovnik alpiyskiy*, *papontik* (russian); *izjubreva trava*, *maralova trava*, *aranay-ubjusu*, *sin-ott*, *nijniy uyman* (natives of Siberia), etc.

In the Siberian and Mongolian folk medicine it composes herbal remedies curing lung and kidney diseases, jaundice, fever, and quinsy [5]. *Leuzea* preparations are recorded in the Drug State register of Russia and some other states. *Leuzea* extracts serve as tonic and stimulating drugs for functional nervous disorders, mental and manual fatigue, impaired organ functions, cardiovascular diseases and endocrine pathologies [6].

The widest popularity was gained by *Leuzea* in the last decades as an adaptogen – its stimulating effect in regard to the central nervous system and general organism functions is a well known fact. Without producing any full-blown effect, adaptogens are most efficient for borderline disturbances, as supportive therapeutic agents, by overexertion, general weakness, and after diseases – in case of different pathologies they recover and optimize impaired organism functions while removing metabolic and energy metabolic imbalance. They increase the efficiency rate of internal homeostasis regulators and prevent possible abnormalities in the organism. Besides, adaptogens are known to increase the endurance power under physical and psychical stress conditions, protect the organism, also the brain, from negative influence on the cell level.

The *Leuzea* preparations are nontoxic and on meeting certain conditions leave no negative aftereffect even by elderly people. By the action efficiency rate and possibility of usage for a great number of pathologies, they have an advantage compared to both plant (*Panax ginseng*, *Eleutherococcus senticosus*, *Schizandra chinensis*, *Rhodiola rosea*, *Aralia elata*, *Echinacea*, *Glycyrrhiza glabra*, *Pfaffia paniculata* etc.) and artificially synthesized remedies [7-8]. Their application has neither age nor seasonal restrictions; repeated overdosing does not lead to any negative aftereffects.

Therapeutic action of the “East medicine living legend”, its safety and absence of side effects proven by long application has provoked its deep scientific study. In the last 20s, work on its cultivating was initiated, whereas in the 40-50s its pharmacological and clinical investigation began [9-10].

Leuzea became especially popular in the 90s, which initiated its broad use as a food additive. The consumer market offers numerous commercial products varying by their application purpose produced by the firms *Gero Vita*, *Natural Elixir*, *Life-Science Technologies*, *Cytodyne Technologies* etc., via extraction from *Leuzea* rhizomes and revealing small differences in the formulas of biopreparations. Part from them are described in work N. Timofeev [11] (2001a); R. Lafont and L. Dinan [12].

1. UNIQUE PROPERTIES OF THE ADAPTOGEN PLANT

1.1. Active agents – ecdysteroids. During the last years, *Leuzea* is being intensively studied for the properties of chemical substances composing it. It was established that its unique biological activity is determined by the complex of substances including mono- and poly-saccharides, inulin,

organic acids, steroids, phytoecdysones, vitamins, poly-acetylenic compounds, caoutchouc, phenol-carboxylic acids and their derivatives, lignin, catechins, tanning agents, kinons, essential oil, alkaloids, coumarins, flavonoids, anthocyanins, fatty oil, waxes, lipids [5], as well as gums, lemon salt crystals, phosphates, macro- and microelements [4].

From this row, phytoecdysteroids are all-important substances [13-14] with the main mass fraction represented by *20-hydroxyecdysone* (*20E*, *ecdysterone*, *beta-ecdysone*, *crustecdysone*). *20-hydroxyecdysone* is present in every plant organ [15] and causes various physiological effects in organisms of human and haematherms. Following the special experiments conducted comparing between nonpurified overground shoots of *Leuzea* and chemically pure ecdysteroid extracts from the same shoots [16], the latter were responsible for the physiological reaction.

Apart from main ecdysteroids, plants contain a wide range, "cocktail" of minor ecdysteroids, including such highly active connections, as: *rapisterone D*, *dachryhainansterone*, *24(28)-dehydro-makisterone A*, *22-benzoate-ecdysterone*, *5-deoxy-kaladasterone*, *polypodine B*, *ajugasterone C*, *makisterone A* и *C*, *integristerone*, *leuzeasterone*, *carthamosterone*, *coronatasterone* with their derivatives, etc.; Fig. 1). A broad spectrum of ecdysteroid forms is accompanied by their conjugations with other secondary metabolic products: inorganic (sulphates, phosphates) and organic acids (acetates, benzoates, cinnamates), sugars etc.

Theoretically possible are any combinations of these derivations in form of thousands of different molecules, responsible for the unique biological activity of the nonpurified extracts. Consequently, the activity rate of the extracts is significantly higher compared to that of the highly purified drugs [17].

1.2. Physiological activity. Ecdysteroids support the life activity of almost all classes of organisms being responsible for a variety of functions. In most cases, they are transferred from ecdysteroid-synthesizing plants to the lower food chain links. Certain is only that *20-hydroxyecdysone* is a true moulting hormone for arthropoda (insects and cancrs).

Some sea inhabitants secrete them for defense and attack. As for mammals, people, and plants, they play some universal hormone-like role, but are not hormones. Ecdysteroids rather control over the hormone balance while taking a higher position in the biologically active substances' hierarchy.

Being introduced into the organism, ecdysteroids are transported within the blood flux to internal organs causing rapid and prolonged effects, lasting for a few minutes or 2-3 days, correspondingly. On subcutaneous injection, elimination starts in 4-10 minutes, in 2 hours the radioactive marker in blood is no more discernable. On oral introduction, absorption proceeds in a slower rate. Elimination presents a through way via liver, intestines, and faeces (urine in part). In a day after introduction, *20-hydroxyecdysone* is completely eliminated from the organism [18]. It is not destructed by the acid-base content of digestive tract and does not affect its inhabitants, e.g. microorganisms' association [19]. A one-time course of treatment for 7-10 days accounts for a period of afteraction up to 2 months [7].

Quite large are therapeutic indications for *Leuzea* as decoctions, tinctures, extracts, and biopreparations. Ecdysteroid-containing preparations regulate mineral, carbohydrate, and protein metabolism, and reveal anti-oxidant and -radical properties [20-21]. They normalize the blood level of glucose being helpful in case of diabetes mellitus [22]; lower the cholesterol level [23]; remove liver inflammation by toxic hepatitis [24]. Ecdysteroids contain substances, which act as vitamin D₃ having an anti-rachitic effect [25].

Extracts from *Leuzea* improve memory and memorization [26] and remove alcoholic intoxication and depression states [27]. Moreover, they hamper tumour development [28-29] and

because of their anti-inflammatory properties are more efficient than many synthetic preparations [30].

Leuzea preparations are effective by poisonings with chlororganic compounds and heavy metals. They have been proven as healing the circulatory system diseases [31], strengthening the processes of haemopoiesis, improving the coronary blood flow by means of decreased blood viscosity, and relaxed blood vessels and internal organs' nonstriated muscles; under critical state they also recover a normal pulse, are helpful by arrhythmia, ischemia heart disease, angina pectoris attacks, prevent myocardial infarction [32-33].

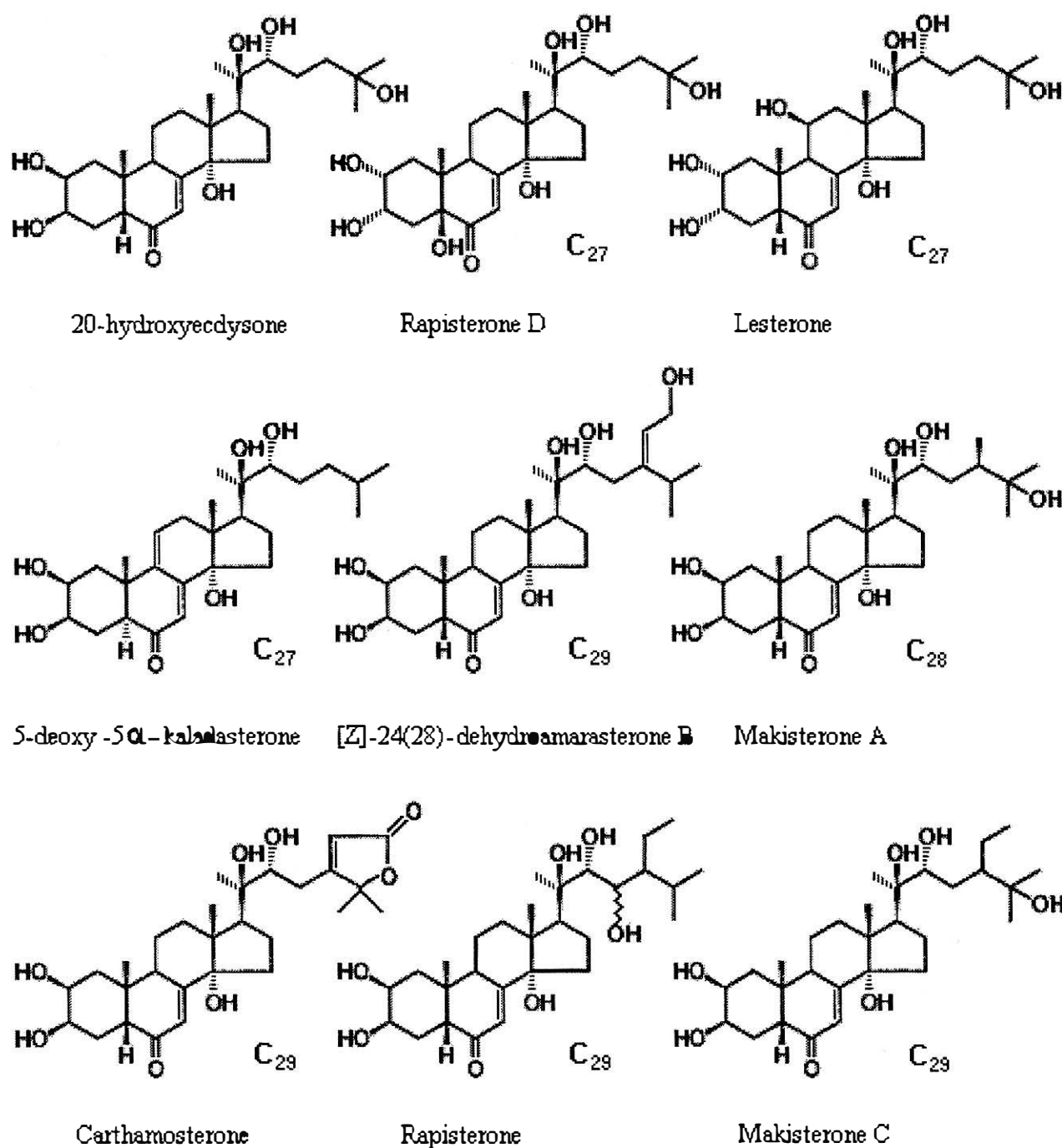


Fig. 1. Ecdysteroids of *Leuzea carthamoides*

Applied for 5-10 days, Leuzea leads to development of nonspecific organism resistance to unfavorable factors of physical, chemical and biological nature, which, in turn, is much hopeful for rehabilitation and change processes in human immune system, humoral immunity development [34]. In regard to healthy people, Leuzea preparations increase the threshold of organism defense against stress conditions, supercooling, superheating, gas pollution, extensive moisture,

atmospheric pressure changes, ionizing radiation exposure, pathogenic microflora aggression etc. The activity rate of the blood protective system elements, lymphocytes and neutrophils, rises [35]; the phagocytosis functions increase [36].

Ecdysteroids produce an anabolic effect in vertebrates stimulating the protein biosynthesis in liver, kidneys, and muscles [37]. This feature is broadly used in professional sport in order to achieve high results [38]. In contrast to synthetic steroids, ecdysteroids (e.g., 20-hydroxyecdysone) cause a high predisposition to protein synthesis in organism without producing any life-dangerous aftereffects. Therefore, they appear to be a deserved substitute for such a popular but forbidden toxic preparation as dianabol (methandrostenolone) used in speed and power sport arts [39-40].

1.3. Application of *Leuzea* preparations. People's health of today is threatened with loss of natural organism resistance to complex unfavorable and even harmful environmental factors. Immunity loss is ascribed considerably to stress situations and nerve overload in social life. Pathologic states can also appear due to extreme production technologies, high tension level of the environment, namely chemical contamination, natural insolation deficiency, abrupt photoperiodic changes, influence of the Earth's magnetic index, electromagnetic cosmic radiation.

All these factors abate the protective organism functions, result in explicit- and implicit-defined diseases, often in untimely ageing and death. Classical direct and all-strong medicaments are often helpless. Strict therapeutic measures produce other side effects and complications; they make one drug-dependent and let the pathologic process develop further in a new, even more severe form. At the same time, the unspecific resistance rate is to be successfully increased via natural immunostimulating drugs. A special position from them occupy plants producing phytoecdysteroids as secondary metabolites.

Official medicine has recognized only few preparations from *Leuzea*; all of them are made from rhizomes: the ethyl extract (70 %), tablets from fined roots only or in a mixture with microcrystalline cellulose. A chemically pure substance (20-hydroxyecdysone) isolated from the *Leuzea* rhizomes as a white creamish crystalline powder was patented under the name "ecdystene" [70].

Further it was used to produce a drug formulation and composed a wide range of biologically active additives, different by form and structure. Clinical trials in acute experiments have shown that even the largest 20-hydroxyecdysone doses do not kill the animals. The LDB50B barrier, which means first negative reactions, varies between 6 to 9 g/kg body weight [12]. The last circumstance presenting evidence for the safety of 20-hydroxyecdysone has opened new ways for its application as food additive.

Note. The consumer market of ecdysteroid-containing compounds from *Leuzea* involves the market segments concerning:

- Human health (anti-depressants, immuno- and sex-stimulants, fat burners, anti-shock, -pain and wound-healing remedies);
- *Physical training and sport (professional and amateur, body-building);*
- *Cosmetics and perfume;*
- Using ecdysteroid-containing compounds in special products (rejuvenating products, physical power and psychical energy concentrators, anti-hypnotism and -sleeping draughts);
- *High biotechnology branches (gene engineering, transplantation of organs, microbiology);*
- *Animal farming (meat and milk cattle-breeding, breeding of animals for furs, silkworm breeding), equestrian sport;*
- *Plant crop protection against insect pests (fruit gardening, forest and barn entomology);*
- *Applying as anti-parasitic (anti-heminth) products;*
- *Applying as plant growth and development regulators.*

Ecdysteroid-containing preparations can compose many clones. Extracts from other adaptogenic, vitamin-containing and aromatic plants, micro- and macroelements, chocolate, vanilla, lipids, honey, flowers pollen, neutral fillers serve as further components.

By production form, they can be tablets, capsules, liquid (in bottles) and dry phytotea, extracts, drinks, creams, balms, lotions and shampoos, alcohol-free tonics and vodka drinks. By induction form to people, they can be induced orally, intramuscularly, intravenously, as well as *via* massage, inhalation, aromalamp. As for domestic animals, they are included into mixed fodders, different healing fodder additives or used as veterinary preparations.

For most of people, the *Leuzea* preparations are necessary to support whole vitality of the organism, remove disturbances associated with metabolic imbalance and menstrual irregularities, for rehabilitation during the postoperative period, to assure recovering after a severe disease. Being introduced as food-additives, they remove irritability states, neuroses, psychastenic conditions, hyperexcitability and flaccidity, fears, consternations, and phobias. An important property is that the *Leuzea* can still pain in the organism, no matter where it is located. The *Leuzea* preparations can be efficiently used at home in case of alcoholic inebriations, food poisoning, as well as to stabilize arterial pressure and the sugar blood level, quicken the wound and fracture healing.

Brain workers who have to memorize a large body of information, concentrate attention, do everything with accuracy, overcome logic problems, need these remedies too. Introduction of the *Leuzea* provides us with an ability to foresee the course of events and events themselves, which is explainable by the intensive brain action without side irritants. The *Leuzea* is recommended for application to the emergency services when the work is to be done in tense psychoemotional surroundings with strong irritants, always time deficiency, and lack (abundance) of information.

The biologically active food additives of *Leuzea* were designed with the purposes of gaining physical power and endurance in professional sport, building up muscle fibers in body-building. Their mode of action here is connected with an active behavior of *20-hydroxyecdysone*, affecting the metabolic processes of protein synthesis and energy consumption in cells and being responsible for removing the muscular tiredness during extensive exercise [38]. These processes also cause burning up excessive fat deposits.

Along with sport medicine, adaptogens take an important part in sea, cosmic, and military medicine as helping healthy people to overcome physical and mental overstrain [41]. Since allowing for repeated concentration of psychical energy *via* refining the organs of sense, and making one sleep-resistant, the preparations-of *Leuzea* can serve as a base component in the "elixir of fearlessness". The *Leuzea* presents an irreplaceable remedy for tourists et al.

Its positive effects on the psychoemotional state, cardiovascular system, and dynamic working capacity of organism make the preparations improving the sexual function and increasing libido. The *Leuzea* is one of best preparations to recover and sustain the sexual activity, to get ride of frigidity and potency disorder. By women, improvement of reproduction functions (capacity to conceive and give birth to new generations) is observed.

Based on the properties of ecdysteroids to strengthen the blood circulation in capillaries, improve its physical and chemical composition, speed up cell regeneration in epidermis and cornea, the *Leuzea* can be used in cosmetic production, namely compose preparations for hair growth (recovery), products curing wounds, sores, and burns, removing wrinkles, rejuvenating and protecting the skin from ultraviolet sun radiation [42].

The *Leuzea* is an ideal remedy for animal farming intensification that has been tested in practice [4, 43-44]. It is used in breeding of animals for furs, cattle and small cattle breeding,

poultry farming, equestrian sport. Also, the preparation forms part of food additives as a bio-stimulant increasing milk yields and average daily weight increments (by 35-40 %), eliminating mortality of newborn animals or birds (by 2.1 times). Induction of the *Leuzea* removes listlessness and reduces the service-period of cattle [45], increases the strength of bee family [46].

Furthermore, the formulations of *Leuzea* can be used as plant growth and development regulators. Judging from their chemical structure, ecdysteroids are the closest analogues of brassinosteroids, a new class of phytohormones, also can have stimulating effect on growth and development of plants [47-48]. The nonpurified extracts containing modified ecdysteroid forms are essentially more active than the chemically pure 20-hydroxyecdysone [49]. In fact, they combine positive features of several classes of phytohormones: increase plant-germinating power, contribute to development of strong photosynthetic apparatus, and make plants resistant to frost and pathogens. The *Leuzea* biopreparations increase the plant productivity rate per unit area and commodity output.

2. PROBLEMS AND THEIR SOLUTION POSSIBILITIES

2.1. Sources of raw materials for ecdysteroid-containing preparations. The commercial preparations based on the chemically pure 20-hydroxyecdysone (*Ecdysten* etc.) are very easy-to-use compared to the rhizomes though extremely expensive and inaccessible to the broad masses. The minimum daily dose costs \$1.2-1.5 and the maximum dose is even more expensive.

The recent deficiency in the crude drug of *Leuzea* contributed to 20-hydroxyecdysone isolated from other ecdysteroid-containing plants. Used are such species as *Achyranthes bidentata*, *Cyanotis arachnoidea*, *Pfaffia paniculata*, *Polypodium vulgare*, *Polypodium decumanum*, *Serratula coronata*; representatives of the genera *Silene*, *Lychnis*, *Ajuga*, *Paris*, *Helleborus* etc. are tested for as well.

In most cases they are low-height grasses growing in scattered groups in shadow taiga forests and hollows, along shadow Russian peat-bogs or in swamps of the Amazon jungle. The dug out rhizomes or overground parts of them are used as crude drug. Some grasses are quite poisonous, others are not recommended for use as drug plants.

By the productivity value, cultivation and processing technological effectiveness, ecdysteroid content in mass organs, these plants cannot compete with *Leuzea*. That what is extremely important for science to discover the biosynthesis pathways of ecdysteroids, in the nearest future has poorly prospects for the industrial production of pharmpreparations. Even if some culture is recommended for cultivation, there are no reasons to consider the preparations from the substitute plants having the same biological activity power as those prepared from *Leuzea* [17].

As it was mentioned above, the physiological effect of crude drug is a combination of thousands of other modified components, in addition to the chemically pure 20-hydroxyecdysone. Complaints of the unstable biological activity of ecdysteroid-containing plants on the Internet-pages may be associated with the alternative sources. Therefore, based upon a wide range of practically valuable reasons, *Leuzea* is commonly considered to take a central position among ecdysteroid-containing plants with no substitutes able to substitute it fully [50-51, 71]. Today's great demand for *Leuzea* at the world market has arisen a question of the cultured source of raw materials for pharmacological industry.

2.2. Overground phytomass instead of rhizomes. When tracing the history of *Leuzea*, it is worth mentioning that it has been researched by scientific organizations already since a year of 1929 as a source of unique pharmpreparations [10]. Its high potential was recognized, but,

unfortunately, it was not put into production. The reasons are as follows:

1. Sub alpine high meadows do not allow for collection the overground plant biomass. For that reason, the enterprises producing the *Leuzea* preparations used only the underground organs as raw, which contributed to a dramatic decrease in area with *Leuzea* [4, 52].
2. The rhizomes are not a technologically reasonable source concerning industrial production. Moreover, the effective doses of *20-hydroxyecdysone* (10-20 mg/kg body weight) in respect of mass production require many thousand area hectares to be destroyed [11].
3. Growing the ecdysteroid-containing plants *in vitro* is attached to many of difficulties [53]; common techniques are not applicable here, while first possibility for crude drug collection appears no earlier than 3-4 years after the agropopulation is placed [54-55]. There are big problems concerning the surviving ability of plants and quality of seeds, which do not allow for placing large industrial plantations [56-58]. The life duration index of plant decreases in *in vitro* conditions by 10-15 times compared to nature [59].
4. Collection, drying and storage of raw materials are accompanied by considerable losses of active substances [60]. Being processed, the species loses in activity.

From the short problem analysis above, it is possible to conclude that new pharmpreparations from *Leuzea* need to be developed in order to solve the existing problems, reasoning from the following approach:

- All technology should be based on the yearly renewable sources of raw materials that could be overground parts of the plants;
- The terms for crude drug collection should be settled taking into consideration both the maximum productivity level and high ecdysteroid concentration in phytomass;
- The raw material collection procedure, conditions when drying and storage are to assure safety of the target substances, especially mobile highly-active fractions;
- Application of crude drug has to be optimized by decreasing the doses.

Thus, it has been revealed as having no prospects to use the rhizomes in mass production of plant crude drug. Scientific research should aim at working out new classes of pharmacological drugs from the overground phytomass, optimization the doses applied by now, and lowering the end price.

2.3. Technological problems of crude drug production. Though they are no less biologically active than the rhizomes, there are no officially recognized pharmpreparations from the overground parts of *Leuzea* except of the green tea preparation "*Maralan*" (*Herba leuzea*) being produced in Czechia [61]. Influence of overground phytomass of *Leuzea* on animals has been already surveyed in the former USSR and abroad. They were experimentally proven as non-toxic if introduced in the doses up to 0.3-0.5 kg dry substance per 1 kg body weight [62-63]. The rats can live on the ration, 50 % of which consists of *Leuzea* grassy flour. In long-term experiments, when cut small green pieces of plants were added to the rations, there were no negative reproduction effects observed.

Ecdysteroids compose all organs of *Leuzea*, and their concentrations can serve as one of most important quality characteristics of crude drug. Ecdysteroid accumulation in different phytomass elements depends on combination of many factors, quite often human-independent. The absolute concentrations of *20-hydroxyecdysone* in crude drug are spread in values from 0.022 to 0.87 % [64].

Quite often it contains only the less active ecdysteroid fraction firmly bound to cell molecules, and no highly active mobile part. Reasoning from concentrations of active substances, the empirical doses are, then, comparable with the classical dose of “firm” *20-hydroxyecdysone* (5-20 mg/kg) and, consequently, if rhizomes, are not applicable to large-scaled production.

The crude drug producer has to: a) form those conditions in cenosis favoring the natural biosynthesis and accumulation of physiologically active ecdysteroid fractions in the particular plant organs; b) retain the initial content of target substances in crude drug during all processes of its collection and conservation; c) provide the end production with technological longevity, i.e. minimize reacting substances' losses during conservation [65]

Under optimal cultivation conditions, the ecdysteroid concentrations reach their stable level beginning with the fourth-fifth living years. Content of ecdysteroids is influenced by weather and climatic conditions: air temperature, spectral composition of light, atmospheric and soil moisture, stress factors [66]. The biosynthesis is followed by ecdysteroid redistribution within vegetative and generative organs, and transition to the roots with escape into the soil afterwards. Agricultural engineering methods (terms, repetition factor and norms of biomass collection, kinds of fertilizers, inter-row treatment) considerably influence concentration and the distribution gradient of ecdysteroids to different spheres.

The ecdysteroid-containing crude drug reveals a strong trophic dependence of retained effective substances on plant age, climatic conditions of cultivation, way of collection, elementary composition of crude drug. The commonly accepted methods of processing do not assure the reacting substances of safety. The kinetics of drying the plant material being of high water-holding ability is in direct proportion to its physical structure, whereas the latter has a negative correlation to ecdysteroid retaining [64].

In general, the drug-processing technology, equipment and modes applied cause multiple variations in ecdysteroid content. The production shelf life depends, in addition to growing conditions, processing and mode of conservation, on the packing, gaseous mixture composition, its physical structure (*20-hydroxyecdysone* can vary within the limits of 0.004 to 0.460 %).

3. NEW PHARMPREPARATIONS FROM LEAVES PART *LEUZEA*

In the past years the scientific bases for agropopulations of *Leuzea* as an industrially cultured drug plant have been developed. Estimated are its life cycle peculiarities, resistance factors in cenosis, biomass structure and ecdysteroid accumulation dynamics in single organs and in ontogenesis; optimal terms and methods of collection, modes of plant material processing, economic factors in production are determined [4, 15, 66-68]. All these moments offer rich possibilities for new and cheap pharmacological preparations with high anabolic and immunostimulating activity, isolated from overground *Leuzea* biomass (Fig. 2; Table 1-4). For example, first two preparations of new generation are already developed – “*Bioinfusin*” and “*BCL-PHYTO*”.

Advanced and ready to application it is thin the crushed powder from leaves parts *Leuzea carthamoides* contains a complex of biologically active substances:

- **Phytoecdysteroids.** It is identified 52 individual ecdysteroids, average concentration makes 0.25-0.30 %. In separate fractions of medicinal raw material concentration can be finished to 0.7-1.2 %.
- **Protein and amino acids.** Contents of protein – 27-31 %. In structure of amino acids contains up to 157 g/kg irreplaceable (lysine – 16.5; threonine – 10.8; leucine – 19.3; isoleucine – 9.5;

phenylalanine – 11.5; histidine – 4.5; tyrosine – 12.5; valine – 13.9; arginine – 11.0). In structure of replaceable amino acids the increased contents proline – 29.2 g/kg is observed; asparaginic – 34.6 g/kg and glutaminic acids – 25.5 g/kg.

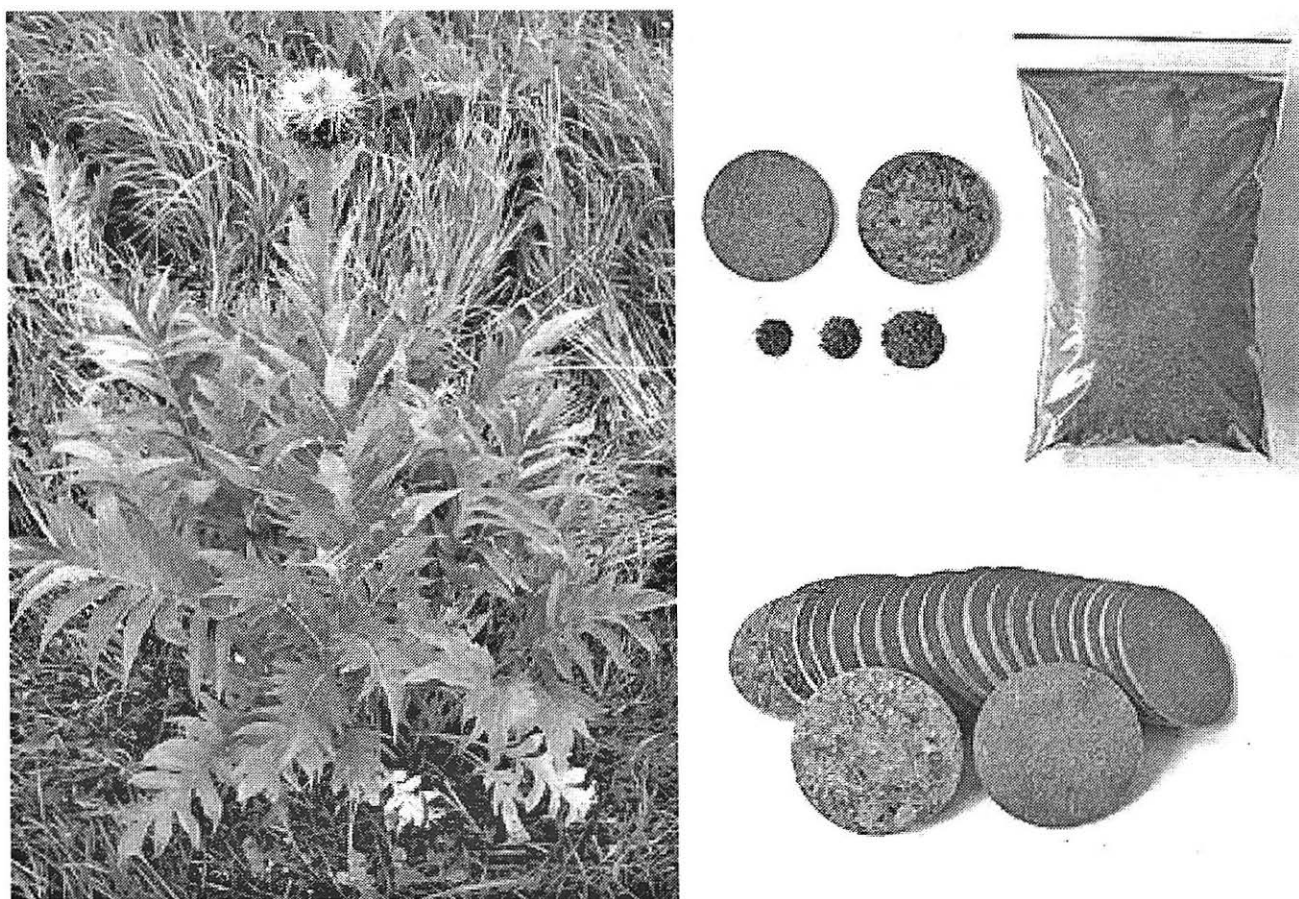


Fig. 2. *Leuzea carthamoides*:
Powdered and tableted drug material from leaves parts

- **Vitamins.** 18 vitamins and vitamin-like substances are identified, including: carotenoids (vitamin A) – 310-650 mg/kg; an ascorbic acid (vitamin C) – 415-620 mg/kg; a chlorophyll – 860 mg/kg; flavonoids (vitamin P) – 4000 mg/kg; a folic acid (vitamin B₉) – 340 mg/kg; riboflavin (vitamin B₂) – 4.6 mg/kg; tocopherol (vitamin E) – 36-62 mg/kg; phyloquinone (vitamin K₁) – 3.2-26.6 mg/kg; thiamine (vitamin B₁) – 8.8 mg/kg; biotine (vitamin H) – 0.06 mg/kg; inositol – 1453 mg/kg; pantothenic acid (vitamin B₃) – 5.6 mg/kg; niacin (vitamin PP) – 115.2 mg/kg; pyridoxine (vitamin B₆) – 2.8 mg/kg, etc.
- **Macronutrient elements.** It is characterized by the increased contents of water-soluble ions kalium, nitrogen, sodium, and phosphorus. The contents of elements: K – 3.1-4.7 %; N – 2.8-3.8 %; P – 0.3-0.5 %; Mg – 0.15-0.39 %; Ca – 1.5-2.9 %; S – 0.11-0.15 %; Si – 0.10-0.14 %; Cl – 0.18-0.60 %; Na – 0.07-0.12 %; Fe – 0.03-0.05 %; Al – 0.003-0.004 %.
- **Microelements.** Except for the basic structural macroelements (Ca, P, Si, K, Na, Cl, S), it is revealed presence of 47 microelements, including 15 vital (I, Cu, Zn, Fe, Co, Cr, Mo, Ni, V, Se, Mn, As, F, Si, Li) and 4 is conditional essentially (Rb, Cd, Pb, Sn). Distinctive feature - presence stimulating and survival rate of the man elements (Li, Ti, Ga, Ge, Rb, Zr, As, Ba, Au, Hg) or elements which deficiency conducts to diseases (Fe, Cu, Zn, Mn, Cr, Se, Mo, I, Co, F, Si).
- **Toxic substances.** Does not contain alkaloids, triterpenoid saponins, narcotic or poisonous substances. The contents of heavy metals (Hg, Cd, As, Ni, Pb, Cu, Zn) do not exceed a

background level. Chlor- and phosphororganic connections are absent. The contents radionuclides ^{90}Sr and ^{137}Cs below a normative level in 1.5 and 100 times. A level of nitrates and nitrites within the limits of norm [72].

Table 1. Direct immunoresistant action of *Leuzea carthamoides* on chickens (murrain level in farm rooms)

Indices	Unit	Female	Male	Infection bird
Control	%	3.25	3.73	13.42
<i>Leuzea</i>	%	2.08	2.5	5.84

Table 2. Immunostimulating aftereffect in production conditions (death rate of young pigs, %)

Indices	nit	Season					
		March	April	May	June	July	August
Control	%	26.2	23.1	27.6	26.2	33.3	24.1
<i>Leuzea</i>	%	22.6	12.5	12.1	13.1	8.1	8.7

Table 3. Anabolic effect of *Leuzea carthamoides* in production conditions (1635 pigs)

Index	Unit	Feeding duration					
		30 days		60 days		90 days	
		control	trial	control	trial	control	trial
Total increase in	on	.8	3.9	1.2	5.2	0.8	5.3

Table 4. Anabolic effect in industrial poultry farming (rooms with 45-61 thousand chickens)

Index	nit	Living mass of chickens by age, days							
		01	10	20	30	40	50	60	70
Female: control	g	36	73	137	206	314	434	568	744
<i>Leuzea</i>	g	36	73	166	280	430	590	720	850
Male: control	g	36	81	153	240	350	540	710	900
<i>Leuzea</i>	g	36	95	200	325	490	650	820	1040

Preparation "Bioinfusin" – reg. No 001047-OP; the liquid form on the basis of *Leuzea carthamoides*. It is meant for intramuscular and intravenous introduction. It is used to increase the

whole organism resistibility during pathologic states of different etiology, strengthen the sexual potency, cure respiratory diseases (table 5). The action mechanism specificity of new preparation lies in a stimulating activity of small doses and inhibiting effects on proliferative organism processes in large doses. The preparation causes a strong biostimulating effect on the organism [69]. This is accounted for by such blood serum indices responsible for natural resistance of organism as whole protein and its lysozymic, bactericidal, neurophyll and antibody-forming fractions, phagocytic cell activity.

On the seventh day of treatment all indices go up by about 15-30 % and more, compared to the control group. The biological activity rate detectable with values for antibody-forming spleen cells and gamma globulins in blood serum exceeds the control figures by 1.5-2 times. One-time introduction has anabolic effect of 10-12 % (table 6).

Intravenous introduction has once a day repetition factor; the course duration includes 5-7 days. The doses comprise 0.02-0.05 ml/kg. Intramuscular introduction needs 2 times higher daily doses. The daily doses for *20-hydroxyecdysone* account for 0.1-0.5 µg/kg (10^{-12} ... $2 \cdot 10^{-13}$ M). Testing the preparation for acute toxicity rate, the LD₅₀ (lethal dose quantity) was equal to 9.5 g/kg proving its absolute safety. The “Bioinfusin” is produced in the hermetically capped glass bottles for 10, 20, 50, 100 and 200 ml.

Table 5. Biochemical blood indices by introduction of the pharmpreparation “Bioinfusin” for respiratory diseases, % (course – 5 days, autumn)

Indices	Control			“Bioinfusin”		
	0 days	12 days	19 days	0 days	12 days	19 days
Erythrocytes, million/µl	100	89.1	78.2	100	117.0	119.2
Hemoglobin, g/%	100	96.1	95.1	100	104.7	103.8
Phagocytic activity, %	100	95.3	90.6	100	112.6	119.7

Table 6. Anabolic activity rate of the preparation “Bioinfusin” by one-time intramuscular introduction, % (trials on white mice)

Dose of <i>Leuzea</i> if 20E, µg/kg	Time of aftereffect, days				Conventional daily dose
	0	10	20	30	
control	100.0	100.4	100.4	103.4	–
387	100.0	89.6	92.2	110.0	$2.7 \cdot 10^{-11}$ M
35	100.0	98.7	104.3	112.0	$2.4 \cdot 10^{-12}$ M

Preparation “BCL-PHYTO” – the powdered form on the basis of preparation *BCL* (*BactoCelloLactin*; reg. No 000313-OP) and high-quality elements leaves parts *Leuzea carthamoides*. It is meant for therapeutic and preventive treatment in veterinary medicine, it is used for gastrointestinal tract diseases of calves, pigs, and birds. Providing additional clinical trials, it can be applied in respect to man. The preparation presents a mixture of strong probiotic preparation *BCL* (three different synergist microorganisms) with *Rhaponticum carthamoides*. It is packed into glass bottles or cellophane packages for 50 to 500 ml. The “*BCL-PHYTO*” has a high antagonistic activity rate against colon bacilli, streptococci, proteus, staphylococci, and dysentery causative agents.

It possesses a high cellulolytic activity rate, which makes impossible the pathogenic and conditional pathogenic microflora development. In addition to antibacterial properties, the preparation produces anabolic and immunostimulating effects, as well. The “*BCL-PHYTO*” does not have a negative influence on the end production quality or cause complications by animals. It serves as a powerful substitute of many antimicrobial drugs: antibiotics, sulfanilamides, nitrofurans, and represents an ecologically safe product. There are no contraindications established by now.

For prevention the preparation is induced 1-2 times a day (added to fodder or drink) on the basis of 0.1 g/kg biomass, age-invariably. The daily dose, if *20-hydroxyecdysone*, is equal to 5-10 µg/kg ($1...2 \times 10^{-11}$ M). The course duration comprises from 3-5 to 30 days. After a long-term introduction period a pause in a month is required. If diarrhea, the effective doses are increased to 1 g/kg and used on dissolution in hot water once a day for 3-5 days.

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