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Siberian Plants and Natural Mineral Salts for Dietary Supplements

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ABSTRACT

With the increasing consumption of dietary supplements, Russian producers looked for ways to utilise Siberian plants and minerals, which have been traditionally employed by the local population to increase energy and vitality. The new dietary supplement made with such valuable active ingredients as Siberian cranberry, burdock root, marsh cinquefoi and natural mineral salts found in Siberian lakes possesses antioxidant and anti-inflammatory properties. The ingredients, formula and the production process of the dietary supplement were tested in Biolit Research and Production Company (Tomsk city). To assess the effectiveness of the dietary supplement, 75 patients were prescribed daily amplipulse therapy with electrode pads soaked in 2% solution made from the dietary supplement. Clinical evidence was evaluated and confirmed the positive trends in gastric motor activity, gastric juice acidity and the overall healing process. The encapsulated powder form of the dietary supplement proved to be easy to use and can be recommended for both healthcare facilities and home treatment.

Key words: *Dietary supplement, Siberian plants, Peptic ulcer disease, Amplipulse therapy*

INTRODUCTION

In recent years the consumption of dietary supplements has experienced an increased growth across the globe. As more people are willing to invest in their health and general well-being, nutritional consultants recommend various dietary supplements to help boost metabolism and improve overall health [1-10]. At the same time, Russian producers of dietary supplements are particularly interested in using local ingredients as such ingredients are readily available and well-adapted to the local environment [11, 12].

MATERIALS AND METHODS

To respond to the growing demand, a new plant-based dietary supplement has been developed. The active ingredients of the supplement include:

1. *Cranberry (Vaccinium oxycoccus).* The bioactive compounds profile of Siberian cranberry is very appealing. The berries contain organic acids, for example, malic, citric, quinic, and benzoic acids are in the range of 2-5%. Benzoic acid derivatives are commonly used for their antibacterial activity. Glucose, fructose, and sucrose represent the sugar content. The fruits contain ascorbic acid and carotenoids (12-20 mg/100g), B vitamins, salts of iron, potassium, manganese, calcium, phosphorus and other mineral micro-and macroelements, triterpene compounds, namely, oleanolic and ursolic acids, tannins, flavonoids, rutin, quercetin, catechin, and hesperidin.

The amount of oil in the seeds reaches 16-28%. Siberian cranberry is successfully used as an anti-inflammatory and multivitamin agent.

2. *Burdock root (Arctium lappa).* The main biologically active constituents of the Burdock root include arctigenin and arctiin (the glycoside of arctigenin), which are phenylpropanoids, and inulin (up to 45%), which is a polysaccharide. The other constituents include salts of magnesium, potassium, calcium, essential oil, and fatty acids (up to 0.18%), stigmasterol and β-sitosterol, proteins (approx. 12%). The Burdock root is used as a choleretic and diuretic agent. Inulin can activate accumulation of glycogen in the liver. Inulin belongs to the fructan group and is broken down to fructose in the gastrointestinal tract. In addition, inulin acts as an enterosorbent and helps remove various toxins and metabolic wastes.

Moreover, inulin possesses other useful properties:

a) Inulin is prebiotic which enhances growth of Bifidobacteria and helps maintain the normal functioning of the gastrointestinal tract;
b) Inulin improves peristalsis, as it helps to stimulate muscle contractions that move food through the digestive tract;
c) Inulin increases magnesium and calcium absorption and retention, contributing to improved bone density;
d) Inulin lowers blood sugar levels, influences the metabolism of lipids, helps reduce risk factors of cardiovascular lesions;
e) Inulin demonstrates the anticancer, immunomodulatory, and hepatoprotective effects.

Inulin and other polysaccharides found in burdock roots lessen the irritation of the gastrointestinal mucosa, exert anti-inflammatory properties, and reduce the absorption of lithogenic substances (oxalates) in the intestine, lowering the chances of oxalate stones formation.

Burdock roots contain arctiin, a lignan glycoside $C_{27}H_{34}O_{11}$, which is hydrolysed by the intestinal microflora to the aglycone arctigenin and glucose. There is good evidence that arctiin and arctigenin possess the antiviral effect and increase the immune response to some influenza viruses [13, 14]. Arctigenin protects nerve cells from damage induced by ethyl alcohol and amyloid, inhibits the synthesis of β-amyloid, reducing its damage during ischemia [15-17]. Additionally, arctigenin is known to possess radioprotective, diuretic, and anti-inflammatory effects [18-24]. Moreover, arctigenin demonstrates antitumor activity. Herbal remedies with burdock roots improve mineral metabolism and stimulate the production of proteases in the pancreas.

Arctiin inhibits the pro-inflammatory mediators - interleukin 1-beta and interleukin 6, nitric oxide, cyclooxygenase - α, by inactivating the nuclear transcription factor, NF-Kb [25]. Previous studies confirm the cytostatic, antiproliferative, and antitumor effects of arctiin [26].

The effect of lignan glycoside in treating streptozotocin-induced diabetes mellitus is recognized; it weakens the intensity of diabetic complications, inhibits diabetic retinopathy. The effectiveness of the treatment of diabetes and its complications is explained by the significant inhibitory potential of lignan glycoside against the activity of aldose reductase. The hypotensive effect of arctigenin is associated with the modulation of nitric oxide synthesis, which underlies the prevention of the development of cerebral artery vasospasm after a subarachnoid haemorrhage [6].

Burdock roots are a source of 20 free amino acids, with asparagine among them. β-asparagine has the antitumor activity which is explained by its cytostatic (the inhibition of cell growth and multiplication) and apoptosis-inducing activity (the induction of cell death).

The essential oil extracted from burdock root is represented by palmitic acid (0.065 - 0.17%), linolenic, lauric, myristic, oleic, stearic, and palmitic fatty acids (0.4 - 0.8%).

Phenolic compounds of burdock root include tannins (4.1 - 7.3%) and flavonoids (1.3 - 2.3%). Moreover, burdock roots contain phenolcarboxylic acids like chlorogenic, isochlorogenic, caffeic, as well as resin, mucilage, saponins, alkaloids, mineral salts, and ascorbic acid.

Burdock roots are rich in acetylenes and polyacetylenes. The chemical composition and functional properties of burdock are still not completely researched and further study is required.

3. *Underground and above-ground parts of marsh cinquefoil (Comarum palustre).* Although all parts of the plant are used for medicinal purposes, the underground parts are the most commonly exploited. The rhizomes of the plant are included in the State Register of Medicines of the Russian Federation (2008). The above-ground part of the plant contains a comaruman (pectin) and monoterpenoids: pinene, terpineol, and citronellal.

All parts of the plant are rich in phenolic compounds: flavonoids (gossypetin, luteolin, kaempferol, quercetin, apigenin, and their glycosides), catechins (epigallocatechin, gallocatechin), and tannins, phenylpropanoids, and phenolic acids (chlorogenic, cinnamic, caffeic, p-coumaric, salicylic, ferulic). The plant also contains coumarins (umbelliferone), triterpene saponins, and sterols.

Water and hydroalcoholic extracts made from above-ground parts of the plant (flowers, leaves) and underground parts (rhizomes) show hypotensive, stress-protective, and antitumor activity. The anti-inflammatory effect is explained by the presence of comaruman, which inhibits neutrophil adhesion to fibronectin. The wound-healing effect should also be noted. Infused water prepared with the leaves of the plant is a good alternative to tea. Extracts made from leaves and underground parts are now commonly used in the cosmetology industry and as active ingredients of dietary supplements. Water extracts of the above-ground parts of the plant show the anticoagulant effect, while hydroalcoholic extracts have the coagulant effect.

To be used in dietary supplement products, the raw materials (leaves) have to meet certain requirements. They should contain at least 1.0% of polyphenolic compounds, 3.0% of tannin, 0.1% of catechins, 15.0% of extractive substances (not less than 8.5% of quercetin, and 6.1% of kaempferol).

4. *Esobel (natural mineral salt found in Siberian lakes).* The extract is made from healing mud found in Siberian mineral-rich lakes and contains a complex of mineral salts: cations (Na +, Ca2 +, Mg2 +, K +), anions (Cl-, SO42, CO32-, HCO3-), and compounds (prostaglandins, fulvic and humic acids, amino acids).

Esobel shows the anti-inflammatory effect (reduces pain and hyperemia), prevents new adhesions, and helps reduce the existing ones. Moreover, Esobel enhances regeneration, influences and restores joint mobility.

For the dietary supplement production, the following quality criteria are to be met. The minimum amount of calcium should be not less than 0.6%; carbonates - 0.55%; magnesium - 4.5%; sulfates - 6.7%; chlorides - 56.0%. Mass fraction of crude fat is 0.8%.

5. *Sorbitol.* Sorbitol is a registered food additive (E420), which is commonly used to substitute sugar in many low-calorie drinks and foods. The substance has become a popular artificial sweetener as it only has 2.6 kilocalories (11 kJ) per 1 gram compared to 4 kilocalories (17 kJ) per 1 gram of usual sugar (64% of the calorie content of sucrose). Sorbitol also has the choleretic effect.

Esobel dietary supplement ingredients include cranberry extract - 5%, burdock root - 1%, underground and above-ground parts of Comarum palustre - 2%; Esobel - 5%; and sorbitol - 87%. The product is marketed in a granular form, with granule sizes ranging from 1 to 4 mm in diameter. The color of the granules varies brownish-grey with dark inclusions with a sweet and salty taste and a distinctive smell.

The physical and chemical properties of the dietary supplement are shown in **Table 1**.

Table 1. The Physical and Chemical Properties of the Dietary Supplement

Indicators	Amount
Water solubility, min, not longer than	10.0
The moisture content of granules (mass fraction), %, not more than	1.0
Lipid content, %, not less than	0.05
Polyphenolic compounds content (calculated as tannin), %, not less than	0.7
Organic acids content (calculated as malic acid), %, not less than	1.5
Magnesium content, %	0.3

The production process consists of the stages shown in **Figure 1**.

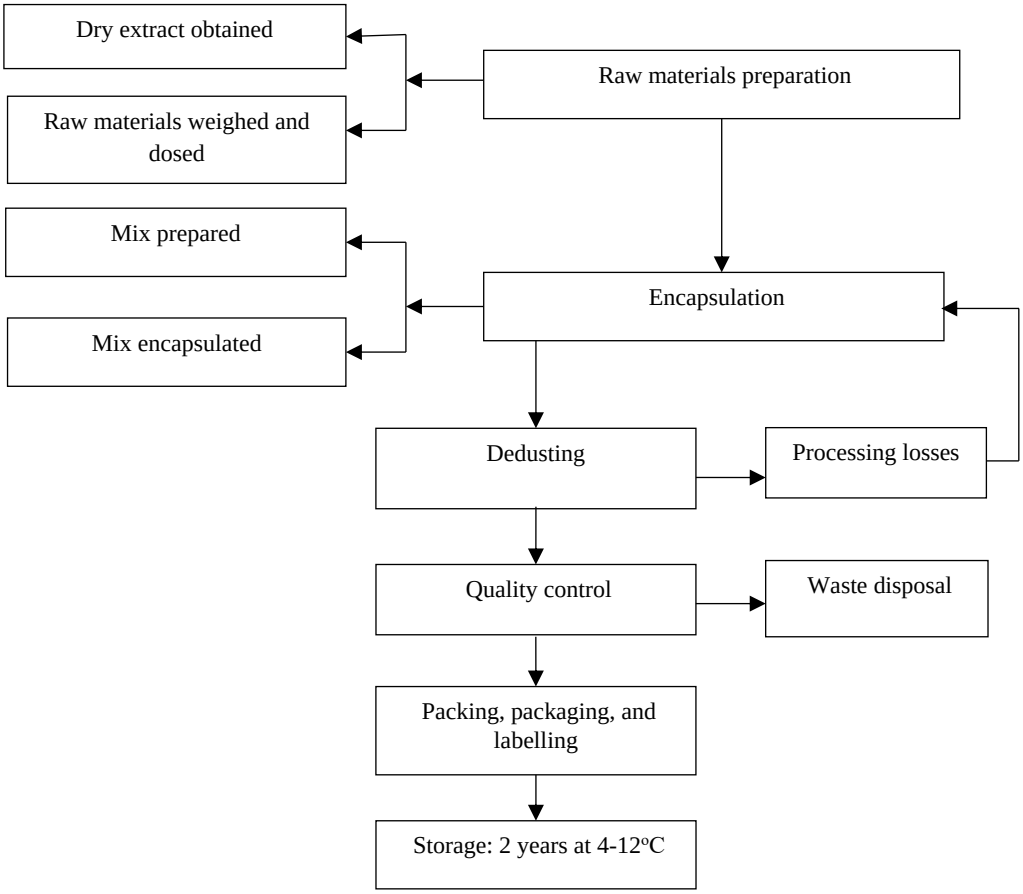

Figure 1. The Dietary Supplement Production Process

Raw materials preparation

Before acceptance, all raw materials are subject to the following quality assurance checks:

- The marking on the packaging (bags, flasks, etc.) indicating the date of manufacture, the name of the raw material, and the manufacturer should be correct and complete;
- The incoming quality and safety control should comply with the specifications (certificates issued by an accredited laboratory);
- The accompanying documents should be marked with a green strip on the label (the statement of production admission).

Preparation of the dry extracts of burdock roots and leaves of comarum palustre

First, burdock roots are ground and sieved to obtain particles of 2.0-3.0 mm. Second, they are put into a food boiler with hot water (60°C) and left to infuse for 2 hours at a steam generator temperature of 80°C with the anchor mixers turned on. The extraction process is then repeated three times at two-hour intervals. The raw materials necessary for the dry extract production are shown in **Table 2**.

Table 2. The Raw Materials for the Dry Extract of Burdock Root

No	Raw material	Amount in kilogrammes
1	Ground burdock roots	58.0
2	Purified water	290.0
	Fluid extract	*180.0*
	Soft extract	*90.0*
	Dry extract	*20.0*

The procedure for the preparation of the dry extract from leaves of Comarum palustre is similar to the preparation of the dry extract from burdock roots, only the size of the particles obtained varies from 1 to 2 mm. The raw materials necessary for the dry extract of Comarum palustre are shown in **Table 3**.

Table 3. The Raw Materials for the Dry Extract of Comarum Palustre

No	Raw material	Amount in kilograms
1	Ground Comarum palustre leaves	133.0
2	Purified water	665.0
	Fluid extract	*430.0*
	Soft extract	*210.0*
	Dry extract	*20.0*

To ensure the quality of the finished product, it is essential to monitor the extraction process length and temperature.

When prepared, the fluid extract is then filtered using a filter unit which consists of a milk filter and a nonwoven filter made of polyester (60%) and polypropylene (40%) for particles smaller than 60 microns. The extract is opalescent, of brown color with a mass fraction of dry substances of 7-10%.

To obtain the soft extract, the fluid extract is boiled at 70-80°C for five hours and then sieved. As it is very important to get a viable dry extract, a freeze-drying technique is used.

When the dry extracts are ready, all the ingredients are checked and dosed in strict accordance with the formula. Then, all the ingredients are loaded into a mixer, where they are mixed for one hour at a speed of 800 rpm.

At the next stage, the finished product is encapsulated, with hard gelatine employed as a shell material. Each capsule is filled with 0.51-0.61g of the product. Following the encapsulation, the capsules are dedusted over a screen to dispose of any residual powder.

For quality assurance, one hundred grams of samples are then taken to the laboratory for assessment. The samples are to comply with the following quality and safety requirements: organoleptic, physicochemical, microbiological, and toxicological. The results of the quality and safety assessment are presented in **Tables 4 and 5** below.

Table 4. Organoleptic Quality Indicators

Indicator	Description
Appearance	Powder in hard gelatine capsules
Colour	Brownish-grey with dark inclusions
Taste	Salty
Smell	The distinctive smell of seafood

Table 5. Dietary Supplement: Physicochemical Quality Indicators

Indicator	Reference value
Polyphenolic compounds content (calculated as tannin), mg/capsule, not less than	15.0
Glucosamine content, mg/capsule, not less than	8.5
Chondroitin sulfate content, mg/capsule, not less than	12.5
Disintegration time, min, not longer than	15.0
Moisture content (mass fraction), %, not more than	5.0

The results of microbiological and toxicological examinations are presented in **Table 6**.

Table 6. Dietary Supplement: Sanitary Safety

Indicator	Reference value	Actual content
Toxic elements, mg / kg, not more:		
Lead	10.0	0.10
Arsenic	12.0	2.9
Cadmium	0.2	0.021

Mercury	0.5	0.001
Pesticides, mg / kg, not more:		
Hexachlorocyclohexane (α, β, γ-isomers)	0.2	Less than 0.005
DDT and metabolites	2.0	Less than 0.005
Heptachlor	not allowed	not found
Aldrin	not allowed	not found
Microbiological		
CFU / g, not more:		
Mesophilic aerobic and facultative anaerobic microorganisms quantity	$1•10^4$	Less than 10
Product weight (grams)		
Coliform bacteria	0.1	not found
Pathogenic, salmonella included	10	not found
E. coli	1.0	not found
Staphylococcus aureus	1.0	not found
CFU / g, not more:		
Yeast and mould	200	Less than 10

The shelf life of the dietary supplement is 2 years when kept at 4-12°C in a dark place.

Nowadays, there is an increasing demand for new approaches to treating Peptic Ulcer Disease (PUD), for this reason, to assess the effectiveness of the supplement in improving trophism and microcirculation in tissues, the gastric motor activity, and the anti-inflammatory and analgesic effects, a clinical trial was performed.

RESULTS AND DISCUSSION

The total number of participants of the clinical trial included 75 patients (49 males and 26 females) aged from 21 to 62 diagnosed with peptic ulcer disease. Fifty-three participants experienced burning pain and thirty-six participants complained about belching. Exacerbation was noted as seasonal in 92% of cases.

Monitoring of the treatment included studying the subjective complaints made by the patients and the assessment of the objective data obtained from the gastroduodenoscopy examinations. The clinical trial was carried out in Medical and Sanitary Unit No 2 located in Tomsk city and the clinical procedures were supervised by A.I. Kareva, Medical and Health Care Department Head, and R.R. Enikeeva, the Department of Endoscopy Head.

The medical treatment chosen for the trial included electrotherapy. Electrotherapy is a popular medical treatment in Russia, with amplipulse and diadynamic therapy being the most popular. Amplipulse therapy (SMT-therapy) is a method of local exposure to an alternating electric current through electrodes and wet hydrophilic pads, which are applied on chosen areas. The participants were prescribed amplipulse therapy to be administered daily. For every session electrode pads were soaked in 10 ml of 2% solution made from the dietary supplement.

A noticeable positive trend was recorded during treatment. The participants stated the reduction of epigastric pain. No pain was recorded when the pyloroduodental zone was palpated. The Student's test was employed to study the data received during the trial.

The epithelialisation process and the complete healing (according to EGD data) were registered in 87% of cases, and the examinations of 4 participants demonstrated the ulcer size reduction. Thus, the positive dynamics were recorded.

When studying the effectiveness of using the dietary supplement in electrotherapy to reduce the gastric juice acidity, we noted that the pH of the gastric acid of 26 participants changed from 1.8 to 3.3, while the secretion of pepsin remained unchanged. No side effects of the treatment during the clinical trial were recorded.

CONCLUSION

The findings of the clinical trial allow us to conclude that amplipulse therapy applied with the dietary supplement is an effective way of improving gastric motor activity, altering gastric juice acidity, and stimulating the healing process.

The encapsulated powder form of the dietary supplement is a convenient and reliable way of using and storing, and eases the dosing process; therefore, it can be successfully employed in different healthcare facilities and health resorts as well as for at-home treatment.

The ingredients, formula, and the production process of the dietary supplement were tested following ISO 9001, 22000, GMP to guarantee the product quality and competitiveness. The assessment was carried out in Biolit Research and Production Company located in Tomsk city.

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ETHICS STATEMENT : Participation in this research was entirely voluntary.

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