ABSTRACT:
Nutriceuticals Based on Siberian Herbs with Immunomodulatory Activities for Prevention and Treatment of Renal Diseases and Cancer

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Two new immunomodulatory nutriceuticals were created based on Siberian plants. The nutriceuticals contain complexes of biologically active substances such as balanced protein-carbohydrate complex, flavonoids, tannins, pectins, hydroquinones, vitamins, microelements, cellulose, etc.

Ecophyt includes extracts of Leather bergenia (Latin name is Bergenia crassifolia) and Prairieweed (L.n. is Pentaphylloides fruticosa), as well as modified chlorophyll of spirulina. Ecophyt showed immunomodulatory and adaptogenic properties. The clinical trial of those therapeutic effects was studied in the complex therapy of bronchial asthma (State Medicinal University, 2004, Kharkov, Ukraine). Ecophyt improves the immunogram indexes, activates mechanism of organism's self defense, kills mutilated and abnormal cells, inhibits tumor cell growth and causes their destruction. In addition to professional investigations, the patients were asked to rate their after treatment life quality, which they described as very high.

Radaclean contains extracts of Leather bergenia and Prairieweed, bioactive complexes of Siberian cedar (L.n. is Pinus sibirica) and Sea-buckthorn (L.n. is Hippophae rhamnoides). Clinical trial of Radaclean was done in Nephrological and Endocrinological Departments of M. Kalinin Samara Regional Clinical Hospital (2004, Samara, Russia). Radaclean's effects were studied on the following diseases: urolithiasis, salt diathesis, and chronic pyelonephritis connected with diabetic nephropathy. The nutriceutical has nephroprotective and hepatoprotective action, gentle stimulation effect on detoxication and excretion body functions, aids normalization of functional condition of nephrons, and improves indexes of lipid exchange.

Both nutriceuticals have been recommended for complex therapy of kidney, liver, cardiovascular pathologies, bronchial asthma, other chronic diseases, and cancer. The adverse side effects of Ecophyt and Radaclean have not been reported.
Chronic diseases and cancer are major health problems in the world. Cancer results from breakdown of the regulatory mechanisms that govern normal cellular homeostasis. The proliferation, differentiation, and survival of individual cells in multicellular organisms are carefully regulated to meet the needs of individual cells in multicellular organisms as a whole. This regulation is lost in cancer cells, which grow and divide in an uncontrolled manner, ultimately spreading throughout the body and interfering with the function of normal tissues and organs. Even though chronic diseases have other pathophysiological mechanisms, they too change homeostasis. Any kind of illness increases the amount of toxic substances. That is why, treatment of any diseases requires excretion of waste materials produced by the body and pathogenic microorganisms. High prevalence of chronic diseases and cancer raises concerns about the efficacy and limitations of conventional health care approaches in preventing and treating these disorders [Nader, 2000]. Such concerns may contribute to the increasing public and professional interest in alternatives to conventional modern medicine [Abdullaev FI, Sep. 1997; J.G. Topliss, 2002].

An ideal agent for preventing or treating cancer and internal pathologies should have gentle immunomodulatory action [Sprengers, 2005; Mark, 2004], selectively accumulate in pathological cells, induce apoptosis (natural cell death process) [Guimarães, 2004], promote excretion of metabolic products, and should not have significant side effects. Natural products are more acceptable for our body then synthetic substances and have less side effects. Natural products, very often, have integrated activities and could be used for treatment of different health problems. This is a very good point to turn the main stream of investigation to the chemistry of natural substances. But it is very hard to receive an integrated effect in one remedy; even if, it is a natural complex. One the ways to solve this problem is creating disease oriented series of herbal products. A main product of each set could be design for treatment of specific disorders such as renal diseases or cancer; supplementary products should increase excretion of metabolic and toxic products. Those supplementary-products could be also used as components of complex therapy for most chronic diseases.

Siberia (Russia) is a huge natural source of well known and unknown plants. Based on Siberian plants the new group of natural products was created by Ukrainian and Russian scientists. The unique properties of Sea-buckthorn (Latin name is Hippophae
rhamnoides), Siberian cedar (L.n is Pinus sibirica Du Tour), Leather bergenia (L.n. is Bergenia crassifolia), Prairieweed (L.n. is Pentaphylloides fruticoso) are well known from centuries past. Modern research already proved several pharmacological activities of those plants, but an investigation goes on [Nikolaeva, 1999.; Patents; 93028222/14, 93010258/14, 96112483/14; Kokoska, 2002; Suslov, 2002; Kolpakov, 2001; Nikolaeva, 1999; Ivanova, 1999; Beveridge, 1999; Kallio, 1999; Stranadko 1996; Bonnett, 1995; Breinholt, 1995].

This article represents materials about two new nutriceuticals Ecophyt and Radaclean. Both of them contain a complex of biologically active substances such as balanced protein-carbohydrate complex, flavonoids, tannins, pectins, hydroquinone, vitamins, microelements, cellulose, etc.). Bioflavonoids and other phenol compounds have antiinflammatory, antioxidant, antiallery, antimutagenic [Rubem Cesar Horn, March 2003], membrane-protection activities. Those types of biological activities stabilize microcirculation in Malpighian bodies and promote glomerular filtration. Phenol compounds effectively slow down the free-radical-reactions. Arbutin has gentle diuretic action and decreases excretion of urea and creatinine in blood. Pectin is also an important part of the new nutriceuticals. It aids in the bonding and excretion of endo- and exotoxins.

Besides Siberian plants one of the nutriceutical includes modified chlorophylls of Spirulina. Experimentally, it had been proved that modified chlorophylls of Spirulina improves humoral immunity. Additionally, modified Spirulina chlorophylls stimulate formation of antibodies which oppose cancer cells and activate regeneration of invaded tissues. Those effects extend the time and quality of cancer patients' lives. In many cases, it was observed that Spirulina's chlorophylls slow down the primary cancerous tumor growth and prevent the spread of metastases.

Ecophyt contains biologically active complexes of Leather bergenia, Prairieweed, and modified Spirulina chlorophylls. As a result of well-chosen combination of Siberian plant extracts and modified Spirulina chlorophylls, Ecophyt activates organism's self defense mechanism, kills dysplasia (abnormal) cells, and inhibits tumor growth.

Another new nutriceutical has the name Radaclean. It contains extracts of Leather bergenia and Prairieweed as well as complex biologically active substances of Sea-buckthorn and Siberian cedar. The nutriceutical has nephroprotective, hepatoprotective actions as well as gentle stimulation effect on detoxication and excretion. Radaclean also aids in normalization of conditions of nephron functioning and improves lipid exchange indexes.

The Goals of investigation were the study of the effects of the nutriceuticals on the primary body functions and the evaluation of their influence on adaptogenic abilities.

CLINICAL OBSERVATION

Ecophyt

Immunomodulatory and adaptogenic effects of Ecophyt were studied on bronchial asthma patients in Kharkov State Medical University in 2004. There were 25 patients with persistent moderate bronchial asthma (BA) in acute exacerbation case (12 of them
had hormone-dependent one). The study was compared to a control group. The patients’ states of health was monitored by clinical analysis of blood, blood serum (urea), and urine as well as biochemical blood screening (total bilirubin, alanine and aspartate aminotransferases, creatinine). The body’s adaptive responses and immunological status had been studied through primary and secondary immunologic screen tests. The content of blood immunoglobulin E (IgE) was performed by enzyme-linked immunosorbert assay. The attending medical doctors were asked to score the quality of patients’ life by scale: 0 - unsatisfactory, 1 - satisfactory, 2 - good, 3 - very good.

The patients were divided into two groups. The first group received standard therapy. The second group was treated by Ecophyt and standard therapy as well. Twice a day the patients received one tea spoon of Ecophyt. The nutriceutical was given on empty stomach 30 minutes before meal with a full glass of water for 14 days. The baseline therapy was the same for both groups. This therapy consisted of inhalant corticosteroids (Budesonid, Flixotide, Beklazone) and bronchodilators (a short-acting - Salbutamol and long-acting beta 2 antagonists - Serevent). Twelve patients received oral corticosteroids, an equivalent to 30 mg prednisolone a day, during last 7-10 years.

Two patient groups were associated on the base of the leukogram analysis according to nonspecific adaptive responses of body:

**first group** - 9 patients had stress reaction, which constitutes 60%,
3 patients had reaction of quiet adaptation, which constitutes 20%,
3 patients had reaction of advance adaptation, which constitutes 20%;

**second group** - 6 patients had stress reaction (60%),
2 patients had reaction of quiet adaptation (20%).
2 patients had reaction of advance adaptation (20%).

Consequently, the composition of investigated groups could be compared by clinical analysis and nonspecific adaptive responses of body. Standard clinical signs, symptoms, and laboratory examinations for each patient were evaluated before (0-th day) and after the treatment (14-th day). All patients showed significant health improvement and reduction of bronchospasm frequency, weakness, fatiguability as well as sleep and physical activity relief. An analysis of nonspecific adaptive responses of body after the treatment showed the following:

**first group** did not have stress reactions (0%),
6 patients had reaction of quiet adaptation (40%),
3 patients had reaction of advance adaptation 20%,
6 patients had training reaction (40%);

**second group** - 2 patients had stress reaction (20%),
5 patients had reaction of quiet adaptation (50%),
2 patients had reaction of advance adaptation (20%),
1 patients training reaction (10%).

It is known that: stress reaction is a sign of disease progression, reaction of quiet adaptation and reaction of advance adaptation show non-stable clinical remission, and the training reaction demonstrates the best adaptation. The dynamic of nonspecific-adaptive-responses-of-body in both patient groups allows to conclude that Ecophyt has adaptogenic activity.
Clinical studies also showed positive influence of Ecophyt in acute period of asthma. Thus in the first patient group, after seven days treatment, the amount of asthma attacks decreased from 3.8±0.12 to 1.6±0.3 per day. According to the peak-fluorophotometry monitoring of the peak expiratory flow rate grew up from 236.5±16.8L/min up to 372.3±11.6 L/min. It also was shown decreasing daily variability of the peak expiratory flow rate.

**Immunological Profile of Studied Groups**

(*asthma*)

<table>
<thead>
<tr>
<th>Table 1.</th>
<th>Verified measure</th>
<th>Control group</th>
<th>First group</th>
<th>Second group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before- treatment (n=8)</td>
<td>Post- treatment (n=8)</td>
<td>Before- treatment (n=8)</td>
<td>Post- treatment (n=7)</td>
</tr>
<tr>
<td>Leucocyte, $*10^9$/L</td>
<td>5.6±0.21</td>
<td>7.28±0.41*</td>
<td>7.61±0.14</td>
<td>7.98±0.25*</td>
</tr>
<tr>
<td>Lymphocyte, %</td>
<td>1.65±0.11</td>
<td>1.48±0.13</td>
<td>1.56±0.12**</td>
<td>1.44±0.12*</td>
</tr>
<tr>
<td>Lymphocyte, $*10^9$/L</td>
<td>29.4±1.11</td>
<td>27.31±4.80</td>
<td>28.10±3.20</td>
<td>26.30±1.30*</td>
</tr>
<tr>
<td>T-lymphocyte, %</td>
<td>67.3±2.81</td>
<td>56.30±6.80*</td>
<td>66.30±8.10**</td>
<td>56.3±3.44</td>
</tr>
<tr>
<td>T-lymphocyte, x$10^9$/L</td>
<td>1.11±0.02</td>
<td>0.96±0.03*</td>
<td>1.04±0.02**</td>
<td>0.93±0.03*</td>
</tr>
<tr>
<td>B-lymphocyte, %</td>
<td>11.57±1.91</td>
<td>18.43±1.32</td>
<td>17.61±1.36*</td>
<td>16.6±4.3*</td>
</tr>
<tr>
<td>B-lymphocyte, $*10^9$/L</td>
<td>0.19±0.00</td>
<td>0.29±0.01*</td>
<td>0.22±0.03*</td>
<td>0.26±0.03*</td>
</tr>
<tr>
<td>T-helper, %</td>
<td>55.86±1.17</td>
<td>69.4±8.41*</td>
<td>57.83±6.07**</td>
<td>66.2±7.41</td>
</tr>
<tr>
<td>T-suppressor, %</td>
<td>18.22±2.11</td>
<td>11.13±0.13*</td>
<td>16.9±0.23</td>
<td>12.12±0.13</td>
</tr>
<tr>
<td>Immunomodulator index</td>
<td>3.11±0.21</td>
<td>6.23±0.12*</td>
<td>3.29±0.29**</td>
<td>5.54±0.11*</td>
</tr>
<tr>
<td>% phagocytic neutrophils</td>
<td>55.30±3.00</td>
<td>29.70±4.80*</td>
<td>48.70±7.60**</td>
<td>28.40±4.80*</td>
</tr>
<tr>
<td>Phagocytic index</td>
<td>1.30±0.05</td>
<td>1.10±0.03</td>
<td>1.30±0.06</td>
<td>1.20±0.04</td>
</tr>
<tr>
<td>RNB test, %</td>
<td>10.00±1.23</td>
<td>19.40±5.60*</td>
<td>13.60±0.07**</td>
<td>18.30±1.45*</td>
</tr>
<tr>
<td>Ig A, g/L</td>
<td>1.89±0.11</td>
<td>1.87±0.09</td>
<td>1.86±0.06</td>
<td>1.88±0.12</td>
</tr>
<tr>
<td>Ig M, g/L</td>
<td>1.00±0.09</td>
<td>0.94±0.06</td>
<td>0.96±0.05</td>
<td>1.10±0.08</td>
</tr>
<tr>
<td>IgG, g/L</td>
<td>9.86±0.21</td>
<td>9.65±0.11</td>
<td>9.79±0.12</td>
<td>9.44±0.31</td>
</tr>
<tr>
<td>IgE, Me/L</td>
<td>96.30±11.50</td>
<td>272.50±9.60*</td>
<td>255.30±11.8</td>
<td>181.30±6.80</td>
</tr>
</tbody>
</table>

*P<0.05 compared with placebo group
**P<0.05 compared with tested group

The data analysis of immuno-grams showed the typical asthmatic signs: decreasing amount of T-lymphocytes, T-suppressors, and percentage of phagocytic neutrophils; increasing in immunomodulatory index and amount of B-lymphocytes, T-helpers, reduction-of-nitroblue-tetrazolium-test results (RNT-test), and total immunoglobulin (IgE). These immuno-gram results were rather similar for both groups.
On the 14-th day, the laboratory analysis showed positive changes in both studied groups. The progress in the first group was most evident: the amount of T-lymphocytes and percentage of phagocytic neutrophils was increasing, while immunomodulatory index and RNT-test results were decreasing. Those laboratory and clinical studies showed that the treatments were done correctly; however, immunomodulatory effect of Ecophyt was well proven by positive changes of immuno-gram and patients' examinations by physicians.

Physicians and patients were questioned about their satisfaction with the treatment and efficiency thereof. Both were ranked as very high. Doctor's scoring of efficacy of treatment was 2.15±0.04. Patients scoring of treatment was 2.75±0.05, while satisfaction with it was 2.91±0.01 (for the experimental group) and 2.85±0.03 (for the control group).

All of these facts allow to draw the conclusion that Ecophyt has an adaptogenic activity. The adverse side effects of Ecophyt have not been reported. The patients were pleased to take the nutriceutical and noted its pleasant taste and scent.

Radaclean

Clinical trial of Radaclean was done in Nephrological and Endocrinological Departments of M. Kalinin Samara Regional Clinical Hospital (2004, Samara, Russia). Forty six patients had been studied, 16 men and 30 women of ages ranged from 20 up to 64 years old. Patients' diagnoses were urolithiasis, salt diathesis, chronic pyelonephritis, chronic interstitial nephritis, chronic pyelonephritis in conjunction with diabetic nephropathy. The patients received regular therapy and Radaclean (6 capsules a day).

The control group consisted of 33 patients chosen within the same age and gender. Several patients expressed a wish to receive Radaclean as a mono-therapy. Standard clinical signs, symptoms, and results of laboratory examinations for each patient were evaluated before, during (10-th day) and after the treatment (21-th day). All patients were regularly examined by physicians, urologists, and nephrologists. The controlled parameters of well being were clinical-blood test, urinalysis (alanine-aminotransferase, aspartate aminotransferase, urea, cholesterol, lipoproteins, gamma-glutamyl-transferase, total protein, and so on), and nephrosonography data. Patients also had been asked to score acceptability of the nutriceutical by ten grade scale. Radaclean was given in 2 capsules each 8 hours before meal. Some laboratory findings for both studied groups are shown in table 2.

As known, at the initial stages of treatment of such diseases the patients' well being worsens. In the studied group Radaclean improved patients' feeling-of-well-being and stabilized laboratory readings permanently. In the control group, improvement took several days and was random. In addition, Radaclean-treated patients evaluated their feeling-of-well-being higher then those in the control one. They noted relief of shortness-of-breath and back pain as well as improvement of appetite and sleep.

Studied patients were divided into two subgroups. Seven patients had chronic pyelonephritis with diabetes complicated by diabetic nephropathy. They received standard hypoglycemic therapy, Enalapril, and Radaclean. The control group received
standard hypoglycemic therapy, Enalapril, and placebo. The Radaclean-treated group showed better laboratory examination rates, namely, improvement of blood forming elements. Physicians observed work of gastrointestinal tract, fats, protein, and salt metabolism, and other signs of health improvement.

### Laboratory Examinations of Studied Groups

Table 2.

<table>
<thead>
<tr>
<th>Verified measure</th>
<th>Studied group</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before treatment</td>
<td>After treatment</td>
</tr>
<tr>
<td><strong>Clinical-blood test:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peripheral blood's erythrocytes, *10^9</td>
<td>4.3</td>
<td>4.3</td>
</tr>
<tr>
<td>Peripheral blood's leukocytes in, *10^9</td>
<td>6.6</td>
<td>5.7</td>
</tr>
<tr>
<td>Hemoglobin, g/L</td>
<td>139</td>
<td>141</td>
</tr>
<tr>
<td>Erythrocyte sedimentation rate, mm/h</td>
<td>18</td>
<td>10</td>
</tr>
<tr>
<td>Total protein, g/L</td>
<td>70</td>
<td>71</td>
</tr>
<tr>
<td>Cholesterin, mmol/L</td>
<td>6.6</td>
<td>6.5</td>
</tr>
<tr>
<td>Alanine aminotransferase, u</td>
<td>38</td>
<td>36</td>
</tr>
<tr>
<td>Aspartate aminotransferase, u</td>
<td>39</td>
<td>40</td>
</tr>
<tr>
<td><strong>Urine analysis:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Density</td>
<td>1018</td>
<td>1016</td>
</tr>
<tr>
<td>Protein, %</td>
<td>0.1</td>
<td>0.033</td>
</tr>
<tr>
<td>Leukocytes leu/ul</td>
<td>10</td>
<td>2</td>
</tr>
</tbody>
</table>

It also was studied a subgroup of patients which expressed a desire for receiving Radaclean as a mono-therapy. That subgroup included patients with the following diagnoses: urolithiasis, secondary chronic pyelonephritis, and saline diathesis. The patients received two capsules of Radaclean three times a day before meal. The treatment duration was 21 days. Laboratory examinations showed increase in hemoglobin contents, seromucoid, and the amount of erythrocytes in blood and urine. Urinary protein excretion became significantly lower. The erythrocyte sedimentation, urea, and creatinine examination rates, as well as liver function test results, were normalized. Ultrasonic examination data also confirmed expulsion of kidney calculi and normalization of an urinary sediment. The patients noted normalization of sleep and temper. The total patients' motor activity was increased as well.

Thus, based on our studies one can conclude that Radaclean has nephroprotective activity, reduces unwanted consequences of drug treatments, and increases body's adaptive ability.

**Conclusion**

According to the data provided by our study it can be concluded that Ecophyt and Radaclean have nephroprotective and adaptogenic effects. The nutriceuticals normalize
main biomedical examination rates of urine and blood, reduce unwanted consequences of
drug treatments, and increase body's adaptive abilities. Ecophyt and Radaclean were
recommended as supplementary medicine for treatment of
- cancer and rehabilitation of cancer patients in post-period of surgery, radio- and
chemotherapy;
- diseases of kidney, liver, and cardiovascular system, including chronic
inflammation processes of different etiology and localization;
- various types of immunodeficiency disorders;
- internal- and external-intoxications (including bacterial intoxication);
- disorder of motility and expulsion mechanism of intestinal;
- chronic fatigue;
- disorder of adaptogenic ability of body caused by frequent changing of time
zones and long term pharmacotherapy;
- influence of occupational and environmental hazards.

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