

THE ADAPTOGENIC SPECIES: THEORETICAL AND PRACTICAL IMPORTANCE. A REVIEW.

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Abstract. Rediscovered at the middle of the last century, the adaptogens are a miraculous plant group. They permit the optimal-maximal expression of the physical and mental capacities of man, being used for the same purpose at some animals (thoroughbred horses). A summary insight in the past indicates they were known and used in different civilizations and philosophical theories. The actual characterization of the adaptogens is found in Ibn Sina's (Avicenna's) concepts. On the basis of recent information, the concept of adaptogen, hypotheses regarding the realization of the non-specific resistance character, the features of the three classes of adaptogens admitted at present: primary, secondary and associated adaptogens, the content of bioactive substances, and others, were defined. The analysis of the relation between the centres of origin of the species and the concomitant presence of several prehuman genotypes in these areas suggest the prehuman population's implication in the selection of species with adaptogenic features. Some commercial products with adaptogenic features are also presented.

Keywords: bioactive substances; species origin centers, adaptogens, humanoid populations, commercial products.

Rezumat. Specii adaptogene: importanță teoretică și practică. O trecere în revistă. Redescoperiți la mijlocul secolului trecut, adaptogenii sunt o clasă miraculoasă de plante. Ei permit exprimarea optimal-maximală a capacităților fizice și mentale ale omului, fiind utilizați în același scop la unele animale (cail de rasă). O sumară incursiune în trecut, arată cunoașterea și utilizarea lor în diferite civilizații și teorii filosofice. Caracterizarea actuală a adaptogenilor se regăsește în conceptele lui Ibn Sina (Avicenna). Pe baza informațiilor recente este definit conceptul de adaptogen, ipoteze privind modul de realizare a caracterului de rezistență non-specifică pe care o induc, caracteristicile celor trei categorii de adaptogeni admise în prezent: adaptogeni primari, secundari și asociați, substanțele bioactive conținute ș.a. Analiza relației dintre centrele de origine a speciilor și prezența concomitentă a mai multor genotipuri preumane în aceste regiuni, sugerează implicarea populațiilor preumane în selecția speciilor având caracter adaptogen. De asemenea, sunt prezentate unele produse comerciale având caracter adaptogen.

Cuvinte cheie: substanțe bioactive, centre de origine a speciilor, adaptogeni, populații humanoide, produse comerciale.

INTRODUCTION

The adaptogens are the most beneficial nutrients of vegetal origin, represented only by a few very rare species. They help the organism to reach optimal mental and physical performances. In actual conception, the adaptogen is a "new class of metabolic regulators which increase the ability of an organism to adapt to environmental factors and to avoid damage from such factors" (PANOSIAN et al., 1999; SAMUELSON & BLOHIN, 2009). They induce a non-specific resistance of the organism to stress factors. The adaptogens were (re)discovered and named by the Russian scientist LAZAREV in 1946, which described the novel effect of dibazol 12-benzyl benzimidazol, an arterial dilator, which produced a "state of nonspecific resistance" (PANOSIAN & WAGNER 1999; PANOSIAN, 2003).

The first studies in the adaptogen field were considered the studies performed by Brekhman on the *Panax ginseng* species, which also elaborated the first definitions: (1) "the adaptogen is a substance which presents a non-specific effect, leading to an increase of the body resistance to physical, chemical or biological stress factors"; (2) "the adaptogen has a normalizing influence on a pathological state, regardless of its nature"; (3) "an adaptogen is a compound which can be inoculated and does not affect the normal function of the body" (BREKHMAN, 1968). Their existence has been signalled since Antiquity, the remedies with an adaptogenic effect being mentioned in traditional Chinese medicine (tonic Qi), African (Manyasi), Tibetan, Ayurvedic (Ramayana) and American Native medicines. Ample studies on some plant species with adaptogenic effect, met in the Russian Far East, have been performed since the middle 20th century in the ex-Soviet Union, in the Primorye region, after the elaboration of the Order No. 4654-p/04.03.1043, issued by the Council of the People's Commissaries of the SSSR (LEBEDEV, 1967). Information about the adaptogen utility was diffused in the seventh decade of the last century. After the study of the flora of the Russian Far East (Primorye region), the adaptogenic effects of seven plant species, used in single or combined administration, the last variant being more beneficial, were described and analyzed. After the ample research performed both in the Russian Far East and in other regions, the number of species with adaptogenic properties increased (MAMEDOV, 2005). The seven species constituting the initial nucleus of adaptogens were:

- *Eleutherooccus senticosus* (Acanthi Root): Called the King of Adaptogens. Counteracts stress, increases productivity and endurance and normalizes body systems.
- *Schizandra chinensis* (Chinese Magnolia Vine): Counteracts stress, increases productivity, and combats fatigue.
- *Aralia elata* var. *mandshurica* (Manchurian Thorn Tree): Increases mental acuity.
- *Rhaponticum carthimoides* (Maral Root): Increases muscle development, improves performance, endurance and circulation.
- *Rhodiola rosea* (Russian Rhodiola): Increases mental and physical performance, normalizes heart rate, improves nervous system function and stabilizes mood.

- *Glycyrrhiza uralensis* (Licorice Root): Neutralizes toxins and balances blood sugar levels.
- *Avena sativa* (Fresh Wild Oat Seed): Strengthens the entire nervous system.

The knowledge about adaptogens was initially applied only in the ex-Soviet Union, remarkable successes in sport, spatial and military programs being obtained. After 1960, the information about adaptogens was also disseminated in other countries (Germany, Sweden, Korea, Japan and the USA). The research performed on a global level led to a higher number of adaptogenic species, the elaboration of many hypotheses about their pharmacological action, the establishment of the active principles which determine the adaptogenic effect, the elaboration of some commercial products with an adaptogenic effect, a/o. BREKHMAN (1968), established the following features of adaptogens:

- adaptogens are safe with no significant side effects or contraindications;
- adaptogens have a general, nonspecific action to improve resistance to stress;
- adaptogens have a balancing, normalizing effect on body functions, regardless of the origin of disruption or the direction of the homeostatic disturbance.

Thus, the adaptogens are nontoxic in normal doses, produce a nonspecific defensive response to stress, and have a normalizing influence on the body. They normalize the hypothalamic-pituitary-adrenal axis (HPA axis). As defined, adaptogens constitute a new class of natural, homeostatic metabolic regulators (BREKHMAN (1968).

The main pharmacological properties of adaptogenic products (particularly extracts of bioactive substances of vegetal origin) were formulated in 1969 by BREKHMAN & DARDYMOV:

- the adaptogen is relatively atoxic for the recipient, regardless of the usage period;
- an adaptogen has a “non-specific” activity and determines the increase of the body resistance to a wide spectrum of physical, chemical and biological noxious agents;
- the adaptogens help the body to adjust or normalize its organ and system functions;
- adaptogens make the stress response less damaging;
- adaptogens help to maintain homeostasis in the face of stress by regulating the body’s adaptive reactions;
- adaptogens reduce most signs of the alarm stage of the stress response and delay or promote avoidance of the exhaustion stage;
- the use of adaptogens eliminates or significantly decreases the classical signs of the prolonged stress reaction described by Hans Selye as “the Stress triad” (SEYLE, 1973);
- adaptogens help the body utilize fuel more efficiently, with fewer toxic or waste by-products (like lactic acid), which can contribute to fatigue and reduced function;
- efficient use of energy means greater reserves that are more readily available.

The practical utilities of adaptogens are:

- **obtaining pharmaceutical products**, for different usages: tonic and stimulating substances for sports medicine; in general medicine, preparations protecting against different stress factors, organism exposure to cold in arctic regions, to the action of different pollutants produced by different industrial activities (mining and energy industries, chemical industry, mechanical vibrations, and others);
- **prevention and treatment** of some lesions or under other abnormal conditions;
- **curative agents** in the treatment of some neurological and mental diseases, such as: asthenia, neurosis, depression, alcoholism, and others, as well as adjuvant in other diseases, such as tuberculosis or in cancer therapy;
- **anti-stress substances**, inducing the increase of tolerance and resistance to physical and mental stress, as well as the reduction of the incidence of its injurious effects on the body;
- **anti-toxic action**, increasing the body tolerance to more chemicals, biological toxins or toxins produced by radiations;
- **normalizing agents**, having the effect of regulating the body functions, if they have the tendency to be fluctuant. In this group there are: the regulation of some endocrine gland activities (hypophysis, thyroid, suprarenal), the regulation of some biochemical parameters (blood pressure, cholesterol and blood glucose level, and others); the changes at the adaptogen level induced a stimulation of the nervous, endocrine and immune systems;
- **prophylactic role**, through the increase of the body resistance to many dysfunctions, having also a therapeutic action: influenza, acute respiratory diseases, atherosclerosis, hypertension, diabetes, obesity, skin diseases, cancer, and others;
- **enhancement of the performance of some thoroughbred animals**, such as horses (KING, 2006).

Pharmacological characterization of adaptogens

The tests involving exposure to heat or cold, atmospheric pressure and oxygen content different from normal, radiations, toxic substances, different storage conditions, psychical stress state, fear and chronic diseases, pointed out that the most important characteristic of adaptogens is the increase of the body resistance capacity, both to the physical stress and to the psychical-emotional stress. The same property resulted from specific biochemical tests (the NO [nitric oxide] content of the blood, spittle and expired air; cortisone level in blood; ACTH [adrenocorticotropic hormone] and other hormones and substances), as well as some cell functions (phagocytosis, *in vivo* and *in vitro* cytokine production). It was also established that the NO donors increase and NO synthesis inhibitors diminish the swimming length time of the rats, affect their survival and their longevity under hypoxia conditions, and increase the induced immobilization of the gastric ulcer in rats.

At present, PAWAR VINOD & HUGAR (2012) considered that the adaptogens represent a new class of bioactive substances, with the following features:

- they reduce the lesions and negative effects induced by stress factors, through the activation of the nervous and endocrine systems;
- they induce the increase of attention and resistance in the situation of diminished performances, determined by extenuation and/or feebleness sensation.

Hypotheses regarding the action mode of adaptogens

Several hypotheses were elaborated to explain the protecting and stimulating effects of the adaptogenic products. Dardymov and Kirkorian (quoted by PANOSSIAN & WAGNER, 1999) consider that the main function of the adaptogens is determined by their antioxidant action, as they are a trap for free radicals. But this conception cannot explain all their medical effects. In the Panossian's postulates (PANOSSIAN & WAGNER, 2003), adaptogens are considered to act mainly on the Hypothalamic/Pituitary/Adrenal (HPA) axis and on the Sympathoadrenal System (SAS). Thus, the adaptogens can fashion the organism response to the stress factor action (physical, environmental or emotional factors), achieving the regulation and interconnection of the endocrine, immune and nervous systems. This (re)regulation of systems disturbed or troubled by stress factors is realized through the action of some chemical mediators (cytokines, catecholamine's, glucocorticoids, cortisol, serotonin, nitric oxide, cholecystokinin, corticotrophin-releasing factor (CRF), or sexual hormones. This theory explains the different effects of adaptogens: anti-inflammatory, antioxidant, anxiolytic, antidepressant, nerving and amphoteric. According to BREKHMAN & DARDYMOV (1969), there are many plants with an amphoteric function, but very few are adaptogens. All adaptogens act as amphoteric with a wide spectrum over the living organisms, but they rarely have a pronounced effect over an organ or specific system. The main differences between stimulating and adaptogenic plants are presented in Table 1.

Table 1. The differences between species with stimulating features and adaptogenic species (after PAWAR VINOD & HUGAR, 2012).

Feature	Stimulating species	Adaptogenic species
Recovery after exhausting physical solicitation	Low	High
Energetic exhaustion	Yes	No
Performance under stress conditions	Low	High
Survival under stress conditions	Low	High
Response quality	Slight	Good
Insomnia	Yes	No
Secondary effects	Yes	No
DNA/RNA and protein syntheses	Low	Increased

The investigations performed by PANOSSIAN & WIKMAN 2009b and PANOSSIAN et al. (2009a, 2010, 2011, 2012) established that the stress-protective activity of adaptogens is associated on the cellular level, via activation molecular chaperones Hsp70, and other key mediators of the stress response such as cortisol, nitric oxide, stress-activated protein kinase JNK (PANOSSIAN et al., 2012) and DAF-16 (PANOSSIAN et al., 2007). Studies have demonstrated that heat-shock factor 1 (HSF1) and Neuropeptide Y might be primary upstream molecular targets of adaptogens in neuroglia cells, but the results were only suggestive, not conclusive (PANOSSIAN et al., 2011, 2012).

As a result of research performed both in the Russian Far East and in the whole world, the number of species with adaptogenic properties increased (MAMEDOV, 2005). In the living world, except the higher plants, there are numerous species, from different organization levels, which present bioactive substances, with antistress or adaptogenic action. Among these: prokaryotes (Cyanophyceae, *Spirulina platensis* [GOMONT] GEITLER; DEMIREL et al., 2012), lower plants (mushroom, *Inonotus obliquus* [ACH. EX PERS.] PILÁT, chaga mushroom; BHAKUNI & RAWAT, 2005), or animals which contain bioactive substances with adaptogenic or anti-stress action (*Mytillus galloprovincialis*, bivalve, KUDRYASHOV & GONCHARENKO, 2004; some amphipods (TIMOFEYEV & STEINBERG, 2006).

CUI et al. (2005) evaluated the protecting potential of *Inonotus obliquus* against the oxidative damage to DNA in a human keratinocyte cell line. The study found the polyphenolic extract from *I. obliquus* protected these cells against hydrogen peroxide-induced oxidative stress. Another study pointed out that the endopolysaccharide of chaga produced indirect anticancer effects via immunostimulation.

TYMOFEYEV et al. (2007) consider that the natural organic matter (NOM) can modify the multixenobiotic resistance (MXR) of an organism. They consider that the MXR system is a general first non-specific line of defence against environmental contaminants. Subsequent research will establish that these are stimulating or adaptogenic species.

Different scientists (MAMEDOV, 2005; TIWARI et al., 2011; YANCE, 2013) distinguish three main categories of adaptogens and use herbs from each of these categories in all formulations to achieve the best possible results.

Primary adaptogens: meet the classical definition of adaptogens.

Secondary adaptogens: meet most of the traditional criteria or have met all of the criteria but lack sufficient scientific validation.

Adaptogen companions: may not meet all of the traditional criteria but play a supporting role by enhancing the HPA axis and anabolic metabolism.

A. Primary adaptogens are represented through the initial nucleus from Primorye region from Far East Siberia, as well as through other species, with similar properties, described in other Terra planet regions. The features of the primary adaptogens are:

- ample scientific research confirmed their adaptogenic character;
- they ensure a “general resistance” in the whole body;
- they have a non-specific action, with a “normalizing” effect toward the action of different stress factors;
- they have the capacity of maintaining or restoring the homeostasis;
- their use is safe and they do not have secondary effects, even after prolonged use.

The activity of primary adaptogens is focused on metabolic regulation through their proven effects on the hypothalamic-pituitary-adrenal (HPA) axis during stress-adaptation responses. They have an ability to maintain or restore homeostasis and allostasis and encourage anabolic restoration. Primary adaptogens enable better response and recovery because they help to smooth out the highs and lows of the neuroendocrine stress response by regulating and normalizing the hormones involved. Primary adaptogens strengthen all systems, promote optimal response and hasten recovery of function, and help to regulate energy use by enhancing cellular energy transfer. Adaptogens enable us to make more efficient use of oxygen, glucose, lipids, and proteins (YANCE, 2013). Arguments for the HPA regulation by primary adaptogens are represented through:

- increasing and modulating the flow of energy throughout the day;
- decreasing feelings of stress;
- increasing endurance;
- supporting mental alertness;
- promoting deep, restful sleep.

The primary adaptogens are represented through the initial nucleus from Primorye region from Far East Siberia, as well as through other species, with similar properties, described in other Terra planet regions. Other adaptogen species, are: *Eleutherococcus sessiliflorus* S. Y. Hu (tincture from root a/o rhizome), *Olopanax elatus* (NAKAI) NAKAI (tincture from root, a/o rhizome); *Panax ginseng* C. A. Mey (tincture from root) (MAMEDOV, 2005), *P. quinquefolius* (standardized root extract), *Withania somnifera* (aqueous ethanol root extract), *Cordiceps sinensis*, *Codonopsis pilosula*, *Glycyrrhiza glabra*, *Ganoderma lucidum*, *Schisandra splenathera* (plant, standardized extract), *Emblica officinalis*, *Aralia schmidtii*, *Bryonia alba*, *Tinospora cordifolia* (plant), *Ocimum sanctum* (leaves), *O. gratissimum* (leaves), *Gymnostemma pentaphylla*, *Rhaphonticum carthamoides* (plant), and others (WINSTON & MAIMES, 2007). Recent information about the species with adaptogenic properties were presented by TIWARI et al. (2011), PAWAR VINOD & HUGAR (2012), MAHAJAN & GAJARE (2012), YANCE (2013).

As a general remark, the adaptogenic species origin is near or in the centre of origin described by VAVILOV. In these centres, the humanoid populations, which had a role in their evolution, were present. In severe climatic conditions, in some species it took place a genetics amplification process, which confers resistance for plants toward extreme environmental conditions. In this resistance, many biochemical compounds, which pass in the consumer bodies, different animal and humanoid populations from the area, are involved. The humanoid populations present in these areas contributed to the evolution of adaptogenic populations through empirical selection of the productive plants, resistant and with a big area. The knowledge about their properties was transmitted in human descend populations, being used in alimentation and for their properties. This hypothesis is supported by some findings. Thus, in the area of Denisova cave (Altai Krai, Russia), 41,000 years ago, three different humanoid populations inhabited: *Homo devisovan*, *H. neanderthalensis* and *H. sapiens sapiens* (KRAUSE et al., 2010), relatively sedentary. In the proximity of this region, there are the **Central Asiatic Centre** of domesticated species, in which there are included Northwest India (Punjab, Northwest Frontier Provinces and Kashmir), Afghanistan, Tajikistan, Uzbekistan, and western Tian-Shan (VAVILOV, 1961). 43 domesticated plants: common wheat, peas, lentil, sesame, cotton, onion, garlic, spinach (three adaptogenic species), carrot, pear, grape, apple, and others. Probably this centre was the largest, in its constitution being also included South Siberia with some classical adaptogenic species (CORNEANU & CORNEANU, 2011). In the **Mediterranean Centre**, which includes the borders of the Mediterranean Sea, there were also domesticated 84 plant species: durum wheat, emmer, oats, pea, rape, olive, cabbage, peppermint, black mustard, Baraka, and others. Baraka (*Nigella sativa* L.) is an adaptogenic species, used since Antiquity. This area was a centre of human origin, being met many human populations. Thus, in Qesem cave, situated near Tel Aviv (Israel), naturally closed 200,000 years ago, eight teeth belonging to *Homo neanderthalensis* and *H. sapiens* were discovered. They belong to some fossils with two distinct ages: (a) 300,000 – 400,000 years and (b) 200,000 - 300, 000 years. As an explanation, many hypotheses were issued: (a) they belong to an archaic population from *Homo* genus; (b) fossils of *H. neanderthalensis* which evolved differently; (c) these teeth belong to a new human species; (d) *H. sapiens* appeared earlier, and thus his migration from Africa in Asia and Europe; (e) the origin sites of the human species is the Middle East, not Africa (CORNEANU & CORNEANU, 2011).

One action path of adaptogens consists, on the one hand, of support of the neural-endocrine system, maintenance of all neural-endocrine hormonal systems and of the vital organs of the organism, and on the other hand, of a stronger vital communication. They can induce a normalizing effect of the system functions, inducing either their hypo- or hyper function. The adaptogens can induce an optimal homeostasis, preventing or delaying any injurious effect

determined by stress factors or by the aging process. Thus, there is a higher probability of disease prevention and treatment, together with a qualitative and quantitative increase of health and life. They are the essential element of vitality, because they assure an equilibrium state of the whole body.

B. Secondary adaptogens

After YANCE (2013), the secondary adaptogens present most of the criteria of primary adaptogens, but not all. Also, although secondary adaptogens demonstrate some normalizing activity, especially of the immune, nervous, and hormonal systems, they may not directly support the HPA axis. The protective effects of secondary adaptogens come with regular use when combined with primary adaptogens. The secondary adaptogens manifest some features (YANCE, 2013):

- they are more numerous than the primary adaptogens;
- they manifest some normalizing activities, especially on the immune, nervous and hormonal systems;
- they were extensively studied for their adaptogenic qualities, but cannot confirm the adrenaline system (thus their activity may not directly support the HPA axis);
- while they may meet some, or most, of the qualifications of primary adaptogens, they have yet to be studied extensively;
- many of these plants are rich in fatty acids, sterols, and phenol compounds;
- many of these plants enhance anabolic metabolism;
- they can offer non-specific protecting effects for all systems and organs, thus completing the benefits induced by primary adaptogens.

Many plant species present the features of secondary adaptogens, toward different stress factors or different affections of organs a/o systems, being used in their treatment. Thus, the roots from *Angelica atropurpurea* are used as a natural remedy for cardiovascular affections, chronic inflammations (especially in rheumatism), lung and urinary systems, and female reproductive affections. *Ginkgo biloba* leaves are a secondary adaptogen for adrenal, pancreatic and cardiovascular diseases, nervous system and as great neurovasodilator. *Hypericum perforatum* (herbs) is used for its adaptogenic features in cardiovascular diseases, for nervous and digestive tract. Recent research (CORNEANU et al., 2012, CORNEANU & CORNEANU, 2013) recommended the use of volatile oils extracted from *Nigella sativa* seeds for their adaptogenic features at the liver level.

C. Associated adaptogens (herbal adaptogen companions)

The medicinal plants from this group offered enormous general benefits, such as tonicity of the entire body, protection of the vital organs and participation in the protection of the entire organism from several stress factors. Their general action can equilibrate or synergize the effects of primary and secondary adaptogens. They are not toxic and their beneficial effects are cumulative for a long period of time. The companion (associated) adaptogens present antioxidant and anti-inflammatory properties.

Many culinary and aromatic plants used in traditional cuisine (officinal rosemary, Indian saffron, green tea, turmeric, ginger, and others), as well as the nutritional agents, are associated adaptogens.

Because the species from this group manifest enormous general health benefits similar to those of primary and secondary adaptogens, but some scientists (YANCE, 2013) consider that they do not meet the criteria to be officially termed adaptogens. YANCE (2013) affirms: "I call them adaptogen companions, because their actions enhance or synergize the effects of primary and secondary adaptogens". This elite group of herbs and nutritional compounds is used in a supporting role to potentiate primary herbs, harmonize formulations, and, most often, to add high nutritive value. When combined with primary and secondary adaptogens they will significantly increase life span and quality of life.

Important Actions of Adaptogens

- **as anti-stressors:** To increase tolerance and endurance to stress, both physical and mental, as well as decrease the incidence of the harmful side effects of stress on the body;
- **as a normalizing agent:** To provide a regulatory effect on body functions, which tend to fluctuate. It has been shown that adaptogens normalize abnormalities of functions including adrenal, thyroid, blood pressure, cholesterol and blood glucose. Scientific data indicates that changes produced by adaptogens are the result of stimulation of the nervous system, endocrine system and immune system;
- **as a prophylactic:** To enhance a wide range of therapeutic action: influenza, acute respiratory disease, atherosclerosis, hypertension, diabetes, obesity, skin disorders and cancer;
- **as an anti-toxic:** To increase the body's tolerance of many chemical, biological and radioactive toxins.

Constituents of adaptogenic extracts. After PANOSSIAN (2003), depending on the bioactive substance, there are three adaptogen types.

(1) Adaptogens with phenol compounds, as phenylpropanoids, phenyl ethane derivatives, and lignans, whose structural resemblance to catecholamines could suggest an effect on the sympathoadrenal system and possibly imply an effect in the early stages of the stress response. In this group, there are included roots and rhizome of *E. senticosus* and *R. rosea*, as well as extracts of *S. chinensis* fruits.

(2) Adaptogens with tetracyclic triterpens similar to cucurbitacin-R-diglucoside, which structurally resemble the specific corticosteroids that inactivate the stress system to protect against overreaction toward stressors. This group of adaptogenic substances is in extracts of *B. alba* and *W. somnifera*.

(3) Adaptogens with oxylipins (an unsaturated trihydroxy) or epoxy fatty acids (structurally similar to leukotrienes and lipoxines). These adaptogenic compounds have been found in *B. alba* and *G. glabra*.

Commercial products with adaptogens

The **oxyfresh Primorye tonic** was the first anti-stress tonic with revigorant properties, prepared by specialists from Russia, United States and Canada. It is consumed daily by a wide people range, from professional athletes and policeman, military, to pensioners. This produce assures mental clarity, enhanced resistance and recovery of organism.

LERA is a product obtained from ten adaptogenic plant species, which vegetate in the virgin forests from East Siberia. It is produced as a liquid elixir, daily administered. The main constituent is *Eleutherococcus senticosus* (Siberian ginseng, the king of adaptogens), together with *Aralia elata* var. *mandshurica* and eight other species. LERA is efficient on the immune system, physical and mental effort capacity, performances, normalizing effect after stress, resistance toward environmental toxins, antioxidant activity, antia-ging effect, effect on the cardio-vascular system, effects on some analyzers (auditory and vestibular, visual and colour perception) and recovery processes.

Ultima Adaptogens contains the three universal adaptogens, having a maximal efficiency (ANONYMOUS, 2013):

- *Eleutherococcus senticosus*, a medicinal plant which prevents the liberation of an excessive amount of corticosteroid hormones, as a result of the presence of some stress factors;
- *Schisandra chinensis*, an adaptogenic plant native from China which increases the amount of energy liberated and tempers fatigue;
- *Rhodiola rosea*, a perennial plant which tempers stress and anxiety;
- Moreover, Ultima Adaptogen contains other three medicinal plants with synergic activity:
- *Angelica* (a biennial or perennial plant, which protects the liver);
- *Liquorice* (a common plant with antioxidant properties, which counteracts the stress effects);
- *Cinnamon* (a plant which reduces the blood pressure, the glycaemia level, cholesterol together with other beneficial activities).

Recommendations for the use of Ultima Adaptogens:

- to enhance the general health and protect from the dangers of stress;
- to protect some vital organs, such as: liver, heart, immune system and brain;
- for athletes, the working at night or partake in physical activity;
- recovery from an illness or injury.

The Ultima Adaptogens assures some advantages:

- no known adverse effects;
- no prohibited and stimulating substances;
- this product is standardized, stable and tested through scientific research;
- can restore the balance of organism in any situation.

Other important benefits adaptogens provide include:

- increasing mental and physical stamina;
- speeding recovery from physical training;
- protecting against illness and injury;
- protecting the heart and liver;
- anti-oxidant, anti-ageing, and anti-cancer properties.

CONCLUSIONS

Adaptogen is a metabolic regulator which increases the ability of an organism to adapt to environmental factors, and to avoid damage from such factors. Environmental factors can be of different nature: physical, chemical, and physiological (external), different injury, aging, anxiety, mental exhaustion, and others.

An adaptogen manifests a normalizing effect, i.e., counteracting or preventing disturbances to homeostasis brought about by stressors. Also, an adaptogen must be innocuous with a broad range of therapeutic effects without causing any major side effects.

The adaptogens act mainly on the hypothalamic/pituitary/adrenal (HPA) axis and on the sympathoadrenal system (SAS). Thus, the adaptogens can fashion the organism response to the stress factor action (physical, environmental or emotional factors), achieving the regulation and interconnection of the endocrine, immune and nervous systems.

This (re)regulation of systems disturbed or troubled by stress factors is realized through the action of some chemical mediators (cytokines, catecholamines, glucocorticoids, cortisol, serotonin, nitric oxide, cholecystokinin, corticotrophin-releasing factor (CRF), or sexual hormones. This theory explains the different effects of adaptogens: anti-inflammatory, antioxidant, anxiolytic, antidepressant, nerving and amphoteric.

The recent investigations established that the stress-protective activity of adaptogens is associated on the cellular level, via activation molecular chaperones Hsp70, and other key mediators of the stress response such as cortisol, nitric oxide, stress-activated protein kinase JNK and DAF-16. Subsequent investigations can evidence also other aspects, regarding the implication of other mediators.

Depending on the bioactive substance, there are three groups of adaptogens: adaptogenic compounds with phenol compounds, tetracyclic terpene and adaptogens with oxylipis or epoxy fatty acids. The presence of different bioactive substances explains the different action of the adaptogens.

Regarding their actions, the adaptogens can be divided into three classes: *primary adaptogens* (manifest the classical features of adaptogens), *secondary adaptogens* (manifest some normalizing activities, especially on the immune, nervous and hormonal systems but lack sufficient scientific validation), *associated adaptogens* or *herbal adaptogen companions* (present antioxidant and anti-inflammatory properties and can equilibrate or synergize the effects of primary and secondary adaptogens).

The adaptogens can present three types of bioactive substances: phenol compounds (phenylpropanoids, phenylethane derivatives, and lignans), tetracyclic triterpens, and oxylipins or epoxy fatty acids.

Many species of prokaryotes, lower plants or animals, present organic substances which confer resistance toward exobiotic factors. The subsequent research will established if these are stimulant species or adaptogenic species.

Some commercial products with adaptogenic features, such as: Oxyfresh Primorje tonic; LERA, Ultima Adaptogens, were also presented.

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