

## The Search for “Herbs Superior” to Improve Cardiovascular Function, Boost Endurance Capacity, and Mitigate Metabolic Dysfunction

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### Abstract

Adaptogen is a term used for specific substances that increase the body’s resistance to nonspecific stress. Adaptogens contribute to a biochemical change in an organism that generates a more effective response than the body might exhibit without them. Noted Soviet researcher, Nikolai V. Lazarev described an adaptogen as “an agent that allows an organism to counter adverse physical, chemical, or biological stressors by raising nonspecific resistance toward such stress, thus allowing the organism to adapt to the stressful circumstances”. Some of the earliest scientific research on natural adaptogens was done on *Panax ginseng* (Asian ginseng) that was found to enhance physical performance in Soviet athletes. Subsequently, thousands of clinical trials were performed on over four thousand plants and the results published in peer-reviewed journals. Adaptogenic herbs can influence the corticosteroidal effect of the adrenal glands through the hypothalamus-pituitary-adrenal axis, enhance endurance capacity, improve cardiovascular function, and alter metabolic function. The bioactive constituents of many adaptogenic herbs fall into two general chemical classes, terpenes or polyphenols, that are secondary metabolites of specific adaptogenic plants. Also, polysaccharides act, in part, as immunomodulators. Adaptogens can increase oxygen and neuroreceptor efficiency, influence the levels and activity of monoamines and opioid peptides, and enhance the physiological response to stressors. Over time, many definitions of adaptogens have been put forth, which demonstrates a lack of consensus regarding adaptogens in the scientific community, specifically to their characteristics and mechanisms of action. However, their beneficial effects in humans seem far-reaching and have been reported by scientists and observed for centuries in Ayurveda and Traditional Chinese Medicine (TCM). There remains the challenge of establishing the efficacy of these adaptogenic herbs as each herb contains numerous constituents; however, an isolated constituent might or might not work as well as the whole phytocomplex. Although many of these herbal remedies have been used for hundreds to thousands of years, the scientific evidence regarding their safety and efficacy is inadequate and inconclusive. Nevertheless, the beneficial effects of long-term administration of specific adaptogenic herbs is more established than those of short-term administration. This review provides a historical backdrop to the research regarding adaptogenic herbs and their proposed (and in some cases confirmed) beneficial applications in the body’s response to stress.

**Keywords:** Ayurvedic; Adaptogen; Ashwagandha; Ginseng; Heart Disease; Hypertension; Immune System

### Abbreviations

CNS: Central Nervous System; CSRS: Central Stress Response System; GAS: General Adaptation Syndrome; HPA: Hypothalamus-Pituitary-Adrenal Axis; iNOS: Ca<sup>2+</sup>-Independent Nitric Oxide Synthase; NKC: Natural Killer Cell; ROS: Reactive Oxygen Species; TCM: Traditional Chinese Medicine; TNF: Tumor Necrosis Factor USP: United States Pharmacopeia

### Introduction

#### The meaning of adaptogen and adaptogenic herb

In the 1940s, Soviet scientists applied the term “adaptogen” to specific substances to describe their actions of increasing the body’s resistance to nonspecific stress [1]. According to Panossian and Wikman (2009), adaptogens contribute to a biochemical change in an organism (resulting from exposure to specific environmental conditions or stressors) that generates a more effective response [2]. The term adaptogen is derived from the Latin word, *adaptare*, meaning, “to adjust” [1–3].

Nikolai V. Lazarev, a noted Soviet scientist, medical doctor, and pharmacologist, conducted experiments on the chemical substance, dibazol, that had been used to treat hypertension and heart disease. Lazarev observed that the drug could increase the resistance of specific organisms to stress. Lazarev went on to define adaptogen as “an agent that allows an organism to counter adverse physical, chemical, or biological stressors by raising non-specific resistance toward such stress, thus allowing the organism to adapt to the stressful circumstances” [4].

In 1968, Israel I. Brekhman and Lazarev proceeded to research adaptogenic natural substances rather than chemical drugs [5,6]. They were tasked with finding ways to help Soviet elite athletes and soldiers become more competitive. They began by investigating Panax ginseng (Asian ginseng). They found that this herb had potential in enhancing physical performance. However, Panax ginseng was not indigenous and did not grow well in their country. Due to the expense and difficulty in acquiring the herb, they were forced to look for other plants that might offer similar properties and physiological effects [5,6].

These scientists conducted thousands of clinical trials, investigating over four thousand plants. About twelve of these investigated plants were identified as being adaptogenic—reputed for their rejuvenating effects and used for centuries, the most notable and practical being Eleuthero (*Eleutherococcus senticosus*), also known as Siberian ginseng, Licorice (*Glycyrrhiza glabra*), Rhodiola (*Rhodiola rosea*), American ginseng (*Panax quinquefolius*, *Panacis quinquefolis*), Astragalus (*Astragalus membranaceus*), and Angelica (*Angelica archangelica*) [1,5,6].

From that period until the break up of the Soviet Union in 1991, research on adaptogenic plants was vigorous, with over fifteen hundred pharmacological and clinical studies formally conducted on adaptogenic plants. These studies concluded that adaptogenic plants could induce higher oxygen utilization, modulate stress responses, improve stamina, and shorten recovery periods from sports activity in the tested Soviet athletes [2,5–7].

Initially, it was theorized that some of the features of these adaptogenic plants in nature could be what makes them effective in humans. For example, many of these plants grew in high altitudes, acrid and dry climates, and in areas of severe environmental variations. Since they demonstrated the ability to survive in such extreme conditions, it was thought that they might impart that same “rebound” quality when consumed by humans [8–10].

### Discussion

#### Mechanism of adaptogenic herbs

A vast number of studies have been performed and peer-reviewed papers published in many countries regarding the physiological benefits of adaptogenic herbs. The most commonly accepted scientific explanation of the beneficial effects of adaptogenic herbs is attributed to the herbs’ influence on the corticosteroidal effect of the adrenal glands through the hypothalamus-pituitary-adrenal axis (HPA). These herbs influence the body’s stress response. A placebo-controlled, double-blind study, conducted by Kuo., *et al.* (2010), found that Eleuthero—given to athletes over eight weeks—enhanced their endurance capacity, improved cardiovascular function, and altered metabolic function [11].

### Terpenes and polyphenols

The bioactive constituents of many adaptogenic herbs fall into two general chemical classes: terpenes and polyphenols [4].

Terpenes represent a broad class of molecular products synthesized by plants as a secondary metabolite. While found in small amounts in living organisms, they play vital roles in plant physiology. Triterpenoid saponins are found commonly in adaptogens. They help plants adapt to and survive in diverse environmental conditions. These saponins are one enzymatic process away from becoming steroidal and, therefore, may function as a precursor in the modulation of hormonal activity in humans, producing adrenocorticotrophic hormonal effects.

Polyphenols are also secondary metabolites of plants, having purported immune-boosting and protective properties. They contain flavonoids that promote various physiological benefits in humans [4,12–14].

### Polysaccharides

Polysaccharides are another principal constituent of adaptogens. Polysaccharides are multiple monosaccharide units that form a large glucose chain. Polysaccharides can be found in many TCM herbs that “tonify” and support immunity, such as Astragalus root and ginseng. Polysaccharides act, in part, as immunomodulators that can affect immune system components, such as cytokines, tumor necrosis factor (TNF), natural killer cells (NKCs), B and T lymphocytes, and granulocytes [4,15].

### The effect in the general adaptation syndrome (GAS)

It has been suggested that adaptogens enhance the physiological response to stressors during the general adaptation syndrome (GAS), including the central stress response system (CSRS) broadly. Also, it has been proposed that their intervention in GAS involves the sympathetic adrenomedullary system, the limbic system, and the central monoaminergic system, suggesting that brain function is the main feature of modulation [7].

### Neurogenic, neurotropic, and central nervous system effects

Other mechanistic characteristics of adaptogens, however, are not directly related to their HPA effect. Increased oxygen and neuroreceptor efficiency have been cited as some reasons these herbs can influence stamina and the stress response. Perfumi and Mattioli (2007) studied the CNS effects of *Rhodiola rosea* and postulated that the herb might influence the levels and activity of monoamines and opioid peptides, such as beta-endorphins [16].

A study by Panossian and Wikman (2010) showed that the adaptogen, *Schisandra chinensis*, exhibited neurotropic and central nervous system (CNS) stimulating activity, in addition to cortisol modulation via the HPA. An earlier placebo-controlled study by Panossian., *et al.* (2007) reported a change in nitric oxide synthase activity with the administration of a variety of adaptogenic herbs [7]. This study showed that the herb’s effect was initiated in the hypothalamus due to alterations in neural Ca<sup>2+</sup>-independent nitric oxide synthase levels (iNOS). Cytokines and lipopolysaccharides can promote iNOS, producing a high level of nitrous oxide that plays a role in the immune response

[17]. Panossian, *et al.* (2007) also noted that a series of enzymatic transactions were moderated, suggesting that the effects of adaptogens may involve more than their HPA axis effect [2,18].

### The search for identity and designation

Since Soviet scientific efforts, many definitions of adaptogens have been put forth. (This lack of consensus shows that the scientific community is not yet in full agreement as to what characteristics and mechanisms of action constitute an adaptogen). In their book, “Adaptogens: Herbs for Strength, Stamina and Stress Relief” published in 2010, authors David Winston and Steven Maimes, reported various and slightly differing definitions for adaptogens that have been offered, as follows:

1. An agent that increases the body’s ability to adapt to environmental and internal stress by strengthening the immune, nervous, and glandular systems. Enhances an organism’s resistance to stress, disease, and environment as well as normalizes metabolic functions and increases metabolic efficiency [4].
2. A prophylactic that heightens in an unspecific way the resistance of the organism to various environmental influences and stimuli and or reduces the disposition or susceptibility to illness [4].
3. (An herb that) enhances the body’s nonspecific resistance to external stress or noxious effects of a physical, chemical, or biological nature [4].
4. A substance that increases the body’s resistance to physical, environmental, emotional, or biological stressors and promotes normal physiologic function [19].
5. An herb that increases resistance and resilience to stress, enabling the body to avoid reaching collapse because it can adapt to the problem [4,7].
6. A substance that helps bring the body into a state of harmony with its environment by introducing chemical, cellular, and systemic balance. This harmonizing function reduces the effects of unfavorable conditions and stimulates the body’s own immune and healing functions. These adaptogenic substances help the body to adapt to various stressful challenges presented by the environment and reduce the damage inflicted on the body. They tend to promote the body’s own ability to cope successfully with stress, thus prolonging well-being [7,19].
7. Adaptogens are strengthening herbs that bring balance back to the body no matter what the direction of imbalance. They combine both tonic and balancing properties. Examples include Siberian ginseng root bark (*Eleutherococcus senticosus*) and jiaogulan leaves and stems (*Gynostemma pentaphyllum*) [4,20].
8. Adaptogens are nontoxic substances that nonspecifically increase the resistance of an organism to a wide range of harmful influences and normalize its functions [4,7].

In 1968, functional characterizations of adaptogens were proposed by Brekhman and Dardymov:

- An adaptogen is nontoxic to the recipient.
- An adaptogen produces a nonspecific response in the body—an increase in the power of resistance against multiple stressors, including physical, chemical, or biological agents.

- An adaptogen has a normalizing influence on physiology, irrespective of the direction of change from physiological norms caused by the stressor [4].

Various theories regarding the functional nature of adaptogens have been reported by scientists and observed for centuries in Ayurveda and TCM. Ayurveda and TCM have valued adaptogenic substances, calling them “superior herbs” [21]. These special herbs have been anecdotally documented for centuries for their ability to promote longevity and restore health; they have been called “elixirs”, capable of curing sickness and extending life.

### The challenge of establishing adaptogens’ efficacy

According to Winston and Maimes (2007): “It is difficult for so-called adaptogen herbs to be understood scientifically, in part due to the reductionist standards that induce bias and poor conclusions concerning the overall proof of an herb’s efficacy. It is important to recognize that plants do not have single constituents and that while not all of them are chemically ‘active’, they may play an important role in the overall efficacy of the herb” [4].

This biochemical-conundrum has been endorsed by Dr. Guiseppi Nacci, as reported by Kerna (2019). According to Dr. Guiseppi Nacci:

A plant constitutes a single therapeutic unit where the active principles from some characteristic phytocomplex, by binding themselves to or interacting with other molecules, are eliminated during the purifying processes. So, the phytocomplex is the “quintessence” of medicinal plants and not their purified “active principle”. A phytocomplex could be considered as a complex biochemical element constituting the whole pharmacological unit of medicinal plants (Guiseppe, 2008).

Dr. Nacci decried that it is the phytocomplex, not just the purified bioactive principle that renders the functional constituents bioactive and effective [22].

The United States Pharmacopeia (USP) acknowledges that some herbal remedies have been used for hundreds to thousands of years. However, it further states, “scientific evidence regarding these products’ safety and efficacy may be rare or nonexistent” [4]. Also, according to Ioannidis (2005), “the great majority of published research is so deeply flawed that it should be considered essentially worthless” [23]. While micro-aspects of an herb’s constituents can be isolated and analyzed, the broad aspects that have been observed for thousands of years in Ayurveda and TCM are still poorly understood scientifically. Much of the research has been conducted on animals that might metabolize these herbs differently than humans, which is another shortcoming of the research on these adaptogenic herbs.

### The effectiveness of long-term versus short-term use of adaptogenic herbs

Panossian and Wagner (2005) suggested that adaptogens might have far-reaching effects on all endocrine activity when taken long-term. A comparison of the short- and long-term administration of three adaptogenic herbs showed a broader-based impact when given long-term [24]. Thus, this study supported the traditional application of these herbs as tonics for the restoration and preservation of health and vitality.

Specific adaptogens have been noted for their beneficial effects on cardiovascular function, in boosting endurance capacity, and mitigating metabolic dysfunction as well as positive effects on cognition, diabetes, immunity, neurodegeneration, cancer (as an anti-cancer or carcinopreventive agent), *Aedes aegypti* (Diptera: Culicidae), mental stress, and sleep deprivation [25–53].

There are numerous adaptogens; however, some of the most notable, widely researched, and utilized adaptogenic herbs—herein termed, the “Soviet-seven”— are listed as follows:

- American Ginseng (*Panax quinquefolius*, *Panacis quinquefolis*) [25,26].

- Angelica (*Angelica archangelica*) [27,28].
- Ashwagandha (*Withania somnifera*) [29–33].
- Astragalus (*Astragalus membranaceus*) [34–36].
- Eleuthero (*Eleutherococcus senticosus*) also known as Siberian ginseng [37–45].
- Licorice (*Glycyrrhiza glabra*) [46–49].
- Rhodiola (*Rhodiola rosea*) [50–53].

These adaptogens share many properties and modes of action as described previously. For a more comprehensive list and thorough descriptions, actions, images, and applications of adaptogens, refer to the link provided in the Supplementary Information section at the end of this paper.

### Conclusion

The health-promoting, therapeutic, and longevity effects of specific adaptogenic herbs have been recorded for thousands of years. In the mid-1900s and onward, scientific investigation into the various health-promoting and resistance and recovery effect of adaptogenic herbs has been robust. Nevertheless, these herbs remain on the fringe of Western and allopathic medicine, where their full health- and cost-benefits are not being realized fully.

### Conflict of Interest Statement

The authors declare that this paper was written in the absence of any commercial or financial relationship that could be construed as a potential conflict of interest.

### Supplementary Information

The “Ultimate Guide to Adaptogens” (<https://drinkmetta.com/blogs/the-elevated-life/the-ultimate-guide-to-adaptogens>).

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