

Harnessing Nature's Power: Adaptogenic and Anti-Stress Effects of Selected Herbal Plants

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Abstract-

According to various surveys, the stress is the major problem for many diseases ranging from psychiatric disorders to endocrine disorders including diabetes mellitus, hypothyroidism, male sexual dysfunction, peptic ulcer, hypertension, ulcerative colitis etc. In Holy *Geeta*, it is seen that *Arjuna* was one of the sufferers from stress during *Mahabharata* war. At that time Lord *Krishna* takes responsibility to counsel him in *Geeta*). It is one of the eight branches of *Ayurveda*. *Rasayana* drugs are claimed to contribute in revitalizing the tissues and even the psyche thereby maintaining the health of the human being. These are stated to possess rejuvenation power which enhance the *Ojas* of the body i.e. vitality. It is similar to the modern concept of Adaptogenic agents which gives the protection to the human physiological system against diverse stressor. The adaptogens improve the response to stress and help the body to adapt by normalizing physiological processes in times of increased stress. *Ashwagandha* is one of the best medicinal herbs for that purpose & is compared well with *Eleutherococcus senticosus* (Siberian Ginseng), *Panax Ginseng* (Chinese/ Korean Ginseng) in its adaptogenic & antistress activity, hence popularly known as Indian ginseng. That's why we take a review of antistress activity of *Ashwagandha*.

Keywords:

Anti-stress and Adaptogenic Activity of *Withania somnifera*, *Emblica officinalis*, *Asparagus racemosus*, *Ocimum sanctum*, *Tribulus terrestris*, *Piper Longum*, *Boerhaavia diffusa*, *Panax ginseng*, *Rhodiola rosea*, *Carum carvi*.

Introduction-

Stress can be described as the sum total of all the reactions of the body to a stimulus, which disturb the normal physiological condition and result in a state of threatened homeostasis and has been defined as a nonspecific response of the body to any demand imposed on it (Selye 1936). In its most simplified sense, stress is what one feels when life's demands exceed one's ability to meet those demands. Stress is an internationally recognized phenomenon fortified by advancement of industrialization in a demanding civilization. In fact, every individual is likely to face stressful situations in day-to-day life from headaches to heart disease and immune deficiency to digestive problems. Thus, stress is a factor in many illnesses (Selye 1998). ⁽¹⁾ An adaptogen produces a non-specific response in an organism; i.e., an increase in 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. An adaptogen is incapable of influencing normal body functions more than required to gain non-specific resistance. ⁽²⁾ In this modern era, stress has become an integral part of human life. It is vital that stress is kept under control and normal functioning is not hampered due to excessive stress. Stress is considered to be any condition which results in perturbation of the body's homeostasis. If the level of stress is extreme, the homeostatic mechanisms of the organism become deficit and the survival of the organism is threatened. Stress has been postulated to be involved in the etiopathogenesis of a variety of disease states, viz; hypertension, peptic ulcer, diabetes, immunosuppression, reproductive dysfunctions and behavioral disorders like anxiety due to involvement of the central nervous system (CNS), endocrine system, and metabolic system ⁽³⁾. As stress is linked to many diseases, research on an effective antistress agent (adaptogen) from plants has gained importance. We report the investigations on the adaptogenic property of a standardized extract of *Bacopa monniera* against acute (AS) and chronic stress (CS) models in rats. Panax root powder (*Panax quinquefolium*) was taken as a standard. Male SD rats, weighing 180–200 g, exposed to immobilization stress for 150 min once only for AS and for seven consecutive days in CS, were fed with *B. monniera* or *Panax* root powder daily for 3 days in AS and for 7 days in CS, 45 min prior to each exposure of stress. Rats were sacrificed immediately after stress, the blood was collected, and the plasma was separated out for biochemical estimation. ⁽⁹⁾ *Rhodiola rosea* is a popular plant in traditional medical systems in Eastern Europe and Asia with a reputation for stimulating the nervous system, decreasing depression, enhancing work performance, eliminating fatigue, and preventing high altitude sickness. *Rhodiola rosea* has been categorized as an adaptogen by Russian researchers due to its observed ability to increase resistance to a variety of chemical, biological, and physical stressors. Its claimed benefits include antidepressant, anticancer, cardioprotective, and central nervous system enhancement. Research also indicates great utility in asthenic conditions (decline in work performance, sleep difficulties, poor appetite, irritability, hypertension, headaches, and fatigue) developing subsequent to intense physical or intellectual strain. The adaptogenic, cardiopulmonary protective, and central nervous system activities of *Rhodiola rosea* have been attributed primarily to its ability to influence levels and activity of monoamines and opioid peptides such as beta-endorphins. ⁽¹⁰⁾ Herbal formulations have been in use for many years not only in Asian countries but also globally for human well-being. The herbal formulations claimed to enhance physical endurance; mental functions and non-specific resistance of the body have been termed as adaptogens. ⁷ The potential utility of safer and cheaper herbal medicines as antistress agents have been reported as they can withstand stress without altering the physiological functions of the body. Various herbs like *Withania somnifera*, *Emblica officinalis*, *Asparagus racemosus*, *Ocimum sanctum*, *Tribulus terrestris* and *Piper longum* are claimed to have immunomodulatory, adaptogenic, anabolic effects and the ability to improve vital energy. ⁽¹¹⁾ The reality of adaptogens is that they are effective tonics and can be taken daily for overall health. In fact, throughout the world millions of people are using these products on a daily basis.



(Fig.1)

Many of the adaptogens that are commonly used today have a history of use that goes back hundreds and thousands of years. Over that time, a vast amount of experience has been gained that has gone toward understanding their therapeutic applications. Adaptogens can greatly increase the effectiveness of some modern drugs, including antibiotics, anxiolytics (anxiety relief), antidepressants, and hypoglycemic agents. They also can reduce, and in some cases eliminate, the side effects of some drugs. They have a proven record of being safe, efficacious, and quite versatile in their treatment of many conditions. ⁽¹²⁾ Studies indicate ashwagandha possesses anti-inflammatory, antitumor, antistress, antioxidant, immunomodulatory, hemopoietic, and rejuvenating properties. It also appears to exert a positive influence on the endocrine, cardiopulmonary, and central nervous systems. The mechanisms of action for these properties are not fully understood. Toxicity studies reveal that ashwagandha appears to be a safe compound. ⁽¹⁵⁾ Stress, as a major cardiovascular risk factor leads activation of sympathoadrenal & hypothalamic pituitary adrenal (HPA) axis & causes oxidative stress induced changes & provide cardio protection in ischemic rats similar to the properties ascribed to adaptogens. Two new glycowithanolides, sitoindoside IX & sitoindoside X, isolated from *Withania somnifera* Dunal, were evaluated for their immunomodulatory & CNS effects like antistress, memory & learning in laboratory animals, because the plant extract was used by practitioners of the Indian system of medicine for similar purpose. Both these compounds (50- 200mg/kg) produced significant anti stress activity in albino mice & rats, augmented learning acquisition & memory retention in both young & old rats. These findings are consistent with the use of *Withania somnifera* in *Ayurveda* to attenuate cerebral function deficits in the geriatrics population & to provide nonspecific host defense. Anti-stress activity associated with glycosides (sitoindoside VII & VIII) present in this plant was reported to the usefulness of *Ashwagandha* as an anti-stress adaptogen. Administered orally (50- 200mg/kg orally) both sitoindoside IX & X compounds also produced significant anti-stress activity in albino mice & rats. They also augmented learning, acquisition & memory retention in both young & old rats. ⁽¹⁶⁾ Shatavari, or *Asparagus racemosus* used for centuries in *Ayurveda* to support the reproductive system, particularly for females, and as a support for the digestive system, especially in cases of excess pitta. In Sanskrit it means “having one hundred roots” and also referred to as meaning “having one hundred husbands”. Shatavari’s name gives reference to its traditional use as a rejuvenative tonic for the female reproductive system. On heavily for all stages of a woman’s reproductive cycle, beginning with the menarche, supporting the female system through lactation and fertility, uterine strength during pregnancy, childbirth and

ample lactation (flow and quantity of milk), and hot flashes, irritability, irregular memory and dryness during menopause. In Ayurveda, Shatavari is uterine tonic.



(Fig. 2)

Pharmacognosy-

1. Scientific Name: *Boerhaavia diffusa* Linn.

Kingdom: Plantae

Family: Nyctaginace

Group: Dicotyledons and

Phylum: Angiosperms.

Other Synonyms of this drug are *B. adsendens*,
B. caribaea, *B. coccinea*, *B. paniculata*, *B. repens*

2. Botanical Name: *Panax quinquefolius*

Family: Araliaceae

Common Names: Sang, Seng

Taste/Energy: Sweet, bitter, slightly cool, and moist.

Parts Used: Root and leaf

Location/Cultivation: American ginseng is native to the eastern United States and Canada, from the Catskill Mountains of New York and the Berkshire Mountains of Massachusetts, north into Ontario, west to Iowa, south to Arkansas and Kentucky, and east through the highlands of Alabama, Georgia, Tennessee, North Carolina, and Virginia.

3. Botanical Name: *Withania somniferae*

Family- Solanaceae

Synonym- Ashwagandha, Asgandh, Asavari

4. Botanical name- *Asparagus racemosus* Wild.

Family- Liliaceae

Synonyms- Bahusuta, Vari, Shatavirya,
Narayani, Bhiru.

5. Botanical name- *Emblica officinalis*

Family- Euphorbiaceae

Synonym- Amla, Indian Goose berry, Avla

Other - American Ginseng • Amla • Ashwagandha • Asian Ginseng Astragalus • Cordyceps • Dang Shen • Eleuthero Guduchi • Holy Basil • Jiaogulan Licorice • Lycium • Prince Seng • Reishi • Rhaponticum Rhodiola • Schisandra • Shatavari • Shilajit.

Methods and several activities -

Antistress / Adaptogenic:

Study of ethanol extracts of roots of *B. diffusa* showed increased stress tolerance in swim endurance test and cold restrains stress. Immunomodulatory activity was shown by increased carbon clearance, indicating stimulation of the reticuloendothelial system. There was an increase in DTH response to SRBC in mice, corresponding to cell mediated immunity and indicating stimulatory effects on lymphocytes and accessory cell types. ⁽⁴⁾ Hydroethanolic extract (80%) of *Boerhaavia diffusa* (HEBD) and a polyherbal formulation (Punarnava mandur) *Boerhaavia diffusa* were compared for their antistress activity using Cold restraint stress model. Punarnava mandur contains *Boerhaavia diffusa*, mandur bhasm, varun, bharangi. Adaptogens seem to be useful during both adrenal hyper stress as well as adrenal hypo fatigue. By definition, an adaptogen implies the capability for be directional or normalizing effects. The most important adaptogens for the adrenals include *Panax Ginseng*, Siberian Ginseng, Ashwagandha, Rhodiola, *Boerhaavia diffusa*, and Holy basil Leaf Extract. *Boerhaavia diffusa* (PUNARNAVA) has the ability to support both adrenal over and under activation. In stressful conditions it has demonstrated the ability to buffer the elevations of serum cortisol and prevent the suppression of the immune system that takes place with elevated cortisol. On the other hand, *Boerhaavia diffusa* has also demonstrated the ability to improve cortisol levels with end stage adrenal exhaustion. The treatment with the watery extract from the root of *B. diffusa* induced leukocytosis with predominant neutrophils, associated to the phagocytosis ability and it was bactericidal to the neutrophils and the macrophages. ⁽⁵⁾ *Boerhaavia diffusa* has the ability to support both adrenal over and under activation. In stressful conditions it has demonstrated the ability to buffer the elevations of serum cortisol and prevent the suppression of the immune system that takes place with elevated cortisol ⁽⁶⁾ Induction of forced swim stress to the animals produced a significant increase in VMA and decrease in ascorbic acid excretion compared with their respective basal excretion in normal condition. Both the parameters were found to return to their normal levels in three to four days after withdrawal of stress. Daily treatment of *Carum carvi*. to the animals under normal condition produced no change in the excretion of VMA and ascorbic acid compared with normal basal levels indicating that *Carum carvi* did not alter excretion of VMA and ascorbic acid in normal condition. Daily administration of *Carum carvi* one hour prior to the induction of stress inhibited the increase in VMA and decrease in ascorbic acid excretion which was manifested during stress alone. The inhibition was found to be significant at all dose levels in a dose dependent manner. ⁽⁷⁾ A variety of stress situations have been employed to investigate the consequences of stress and to evaluate antistress agents, and the lack of consistency of stress protocols and their biological consequences is astounding. Acute or short-duration stress appears to have limited aversive effects on the individual since the body sets in motion an array of physiological, biochemical and endocrine responses to counter stress effects. However, chronicity and excessiveness of the stressor, and the inability of the organism to cope with the stress. As such, a workable model of experimental stress has to incorporate the factors of chronicity, unpredictability and the inability to escape from the stressor. The experimental model

used in this study fulfils these criteria and has been shown in earlier studies to induce significant physiological, biochemical and neurochemical perturbations that could be attenuated by putative adaptogenic agents comprising of herbal rasayana formulations in rats. ⁽⁸⁾ The pretreatment of *B. monnierea* at lower dose reversed the AS-induced ulcer index, adrenal hypertrophy, hyperglycemia, AST, and CK activities. This clearly demonstrates its potential antistress activity. The same extract at higher dose was able to revert AS-induced adrenal hypertrophy, atrophy of spleen, hyperglycemia, ALT, and AST activities. The decrease in the adrenal gland weight shows its potential role in attenuating the activation of HPA axis. The involvement of HPA axis during stress causes adrenal enlargement, spleen atrophy ulcers, and metabolic changes. Pretreatment with *P. quinquefolium* only reverted AS-induced spleen atrophy, ALT, AST, and CK activities but was unable to produce any significant effect on ulcer index, adrenal hypertrophy, and hyperglycemia. Thus, it seems to have a direct action on the peripheral metabolism and enzymes in AS. The main axis of stress was not attenuated by this pretreatment during AS. CS leads to a prolonged activation of HPA axis; thus, more pronounced effect on ulcer index and adrenal gland weight was found. The prolonged activation of stress hormones results in gluconeogenesis after utilization of the primary carbohydrate source during the AS demand on the first exposure. Thus, it mobilizes the lipids' sources for energy substrate. Pretreatment with *B. monnierea* extract at low dose was able to restore CS-induced ulcer index and AST activity only, while the same at higher dose reverted ulcer index, adrenal hypertrophy AST, and CK activities. Pretreatment with *B. monnierea* in CS resulted in the elevation of the glucose level in the circulation, which can be easily available energy substrate and help the organism to combat the stress demand at its internal and external environment. This elevation of the glucose in the CS by bacopa treatment represents its restorative properties, which can be achieved by enhancing the enzymes involved in glycogenolyses and gluconeogenesis, which are the main rate-limiting step in conversion of the noncarbohydrate source to carbohydrate. Pretreatment with *P. quinquefolium* also reversed ulcer index, adrenal hypertrophy, AST, and CK. Similarly, other adaptogens such as *W. somnifera* and *O. sanctum* has been reported to be effective against stress-induced gastric ulcers and adrenal gland hypertrophy; therefore, the profile of the *B. monnierea* is similar to *W. somnifera* and *O. sanctum*. Here, *B. monnierea* at higher dose and *P. quinquefolium* are showing antistress effect by attenuating the systemic HPA axis response. This shows that *B. monnierea* is effective in both. As well as in CS via attenuating the HPA axis. *P. quinquefolium* treatment attenuates the HPA axis response only in case of CS but fails during AS. The other reversal during the AS may be the peripheral effects of the *P. quinquefolium*, which may be the same in case of low dose of *B. monnierea* treatment during the CS. ⁽⁹⁾ *Rhodiola rosea* appears to offer generalized resistance against physical, chemical and biological stressors in rats and other animals studied. Evidence also suggests cardioprotective and anticancer benefits in animals. In the test of swimming "to the limit," *Rhodiola rosea* administration increased the swimming time of rat's 135-159 percent. Working capacity of the rats consistently improved throughout the supplementation period. ⁽¹⁰⁾ When a person is under stress, more stress hormones are released and manufactured. Adaptogens help the adrenal glands respond more effectively and efficiently to the excess in hormones. When stress stops, adaptogens help the adrenal glands shut down more quickly.

Immunomodulatory activity:

Adaptogens also support adrenal function by allowing cells access to more energy and preventing oxidative damage. Amla is used to prevent and treat damage associated with connective tissue

disorders such as rheumatoid arthritis and lupus. Ashwagandha is used to treat fibromyalgia and autoimmune diseases such as rheumatoid arthritis and polymyositis. Guduchi is used to modulate excessive immune response in autoimmune diseases such as rheumatoid arthritis. It can also enhance uric acid excretion and relieve arthritis with accompanying gout. Holy basil oil is used topically for arthritis. ⁽¹²⁾ It is worth noting that, along with the common feature associated with all plant adaptogens, namely, induction of a state of non-specific resistance in stress, these drugs exhibit various specific effects under different conditions. For example, it seems that the most important effects of *R. rosea* extract related to improvements in mental performance, memory and learning. Although adaptogens are not officially accepted in modern medicine, PG finds extensive use as an antistress remedy. Ayurveda documents several plants, including WS, which are categorized as rasayanas. The properties ascribed to rasayanas in Ayurveda are remarkably similar to those of adaptogens. WS has been subjected to experimental studies using acute stress paradigms and shown to have significant stress-attenuating activity in addition, WS has several properties generally associated with adaptogens including immunomodulatory, cognition-promoting anti-inflammatory antioxidant radiosensitizing and mood stabilizing behavioral effects in experimental animals. Limited clinical studies appear to confirm the adaptogenic antistress action of WS. A variety of stress situations have been employed to investigate the consequences of stress and to evaluate antistress agents, and the lack of consistency of stress protocols and their biological consequences is astounding. Acute or short-duration stress appears to have limited aversive effects on the individual since the body sets in motion an array of physiological, biochemical and endocrine responses to counter stress effects. However, chronicity and excessiveness of the stressor, and the inability of the organism to cope with the stress, appear to induce the syndromal state described by Selye in 1936. As such, a workable model of experimental stress has to incorporate the factors of chronicity, unpredictability and the inability to escape from the stressor. ⁽¹³⁾

Antistress Effect -

To evaluate the antistress effect of WS, an alcohol extract from defatted seeds of WS dissolved in normal saline was given (100 mg/ kg intraperitoneally as a single dose) to 20-25 g mice in a swimming performance test in water at 28°-30°C. Controls were given saline. The extracts approximately doubled the swimming time when compared to controls. In another study, WS prevented both a weight increase of the adrenals and a reduction in ascorbic acid content of the adrenals normally caused by this swimming test. The authors suggested that WS induced a state of nonspecific increased resistance during stress. Glycosides of WS (sitoindoside VII and VIII, 50 to 100 mg/kg) exhibited significant antistress activity in forced swimming induced immobility in mice, restraint stress induced gastric ulcers in rats, restraint-induced *Withania somnifera* (Ashwagandha) The alcohol extract of WS (100 mg/ kg, twice daily orally on day reduced stress-induced increases in blood urea nitrogen levels, blood lactic acid, and adrenal hypertrophy, but did not affect changes in thymus weight and hyperglycemia in rats. WS reversed the cold swimming-induced increases in plasma corticosterone, phagocytic index, and avidity index to control levels. WS root powder (100 mg/kg orally as an aqueous suspension daily for seven days) given before the swimming test in water at 10°C also increased total swimming time, indicating better stress tolerance in rats. These results indicated a significant increase in plasma corticosterone level, phagocytic index, and avidity index in control rats, whereas these levels were near normal in WS rats subjected to the same test. In a comparative study for antistress activity, finely powdered roots

of WS and *Panax ginseng* (PG), suspended in 2-percent acacia (100 mg/kg in 1.00 mL orally) were given to 18-20 g mice daily for seven days; the swimming test was given on day 8.25 Significant antistress activity, as measured by the swimming endurance test, was found for both compounds. The swimming time was 536.6 minutes for PG, 474.1 minutes for WS, and 163.3 minutes for controls; all differences between groups were significant ($p < 0.05$). Anabolic activity, measured as an increase in body weight, was significant for both herbal extracts but was better in the WS group than in the PG group. If these results could be reproduced in humans, it would support the use of WS in nervous exhaustion due to stress and in cachexia to increase body weight. (15)

The Anti-peroxidative & Antioxidant action of *Withania somnifera* could be attributed to withanolides (sitoindoside VII-X) & withaferin-A (glycowithanolides) present in *Withania somnifera* extract. Besides the presence of other potential sources of antioxidant compounds such as polyphenols, flavonoids & alkaloids, vitamin-C can attribute to the antioxidant efficacy of *Withania somnifera* as In-vitro exposure of goat blood to 1, 4-dioxane & TCE can alter the biochemical parameters, induce oxidative imbalance by reducing antioxidant dioxane / TCE induced oxidative stress. *Ashwagandha* supports sound sleep and antistress effect due to alkaloids and glycosides which can affect elements of the central nervous system and immune system. An important active principle of *Withania somnifera* is *Withaferin-A*, have been shown to possess a remarkable range of therapeutic properties i.e. antistress, antioxidant, immunomodulatory. From this, it is seen that it will be used in *Vata Dosha Pradhana Samprapti*. Clinical trials using *Ashwagandha* for a variety of conditions should also be conducted (16). Shatavari improves varna (complexion), oja and bala (strength). This aids to improve body immunity, vigor and vitality. Charaka have mentioned it under the *vayasthapana mahakashaya* thereby focusing on its rejuvenating and anti-ageing property. (13) Shatavari forms the principle ingredient in many of the Ayurvedic formulations mentioned in the treatises which are basically indicated in various types of gynecological disorders it relieves women stress (14) *Emblca officinalis* have potent antioxidant activity due to the presence of tannoids, tannins, vitamin C and flavonoids.

The pharmacological studies on *Emblca officinalis* fruit have revealed that it has good x Antioxidant, Cytoprotective and immunomodulatory, Antidiabetic, Hypolipidemic, Antitussive, Anticancer, Cardioprotective, Antiulcerogenic, Antiepileptic and Hepatoprotective activity. The root contains ellagic acid and lupeol and bark contains leucodelphinidin. The seeds yield a fixed oil (16%) which is brownish-yellow in color. It has the following fatty acids: linolenic (8.8%), linoleic (44.0%), oleic (28.4%), stearic (2.15%), palmitic (3.0%) and myristic (1.0%). Since *Emblca officinalis* has a number of medicinal properties and is a potent anti-oxidant, the present study was undertaken to evaluate the potential usefulness of fresh fruits of *Emblca officinalis* for antistress and adaptogenic activity in experimental animals. *Withania somnifera*, an established ayurvedic herb used as an adaptogen is used as reference standard. (17)

Conclusion:

The results of review articles are very encouraging & indicate that this herb should be studied more extensively to con-firm these results & reveal other potential therapeutic effects. According to Guna Karma of *Ashwagandha*, due to Snigdha Guna (Unctuous), Balya (Tonic) and Vaya-Sthapana (Anti-aging) properties of *Ashwagandha*, it directly acts as Rasayana. This along with

Tikta Rasa (Bitter) and Laghu Guna (Light) acts on Dhatwagni for Sukshma Pachana karma (Metabolism) to produce Prakrut Dhatu (seven primitive matter). It ultimately results in Ojas Nirmiti (governing the immune system). It will break the pathology and help to maintain the strength of the body to stand during stress. Also, Ashwagandha supports sound sleep and anti-stress effect due to alkaloids and glycosides which can affect elements of the central nervous system and immune system. An important active principle of *Withania somnifera* is Withaferin-A, have been shown to possess a remarkable range of therapeutic properties i.e. antistress, antioxidant, immunomodulatory. From this, it is seen that it will be used in Vata Dosha Pradhana Samprapti. Clinical trials using Ashwagandha for a variety of conditions should also be conducted.

References:

1. Koppula S, Kopalli SR, Sreemantula S. Adaptogenic and nootropic activities of aqueous extracts of *Carum carvi* Linn (caraway) fruit: an experimental study in Wistar rats. *Australian Journal of Medical Herbalism*. 2009;21(3):72.
2. Desai SK, Desai SM, Navdeep S, Arya P, Pooja T. Antistress activity of *Boerhaavia diffusa* root extract and a polyherbal formulation containing *Boerhaavia diffusa* using cold restraint stress model. *Int J Pharm Sci*. 2011;3(1):130-2.
3. Murti K, Panchal MA, Lambole V. Pharmacological properties of *Boerhaavia diffusa*-a review. *Int J Pharm Sci Rev Res*. 2010;5(2):107-10.
4. Rajpoot K, Mishra RN. *Boerhaavia diffusa* roots (Punarnava mool)–review as rasayan (rejuvenator/antiaging). *International Journal of Pharmaceutical and Biomedical Research*. 2011 Oct;2(4):1451-60.
5. Rao PP. Ophthalmic uses of *Boerhaavia Diffusa* L. (Punarnava).
6. Koppula S, Kopalli SR, Sreemantula S. Adaptogenic and nootropic activities of aqueous extracts of *Carum carvi* Linn (caraway) fruit: an experimental study in Wistar rats. *Australian Journal of Medical Herbalism*. 2009;21(3):72.
7. Pawar VS, Shivakumar H. A current status of adaptogens: natural remedy to stress. *Asian Pacific Journal of Tropical Disease*. 2012 Jan 1;2: S480-90.
8. Bhattacharya SK, Muruganandam AV. Adaptogenic activity of *Withania somnifera*: an experimental study using a rat model of chronic stress. *Pharmacology Biochemistry and Behavior*. 2003 Jun 1;75(3):547-55.
9. Rai D, Bhatia G, Palit G, Pal R, Singh S, Singh HK. Adaptogenic effect of *Bacopa monniera* (Brahmi). *Pharmacology Biochemistry and Behavior*. 2003 Jul 1;75(4):823-30.

10. Deepak R, Bhatia G, Palit G, Pal R, Singh S, Singh HK. Adaptogenic effect of *Bacopa monniera* (Brahmi). *Pharmacol Biochem Be.* 2003 Jul; 75:823-30.
11. Desai SK, Desai SM, Navdeep S, Arya P, Pooja T. Antistress activity of *Boerhaavia diffusa* root extract and a polyherbal formulation containing *Boerhaavia diffusa* using cold restraint stress model. *Int J Pharm Sci.* 2011;3(1):130-2.
12. Winston D. *Adaptogens: herbs for strength, stamina, and stress relief.* Simon and Schuster; 2019 Sep 17.
13. Bhattacharya SK, Muruganandam AV. Adaptogenic activity of *Withania somnifera*: an experimental study using a rat model of chronic stress. *Pharmacology Biochemistry and Behavior.* 2003 Jun 1;75(3):547-55.
14. Ganguly S, Khakhlary K. SHATAVARI (*Asparagus Racemosus* Wil).
15. Mishra LC, Singh BB, Dagenais S. Scientific basis for the therapeutic use of *Withania somnifera* (ashwagandha): a review. *Alternative medicine review.* 2000 Aug 1;5(4):334-46.
16. Gajarmal Amit Ashok, Shende M.B., Chothe D.S. A Review Antistress Activity of Ashwagandha (*Withania Somnifera* Dunal) –
17. N. Naidu 1, P. Padmabhushanam 2, Shaik Harun Rasheed 3 Adaptogenic Activity of Ethanolic Extract of *Emblca Officinalis* Fruits.
18. Al-Hindawi MK, Al-Khafaji SH, Abdul-Nabi MH. Anti-granuloma activity of Iraqi *Withania somnifera*. *J Ethnopharmacol* 1992; 37:113–6.
19. Anisman H, Kokkinidis L, Sklar LS. Neurochemical consequences of stress. In: Burchfield SR, editor. *Stress. Psychological and physiological interactions*; 1984. p. 67–98.
20. Begum VH, Sadique J. Effect of *Withania somnifera* on glycosaminoglycan synthesis in carrageenin-induced air pouch granuloma. *Biochem Med Metab Biol* 1987; 38:277.
21. Bhattacharya SK. Evaluation of adaptogenic activity of *Trasina*, an Ayurvedic herbal formulation. In: Mukherjee B, editor. *Traditional medicine.* New Delhi: Oxford and IBH Publishing; 1993. p. 320–6.
22. Bhattacharya SK. Nootropic effect of *Mentat*, a psychotropic formulation, on cognitive deficits induced by prenatal undernutrition, postnatal environmental impoverishment and hypoxia in rats. *Indian J Exp Biol* 1994; 32:31– 6.
23. Bhattacharya SK. Behavioural and physiological perturbations induced by chronic unpredictable footshock stress in rats. Effect of a standardized extract of *Withania somnifera*

(Ashwagandha). Proceedings of international conference on stress adaptation, prophylaxis and treatment, Bose Institute, Calcutta; 1998. p. 39.

24. Bhattacharya SK, Kumar A. Effect of Trasina, an Ayurvedic herbal formulation on experimental models of Alzheimer's disease and central cholinergic markers in rats. *J Altern Complement Med* 1997; 3:327– 36.

25. Bhattacharya SK, Goel RK, Kaur R, Ghosal S. Antistress activities of sitoindoside VII and VIII, new acyl stearyl glucosides from *Withania somnifera*. *Phytother Res* 1987; 1:32– 3.

26. Bhattacharya SK, Kumar A, Ghosal S. Effects of glycowithanolides from *Withania somnifera* on an animal model of Alzheimer's disease and perturbed central cholinergic markers of cognition in rats. *Phytother Res* 1995a; 9:110– 3.

27. Bhattacharya SK, Kumar A, Jaiswal AK. Effect of Mentat, a herbal formulation, on experimental models of Alzheimer's disease and central cholinergic markers in rats. *Fitoterapia* 1995b; LXVI:216– 22.

28. Bhattacharya SK, Satyan KS, Ghosal S. Antioxidant activity of glycowithanolides from *Withania somnifera*. *Indian J Exp Biol* 1997a; 35:236– 9.

29. Bhattacharya SK, Satyan SK, Chakrabarti A. Effect of Trasina, an Ayurvedic herbal formulation, on pancreatic, islet superoxide dismutase activity in hyperglycemic rats. *Indian J Exp Biol* 1997b; 35:297– 9.

30. Bhattacharya SK, Bhattacharya A, Sairam K, Ghosal S. Anxiolytic– antidepressant activity of *Withania somnifera* glycowithanolides: an experimental study. *Phytomedicine* 2000a; 7:463– 9.

31. Bhattacharya A, Ramanathan M, Ghosal S, Bhattacharya SK. Effect of *Withania somnifera* glycowithanolides on iron-induced hepatotoxicity in rats. *Phytother Res* 2000b; 14:470– 568.