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# ADAPTOGENIC AGENTS OF PLANT ORIGIN: THERAPEUTIC POTENTIAL AND APPLICATION

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**ABSTRACT:**

Although they can enhance the body's resilience to biological, chemical, and physical stressors while preserving physiological homeostasis, plant-derived adaptogenic drugs have attracted considerable scientific and medical interest. Plant-based adaptogens, which have long been used in traditional medical systems such as Ayurveda, Traditional Chinese Medicine, and folk medicine, are currently being thoroughly studied for their wide range of therapeutic potential. Withania somnifera, Panax ginseng, Ocimum sanctum, Rhodiola rosea, and Eleutherococcus senticosus are examples of well-known adaptogenic herbs that display a variety of pharmacological activities, including anti-inflammatory, immunomodulatory, neuroprotective, anti-fatigue, and anti-stress properties. Modulation of the hypothalamic-pituitary-adrenal axis, control of stress mediators, and enhancement of cellular energy metabolism and immunological responses are the mechanisms that underlie adaptogenic activity. Plant adaptogens have demonstrated promise in the prevention and treatment of stress-related disorders, metabolic syndromes, cognitive impairment, and chronic degenerative diseases due to their multi-targeted effects and favourable safety profiles. Their wider medicinal applicability is hindered by issues like a lack of standardization, diversity in phytochemical content, and a lack of large-scale clinical evidence, despite promising preclinical and clinical findings.

**KEYWORDS:** Adaptogenic Agents; Natural adaptogens, plant origin, phytochemicals, herbal medicine.

## 1. INTRODUCTION:

Non- toxic plants are known as “adaptogens” and claim to help the body withstand stimuli of all kinds, including physical, chemical, and biological ones. These plants and roots have been utilised for ages, in Ayurvedic and Chinese medical practises, but they are currently seeing a revival.

### Adaptogenic plants' benefits:

By maintaining a stable balance in the hypothalamus, pituitary, and adrenal glands, adaptogens exert their molecular action. These play a role in the stress reaction. They function by manipulating the body’s reaction to stress.

We typically experience three levels of stress when our bodies are under pressure

1. Phase of warning and resistance
2. The depletion phase.

The use of herbs as “adaptogens” to reduce stress-related morbidity is one possible benefit of herbal medicine. According to a herbalist, an adaptogenic therapeutic goal is to encourage a healthy physiological response to both internal and external stimuli. In essence, the adaptogen adapts to its surroundings.

Animals and isolated neural cells have been used in studies on adaptogens. They have several physiological consequences, according to researches depends sources:

- Neuroprotective substance
- Anti-fatigue and anti-depressive qualities
- Central nervous system stimulant
- They lessen stress and exhaustion, improve focus, and increase mental work capacity.

Adaptogens aid in your ability to adjust to various types of stress, as the name suggests. They “normalise” a lot of the body's activities and aid in maintaining homeostasis, which is another way to explain how they function.[1]

They accomplish this, among other things, by interacting with the HPA axis, which regulates the release of numerous hormones, one such hormone is cortisol, a main “stress hormone” that also plays a role in aging signs. When we experience the fight or flight reaction.

Cortisol levels increase, which activates our sympathetic nervous system and our adrenal glands.

People who frequently engage in the fight or flight reaction may be in a constant state of stress, which can strain the digestive system and stress the adrenal glands, as well as lead to a variety of problems like exhaustion, weight gain, decreased libido, and acne.

Those in need of an adaptogen:

Young parents, university students, primary caregivers, such as nurses or family members caring for ill patients or relatives, are some of those most susceptible to adrenal difficulties.

Essentially, adaptogens protect us against the negative effects of stress and, as a result, increase our resilience and overall health.[2]

**2. Modals for evaluation of adaptogenic activity:**

Mice responded favourably to both doses of clove extract's anti-stress effects. Using clove extract to prevent anoxic stress-induced convulsions in mice was also successful [3]. Swimming endurance of mice. Pre-treated mice with S. cardifolia extract showed significant swimming improvement, as well as a reduction in increased WBC length, plasma cortisol, and blood sugar [5]. Adult male Wistar rats underwent a modest random footshock treatment once a day for 21 days [6]. In a rat model, rhodiola rosea extracts first showed an anti-inflammatory activity in formaldehyde-induced arthritis, carrageenan-induced paw oedema, and nystatin-induced paw oedema. COX-2 and phospholipase A2 activity were inhibited more successfully by rhodiola rosea extraction than COX-1 activity. Salidroside also reduced inflammation in mice exposed to lipopolysaccharide by reducing the generation of pro-inflammatory cytokines (TNF, IL-1, and IL-6) and in vivo by blocking the NF-B and MAPK signalling pathways [21].

**3. Pharmacology of adaptogens:**

The ability of the body to withstand and adjust to physical, chemical, biological, and psychological stressors is improved by adaptogens, a special class of pharmacologically active compounds that are mostly derived from plants. Adaptogens have pleiotropic effects and help restore normal physiological functioning without upsetting normal homeostasis, in contrast to traditional medications that target certain targets.

The hypothalamic-pituitary-adrenal (HPA) axis, which is essential to the stress response, is modulated by adaptogens at the molecular and cellular level. They inhibit excessive activation of stress pathways and lessen stress-induced damage by controlling the release of stress hormones, including cortisol and catecholamines. Additionally, adaptogens

improve energy metabolism and stress tolerance by influencing the sympathoadrenal system.

Through scavenging free radicals and boosting endogenous antioxidant defense mechanisms, including superoxide dismutase, catalase, and glutathione, adaptogens significantly reduce oxidative stress. These processes shield tissues and cells against oxidative damage brought on by stress and aging-related deterioration.

Additionally, by boosting both innate and adaptive immune responses, adaptogens exhibit immunomodulatory effects. They increase resistance to infections and inflammatory situations by controlling the synthesis of cytokines, boosting the activity of macrophages and natural killer cells, and enhancing immunological surveillance. By inhibiting pro-inflammatory mediators, including prostaglandins, nitric oxide, and inflammatory cytokines, many adaptogens also have anti-inflammatory qualities.

Adaptogens have neuroprotective, anxiolytic, and cognitive-enhancing effects from a neuropharmacological perspective. They increase mood, memory, mental performance, and resistance to mental tiredness by modulating neurotransmitters like serotonin, dopamine, and gamma-aminobutyric acid (GABA). Additionally, adaptogens promote cellular energy metabolism and mitochondrial activity, which increases physical endurance and lessens weariness.[29]

**4. Molecular targets of the effectors that mediate adaptogenic effects**

The stress hormones cortisol and neuropeptide Y (NPY), as well as several significant adaptogenic stress response mediators, including nitric oxide, stress-activated protein kinases, heat shock proteins (HSP70 and HSP25), and the FOXO (DAF-16) transcription factor, have been implicated in mediating the adaptogenic effects of plant extracts in both human and animal studies (e.g., Rhodiola, ginseng, Withania, etc.). The process of stress adaptation is orchestrated by several mediators (which may also be involved in ageing or disease pathology), and none of their contributions can be calculated with any degree of confidence.

On the basis of the findings of in vitro and ex vivo investigations utilising cells of both human and animal origin, several reviews outline the potential mechanisms of action of adaptogens. Antiaging medications are thought to have as their pharmacological targets HSP70 and heat shock factor-1 (HSF1). The intended patient population, such as elderly people who are more vulnerable to stress, cannot employ the compounds used to increase

HSP70 because they are often cytotoxic and do not protect against stress. Fortunately, plant adaptogens can be administered repeatedly and at a very large dose range (up to 3000 mg/kg of rat body weight) (over several months).

It has been demonstrated that adaptogens have anti-stress properties that prevent the death of Lymnaea stagnalis pond snail eggs from heat shock, menadione-induced oxidative stress, and heavy metal intoxication.

Adaptogens, however, were unable to change how heat shock proteins were expressed in the growing organism. Given that HSP70 expression under stressful settings is already maximal in young organisms and only decreases with ageing, this may be expected. HSP70 is greatly raised by other adaptogens. rats' focus and increases their endurance, exhausted from prolonged swimming [29] [30].

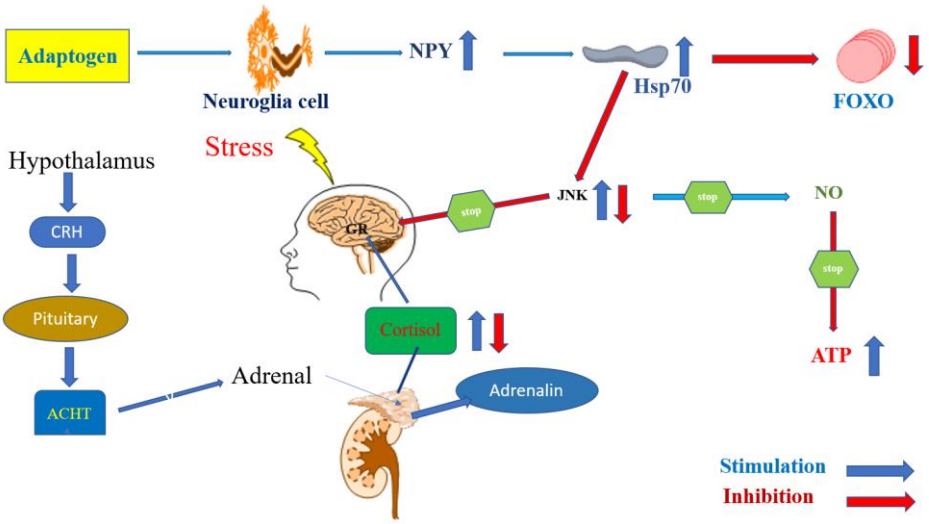
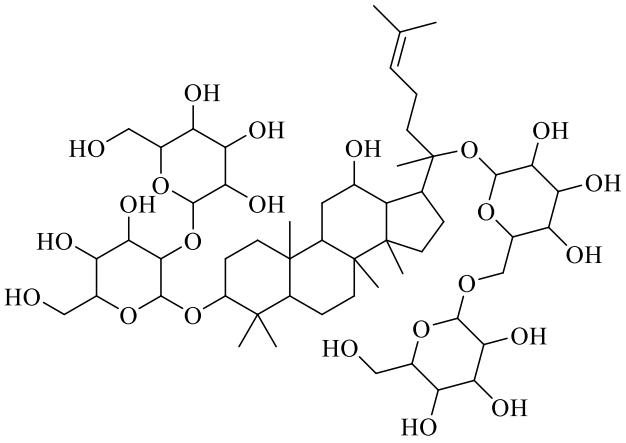


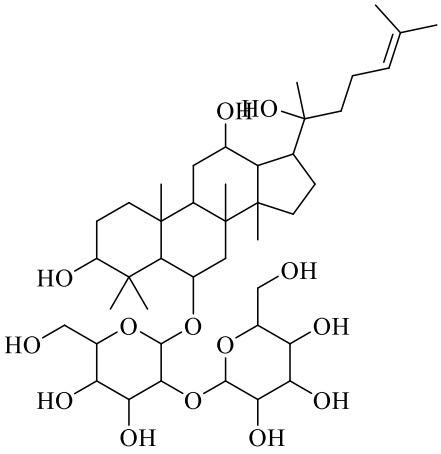

**Figure 1. Hypothetical action of adaptogens.**

**5. Active Molecules:**

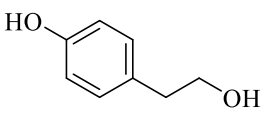
Chemically, the adaptogens are often either tetracyclic triterpenoids/steroids or complex phenolics. Phenylpropanoids and derivatives of phenylethane are among the phenolic chemicals. The protopanaxadiol (PPD), (Rb1, Rb2, Rc, Rd, Rg3, Rh, Rh3, etc.) and protopanaxatriol (PPT), (Rg1, RE, Rf, Rg2, Rh1, etc.). gingerol, shogaol,5- lipoxygenase or prostaglandin, gingerols, Rhodiola rosea (p- tyrosol and phenolic glycoside rhodioloside), ginseng (ginsenoside), and garlic (14 KD–Glycoprotein) [28] [29].



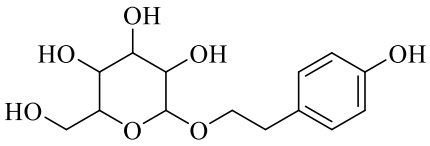
Ginsenoside Rb1



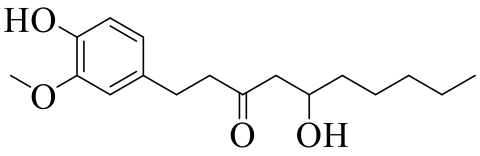
Ginsenoside Rf



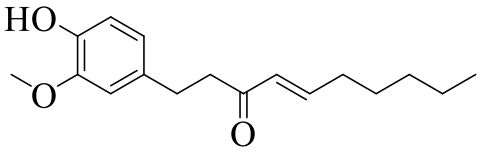
P-Tyrosol



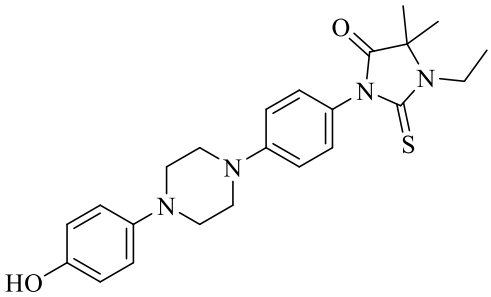
Salidroside



Gingerol



Shogaol



5-Lipoxygenase

**6. Plants having adaptogenic properties:**

**6.1 Clove:** Biological source: *Eugenia caryophyllus.*

Family- Myrtaceae.

Plant parts used – Bud

The goal of the current investigation was to determine whether clove hydroalcoholic extract has any anti-stress properties. The impact of cold was assessed. Stomach ulcers brought on by restriction, sound stress, induced biochemical changes, and anoxic stress induced convulsions.

200 and 100 mg/kg of clove extract were the two distinct oral doses that were given

The typical medication was Zeetress, a well-known anti-stress formulation (14mg/kg p.o.). All of the tested mice responded favourably to both doses of clove extract's anti-stress effects. Clove extract suppressed sound stress-induced biochemical alterations, such as in plasma levels of aspartate aminotransferase, alanine aminotransferase, alkaline phosphate, glucose, cholesterol, and corticosterone, as well as the formation of cold restraint-induced stomach ulcers. Increasing the delay of anoxic stress-induced convulsion in mice using clove extract was similarly successful. [3]

**6.2Green tea:** Biological source: *Camellia sinensis*

Family -Theaceae

Plant parts used – leaves

This study looked into how Ocimum sanctum and Camellia sinensis affected anxiety and depression brought on by stress. Male albino rats weighing 200g or less were used in this investigation.

The elevated plus maze (EPM), open field (OFT), forced swim (FST), and tail suspension test were used to assess the effects of Ocimum sanctum and Camellia sinensis on anxiety and depression. Aqueous extract of O. sanctum C. sinensis (100mg/kg for 6 days) was administered after restraint stress (3 hours per day for 6 days) to significantly increase the % of entry and the amount of time spent in open arms in the EPM. Increased latency and decreased ambulation and rearing were both effective measures of restraint stress, respectively.[4]

**6.3 Bala:** Biological source: *Sida cordifolia*

Family- Malvaceae

Plant parts use – Root

Analysis of Sida cordifolia root's ethanol extract for antistress and adaptogenic use of cold activity to manage stress, and mice swimming stamina pre-treated mice with S. cordifolia

extract displayed substantial swimming improvement, reduced the higher WBCs, plasma cortisone, and blood sugar.[5]

**6.4 Ashwagandha:** Biological source: Withania somnifera

Family- Solanaceae

Plant parts use – Root

Withania somnifera is dual categorised as a rasayana in Ayurveda, the traditional Hindu medicinal system.

Rasayanas are a class of plant-derived medication thought to enhance physical and mental health, increase resistance of the body to disease and various harmful environmental factors, revitalise the body in debilitated conditions, and lengthen lifespan. These qualities are strikingly comparable to those of adaptogens like Panax ginseng (PG), which are said to have in modern medicine. So, against a rat model of chronic stress, the adaptogenic activity of a standardised extract of W. Somnifera root was studied.

Adult male Wistar rats underwent a modest random footshock treatment once a day for 21 days. [6]. Cold swimming stress is known to raise plasma corticosterone levels. Cold swimming stress has also been shown to increase the phagocytic index and avidity index. The current study shows that the above stress indices have been restored in W. somnifera-treated rats. Furthermore, an increase in total swimming time indicates improved stress tolerance in these rats. A similar increase in total swimming time has been reported in mice subjected to swimming stress [27].

**6.5 Tulsi:** Biological source: Ocimum sanctum

Family -Lamiaceae

Plant parts used – leaves

By measuring agglutinating antibodies. Using the widely used agglutination and the sheep erythrocyte agglutination tests and E-rosette formation in albino rats, a methanol Extract and an aqueous suspension of Ocimum Sanctum fear leaves were examined for their immunoregulatory profile to on and sheep erythrocytes.

The results of the study show that humoral immunology is stimulated, as shown by me in antibody titre in the Widely Grad sheep erythrocyte agglutination tests, as well as by the cellular immunologic response, which is shown by the production of Erosettes and lymphocytosis. The study's findings suggest that Ocimum has immunostimulant properties, which may help to explain why the herb has adaptogenic properties [7].

**6.6 Ginger**: Biological source: Zingiber officinale

Family – Zingiberaceae

Plant parts used – Rhizome

Ginger can treat a variety of conditions, including cancer, diabetes mellitus, degenerative diseases like arthritis and rheumatism, digestive problems like indigestion and constipation, ulcers, and cardiovascular diseases like atherosclerosis and hypertension.

It also possesses anti-microbial capabilities, which can aid in the treatment of infectious disorders, and possesses anti-oxidative and ant-inflammatory qualities to slow down the ageing process.

Oxidative stress, which is a key factor in heart diseases, cancer, and the ageing process, is caused when the production of free radicals or reactive oxygen species (ROS) during metabolism exceeds the antioxidant capacity of a biological system. Ginger bioactive compounds, such as **gingerols,** have demonstrated antioxidant action in several models.[8]

**Anti-oxidative stress effects:**

A free radical scavenger is present in the complex phytochemistry, which is created by biological processes. Some free radicals produced during the oxidation process are necessary for the creation of energy [8]. Oxidative stress is brought on by an increase in free radical production, and it can cause DNA damage in such an unbalanced condition. Antioxidant supplementation through dietary components is crucial for maintaining an organism's life [10]. Numerous in vitro and vivo studies have been conducted to examine the anti-oxidative capabilities of ginger and its constituents. The body’s defences can be strengthened by increasing antioxidant status, which will surely shield people from numerous chronic ailments [11] because it has an alpha, beta- unsaturated ketone moiety. Ginger 6-shogaol has shown to have the strongest anti-inflammatory and anti-oxidant capabilities [12].

In one trial, Z. officinal ethanol extract, both by itself and in conjunction with vitamin E, partially reduced the nephrotoxicity brought on by **cisplatin.** The antioxidant defence mechanism in the kidneys mediates this protection [13].

The protective effect of ginger extract against $CCl_4$ and acetaminophen-induced liver damage was investigated in another study, and the results suggested that Z. officinale may help prevent acute liver injury [14].

**Anti-inflammatory effects:**

Through the inhibition of 5- lipoxygenase or prostaglandin synthetase, gingerol, shogaol, and other structurally similar compounds in ginger prevent the formation of prostaglandin and leukotrienes [16]. They also prevent the production of pro-inflammatory cytokines such as IL-1, TNF, and IL-8 [15].

Lantz et al. Demonstrated that extracts containing shogaol do not affect COX-2 expression, while gingerols can decrease LPS- induced COX-2 expression. These findings show that significant ginger constituents can reduce PGE (2) generation [17]. Studies examining the utility of ginger in osteoarthritis patients have shown mixed results. In a single trial, ginger extract was found to significantly lessen the symptoms of knee osteoarthritis [18].

**6.7 Roseroot:** Biological source: Rhodiola rosea

Family- Crassulace

Plant parts used – Rhizome and Root

With a reputation for energising the neurological system, lowering depression, improving work performance, eradicating exhaustion, and preventing high altitude sickness, rhodiola rosea is a common plant in traditional medicine systems in eastern Europe and Asia.

Russian researchers have classified R. rosea as an adaptogen because of it's know capacity to boost defence against a range of chemical, biological, and physical stressors.

The benefits it is said to provide include antidepressant, cancer prevention, cardioprotective, and improved central nervous system. 12 novel compounds have been isolated out of 28 isolated compounds from the root and above-ground parts of R. rosea. The biologically active substance contains in the roots include organic acids, flavonoids, tannin, and phenolic glycosides.

The 2 compounds isolated from its roots for the stimulating adaptogenic properties of R. rosea were identified as p-tyrosyl and the phenolic glycoside rhodioloside [20].

At a dose of 250mg/kg body weight in a rat model, rhodiola rosea extracts initially demonstrated their anti-inflammatory effect in formaldehyde induced arthritis, carrageenan, and nystatin- induced paw oedema. Cyclooxygenase-2 (COX-2) and phospholipase $A_2$ activity were more successfully suppressed by rhodiola rosea extraction than COX-1 activity.

Salidroside also reduced inflammation by preventing the synthesis of pro-inflammatory cytokines (TNF, IL-1and IL-6) and in vivo in mice exposed to lipopolysaccharide, via blocking the NF-B and MAPK signalling pathway [21].

**6.8 Ginseng:** Biological source: Panax ginseng

Family- Araliaceae

Plant parts use – Root

The primary functional elements of ginseng are a class of saponins called ginsenosides (panaxoside). They are steroid glycosides having a carbohydrate chain and a recognisable steroid core. Ginsenosides can be divided into two groups, the four -ring carbon skeleton dammarane and the five-ring carbon skeleton oleanane, based on their aglycones (non-sugar moiety). The protopanaxadiol (PPD), (Rb1, Rb2, Rc, Rd, Rg3, Rh2, Rh3, etc.), and the protopanaxatriol (PPT), (Rg1, Re, Rf, Rg2, Rh1, etc.), are two further kinds of dammarane [22].

P. quinquefolius L. root methanol extract was tested for its hypoglycaemic effects in a mouse model of type-2 diabetes. Blood glucose, plasma cholesterol, and low-density lipoprotein (LDL) levels were significantly reduced in the treated group, whereas the levels of glycogen and high-density lipoprotein (HDL) were significantly higher. In a mouse model of Type-1 and Type-2 diabetes, the preventive benefits of P-quinquefolium on diabetic nephropathy were assessed.

Alcoholic extract (200mg/kg) was given orally for two or four months, which significantly reduced NF-B levels and prevented oxidative damage. Ginseng dramatically reduces the extracellular matrix protein and vasoactive factor upregulation brought on by diabetes in the kidneys [23].

**6.9 Garlic:** Biological source: Allium sativum

Family- Liliaceae

Plant parts used – Rhizome

It is regarded as a strong spice and a medication with a wide range of medicinal qualities, including antibacterial, anticancer, and anticoagulant effects.

The 14-KDa glycoprotein, one main protein, has been identified and purified. There is evidence that this protein possesses immunomodulatory properties. Two types of garlic were employed in this study: freshly produced garlic and commercial garlic tablets. Both sources of garlic increased the delayed type hypersensitivity (DTH) response, with 20mg/kg exhibiting the greatest augmentation [24].

**6.10 Turmeric:** Biological source: Curcuma longa

Family- Zingiberaceae

Plant parts used – Rhizome

Anti-inflammatory, antioxidant, anticancer, anti-viral, and antibacterial activities are all present in turmeric. Additionally, it could be therapeutic, which has advantages in daily life. When disinfecting burns and cuts, it functions as an antiseptic. It possesses antidiabetic, antiapoptotic, antiangiogenic, and immunomodulatory characteristics because it controls insulin levels. It lessens the risk of childhood leukaemia, melanoma, cancer cell metastasis, and platelet aggregation (antithrombotic). Due to its anti-inflammatory qualities, it also functions as a natural pain reliever. As a result, it is employed in the management of arthritis. It lowers blood cholesterol, aids in liver and fat metabolism cleansing, builds immunological strength, and improves wound healing, among other things [25].

**Antioxidant activity of turmeric:**

| S. No. | Common name | Adaptogenic plants | Part used |
|---|---|---|---|
| | Clove | Eugenia caryophyllus | Bud |
| | Green tea | Camellia sinensis | Leaves |
| | Bala | Sida cordifolia | Root |
| | Ashwagandha | Withania somnifera | Root |
| | Tulsi | Ocimum sanctum | Leaves |
| | Ginger | Zingiber officinale | Rhizome |
| | Roseroot | Rhodiola imbricata | Root |
| | Ginseng | Panax ginseng | Root |
| | Garlic | Allium sativum | Rhizome |
| . | Turmeric | Curcuma longa | Rhizome |

Curcumin has been demonstrated to be a potent oxygen-free radical scavenger. It performs an antioxidant role similar to that of vitamins C and E. It can guard against haemoglobin or lipid-induced oxidants. It is possible to drastically reduce the production of reactive oxygen species (ROS) like $H_2O_2$, superoxide anions, and nitrite radicals by activated macrophages.

**Anti-cancer effect of turmeric:**

Turmeric and curcumin can reduce the activity of numerous prevalent mutagens and carcinogens. Direct anti-inflammatory and free radical scavenging effects, as well as indirectly raising glutathione concentrations, have been linked to the anticancer properties of turmeric and curcumin, assisting in the liver's detoxification of mutagens and carcinogens and preventing the synthesis of nitrosamines. In addition, established that curcumin reduces the mutagenic effects of UV radiation on induration impact [26].

## 7. CONCLUSION:

Plant-based adaptogenic agents offer a viable and comprehensive strategy for strengthening the body's defences against biological, chemical, and physical stresses. Plant-based adaptogens like Withania somnifera, Panax ginseng, Ocimum sanctum, Rhodiola rosea, and Eleutherococcus senticosus modulate the neuroendocrine immune axis, maintain homeostasis, and enhance general physiological resilience, according to a wealth of experimental and clinical data.

They are useful in the treatment of stress-related illnesses, metabolic dysfunctions, cognitive impairment, and chronic degenerative diseases due to their diverse pharmacological activities, which include antioxidant, anti-inflammatory, immunomodulatory, neuroprotective, and anti-fatigue qualities.

Plant adaptogens have therapeutic uses in modern healthcare, nutraceuticals, and preventative medicine in addition to traditional medicine. Long-term usage is supported by their generally good safety profile and natural origin, especially when compared to synthetic drugs that could have negative side effects. However, there are still major obstacles to their broader acceptability and regulatory approval, including inconsistent phytochemical content, a lack of standardization, and a dearth of large-scale clinical trials.

To demonstrate efficacy and safety, future research should focus on thorough pharmacological evaluation, extract standardization, clarification of specific molecular pathways, and carefully planned clinical trials. The therapeutic potential and practical application of plant-derived adaptogenic agents will be further enhanced by integrating traditional knowledge with contemporary scientific methods, establishing them as significant contributors to stress management and overall health promotion.

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