

# An Ayurvedic Perspective on the Function of Immunomodulator Herbs in Cancer

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## Abstract

Humans have relied on herbal remedies for countless years to treat a wide range of illnesses. Plants are a vital source of phytochemicals with a wide range of pharmacological applications, such as alkaloids, polyphenols and glycosides. It is demonstrated by clinical research that certain active ingredients have immunomodulatory properties. A complex phenomenon that can affect any region of the body, cancer is a multifactorial disease. As per the World Health Organization, cancer is the primary cause of death. Recently, there has been an upsurge in the prevalence of cancer disease due to unhealthy eating habits, alcohol and cigarette use, pollution, pesticide exposure, and food residue. Even with the daily advancements in organic food, eating a healthy diet, and treatment protocols, cancer prevention or cure remains a huge global concern in the current context. Thus, the goal of this review study is to use *Rasayana* herbs with immunomodulator activity to enhance immune response, thereby lowering the risk of cancer and improving quality of life for cancer patients.

**Keyword** - *Rasayana*, herbal remedies, immune modulators, and cancer.

## Introduction :

*Rasayana* is known as rejuvenation therapy since it fortifies the body's internal systems, improving longevity, memory, intelligence, skin condition, and energy levels<sup>1</sup>. There is published evidence of a medicinal plant with immunostimulant effects that modulates both specifically and non-specifically. According to descriptions, plants with immunomodulatory qualities such *Asparagus racemosus*, *Withania somnifera*, and *Tinospora cordifolia* having *Rasayana* Properties.

A complex phenomenon that can affect any region of the body, cancer is a multifactorial disease. In the world, it is one of the main causes of sickness and mortality. The difficulty of curing it through many treatment modalities used by different medical systems is a challenge to the medical profession. Cancer treatment involves three fundamental treatment modalities: surgery to remove the afflicted portion, chemotherapy, and radiotherapy. Cancer patients with higher survival rates thanks to radiation or cytotoxic medication therapy experience a decline in quality of life at the same time. When combined with chemotherapy and radiation therapy, *Rasayana* herbs can be beneficial for these individuals. The World Health Organization states that unhealthy diet, alcohol

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consumption, physical inactivity, smoking, and air pollution are common risk factors thought to be connected to cancer. As a result, the body produces more free radicals, which harm tissue and eventually result in illness.

Pesticide use has been strongly linked to cancers such as leukemia, breast cancer, pancreatic cancer, lung cancer, brain cancer, kidney cancer, and non-Hodgkin lymphoma<sup>2</sup>. Certain mutations in genes that control how our cells behave, particularly how they divide and develop, indicate a genetic component to cancer in certain individuals. While there is currently no way for us to fully protect ourselves from this issue, we can lower our risk by adopting certain dietary practices or using immunomodulators, which are drugs that strengthen the immune system. Along with its therapeutic benefits, *Ayurveda* has traditionally placed a strong emphasis on health promotion and prevention. While there is currently no way for us to fully protect ourselves from this issue, we can lower our risk by adopting certain dietary practices or using immunomodulators, which are drugs that strengthen the immune system. Along with its therapeutic benefits, *Ayurveda* has traditionally placed a strong emphasis on health promotion and prevention. Through improving immunity and reviving the metabolism, *Rasayana tantra* is a branch of *Ayurveda* that is only focused on maintaining and promoting health. *Rasayana dravya*, which is referenced in the *Samhita* and other texts, is one of the most valuable immunomodulatory medications found in *Ayurveda*.

#### Data Source<sup>1</sup> :

A variety of research articles from online journals, scientific journals, Ayurvedic Samhitas, and contemporary medical literature were consulted in order to comprehend the concepts of cancer, immunity, immunomodulators, and modern Ayurvedic aspects, as well as the *Rasayana* idea. Evidence-based research was conducted by compiling the immunomodulator and anticancer

effects of *Rasayana* plants. In conclusion, drugs called immunomodulators are used to help the immune system become more balanced or normal. *Rasayana* herbs, which are referenced in old *Ayurvedic* literature, are highly effective immunomodulators against cancer.

#### Material & Methods<sup>2</sup> :

A comprehensive review of books, journals, the internet, research portals, and previous data related to the concept of cancer, immunity, and immunomodulators in *Ayurveda* and a modern aspect was done. Those plants having been considered as *Rasayana* in *Samhita* and *Bhavprakash Nighantu* were selected. Research articles were referred to compile *Rasayana* plants mentioned in *Ayurveda* text which had proved immunomodulatory activities and the anticancerous effect.

#### Ayurvedic concept of cancer

As per the World Health Organization, the term “cancer” encompasses a broad range of illnesses that can impact any region of the body. It is the fast emergence of aberrant cells that expand beyond their typical bounds and have the ability to infect nearby bodily regions and spread to other organs. As a result, the term “cancer” is not used in *Ayurveda*; rather, we can associate it with “*arbuda*” (which means “a lump or mass”) based on certain shared features. *Acharya Sushruta* states that *arbuda* is a slowly growing, large-sized, spherical, deeply entrenched, non-suppurative mass that can cause irregular, mild pain in any portion of the body<sup>3</sup>. The *Doshic* concept— *Vata Pitta, Kapha*— is the fundamental basis of it. Following the manifestation of *Arbuda*, the *doshas* (*Vata*, *Pitta*, and *Kapha*) are vitiated by *mithya ahara* and *vihara* involving *Dhatu*s such as *Mamsa*, *Meda*, *Rakta*, etc. They can be divided into six categories based on the involvement of *dosha* and *dhatu*: *Vataja*, *Pittaja*, *Kaphaja*, *Mamsaja*, *Medaja*, etc. The two categories of *Arbuda* described in *Ayurvedic* texts are *Asadhya*

(incurable) and *Sadhya* (curable), based on the prognosis of the various forms. *Mamsaarbuda*, *Raktaarbuda*, or immovable objects situated in important locations or canals are regarded as *Asadhya* (incurable).

### Concept of Immunity and Immunomodulators

In order to defend animals from invasive germs and prevent organ and tissue damage, the immune system developed (Ford MN and Roach SS. Introductory clinical pharmacology). The immune system's cells include neutrophils, basophils, mast cells, lymphocytes, monocytes, macrophages, and eosinophils. The human immune system's master cell is a lymphocyte. Though they have a similar morphology, lymphocytes are classified into two main populations: T and B lymphocytes, which represent the majority of the population functionally, and NK (natural killer) cells, which make up a tiny portion of circular lymphocytes, the third kind. From lymphoid precursor cells in the bone marrow, these three subtypes of lymphocytes originate. T cells proceed to the thymus, whereas B lymphocytes stay in the bone marrow .

According to Harsh Mohan Textbook of Pathology, there are two primary types of immune systems: 1) natural (nonspecific) and 2) adaptive (specific), which are linked in their physiological roles. Antigen-specific immunity, also known as natural or innate immunity, is thought to be the initial line of protection. It consists of two main parts: humoral (hampered by complement) and cellular (made up of natural killer (NK) cells, neutrophils, and macrophages). "The antigen specificity factor takes adaptive (specific) into consideration. Humoral (made up of antibodies produced by B cells) and cellular (mediated by T cells) are its other two primary components.

According to D. Kumar et al. (2012), immunomodulators are biotic or synthetic substances that have the ability to activate, inhibit, or modify any part of the immune response. Together, they are currently regarded as some of the

most effective instruments available to contemporary medicine for the treatment of illness and wellness. They fall into three broad categories: immunostimulants, immunoadjuvants, and immunosuppressants. By raising the essential level of the immune response, immunostimulants have the potential to operate as preventive and promoter agents, in healthy individuals. Immunotherapeutic drugs are anticipated to be those with immune response impairments (Juyal PD and Singla LD). The mechanisms involve the following: phagocytic activity, natural killer cell activation, immunostimulatory effect on peritoneal macrophages, elevation of serum immunoglobulin level, stimulation of lymphoid cells, modulation of cytokine gene expression, enhancement of cellular immune function, and nonspecific cellular immune system effect (Phatru Patel et al. 2010; G.K. Mallaiah et al. 2016). It may be possible for healthy individuals to maintain a condition free from disease by modulating immune responses through the stimulatory or suppressive action of the medication.

### Concept of Immunity in Ayurveda

*Oja* and *Vyadishamatva* are associated with immune factor in *Ayurveda*. The *parama teja* of the *saptadhatus* is indicated by *Ojas*, which also symbolizes an individual's "Bala" or biological strength. All the *dhatu*s within the body are contained in its essence, or *Sara*. Increasing the body's *Oja-Bala*, which is necessary to protect it against illness, is therefore the main prerequisite. Three categories of *Bala* have been identified by *Acharya Charaka*: *Yuktikrut Bala* (Artificial Strength), which is obtained by a nutritious diet and regular exercise, *Kalaja Bala* (Acquired Strength), which is dependent on external conditions, and *Sahaja Bala* (Natural Strength) which is gained from generation to generation<sup>3</sup>.

When discussing *Vyadhi shamatva*, *Chakrapani Datta*, a commentator on *Charaka*, stated that it signifies *Vyadhi bala virodhitvam* and *Vyadhi*

*utpada* *pratibandhakatvam*<sup>4</sup> .(I) *Vyadhi-balavirodhitvam*: This is the ability to control or endure the intensity of the illness, that is, the ability to impede the illness's advancement.(II) *Vyadhi-utpada* *pratibandhakatva*: The body's ability to withstand medical intervention and prevent the sickness from developing again.

### Concept of Rasayana

The word *Rasayana* is composed of the words *Rasa* and *Ayana*, where *Rasa* can be understood as *Rasa Dhatu* and *Ayana* as carrying. *Rasayana*, thus, refers to that which creates *Rasa Dhatu* as an *Ayana* to provide nourishment to the *Dhatu* that follows<sup>5</sup>. It functions at the *agni* level to improve the nutritional value of *ahara* *rasa* and aids in improved cellular nutrient absorption and circulation. In this

way it feeds the *sapta Dhatu* and finally raises the *Oja* (the body's vital power).

*Rasayana Tantra* is one of the eight clinical Specialties of *Ayurveda*. It refers to nutrition, Natural resistance and geriatrics. Apparently, *Rasayana* means an improved state of Nourishment, which in turn upholds increased Immunity and youthfulness. *Rasayana* can be A drug, diet or even a life style and conduct i.e., *Achar rasayana*, which may be helpful in achieving the above goal. The *Rasayanas* are supposed to strengthen *Oja* and *Bala* i.e., vitality and bio strength with natural resistance against aging and disease. The other benefits of this therapy are the promotion of memory and intelligence, the preservation of youth, luster, complexion and voice.

Given below is the list of some medicinal plants with *Rasayana* action (Rejuvenating action) and proved to have an immunomodulatory effect and anti -cancerous effects (table 1).

Plants / Botanical Name	Family	Chemical constituents	Immunomodulator Activity Researches
<i>Tulsi</i> <i>Ocimum Santum</i>	<i>Labiatae</i>	Essential oils such as eugenol, cavacrol, derivatives of ursolic acid & apigenin	1]Evaluation of immunomodulatory potential of <i>Ocimum sanctum</i> seed oil and its possible mechanism of action (PK Mediratta, KK Sharma, S Singh - Journal of Ethnopharmacology, 2002 – Elsevier)
<i>Guduchi</i> <i>Tinospora cordifolia</i>	<i>Menispermaceae</i>	Alkaloidal constituents such as berberine, tinosporic acid	1] Pharmacological study of <i>Tinospora Cordifolia</i> as an immunomodulator (V D Vaibhav et al. 2010) 2]Immunomodulatory effects of <i>Tinospora cordifolia</i> ( <i>Guduchi</i> ) on macrophage activation (More P, Pai K 2011)
<i>Haridra</i> <i>Curcuma Longa</i>	<i>Zingiberaceae</i>	<i>Curcuminoids</i>	1] Immunomodulatory activity of curcumin (S Antony et al. 1999) 2] Curcumin-albumin conjugates as an effective anti-cancer agent with

			immunomodulatory properties (Aravind SR et al. 2016)
<i>Amalaki</i> <i>Emblica officinalis</i>	<i>Euphorbiaceae</i>	Tannis , vitamin C	1]Immunomodulator role of <i>Emblica officinalis</i> in arsenic-induced oxidative stress and apoptosis in thymocytes of mice (Singh et al. 2013) 2] Evaluation of Immunomodulatory potential of <i>Emblica officinalis</i> fruit pulp extract in mice (R.S Suja et al. 2009)
<i>Neem</i> <i>Azardica Indica</i>	<i>Meliaceae</i>	Azadirachtin , nimbin ,gedunin , Gallic acid , catechin, NB – 2 peptidoglycan	1]Enhancement of immune responses to <i>neem</i> leaf extract ( <i>Azadirachta indica</i> ) correlates with antineoplastic activity in BALB/c-mice (J Beuth, H Schneider, HL Ko – in vivo, 2006 – iv.iarjournals.org)
<i>Yashtimadhu</i> <i>Glycyrrhiza glabra</i>	<i>Leguminose</i>	Glycyrrhizin, polysaccharide	1]Evaluation of immunomodulatory activity of <i>Glycyrrhiza glabra</i> L roots in combination with zing (Mazumder papaya et al. 2012) 2] The immunomodulatory activities of licorice polysaccharides ( <i>Glycyrrhiza uralensis</i> Fisch.) in CT 26 tumor bearing mice (Ayeka et al. 2017)
<i>Ashwagandha</i> <i>Withania Somnifera</i>	<i>Solanaceae</i>	Alkaloids,saponins, Steroidal lactones	1]In Vivo Effects of <i>Ashwagandha</i> ( <i>Withania somnifera</i> ) Extract on the Activation of Lymphocytes(J Mikolai,

			A Erlandsen, A Murison... - The Journal of ..., 2009 – liebertpub.com)
<i>Shatavari</i> <i>Asparagus racemosus</i>	<i>Asparagaceae</i>	Asparagamine A Steroidal saponins, shatavaroside A, shatavaroside B, filiasparsoside C, shatavarins,	1]Immunomodulatory activity Of <i>Asparagus racemosus</i> on systemic Th1/Th2 immunity: Implications for Immunoadjuvant Potential (Gautam Manish et al. 2009) 2]Immunomodulatory activity steroidal saponins from <i>Asparagus racemosus</i> (Sharma U, Kumar N et al. 2013)
<i>Bala</i> <i>Sida cordifolia</i>	<i>Malvaceae</i>	$\beta$ -phenethylamine, ephedrine, pseudoephedrine, S- (+)-Nb- methyltryptophan methyl ester, hypaphorine, vasicinone, vasicinol, choline, and betaine	Extract of <i>Sida cordifolia</i> contain Polysaccharides Possessing Immunomodulatory Activity and Anti-cancer activity (G. Rosmarinic Acid Compounds with Antibacterial Activity (Haroon Iqbal er al. 2021)
<i>Vasa</i> <i>Adhatoda</i> <i>Vasica</i>	<i>Acanthaceae</i>	vasicine, a quinazoline alkaloid, Bromhexine, alkaloids, tannins, saponins, phenolics and flavonoids	Immunomodulatory & anti oxidant properties of methanolic extract of <i>Adhatoda vasica</i> leaf after particulate antigen stimulation in mice(Rana Adhikary et al 2014)

### Guduchi (*Tinospora cordifolia*)<sup>5</sup> :

Anticomplementary and immunostimulating properties have been discovered in the active ingredients of *Guduci* (*Tinospora Cordifolia*), a significant *rasayana* medication. *Guduci* extracts have been the subject of prior research that revealed antidiabetic, anti-inflammatory, and hepatoprotective properties. The in vitro immunohaemolysis of antibody-coated erythrocytes was inhibited by syringin (TC-4). It was discovered that inhibition of the classical complement pathway's C3-convertase was the

cause of the decreased immunohaemolysis. The compounds caused the serum's level of IgG antibodies to significantly rise. Additionally, there was a dose-dependent enhancement of cellular and humoral immunity. Cordioside (TC-2), Cardiofolioside A (TC-5), and Cordiol (TC-7) have all been shown to exhibit macrophase activation. These substances activated the peritoneal macrophases, which resulted in a notable increase in phagocytic activity (Kapil A. and Sharma S., 1997). Remember that both specific and nonspecific immune responses are significantly influenced by

macrophages. Within the context of innate immunity, the phagocytosis of foreign substances by macrophages and other phagocytes plays a role in the control of cellular and humoral immune responses. As effector cells, macrophages provide immunological surveillance against tumor cells.

*Yashtimadhu (Glycyrrhiza glabra)*

It has been discovered that another significant *Rasayana* medication, *Yastimadhu (Glycyrrhiza glabra)*, is immunostimulative. This means that it speeds up the activation of macrophages through lymphocytic transformation and raises leucocyte counts. According to Yamamoto M. (1975), it also possesses antioxidant, anti-inflammatory, and antiallergic properties. Infants' immunoglobulin levels increased in a controlled clinical study using the *Rasayana* drugs *Amalaki*, *Vidang*, and *Atibala (Amalaki compound)*, which is much higher than in situations where multivitamins were used (Tuteja V., 1993).

#### **Curcuma longa L<sup>6,7</sup>:**

*Curcuma longa*, also known as *turmeric (haldi)*, is a herb grown for its rhizome in India. It is a member of the *Zingiberaceae* family. The fragrant, stimulant, antiperiodic, and carminative rhizome is used to treat urinary problems, diarrhea, jaundice, Alzheimer's disease, and liver problems. Turmeric contains a yellow-orange compound called *curcumin*. *Curcumin* has been shown to have nematocidal qualities and to prevent the proliferation of parasites. Because *curcumin* binds to cholesterol receptors on all immune cells, it aids in maintaining the body's homeostasis as the body mounts an immunological response. Prevents pro-inflammatory complex and reactive oxygen species (ROS) from being produced. Turmeric rhizome methanol extract (200 mg/kg) stimulates the innate and adaptive immune systems in a beneficial way. When rhizome extracts were administered to tuberculosis patients, dendritic cell inhibition and T-cell activation were seen.

In equal proportions, a combination of four significant *Rasayana* drugs was discovered to potentiate the cellular and humoral components of immunity: *Guduci (T. Cordifolia)*, *Ashwagandha (W. somnifera)*, *Amalaki (Emblia officinalis)*, and *Tulasi (Ocimum Sanctum)* (Chatterjee S. & Das S.N., 1996). Increases in circulating levels of globulins and other components, as well as neutrophils' microbicidal activity, are noteworthy. In addition to improving T-cell memory, it also markedly increased the number of lymphocytes. According to the study on macrophage function, administering this combination resulted in a significant increase in macrophage cell size, quantity, and phagocytic activity. The results of the chemotaxis test for leucocytes using a phagocytic cell demonstrated a positive result (Gomes A., 1966).

#### **Discussion :**

Cancer is a serious illness that is challenging to fully treat. In a multistage process that often advances from a precancerous lesion to a malignant tumor, it rises from the conversion of normal cells into tumor cells. *Rasayana* dravya has the therapeutic ability to halt the progression of illness and stop it from coming back. It has to do with food and how the body processes it. *Rasayana* Dravyas anticipated working at the level of pathological alterations occurring at the *agni* and *srotus* levels. Better nutrition is made possible by improving the body's metabolism and digestion through the enhancement of *agni*. *Rasayana* dravya functions at the *srotus* level by enhancing microcirculation and supplying the tissues with the right nutrition. The distribution of *Ojas* to the *Dhatus* depends equally on the integrity of the pathways. As such, their purpose is to provide natural resistance against sickness, strengthening *Oja* (vitality) and *Bala* (bio strength).

According to V Praveen Kumar et al. (1998), *Rasayana dravyas* were found to significantly enhance the proliferation of spleen cells, especially when mitogen was present. One component of the

lymphatic system, which is a component of the immune system, is the spleen. It produces white blood cells that fend off infections in addition to storing and filtering blood. Additionally, it was discovered that giving mice *Rasayana* Dravyas boosted the esterase activity in their bone marrow cells, indicating a greater development of lymphoid linkage cells (V Praveen Kumar et al. 1998). *Rasayanas* are effective immunostimulants, as demonstrated by these two functions. The listed plants' immunomodulatory activity was tested in both an in vivo and an in vitro setting.

These plants not only have immunomodulatory properties, but they have also been shown to have anticancer properties against several cell lines. Shiva Aliza deh Nazmi et al. (2018) reported that *Glycyrrhiza glabra* shown anticancer effects on HT-29 Colon Cancer and MCF-7 Breast Cancer Cell Lines, while G. Mallikarjuna et al. (2013) reported on *Sida cordifolia* L.'s role in hepatocellular carcinoma. (Debaashish, Biswas et al., 2018) *Asparagus racemosus* root extracts showed antitumor activity in non-small cell lung cancer A549 c.

Colon cancer cells may be resistant to the anticancer effects of *berberine* derived from *Tinospora cordifolia* (Annalisa Palmieri et al. 2019). The *bilvaleaf* (*Aegle marmelos*) shown cytotoxic effect on the human hepatocellular carcinoma cell line (*Kulprachakarn* K et al. 2020), whereas the extract from *bilva* fruit protected rats against breast cancer caused by DMBA. (Arun Kumar et al., 2020). While *Centella asiatica* extract showed anticancer activity against many tumor types, *Bacopa monnieri* L. demonstrated anticancer potential against MCF-7 and MDA-MB 231 cell line (Md. Nasar Mallick et al. 2015). In liver cancer cells, an aqueous extract of *Tribulus terrestris* Linn was reported to be beneficial (Kim HJ et al. 2011).

There are many different therapeutic applications for *Rasayana* herbs. *Rasayana* may provide protection through immunomodulation, the suppression of free radicals, the strengthening of

cellular detoxification systems, the repair of injured nonproliferation cells, and the replenishment of damaged or mutated cells with new ones. Many of the herbs indicated above have effects that are *deepana* (appetiser), *panchana* (digestion), *balya* (tonic), *brimhaniya* (nourishing), *Medhya* (brain tonic), and *oja vardhaka* (increases vitality), as even the *Ayurvedic* book verifies.

## Conclusion

Numerous risk factors are included in the vast category of disorders known as cancer. While it is impossible to cure cancer or stop it from happening completely, one can try to reduce the risk factors by employing immunomodulator medications to modify the immune system on a daily basis. The potential of *rasayana* plants as immunomodulators is enormous. Combinations like *Chyavanaprash*, *Amalaki Rasayana*, *Gokshura Rasayana*, *Jivanti Rasayana*, and *Bramhi Rasayana* that use these herbs in the form of *avaleha* or *churna* (powder) might be used as adjuvant therapy to contemporary cancer treatment. Furthermore, we should include herbs like *punarnava*, *guduchi*, *bramhi*, *amalaka*, *jivanti*, and *haridra* in our regular diets by preparing energizing dishes like soups or vegetables. It was also discovered that some cancers have a genetic background. Research utilizing these plants as a preventive approach in such individuals with a family history of cancer should be rationally pursued.

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