ISSN 2456-3110
Vol 8 · Issue 3
March 2023

JAiMS
INTERNATIONAL

Journal of Ayurveda and Integrated Medical Sciences

www.jaims.in

JAIMS

An International Journal for Researches in Ayurveda and Allied Sciences

Maharshi Charaka
Ayurveda

Indexed

Journal of
Ayurveda and Integrated Medical Sciences
ISSN 2456-3110
REVIEW ARTICLE March 2023

Role of Ayurvedic Medicinal Plants in Auto-immune disorders and their management

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ABSTRACT

Auto-immune disease is an abnormal condition in which immune system start producing auto-antibodies against constituents of its own tissues. Under normal circumstances immune system will not destroy self-antigens, but in Auto-immune disease breakdown of mechanisms responsible for self-tolerance and induction of an immune response against component of the self-body tissues. Activation of self- reactive clones of T or B lymphocytes generating humoral or cell mediated response against self-antigen. Worldwide up to 700 million peoples are estimate to be suffering from auto-immune disease. According to *Ayurveda* cause of auto-immune disease is due to mechanism of aberrant '*Agni'* and '*Ama'* production may occur at macro and micro level. That *Ama* is full of antigen or the molecules which are mimicking the shape and structure of our healthy tissues. Those molecules are intermediary harmful metabolites which are attacked by our immune system to neutralize. That's how the autoimmune diseases are start. Also, in auto-immune disease different *Dhatvagnis* are involved and *Dhatus* and related *Shrotas* suffer, resulting *Dhatukshay, Ojakshay* occurs and further multiple *Koshtang* and there *Avayav* affected. *Ayurvedic* principles are specific and provide numerous medicinal plants which have immuno-modulator properties, like *Ashwagandha, Amalaki, Guduchi, Pippali, Punarnava, Yashtimadhu, Vidang* etc. the present paper deals with various researches done on *Ayurvedic* medicinal plants in management of Auto immune disease. Detailed description of all these drugs on Auto-immune disease will be mentioned in full paper.

Key words: *Auto-immune disease, Ama, immune-modulator, Ojakshaya*

INTRODUCTION

The immune system usually guards against bacteria and viruses. When it senses the foreign invaders, the immune system sends out fighter cells to attack them. Usually, the immune system know the difference between foreign cells and own cells. In an Autoimmune disorder, the immune system mistakes to recognized, part of your body, like your joints or skin or tissues, as foreign. It releases protein called auto-antibodies that attack healthy cells and further caused variety of diseases. The disease and progression vary from person to person.

Ayurveda based on a holistic view. *Ayurvedic* principles are specific and yet broad enough to facilitate application to and analysis of even the new and emerging disease and syndrome. According to *Ayurveda* cause of auto-immune disease is due to mechanism of aberrant '*Agni'* which produced *Ama* and weak *Ojas.* Also, in auto-immune disease different *Dhatvagnis* are involved. *Ayurvedic* principles are specific and it treats the root cause of disease rather than the symptoms of autoimmune disease. *Ayurveda*

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Submission Date: 14/01/2022 Accepted Date: 22/02/2023

Access this article online

Quick Response Code

Website: www.jaims.in

DOI: 10.21760/jaims.8.3.20

ISSN: 2456-3110 REVIEW ARTICLE March 2023

focuses on restoring, balancing and strengthening the immune system, threw work on *Agni* and *Ojas.* The modulation of immune system response by using *Ayurvedic* herbal medications as a possible therapeutic measure has now become a subject of scientific investigation. It provides numerous medicinal plants which have immuno-modulator properties, like *Ashwagandha, Amalaki, Guduchi, Pippali, Punarnava, Yashtimadhu, Vidang* etc. The present paper deals with various researches done on *Ayurvedic* medicinal plants in management of Auto immune disease.

Auto-immune disease

Autoimmune disease is a condition which is triggered by the immune system initiating an attack on self-molecules due to the deterioration of immunologic tolerance to auto-reactive immune cells.[1] The initiation of attacks against the body's self-molecules in autoimmune diseases, in most cases is unknown, but a number of studies suggest that they are strongly associated with factors such as genetics, infections and/or environment. Autoimmunity is characterized by the reaction of cells (auto reactive T-lymphocytes) or products (autoantibodies) of the immune system against the organism's own antigens (auto antigen). It may be part of the physiological immune response (natural autoimmunity) or pathologically induced, which may eventually lead to development of clinical abnormalities (autoimmune disease).[2]

ADs may be either organ-specific (e.g., thyroid, β-cells of the pancreas), where unique tissue-specific antigens are targeted, or may be more systemic, in which multiple tissues are affected, and a variety of apparently ubiquitously expressed auto antigens are targeted.[3]

Common type of Auto-immune disease are - Type 1 diabetes, Rheumatoid arthritis, Pernicious anemia, Celiac sprue disease, Vitiligo, Scleroderma, Psoriasis, Inflammatory bowel disease, Addison's disease, Hashimoto's disease and many more.

Factor affecting Auto-immune disease

The exact cause of autoimmune disorders are unknown, but some factors may trigger changes that confuse the immune system. Genetic predisposition, environmental factors (including infections) and gut dysbiosis play major role in the development of autoimmune disorder.

For example, one of the most common genetic associations with autoimmune disorder is the protein tyrosine phosphatase gene PTPN22 expressed in lymphocytes. It has been found in patients with many autoimmune disorder, Including Type-1 Diabetes mellitus, Rheumatoid arthritis (RA), Systemic lupus erythematosus (SLE), and autoimmune thyroiditis.[4]

Also, there are a host of environmental factors that trigger autoimmune disorder including Chemical toxicants, heavy metals, viruses, bacteria, emotional stress and drugs etc. For example, Smocking is a known risk for RA. Cigarette smoking may induce citrullination of proteins in pulmonary alveolar cells, which are highly specific for RA as are the HLA associations that are related to the development of these auto-antibodies.[5]

Also, it is clear that the gut micro biota has a profound and long term effect starting at birth on the host immune system. It is also evident that it plays a significant role in auto immune disease both inside and outside the gut.

Autoimmune diseases in Ayurveda - According to Ayurveda

समदोषः समाग्निश्च समधातु मलः क्रियाः।
प्रसन्न आत्मेद्रिय मनः स्वस्थ्यइतिअभिधीयते॥

(सु.सुत्र.15)

The person who is in a state of equilibrium of body's; *Doshas* (humors), *Agni* (digestive fire), *Dhatus* (tissues), *Malah Kriya* (Physiological functions of excretions etc.) and whose *Aatma* (soul), *Indriya* (senses) and *Manah* (mind) is happy all are considered as healthy person. Impaired *Doshas, Agni, Dhatu* and *Malah Kriya* caused diseases.

According to Ayurveda, Autoimmune disorder caused by impaired *Agni* which may produce endotoxins called '*Ama*". That *Ama* full of antigen or the molecules which are mimicking the shape and structure of our healthy

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tissues. Those metabolites they are attack by our immune system to neutralize and same in other tissues. That's how the autoimmune disease start.

Also, in Autoimmune disease different *Dhatwagnis* are involved and *Dhatus* or related *Shrotas* may suffer. When *Agni* turns against normal *Dhatus*, destruction of *Dhatus* and their *Avayav* takes place, because in normal health there is a coordinated hormonal control over *Agni*. This controll is maintained by *Doshas-Dhatus-Malas* and *Ojas.* In autoimmune disease this control is lost at different domains.

In auto immune disorder the *Doshas* we can see how individuals with a *Pitta* predominant constitution would be prone to Autoimmune disorders. But *Pitta* doesn't act alone. When *Vata Doshas* increases in the presence of high *Pitta*, it's like wind blowing on a fire. The inflammation spreads throughout the body. Eventually the *Agni* deposit in a weak spot and the disease progresses at that site.

In initial stage due to constant unhealthy life style and *Virudh Aahar* accumulation of *Mala* [*Mala Sanchay*] and impaired *Jatharagni* begins formation of *Ama* in the body. In secondary stage due to *Pitta* dominancy over activity of *Agni Bhav* takes place resulting destruction of *Dhatu* function, *Dhatukshaya* and *Ojakshaya* occurs. In this stage inflammation take place. In advance stage of Autoimmune disease *Vata Prakopa* will lead to further pathologies in different *Shrotas*. *Agni* will go beyond its controlled. *Samagni* become *Tikshagni* and it is responsible for excessive *Dhatupaka* and multiple *Koshtangs* under going to be *Paka* as well as *Koshtanga* related organs.

Management of autoimmune disease in *Ayurveda*

Modulation of immune response by using *Ayurvedic* herbal medications as a possible therapeutic measure and it is being really practiced by the *Ayurvedic* practitioners for centuries. Enhancement of immune responsiveness of an organism against a pathogen by non-specifically activating the immune system using immuno-modulatory agents of plant origin is concept behind treating Autoimmune disorders in Ayurveda.[6]

Herbs, which affect the immune system in specific or non-specific mode, can be categorized under immuno herbs that are covered under the broad umbrella of *Rasyana* in *Ayurveda*.[7] Here we have described the potential role of the *Ayurvedic* medicinal plants against Autoimmune disorders as immuno-modulators. As discussed below, several medicinal plants exhibit not only immunomodulatory activity but also a wide range of antioxidant, antiasthmatic, antiarrhythmic, anti-inflammatory, hepatoprotective, hypocholesterolemic, antifungal, cardiotonic, diuretic, and other medicinal activities.

1. ***Abutilon indicum* linn. (Malvaceae) -** Stimulates immune system, affects humoral immunity as shown by its effect in the indirect hemagglutination test, serum immunoglobulin levels. Also affects cell-mediated immunity, showing significant increase in neutrophil adhesion and carbon clearance.[8]

2. ***Adhatoda vasica* Nees (Acanthanceae) -** The alcoholic extract of *A. vasica* is reported to reduce the count of neutrophils, thus diminishing the phagocytosis activity. The extract was found responsible to decrease in delayed-type hypersensitivity reactions and inhibitory effect on T lymphocytes and also reported to possess human immunodeficiency virus (HIV) protease inhibitory activity.[9]

3. ***Acacia catechu* (Leguminosae) -** Aqueous extract affects humoral immunity as shown by its effect in the indirect hemagglutination test, serum immunoglobulin levels and mice lethality test. It also has effect on the cell-mediated immunity, showing significant increase in the neutrophil adhesion, carbon clearance and a reduction in cyclophosphamide induced neutropenia.[10]

4. ***Achillea millefolium* C. Koch (Compositae) -** Extract exhibits significant stimulatory effect on both humoral and cellular immune functions in mice. Aqueous extract of plant shows significant increase in the delayed type of hypersensitivity response at a dose of 100 mg/kg. In the hemagglutination test, plant extract shows stimulatory effect in all doses.[11]

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5. ***Actinidia macrosperma* (Actinidiaceae) -** Acts as immunomodulator by lymphocyte proliferation stimulation and by activating NK cells.[12]
6. ***Allium hirtifolium* Boiss. (Alliaceae) -** Hydro alcoholic extract Increase in footpad thickness due to immunomodulatory Activity.[13]
7. ***Aloe vera* Tourn.ex Linn. (Liliaceae) -** Acemannan (primary polysaccharide from Aloe vera gel) incubated on special type of mouse macrophage cell line, RAW 264.7 for 24 h causes immunostimulation due to activation of Macrophages.[14],[15],[16]
8. ***Alternanthera tenella* Colla (Amaranthaceae) -** Immunostimulation through modulation of B-lymphocyte functions was achieved using aqueous extracts of A. tenella.[17]
9. ***Andrographis paniculata* Nees (Acanthaceae) -** Andrographolide acts as inhibitor of TNF-a and induces significant stimulation of both "antigen specific" and "antigen nonspecific" types of immune responses in mice, showing effectiveness against a variety of infectious and oncogenic (cancer causing) agents.[18]
10. ***Asparagus racemosus* Wild. (Liliaceae) -** The aqueous extract of *A. racemosus* showed significant increase of CD3(+) and CD4/CD8(+). This effect is proposing its effect on T cell activation. Higher antibody titres and delayed-type hypersensitivity (DTH) responses were also reported along with the effect on activated lymphocytes.[19]
11. ***Bauhinia variegata* Linn. (Caesalpiniaceae) -** Increase in macrophage stimulatory activity, neutrophil adhesion and hemagglutination antibody titer confirms its immunomodulatory potential.[20]
12. ***Boswellia spp*. (Burseraceae) -** Stimulatory effect on lymphocyte proliferation.[21]
13. ***Chlorophytum borivilianum* Sant. (Liliaceae) -** Observed an increase in DTH, % neutrophil adhesion and in vivo phagocytosis by carbon clearance method after treatment with extracts, proving its potential as an immunomodulator.[22]
14. ***Cissampelos pareira* Linn. (Menispermiaceae) -** Stimulates immune system, affects humoral immunity as shown by its effect in the indirect hemagglutination test, serum immunoglobulin levels. It also affects cell-mediated immunity.[23]
15. ***Citrus natsudaidai* Hayata (Rutaceae) -** Immunostimulatory effect on lymphocyte proliferation, induction of cytokine (TNF-α, INF-β).[24]
16. ***Cleome gynandra* Linn. (Capperdiceae) -** Stimulatory effect on both humoral immunity as well as cell-mediated immunity by stimulating phagocytosis, increases in DTH (delayed type hypersensitivity response).[25]
17. ***Cordia superba* Cham. And C. rufescens A. DC. (Boraginaceae) -** methanolic Extract showed a significant immunomodulation by stimulating the NO (nitric oxid), IFN-γ and lipopolysaccharide.[26]
18. ***Couroupita guianensis* Aubl. (Lecythidaceae) Naglingam -** Extract showed immunostimulation in vitro and in vivo and increased phagocytic activity thus an increase in phagocytic index and in DTH.[27]
19. ***Curcuma longa* L. (Haridra) -** Curcumin, one of the main active principle of *C. longa* is reported to inhibit NF-κB activation post exposure of various inflammatory stimuli in 117 randomized control trials. There was a significant reduction in TNF-α, IL-6, TGF-β and MCP-1 following curcumin supplementation.[28]
20. ***Ganoderma lucidum* (Fr.)P. Karst. (Polyporaceae) -** Induction of cytokine (TNF-α, IFN-γ) by Ganoderma suggests its immunomodulatory potential.[29]
21. ***Glycyrrhiza glabra* L. (*Yastimadhu*) -** Glycyrrhizin, the main active constituent of the plant, is reported to interfere with immune responses by targeting dendritic cells. It also upregulate the expression of CD40, CD86 and MHC-II maturation markers on dendritic cells as well as enhances the

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production of IL-12 by these cells. It also increases the IFN-γ and IL-10 and further reduces IL-4 production.[30] The root extract of *G. glabra* in association with zinc has also shown immunomodulatory activity.[31]

22. ***Gymnema sylvestre* R.Br. (Asclepiadaceae) -** Aqueous Extract showed significant immunomodulation at all concentrations in various in vitro models by exerting a stimulating effect on phagocytic activity, neutrophil locomotion and chemotaxis.[32]
23. ***Hibiscus rosa* sinensis Linn. (Malvaceae) -** Stimulatory effect on both humoral immunity as well as cell mediated immunity by stimulating phagocytosis, increases in DTH.[33]
24. ***Hyptis suaveolens* (L.) Poit., (Lamaceae) -** Potentially suppresses immune system affecting both humoral immunity and cell-mediated immunity as shown by its effect in indirect hemagglutination test.[34]
25. ***Lagenaria siceraria* Mol. (Cucurbitaceae) -** Ethanolic Extract showed immunostimulation in vitro and in vivo by increasing the DTH.[35]
26. ***Morus alba* Linn. (Moraceae) -** Methanolic Extract affects humoral immunity as shown in the indirect hemagglutination test, serum immunoglobulin levels and mice lethality test. It also affects cell-mediated immunity, showing significant increase in the neutrophil adhesion, carbon clearance and a reduction in cyclophosphamide induced neutropenia.[36]
27. ***Murraya koenigii* (L) Spreng. (Rutaceae) -** Methanolic Extract showed immunostimulation in vitro and in vivo. Significant increase in NO production by mouse peritoneal macrophages is detected in cultures. Supernatants indicated increase phagocytic activity of macrophages thus increase in phagocytic index by rapid removal of carbon particles from blood stream.[37]
28. ***Nyctanthes arbor-tristis* L. (Oleaceae) -** Potentially stimulates immune system and affects both humoral immunity as well as cell-mediated immunity as shown by its effect in the indirect hemagglutination test and serum immunoglobulin levels.[38]
29. ***Ocimum sanctum* Linn. (Labiateae) -** Aqueous/alcoholic Extract shows increased DTH to sheep red blood cells SRBCs. Alcoholic extract was more potent than aqueous in producing delayed type hypersensitivity response. Both extracts have marginal stimulatory effect on humoral immunity.[39]
30. ***Phyllanthus emblica* L. (Emblica officinalis) (Aamlaki) -** *P. emblica* is reported to enhance NK cell activity and antibody-dependent cellular cytotoxicity in syngeneic BALB/c mice.[40] E. officinalis stimulates humoral and cell-mediated immunity along with macrophage phagocyte.[41]
31. ***Picrorhiza scrophulariiflora* Benth. (Scrophulariaceae) -** Strong inhibitory activity of *P. scrophulariiflora* towards the classical pathway of complement, chemiluminescence and T-cell proliferation assay was observed for the diethyl ether extract.[42]
32. ***Randia dumetorum* Lamk. (Rubiaceae) -** Modulates immune system depending upon fractions and mechanism involved in stimulation and increase in DTH response.[43]
33. ***Stereospermum suaveolens* DC. (*Patla*) -** The root extract is reported to increase the total leukocyte count and the population of monocyte and neutrophil in experimental studies. Immunostimulatory potential is reported via DTH response, phagocytic activity and intracellular killing potential of phagocytes.[44]
34. ***Terminalia arjuna* Roxb. (Combretaceae) -** Plant showed immunomodulation by increasing the secondary immune response as evidenced by an increase in Anti- SRBC antibody titre (ASRBs) antibody titer but failed to modulate primary immune response.[45]
35. ***Terminalia chebula* Retz. (*Haritaki*) -** The aqueous extract of dried fruits of *T. chebula* was reported to increase humoral antibody titre and DTH in mice.

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Another study also reported enhanced expression of Th1 cytokine, INF-γ; decreased IL 4; increased percentage of CD4+ cells; lymphocyte proliferation; macrophage phagocyte response; and DTH response in mice.[46]

36. ***Tinospora cordifolia* Miers. (Menispermiaceae) -** Improves the phagocyte function without affecting cell-mediated and humoral immune systems and also causes inhibition of C3 canvertase of the classical complement pathway, hence acts as immunomodulator.[47] The aqueous extract of *T. cordifolia* is reported to influence the cytokine production, mitogenicity, stimulation and activation of immune effector cells. In vitro evidence also supports it by showing upregulating effect on the IL-6 cytokines facilitating the acute response to injuries, inflammation, activation of cytotoxic T cells and B cell diffraction.[48]

37. ***Withania somnifera* (L.) Dunal (*Ashwagandha*) -** The aqueous extract of roots of *W. somnifera* was reported to upregulate Th1-dominant polarization, thus supporting the humoral immunity and cell-mediated immune responses in BALB/c mice.[49] The methanolic extract of the roots enhances the level of IFN-γ, IL-2 and granulocyte macrophage colony-stimulating factor in mice.[50] Another study reports that the aqueous extract enhances nitric oxide synthetase activity of the macrophages, activates and mobilizes macrophages for rendering increased phagocytic activity and potentiates activity of lysosomal enzymes.[51]

Discussion

For Autoimmune disease one of the therapeutic strategies in *Ayurvedic* medicines is to enhance the body's overall natural resistance to the disease causing agent rather than directly neutralizing the agent itself. In *Ayurveda* Toxin removal through *Panchkarma*, improving metabolic activities using herbal medicine like *Neem, Guggulu, Vasa, Patolpatra* etc., increasing *Ojas* production with the help of *Guduchi, Amalaki, Yashtimadhu, Pippali* etc. and immune system correction with the help of herbal medicine are helpful to treat the autoimmune disease. Ayurveda describe a number of drug as *Rasayan* and *Ojovardhak* which are claim to possess immunomodulory effect. *Rasayana* work at the level of *Rasa, Agni* and *Srotas* to achieved the immune enhancement. Also balanced lifestyle and diet prevent autoimmune diseases.

Conclusion

Ayurveda is based on a holistic view of treating an individual by understanding the interplay between the body, mind and consciousness. Ayurveda has its own fundamental principles to diagnosed a disease and treat them with the help of its own Materia- medica and methodology.

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How to cite this article: Nivedita Rawat, Sharddha Sharma. Role of Ayurvedic Medicinal Plants in Auto-immune disorders and their management. J Ayurveda Integr Med Sci 2023;03:108-115.
http://dx.doi.org/10.21760/jaims.8.3.20

Source of Support: Nil, **Conflict of Interest:** None declared.

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