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RESEARCH ARTICLE

REVIEW ON AYURVEDIC PLANTS AS IMMUNOMODULATORS

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Abstract

In today's era use of immunomodulators has tremendously increased to treat various human and animal diseases like viral diseases,cancer, autoimmune diseases, inflammantary conditions etc. Immunity is the body's natural ability to identify and resist various infectious disease and disorders. Immunomodulators are biological or synthetic substances that can stimulate, suppress or modulate any aspect of immunity including adaptive as well as innate immunity. Various factors such as balanced diet,environmental temperature,stress, pathogenic and non-pathogenic bacteria,proper exercise affect the immunity. Natural drugs are used since ancient times for treatment of various diseases because of minimal side effects. Natural compounds are also used enormously as immunomodulators. There are about 1000 natural compounds having immunomodulatory effect they either affect the immune cells or affect the antibody secretion and influence the immune response. Here in this review we have discussed in detail definition of immunity,concept of immunomodulators,classification of immunomodulators,correlation between immunomodulators and Ayurveda and Ayurvedic plants having immunomodulatory activity. The main purpose of this review is to highlight efficacy of available literature on Ayurvedic plants as immunomodulators.

Introduction:-

Since a long time, the traditional medicinal plants have been in the treatment regimen for healthcare of people, to cure variety of diseases.[1] Herbal medicines (drugs) have immunomodulatory property because they stimulate both specific and non specific immunity.[2] Usually India is known for it's traditional healthcare system – Ayurveda, Siddha and Unani.Ayurveda is probably one of the best known and it is believed to have originated over 6 thousand years ago. Ayu-Life,Veda-Knowledge ..Knowledge of life.[3] Ayurvedic herbal medications are widely used for modulation of immune response.[4]

Immunnomodulation of immune response come up with a substitute for a variety of disease conditions and with immunodeficiency and also the herbal immunostimulants getting more importance and visibility.[2,5] Modulation of immune system refers to any change in immune response such as suppression, expression, agumentation of immune system.[6] The review has focused on plants having Immunomodulatory Activity.[7] Immunity is the body's natural ability to identify and resist various infectious disease and disorders.[8] Immunity comprises of both specific and non-specific components.[9] As the infant grows his immune system continues to develop.[10] Immunomodulators are

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biological or synthetic substances that can stimulate, suppress or modulate any aspect of immunity including adaptive as well as innate immunity.[11-13]

Immunity:
Immunity refers to the state of protection against infectious disease.[14] In Ayurveda immunity has been explained by Acharya Chakrapani in terms of Vyadhikhamatva. Basic pathway of immunity.[10]

Immune System :
The immune system is designed to defend host from invading pathogens and to eliminate disease, it also maintains homeostasis within the body of healthy organism.[15,16] The structure of immune system is multilayered, with defenses on several level.

First barrier against infection is skin.

Second one is physiological, where conditions like the temperature and pH of body provide unsuitable conditions for foreign organisms.[8]

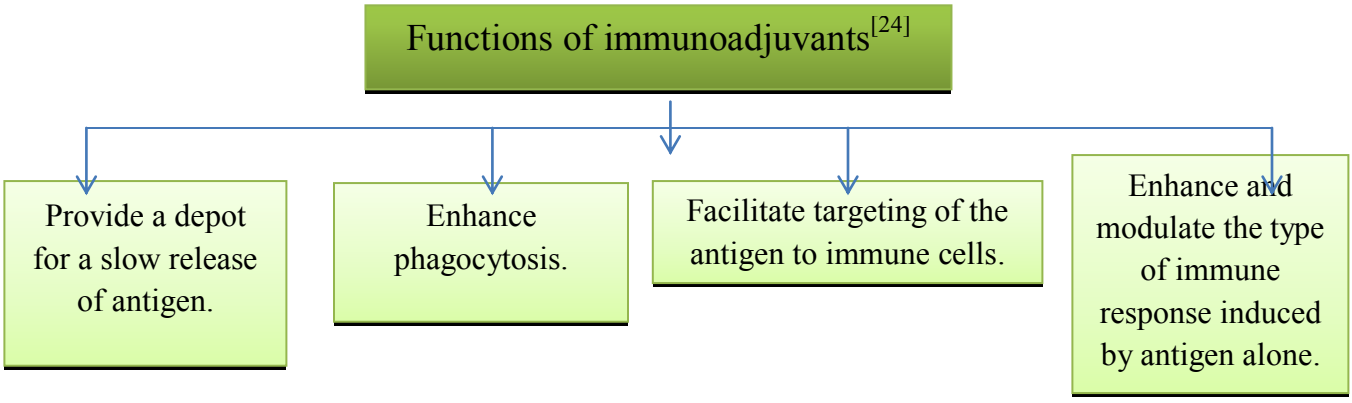
The immune system has been categorized into innate (non-specific) and adaptive immunity (specific).[17]

1. The innate immune system- Innate immunity consist of a series of host defenses including barrier function, cytokines, phagocytes, natural killer cells(NK)cells and gamma delta (gd) T cells to provide the initial (nonspecific) response to a pathogen or injury.[13]
2. The adaptive immune system- Adaptive immunity is called as acquired immunity. The adaptive immune system differs from the innate response as it is specific, has an element of memory and is unique to vertebrates.[18]

Concept of immunomodulators:
Immunomodulators arebiological or synthetic entities which can influence any component or function of the immune system in a specific or non specific method.[19,20] Immunomodulators shows their activity in the following manner.

Administration of immunomodulators → activates macrophage and granulocytes → increasing phagocytosis.[21]
In other words immunomodulators can be called as an active agent of immunotherapy.[22]

Classification of immunomodulators:
Immunoadjuvants:
Immunoadjuvants are used to enhance efficacy of vaccines therefore considered as specific and true immunomodulators of immune system.[11,23]



Immunostimulants:
Immunostimulants are also known as immunomodulators.[15] The substance (drug and nutrient) which stimulate immune system by inducing activation or increasing activity of any organ.[21] They can act through innate as well as adaptive immune response.[25] Immunostimulants can act as immunotherapeutic agent, in those who have an immune impairement.[26] In normal healthy individuals, they are expected to serve as prophylactic and promoter agents i.e. as immunopotentiators.[25,27]

Immunosupressants:
Immunosupressants are structurally and functionally heterogeneous group of drugs which are often administered in combination regimens to suppress the immune response and to treat various type of organ transplant rejection and autoimmune diseases.[28,44]

Correlation Between Immunomodulators And Ayurveda:
Now a day's Ayurvedic immunomodulators are widely used in the management of health and disease.[24] Ayurveda is a most ancient and currently most important tradition practiced widely in India and other countries.[8] The basic concept of immunomodulation is existed in Ayurveda as well as is being practiced by the Ayurvedist for centuries. In Ayurvedic practice immunity can be enhanced by using Rasayana, Lehan and Ojovardhaka remedies. Immunomodulatorsare becoming a central part of 21st medicine.[29] The detailed description of over 700 herbs is given in the Atharvaveda (around 1200Bc), Charak Samhita and Sushrut Samhita.[8]

List of common plants having immunomodulatory activity:

Botanical Name	Common name	Family	Part used	Other Biological Properties	Chemical Constituents	Ref
Ocimum sanctum Linn.	Tulsi	Labiateae	Whole plant	Carminative, stomachic, antispasmodic, antiasthmatic, hepatoprotective	Essential oils such as eugenol, cavacrol, derivatives of ursolic acid, apigenin	[13,18,35]
Morus alba Linn.	Brahmdaru	Moraceae	Fruits, leaves, bark	Immunonutritive, hepatoprotective, Expectorant, hypocholesterolaemic, diuretic	Flavonoids, anthocyanins	[8,15,43]
Panax ginseng Wall.	Ninjin	Araliaceae	Fruits, root	Adaptogenic properties, antiarrhythmic.	Saponins such as ginsenosides, panaxdiol, panaxtriole and oleanolic acid	[13,37,25]
Achilleamillefolium C. Koch	Yarrow	Compositae	Leaves	Anti-inflammatory, antispasmodic, antipyretic, diuretic.	Flavonoids, alkaloids, polyacetylenes, coumarins, triterpenes	[8,38]
Aloe veraTourn.ex Linn.	Kumaari	Liliaceae	Gel from leaves	Purgative, emmenagogue, emollient, antinflammatory.	Anthraquinone glycosides	[13,34,35, 21]
AndrographispaniculataNees	Kaalmegha	Acanthaceae	Leaves	Hepatoprotective, antispasmodic, blood purifier, febrifuge.	Diterpenes	[12,13,26, 39,41]
Asparagus racemosus Wild.	Shatavaari	Liliaceae	Roots	Antioxidant,ulcer healing agent, nervine tonic, antigout.	Saponins, sitosterols	[8,10,13,22]
Murrayakoenigii (L) Spreng.	Surabhini-nimba	Rutaceae	Leaves	Antifungal, insecticidal, insecticidal.	Coumarin, carbazole alkaloids, glucoside	[8,38]
Couroupitaguianen	Nagalinga	Lecythidac	Fruits,	Antifungal.	Steroids,	[8,15,43]

sisAubl.		eae	flowers		flavonoids, phenolics	
Tinosporacordifolia Miers.	Amrita, guduuchii	Menispermiaceae	Entire herb	Hypoglycaemic agent, antipyretic.	Alkaloidal constituents such as berberine, tinosporic acid	[13,6,22,41]
Lagenariasiceraria Mol.	Katu-tumbi	Cucurbitaceae	Leaves, fruit	Purgative, emetic.	Cucurbitacin, beta-glycosidase	[8]
TerminaliaarjunaRoxb.	Arjuna	Combretaceae	Leaves, bark	Cardiotonic, diuretic, prescribed for hypertension.	Flavonoids, oligomericproanthocyanidins.	[8,13,38]
Bauhinia variegata Linn	Kaanchana	Caesalpiniaceae	Roots, bark, buds	Antifungal, astringent.	Flavonoids, beta-sitosterol, lupeol	[13,38]
Urenalobata Linn.	Naagabala	Malvaceae	Roots, fruits, flowers	Diuretic, emollient, antispasmodic.	Flavanoids and glycosides	[8,38]
Gymnemasylvestre R.Br.	Gurmaar	Asclepiadaceae	Leaves	Antidiabetic, diuretic, antibilious.	Sapogenins	[8,38]
CordiasuperbaCham. and C. rufescens A. DC.	Shleshmaataka	Boraginaceae	Leaf, fruit, bark	Anti-inflammatory, antimicrobial.	Alpha-amyrin	[8,13]
PicrorhizascrophulariifloraBenth.	Kutki	Scrophulariaceae	Whole plant, roots	Antioxidant.	Iridoid glycosides, amphicoside	[8,36]
Heracleumpersicum Desf.	Golpar	Apiaceae	Shurb, whole plant	Antimicrobial.	Flavonoids, furanocoumarins	[13,36]
Cissampelospareira Linn.	Paatha	Menispermiaceae	Roots	Antipyretic, analgesic, antilithic	Hayatine alkaloids	[8]
Abutilon indicumlinn.	Atibalaa	Malvaceae	Whole plant	Diuretic, antibacterial	Flavonoids, triterpenoids	[13]
Chlorophytumborivilianum Sant. F	Safedmusli	Liliaceae	Roots	Antifungal.	Sapogenins	[8,43]
AlternantheratenellaColla	Snow Ball	Amaranthaceae	Herb	Antitumor, anti-inflammatory.	Flavonoids, triterpenes	[8]
Ganodermalucidum (Fr.) P. Karst.	Reishi mushroom	Polyporaceae	Whole plant	Antioxidant	Flavonoids, triterpenes	[13]
Nyctanthes arbor-tristis L.	Paarijaata	Oleaceae	Leaf, seeds	Antiviral,hepatoprotective,anti-inflammatory, antispasmodic.	Iridoidglucosides	[8,42]
Actinidiamacrosperma C. F. Liang	Actinidia	Actinidiaceae	Fruits/whole plant	Antileprotic.	Alkaloids, saponins	[13,36]
Acacia catechu Willd.	Khadira	Leguminosae	Leaf	Hypoglycaemic, astringent	Flavonoids, tannis, quercetin	[8,13,38]
Boswellia spp.	Shallaki	Burseraceae	Gum resin	Hypoglycaemic.	Triterpenes, ursanes	[8]
Hibiscus rosasinensis Linn.	Japaa	Malvaceae	Flowers	Antidiarrheal, anti-	Cyclopropanoids	[13]

				inflammatory.		
Cleome gynandra Linn.	Tilaparni	Cleomaceae	Aerial parts	Anti-inflammatory Anticancer	Hexacosanol, kaempferol	[8,38,40]
Hyptissuaveolens (L.) Poit.	Tumbaaka	Lamaceae	Leaf, flowers	Carminative, antispasmodic.	Lupeol, beta-sitosterol	[13]
Randiadumetorum Lamk.	Madana	Rubiaceae	Fruits	Chlorosis, antiarthritic.	Saponins, triterpenes	[13]
Allium hirtifoliumBoiss.	Persian shallot	Alliaceae	Herb	Antirheumatic, anti-inflammatory.	Thiosulfinates, flavonoids	[8,13,37]
Citrus natsudaidaiHayata	Japanese summer grape fruit	Rutaceae	Fruits	Antioxidant	Auraptene, flavonoids	[13,37]
Acanthopanaxsessiliflorus (Rupr. & Maxim.)	Prickly spine	Araliaceae	Shoots and roots	Lympho-proliferative activity.	Biopolymers	[13,38]
Agelasmauritianus	Agelas	Porifera	Sponge	Phagocytotic activity.	Glycolipid (a-galactosylceramide)	[13]
Aphanothecehalophytica		Chroococcales	Cyanobacterium	Inhibits influenza virus.	Exopolysaccharide	[8,13]
ApiumgraveolensLinn.	Celery Seeds	Apiaceae	Leaves, seeds	Anti-inflammatory.	Flavonoids, coumarins	[8,13]
Genus Ardisia	Marlberry	Myrsinaceae	Shrub, Branches and leaves	Antimetastatic drug, anti-HIV property.	Peptides, saponins, Isocoumarins, quinones and alkyl phenols	[8]
Genus Aristolochia	Pipevine	Aristolochiaceae	Leaves	Antiangiogenic, employed in prostate Cancer.	Aristolochic acid	[8,13]
Artemisia annuaLinn.	Wormwood	Composite a	Herb	Immunosuppressive.	Artemisinin	[8,13]
Genus Aspergillus	Aspergillus	Trichocomaceae	Fungus	Antifungals	Polyene, triazole	[8]
Botryllusschlosseri	Botryllus	Botryllidae	Tunicates	Antioxidant, antiviral, antimicrobial and Antitumoral.	Cytokines	[8,13]
BidenspilosaL.	Beggar-ticks	Asteraceae	Flowers, leaves	Anti-inflammatory, immunosuppressive, antibacterial and antimalarial.	Polyacetylenes	[8]
Boerhaaviadiffusa	Punarnava	Nyctaginaceae	Herb	Immunostimulatory	Alkaloid	[13,25]
BugulaneritinaL.	Brown bryozoans	Bugulidae	Marine invertebrates	Immunomodulator.	Macrocycliclactones	[8]
ByrsonimacrassaNied.	Byrsonima	Malpighiaceae	Leaves	Antimicrobial, antioxidant.	Flavonoids, tannins, terpenes	[8,13]
Calendula	Garden	Asteraceae	Flowers	Antitumor	Polysaccharides,	[13,38]

OfficinalisL.	Marigold			antiviral activity, anti-HIV properties.	proteins, fatty acids, carotenoids, flavonoids, triterpenoids	
Camellia sinensisL.	Tea	Theaceae	Leaves	Anticancer activity, lipid lowering activity, anticataract activity, hepatoprotective and antioxidant.	(_)Epigallocatechingallate, quercetin, gallicacid	[12,13,15]
Cannabis sativa	Common hemp	Cannabaceae	Leaves	Immunomodulatory.	Cannabinoids	[8]
Carpobrotusedulis L.	Fig Marigold	Aizoaceae	Flowers, fruit	Immunomodulator.	Alkaloids	[8,13]
CentellaasiaticaLinn.	Brahmi	Umbelliferae	Herb	Immunomodulator.	Triterpenoidsaponins	[8,13]
Cistanchedesertcola	Cistanche	Orobanchaceae	Herb	Immunomodulator, mitogenic and comitogenic activities.	Polysaccharide	[13]
Clionacelata	Borimg sponge	Clionaidae	Sponge	Antibacterial activity.	Clionamide, dehydrodopamine	[8]
Cordycepsmilitaris L.	Militaris	Clavicipitaceae	Fungus	Anti-inflammatory.	Cordycepin, cordyceps acid	[8]
Crinum latifoliumAndr.	Milk and Wine Lily	Amaryllidaceae	Herb	Immunomodulator	Alkaloids	[8,13]
DracocephalumKotschyi	Dragon-Head	Lamiaceae	Herb	Immunomodulator	Essential oil	[8,13]
Echinacea angustifolia	Cone flower	Asteraceae	Flowers	Treatment for common cold, immunomodulator.	Polysaccharide	[8,13]
Eclipta alba L.	Bringraja	Compositae	Leaves	Anticancer, antileprotic, analgesic, antioxidant,antimyotoxic.	Triterpenoidglucoside	[13,38]
Euphorbia hirtalinn.	Asthma weed	Euphorbiaceae	Herb	Anti-inflammatory activity, sedative and anxiolytic activity.	Quercitol, myricitrin, gallic acid	[8,38]
EvolvulusalsinoidesLinn.	Shankhpushpi	Convolvulaceae	Herb	Brain tonic.	Alkaloids	[8,13]
Haussknechtiaelymatica	Haussknechtia	Apioideae	Herb	Immunomodulator.	Phenolics	[8]
Inonotusobliquus Pers.	ChagaMushroom	Hymenochaetaceae	Mushroom	Antitumor.	Polysaccharide	[13]
LarreadivaricataDC.	Creosote Bush	Zygophyllaceae	Herb	Anti-inflammatory.	Lignans	[13]
LyciumbarbarumLinn.		Solanaceae	Fruits	Antioxidant.	Polysaccharide-protein	[8,13]

					complexes	
Matricariachamomilla	Chamomile	Rhabdoviridae	Flowers	Immunomodulator.	Protein	[13]
Mollugoverticillata L.	Carpetweed	Molluginaceae	Herb	Immunomodulator.	Quercetin, triterpenoid glycosides	[13]
MoringaoleiferaL.	Sahijan	Moringaceae	Leaves	Antioxidant.	Vitamin A, B, C, carotenoids, saponins	[8,28]
Pestalotiopsisleucothes		Amphisphaeriaceae	Fungus	Immunomodulator	Terpenes	[8]
Piper longumL.	Pipali	Piperaceae	Fruits	Antioxidant	Alkaloids	[8,9,35,36,38]
Rhodiola imbricate Gray.	Roseroot	Crassulaceae	Rhizomes	Immunostimulating properties.	Phenolics	[13]
Silybummarianum L.	Milk Thistle	Asteraceae	Flowers	Antioxidant.	Flavonoid	[13,38]
Salicorniaherbacea	Glasswort	Chenopodiaceae	Herb	Immunomodulator.	Polysaccharides	[13]
Viscum album L.	Mistletoe	Loranthaceae	Leaves and young twigs, berries	Antitumoral effect.	Viscotoxins, polyphenols, polysaccharides	[8]
ThujaoccidentalisL.	White cedar	Arborvitae	Leaves	Immunomodulator	Polysaccharides	[8,13]
Curcuma longa L.	Turmeric	Zingiberaceae	Rhizome	Anticancer,antioxidant anti-angiogenic,antiproliferative	curcuminoids	[16,30,34,45]
Allium sativum	Lahsuna	Amaryllidaceae	Bulb	Antiviral, antihypertensive, carminative, stimulant, antibiotic	Scordinin, alliin, acrolein, diallyl-trisulphide, diallyl-disulphide	[12,15,21]
Emblicaofficinalis	Amalaki	Euphorbiaceae	Fruit	Immunomodulator, diuretic, laxative	Tannins, vitamin C	[15,22]
Withaniasomnifera	Ashwagandha,Indian ginseng	Solanaceae	Whole plant	Antibacterial, hypolipidemic	Alkaloids, steroidal lactones, saponins	[22,31,41,42,46]
Glycyrrhizaglabra Linn.	Liquirice sweet root	Leguminosae	Roots, stolons	Antioxidant	Glycyrrhizin, polysaccharide	[21,22,28]
Azardicaindica	Neem	Meliaceae	Leaf	Immunopotentiator, anti infective, anxiolytic	Azadirachtin, nimbin, gedunin,gallic acid, catechin, NB-2 peptidoglycan	[22,23,31]

Future prospects:

From ancient times plant derived medicines and folklore medicines have been used for the drug design and development of therapeutic agents.[1,30] Herbal and traditional botanical products are good alternatives to conventional chemotherapy.[31] Presently researchers are fascinated towards plant derived therapeutics and the

research is based on investigation for some plant biochemical in the form of the single compound as lead molecule concerned with particular target linked with disease.[1,30] Numerous plant derived compounds have been identified over the years which possess immunomodulatory characteristics but the systematic, proper and multidisciplinary approach is required for picking out active constituents from different medicinal plants and their different medicinal effects using modern techniques.[16,32] Two approaches can be followed for developing successful drugs from medicinal plants. First one is the phytochemical approach, which depends on identifying the active principle and developing pure phytochemicals as drugs. Yet this type of drug discovery is costly and also time consuming. The second approach is a phytotherapeutic approach wherein standardized crude drug preparations can be used as drugs with modern standards of safety and efficacy. As far as the Indian medicinal plants are concerned, the second approach could be followed.[33]

0Conclusions:-

Herbal plants or extracts having immunomodulatory activity and when co-administered with vaccines may be helpful in obtaining higher protective antibodies against different infections caused by viruses, bacteria etc. Natural immunomodulators are used widely because of high efficacy, low toxicity, low cost.

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