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A BOON IN DISGUISE; PLANTS HAVING IMMUNOMODULATORY ACTIVITY!!! (SCIENCE HAS ALWAYS EVOLVED WITH NATURE)

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Abstract
Immunomodulation is the process of altering a living organism's immune system through functional modifications. You may become less immune-friendly or more immune-friendly as a result. Immunomodulators, which assist in regulating the immune system, are available for purchase. Accordingly, an immunomodulator promotes optimal function of the immune system in the body. Things known as immunomodulators alter how your body reacts to external stimuli. They fortify the body, aiding in the defence against illness. The precise balance between your body's effector and regulatory cells determines how well your immune system functions. In cases where this process is out of balance, illness may ensue. Comprising a multitude of distinct cell types, the immune system functions to protect the body against pathogens, fungi, viruses, bacteria, and cancer cells.

Keywords: Immunoglobulin, Alzheimer Disease, Immunomodulators, leukocytosis, Acetyl cholinesterase

INTODUCTION

IMMUNOMODULATIORS

A class of medications known as "immunomodulators" modifies the immune system's response in one way or another. They can be described in two ways: intrinsic and extrinsic. The immune system's functionality can be changed by combining immunosuppressants, immunostimulants, and tolerogens [1].

Immunostimulant

Immunostimulants or immunostimulators are substances that stimulate or raise immune system component activity. One such instance is granulocyte macrophage colony-stimulating factor. Immunostimulants can be divided into two main groups:

1) **Specific immunostimulant** provides antigenic specified in the immune response, such as vaccines or any antigen that can be found

2) Non- specific immunostimulants - Non-specific immunostimulators and adjuvants, for instance, function despite lacking particular antigenic characteristics. Adjuvants, for example, stimulate immune system components without specific antigenic characteristics, but they can enhance the immunological response to another antigen. 21 Many of the chemicals found in the body are not particular immunostimulators. For instance, it is believed that the innate and adaptive immune systems of the body function better when female sex hormones are present. The body's immune system may also be impacted by other hormones such prolactin, growth hormone, and vitamin D [2].

IMMUNOSUPPRESSANT

Drugs classified as immunosuppressive agents inhibit or reduce the function of the immune system. Immunosuppressive therapy uses them to reduce the body's ability to fight off infections.

1) Ensure that organ transplants (heart, kidney, liver, etc.) are not rejected.
2) Address autoimmunity or conditions that are most likely to result from it (such as ulcerative colitis, myasthenia gravis, and rheumatoid arthritis). Treating another non-autoimmune inflammation (such as long-term allergic asthma control) is the third course of action.[1]

The immune system

Your body's chemicals and cells cooperate to fend off infections. People respond to germs in two somewhat distinct ways. No matter how frequently the infectious agent is seen, natural reactions still occur. However, this is not the case with learned (adaptive) responses. The more times they are exposed to the same virus, the better they get. B and T lymphocytes specific for an antigen begin to proliferate as soon as their surface receptors come into contact with the antigen. Particularly specialised cells called antigen-presenting cells present the antigen to lymphocytes and assist them in combating it. Immunoglobulins, which are antigen-specific antibodies that eradicate extracellular bacteria and maintain our health, are produced by B cells in the body. T cells assist B cells in the production of antibodies. They grow more hazardous when two virus-infected cells are eliminated and macrophages are activated. Innate and learnt responses typically cooperate to eliminate infections, although this isn't always the case [2].

LEVEL OF DEFENCE

Mucus and enzymes that are either antibacterial or hinder the microbe's ability to attach must be overcome by the pathogen before an infection can begin. The keratinized skin surface and the mucus-lined internal cavities are unsuitable environments for most organisms to survive in, thus bacteria must pass through them in order to reach the ectoderm. When an organism gets past this

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first line of defence, it encounters the innate and acquired immune responses, which are two additional layers of defence [3].

THE INNATE RESPONSE

Neutrophil Recruitment

The innate response is responsible for activating and delivering neutrophils to the infection site. How can infections be eliminated? Activated macrophages are critical because they release cytokines that aid in the early phases of a disease's resistance to the virus. These are the motivating factors for granulocyte and granulocyte macrophage colonies, and that's why. The bone marrow produces myeloid precursors, which cause leukocytosis, or an excess of white blood cells, by releasing many cells into the bloodstream. To reach a state where they can combat an infection, they go through a number of stages. These include, among other things, chemokines, sticky molecules, chemo attractants, and pro-inflammatory mediators. As a result of the majority of the work being done with neutrophils, it is now clear that all leucocytes, including lymphocytes, locate themselves using this method. We term this process "localization." Their function is to consume bacteria by enclosing them in membrane-bound vesicles, called pseudopodia. The phagolysosome, which is created when a virus enters your body, is the result of all of this assembly [4].

Complement

Innate immunity is significantly influenced by the complement system. At least 20 serum glycoproteins are present, some of which are significant. These are switched on in a "cascade" fashion, with the power of each one increasing. Most often, a foreign material triggers your body's complement system to activate through antigen-antibody interactions. Your body may also begin to function in this manner as a result of polysaccharides from bacteria. Recent discoveries of mangan-binding lectins activate the classical sequence by improving its functionality [5].

Eosinophils

Eosinophils are critical for the body's defence against parasite infections because they trigger the creation of antigen-specific IgE, which coats the parasite, in the body.

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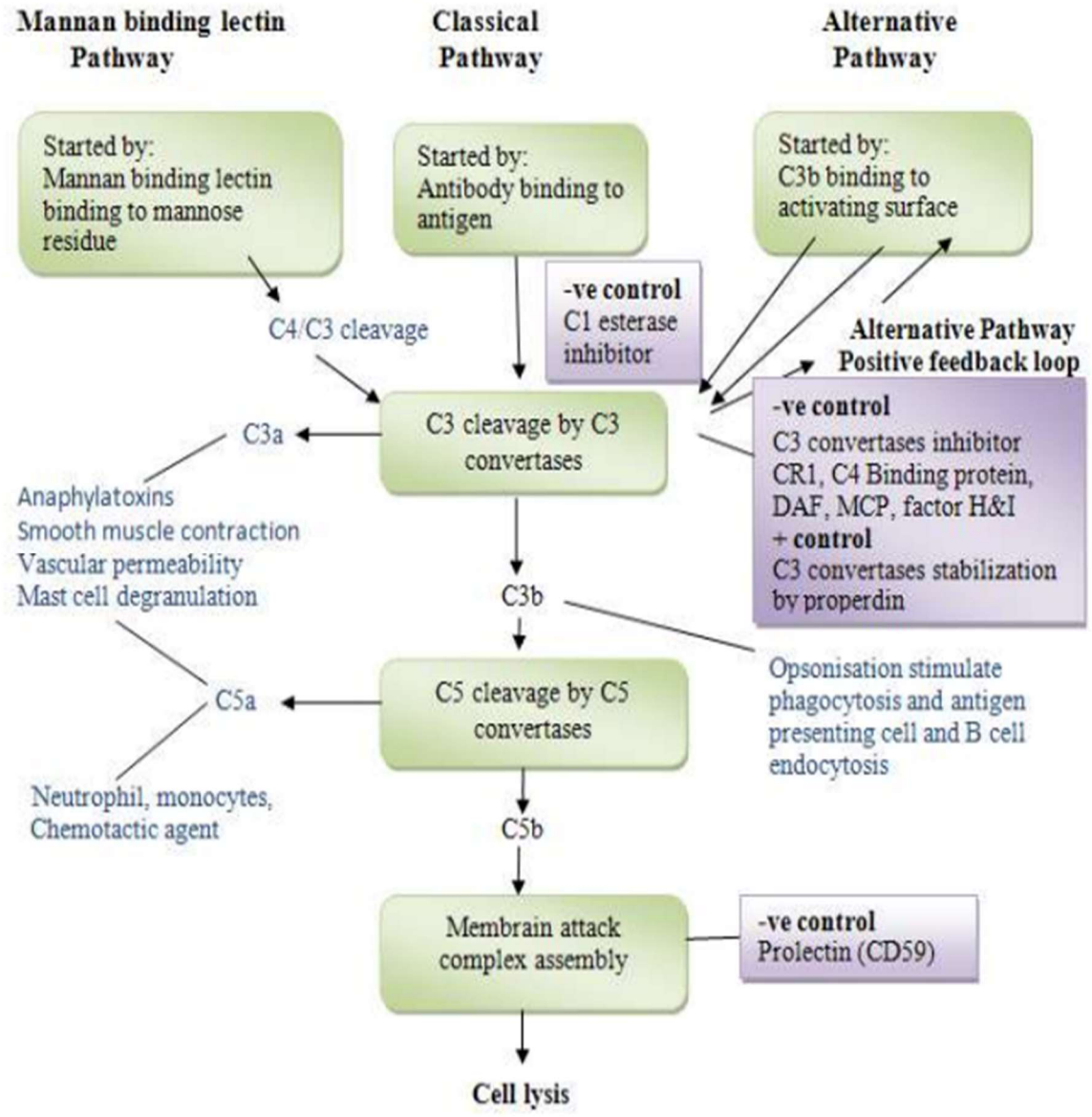

Figure 1: The three pathways of complement activation

Mast Cells Basophils

A mucosal mast cell, or T mast cell, is the sole kind of mast cell. It has trypsin in it. Check out this video to learn more about mast cells in your connective tissue. A receptor known as IgEFcRI (CD23) is present on basophils and mast cells. This receptor immediately consumes up any IgE that is in the region. This happens when an antigen is bound to IgE, which causes these receptors to degranulate and release already-made mediators, such as histamine and serotonin, which can cause a heart attack, as well as other things. In addition, membrane-based mediators, such as leukotrienes B4 and leukotrienes C4 and leukotrienes D4 and leukotrienes E4 are made. An inflammatory reaction may result from tightening of the bronchi and increased blood vessel permeability [6].

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Natural Killer Cells

Naturally occurring killer cells possess receptors for more than only viruses. Two methods exist for them to determine whether there are malignant cells: The FcR (immunoglobulin receptor): Their FcR can connect to targets coated with antibodies, causing antibody-dependent cell lysis. This is the first reason they have it. Some further points: Additionally, the first MHC class 1 receptor is present on their exterior. The binding of this receptor is necessary for the natural killer cell to execute a cell. A cell cannot survive if this receptor is not bound. A cell's surface is coated with perforins, which are natural killer cells that adhere to it. Perforin-producing cells have punctured the cell membrane with their own perforins. Granzymes are inserted into holes through pores. The granzymes cause the cell they are in to die [7]. Perforin-producing cells have punctured the cell membrane with their own perforins. Granzymes are inserted into holes through pores. The granzymes cause the cell they are in to die [8]

Table1: Immunomodulator plants found in India

S. N.	Name of Plants	Family	Parts Used	Chemical Constituents	Mechanism Of Action	Pharmacological Uses	Ref.
1	***Acorus calamus*** (Common name: sweet flag)	Acoraceae	Rhizomes	α, β Asarone, Cis and trans isoeugenol	Active constituents degrade Acetyl cholinesterase in the synapses	Memory related disorders, Anti-oxidant, Insecticidal activity, Relives stomach ache and dysentery	9-14
2	***Bacopa monniera*** (Common name: Thyme-leafed gratiola, water hyssop, Brahmi, Indian pennywort	Plantaginaceae	Leaf extracts	Brahmine, herpestine, nicotine, Alkaloids like B-sterols, betulic acid, *Bacopa* saponins (bacopasides A, B, C, I, II, X, and N2), and *Bacopa* saponin E (III, IV, V, and N1) were scrutinized	The involvement of the micro-RNA 124-CREB pathway and serotonergic receptor in the memory enhancing mechanism of standardized extract has also been reported.	Antioxidant, Antilipoxygenase	15-17

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				from the leaf extract of *B. monnieri*			
3	***Celastrus paniculatus*** (Common name: jyotismati, Jyoti Teja)	Celastraceae	Bark and seeds	Sesquiterpenoid polyalcohols, Esters (malkangunionl, malkangunin, Polyalcohol A–D and celapnin); Alkaloids (paniculatine and celastrine); phenolic Triterpenoids (celastrol and paniculatadiol); fatty acids (oleic, linoleic, linolenic, palmitic, stearic and lignoceric acid) and agarofuran derivatives.	Administration of *Convolvulus pluricaulis* increased acetylcholinesterase activity in hippocampal CA1 and CA3 regions associated with the memory function and learning abilities.	Neuroprotective, anti-infertility, antiarthritic, wound healing, anti-inflammatory, antioxidant, analgesic, antimalarial, antibacterial and fungicidal, action hypolipidemic,[26]	18-20
4	***Centella asiatica*** (Common name: Gotu kola, Kodavan, India Pennyw	Apiceae	Leaf extract	Asiaticosides, Asiatic acid, madecassoside and madasiatic acid brahmoside and brahminoside	Reduces apoptosis and hippocampal Aβ levels in vitro and in vivo. Enhances learning and	Anti-inflammatory, antioxidative stress, antiapoptotic effects, neuroprotective effects, wound healing,	21-22

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	ort, Asiatic Pennywort), (In India Manduk parni, Jal Brahmi)			, isothankunisi de, thankuniside and centelloside	memory function in mice models of AD. Potential use in the prevention and treatment of beta-amyloid toxicity and AD	antipsoriatic, antiulcer, hepatoprotective, antidepressant activity, anticonvulsant, sedative, immunostimulant, cardioprotective, antidiabetic, cytotoxic	
5	***Clitoria ternate*** (commo n name: Aparajit (Hindi), Aparajit a (Bengali) and Kakkatta n in Indian tradition al medicine)	Fabaceae	Root s leaf extra ct and aerial parts of c. ternat ea	Taraxerol, Teraxerone, ternatins, delphinidin-3, delphinidin-3ß-glucoside, malvidin-3ß-glucoside, 3 monoglucosi de, 3-rutinoside, 3-neohisperidos ide, 3-o-rhamnosyl Glycoside, kaempferol-3-o-rhamnosyl, aparajitin, beta-sitosterol, malvidin-3ß-glucoside, kaemphferol, p-coumaric acid, etc., are	C. ternatea behaved as brain tonic owing to their potential in increasing levels of acetylcholin e in the brain.	nootropic, anticonvulsant, antidepressant, antianxiety, antistress, antioxidant, anti-inflammatory, antihyperlipidemic , antidiabetic, antiasthmatic, analgesic, immunomodulator y, cytotoxicity, platelet aggregation inhibitory, antimicrobial, gastroprotective and hepatoprotective	2 3-2 4

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				isolated from C. ternatea			
6	***Convolvulus pluricaulis*** (Common name: Shankhpushpi)	Convulvulaceae	Leaf extract	Shankhpushpine, Convolamine, phytosterol, amino acids, fatty acids, scopoletin, beta-sitosterol, Volatile oils, favanoid-kampferol.	Its administration for 3 months at the dose of 150 mg/kg prevented aluminum chloride induced neurotoxicity by decreasing AChE activity, reducing oxidative stress and preserving the activity of ChAT and Nerve Growth Factor-Tyrosine kinase A receptor (NGF-TrkA) [242].	Nootropic, antistress, anxyiolytic, anticonvulsant sedative activities, antiulcer, antibacterial, immunomodulatory, cardiovascular activity, antidepressant, antiamnesic, anticatatonic.	25-27
7	***Coriandrum sativum L.*** (Common name- Cilantro, Chinese parsley)	Apiaceae	Leaf extract, volatile oil	Petroselinic acid, linalool, fatty acids	Ethanolic extract (volatile oil) were assessed in the β-amyloid rat model of Alzheimer's	Antioxidant, Antidepressant, and Anxiolytic proprieties	28-29

					disease. The anxiolytic and antidepressant effects were evaluated in vivo, and the antioxidant property was estimated by the total content of the reduced glutathione in the hippocampus. The experiment revealed that the anxiolytic and antidepressant-like effects decreased catalase activity and increased glutathione levels in the hippocampus of the rat brain.		
8	***Curcuma longa L.*** (Common name:	Zingiberaceae	Rhizomes extracts	Curcumins (Diferuloylmethane), Flavonoids Phenols	It was found that oral administration of curcumin	Neuroprotective, Anti-Inflammatory,	30

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	Turmeric)			Dimethoxy curcumin, bisdemethoxy curcumin, glycosides and terpenoids	inhibits Aβ fibril deposition and hyperphosphorylation of tau proteins that is an important pathway.	Protein Hyperphosphorylation Inhibitor, In cough, hepatic disorders, Diabetes.	
9	***Desmodium gangeticum*** (Common name:Salpani)	Fabaceae	Powdered root, leaf paste	Alkaloids (tryptamines and phenylethylamines), phospholipids, sterols, flavone, Pterocarpanoids (gangetin, desmodin), and glycosides.	Elicits AChE inhibitory activity. Improves learning and memory in scopolamine and ageing models.	Antileishmanial, immunomodulatory, antioxidant, anti-inflammatory, antinociceptive, cardioprotective, antiulcer, antiamnesic and hepatoprotective	31-33
10	***Eclipta alba (L.)*** (Common Name: Bringharaj, Hassk)	Asteraceae	Flower extract	Coumestans, flavonoids, alkaloids, volatile oil, sterols, triterpenoid saponins.	Butanol fraction increased ACh content, decreased MAO-B activity and reduced oxidative stress in the rat brain. Lipid lowering and antioxidant activities of Eclipta	It has good antimicrobial properties like antibacterial, antifungal and antimalarial. It also shows antidiabetic, hepatic disorders, hypolipidemic, anticancer, atherosclerosis, hair growth promoting and memory enhancement and immunomodulatory properties	34-36

					plants have also been reported		
11	***Evolvulus alsinoides*** (Common name- Dwarf morning glory, Shankhpushpi)	Convolvulaceae	Leaf exact	Octadecanoic acid, n-hexadecenoic acid, squalene, cholesterol, Piperine, Ethyl oleate	The methanol and water extract exhibit acetylcholinesterase activity, supporting its potential in reverting neuronal dysfunctions.	Antioxidant immunomodulatory,adaptogenic, antiamnesic and antiulcer	37-43
12	***Ginkgo biloba L.*** (Common name: Maidenhair tree)	Ginkgoaceae	Leaf extracts	Terpenes, bilobalide, ginkgolide	These compounds possess remarkable anti-AChE and antioxidant properties. Further clinical assessment was suggested for the methanolic extract of G. biloba upon revealing in vitro anti-AChE and antioxidant properties when tested	Antioxidant, AChE inhibitor	44

13	***Lavandula angustifolia* Mill**	Lamiaceae	Arial part extract	Linalool, tannins, linalyl acetate, camphor, coumarins, triterpenes, flavonoids.	Lavender extract treatment reversed levels of 10 metabolite markers nearly to control including carnitine, pantothenate, isobutyrate, glutamine, alanine, isoleucine, serine, valine, glucose, and asparagine involved in AD pathogenesis.	Antioxidant, neurotransmitter, antianxiety, hypnotic, anticonvulsant	445-447
14	***Moringa oleifera (M. oleifera)*** (Common name: Drum stick)	Moringaceae	Leaf extract	Vitamins (Vitamin A and C), polyphenols flavonoids, chlorogenic acid and phenolic acids), alkaloids, glucosinolates, isothiocyanates, tannins and saponins	Pre-treatment with *M. oleifera* at an oral dose of 250 mg/kg prevented hypoxia induced memory impairment in rats by maintaining the monoamines	nootropic, anti-inflammatory, hypocholesterolemic, hypotensive and antioxidant, hypolipidemic, antiobesity, antidiabetic, anti-inflammatory, immunomodulatory and anticancer effects.	485-555

					levels in the brain		
15	**Morinda *citrifolia*** (Common name: Cheese fruit, Indian mulberry, Noni)	Rubeaceae	Each part of the tree has medicinal value	Alkaloids, Lignans, Oligo and polysaccharides, flavanoids, additional it's a plant with high nutrition value it contains carbohydrates, dietary fibers, vitamin A, B3, C, Iron, potassium.	It also inhibits the metabolism of Acetyl choline by interfering with the action of Acetylcholine esterase	Anti-oxidant, Repairs broken joints, Appetite stimulant, Treats burns, swelling, boils.	56-61
16	***Matricaria chamomilla***: (Common name: Chamomile)	Asteraceae	flower	Terpinoids like α-Bisbolol, α-Bisbolol oxide A and B, Sesqueterpenes, Luteolin, Coumarins, Umbelliferone and polysaccharides	Phytoconstituents of this plant extracts are responsible for Neuroprotective and Anti-oxidant activity.	Mild laxative Anti-mutagenic Anti-spasmodic Anxiolytic Anti-inflammatory Treats sore stomach	62-69
17	***Salvia officinalis*** Common name: Garden sage	Lamiaceae	Flower	Carnosic acid and Rosmarinic acid, 1,8 cineole, camphor, α and β-thujone,	Protects PC12 cells from neurotoxicity and tau protein hyperphosphorylation.	These compounds are thought to protect the brain from oxidative damage Anti-fungal activity, Anti-viral activity, Anti-anxiety	70-71

				vridiflorol, α-pinene		activity, Memory improvement infertility, diuretics, and local anesthetic for skin, styptic, anti-oxidant.	
18	***Tinospora cordifolia*** (Common name: Giloy, Guduchi, Heart leaved moonseed)	Menispermaceae	Root's part	Steroids, Alkaloids, Polysaccharides, and Glycosides.	*Tinospora Cordifolia*'s mechanism for cognitive enhancement is by immunostimulation and synthesis of acetylcholine, this supplementation of choline enhances the cognitive function.	Treats hay fever and related symptoms Anti-viral, Anticancer, Anti-hypertensive, Vasorelaxant.	72
19	***Withania somnifera (L.) Dunal*** (Common name: Medhyar asayan (Nootropic herb), Ashwagandha, Winter cherry,	Solanaceae	Root extract	Sitoindosides, withaferin	Its extract containing sitoindosides VII–X and withaferin A (50 mg/kg, p.o for two weeks) reversed ibotenic acid-induced cognitive deficit and reduction in cholinergic markers	Antioxidant, leukotriene signaling inhibitor, apoptogenic anti-inflammatory, antioxidant, neuroprotective, antischemic, anti-Parkinson's, antiepileptic, anxiolytic, antidepression, antiarthritic, cardioprotective, antidiabetic, anticancer,	73-80

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	Indian Ginseng)				(e.g., ACh and ChAT) in rats [156]. Sitoindosides VII-X and withaferin differentially (40 mg/kg for 7 days) but favorably altered the AChE activity and enhanced M1- and M2-muscarinic receptor-binding in various brain regions.	antistress, nephroprotective, heptoprotective, antihypoxic, immunomodulatory, hypolipidaemic and antimicrobial [152].	
20	Zingiber officinalis Rosc. (Zingeberaceae) common name: Sonth	Zingiberaceae	Rhizome extractss	s, flavonoids, phenols	Exerts Aβ aggregating, antioxidant and AChE inhibitory activity.	Neuroprotective, antiinflammatory, protein hyperphosphorylation inhibitor	81-82

CONCLUSION

The primary sources of innovation in the creation of therapeutic agents are natural goods and traditional medicinal remedies. Over time, a number of substances with immunomodulatory properties derived from plants have been found. Medicinal herbs can be used to induce immunomodulation as an alternative to chemotherapy for a variety of conditions. The possibility exists to mitigate the negative effects and high expense of synthetic molecules by the identification and isolation of more targeted immunomodulatory medicines derived from plants. The importance of medicinal plants as producers of immunomodulatory molecules with a wide range of chemistries and potential applications in the treatment of humans and animals is highlighted in

this review. It is necessary to resolve the obstacles that arise while applying plant-derived immunomodulators. However, there are times when the transition from traditional remedies to modern pharmaceutical techniques is difficult. Plant secondary metabolite profiles often have a considerable dependence on environmental cues, which can interfere with the reproducibility of extract-based results and explain the inconsistent reactions of phytomedical practices. If the enriched fractions and extracts standardization guidelines are strictly followed, this can be reduced.

Adequate microbiological contamination control techniques were not used in the majority of investigations done to ascertain the impact on the immune system. According to research, the immune system's parameters can be altered by microbial endotoxins.

To combat the microbiological contamination, the proper safety measures must be implemented. Another aim is to classify immunomodulatory drugs generated from plants into a particular class or classes according to intrinsic risk. The cumulative knowledge of meta-analyses of clinical trials, national registries, and clinicians can be used to attempt this risk-level classification of novel plant-derived immunomodulatory drugs. Inadequate quantities required for development and clinical usage are a major limitation with natural products. Researchers must thus focus more on the creation of innovative separation strategies to increase the number for medicinal applications. These drugs' limited bioavailability is a significant therapeutic constraint. To increase their effectiveness when given to people, nanotechnology and other delivery methods are being used. In order to ensure the purity and efficacy of medicinal compounds obtained from plants for potential pharmaceutical uses, there is a lack of standard checking and quality control processes. It can be difficult to achieve consistent quality in every batch of some plant-derived substances because of their excessive molecular weight and structural diversity, such as polysaccharides. Improvements would be driven by the growing demand for these plant-derived products in order to overcome these barriers to market entry.

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