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Nutraceuticals As Immune Booster And Therapy In Disease Treatment

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Abstract: Immunology explores the intricate defenses our body deploys against illness, showcasing the remarkable complexity of the immune system. At its core, immunomodulation adjusts how the immune system reacts—either by amplifying or dampening its responses. The burgeoning field of immunopharmacology is focused on crafting new treatments to address the limitations of existing cytotoxic drugs, which frequently come with problematic side effects. In this context, traditional remedies, especially those from plants, are proving to be valuable alternatives. The case of salicylic acid derived from willow bark, which led to the creation of aspirin, is a prime example of how plant-based compounds can offer therapeutic benefits. There is a growing interest in exploring plant-derived immunostimulants and immunosuppressants, including substances like alkaloids, flavonoids, and polysaccharides. These natural agents hold promise for providing safer and more effective methods for managing immune functions and chronic illnesses. By combining time-tested medicinal practices with contemporary scientific innovations in immunotherapy, we stand to advance new treatment options and enhance overall health outcomes.

Index Terms **-** Nutraceuticals , Immunomodulators, Immunity.

I. INTRODUCTION

Nutraceuticals, a fusion of "nutrition" and "pharmaceutical," are products derived from herbs, nutrients, diets, processed foods, and beverages that offer both nutritional and medicinal benefits. These substances include a variety of bioactive components such as antioxidants, phytochemicals, fatty acids, amino acids, prebiotics, and probiotics, which have therapeutic properties that can positively impact the immune system. The health benefits of nutraceuticals are attributed to their active compounds, including carotenoids, collagen hydrolysate, and dietary fibers, which contribute to both enhanced nutrition and medicinal effects [1].

Nutraceuticals are classified based on their source, nature, and application, with their modes of action including anti-cancer, anti-inflammatory, antioxidant, and anti-lipid activities. They can enhance the immune system and help prevent a range of conditions, such as cancer, neurological disorders, gastroenterological issues, inflammatory diseases, and infections[1]. Additionally, they act as immunomodulators, influencing the immune system's response to support overall health[2].

1.1 Advantages of Nutraceuticals:

- **Nutritional Support**: Address nutrient deficiencies, enhance nutrient absorption, and provide tailored nutrition.
- **Disease Prevention**: Offer antioxidant protection to reduce risks of chronic diseases and boost immune system function.
- **Chronic Disease Management**: Assist in managing conditions like diabetes, high blood pressure, and arthritis.

- **Improved Overall Health**: Support digestive health, provide an energy boost, and aid in weight management.
- **Convenience and Accessibility**: Available in various forms (pills, capsules, powders) and easily accessible through health stores and online retailers [10].

1.2 Disadvantges of Nutraceuticals:

- **Quality and Regulation Issues**: Nutraceuticals lack stringent regulation compared to pharmaceuticals, leading to unverified health claims and inconsistent quality control.
- **Bioavailability**: Some nutraceuticals may have poor bioavailability, with limited data on their pharmacokinetics and pharmacodynamics.
- **Placebo Effect**: Consumers may experience perceived benefits due to the body's natural recovery processes or placebo effects, rather than the actual efficacy of the nutraceuticals.
- **Safety and Interactions**: Potential side effects and drug interactions can occur due to inadequate regulation, which may also impact their effectiveness in treating disorders [10].

Immunology is the study of the body's natural defense mechanisms against diseases, with the immune system being the most complex biological system in humans. This highly advanced system is capable of producing a diverse array of cells to combat a wide range of infections and foreign substances. Immunomodulation involves altering immune system functions, either enhancing or suppressing immune responses. Immune stimulation boosts non-specific immune components like granulocytes and macrophages, while immunosuppressant reduces immune activity, often due to environmental factors or chemotherapy[4].

This emerging field of immunopharmacology focuses on developing new immunomodulatory agents to address the limitations of existing cytotoxic drugs, which have significant adverse effects[4]. Traditional medicines, known for their long history and minimal side effects, offer promising alternatives[3]. Plant-derived substances have shown potential in modulating the immune system effectively. For instance, the bark of the willow tree, rich in salicylic acid, serves as a precursor to aspirin and illustrates the therapeutic value of plant chemicals. Research into plant-based immunostimulants and immunosuppressants is increasing, as these natural compounds, including alkaloids, flavonoids, and polysaccharides, may offer safer and more effective solutions for regulating immune function and treating chronic diseases. This growing interest underscores the importance of integrating traditional medicinal knowledge with modern scientific advancements in immunotherapy[2]..

II. IMMUNITY

Immunity refers to the body's ability to resist or defend against harmful invaders such as pathogens (bacteria, viruses, fungi, and parasites) and toxins. It encompasses a complex network of cells, tissues, and organs that work together to recognize and eliminate these threats, maintaining overall health and preventing disease [5].

2.1 Types of Immunity:

The three types of immunity are innate, adaptive, and passive [5,6] [Figure-1].

a) **Innate or Natural immunity,** is the protection that you are born with. Your body's initial defense mechanism consists of several key components. It features physical barriers like the skin and mucous membranes that prevent harmful substances from penetrating the body. Additionally, this defense system comprises various cells and chemicals designed to identify and attack foreign invaders. It has two major components:
   - ***Humoral:*** comprised by complement.
   - ***Cellular:*** consists of neutrophils, natural killer (NK) cells, and macrophages.

b) **Active immunity**, also called adaptive immunity, develops when you are infected with or vaccinated against a foreign substance. Active immunity is usually long-lasting. For numerous diseases, it can persist throughout your entire lifetime.It too has two main components:
   - ***Humoral:*** Composed of antibodies produced by B cells.
   - ***Cellular:*** mediated by T cells.

c) **Passive immunity,** happens when you receive antibodies to a disease instead of making them through your own immune system. For example, newborns receive antibodies from their mothers, and individuals can also obtain passive immunity through blood products rich in antibodies. This type of immunity provides immediate protection.

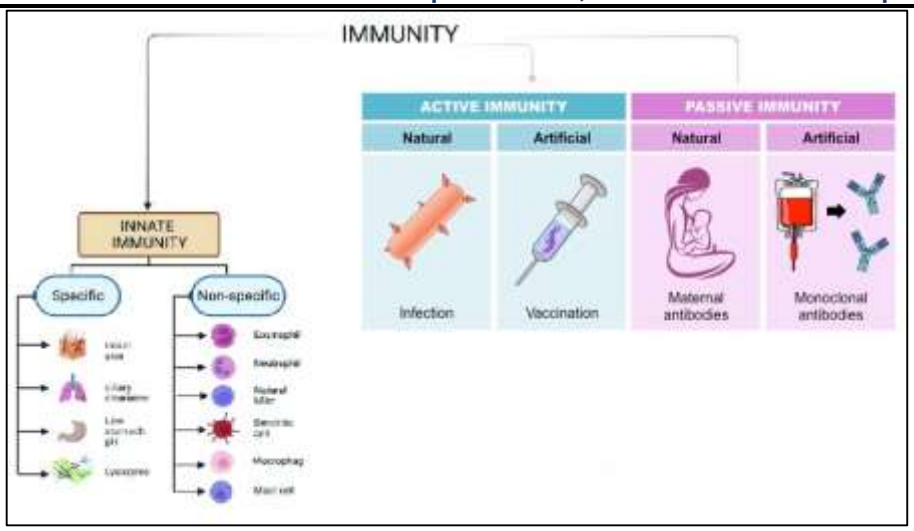

figure-1

2.2 Overview of Immune System Cells:

The immune system comprises a diverse array of specialized cells, each playing a unique role in defending the body against pathogens and maintaining overall health.

a) **Lymphocytes:** Lymphocytes are central to the immune response and are classified into three main types:
   - **T Lymphocytes (T Cells):** These cells are crucial for cell-mediated immunity, helping to directly kill infected cells or regulate other immune cells.
   - **B Lymphocytes (B Cells):** B cells are responsible for humoral immunity by producing antibodies that target specific antigens.
   - **Natural Killer (NK) Cells:** NK cells, also known as large granular lymphocytes, are involved in the innate immune response and can directly kill virus-infected and tumor cells [6].

b) **Monocytes and Macrophages:** Monocytes are large white blood cells that circulate in the blood and differentiate into macrophages when they enter tissues. Macrophages are key players in both innate and adaptive immunity, with subpopulations including:
   - **Dendritic Cells:** Found in lymphoid tissues, these cells are essential for antigen presentation and initiating adaptive immune responses.
   - **Langerhans Cells:** Located in the epidermis, they play a role in detecting and responding to pathogens at the skin's surface [6].

c) **Mast Cells and Basophils:** Both mast cells and basophils are involved in allergic reactions and inflammation:
   - **Basophils:** These circulating granulocytes (0-1% of leucocytes) release histamine and other mediators in response to allergens.
   - **Mast Cells:** Present in tissues, particularly around blood vessels and in mucosal areas, mast cells also release histamine and other inflammatory mediators upon activation [6].

d) **Neutrophils:** Polymorphonuclear neutrophils (PMNs) are the most abundant white blood cells (40-75% of circulating leucocytes). They are the first responders to infections, especially bacterial, and are equipped with granules containing various enzymes and antimicrobial substances. Neutrophils are effective against bacteria and small particles but are less effective against viruses and larger particles [6].

e) **Eosinophils:** Eosinophils (1-6% of leucocytes) are involved in combating parasitic infections and modulating allergic responses. Their granules contain enzymes and inflammatory mediators that are released upon encountering allergens or parasites, contributing to inflammation and immune response [6].

Each of these cell types plays a distinct and crucial role in the immune system, ensuring a well-coordinated defense against a broad spectrum of pathogens and maintaining the body's health.

2.3 Diseases of Immunity:

The immune system is essential for safeguarding the body from infections and diseases. When this system malfunctions, it can lead to various immune system disorders. These disorders are broadly categorized into

four main groups: immunodeficiency disorders, hypersensitivity reactions, autoimmune diseases, and possible immune disorders.

a) **Immunodeficiency Disorders:** Immunodeficiency disorders occur when the immune system fails to respond effectively, leading to increased susceptibility to infections. These disorders are categorized into two types:
   - **Primary Immunodeficiencies**:
     These are typically congenital, resulting from genetic or developmental abnormalities in the immune system. Examples include Severe Combined Immunodeficiency (SCID) and X-linked agammaglobulinemia [11]. These conditions often manifest early in life, with patients experiencing recurrent and severe infections.
   - **Secondary Immunodeficiencies**: These arise from factors that suppress an otherwise normal immune system. Causes include infections (e.g., HIV/AIDS), malnutrition, or the use of immunosuppressive drugs. Since the identification of primary immunodeficiency by Bruton in 1952, numerous conditions have been recognized, including AIDS, which was first described in 1981 [6].

b) **Hypersensitivity Reactions:** Hypersensitivity reactions involve an exaggerated or inappropriate immune response to antigens, leading to tissue damage. These reactions are divided into four categories:
   - **Immediate Hypersensitivity (Types I, II, III)**:
     Type I: Mediated by IgE antibodies, resulting in allergic reactions such as asthma and hay fever. Reactions occur within minutes of exposure.
     Type II: Involves IgG or IgM antibodies directed against cell surface or matrix antigens, causing conditions like autoimmune hemolytic anemia.
     Type III: Characterized by immune complex deposition in tissues, leading to diseases like systemic lupus erythematosus.
   - **Delayed-Type Hypersensitivity (Type IV)**: Mediated by T cells rather than antibodies. Reactions develop 24-48 hours after exposure and include conditions such as contact dermatitis and tuberculosis skin tests [6].

   Mechanisms of Hypersensitivity Reactions:
   Hypersensitivity reactions can be triggered by both exogenous antigens (e.g., dust, pollen, drugs) and endogenous antigens (e.g., self-tissues). Exogenous antigens can lead to mild discomfort, such as itching, or severe conditions, such as bronchial asthma. Endogenous antigens can trigger autoimmune diseases or graft rejection [6].

c) **Autoimmune Diseases:** Autoimmunity occurs when the immune system mistakenly attacks the body's own tissues. This loss of self-tolerance results in the formation of auto-antibodies. Autoimmune diseases are divided into:
   - **Organ-Specific Diseases**: Autoantibodies target specific organs or tissues, leading to chronic inflammation. Examples include Hashimoto's thyroiditis and Type 1 diabetes.
   - **Organ Non-Specific (Systemic) Diseases**: Autoantibodies affect multiple tissues, causing systemic damage. Conditions like systemic lupus erythematosus and rheumatoid arthritis fall into this category [6].

d) **Possible immune disorders:** These are the disorders in which the immunologic mechanisms are suspected in their etiopathogenesis. A classic example of this group is *amyloidosis.*

III. NOTE ON IMMUNOMODULATING AGENTS

Immunomodulating agents influence the immune system in either a suppressive or stimulating manner, depending on their function and application [9].

3.1 Immunosuppressors:

They are agents that inhibit or reduce the activation of immune responses. They are crucial in managing conditions where the immune system inappropriately attcks the body's own tissues, such as in autoimmune disorders or during organ transplantation. By suppressing overactive immune responses, these agents help restore balance and prevent damage to self-tissues. For example, vitamin D has demonstrated efficacy in modulating abnormal immune responses in systemic lupus erythematosus and providing benefits in atopic dermatiotis, all while preserving overall immune function [8].

Two types of immunosuppressant:

a) **Non-specific immunosuppressant:** This immunosuppressant invariably takes places, particularly in the natural instances related to immune deficiency disorders, or may even be induced by the gradual

depletion of lymohoid tissue or by the administration of immunosuppressive drugs. It has been observed adequately that undue radiation exposure gives rise to significant depletion of lymphocytes.

b) Specific immunosuppressant: Specific immunosuppressant is usually induced either by antigen or antibody. Azathiopurine and corticosteroid combination therapy is commonly used in tissue transplantation to inhibit cell-mediated immunity [CMI]. Cyclosporine is commonly used in immunosuppressive agent after organ transplantation in human [9].

3.2 Immunostimulants:

Immunostimulants, on the other hand, enhance the body's natural immune defences. They are particularly beneficial for individuals with comnprised immune systems, helping to boost their ability to fight infections. Immunostimulants can also serve as preventive measures for healthy individuals. or those at higher risk of infections. A notable application is in the context of the SARS-CoV-2 pandemic, where vaccines have been utilized to induce "trained immunity" [7]. This process improves the body's antiviral defenses and reduces susceptibility to infections by enhancing the overall immune response.

They are two types of Immunostimulants:

a) Specific Immunostimulants: It provides antigenic specificity in immune responses e.g. antigen, vaccines.

b) Non-Specific Immunostimulants: These agents enhance the immune response by acting independently of antigenic specificity, either by boosting the response to other antigens or by stimulating immune system components without targeting specific antigens e.g. Adjuvants [9].

Both types of agents play essential roles in managing immune system function, whether by mitigating excessive immune activity or by boosting immune defenses to maintain health and prevent disease.

table-1 A concise overview of immunomodulators sourced from nutraceuticals

Common Name	**Botanical name (Family)**	**Part used**	**Chemical constituents**	**Other Biological Activity**	**Ref. no.**
Tea	*Camellia sinensis*L. (*Theaceae)*	Leaves	Epigallocatechingallate, Quercetin, Gallic acid	Anti-Oxidant	12
Tulsi	*Ocimum sanctum* L.*(Labiateae*)	Entire plant	Essential Oil such as eugenol,Cavacrol	Immunomodulator	13 (14.14)
Ginger	*Zingiberofficinale roscoe (Zingiberaceae*)	Dried Rhizome	Camphene, Citral, Borneol, Cineolc	Anti-Oxidant	14 (4.39-4.42)
Garlic	*Allium sativum (Liliaceae)*	Bulbs	Diallyl disulfide, Diallyltrisulfide, Zinc, Vit-A	Anti-Oxidant Immunomodulator	14 (4.45-4.46)
Turmeric	*Curcuma langa (Zingiberaceae*)	Rhizome	Curcumin Hydrophobic	Anti-Oxidants Anti-Inflammatory	14 (7.6)
Amla	*Emblicaofficinalisgaetan (Euphorbiaceae)*	Fruit	Tannins, Punigluconin, pedunculagin	Anti-Oxidant	14 (4.50-4.51)
Pepper	*Piper nigrum (Piperaceae)*	Fruit	Volatile Oil, Guineensine, Limonenecamphene, Eugenol	Anti-Oxidant	14 (5.21)
Tomato	*Solanumlycopersicum (Solanaceae)*	Fruit	Lycopen, Lipophilic	Anti-Oxidant	14 (6.15)

Alfalfa	*Medicago sativa Linn. (Leguminosae)*	Herb	Vit.K, Vit.C, Thiamin, Riboflavin	Immunomodulator	14 (4.34-4.35)
Chicory	*Cichoriumintybus L. (Asteraceae)*	Root	Sucrose, Cellulose, Protein, Volatile oil, Chicoric acid	Anti-Oxidant, Immunomodulator	14 (4.36-4.39)
Fenugreek (Methi)	*Trigonellafoenumgraceum L (Fabaceae)*	Herb	Ascorbic acid, B Carotene, Fibers, Graicunins	Immunomodulator	14 (4.42-4.44)
Amra (mango)	*Mangiferaindica Linn. (Anacardiaceae)*	Bark	Tannin, Catechin, Mangiferin	Anti- Oxidant	13 (10.3)
Ashoka	*Saracaindica Linn. (Leguminosae)*	Dried Stem Bark	Tannin, Haematoxylin, Ketosterol, Saponin	Immunostimulant	13 (10.14-10.16)
Ginseng	*Panax ginseng (Araliaceae)*	Root	Ginsenosides, Ginsenine, β-sitosterol	Anti-Oxidant, Immnomodulator	13 (9.50-9.52)
Ashvagandha	*Withaniasomnifera dunal (Solanceae)*	Root	Withanolides, Withaferin-A, Amino acids	Immunomodulator	14 (4.56-4.58)
Roseroot	*Rhodiola imbricate gray (Crassulaceae)*	Rhizomes	Phenolics	Immunostimulating Property	15
Dragon Head	*Dracocephalumkotschyi (Lamiaceae)*	Herb	Essential oil	Immunomodulator	12
Bay leaves (Tejpata)	*Cinnomomumtamala (Lauraceae)*	Leaves	Eucalyptol, Terpineol, Eugenol	Immunosuppressant	16
Cumin (jira)	*Cuminumcyminum L. (Apiaceae)*	Seeds	Cymol, Cuminol	Immunostimulant, Immunosuppressant	17
Tamarind (Imali)	*Tamarindusindica L. (Leguminosae)*	fruits	Compesterol, seven hydrocarbon, acetic acid, tartaric acid	Antioxidant, Immunomodulator	18,19

3.3 Exploring Natural Compounds with Immunomodulatory Properties:

The quest for enhancing immune function has led to the exploration of various natural compounds derived from plant and animal sources. These compounds, known for their diverse biological activities, hold potential for developing new therapeutic strategies to modulate immune responses. Among these, glycosides, flavonoids, coumarins, sapogenins, alkaloids, thiosulphinates, volatile oils, terpenoids, and polysaccharides stand out due to their unique properties and benefits.

a) Glycosides:

Glycosides are organic compounds that, upon hydrolysis, yield one or more sugar moieties, known as glycone parts. These compounds are pivotal in numerous biological processes, including immune modulation. Several types of glycosides exhibit immunomodulatory activities:

- **Picrorhizascrophulariiflora**: This plant contains anthraquinone glycosides known for their potential immune-enhancing effects.

- **Dendrobiumnobile**: The stems of this plant provide three novel sesquiterpene glycosides with promising immunomodulatory properties.
- **Andrographispaniculata**: Known for its active compound, Dendroside, and Dendronobilosides, which contribute to its therapeutic benefits [2].

b) Flavonoids:

Flavonoids, characterized by a 15-carbon skeleton with two phenyl rings, play significant roles in immune system modulation. They exhibit a range of immunomodulatory activities:

- **Apigenin**: A well-known flavonoid with documented immunomodulatory effects.
- **OligomericProanthocyanidins**: These compounds, found in various plants, contribute to the overall immune-enhancing effects.
- **Isoflavonoids, Flavones, and Anthocyanins**: Found in plants such as **Terminalia arjuna**, these flavonoids help modulate immune responses through various mechanisms [2].

c) Coumarins:

Coumarins are glycosides derived from benzo-a-pyrone and include furanocoumarins, which are formed by fusing a furan ring to a coumarin molecule. These compounds are known for their immunomodulatory activities.

- **6,7-Dihydroxycoumarin (Esculetin)**: Extracted from plants like **Artemisia capillaris** and **Citrus limonia**, esculetin exhibits a broad range of biological activities, including inhibition of lipoxygenase, suppression of oxidative DNA damage, and antitumor effects.
- **Angelica dahurica**: The root of this plant is used to assess cytotoxic coumarins, which also show potential in modulating immune responses [2].

d) Sapogenins:

Sapogenins, including triterpenoidsaponins and diterpenes, are known for their broad-spectrum immunomodulatory activities. Notable examples include:

- **Gymnemasylvestre**: Known for its role in modulating immune functions.
- **Chlorophytumborivilianum**, **Boswellia spp.**, and **Randiadumetorum**: These plants contain sapogenins that contribute to their immunomodulatory properties [2].

e) Alkaloids:

Alkaloids are nitrogen-containing compounds with significant physiological effects. They are found in both natural and synthetic forms and include:

- **Achilleamillefolium**, **Murrayakoenigii**, **Cissampelospareira**, and **Actinidiamacrosperma**: These alkaloids have demonstrated various immune-modulating effects, enhancing their therapeutic potential [2].

f) Thiosulphinates:

Thiosulphinates, found in plants like **Allium hirtifolium**, are noted for their potent immunomodulatory and adaptogenic effects. These compounds contribute to the overall enhancement of immune function [2].

g)Volatile Oils and Terpenoids:

Terpenes and terpenoids are hydrocarbons with oxygenated derivatives found in plants and animals. They have shown significant immunomodulatory activity:

- **Eugenol**: Derived from **Ocimum sanctum**, this compound exhibits notable immunomodulatory effects, contributing to its therapeutic benefits [2].

h) Polysaccharides:

Polysaccharides, particularly those derived from both microbial and botanical sources, play a critical role in immune regulation. They are known to bind to surface receptors on macrophages, inducing various immunomodulatory responses:

- **Botanical Polysaccharides**: These compounds activate monocytic cells and induce their differentiation into macrophages, providing a unique opportunity to discover novel therapeutic agents with immunomodulatory properties [2].

IV. CONCLUSIONS

The convergence of nutraceuticals and immunology represents a promising advancement in health optimization through natural compounds with immunomodulatory effects. Nutraceuticals, which include extracts from herbs and dietary sources, offer notable nutritional and therapeutic advantages due to their bioactive components such as antioxidants, phytochemicals, and dietary fibers. These elements support immune function, reduce inflammation, and safeguard against chronic illnesses.Classifying nutraceuticals by their source, nature, and application underscores their diverse therapeutic potential, particularly in

modulating immune responses. They can either enhance or temper immune activity, providing valuable interventions for a wide range of health issues from cancer and neurological disorders to inflammatory diseases. However, challenges such as ensuring quality control, enhancing bioavailability, and addressing safety concerns highlight the need for more rigorous research and regulatory oversight in this field.

Immunology, which explores the immune system's intricate mechanisms, reveals the importance of immunomodulation in maintaining immune balance and treating autoimmune conditions. Natural compounds, including plant-derived substances like salicylic acid from willow bark, demonstrate promising potential in modulating immune responses with potentially fewer side effects compared to conventional drugs. Exploring compounds such as glycosides, flavonoids, and polysaccharides further emphasizes the therapeutic promise of nutraceuticals. Integrating traditional knowledge with modern scientific insights could enhance disease management and prevention, ultimately contributing to a more effective and balanced healthcare approach. Continued research in this area is crucial for fully leveraging the benefits of these natural compounds.

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