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ADVANCES IN POLYHERBAL FORMULATIONS FOR IMMUNE ENHANCEMENT: A COMPREHENSIVE REVIEW

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ABSTRACT

A well-functioning immune system is essential for maintaining health, preventing infections, reducing inflammation, and ensuring rapid recovery from diseases. However, factors such as stress, poor nutrition, pollution, and lifestyle disorders can compromise immune function, increasing susceptibility to illness. In recent years, there has been growing interest in plant based immunomodulators as safer and holistic alternatives to synthetic agents. Polyherbal formulations, which combine two or more medicinal plants in specific proportions, are designed to enhance therapeutic efficacy through synergistic interactions among bioactive phytoconstituents. Unlike single-herb preparations, polyherbal combinations provide a broad spectrum of phytochemicals such as flavonoids, phenolics, alkaloids, glycosides, terpenoids, vitamins, and essential oils that collectively strengthen immune responses. These formulations modulate both innate and adaptive immunity by regulating cytokine production, enhancing macrophage and lymphocyte activity, improving antibody responses, reducing oxidative stress, and suppressing chronic inflammation. This review discusses the growing acceptance of herbal immune boosters, which are natural remedies derived from plants. Through a synergistic method, oxidative stress is decreased, cytokine production is regulated immune cell activation is improved and macrophage and lymphocyte function is improved. Moreover, polyherbal formulations frequently balance dosage to minimize side effects while increasing bioavailability and medicinal efficiency.

Keywords: Immune System, herbs, immunity booster, antioxidant, immunomodulatory.

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INTRODUCTION

A complex network of diverse immune cells and chemicals that defend against infections and other invaders is known as the immune system, [1]. The innate immune system stimulates immune cells such as neutrophils, monocytes, dendritic cells, macrophages, and epithelial cells by using pattern recognition receptors to recognize the molecular patterns of pathogens. Both host-derived damage-associated molecular patterns and pathogen-derived, pathogen-associated molecular patterns are also targeted by PRsI [2]. The two main classifications for immune systems are innate (non-specific) and adaptive (specific). Immunoglobulins (Ig), which are generated by B cells in response to antigenic onslaught from allergens and pathogens, are associated with specific immunity. The classes IgA, IgG, and IgE are further separated after activation through isotype swapping. Since IgAs are present in mucosal secretions, breast milk, perspiration, tears, and saliva, they are the most pertinent to the current review. Furthermore, the

IgAs help control commensal microbes at mucosal sites and prevent infections [3]. White blood cells (leukocytes), which are part of the immune system, made up of cells, tissues, and organs, move throughout the body to defend against invaders and infectious organisms [4]. Plants high in antioxidants, vitamins, proteins, carbohydrates, dietary fibre, amino acids, minerals, steroids, alkaloids, and antiviral and antibacterial phytochemicals include garlic, Margosa Neem, Tulsi, Giloy, Clove, Ginseng, Betel vine, Black pepper, Black cumin, Ashwagandha, Liquorice, Astragalus [5].

TYPES OF IMMUNITY

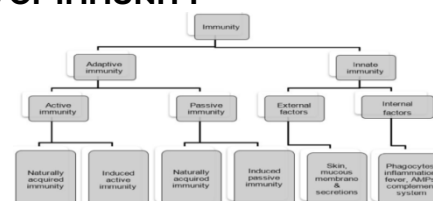


Figure 01: Types of immunity [6]

INNATE IMMUNITY

Natural immunity, sometimes referred to as in-born immunity, is a person's defense system against pathogenic microorganisms and includes all defense systems that shield the host from dangerous pathogens [6]. To protect human hosts against viral assaults, innate immunity also referred to as nonspecific immunity now works in tandem with the adaptive immune system. An important regulator of human inflammatory illnesses, such as asthma, atopy, and autoimmune conditions like type 1 diabetes, inflammatory bowel disease, and systemic lupus erythematosus, innate immunity is essential for host defense against viral threats [7]. Numerous cells, such as phagocytes, dendritic cells, mast cells, basophils, eosinophils, natural killer (NK) cells, and lymphocytes (T cells), are essential to the innate immune response. Neutrophils and macrophages are the two primary cell types that make up phagocytes. Neutrophils have granules that aid in the removal of harmful microorganisms, and both have the ability to phagocytose microorganisms. Conversely, macrophages are long-lived cells that deliver antigen to T cells and engage in phagocytosis [8].

ADAPTIVE IMMUNITY

Immunoglobulin (Ig), a Y-shaped figure, is the first antigen-specific receptor. The immune system uses a variety of receptors, including antibodies, to monitor the environment. The Ig domain, commonly used template for a variety of molecules in the immune system. It is made up of three globular domains joined by flexible linkers. Ig domain-containing proteins are members of the immunoglobulin super family, that communicate with immune cells by binding to an antigen [9]. Customized receptors produced by somatic recombination of gene segments are essential for adaptive immune responses. These developed as a result of vertebrate gene duplication, producing extremely precise and adaptable reactions. Cells that express these receptors can remain in the host for life after coming into contact with a pathogen [10]. Antigen-specific receptors on T and B cell surfaces, which are produced by somatic rearrangement of germline gene elements and enable the production of millions of distinct antigen receptors, give the adaptive immune system remarkable specificity for antigens [11].

HERBS USED AS IMMUNITY BOOSTER

Probiotics and prebiotics, melatonin, medicinal herbs, beekeeping products, and other naturally occurring substances with immunomodulating qualities could investigate novel treatment approaches to boost immunity against a range of illnesses. Numerous vitamins and minerals are also highly useful in promoting healthy immune system function [11]. Numerous species in a number of botanical families, including Asteraceae, Myrtaceae, Rutaceae, Phyllanthaceae, Piperaceae, Labiatae, Solanaceae, Liliaceae, Zingiberaceae, Argliaceae, Lamiaceae, Euphorbiaceae, etc., have been shown to have immunomodulatory properties. In

recent years, a growing number of herbs with immunostimulant properties have been studied and discovered for use in traditional medicine, based on the study of plant species from all over the world. Herbal remedies are thought to be efficient and affordable natural immunomodulators [12].

Table 01: Enclosing the list of herbs used as immunity boosters

Stevia	<i>Stevia rebaudiana</i>	Asteraceae	Stevioside, Rebaudiosides, Caffeic acid, Quercetin, Luteolin.	Immunomodulatory activity, antioxidant, anti-inflammatory, antidiabetic, anticancer, anti-obesity [23-28].
Jamun	<i>Syzygium cumini</i>	Myrtaceae	Ellagic acid, Gallic acid, Ferulic acid, Myricetin, Rutin, Quercetin, Kaempferol.	Immune boosting activity, antioxidant, antibacterial, antifungal, antiulcer, antihyperlipidemic, antidiabetic, Hepatoprotective, CNS activity [50-54].
Bael	<i>Aegle marmelos</i>	Rutaceae	Gallic acid, Ferulic acid, Caffeic acid, Marmelosin, Umbelliferone, Scopoletin, Aegeline, Quercetin.	Immunostimulant activity, anti-cancer, anti-diabetic, antibacterial, antifungal, anti-oxidant, cardioprotective, neuroprotective [56-57].
mla	<i>Phyllanthus emblica</i>	Phyllanthaceae	Emblicanin A, Emblicanin B, Chebulinic acid, Rutin, Ascorbic acid, Quercetin.	Immune-boosting activity, cytoprotective, anti-inflammatory, antidiabetic, anticancer, cardioprotective, dermatological and hair care, gastroprotective [61-63].
Fenugreek	<i>Trigonella foenum graecum</i>	Fabaceae	Diosgenin, Yamogenin, Tigogenin, Trigonelline, Choline, Gentian Ine.	Anti-diabetic, hypoglycaemic, anti-hyperlipidemic, anti-inflammatory and anti-oxidant, anti-parasitic, anti-cancer [74].
Peppermint	<i>Mentha</i>	Lamiaceae	Menthol, Menthone, Rosmarinic acid, Caffeic acid, Hesperidin,	Immunomodulatory, anti-inflammatory, antimicrobial, antioxidant, analgesic and

	<i>piperita</i>		Luteolin, Apigenin.	topical, anti-tumour and antidiabetic [71-73].
Ashwagandha	<i>Withania somnifera</i>	Solanaceae	Withanolide s, Withaferin A, Withanolide A, Withanolide D, Somniferine, Tropine, Cusco hygrine.	Immunostimulant, adaptogenic and antistress, neuroprotective and cognitive enhancer, anti-inflammatory, anti-oxidant, cardioprotective [75].
Moringa	<i>Moringa oleifera</i>	Moringaceae	Quercetin, Kaempferol, Chlorogenic acid, Gallic acid, Myricetin, Rutin, Glucomorinin, Moring in.	Potent anti-oxidant, anti-inflammatory, antioxidant, hepatoprotective, antidiabetic, anticancer, cardioprotective and neuroprotective [76].
Tulsi	<i>Ocimum Sanctum Linn</i>	Labiatae	Eugenol, Methyl eugenol, Linalool, Rosmarinic acid, Apigenin, Luteolin, Ursolic acid, Oleonic acid, Vicianin, Orientin.	Anti-stress and adaptogenic, antimicrobial and antiviral, anti-inflammatory and antioxidant, cardioprotective, antidiabetic, anticancer [77].
Cardamom	<i>Elettaria Cardamomum</i>	Zingiberaceae	1,8-Cineole, α -Terpinyl acetate, Gallic acid, α -Pinene, β -Pinene, Quercetin.	Anti-oxidant and anti-inflammatory, antimicrobial and antifungal, cardiovascular and metabolic health, neuroprotective and gastroprotective [78].
Gingseng	<i>Panax Gingseng</i>	Argliaceae	Ginsenosides, Panaxosides, Panaxes, Maltol.	Immune system modulation, anti-inflammatory and anti- -cancer, antiaging, adaptogenic and stress, antioxidant, anti-cancer [79].
Turmeric	<i>Curcuma longa linn</i>	Zingiberaceae	Curcuminoids, Desmethoxycurcumin, Tumerone, Ferulic acid, Quercetin, Curcumin.	Strong anti-inflammatory, anti-oxidant, anticancer, antimicrobial, neuroprotective, cardioprotective, anti-viral [80].

PLANT PROFILES

1) Stevia Leaves (*Stevia rebaudiana*) [8]



Figure 01: Stevia Leaves (*Stevia rebaudiana*)

Introduction

The leaves of the Brazilian and Paraguayan plant *Stevia rebaudiana* are used to make stevia. As a natural sweetener, stevia can be used in place of sugar. In India, stevia leaves are also known as Meethi Tulsi. Stevia's active ingredients, which include the di-terpene glycosides stevioside, rebaudiosides A-F, steviolbioside, and dulcoside, are 30–150 times sweeter than sugar and have been shown to be heat, pH, and unfermentable. Stevia glycosides were discovered in 1931 and gives sweetness

to stevia. Since the glycosides in stevia are not metabolized by the human body, it has no calorific value. Stevia has a slower-onset and more enduring flavor than sugar. Some of its extracts may also taste bitter or licorice-like at greater doses [13-15].

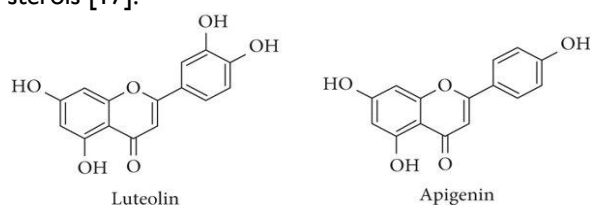
Description

Stevia is a long-lasting plant that can reach a height of about 1 meter and leaves of 2 - 3 centimetres long. The leaves are attached directly to the stem and are green in colour. They do not

have any scent. The taste is a bit sweet. The size of the leaves is 5 centimetres long and 3 centimetres wide. The leaves have an oval shape. Additionally, the leaves have pointed ends and a petiole that connects them to the stem, and their surfaces are smooth. The flowers are white and have a funnel shape with lobed parts [16].

Chemical Constituents

Stevia contains a wide range of natural plant compounds, including terpenes and flavonoids, which contribute to its biological properties. Its sweetness mainly comes from glycosides such as stevioside (about 5–10%) and rebaudioside A (around 2–4%), both of which provide a strong sweet taste without adding calories. Other sweet components include steviolbioside, rebaudiosides (A–F), and dulcoside A. Despite its sweetness, stevia can have a slight bitter aftertaste due to the presence of tannins, flavonoids, and certain volatile compounds. It also contains various bioactive substances like apigenin, caffeic acid, beta-sitosterol, kaempferol, quercetin, luteolin, chlorophyll, and steviol derivatives, along with plant sterols [17].



Nutritive Values

Stevia leaves are a natural low-calorie sweetener that provide about 2.7 kcal/g in dry form. They contain useful nutrients such as carbohydrates, proteins, fibre, and small amounts of fat. These nutrients help in supporting overall health and may reduce the risk of certain diseases. Stevia also has oligosaccharides, which may help in controlling blood sugar and lipid metabolism. In addition, it contains essential minerals that are important for growth, body functions, and tissue development [20–21].

Medicinal Uses

Stevia has drawn the attention of health-conscious fitness lovers all over the planet as a non-caloric sweetener. It is regarded as replacing saccharin worldwide. The major sweet compounds that are isolated from the stevia leaves are several glycoside compounds including steviolbioside [22].

Pharmacological Activities

1) Anti-diabetic & Antioxidant Action:

Stevia rubidiana Bertoni has been utilized for managing diabetes. The results show a drop in blood sugar levels, ALT and AST, alongside a rise in insulin levels. Stevia leaves protect rats from diabetes, reduce stress risks, and improve liver and kidney health. It also has antioxidant qualities [23].

2) Antimicrobial & Larvicidal Actions:

The leaf extracts of *Stevia rubidiana* Bertoni have demonstrated the ability to fight against various germs (12 types of Streptococci and 4 types of Lactobacilli) using the well diffusion technique. Secretory Immunoglobulin A (sigA), a key antimicrobial antibody, showed levels ranging from 100–400 µg/mL under normal conditions and increased up to 450 µg/mL following

treatment, indicating enhanced antimicrobial defense. The area of inhibition was also examined in this study [24].

3) Anti-inflammatory & Immune Modulation Actions:

Indicate that the anti-inflammatory properties of sativoside in cases of LPS-induced lung injuries are due to the blockage of the NF- κ B signalling pathway. Steviside could be considered for treating acute lung injuries (25).

JAMUN LEAVES (*Syzygium cumini*)

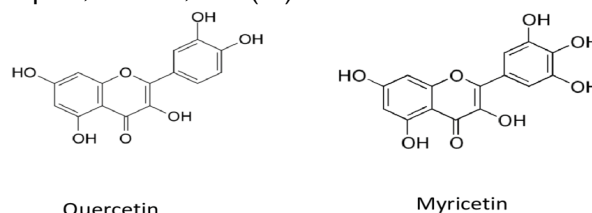


Figure 02: Jamun Leaves (*Syzygium cumini*)

Angiosperms are a diverse group of plants encompassing more than 300,000–400,000 species, which represent about 80% of all living green plants on Earth. (28–29) The World Health Organization has identified 21,000 medicinal plants, and India is an abode for 2,500 important medicinal plants in the world. Angiosperms have the unique ability to synthesize numerous bioactive compounds that can be of medicinal and healthcare importance to humans. The use of plants and natural products dates back at least 5,000 years, and the Atharva Veda lists at least 50 plants used for the treatment of different ailments. (30–31) The Myrtaceae family consists of 121 genera and 5,800 species of perennial trees and shrubs that are distributed widely in the subtropical and tropical regions of the world. This family consists of plants that bear edible fruits, which are a berry type with pulp. The plants have a characteristic aroma and are of great agro-industrial importance [32–33].

Chemical Constituents

It has been documented that *S. cumini* seeds possess glycoside jambolin (antimale), alkaloid jambosine, and ellagic acid. Furthermore, the presence of flavonoids, phenolics, protein, and calcium has also been noted. Anthocyanins, which give the fruit its colour, are present in the fruits, along with gallic acid, malic acid, glucose, fructose, raffinose, petunidin, malvidin, petunidin 3-gentiobiose, and malvidin 3-laminaribioside. Moreover, the fruits have also been shown to contain a range of nutrients, including carbohydrates, fibre, calcium, magnesium, phosphorous, sodium, potassium, copper, sulphur, chlorine, iron (42).



Description

Jamun grows best in deep, well-drained loamy soil and is cultivated in countries such as the USA, Israel, and the West Indies for its fruit and valuable wood. It is a large

tree that takes many years to fully mature and can reach up to 100 feet in height with a broad canopy. The trunk is thick, with rough, cracked bark that peels off and changes from mottled near the base to smooth pale grey above. Its branches often begin close to the ground, giving the tree a wide spread. The leaves are opposite, oblong to elliptical in shape, and measure about 8–10 inches long, with rounded or pointed tips [43-45].

Nutritive Values

Jamun fruit pulp is highly nutritious, though its exact composition can vary depending on where and when it is grown. It contains a high amount of moisture (around 79–86%), making it very hydrating. The pulp has modest levels of natural sugars and carbohydrates, along with small amounts of fats (about 1.28%), proteins (around 0.65%), and fibre [46-48].

Medicinal Uses

Stem bark is recommended for Antisera (diarrhoea) and Rakta pitta (bleeding disease), seeds have been used to treat Madhumita (diabetes) and Gudakesha. Sushruta suggested the fruit for internal bleeding, menstruation problems, obesity, and vaginal discharge. Charaka employed the bark as an astringent and fruit, seed, and leaf decoctions to treat diarrhoea [49].

Pharmacological Activities

1. Immunomodulatory activity

Oral treatment of Jamun's methanol seed extract at dosages of 100, 200, 300, 400, and 500 mg/kg showed immunomodulatory action in mice and rats. In a dosedependent way, the methanol seed extract improved the hemagglutination titre and carbon clearance in mice as well as the delayedtype hypersensitive reaction in rats. White blood cell and lymphocyte counts were considerably increased by the seed extract [50].

2. Antioxidant activity

Many diseases are linked to oxidative stress caused by harmful free radicals. Jamun has shown strong antioxidant activity, helping to neutralize these reactive species. Studies indicate that extracts from its leaves and seeds using solvents like methanol, dichloromethane, and hydro alcohol can reduce nitric oxide free radicals in a dose-dependent manner. Different leaf extract fractions have also demonstrated the ability to enhance antioxidant power and scavenge free radicals such as DPPH. Ethanol extracts further improve reducing capacity. Jamun leaf extracts are effective in neutralizing various radicals, including hydroxyl, superoxide, DPPH, and ABTS, depending on their concentration [51].

BAEL FRUIT (*Aegle marmelos*)

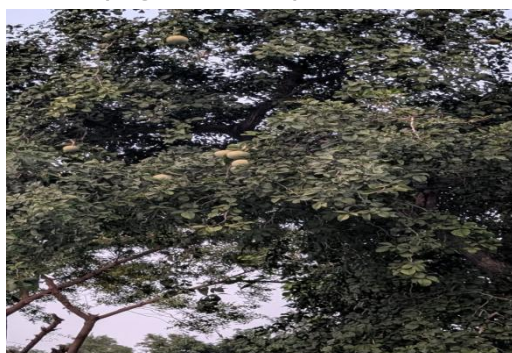


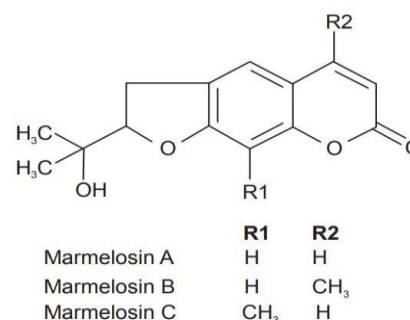
Figure 03: Bael Fruit (*Aegle Marmelos*)

Aegle marmelos (Bael), a subtropical fruit of the Rutaceae family, has been an important culinary and medicinal plant in India for over 5000 years. Its pulp is widely used to make murabba, puddings, juices, and other desserts, and the fruit is valued for its dietetic properties. Known by various regional names, Bael is also recognized as an important natural source of antioxidants [55].

Description

The fruit is generally round to oval in shape and has a pleasant aromatic smell with a pale orange color. It may appear fibrous and can range from oval, oblong, to pear-shaped forms, usually measuring about 5–20 cm in diameter. In the initial stages of development, the surface is grayish-green, which gradually changes to yellowish-orange or deep orange as the fruit matures [56].

Chemical Constituents



MARMELOSIN GALLIC ACID

Aegle marmelos is a spiny, slow-growing, medium-sized tree belonging to the family Rutaceae. The plant grows up to 12-15 meters in height and 90-120 centimeters in girth. The trunk is short, thick, soft, with flaking bark and spreading, spiny branches. The spikes present are long, sharp, and axial [56].

Nutritive Values

Numerous bioactive compounds have been isolated from the Indian medicinal plant known as Bael, which has been traditionally used to treat a variety of illnesses. Bael, which is extremely rich in vitamins like A, B group, and C, has been shown to function as an antioxidant, reducing rancidity and color loss. Alkaloids (Aegelin, Frangine, Aegeline), coumarins (marmelide, psoralen, imperatorin), and terpenoids (cineol and caryophyllene), among others, are present in *A. marmelos* [55].

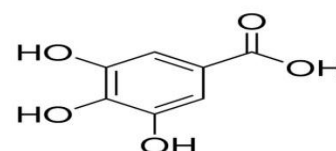
Medicinal Uses

The fruit bael contains many anti-inflammatory, and digestive qualities. It is mostly used to treat peptic ulcers, constipation, dysentery, and chronic diarrhoea. It also aids in the treatment of respiratory conditions like asthma, diabetes, fevers, and cholesterol [58-59].

Pharmacological Activities

1. Immunostimulant activity:

The



methanolic extract of the fruit was investigated for immunostimulant activity against Wistar albino rats using the carbon clearance assay and neutrophil adhesion test. It was found that the extract at a dosage of 500 mg/kg showed immunomodulatory activity in the rat model by increasing the production of neutrophil adhesion and the phagocytic index in the carbon clearance assay [56].

2. Anti-cancer activity

The *A. marmelos* of methanol and acetone extract of cytotoxicity against HepG-2, MDA-MB-231, and Vero cells were investigated. The IC_{50} of the methanol extract of *A. marmelos* was 47.08 g/ml, whereas the IC_{50} for the acetone extract of *A. marmelos* was 79.62 g/ml, making HepG-2 cells more sensitive to it. Both extracts of *A. marmelos* are toxic to cancer cells; however, Vero cells can survive 24 hours [57].

3. Anti-oxidant activity:

The fruit pulp extracts of *Aegle marmelos* prepared using methanol and ethanol have shown significant antioxidant activity in experimental studies. These extracts were evaluated using several standard methods such as DPPH radical scavenging assay, nitric oxide scavenging assay, hydrogen peroxide scavenging assay, ABTS assay, superoxide radical scavenging assay, and reducing power assay. The results indicated that both methanolic and ethanolic extracts effectively neutralize free radicals, demonstrating strong antioxidant potential. This activity helps in protecting cells from oxidative stress and damage caused by harmful reactive oxygen species. Interestingly, the extract obtained from unripe fruits was found to possess stronger inhibitory and antioxidant effects compared to that of mature fruits [56].

AMLA FRUIT(*Phyllanthus emblica*)



Figure 04: Amla Fruit(*Phyllanthusemblica*)

Introduction

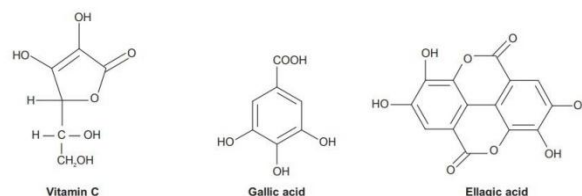
Amla commonly known as Indian gooseberry, is a wonder herb and one of the precious gifts of nature to human health. It belongs to family Euphorbiaceae. According to believe in ancient Indian mythology, it is the first tree to be created in the universe. The species is native to India and also grows in tropical and subtropical regions including Pakistan, Uzbekistan, Srilanka, South East Asia, China and Malaysia. It grows about 8-18m height with thin light grey bark, leaves are simple, light green, subsessile, closely set along the branchless looks like pinnate leaves; flowers are greenish yellow; fruits are globose, fleshy, pale yellow with six obscure vertical furrows enclosing six trigonous seeds in two seeded three crustaceous cocci [60].

Description

Amla (*Phyllanthus emblica*), or Indian Gooseberry, is a small to medium-sized deciduous tree known for its unique, sour, bitter, astringent fruit, rich in Vitamin C and antioxidants, used heavily in Ayurvedic medicine and cuisine (chutneys, preserves). The plant features delicate, light green leaves that look like pinnate leaves, greenish-yellow flowers, and smooth, spherical, greenish-yellow fruits with six vertical stripes or furrows [60].

Chemical constituents:

The fruit of *Emblia officinalis* (amla) is especially rich in tannins, making up a significant portion of the plant's total tannin content. It contains important compounds like emblicanin A and B, which are known for their strong antioxidant effects. When broken down, these compounds release beneficial substances such as gallic acid, ellagic acid, and glucose. Another compound present in the fruit is phyllemblin. Not just the fruit, but the leaves and bark are also high in tannins, while the roots contain ellagic acid and lupeol, and the bark includes leucodelphinidin. The seeds produce about 16% fixed oil, which is brownish-yellow and made up of fatty acids like linoleic, oleic, and linolenic acids, along with smaller amounts of others [62].



Nutritive values

Amla (Indian Gooseberry) is a nutritional powerhouse, exceptionally rich in Vitamin C (600-700mg per 100g), antioxidants like flavonoids & polyphenols, and fiber, with small amounts of protein, carbs, calcium, iron, and potassium, offering benefits for immunity, digestion, and overall health while being low in calories and fat. Per 100 grams, amla offers around 44 calories, about 10 g of carbohydrates, 0.9 g protein, 0.6 g fat, and over 4 g of dietary fibre. It is especially rich in vitamin C (600–700 mg), along with smaller amounts of vitamins A and B-complex. It also contains important minerals such as calcium, potassium, phosphorus, magnesium, and iron. Amla is widely valued for its medicinal benefits. Its strong antioxidant properties help protect cells from damage and support overall health [6].

Pharmacological activities:

1. Antioxidant and free radical scavenging activity:

The fruit and seed of *E. officinalis* possess excellent antioxidant properties and are important free radical scavengers that are necessary for the maintenance of redox homeostasis, which is responsible for a variety of degenerative diseases. Galic acid, which is equivalent to the total phenolic content in milk, is one such component [61]

3. Cardioprotective activity:

Rat hearts were used to study the effects of a long-term oral fresh fruit homogenate of Amla on the heart's antioxidant system and oxidative stress brought on by ischemic-reperfusion injury (IRI). By increasing endogenous antioxidants, chronic EO treatment causes myocardial adaption and shields rat hearts from the

oxidative damage brought on by IRI. The main factor causing atherosclerosis to develop is low density lipoprotein (LDL) cholesterol. Because they prevent oxidative stress, antioxidants are thought to be a great therapeutic option for atherogenesis [63].

4. Anticancer activity:

Breast, uterine, pancreatic, stomach, and liver cancers are among the tumors that amla prevents from growing and spreading. It helps lessen or avoid the negative effects of radiation and chemotherapy. When used in conjunction with cyclophosphamide treatment, EO or its pharmaceutical formulations may be advantageous for cancer patients [63].

5. Immunomodulatory activity:

Immune activation is as effective as well as protective approach against emerging infectious diseases. *E. officinalis* has been reported to inhibit chromium-induced free radical production, and it restored the antioxidant status back to control level. It also inhibited the apoptosis and DNA fragmentation induced by chromium [61].

PEPPERMINT LEAVES (*Mentha Piperita*):



Figure 05: Peppermint Leaves (*Mentha Piperita*)

Mentha piperita L., also known as peppermint, is an important medicinal herb from the Lemnaceae family. It was named the "Medicinal Plant of the Year" in 2004 and has been used for centuries in both Eastern and Western medicine, though it was first described in 1753 by Carolus Linnaeus. Besides its medicinal uses, peppermint is also popular as a flavouring agent in products like chewing gum and mints, as well as in cosmetics and pharmaceuticals. This plant is a natural hybrid between *M. aquatica* and *M. spicata*. Known as "hierba buena" (meaning "good herb"), peppermint produces peppermint oil, which is mainly made up of menthol (C₁₀H₂₀O), a waxy white crystalline substance that is solid at room temperature. The oil is found in the peltate glandular trichomes of the plant's aerial parts and is one of the most commonly used volatile oils [64-65].

Description

Peppermint (*Mentha piperita*) is a vigorous, aromatic hybrid mint known for its strong, cooling flavour from high menthol content, used in teas, foods, and remedies for digestion, headaches, and congestion. This perennial herb features square stems, dark green leaves, and purple flowers, spreading aggressively, so it's often grown in containers to control its spread. It thrives in moist soil with partial sun and is cultivated globally for its medicinal, flavouring, and fragrant properties, with harvesting best done in the morning for peak oil concentration [67].

Chemical constituents

Peppermint (*Mentha piperita*) is a perennial herb that belongs to the mint family, Lemnaceae, as shown in Fig.

01. It is known for its strong antioxidant and antimicrobial properties, as well as its active compounds. Peppermint plays an important role in boosting the immune system and improving Appetit. The plant is a hybrid cross between water mint (*Mentha aquatica*) and spearmint (*M. spicata*). The aerial parts of mint are used to extract polyphenols, such as Rosmarinus acid, eriocarpin, cinnamic acid, caffeic acid, and naringin-7-O-glucoside. Other compounds include luteolin-diglucuronide and eriodictiol glucopyranosyl rhamnopyranoside. Different species of mint contain varying amounts of these compounds. The chemical composition of mint plants can differ based on factors like physiological differences, environmental conditions, geographic location, and genetic variations [68].

Nutritive values

Peppermint is low in calories but rich in vitamins A, C, and K, minerals like iron, manganese, and potassium, fiber, and antioxidants, making it great for digestion, headaches, and freshening breath due to its active compound, menthol, though large amounts aren't typically consumed, so its benefits come from essential oils in teas or extracts, not bulk. Provides significant Vitamin A (for vision/immune), Vitamin C (antioxidant), and K (blood clotting). Offers Iron (oxygen transport), Potassium (fluid balance), and Manganese (metabolism) [70].

Medicinal uses:

Peppermint (*Mentha piperita*) offers medicinal benefits primarily for digestive issues like IBS, nausea, and bloating, thanks to its smooth muscle relaxing and antimicrobial properties, especially its active ingredient, menthol, which also helps with headaches, sinus relief, and pain. It's used in teas, essential oils (often enteric-coated for gut use), and topical applications for its cooling, anti-inflammatory, and invigorating effects on the brain, muscles, and respiratory system, though it's important to use appropriate forms for specific conditions [70].

Pharmacological Activities:

1. Immune boosting:

It supports the function of immune cells, such as macrophages, which are crucial for innate immunity. Peppermint (*Mentha piperita*) leaves boost the immune system through their potent antioxidant, antiviral, and antibacterial properties, with key compounds like menthol inhibiting pathogens, reducing inflammation, and supporting overall immune response. Studies show peppermint oil effectively fights bacteria (like *E. coli*) and viruses (including influenza, coronavirus), while also providing antioxidants that combat cellular damage, making it a valuable natural agent for preventing illness and supporting recovery [71].

2. Anti-bacterial activity

Medicinal plants have long been used in traditional medicine, and their secondary metabolites are becoming more popular as antimicrobial agents. Peppermint, in particular, has attracted attention from scientists studying infectious diseases due to its biologically active compounds. Peppermint oil (PO) and extracts have shown strong antimicrobial activity against a variety of bacteria, including *Escherichia coli*, *Salmonella pullorum*, *Streptococcus faecalis*, *Staphylococcus aureus*, *Salmonella typhi*, *Proteus vulgaris*, and many others. Studies have found

that peppermint leaf extracts are more effective against Gram-negative bacteria than stem extracts. The essential oil from peppermint leaves has the highest antibacterial activity, with inhibition zones ranging from 11.58 to 17.24 mm, while the stem extract has an average inhibition zone of 15.82 mm [72].

3. Anti-plasmid activity:

The anti-plasmid properties of peppermint were studied using the *E. coli* bacterial strain. Three different peppermint oils showed anti-plasmid activity, while all oils showed antimicrobial effects. Using a method called the checkerboard approach, researchers tested how menthol and peppermint oil affected antibiotics in the same bacterial strain. The tests confirmed that both peppermint oil and menthol have anti-plasmid effects. This suggests that menthol-containing compounds could help eliminate bacterial plasmids that cause antibiotic resistance. The unique way menthol works to eliminate these plasmids is a key feature, as it makes bacteria with plasmids more sensitive to menthol, leading to their destruction. Research also found that peppermint leaf extract has stronger antibacterial activity than peppermint stem extract, especially against Gram-negative bacteria [72].

ADVANTAGES OF POLYHERBAL FORMULATION

Synergistic impact: Several herbs combine to improve the total medicinal effect. Efficacy is increased because the combined effect is frequently larger than the separate effects (synergy). **Wide range of activity:** Polyherbal formulations can simultaneously target pathways or disorders, such as immunomodulatory, anti-inflammatory, antioxidant actions.

DISCUSSION

The immune system is a complex network of cells, tissues, and biochemical pathways that protect the body against infections and diseases. Immune boosting refers to enhancing the body's natural defense mechanisms through nutritional, herbal, and lifestyle interventions. The present study highlights the growing importance of polyherbal formulations in enhancing immune response through natural and holistic approaches. The immune system, being a complex network of cells and signalling molecules, requires balanced regulation to effectively protect the body against pathogens. The use of multiple medicinal plants in a single formulation offers a synergistic effect, where different phytochemicals work together to improve overall immunity rather than acting individually. These constituents are known to play a significant role in reducing oxidative stress, which is one of the major factors responsible for weakened immune function. By scavenging free radicals, these herbs help maintain cellular integrity and support immune cell activity. Another important observation is the immunomodulatory action of these plants, which involves regulation of cytokine production and stimulation of immune cells such as macrophages, lymphocytes, and neutrophils. This balanced modulation is crucial because both underactive and overactive immune responses can lead to disease conditions. The presence of antioxidant and anti-

inflammatory properties further strengthens their therapeutic potential by preventing chronic inflammation and tissue damage. Experimental studies discussed in the article also support the pharmacological benefits of these plants, including antimicrobial, antidiabetic, and hepatoprotective activities. Such multifunctional properties make polyherbal formulations more effective compared to single drug therapy. Additionally, the natural origin of these herbs contributes to better safety profiles and reduced side effects. Overall, the findings suggest that polyherbal formulations can serve as promising alternatives or complementary approaches to conventional immunotherapy. Natural immune boosters, especially plant-based formulations, have gained attention due to their safety and multi-targeted actions. Medicinal plants such as *Stevia rebaudiana* (Stevia), *Phyllanthus emblica* (Amla), *Syzygium cumini* (Jamun), and *Mentha piperita* (Peppermint), *Aegle marmelos* (Bael) contain bioactive compounds like flavonoids, phenolics, alkaloids, and vitamins that exhibit antioxidant, anti-inflammatory, and immunomodulatory properties. These phytochemicals help in neutralizing free radicals, reducing oxidative stress, and enhancing the activity of immune cells such as macrophages, lymphocytes, and natural killer cells. Additionally, certain herbs stimulate cytokine production, improving the body's ability to respond to pathogens. However, further clinical studies and standardization are necessary to validate their efficacy, optimize dosage, and ensure quality control. This approach could play a significant role in developing affordable and effective immune-boosting therapies in the future.

CONCLUSION

This study concludes by demonstrating that polyherbal formulations provide a balanced and natural approach to immune system support. The formulation reduces oxidative stress, controls inflammation, and boosts immune cell function by mixing plants such as *Stevia rebaudiana*, *Syzygium cumini*, *Aegle marmelos*, *Phyllanthus emblica*, and *Mentha piperita*. They are more successful than single-ingredient treatments because of their combined (synergistic) action. Because of their natural origin, these plant-based formulations tend to have less adverse effects in addition to strengthening the body's defense mechanisms. Their therapeutic value is further enhanced by their other advantages, which include metabolic support and antibacterial properties. Further clinical studies and appropriate standardization are required to verify their efficacy, safety, and ideal dosage.

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