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IMMUNOBOOSTING ROLE OF TURMERIC

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Running title:

A review on immunoboosting activity of herbs: Turmeric, Garlic and Ginger

ABSTRACT

For centuries, people of India have venerated turmeric as a spice and as a medicine. Turmeric has been utilised in traditional medicine since the dawn of mankind. Turmeric and its value-added derivatives are produced, marketed, and exported in large quantities by India. *Curcuma longa* (Turmeric) is a popular and widely available rhizomatous medicinal herb from India that belongs to the *Zingiberaceae* family. Turmeric is made up of curcumin, demethoxycurcumin, and bisdemethoxycurcumin, which are all known as curcuminoids. Turmeric has been recommended as a natural antibiofilm and antioxidant agent. One of the main constituents of turmeric, curcumin shows great immunoboosting activity and anti-inflammatory action. The chemical changes in the structure of curcumin may lead to effective modification in its antioxidant as well as water solubility which increases its bioavailability. Turmeric has long been used as a home remedy for coughs, sore throats, and respiratory illnesses and it may also be a good immune booster against SARS-CoV-2 treatments in the current pandemic. Thus, turmeric and its compounds have the potential to be used in modern medicine to cure a variety of illnesses.

Keywords: Herbal plants, Immunoboosters, Traditional medicines, Turrneric, Curcumin,

Immunomodulation.

INTRODUCTION

It is vital to have a healthy immune system in order to fight off several harmful illnesses. Immunity does not develop in a day or a week, but eating a well-balanced diet to maintain good physical and mental health strengthens our immune system . The immune system is made up of a complex network of cells, tissues, proteins, and organs . Immunity is a condition of protection from infectious disease imparted by an immune response triggered by immunisation or past infection, as well as other non-immunological variables .Good diet is essential for good health, especially when the immune system is under attack.[1]

Turmeric and other therapeutic plants are referred to as "Gifted Gods" for their ability to heal, sustain, and rehabilitate patients.[2]Turmeric, a golden spice, has a long history of use, not just as a spice but also as a medicinal herb. Traditionally, these spices have been used as a herbal cure for a range of skin, pain, lung, liver, and gastrointestinal issues like stomach cramps, diarrhoea, constipation, cough, and indigestion. Turmeric is a natural anti-inflammatory substance that works by modulating the immune system. Furthermore, current science has demonstrated that curcumin and cinnamaldehyde, two of the spice's key chemical ingredients, govern a variety of biological functions, including increased metabolism. Many medicinal chemists are still interested in turmeric because of its vast spectrum of pharmacological effects, including antiinflammatory, antidiabetic, anticancer, antiangiogenesis, antioxidant, and antiviral.In a nutshell, turmeric is a wonder spice with incredible health advantages that are essential for everyone. [3]

TURMERIC

Among Ayurveda and any other conventional medicine, Curcuma is one of the more common,primary medicines. Turmeric, also known as Haridra" or "Haldi Turmeric" is an ancient flavour obtained from the long turmeric rhizomes, which is a member of *Zingiberaceae*.[4] *Curcuma longa* (curcuma) is cultivated in

the tropics and subtropics. The world's largest producer of turmeric is India, where it has been used as a home-based recourse for several diseases for times. Short-lived turmeric perennial with huge oval leaves, and carries oval leaves, and oval bears, pyriformes, or oval rhizomes are regularly stretched and earthy yellow in color.[5]

Indications:

One of the most notable compounds found in turmeric is curcumin and it also shows antibiotic and antiviral activity. Turmeric powder has a restorative effect in both aseptic and septic lesions. It is primarily used as an anti-inflammatory agent and together for the cure of jaundice, menstrual difficulties, hematuria, hemorrhage. [6]

It is mainly used to cure digestive, skin, liver disorders. One of the major indications is as an immunomodulating agent. It is used in the treatment of arthritis and psoriasis. Traditionally it s used in the treatment of menstrual problems, epilepsy, asthma, cough, and kidney stones.[7] It is also useful as stomachic and blood purifier. Paste form of turmeric roots are used for cleaning and undergoing disinfection of the skin.[8] The above indications are illustrated in Figure 1.

Constituents:

Phytochemistry studies indicate that turmeric contains mostly curcuminoids, sesquiterpenes and terpecurcumins.[9] The flavonoid curcumin (diferuloylmethane), yellow coloring agent is the active element in turmeric. Curcumin (diferuloylmethane), DMC (demethoxycurcumin), BDMC (bisdemethoxycurcumin), and a variety of volatile oils, including tumerone, atlantone, and zingiberone, are the active components in turmeric. The principal colourless metabolite of curcumin is tetrahydrocurcumin (THC). Curcumin has been proven to have a wide range of pharmacological properties, including antioxidant, antiinflammatory, and chemopreventive, as well as neuroprotective properties. [10] Pharmacological activity of curcumin is

identified using PASS Way 2 Drug approach and illustrated in Table 1. Curcumin and curcuminoid's structures were discovered to be diferuloyl methanes in 1910. C21H20O6 is the molecular formula for curcumin. The price of turmeric goods is entirely determined by the amount of curcumin present. [11]

Turmeric powder has 3.60 grams of protein and 5.14 grams of fat. It is also mineral-rich (19 mg/100g iron; 3 mg/100g zinc). Vitamin levels are also elevated. Riboflavin is 0.23 milligrams per 100 grams, niacin is 5.14 milligrams per 100 grams, and folic acid is 39 micrograms per 100 grams.[12,13]

Chemistry of Curcumin:

Curcumin's powerful antioxidant properties are responsible for many of its medicinal effects. Curcumin is one of the few antioxidative compounds that has both phenolic and beta-diketone groups in one molecule.[14] In oxygen radical reactions, curcumin exhibits both antioxidant and pro-oxidant properties, functioning as a scavenger of radicals or a catalyst in the synthesis of radicals, depending on the experimental conditions.[15] Curcumin's antioxidant action is thought to be due to its ability to scavenge biological free radicals. Curcumin is the greatest antioxidant among natural curcuminoids and tetrahydrocurcumin has the strongest antioxidative activity among hydrogenated curcuminoids, according to studies.[16]

The highest potency was tetrahydrocurcumin, showing that hydrogenation of curcumin and demethoxycurcumin boosted their antioxidative ability. Both natural curcuminoids and tetrahydrocurcuminoids had lower antioxidant activity when one or both methoxy groups were missing.[17]Curcumin's antioxidant activity was also boosted by the presence of methoxy groups in the phenyl rings. [18]

Curcumin has a chemical structure that is both compact and distinctive, with two phenols and potentially enolizable –diketone moieties. Two allylic double bonds connect these functional groups. Because of the conjugated olefin, diketone, and phenol components, curcumin has a distinct reactivity.[19] Vanillin, p-

hydroxybenzaldehyde, ferulic aldehyde, p-hydroxybenzoic acid, vanillic acid, and ferulic acid were produced by photo-oxidation of the three major curcuminoids (curcumin, demethoxycurcumin, and bis-demethoxycurcumin) in sunlight, which were derived from oxidative cleavage of the conjugated alkyl part of the curcuminoids.[20] The chemical structure of Curcumin, demethoxycurcumin, and bis-demethoxycurcumin are illustrated in Figure 2.

Curcumin has a low water solubility, which limits its use in biological systems. It is soluble in alkaline aqueous solutions; however this reduces its stability, resulting in the formation of different breakdown products. Curcumin has the highest rate of degradation among the various curcuminoids at pH 10.2. Curcumin's solubility in aqueous solutions can also be improved by substituting it with water-soluble biomolecules. The use of heat to increase the solubility of curcumin could be a solution to the problem of bioavailability. Curcumin's full pharmacological potential is limited due to its extremely low water solubility; hence it's being explored for oral administration to patients in clinical trials. [21]

Structure Activity Relationship of curcumin:

- The presence of OH groups in the phenolic ring (entries 4 and 4') determines curcuminoids' anticancer effects. These groups help liberate radicals by donating electrons.
- The methoxy group at positions 3 and 3' improves curcuminoid's antioxidant properties
- Substitution at positions 2 and 2' improves all activities compared to unsubstituted analogues
- Cyclization in the central part of the compound and the introduction of heteroatoms (oxygen and nitrogen) leads to the formation of compounds with enhanced antitumor and anti-angiogenic properties.
- The cytotoxicity of curcuminoids is caused by the addition of groups to the OH group in positions 4 and 4'

- The removal of one of the methoxy groups exposes the Tuberculosis impact.
- The anti-HIV action is increased when methoxy groups are converted to hydroxyl ones. [22]

The structure activity relationship of curcumin is illustrated in Figure 3.

Immunoboosting activity of curcumin:

Curcumin's immunoregulatory properties have been explored extensively since they were initially described in 1999[23]. Through regulation of Th2-, immunoglobulin E (IgE), and mast cell-mediated immune responses, turmeric and curcumin improved allergic rhinitis [24], asthma [25], food allergy, allergic conjunctivitis and allergic contact dermatitis. Curcumin toxicity was not observed in human trials including doses ranging from 800 to 2500 mg per day for three months. It's an antiviral with the ability to stop viruses from replicating. Curcumin possesses renoprotective and cardioprotective characteristics, according to research. However, because of its limited absorption and metabolic instability, it has low bioavailability. When taken two to three times a day, one teaspoon of turmeric powder combined in hot milk increases protection against viral illness. [26]

Curcumin's immunomodulatory properties stem from its interactions with a variety of immunomodulators, including dendritic cells, macrophages, and both B and T lymphocytes, to name a few. The sign transducers and activators of transcription signalling is a signal transduction pathway that modulates a wide range of cytokines and growth factors involved in cell proliferation, differentiation, cell migration, and apoptosis, and are directly involved in cellular homeostasis and immune responses. [27]

T and B cells, macrophages, neutrophils, dendritic cells (DC), and natural killer cells can all be affected by curcumin. Curcumin inhibits the production of pro-inflammatory cytokines such IL-1, IL-2, IL-6, IL-8, IFN-γ, monocyte chemotactic protein 1-1 (MCP-1), iNOS (Nitric oxide synthase), and NO in a variety of clinical

situations.[28-30] Curcumin stops lymphocytes from proliferating and secreting IL-4, IL-5, and granulocyte-macrophage colony-stimulating factor (GM-CSF). Curcumin, on the other hand, can increase the expression and synthesis of IL-10, which can help to reduce inflammation. Curcumin inhibits angiotensin-converting enzyme (ACE) and reduces TNF-, IL-12 activity, and macrophage infiltration, among other anti-inflammatory actions. TGF and NF-B signalling, as well as the expression of smooth muscle actin and Tenascin-C, an antiadhesive protein, are all inhibited by curcumin.[31-33] The overall immunoboosting activity of turmeric is shown in Figure 4.

TABLES

Table no. 1: PASS analysis of Curcumin

Pa	Pi	Activity
0,936	0,003	Feruloyl esterase inhibitor
0,898	0,001	Beta-carotene 15,15'-monooxygenase inhibitor
0,900	0,008	Aspulvinone dimethylallyltransferase inhibitor
0,887	0,014	Membrane integrity agonist
0,872	0,003	Monophenol monooxygenase inhibitor
0,864	0,003	Reductant
0,833	0,003	Carminative
0,832	0,005	Linoleate diol synthase inhibitor
0,833	0,010	Gluconate 2-dehydrogenase (acceptor) inhibitor
0,826	0,003	HMOX1 expression enhancer
0,833	0,014	Chlordecone reductase inhibitor
0,836	0,021	Ubiquinol-cytochrome-c reductase inhibitor
0,812	0,002	Vanillyl-alcohol oxidase inhibitor
0,814	0,004	Antimutagenic
0,816	0,014	Mucomembranous protector
0,805	0,003	MMP9 expression inhibitor
0,803	0,008	Apoptosis agonist
0,783	0,003	Steroid N-acetylglucosaminyltransferase inhibitor
0,777	0,003	GST M substrate
0,778	0,012	GST A substrate
0,766	0,003	Free radical scavenger
0,764	0,004	TNF expression inhibitor
0,747	0,009	Caspase 3 stimulant
0,747	0,011	UDP-glucuronosyltransferase substrate

0,737	0,004	MAP kinase stimulant
0,736	0,007	Antihypercholesterolemic
0,731	0,013	Fibrinolytic
0,708	0,003	4-Coumarate-CoA ligase inhibitor
0,706	0,002	HIV-1 integrase (Strand Transfer) inhibitor
0,724	0,029	Membrane permeability inhibitor

Pa: Probability of Activity Pi: Probability of Inactivity

FIGURES

Figure 1: Indications of Turmeric

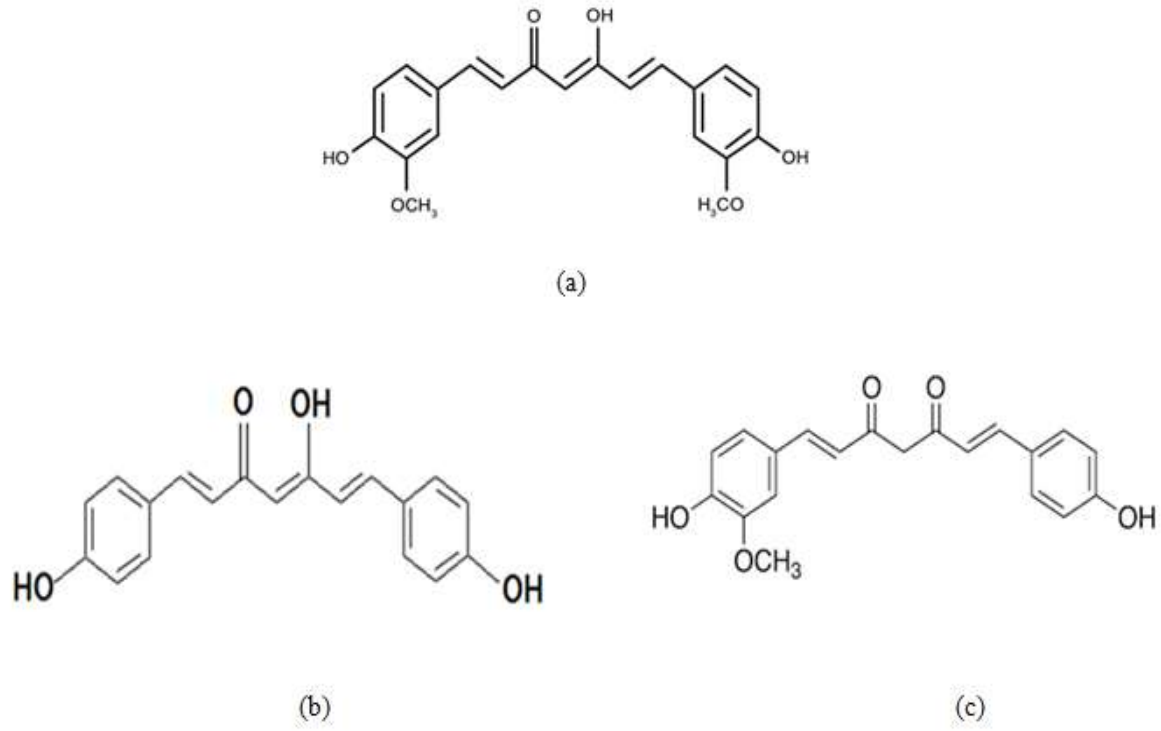

Figure 2: Chemical structure of: (a) Curcumin (b) Bisdemethoxycurcumin(BDMC) (c) Demethoxycurcumin(DMC)

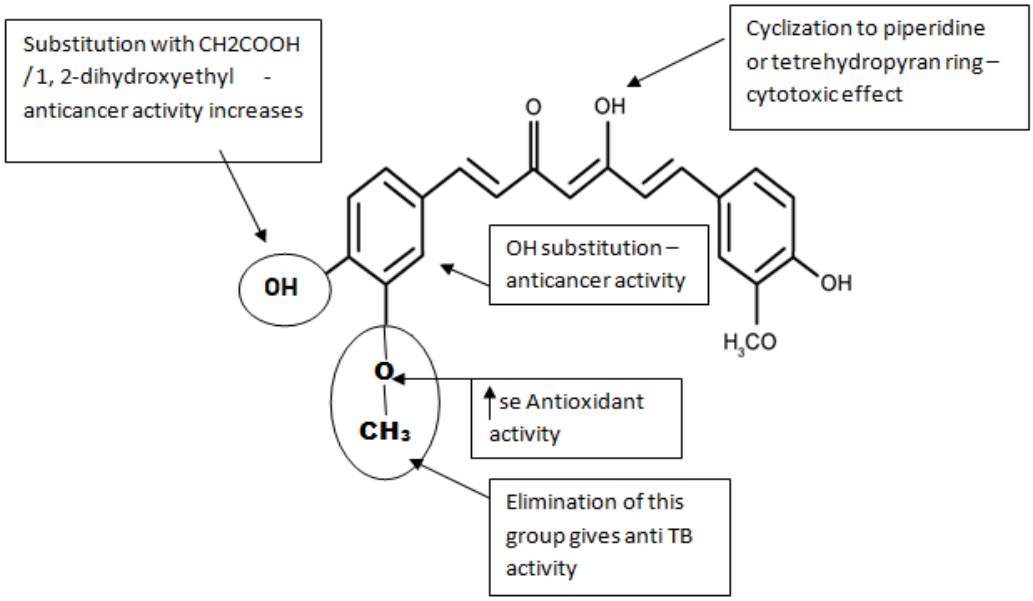

Figure 3: Structure activity relationship of curcumin

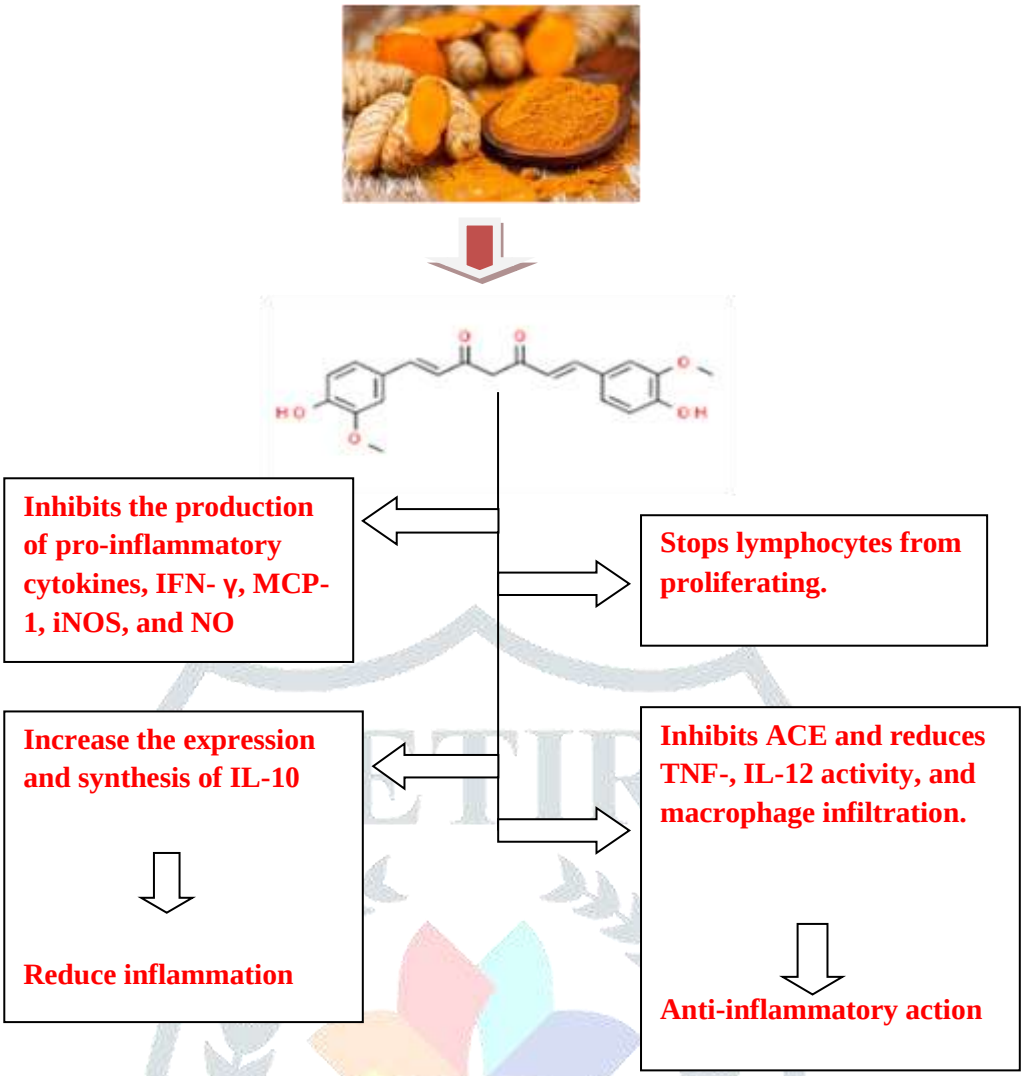

Figure 4: Immunoboosting activity of Curcumin

CONCLUSION

Curcumin, an orange-yellow polyphenol found in curry spice Curcuma longa, has a long history of medicinal usage in Ayurvedic and Chinese medicine. Numerous research undertaken over the last 30 years have backed both the wisdom and scientific credentials of this method. Curcumin has been discovered to have antioxidant, antiinflammatory, anticancer, and other properties. Curcumin uses several pathways to leave its imprint on biological systems, according to mechanistic research, which also suggests that it could be used as a modern benign chemotherapy for a variety of diseases. Curcumin's therapeutic actions are principally mediated by blocking IB degradation and consequent inactivation of NF-B, which sets off a chain of downstream inflammatory and immunogenic events. Curcumin's inhibition of NF-B activation causes the expression of various proinflammatory cytokines (e.g., TNF, IL-1, IL-2, IL-6, IL-8, and IL-12) to be inhibited, as well as the mRNA expression of several proinflammatory enzymes to be down regulated (e.g., COX, LOX, MMPs, and NOS). Curcumin's immunogenic response is boosted even further by its capacity to block TLRs. Finally, curcumin has been shown to have proimmune activity in Alzheimer's disease, multiple sclerosis, cardiovascular disease, diabetes, allergy, asthma, inflammatory bowel disease, rheumatoid arthritis, renal ischemia, psoriasis, and scleroderma, among other autoimmune disorders. Overall, these data imply that curcumin should be investigated further as a possible immunoregulatory treatment for a variety of immunological diseases. Curcumin, volatile oil, and curcuminoids, among other chemicals discovered through phytochemical research of turmeric, have been proven to have powerful pharmacological activities.

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