Trends in Immunotherapy 2024, 8(2), 4190.
https://doi.org/10.24294/ti.v8.i2.4190

Article

Concept and role of immunomodulatory medicinal plants used in Ayurvedic health care system

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CITATION

Sachin, Kumar V, Sharma M, et al. Concept and role of immunomodulatory medicinal plants used in Ayurvedic health care system. Trends in Immunotherapy. 2024; 8(2): 4190. https://doi.org/10.24294/ti.v8.i2.4190

ARTICLE INFO

Received: 1 January 2024
Accepted: 15 July 2024
Available online: 12 August 2024

Abstract: The statement "prevention is better than cure" and its applications is not a new for Ayurvedic health care system. The statement defines the aim and objectives of Ayurvedic health care system in a nutshell "swasthasya swasthya rakshanam aaturasya vikara prashamanam". The immune system is certainly considered one of our most discreet biological systems withinside the body. Immunizations may be obtained by us actively or passively. Active immunization includes stimulating with an antigen to generate immunological defenses against a destiny exposure, rather than passive vaccination, which includes administering antibodies to someone who has already been exposed to an antigen. Both plant and animal sources produce immunomodulatory effects to boost the body's immunological reactivity against infections by engaging the non-specific immune system. Herbal immunomodulators are substances that either activate or suppress innate and adaptive immune responses in the body. Different ailments including allergies, asthma, rheumatoid arthritis, cancer, and other infectious disorders are caused by immune system failure. Therefore, regulating the many infectious illnesses requires significant immune response modification. Global scientific study is currently focused on how various medicinal plant components might alter the immune system. Numerous Indian and "Rasayana" and medicinal plants may have immunomodulatory characteristics. Some of these plants are *Tinospora cordifolia*, Morus alba, Acacia catechu, Allium sativum, and Mangifera indica. There are many more that are still undiscovered and offer space for greater study.

Keywords: immunomodulators; immunization; herbal immunomodulators; Ayurveda; Ayurvedic health care system

1. Introduction

The old Indian medical system (Ayurveda) played a significant part in both the prevention and treatment of disease [1]. Numerous plants are exhibiting immunomodulatory effects [2]. Despite being an option, conventional immunomodulatory chemotherapy is more expensive and typically out of the reach of the average person with poor income. Therefore, the regulation of the immune system by traditional medicinal plant products has been a focus of contemporary scientific research around the globe [3,4]. In the traditional texts of Siddha and Ayurveda, several medicinal plants have been recommended for the treatment of disorders that cause immune weakness [5]. The current study reviewed the usage of Ayurveda and Siddha as immunomodulators in the healthcare sector. The focus of Indian traditional

medicine is illness prevention [6,7]. The term "Rasayana" refers to a collection of the many healthcare practices that an individual should follow. Rasayana is a Sanskrit word that, when translated, refers to the movement of rasa [4]. Nutrients and these nutrients penetrate tissues and cells as well as the different sections of the body. Some of those nutrients, both macro and micro, support the body's healthy operation and disease resistance. Sushruta was more explicit when he defined a Rasayana as a practice that prevents aging, lengthens life expectancy, boosts resistance to sickness, fosters intellect and memory [8]. The ayurvedic system of medicine is a very old yet very important traditional system of treatment practiced in India, Sri Lanka, and other nations. It has a strong experimental and philosophical foundation [9].

1.1. Immunity

Immunity refers to an organism's capacity to fend away dangerous microorganisms. These microorganisms behave as alien bodies for living cells, which then strive to eradicate those microorganisms. It is also known as the organism's protective mechanism to protect itself from an outside threat. Both particular and general components have a role in immunity [10]. The non-specific components serve as deterrents or barriers to the variety of pathogens with different genetic make-up and nature, whereas specific immunity is only produced when a pathogen causes infection and, in order to combat it, specific immune cells become active and produce resistance to that pathogen.

A complex biological system of the body called immunity is capable of recognizing and tolerating substances that are native to the body and beneficial to the cells, as well as recognizing and rejecting substances that are foreign. Immunity is also capable of identifying substances that are harmful to the body (non-self) [11–17].

1.2. Immunomodulator

These are biological or artificial compounds that have the power to activate, inhibit, or modify the immune system's innate and adaptive components [5].

Classifications of immunomodulator, there are three categories for immunomodulators:

- Immunoadjuvants
- Immunostimulants
- Immunosuppressant

Immunoadjuvants—They are particular immune stimulants because they are used to increase the effectiveness of vaccinations. The possibility exists that immunoadjuvants will really be the ones to modulate the immune response [18,19].

Immunostimulants—They have the ability to strengthen the immune system to fight against diseases and infections [20,21].

Immunosuppressant—They have the ability to produce immunosuppression activity and keep our immune system in check [22].

2. Mode of action of *Rasayanas*

Rasayana (Immunomodulator) (**Figure 1** and **Table 1**) medications influence the immunological system. The therapeutic benefits of *Rasayana* are felt when a skilled

Ayurvedic doctor administers the right formulation of the *Rasayana* at the right season. The medications are said to provide many benefits, including the ability to prevent life, enhance mental performance, and provide relief from a variety of illnesses, including those brought on by infections, according to the ancient *Ayurvedic* literature [8,9,23]. The scientific mind finds it difficult to believe that one plant could have such a wide range of seemingly unrelated benefits, almost as if it were a magic remedy. The only way it made sense was if the medications were altering the body's endocrine system, causing a series of events to take place that will affect many organs and result in its wide range of activities. The scientific mind finds it difficult to believe that one plant could have such a wide range of seemingly unrelated benefits, almost as if it were a magic remedy. The only way it made sense was if the medications were altering the body's endocrine system, causing a series of events to take place that will affect many organs and result in its wide range of activities [4,8,9,23,24].

Table 1. Herbal drug related to immunity and different properties.

Common name	Biological name	Family	Parts used	Chemical constituents	Biological activity
Kumari	Aloe vera	Liliaceae	Gel obtained from leaf	Saponins, anthraquinone glycosides, salicylic acid	Anti-inflammatory, emollient, Purgative, emmenagogue, immunomodulator [25]
Brahmdaru	Morus alba	Moraceae	Fruit, leaf, bark	Triterpenoid saponins, Flavonoids, anthocyanins, bacosides	Diuretic, hypocholesterolemic, expectorant, immunomodulator [26,27]
Ninjin	Panax ginseng	Araliaceae	Fruits, root	Glyrrhizic caid, saponins such as ginsenosides, panaxdiol, panaxtriole, oleanolic acid, paenoflorin	Antiarrhythmic, adaptogenic characteristics [28,29]
Yarrow	Achillea millefolium	Compositae	Leaves	Flavonoids alkaloids, linoleic caid polyacetylenes, coumarins, triterpenes	antihypertensive, anti-pyretic, antispasmodic, and anti-inflammatory [30]
Kaalmegh	Andrographis paniculata	Acanthaceae	Leaves	Andrographolide,diterpenes,kalmeghin	Febrifuge, blood purifier, immunomodulator, antispasmodic, hepatoprotective [31,32]
Surabhini-nimba	Murraya koenigii	Rutaceae	Leaves	Nimbidol,nimbolinin,coumarin, carbazole alkaloids, glucoside	insecticide, anti-fungal, immunomodulator [33]
Nagalinga	Couroupita guianensis	Lecythidaceae	Fruits, flowers	Steroids,lignans, alkaloids flavonoids, phenolics	Anti-fungal, anticancer, antifertility, antidepressant, immunomodulator, insecticidal, anthelmintic [34]
Katu-tumbi	Lagenaria siceraria	Cucurbitaceae	Katu-tumbi	Aglycones,cucurbitacin, beta-glycosidase	Laxative, aperient, anticarcinogenic, anti-HIVA, antioxidant, cardioprotective, prebiotics, immunomodulatory [35]
Kaanchana	Bauhinia variegate	Caesalpiniaceae	Roots, bark, buds	Flavonoids,lupeol, beta-sitosterol,vitamin c	Anti-fungal, anti-microbial, anti-oxidant, immunomodulator [36]
Naagabala	Urena lobata	Malvaceae	Roots, flowers	Quinazoline,flavanoids, linoleic	Diuretic, humectants, antis-pasmodic, immunomodulator, wound healing, antioxidant [37]
Gurmaar	Gymnema sylvestre	Asclepiadaceae	Leaves	Tannins, sapogenins, flavonoids	Ant-diabetic, diuretic, anti-bilious, antiarthritic, anticancer, immunostimulatory, hepatoprotective [38]

Table 1. (*Continued*).

Common name	Biological name	Family	Parts used	Chemical constituents	Biological activity
Shleshmaataka	Cordia superba	Boraginaceae	Leaf, fruits and bark	Chlorophyll,alpha-amyrin,sitasterol	Anti-inflammatory, antimicrobial, immunomodulator [39,40]
Golpar	Heracleum persicum	Apiacea	Shrub	Hexyl butyrate, flavonoids, octyl acetate Furanocoumarins	Antibacterial, antimicrobial, immunomodulator, neurological, gastrointestinal, respiratory, rheumatological and urinary tract diseases, immunomodulator [41,42]
Patha	Cissampelos Pareira	Menispermiaceae	Root	Saponins, hayatine, alkaloids, pareirine	Anesthetic, antipyretic, antilithic, anti-inflammatory, antiarthritic, antiulcer, antidiabetic, anticancer, antifertility, antimicrobial, antioxidant [43,44]
Atibala	Abutilon indicum	Malvaceae	Whole plant	Asparagines,flavanoids, alkaloids,geraniol Triterpenoids	Diuretic, antimicrobial, antifungal, cardioprotective, immunomodulator, hepatoprotective, analgesic, anti-Inflammatory [45]
Safed musli	Chlorophyyum borivilianum	Liliaceae	Root	Sapogenins, carbohydrates, proteins	Fungicide, immunomodulator, rejuvenating, aphrodisiac [46,47]
Snow ball	Alternanthera tenalla colla	Amaranthaceae	Herb	Flavanoids, Triterpenes	Anti-inflammatory, antitumor, immunomodulator [48]
Tejpata	Cinnamomum tamala	Lauraceae	Leaves	Eugenol, linalool, eucalyptol	Carminative anti-flatulent ,diuretic, immunomodulator, antimicrobial, cytotoxic, thrombolytic [49,50]
Gunja	Abrus precatorius	Fabaceae	Seed, leaves, root	Amino acid, glycyrrhizin	Anti-diabetic, anti-oxidative, bronchitis, immunomodulator, jaundice, hepatitis, abortion, malaria [51,52]
Patol	Trichosanthes diocia	Cucurbitaceaec	Fruits and leaves	Protens, carbohydrats, fats fixed oil	Antipyretic, diuretic, cardiotonic, laxative, ulcer- and inflammation-killing, immunomodulator, antidiabetic [53]
Lavanga	Syzigium aromaticum	Myrtaceae	Flower buds	Tannins,essential oil,	Antimicrobial, immunomodulator, antiulcer, antidepressant, antioxidant, anticancer [54,55]
Jeeraka	Cuminum cyminum	Umbellifera	Dried seed	Volatile oil,fixed oil, proteins	Digestion track disorder, antimicrobial, insecticidal, antioxidant, antidiabetic, immunomodulator [56,57]
Kamal	Nelumbo nuccifera	Nymphaceae	Flower, seed, root	Alkaloids, sugars, vitamins	Immunomodulator, digestive, antioxidant, antiviral, diuretic hepatoprotective [58,59]
Shigru	Moringa olifera	Morangaceae	Dried leaves, root bark	Carbohydrates, carotin,	Skin problems, wormicidal, itching, calculi, anti-inflammatory, immunomodulator [60,61]
Kutki	Picrorrhiza kurroa	Plantaginaceae	Roots, rhizomes	Glycoside, kutakoside, kutkin	Immunomodulatory, antioxidant, antidiabetic, hepatoprotective, antiarthritic [62]
Glassworth	Salicornia herbacea	Chenopodiaceae	Herb	Polysaccharides	Immunomodulator [63]
Mistletoe	Viscum album	loranthacea	Leaves, Young twigs, Berries	Viscotoxine, Polyphenols, Polysaccharides	Immunomodulator [64]
Roseroot	Rhodiola imbricate	Crassulaceae	Rhizomes	Phenolics	Immunomodulator [65]
White cedar	Thuja ossidentalis	Arborvitae	Leaves	Polysaccharides	Immunomodulator and microbicidal [66]

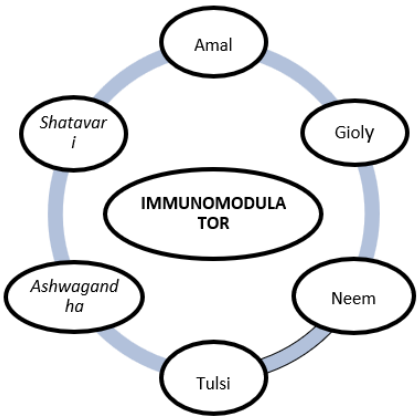


Figure 1. Some plants act as immunomodulator.

2.1. Gioly (*Tinospora cardifolia*)

Part used: Roots:

The herb *Tinospora cordifolia* (TC) is used to cure infections, diabetes, anemia, emaciation, and skin conditions. It is well known that plant extracts may activate macrophages and help us by improving phagocytic activity and increasing their intracellular killing activity. Immunosuppression accompanied by abnormal hepatic function and sepsis revealed poor surgical outcomes in obstructive jaundice. The active phytochemicals present in Gioly (*Tinospora cardifolia*) were shown to have immunomodulatory [67] and anticomplementary properties, and it has been claimed that they strengthen host defences, hence improving surgical outcomes. The traditional complement pathway was blocked by cordiol (TC-7) and syringin (TC-4). Immunoglobin G (IgG) antibodies in serum increased significantly as a result of the substance. There was a dose-dependent improvement in humoral and cell-mediated immunity. According to research, *T. cordifolia* stimulates mononuclear cells to generate cytokines including GM-CSF and IL-1. The aqueous extract is able to produce a remarkable therapeutic potential against obstructive jaundice (Kamala), TB (Rajayakshma), and complication occurs after chemotherapy. It has also been demonstrated that *T. cordifolia* selectively activates macrophages and increases their phagocytic activity. It was also demonstrated in a recent double-blind randomized controlled experiment to boost nitric oxide generation in TB patients, leading to greater macrophage stimulations. In comparison to standard anti-TB treatment alone, TB patients who received *T. cordifolia* extract also demonstrated improved radiological recovery and sputum consistency [67–70].

Active compounds of *Tinospora cardifolia* (Gioly)

Terpenoid (**Figure 2**), alkaloid (**Figure 3**), lignans (**Figure 4**), and steroids (**Figure 5**) are the main components of *Tinospora cordifolia* [71].

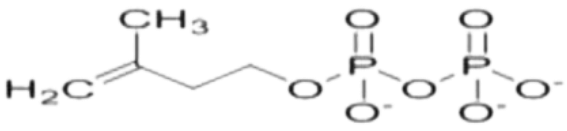


Figure 2. Terpenoid.

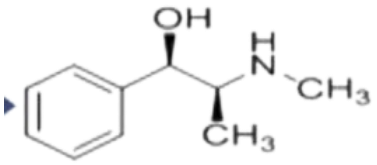


Figure 3. Alkaloid.

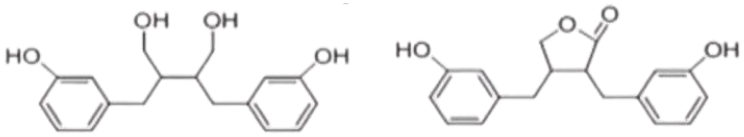


Figure 4. Lignans.

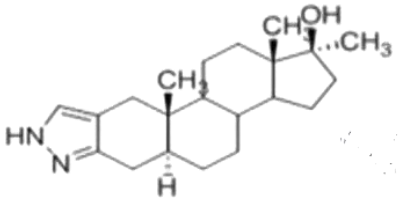


Figure 5. Steroids.

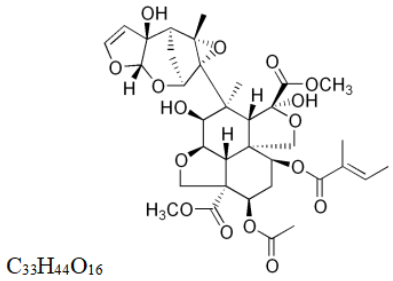
2.2. *Neem* (*Azadirachta indica*)

Part used: Leaves, stem bark:

Margosa is another name for it. It is a fixed oil made from completely grown seeds of the *Azadiracta indica* plant, a member of the meliaceae family. India and other tropical nations are home to the *Neem* plant. The medicinal properties of Azardicta indica are said to include anti-infective, anxiolytic, and general immunopotentiating properties. It is extensively researched for a variety of advantageous characteristics. The aqueous *Neem* leaf extracts boost macrophages' phagocytic activity. It has been discovered that *Neem* increases IL-2, IFN-, and TNF-a production. In 21 days, it boosted the total lymphocyte and T-cell counts in human volunteers, stimulating both cell-mediated immunity and humoral immunity by raising antibody levels. *Neem*'s ability to heal is mediated by how it is work on the immune system and produces the Rasayana karma [72–74].

Active compounds of *Azadirachta indica* (*Neem*)

Neem, *Azadirachta indica* L., plays a therapeutic role in the management of health since it is a rich source of many different kinds of substances. The most important chemical constituent is azadirachtin (**Figure 6**) [75].



$C_{33}H_{44}O_{16}$

Figure 6. Azadirachtin.

2.3. Tulsi (*Ocimum sanctum*)

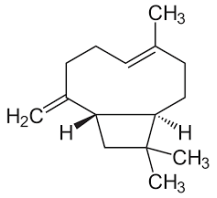
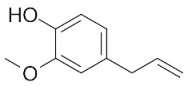
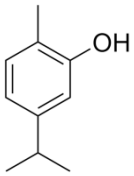
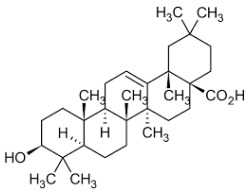
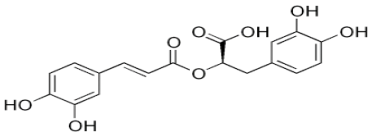
Part used: Whole plant:

It also goes by the name of holy basil. Tulsi is made up of both fresh and dried leaves from the Lamiaceae plant *Ocimum sanctum*. It is an annual herbaceous plant that is branching and tiny and is found all throughout India. Hindus regard this plant as holy. It is frequently planted in temples and in gardens. It is used as antistress, antioxidizing, and immunomodulatory agent. The alterations in plasma levels of corticosterone brought on by exposure to both acute and chronic stress were reversed by the ethanolic extract of *O. sanctum*. The modulatory effects of the alcoholic extract of leaves of *O. sanctum* on different enzyme levels in the liver, lung, and stomach of mice have been investigated by Banerjee et al. The activities of cytochrome P450, cytochrome b5, and arylhydrocarbon hydroxylase were all markedly increased by oral administration of the extract. These enzymes are crucial for the detoxification of both mutagens and carcinogens. These findings imply a possible function for leaf extract or its active ingredient in the chemoprevention of chemical carcinogenesis [76–80].

Active compounds of *Ocimum sanctum* (Tulsi)

The primary chemical components of Tulsi include -caryophyllene, Eugenol, Carvacrol, Oleanolic acid, Ursolic acid, and Rosmarinic acid (**Table 2**) [77,78]

Table 2. Phytochemicals present in Tulsi [76,78–82].

S. No.	Chemical name	Chemical formula	Structure
1	Caryophyllene	$C_{15}H_{24}$	
2	Eugenol	$C_{10}H_{12}O_2$	
3	Carvacrol	$C_{10}H_{14}O$	
4	Oleanolic acid	$C_{30}H_{48}O_3$	
5	Rosmarinic acid	$C_{18}H_{16}O_8$	

2.4. Ashwagandha (*Withania somnifera*)

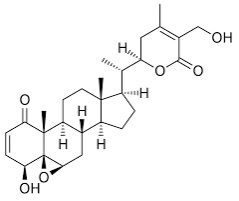
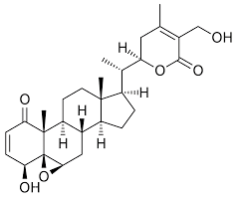
Part used: Roots:

One widely respected Rasayana is *Withania somnifera*. As an immunomodulator, anti-inflammatory, and antioxidant, *W. somnifera* is also used. Inflammatory processes are well inhibited by *Withania somnifera*. In contrast to commonly prescribed nonsteroidal anti-inflammatory medicines (NSAIDs), it can also specifically reduce the production of a-2 macroglobulin and has antioxidant properties. The plant is characterized as acting as Rasayana and mediya. Ashwagandha was discovered to lessen the signs and symptoms of anxiety in a clinical investigation of anxiety neurosis patients. The medicine has demonstrated symptomatic alleviation in mental tiredness and an immediate improvement in memory span after one month of therapy. The herb has been demonstrated to be helpful in treating depression in a different investigation. It was discovered that the test extract shown an excellent improvement in mental processes in yet another double-blind placebo-controlled clinical investigation on the extract of Ashwagandha that included both normal and depressed subjects. In tests, Ashwagandha extracts shielded mice from infections both in healthy states and in immunosuppressed conditions brought on by hemisplenectomy or other surgeries. Along with producing leucopenia brought on by cyclophosphamide-induced leucopenia, this plant also produced leucocytosis with a neutrophilic predominance.

Active compounds of *Withania somnifera* (*Ashwagandha*)

The primary chemical components of Ashwagandha include: Withaferin-A, Withanone (**Table 3**).

Table 3. Phytochemicals present in *Ashwagandha* [83–88].

S. No.	Chemical name	Chemical formula	Structure
1	Withaferin-A	$C_{28}H_{38}O_6$	
2	Withanone	$C_{28}H_{38}O_6$	

2.5. Shatavari (*Asparagus racemosus*)

Part used: Whole plant:

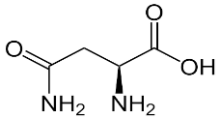
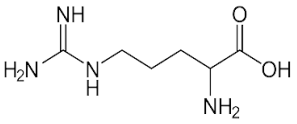
Shatavari used as an antioxidant and immunomodulator. *Asparagus racemosus* whole plant aqueous extract offers defense against biological, physical, and chemical stressors. After 17 weeks of ochratoxin A therapy, *Asparagus racemosus* treatment prevented the reduction of chemotactic activity and the generation of IL-1 and TNF-a by murine macrophages. According to research on the mechanisms of action, it

induced immunostimulation. Additionally, it has been discovered that aqueous extracts of Asparagus racemostes inhibit the myelosuppressive effects of both single and double doses of cyclophosphamide.

Active compounds of *Asparagus racemosus* (*Shatavari*)

The essential oils, asparagine, arginine, tyrosine, flavonoids (kaempferol, quercetin, and rutin), resin, and tannin are the main chemical components of asparagus (**Table 4**).

Table 4. Phytochemicals present in Shatavari [15,89–93].

S. No.	Chemical name	Chemical formula	Structure
1	Asparagine	$C_4H_8N_2O_3$	
2	Arginine	$C_6H_{14}N_4O_2$	

2.6. Amal (*Emblica officinails*)

Part used: Fruit pulp:

Embellica officinalis, a plant of the Euphorbiaceae family, is the source of both dried and fresh amla. It is a little tree that may be found in India's whole deciduous forest. Additionally, Myanmar and Sri Lanka contain it. The fruits start off green but become golden and brick red as they ripen. having an astringent flavour that is painful. It functions as an antibacterial, rejuvenator, and booster of energy. helps prevent pancreatitis, Positive nitrogen balance is induced, metal toxicity is protected, and increase cellular toxicity based on NK cells and antibodies against the Dalton lymphoma ascites tumor [94,95].

Active compounds of *Emblica officinails* (*Amal*)

The main chemical components of Amal include: vitamin C (ascorbic acid) $C_6H_8O_6$ (**Figure 7**).

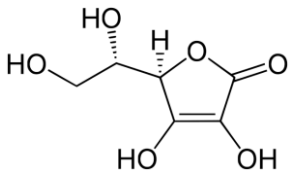


Figure 7. Ascorbic acid.

3. Conclusion

Instead of using an allopathic diagnosis method, we may treat a variety of ailments using a traditional approach that is more economical for general populations. The Siddha, Unani and Ayurveda systems used medicinal plants for treatment and diagnosis, and they are widely accessible in Indian forests. A class of pharmaceutical preparations known as Rasayana has been used successfully and widely for centuries.

They are immunostimulants and can able to stop the development of a variety of illnesses, including premature aging.

Author contributions: Conceptualization, DSB; methodology, SS, KS and BK; formal analysis, DSB; investigation, DSB; resources, NKP and SKS; data curation, DSB; writing—original draft preparation, S, VK, MS, V and PC; writing—review and editing, S, VK, MS, V and PC; supervision, NKP, AKC and DSB; project administration, AKC and DSB; funding acquisition, BK. All authors have read and agreed to the published version of the manuscript.

Acknowledgments: The authors would like to thank the School of Pharmaceutical Sciences, Lovely Professional University, Punjab for organizing 3rd International Conference of Pharmacy (ICP-2022).

Conflicts of interests: The authors declare no conflict of interest.

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