

IMMUNOMODULATORY NATURAL PRODUCT: REVIEW**SURYA PRATAP GOND, SUDHANSHU SAHU, SUDEER RAWAT, A. RAJENDIRAN, ANJU SINGH***

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Received: 09 February 2022, Revised and Accepted: 23 March 2022

ABSTRACT

Immunomodulation is also known as immune system modulation that is preceding changes the immune response result helps the tissue damage and immoderate response that is obtained by natural and unnatural (human-made) from. The review on an immunomodulatory natural products that is attention on anti-infective treatments for various numbers of justifications. Various traditional natural medicines are used for the immune response directly or indirectly impact antigen through adaptive defense mechanism of the host cell. And there currently various medicinal plants used for anti-effective such as *Aloe Vera mill*, *Panax ginseng*, *Andrographispaniculata*, and *Clausenaexcavate* that are gives immunomodulatory and anti-infective. Response and these responses have been modulated by using in their past and further developed by research change their modulation effects and many natural phytoconstituents used for immune system modulation and seen their activity on the various disease and effects and action and modulation.

Keywords: Introduction, Immunomodulator, Immunosuppressant, Natural products, Chemical constituent.

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INTRODUCTION

Immunomodulation by natural product is used for modulation of the human immune system by traditional medicinal herbs including own natural products and chemical constituents in the earliest have various natural sources used for many disorders, illness. At present, immunomodulation is their immunological response that delivers by their common therapy based on their disorder and illness state for immunological response triggered by a host defense mechanism that produces an immune suppressor produces a state as auto immune ailments. immunity is the self-defense mechanism that neutralizes antigen and protects the body [1] Immunomodulation is indicated the straighten of repression that pointed out humoral immunity, cellular, non-specific protection constituent and this are medicinal agents and depend on the dose and exhibit immunomodulatory results [2,3] immunomodulator are worked as immunosuppression and immune-stimulators that shows reversible activity and they are biologically active [4] both substances have special activity based on their sources and substances [5].

CLASSIFICATION OF IMMUNOMODULATOR

Immunomodulators are clinically categorized into three types.

IMMUNOSTIMULANT

Those agents work as stimulate the human immune system and enhance the body's resistance to microorganisms (germs, bacteria, fungi, etc.) and these are specific (work on specific allergen) and nonspecific (does not have specific allergen). They are immune protective and immune promoters [6].

IMMUNOSUPPRESSANT

That agent suppresses the immune system and their structurally and functionary heterogeneous class of medication that is used for the treatment of several kinds of corneal transplant of surgery transplant surgical operation autoimmune disorder [7].

IMMUNOADJUVANTS

Those agents are improving the strength of vaccines and work as specific immune stimulants (act on specific antigen) they are real

modulators of immune response and that is chosen between hormonal and cellular worker T1 and T2 cells immune destructive, immune protective counter IG types of the immune response [8].

HISTORY OF IMMUNOLOGY

The study of the immune system includes their properties and sources their function and structure in the first known about Immunity in ancient Time was a plague of Athens have infectious disease in 430 BC. Thucydides was an Athenian historian who noted the fact that individuals were getting recovered from the period of disease, were not getting sick from same disease another time [9]. 18th-century French mathematician and philosopher Pierre Louis Maupertuis is researched scorpion venom and observed the immunity to this venom on dogs and mice [10] after that observation, immunity developed by Louis Pasteur gives germ theory of disease and make the development of vaccination [11] after that determine the microorganism are show infectious disease virus determine for pathogens.

IMMUNOMODULATORY NATURAL PRODUCT (TABLE 1)

Number of immunomodulatory compound have been identified in various natural plants through in vivo and in vitro studies. Table 1 summarises the list few chemical compounds with their source plant species.

CONCEPT OF TRADITIONAL HERBAL DRUGS AND CORRELATION WITH AYURVEDA MEDICATION

This is the most ancient tradition, Hindu medication system that is used in India, Sri Lanka, etc., and various meditational plants used for Ayurveda Rasayana means the path of essences that enhance the body resistance and used for the enhance memory, intelligence, and promoted and improve the immune system, prevent the aging normally that used for in decline phase age 45 years for a human. Coumarin and Esculetin have a natural product that has provided immunomodulatory action (Fig. 1 and Table 2) [13].

ALOE VERA

About more than 300 types of medicinally potent found in the earth and *Aloe vera* obtained from the plant of *Aloe Barbadosis* Miller

Table 1: On the bases of Wanger immunostimulatory natural product^[12]

Low molar mass natural product		High molar mass natural product	
Category	Immunostimulatory, Natural product	Category	Immunostimulatory product
Alkaloids	Vincristine, Cocaine	Lectins	Concanavalin A
Terpenoids	Sesquiterpene lactones, diterpenes, Triterpenes	Polysaccharides	Latina's, angel an, Arabgalatans
Phenolics	Flavonoids, coumarins, quinolones tannins	Nucleotides	Poly I.C

Table 2: Immunomodulatory natural product

Chemical compound	Species	References
Phenolics		
Coumarin		[14-16]
7-hydroxycoumarin		[17]
Scopoletin	<i>Artemisia Freddie</i> , <i>Asteraceae</i>	[18,19]
Oxypeucedanin	<i>C. hystrix</i> , <i>Rutaceae</i>	[20]
Iridoid glycosides		
Oleuropein	<i>O. europaea</i> , <i>Oleaceae</i>	[21,22]
Saponins		
Ginseng saponins	<i>P. ginseng</i> , (<i>Araliaceae</i>)	[23]
Seikosaponins	<i>Bupleurum chinense</i> , (<i>Apiaceae</i>)	[24]
Esculentoniside	<i>P. Americana</i> (<i>Phytolaccaceae</i>)	[26]
Bryostatins	<i>B. neritina</i>	[27]
Glycoprotein's		
Viscotoxins	<i>V. album</i> , <i>Viscaceae</i>	[28,29,30]
Ginsengs	<i>P. ginseng</i>	[31]
Aliphatic		
Organosulfur compounds	<i>Allium spp.</i> , <i>Alliaceae</i>	[32,33]

C. hystrix: *Citrus hystrix*, *O. europaea*: *Olea europaea*, *P. ginseng*: *Panax ginseng*, *P. Americana*: *Phytolacca Americana*, *B. neritina*: *Bugula neritina*, *V. album*: *Viscum album*

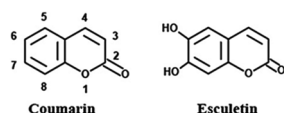


Fig. 1: Structure of Coumarin and Esculetin [46]

family Liliaceae and Aloeaceae and that also called Cape aloe, Curacao aloe isolation of dihydrocoumarin derivative from aloe Vera and their structure resolved by X-ray crystallographic diffraction analysis, 1D extensive, and 2DNMR spectroscopy are gives the antioxidant effects on mostly hydroxyl, superoxide radicals, and immunomodulatory effect show by 1 compound that mostly shows increase phagocytic action and increase the superoxide anions oxygen respiratory burst of rat peritoneal macrophages [34].

Andrographis paniculata (kalmegh)

Andrographis paniculata is commonly known as Kalmegh, and belongs to Acanthaceae family. It finds its importance and use in homeopathic and Ayurvedic medicine system. It contains chemical constituent like andrographolide and neoandrographolide. These compounds are very bitter in taste, colourless and crystalline in nature. Chemically they have diterpene lactone and show the bactericidal activity recently in research. *Andrographis paniculata* on mice that work as an immune stimulator as two types first is antigen-specific response (as work against the specific antigen and neutralize and make an antibody for a specific antigen) and antigenon-specific (destroyed invaders macrophage cells scavenge) and they work against microbial infection and cancers substances. And that work provided by adrenal activity, show the immunostimulatory, anti-inflammatory effect [36,37].

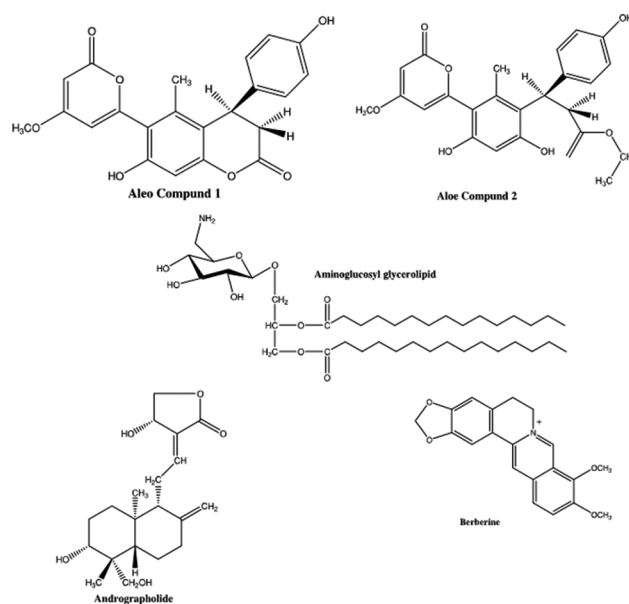


Fig. 2: Natural immunomodulatory phytoconstituents

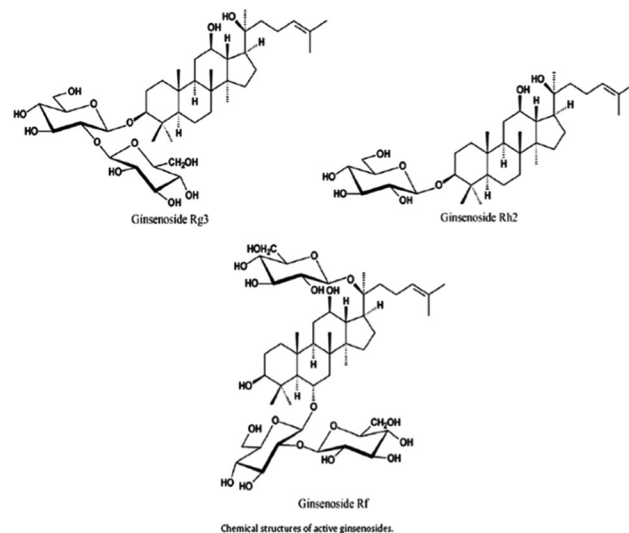


Fig. 3: Different constituents in ginseng

Camellia sinensis (Tea)

They are obtained by aqueous extract of *Camellia sinensis* are that are also show immunostimulatory activity and increases neo protein production and in unstimulating human peripheral mononuclear *in vitro* that reduces the neo protein production observed in cell stimulant together mitogens [38].

Clausena excavate

They are obtained from the wild shrub of *Clausena excavate* family Rutaceae and basically, they are obtained in Southern Asia [39] and these are also isolated phenolic compounds

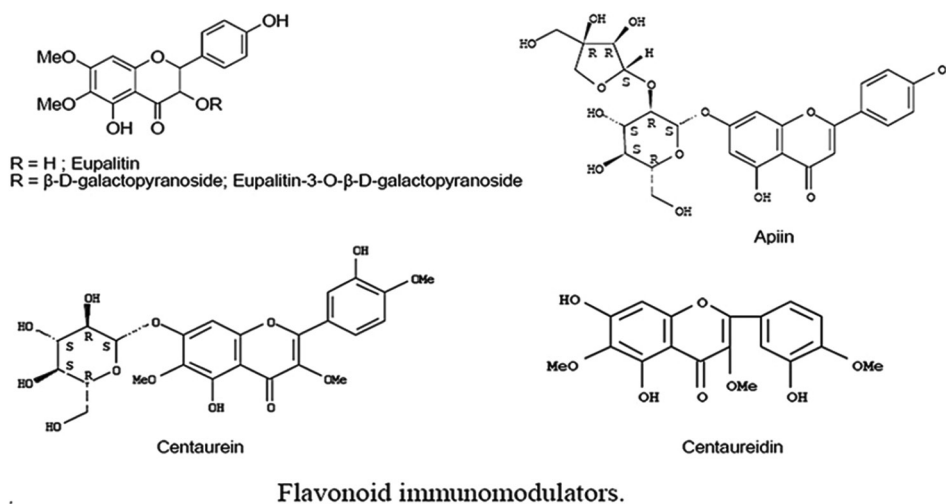


Fig. 4: Flavonoids are used for the immunomodulatory activity

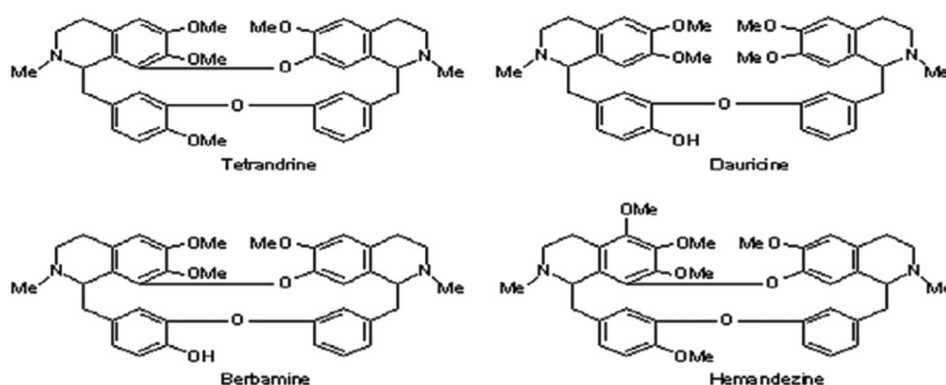


Fig. 5: Alkaloids are used for immunomodulatory activity

such as Furanocoumarins, flavonoids, and carbazole [40,41] mostly these agents are stimulating and suppress the immune system and influence enzymatic order and their outcome have immunomodulating and phagocytic activity [42].

Acacia catechu

The extract of acacia catechu is used for increasing neutrophilic adherence that nylon fibers, they are also increasing the phagocytic effect and produces defense beside cyclophosphamide encourage neutropenia result cell to mediate immunity and they are also used for that increase serum immunoglobulin levels [43].

Plantagoasiatica L.

They are obtained from seeds of *Plantagoasiatica* L their extract is used for the immunological response they are shown an immunomodulatory effect basically in which their main purpose of study extract seeds of *Plantago asiatica* L. there examines on the maturation of dendritic cells [44].

CYNODONDACTYLON

Freshly prepared juice of grass is used for the historical medication or regulate for solid content. Their amount of phenol is measured by the Folin-Ciocalteu technique and this juice is also used to examine the action of Doxorubicin to cause DNA damage *in vitro*. Their immunomodulatory activity was observed on mice through humoral antibody response that is determined by hemagglutination antibody titer and spleen cell assay [45].

GINSENG SPECIES

Ginseng is Chinese traditional used been number of medication conditions Ginsenosides is a main chemical constituent of the ginseng are used for that verify potential health anti-inflammatory, immunomodulatory, antihypertensive and there critical role in its diverse physiological action 70% ethanol extract of ginseng inhibit transcription and secretion of CXCL -10 following TNF - alpha stimulation [46] they did their best immune modulating effect than other herbal drugs and ginseng are show immune stimulant and immunomodulation, immunosuppressants effect and their immunostimulant activity show by polysaccharides fraction work as macrophage, b lymphocyte [47-49].

GOLDENSEAL

Goldenseal is obtained from *Hydrastis Canadensis* family Ranunculaceae and they are used for the treatment of colds and flu and berberine are show immune-stimulating activity [50] in the recent study of berberine are show the that improve the activity of macrophage and improve the blood supply of spleen [51,52].

Ecliptaalba

Eclipta alba's common name is bhringraj and their family Asteraceae their dried herb is used for liver disorders like jaundice [53] these are the main natural product are wedelolactone and dimethyl wedelolactone and declaration and they mostly increased phagocytic activity [54].

Terminalia arjuna

They are used for the improve anti-SRBC antitoxin secondary phase of immune response and their bark powder is decreased formalin-induced

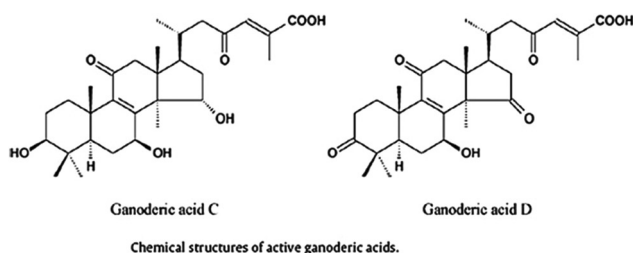
paw edema at 24 h but not carrageenan-induced paw edema this same is used for reduced that licks and bite in both phases of formalin-induced pain response and these are the antagonist of pretreatment with naloxone and there has a hypothesis for anti-inflammatory activity and these are category included in flavonoids and their various flavonoids are included work like immunomodulatory activity [55].

Alkaloids

Alkaloids are naturally occurring organic compounds which present in plants. Structurally, it contains at least one nitrogen atom in their heterocyclic ring. Alkaloids have different action in human and animal species. Along with different chemical and pharmacological actions, alkaloids are also used for immunomodulatory activity [56].

Ganoderic acid

Ganoderic acid is obtained in Ganoderma mushrooms and they have commonly used in Chinese traditional medication they are also producing immunomodulatory activity



CONCLUSION

This review is about immunomodulatory herbs and plants and briefly study the various medicinal plant used in the treatment of immune disorder and their natural chemical constituents and activities on immunomodulation.

ACKNOWLEDGMENT

The authors acknowledge the support from the School of Pharmaceutical Sciences, CSJM University, Kanpur, Uttar Pradesh, India, 208024.

AUTHOR'S CONTRIBUTIONS

All authors contributed equally to writing the manuscript, analyzing the data, read, and approving the manuscript.

CONFLICT OF INTEREST

None.

FUNDING

None.

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