

A Review on Herbal Immunomodulators in Cancer

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Abstract: *Natural products with immunomodulatory activity are widely used in treatment of many diseases including autoimmune diseases, inflammatory disorders in addition to cancer. They gained a great interest in the last decades as therapeutic agents since they provide costly effective and less toxic products than the synthetic chemotherapeutic agents. Immunomodulators are the agents that have the ability to boost or suppress the host defence response that can be used as a prophylaxis as well as in combination with other therapeutic modalities. The anticancer activity of these immunomodulators is due to their anti-inflammatory, antioxidant, and induction of apoptosis, anti-angiogenesis, and anti-metastasis effect. These natural immunomodulators such as genistein, curcumin, and resveratrol can be used as prophylaxis against the initiation of cancer besides the inhibition of tumor growth and proliferation. Whereas, immunostimulants can elicit and activate humoral and cell-mediated immune responses against the tumor that facilitate the recognition and destruction of the already existing tumor. This review represents the recent studies on various natural immunomodulators with antitumor effects.*

Keywords: Immunomodulator, Apoptosis, Antioxidant, Antitumour

I. INTRODUCTION

The main purpose of Ayurveda, the ancient Indian medical system is to prevent the disease process system and explore various natural resources, both medical and non-medical, in order to improve the natural abilities of biological systems, to change the quality of life. The modern medical system has always been keen to arouse the indirect immunity of human health sciences, which has led to the development of effective vaccines using microbial correction to improve the immune system of the invader.

Immunology is one of the fastest growing areas of medical biotechnology research and has great promises regarding the prevention and treatment of various diseases such as inflammation of the skin, intestines, respiratory tract and central organ. Infectious diseases are now considered primarily as immunological diseases while neoplastic disease and organ transplantation and several autoimmune diseases.

1.1 Immunomodulation

Immunomodulation is a therapeutic approach in which we try to intervene in auto regulating processes of the defence system. Immunomodulator are the extrinsic or intrinsic substances which regulate or alter the scope type duration or competency of the immune response. Immunomodulator correct immune system that is out of balance. Immunomodulators modulate the activity of the immune system. That, in turn decreases the inflammatory response.

Immunosuppressant: Immunosuppressant is already employed in surgery for implantation. An immunosuppressant is any substance that activates the immune system. They may be external, such as immunosuppressive drugs, or endogenous, such as, e.g., testosterone. Immunosuppressants are agents that suppress the immune system and are used to control the pathological response to autoimmune disease.

Anticancer and immunomodulatory herbal immunomodulators

1. Withania somnifera
2. Morus alba linn.

3. Panax ginseng.
4. Curcuma longa.
5. Catharanthus roses.
6. Syzygium aromaticum.

A. *Withania somnifera*

Withania somnifera also known as winter cherry or ashwagandha. This plant grows in india and Africa. It belongs to kingdom plantae, order - solanales and family - solanaceae. Genus and species are withania and somnifera respectively. Roots are collected from the respective plant ashwagandha then it is cleaned and dried properly. Preparation of powder from root of ashwagandha and different pharmaceutical activities are performed. Even marketed preparations are available.



Fig 01- Root powder

MOA

The powder formulation of *withania somnifera* inhibits the fatty acid synthesis and proliferation of the cancerous cells formed in cancer treatment. Root extract contains phytoconstituents such as withaferin A, withanolide A, withanolide B, withanolide C and withanone. These constituents lead to a mechanism of apoptosis. After occurrence of apoptosis, DNA sequencing changes and ICD induction takes place. Finally, adenosine triphosphate is released and cell activation continues.

B. *Morus alba linn*

Morus alba also called as silkworm mulberry, common mulberry and white mulberry. The lifespan of this plant is short. Some plant specimens are identified by humans more than 250 years ago. This plant is found in countries like United States, Mexico, Australia, India, Iran, Turkey and many more. The kingdom of this plant is plantae, order - rosales, family - moraceae. Genus and species of this plant are *Morus* and *alba* respectively. For the production of commercial silk, the white mulberry is widely cultivated to feed the silkworm.



Fig 02 – Fruits of *Morus alba linn*

MOA –Ways of mechanism

1. The formulation is obtained from *Morus alba* fruits. In cancerous cells TLRA activates in macrophasic state, and afterwards tumour cells starts to die. The proliferation of the new cell generation continues.
2. In second mechanism, firstly TLDA activates in macrophasic state. In cancerous cells, antigen is present which is directly attacked and killed by Mulberroferan G which is present in *Morus alba L* fruits.
3. In third mechanism, TLDA is activated in macrophasic state. In Nk cells, antigens are present on cytokinin. Where as cytokinins are occurred in plasma cells and those cells breakdowns the tumor cells.

C. *Panax ginseng*

Panax ginseng is called as Chinese ginseng and Asian or Korean ginseng. The active constituents from roots are extracted for treatment of cancer. This plant generally grows on mountain. Lifespan of this plant is very high. It have kingdom-plantae, order-apiales, family-araliaceae. Genus and species is panax and ginseng respectively.



Fig 03 – Roots of *Panax ginseng*

MOA

20(s) Rh2 (rhodium ion) is the main constituent of *P ginseng* which is isolated from roots of *P ginseng*. The rhodium ion is carried by IL6 (interlukin). Forkilling of cancerous cells jack2 and stat3 pathways are followed. After this, tumor invasion takes place which kills cancerous cells.

D. *Curcuma longa*

It is a flowering plant, family of this plant is zingiberaceae. Rhizomes of *curcuma longa* is used in Indian spices. It is found in the region of southeast asia. Temperature required for the growth of this plant is 20 to 30⁰c. Genus and species of this plant is *curcuma* and *longa* respectively. Rhizome are collected from the plant of *curcuma longa*, they were cleaned properly and boiled. After this, rhizomes were properly dried and grinded in mill, and atlast powder were collected.



Fig 04 – Rizome and powder of *Curcuma longa*

MOA

Curcumin is a polyphenol extracted which is obtained from *curcoma longa*, which shows the antioxidant activity .The present review focuses on the cell signalling pathway belonging development and proliferation of new cell in cancer treatment. The drug is binded to EGFR (epidermal growth factor receptor). Ras protein are protooncogen mutated in the human cancer cell. This leads to occurrence of apoptosis in cancer cells, which leads to death of cancerous cells.

E. *Catharanthus roseus*

Catharanthus roseus is also called as rose periwinkle, pink periwinkle, old maid, madagaskar. It is the flowering plant belonging to family apocynaceae. Vincristine and vinblastine are the main constituent present in this flower. Genus and species of this plant is catharanthus and roseus respectively.



Fig 05 Flower of *Catharanthus roses*

MOA

The mechanism of action of vincristine and vinblastine is they binds to the microtubular protein tubulin in a dimeric form. The drug tubulin complex gets add to the forming terminal end of the microtubules to eliminate assembly. After this there is depolarization of microtubules. The results inobtain a mitotic arrest at the phase of metaphase which leads to dissolution of the mitotic spindle and interference which leads to segregation of chromosomes.

F. *Syzygium aromaticum*

Cloves are the aromatic flower buds of plant belonging to the family myrtaceae. It is found in the region of Indonesia, India and Maluku island. It is used as a spice flavouring agent or fragrance in consumer product like soap, toothpaste etc. Genus and species of this plant is syzygiumand aromaticum respectively.



Fig 06 - *Syzygium aromaticum*

MOA

Eugenol is the active constituent present in clove (76%) which shows antioxidant activity in cancer treatment. In antioxidant anticancer activity there is inhibition of Nf-Kb activating factor i.e primarily initiated by bacterial endotoxin such as tumour necrosis. After this, the prostaglandin synthesis is reduced and decrease COX-2 activity. Occurrence of induction in cell cycles arrest in S-phase and induction of apoptosis cells cause death by reducing inflammatory cytokinin and enhancing the activity of cysplatin.

II. ACTIVE CONSTITUENTS PRESENT IN ABOVE PLANTS

PLANTS	PHYTOCONSTITUENTS
1. <i>Withania somnifera</i>	Withanolides and withaferins have potential benefits against cancer. Withasomniferin-A and 5-dehydrocy withanolide-R from aerial plant parts have been studied for immunomodulatory effects. Withanolide D causes apoptosis in pancreatic cancer cells. Withanolide 5,6-de-epoxy-5-en-7-one-17-hydroxy have found out activity against cancer of liver, breast, colon and prostate. Root extract of ashwagandha has been reported to be effective against cervical cancer.
2. <i>Morus alba linn</i>	Phytochemical study have identified that it consist of terpenoids such Betulinic acid, Ursolic acid in root bark. Alkaloids such as Morroles B-F, 2 α , 3 β -Dihydroxynortropane, 2 β , 3 β -Dihydroxynortropane, etc in fruits. Flavonoids such as Gallocatechin, Gallocatechin gallate, Kaempferol glucuronide, Morin, Quercetrin, etc in fruit. Phenolic acid such as Ferulic acid, Gallic acid, etc in leaf and fruits.
3. <i>Panax ginseng</i>	Phytochemical study have identified that it consist of alkanes, alkynynes, sterols, fatty acids, monoterpenes, lipids, carbohydrates, amines, flavonoids, vitamins, amino acids, nucleic acids, inorganic compounds and various enzymes.
4. <i>Curcuma longa</i>	Phytochemical study have identified that it consist of terpenoids, flavonoids, phenolic compounds, organic acids, anthocyanin, tannins and inorganic compounds. It consist of demethoxycurcumin and bisdemthoxycurcumin. Xanthorrhizol, a bisabolane type of sesquiterpenoid compound is present. Other compounds include xanthorrhizol, turmeronol, curdione, curcuzedoalide, curcumenol and germacrone.
5. <i>Catharanthus roseus</i>	It consist of anticancer agents such as bisindole/monoteroene, vincristine, vinblastine, vindesine and vinorelbine. Leaves of <i>Catharanthus roseus</i> (vinorelbine)cures breast cancer. It contains more than 120 terpenoid indole alkaloids.
6. <i>Syzygium aromaticum</i>	Clove has main source of phenolic molecules like flavonoids, hidroxibenzoic acids, hidroxiphenyl propens, eugenol. This have major bioactive molecules such as gallic acid derivatives like hidrolizable and tannins. Clove contains flavonoids such as quercetin and kamepfreol and phenolic acids like ferulic, caffeic, ellagic and salicylic acids. Clove flower buds consist of 18% of essential oils such as eugenol acetate, eugenol and β -cariofileno.

Table 01: Phytoconstituents present in above plants

III. CONCLUSION

There are several therapeutic procedure are available for the treatment of Cancer That is chemotherapy radiotherapy and Immunotherapy. In most cases undesirable side effect like gastrointestinal disorder kidney damage and other complications are associated with This compound include alkaloid phenol compound and and In addition to the indicator suggestion in vincristine,vinblastine, taxol,mulberofuran G,withaferins, butenolic acid,trmeronol all boswellic acid and compound such as catech in camapheral,Thymol This compound have the antioxidant property and inhibition of damage to DNA cell cycle induction of apoptosis inhibition of angiogenesis in tumor cell and its anti cancer effect are new and more effective.

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