

Analysis of Inhibitory Effects of Flavonoids and Their Derivatives on Melanoma

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Abstract

Flavonoids and Their Derivatives are Effective Platelet Function Inhibitors, Which are Of Great Significance to the Treatment of Vascular Embolism, Chronic Cardiovascular and Cerebrovascular Diseases, Etc. Melanoma is a Type of Tumor Caused by Abnormal Proliferation of Melanocytes, With a High Degree of Malignancy. It Is Easy to Metastasize, has a Poor Prognosis, And Has a High Mortality Rate. The Number of Cases has been Increasing in Recent Years. Tumor Metastasis is a Particularly Complex Process Involving Multiple Steps and Factors. This Whole Process is Affected by Many Factors, Such as the Tumor Itself and the Host Environment. Metastasis, The Scariest Aspect of Cancer, Is The Spread Of Cells From A Primary Tumor To Distant Organs And Continues to Grow Without Interruption. Melanoma is a Common Skin Tumor Caused by Abnormal Proliferation of Melanocytic Cells. Certain Factors, Such as Exposure to Uv Radiation, Smoking, And Chronic Viral Infection, Can Damage Key Genes Involved in Dna Replication and Repair, Resulting in Abnormal Cell Growth.

Keywords

Flavonoids; Melanoma; Inhibitory Analysis.

1. Introduction

Melanoma has a history of more than 100 years, and the prevalence of highly pathogenic strains may lead to all deaths of infected people[1]. The basic structure of flavonoids is not easy to decompose, which widely exists in many cells and belongs to plant secondary metabolites[2]. Flavonoids are widely used in clinic at present because of their wide sources, many biological activities, little toxic and side effects, etc[3]. In response, the body will initiate a coordinated innate and adaptive anti-tumor immune response, leading to the production of interferon- γ (IFN- γ). IFN- γ is a key cytokine produced by activated T cells, natural killer cells (NK) and NKT cells in tumor microenvironment, and plays an important coordinating role in this process[4]. However, these will more or less cause melanoma, and the adaptability of tumor initiation can make use of the delicate balance of positive and negative immune signal factors to activate the immunosuppressive cell pathway and escape the host immunity[5]. The same IFN- γ signaling process will eventually induce feedback inhibition, thus damaging anti-tumor immunity. Flavonoids are tricyclic natural organic compounds in the form of Ce-C3-c6 in nature, which widely exist in flowers, leaves and fruits of many plants, including fruits, vegetables and grains, and are secondary metabolites of plants. It can be seen that flavonoids inhibit the activities of bacteria, viruses and fungi and the possible mechanism of action, and the relationship between the structure of flavonoids and antibacterial activity[6]. The results showed that flavonoids had antibacterial effect by inhibiting bacterial DNA gyrase, the function of bacterial plasma membrane and the energy metabolism of bacteria. Flavonoids have a strong inhibitory effect on melanoma, and the IC50 is only 40.35mg. . Traditional Chinese medicine with abundant resources and definite curative effect is a precious drug treasure house. Flavonoids have low toxicity and are potential anti-melanoma drugs[7].

2. Analysis of curative effect of flavonoids

2.1. Main uses and advantages of flavonoids

It can be found that flavonoids can be used to study the inhibitory effect of arsenic trioxide on proliferation and anti-metastasis of human malignant melanoma cells, and provide new theoretical and experimental basis for flavonoids and their compounds to treat malignant melanoma[8]. Arsenic trioxide (As_2O_3) is the main component of Chinese medicine arsenic. It has been used in the clinical treatment of acute promyelocytic leukemia (APL) and chronic myelogenous leukemia (CML), and has achieved good results[9]. A large number of studies have shown that a class of polyphenols, namely, flavones, widely exist in plants, have a good anti-tumor effect, and inhibit tumor cell proliferation, new blood vessel formation, invasion and metastasis, and so on. Melanoma metastasis is a complicated process[10]. Circulating tumor cells (CTCS) remaining in sub-healthy human body after primary tumor operation are the fatal source of tumor metastasis in the future. Flavonoids have entered clinical trial abroad because of their strong therapeutic effect. In-depth research on flavonoids in China also shows that they have a good application prospect. The inhibitory process of flavonoids on bacteria is shown in the figure 1.

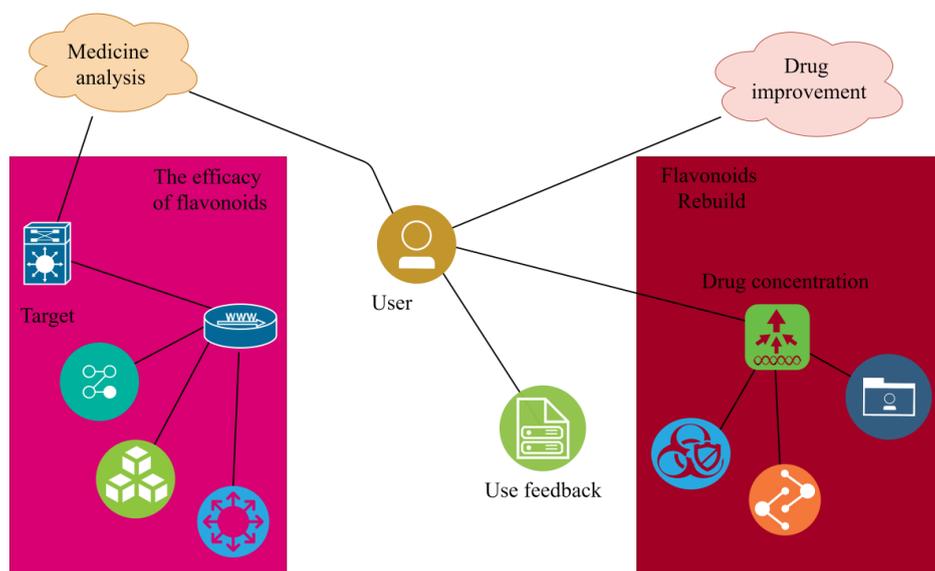


Fig. 1 Inhibition diagram of flavonoids

In recent two years, it is precisely because melanoma exists in different areas of China that it has attracted increasing attention from the domestic medical community. Because melanoma has many clear types and is easy to mutate, it brings great difficulties to the development and application of vaccines. Even a successful vaccine can only protect against the virus attack of one subtype, but it cannot protect against other subtypes. Therefore, the use of flavonoids and their derivatives to apply targeted therapy is also recognized as a feasible method in the current medical community. Flavonoids can effectively reduce the frequency and frequency of arrhythmia in myocardial ischemia-reperfusion injury tissue, and can resist arrhythmia induced by aconitine, ouabain and chloroform. Types and structures of flavonoids. Flavonoids, also known as bionavonoids, generally refer to a series of malodorous 15 compounds formed by connecting two benzene rings (ring A and ring B) with phenolic hydroxyl groups with three central carbon atoms, and their basic mother nucleus is 2-phenyl-chromones.

2.2. Research prospect of flavonoids and their derivatives

Flavonoids are a kind of important natural products produced by plants in their own biochemical metabolism. They are widely found in vegetables, fruits and medicinal plants, and are also a kind of important effective components of Chinese traditional medicines, such as

Huangpi, Pueraria, Pericarpium Citri Tangerinae, Psoralea corylifolia, Honeysuckle, Hippophae rhamnoides, Sophora japonica, Hawthorn, Ginkgo biloba and Euphorbia helioscopia. Natural flavonoids, except a few free ones, are mostly combined with sugar to form O- glycosides. Flavonoids have complex molecular structures and can be modified in many places, so the structures of flavonoids and their derivatives are diversified. Flavonoids isolated from natural plants are mostly polyhydroxy or methoxy substituted products. Melanoma viruses, as lower microorganisms, lack enzyme system, so they can't metabolize independently. They must be parasitic in host cells and rely on their enzyme system to reproduce.

Total flavonoids have the effect of angiotensin converting enzyme inhibitor (ACEI), inhibit the production of endothelin (ET), dilate coronary vessels, improve blood oxygen supply of myocardium, and improve cardiovascular system. Flavonoids and their derivatives have antioxidant and free radical scavenging effects. Reducing the formation of free radicals and scavenging the antioxidant activity of free radicals are the most fully studied biological activities of flavonoids, and they are also important ways for flavonoids to achieve broad biological activities such as anti-cardiovascular and cerebrovascular diseases, anti-aging, anti-radiation and anti-cancer. The drug resistance of melanoma has become a serious global challenge. Melanoma is a kind of poison, which is easy to combine with sulfhydryl-containing enzymes in the body, so that the enzyme activity is inhibited. Arsenic can combine with DNA polymerase, affect DNA synthesis and repair, and induce chromosome aberration and DNA damage. Melanoma is a highly malignant skin cancer, which can be transferred to various organs and mucous membranes of the whole body through blood and lymph. Its clinical chemotherapy effect is very poor, and the effective rate is less than 25%. Flavonoids (also called flavonoids) widely exist in the plant kingdom, which is one of the main components of Chinese herbal medicines and has strong biological activity. Flavonoids can inhibit cell wall synthesis by inhibiting the activity of D-alanine-D-alanine ligase. In order to stop the reproduction and growth of melanoma.

3. Analysis of melanoma inhibitory effect

3.1. Methods and measures of inhibiting melanoma

Melanoma cells can compensate for IFN γ -induced tryptophan deficiency by up-regulating the expression of several amino acid transporters and WARS (tryptophan acyl tRNA synthetase). Once tryptophan is supplemented, it can improve cell survival rate and accelerate recovery. Malignant melanoma is a kind of skin cancer with high malignant degree, and the effect of chemotherapy is very poor. Immunotherapy and gene therapy are the main methods in foreign countries, while arsenic is used in the treatment of malignant melanoma, which has not been reported at home and abroad. Angiogenesis plays an important role in the proliferation of melanoma. It can provide rich nutrition and blood supply for the growth of melanoma to meet the needs of rapid growth of melanoma cells. The inhibitory effect of melanoma is shown in Figure 2.

Once the angiogenesis of melanoma tissue is blocked, the growth of melanoma cells will slow down due to the lack of nutrition and oxygen supply, and even apoptosis and necrosis will occur. Melanoma is a common skin tumor with high malignant degree, which is caused by excessive proliferation of abnormal melanocytes. It is an important cause of skin tumor death. In recent years, more and more foreign scholars have carried out many studies on its anti-tumor effect, and found that regular consumption of foods rich in flavonoids can prevent the occurrence of some tumors. Epidemiological studies show that dietary intake of flavonoids can reduce the risks of breast cancer, colon cancer, lung cancer, prostate cancer and pancreatic cancer. A large number of in vitro and in vivo experiments have proved that flavonoids can interfere with the process of cancer, and the use of flavonoids and their derivatives can also play an important

role in inhibiting melanoma. Many studies have shown that flavonoids and their derivatives can up-regulate the expression of downstream factor genes in p53 pathway, especially Puma gene, suggesting that solanine can promote cell apoptosis through p53, Puma and so on to inhibit the growth of melanoma cells. The antibacterial effect of flavonoids and their derivatives is related to the existence of phenolic hydroxyl groups with affinity for protein, and they can be used as inhibitors of microbial enzymes and biosynthetic pathways. In addition, the substitution of the cyclization system of flavonoids containing isopentenyl groups is to increase their lipophilicity and improve their antibacterial activity through the interaction with cell membrane, thus achieving the effect of effectively curing melanoma.

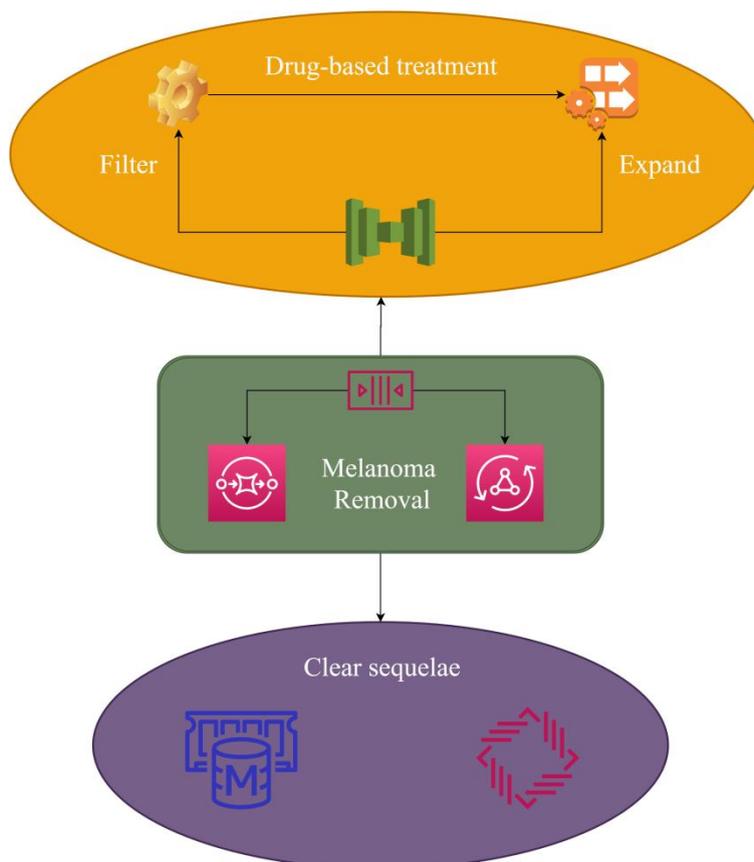


Fig. 2 Melanoma inhibition map

3.2. Research and development plan for inhibiting melanoma

Flavonoids have good antibacterial effect, especially the bacteria resistant to antibiotics are still sensitive to them, and these compounds are not easy to produce drug resistance and widely exist in nature, which has gradually become a research hotspot. The surface proteins of melanoma bacteria are also closely related to their pathogenicity. Many surface proteins of melanoma bacteria are assembled on the cell wall under the catalysis of sorting enzymes, so reducing the activity of sorting enzymes may reduce the pathogenicity of melanoma bacteria. Flavonoids also have different effects on different human bodies, and the drug effects on various special groups are shown in Table 1.

Table 1 Drug action

Drug percentage	General population	Special population
Sequelae	24.45	24.31
No sequelae	12.57	54.32

The results showed that flavonoids and their derivatives changed the cell morphology of *Vibrio harveyi* and inhibited the synthesis of protein. At the same time, it was found by isotope labeling that genistein could inhibit the synthesis of DNA, RNA and protein of *Staphylococcus aureus*, but it had little inhibitory effect on protein, mainly by inhibiting the synthesis of DNA and RNA and then protein. The antigenicity of melanoma cells is mainly the result of changes in their genetic, transcriptional and functional characteristics. On the one hand, these intrinsic factors of tumor cells determine the induction and maintenance of the natural anti-tumor T cell response, on the other hand, they may also lead to drug resistance to targeted drugs. The mutation rate of melanoma is the highest among all cancer types. However, although mutant antigens have therapeutic potential, they are highly patient-specific, and the number of identified shared mutant antigens derived from recurrent melanoma mutations is still low. In vitro administration of total flavonoids can inhibit platelet aggregation caused by arachidonic acid and collagen fibers, improve hemorheology and prolong prothrombin time. It has good effect on inhibiting melanoma.

4. Conclusion

Melanoma is a highly immunogenic tumor because of its mutation load. However, there are still many gaps in the understanding of melanoma cell autonomy factors (which play a role in the immunogenicity of melanoma cells) and how these factors affect the immune response. At present, the research progress of flavonoids and their derivatives is relatively smooth, but because the research of their antibacterial mechanism is still in the primary stage, and most of the current research is conducted in vitro, the research in vivo is relatively few, and some theories have not been fully clarified. Flavonoids and their derivatives extracts can effectively inhibit the growth of *Candida albicans*, *Rhizopus nigricans*, *Botrytis cinerea*, *Penicillium italicum* and other fungi in vitro. Through the study of structure-activity relationship, it is found that there is a certain relationship between flavonoids and antibacterial activity, and flavonoids can inhibit many targets of bacteria. Flavonoids may exert antibacterial synthesis by inhibiting cell membrane function, and B ring may play a major role in inhibiting nucleic acid. After flavonoids and their derivatives and compounds provide new theoretical and experimental basis for the treatment of malignant melanoma, the mechanism of inhibiting malignant melanoma cells needs further study.

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