



## Herbal drug used in management of skin cancer

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### ABSTRACT :

Skin cancer is a condition where the skin's cells grow abnormally. It is one of the most common types of cancer worldwide. It often occurs in areas exposed to sunlight, but it can also appear in places not usually exposed to sunlight. Many studies have looked into the effectiveness of herbal medicine as a supplementary treatment for skin cancer. Herbal medicine uses plants, or mixtures of plant extracts, to treat illness and promote health. Its popularity has increased over the past few decades due to its important role in cancer prevention and treatment. As a result, herbal remedies are being extensively researched and used to treat skin cancers globally. (Norbayu Mansori J. J., nov 2022) This article discusses the cancer-fighting effects of herbal medicine as a supplementary treatment for skin cancer. It also explores how their bioactive components may boost immunity and destroy cancer cells. Additionally, this study provides an overview of plant-based anti-cancer compounds that have shown potential anti-cancer properties in various skin cancer cell lines and animal models. This review aims to raise awareness of herbal medicine as a supplementary treatment for cancer and to offer more information for developing more effective anti-cancer drugs. Future research using herbal medicine in different forms and at various levels must be conducted. These studies need careful design, including strict quality control and standardized models at the cellular, organic, animal, and clinical levels to fight skin cancer effectively. (Chauhan, Skin cancer and role of herbal medicines, jun 2018)

**KEYWORDS :** Traditional Management, Garlic, Green tea, Amla

### INTRODUCTION

Cancer is a leading cause of death around the world. The rate of skin cancer is rising in countries where these tumors are common. From 1970 to 2007, melanoma had the second highest increase in death rate among all documented cancers in Canada. It is estimated that skin cancer is the most common cancer in the United States. According to Erb et al., skin cancers are the most frequently diagnosed cancers in Caucasians globally, and their rates continue to rise due to increased exposure to ultraviolet (UV) radiation. Skin cancer occurs when there is an imbalance, with too little cell death or too much cell growth and survival in the epidermis. UV radiation is the main cause of skin cancer, but other factors include viruses, harmful substances in food, chemicals, and genetic factors. We can prevent skin cancer by controlling or eliminating these causes. We can also effectively remove skin cancer by cutting off the blood supply to the tumor, which slows tumor growth and improves patient survival. Many cancer cells find ways to avoid cell death or have faulty cell death mechanisms. This allows them to grow uncontrollably. Therefore, promoting cell death is a key goal of cancer treatments. (Tawona N. Chinembiri, jul 2014) Currently, we treat skin cancer through surgery, radiation therapy, chemotherapy, or cryosurgery, among other methods. Both 5-fluorouracil and imiquimod are used in topical treatments for superficial basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) in situ. Only imiquimod is approved for topical therapy of cutaneous malignant melanoma (CMM). Each treatment option has its pros and cons. Choosing the right treatment is never straightforward and depends on factors such as where the cancer is located, the patient's health, and the opinions of both the patient and the doctor. (Tawona N. Chinembiri, jul 2014)

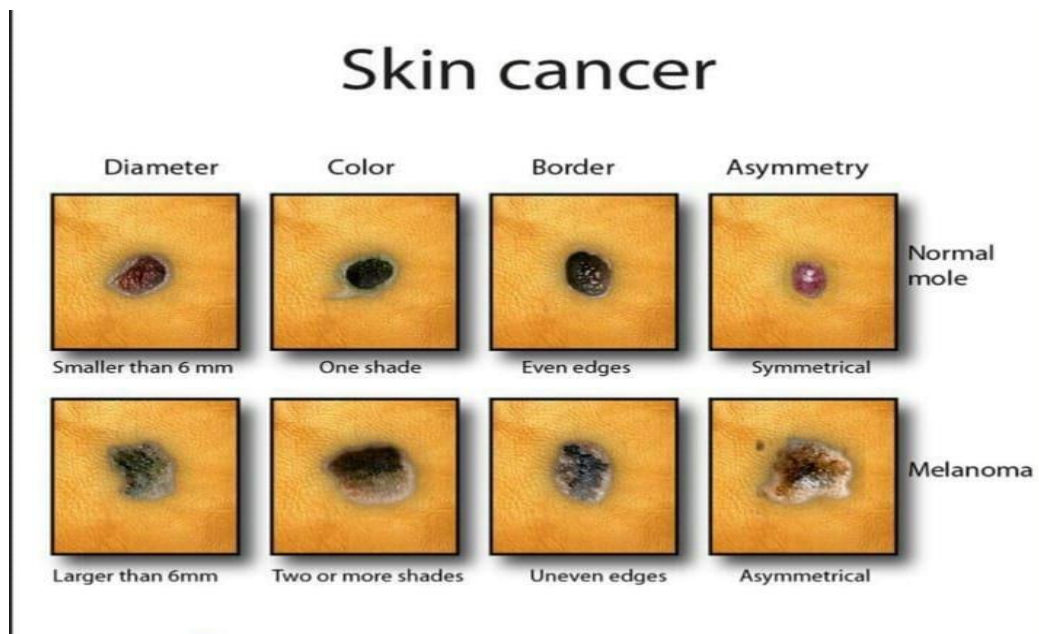
Chemotherapeutic agents often cause severe side effects and can lead to multi-drug resistance. Cancer cells can become resistant to treatments through methods such as pumping out the drugs, increasing drug targets, or altering drug handling. Various strategies have been tried to overcome drug resistance, including nanoparticles, liposomes, and micellar drug delivery systems, with some successes. We can manage the side effects of cancer chemotherapy symptomatically, but sometimes these additional treatments can be very toxic, which some patients find unacceptable. (Tawona N. Chinembiri, jul 2014)

There is growing interest in complementary and alternative medicines (CAM) because of the downsides of standard cancer treatments and the perceived benefits of more natural options. Plant extracts contain phytochemical compounds that show promise as anti-cancer drugs or as starting points for new drug development. They are often used in traditional medicinal forms like homemade tinctures, teas, or crude extracts. However, natural products and traditional medicines have some drawbacks, such as variations in preparation methods leading to differing chemical compositions, difficulties in determining and adjusting doses, and issues with the best way to administer them. While much research is underway to develop new drugs from natural compounds, it is crucial to also focus on optimizing dosages for specific administration routes and designing the most effective dosage forms. The rise in the use of CAM worldwide is largely due to the mistaken belief that natural products are safe, even though there is little scientifically proven information about the clinical effects of many CAMs. Figure 1 provides an overview of the anti-melanoma natural products discussed in this review. (Tawona N. Chinembiri, jul 2014)

A virtual environmental interface, the skin, covers almost 16% of the body mass. It protects our internal organs from various threats. The skin has three layers: the epidermis, dermis, and hypodermis. The epidermis, which comes from the ectoderm, acts as the body's armor and serves as a barrier against environmental stressors. Keratinocytes, which are tightly connected by desmosomes and tight junctions, are plentiful in this layer. The dermis, which comes from the mesoderm, sits beneath the epidermis and supports several appendages, including hair follicles, nerves, sebaceous glands, and sweat glands. Immune cells and fibroblasts are also found in this layer, playing a role in many physiological responses in the skin. Keratinocyte stem cells in the basal layer of the epidermis divide and differentiate as they move outward through the skin's surface, ultimately forming corneocytes. These are tightly linked dead cells that are intact and make up the main barrier of the epidermis. Because the skin is the most exposed organ of the body, UV rays, harmful substances, and toxins can damage it. These factors cause molecular and biochemical stress, leading to changes in the DNA of skin cells and resulting in skin cancer. The change of human skin cells into cancerous ones is a complex process that includes initiation, promotion, and progression. This process is believed to be triggered by oxidative stress in cells, resulting in transformation, survival, and spread of cancer. Exposure to ultraviolet radiation (UVR) is a major cause of skin cancer. UVA (315 to 400 nm, produces reactive oxygen species) and UVB (280 to 315 nm, causes DNA mutations by covalently binding adjacent pyrimidine base pairs C-T, CC-TT transition) are both harmful, while the ozone layer absorbs most of the UVC (100 to 280 nm). UVB causes the most direct DNA damage, as well as oxidative stress and immune suppression. The cell's natural DNA repair mechanism is believed to fix UVR-induced DNA damage. However, if DNA damage goes unrepaired due to random or genetic factors, the cell can develop permanent mutations. Moreover, the risk of skin cancer increases significantly with age. (Aniqa, Kaur, & Sadwal, mar 2023)

### SKIN CANCER

In 1999, around 1 million new cases of basal cell and squamous cell carcinoma were diagnosed in the United States. There were also about 44,000 new cases of malignant melanoma. Melanoma is the sixth leading cause of cancer deaths, and both melanoma and other skin cancers are becoming more common. In the U.S., the lifetime risk of being diagnosed with melanoma is 1.74% for white men and 1.28% for white women. The lifetime risk of dying from melanoma is 0.36% for white men and 0.21% for white women. Data from the California Cancer Registry shows that from 1988 to 1993, the average annual, age-adjusted incidence rates per 100,000 population were 17.2 for men and 11.3 for women among non-Hispanic whites. For Hispanics, the rates were 2.8 for men and 3.0 for women, while for Asians the rates were 0.9 for men and 0.8 for women. Non-Hispanic blacks had rates of 1.0 for men and 0.7 for women. Between 1973 and 1995, the incidence of melanoma in the United States rose by about 4% each year, increasing from 5.7 per 100,000 in 1973 to 13.3 in 1995, according to the Surveillance, Epidemiology, and End Results program (SEER) from the National Cancer Institute. Elderly people, especially older men, face a greater share of illness and deaths from melanoma. In 1995, the age-adjusted incidence rate was 68.7 per 100,000 for white men over 65 and 30.6 per 100,000 for white women over 65. Men over 65 make up 5.2% of the U.S. population but account for 22% of new malignant melanoma cases each year. Women over 65, who are 7.4% of the population, account for 14%. In the U.S., about half of melanoma deaths are in men aged 50 and older. Some experts believe older adults, especially older men, may have less awareness of skin issues and lower rates of skin self-examinations, leading to higher occurrences of advanced melanoma. (Mark Helfand MD, 2001)



Given the increasing number of skin cancer cases and the importance of early detection, it is essential to create an effective way to automatically classify skin cancer. As the largest organ in the human body, the skin protects other systems, which makes it more vulnerable to disease. Melanoma was the most common cancer in both men and women, with about 300,000 new cases diagnosed worldwide in 2018. In addition to melanoma, two other major skin cancers, basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), also had a high incidence, with over 1 million cases in 2018. Reports show that more skin cancers are diagnosed each year than all other cancers combined in the United States. Luckily, if detected early, the chances of a cure increase significantly. Melanoma has a 5-year survival rate of 99% when it doesn't spread. If it does spread to other organs, the survival rate drops to 20%. However, early signs of skin cancer are not always obvious. As a result, diagnostic outcomes often rely on the

dermatologist's skill. For less experienced practitioners, an automatic diagnosis system is a crucial tool for more accurate results. Furthermore, diagnosing skin cancer by sight is highly subjective and rarely reliable. Therefore, it is necessary to create an automatic classification method for skin cancer that is more precise, affordable, and quicker. Additionally, using such automated diagnostic systems can significantly reduce mortality from skin cancers, benefiting both patients and healthcare systems. (Yinhao Wu 1, jul 2022)

Skin cancer is one of the most common types of cancer that starts with the uncontrolled growth of skin cells. It can develop due to ultraviolet radiation from sunlight or tanning beds, leading to the multiplication of skin cells and the formation of malignant tumors. Skin cancer is a leading cause of death globally. According to statistics, 97,160 Americans were diagnosed with skin cancer in 2023, which accounts for 5.0% of all cancer cases reported in the United States. Additionally, 7,990 people died from skin cancer, representing 1.3% of the total deaths due to this disease in the country. Melanoma is one of the most common and dangerous forms of skin cancer, known for its ability to spread quickly to other parts of the body. Between 2016 and 2020, approximately 21 out of 100,000 melanoma cases were diagnosed in the United States. The death rate for melanoma was 2.1 per 100,000 diagnosed cases, and in 2020, 1,413,976 people were living with melanoma. The five-year survival rate for skin melanoma is 93.5%, which is relatively high. When skin melanoma is detected early, the five-year survival rate jumps to 99.6%. Survival chances are higher when skin melanoma is localized, meaning it has not spread to other parts of the body, but only 77.6% of skin melanomas are diagnosed at this local stage. The number of deaths from skin melanoma can be lowered if it is identified in its early stages. (Maryam Naqvi 1, may 2023)

Skin cancer is one of the most common types of cancer today. Since the skin is the body's largest organ, it makes sense that skin cancer is the most frequent type of cancer in humans. It is generally divided into two main categories: melanoma and nonmelanoma skin cancer. Melanoma is a serious, rare, and deadly form of skin cancer. According to the American Cancer Society, melanoma cases make up only 1% of total cases but result in a higher death rate. Melanoma starts in cells called melanocytes. It begins when healthy melanocytes grow uncontrollably, forming a cancerous tumor. This type of cancer can affect any part of the body, often appearing in areas exposed to sunlight, such as the hands, face, neck, and lips. Melanoma can only be cured if diagnosed early. If not, it spreads to other parts of the body and can lead to a painful death. There are various types of melanoma, including nodular melanoma, superficial spreading melanoma, acral lentiginous melanoma, and lentigo maligna. Most skin cancer cases fall into the nonmelanoma category, which includes basal cell carcinoma (BCC), squamous cell carcinoma (SCC), and sebaceous gland carcinoma (SGC). BCC, SCC, and SGC develop in the middle and upper layers of the epidermis. These cancer cells are less likely to spread to other parts of the body. Nonmelanoma cancers are generally easier to treat than melanoma cancers. (Mehwish Dildar 1, may 2021)

## MEDICINAL HERBS USED IN TRADITIONAL MANAGEMENT OF SKIN CANCER

### 1) CURCUMIN



[ Figure 3 Curcumin ]

In the study, three melanoma cell lines (A375, MV3, and M14) were treated with different concentrations of curcumin for 24, 48, 72, and 96 hours to assess its impact on cell growth. The normal human lung fibroblast cell line MRC5 was used as a control. MTT assays measured cell proliferation. The results showed that curcumin reduced growth in melanoma cells in a time- and dose-dependent manner. After 48 hours, the IC<sub>50</sub> concentrations of curcumin for the melanoma cells (A375, MV3, and M14) were 8.29, 18.29, and 14.25  $\mu$ M, respectively. At concentrations between 5 and 30  $\mu$ M, there was no significant growth inhibition in MRC-5 cells under similar conditions. This indicates that curcumin can selectively inhibit the growth of melanoma cells without affecting normal cells at lower doses. The findings suggest that curcumin's ability to reduce cell growth and promote apoptosis comes from blocking the NF- $\kappa$ B and p38 MAPK signaling pathways, downregulating anti-apoptotic proteins Mcl-1 and Bcl-2, increasing p53 and Bax levels, and activating caspase-3 and caspase-8. Curcumin leads to cell death in melanoma cells by interfering with various signaling pathways. Therefore, curcumin may have anti-tumor properties and could be a promising treatment for melanoma. (Norbayu Mansori J. J., nov 2022)

Curcumin is a bright yellow compound found in turmeric plants (*Curcuma longa* L.) from the Zingiberaceae family. Turmeric has been used for a long time in herbal medicine to treat skin and digestive issues, weight management, and inflammation. Recently, conventional medicine has focused on finding new, affordable, and safe substances for treating inflammatory, cancerous, and infectious diseases. A number of lab and animal studies have looked into curcumin's anti-inflammatory, anticancer, and antimicrobial effects, both on its own and in combination with standard treatments. This paper aims to summarize the current understanding of curcumin's impact on skin conditions, as well as its bioavailability and safety profile, based on the most relevant studies published so far. It also offers suggestions for future research.

Currently, there are no molecular docking studies available that describe how curcumin interacts with the molecular targets related to skin disorders. Therefore, we have included our own findings from molecular docking analysis, showing how curcumin binds and interacts with six key enzymatic targets, which are linked to several skin conditions. (Laura Vollono 1, sep 2019) The American Cancer Society estimates that 1 to 1.3 million cases of nonmelanoma skin cancer (NMSC) will be detected each year. Cutaneous SCC makes up nearly 20% of all skin cancers, and apart from melanoma, it accounts for 75% of all deaths linked to skin cancers. Unlike the more common basal cell carcinoma (BCC), SCC is an aggressive tumor that spreads in about 12.5% of cases. It's more common in light-skinned Caucasians, with lower rates reported in people with darker skin, including Asians and Africans. Cutaneous SCC on the face often spreads to parotid lymph nodes, which can harm the facial nerve during treatment, as well as to nodes in the neck, due to the rich lymphatic system in the head and neck area. Treatment for NMSC may include cryotherapy, electrosurgery, topical 5-fluorouracil, photodynamic therapy, imiquimod, and radiation therapy; however, surgery is the main treatment option. When treated early, the five-year cure rate exceeds 90%. The chance of NMSC coming back ranges from 8 to 16%. In some cases, the rate of second lesions returning can be as high as 75% in the first two years and 95% by the fifth year. (Kunal Sonavane, dec 2012)

CUR shows strong anti-cancer effects by specifically targeting tumor cells while leaving normal cells unharmed. It can trigger apoptosis through the caspase activation pathway, which includes caspase-8, 3, and 9. It disrupts cell survival by lowering levels of anti-apoptotic proteins. CUR also affects cell growth by targeting cyclin D1 and c-myc, and it improves the function of tumor suppressor proteins like p53 and p21. Additionally, it regulates death signaling by increasing the levels of death receptors DR4 and DR5. It disrupts mitochondrial function to cause cell death and alters kinase signaling pathways. The ability of CUR to focus on tumor cells rather than normal cells is mainly due to how these cells differ in their expression and sensitivity to the pathways CUR impacts. This makes CUR a promising therapy for cancer with few side effects. (Zhiming Mo, may 2024)

## 2) Olive oil



[Figure 4 Olive oil ]

Olive oil comes from the fruits of trees. It consists mainly of oleic acid, along with smaller amounts of other fatty acids like linoleic acid and palmitic acid. More than 200 different chemical compounds have been found in olive oil. These include sterols, carotenoids, triterpenic alcohols, and phenolic compounds. Hydrophilic phenols are the most common antioxidants in olive oil. (Chauhan, Skin cancer and role of herbal medicines, jun 2018)

The olive tree (*Olea europaea*) and its products are essential to the Mediterranean diet. Right now, the biggest producers of olives and extra virgin olive oil (EVOO) are Spain, Greece, and Italy. The fats found in the fruit and other components from olive by-products are widely used for their many health benefits. These include anti-inflammatory, antimicrobial, and antioxidant effects. The oil extraction process produces two main products: olive pomace (OP) and olive mill wastewater (OMW). OP is a by-product of extra virgin olive oil (EVOO) production. It contains a lot of pulp, skin, pits, and water. OP is a good source of phenolic compounds, sterols, pentacyclic triterpenes, carotenoids, and both mono- and polyunsaturated fatty acids. These elements give it anti-inflammatory, antioxidant, liver-protecting, stomach-protecting, anti-diabetic, and cholesterol-lowering effects. OMW is a liquid waste that has a strong polluting effect. It contains heavy metals and a high level of phenolic compounds. (Lucía Melguizo-Rodríguez† ab, September 2022). The skin is an organ in the integumentary system that serves as the first protective barrier against outside agents and helps maintain balance in the body. It has three layers: epidermis, dermis, and hypodermis. Depending on the body's needs, this organ can change some of its features, such as thickness, color, or texture. Various factors can affect this natural barrier. Biological factors like age or immune status, as well as external factors such as chemicals, physical elements, or various injuries, can have an impact. In this regard, olive and its derivatives have been used for a long time to treat skin conditions like acne, psoriasis, rosacea, and eczema. Thanks to its moisturizing properties and the antioxidant effects of its phenolic compounds, it is valuable as an ingredient in skin care and cosmetic products. (Lucía Melguizo-Rodríguez† ab, September 2022)



### 3) Sunflower oil



[ Figure 5 Sunflower oil ]

Sunflower seed oil comes from the seeds of *Helianthus annuus*. The main components of sunflower oil are oleic and linoleic acids. Sunflower seed oil has a higher concentration of linoleic acid compared to olive oil. This makes sunflower oil a good ingredient for skin products because of the benefits of linoleic acid. Sunflower seed oil also showed a chemopreventive effect in a mouse model of skin cancer with two-stage carcinogenesis. Sesamol, one of its components, plays a specific role in these chemopreventive effects (Kapadia et al., 2002). (Chauhan, Skin cancer and role of herbal medicines, jun 2018)

### 4)Resveratrol



[ Figure 6 Resveratrol ]

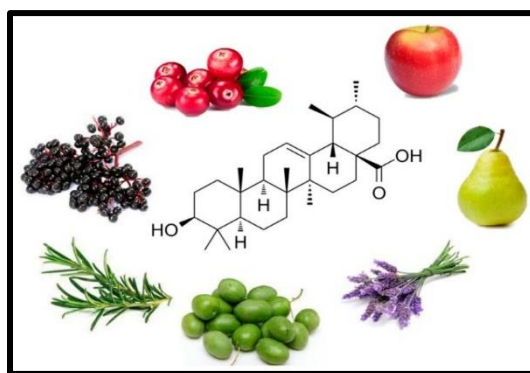
Nonmelanoma skin cancer (NMSC) is the most common type of skin cancer worldwide, with basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) being the most frequent forms. According to the World Health Organization (WHO), about 2 to 3 million cases of malignant skin tumors are diagnosed each year, though this number may be low. Additionally, the GLOBOCAN project, run by the International Agency for Research on Cancer, reported 1,198,073 new cases of NMSC (excluding basal cell carcinoma) globally in 2020.

Moreover, resveratrol has shown antioxidant properties, which help counter the effects of reactive oxygen species (ROS) caused by UV radiation, thus reducing DNA damage and mutations (Tong et al. 2015; Brand et al. 2018). Resveratrol has also been reported to link apoptosis and autophagy, offering a diverse strategy to fight SCC (Szulc-Musiol and Sarecka-Hujar 2021). Research suggests that resveratrol may enhance the effectiveness of chemotherapy drugs, like 5-FU, in treating and controlling skin cancer (Iqbal, Iqbal, Anjum, et al. 2021; Iqbal, Iqbal, Imtiyaz, et al. 2021). In lab studies, resveratrol effectively inhibited the growth and spread of various tumor cell types, including human cutaneous SCC A431 cells, and triggered programmed cell death (Zhang et al. 2018; Zhai et al. 2016). Also, in vivo studies using nude mice with human skin SCC A431 xenograft models showed that resveratrol significantly slowed tumor growth (Hao et al. 2013). This slowing effect was linked to increased expression of p53 and ERK while reducing survivin expression, leading to tumor cell death (Hao et al. 2013). Resveratrol was shown to significantly decrease the UV-B-induced rise in Ki-67 protein levels, a marker of cell growth associated with cancer (Aziz, Afaq, and Ahmad 2005). Kim et al. (2011) found that giving resveratrol orally to mice delayed UV-triggered skin tumor formation and reduced the conversion of benign papillomas to SCCs. Their study also noted increased TGF- $\beta$ 2 expression in UV-induced SCCs, which was later suppressed after resveratrol treatment. (Mohammad Yasin Zamanian, oct 2024)

Another approach for increasing the use of resveratrol-based therapy is to use nanomedicine. Due to the low water solubility and instability of resveratrol and its derivatives, nanoencapsulation has proven to be an effective way to enhance its solubility, bioavailability, and other biological

functions. Incorporating resveratrol in nanocarriers can achieve greater stability, controlled release, and better targeting of tissues or organs, which can lead to fewer side effects. To improve the skin absorption of resveratrol, some nanoformulations, such as liposomes, niosomes, solid lipid nanoparticles (SLNs), nanostructured lipid carriers (NLCs), nanoemulsions, polymeric nanoparticles, and dendrimers, are used to support the potential application of topical resveratrol. Liposomes and niosomes are classified as nanovesicles with bilayers and aqueous cores. SLNs, NLCs, and nanoemulsions are lipid-based nanocarriers that contain lipids in their cores. The polymer-based nanocarriers include poly(lactic-co-glycolic acid) (PLGA), polylactic acid (PLA), and dendrimers, which are commonly used in medical research because of their safety and adjustable size. In recent decades, significant progress in studying resveratrol and its derivatives has shown that they hold great promise for skin use. This review highlights the topical use of resveratrol and its naturally occurring derivatives for treating skin disorders. We focus on reports of skin diseases treated with these stilbenoids through different evaluation methods, including in vitro, ex vivo, and in vivo studies. The potential associated with this emerging application is also discussed in this study. Additionally, the development of nanocarriers to improve skin absorption and therapeutic effectiveness of topical resveratrol is introduced in this review article.(Ming-Hsien Lin a, 2021)

## 5) Ursolic acid



[Figure 7 Ursolic acid ]

A number of ursolic acid derivatives showed strong anticancer effects against three human cancer cell lines. 2 $\alpha$ -hydroxyursolic acid showed higher ability to stop the growth of HepG2 cancer cells. Four ursolic-type triterpenes displayed a significant anti-inflammatory effect on 12-O-tetradecanoylphorbol-13-acetate (TPA)-induced inflammation in mice. Researchers evaluated ursolic acid and its lipophilic 3-O-fatty acid ester chains (C12–C18) for their ability to fight microbes against various Gram-positive and Gram-negative bacteria. Notably, these compounds were effective against the Gram-negative bacteria *Pseudomonas syringae*. Ursolic acid acetate, 11,12-dehydroursolic lactone, and 3-O-acetyl-9,11-dehydro-12 $\alpha$ -hydroxyoleanolic lactone exhibited strong activity against  $\alpha$ -glucosidase. The presence of free hydroxy or carboxy groups is necessary for the trypanocidal activity of ursolic acid, as indicated by the effects of acetates, methyl esters, and aldehyde derivatives. Ursolic acid has been modified at the C-3 position to create cinnamate-based esters. The results showed that changing the parent structures of ursolic acid to the p-coumarate and ferulate ester analogues led to high antimycobacterial activity. The study examined the antitumor effect of ursolic acid and the changes it causes in tumor physiology in mice with tumors. We used the MTT colorimetric assay, clonogenic assay, and growth-delay assay to assess the tumor-killing effects of ursolic acid. Ursolic acid shows promise as an antitumor agent. It can induce apoptosis in tumor cells while also preventing normal cells from becoming cancerous. Additionally, it disrupts many enzymes, including those involved in DNA synthesis. This compound can inhibit growth and trigger apoptosis in various tumor cell lines. Research has shown that it acts at different stages of tumor development. It effectively hinders angiogenesis, tumor cell invasion, and metastasis. It is relatively safe and could be used as a chemopreventive or chemoprotective agent in clinical practice.

## 6) Capsaicin

[ Figure 8 Capsaicin ]



There is conflicting scientific evidence about capsaicin's role as a cancer-causing agent and its potential for both preventing and treating cancer. Hwang et al. showed in a mouse model that applying capsaicin to the skin stimulated skin cancer by activating tyrosine kinase EGFR and COX-2. However, other studies found different results. Some researchers observed no significant increase in skin cancer growth when compared to control subjects and even noted a significant decrease in papilloma formation in mice, suggesting that capsaicin might help inhibit skin cancer. Capsaicin has shown effective chemopreventive and therapeutic properties by influencing cell cycle arrest, triggering apoptosis, and slowing cancer cell growth. It reduces

the expression of NF- $\kappa$ B, AP-1, STAT3, and COX-2, which contributes to its benefits. Additionally, capsaicin causes caspase-mediated cell death in human cutaneous SCC cell lines and shows anti-mitogenic activity in metastatic MM cells by down-regulating phosphatidylinositol 3-kinase (PI3-K) expression. Its combined effects with HA14-1 in inducing caspase-mediated cell death in MM cell lines further highlight its potential.

Researchers are looking into further studies and epidemiological investigations to clarify capsaicin's role in cancer treatment. However, there are not many extensive studies on the topical use of capsaicin for treating skin cancer. Current experiences from its use in other areas point to some potential issues. One review noted that one in three patients experienced higher rates of side effects such as stinging, redness, and burning when compared to a placebo with topical capsaicin. These negative reactions might limit its use in both skin cancer prevention and treatment. Therefore, exploring new drug delivery systems, designs, and formulations that combine capsaicin with other agents that have fewer side effects may provide a fresh path for skin cancer treatment.(Piyushkumar Sadhua\*, 2024)

## CONCLUSION

The exploration of herbal remedies for skin cancer presents a promising frontier in the quest for effective treatments. The utilization of bioactive compounds derived from medicinal plants unveils a potential avenue for inhibiting the development and progression of skin cancer cells. This avenue aligns with the World Health Organization's dietary recommendations, advocating for the integration of phytochemicals from natural sources into daily consumption for their chemopreventive and chemotherapeutic properties. Epidemiological studies consistently underscore the significance of regular fruit and vegetable intake in lowering the risk of cancer development, further emphasizing the potential of plant-derived compounds in this context. These phytochemicals, found in various natural sources, play pivotal roles in regulating molecular processes fundamental to skin cancer, offering a nuanced and multi-faceted approach to combating this disease. Their ability to influence angiogenesis, metastasis, proliferation, apoptosis, and cell cycle arrest positions these herbal remedies as potential candidates for targeted and comprehensive treatment strategies. As research continues to unravel the specifics of these compounds and their mechanisms of action, the integration of herbal remedies into skin cancer treatment protocols holds promise for more effective and holistic approaches to combating this pervasive disease.

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