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REVIEW

Aloe Vera and Cancer

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SUMMARY

Aloe vera, a succulent plant species, has a long history in folk medicine. Its clear, viscous liquid has been used to treat skin problems and other disorders since ancient times. In the last century, oral consumption and the injection of aloe have also come to popular attention. Its topical use is effective in the treatment of burns and abrasions, and oral use is effective in the treatment of constipation. However, it has not been found to be superior to standard treatments. Most recently, claims of anti-cancer properties are prevalent. It has been found to inhibit proliferation and angiogenesis, and to induce apoptosis in cancer cells. Yet other clinical studies indicate that Aloe vera did not prevent or reduce the number of radiotherapy-related lesions; it merely delayed onset. Furthermore, many instances of toxicity and mortality have been reported in the literature. Today, it is better to avoid it, especially forms taken orally or by injection.

Keywords: Aloe barbadensis; Aloe capensis; Aloe vera; alternative medicine; cancer; phytotherapy.

Introduction

Aloe vera, sometimes also known as Aloe barbadensis or Aloe capensis, is a cactus-like perennial plant with fleshy leaves that belongs to the family Asphodelaceae. The Aloe vera plant has been used in folk medicine for thousands of years, dating back to the times of ancient Egypt. Of South African origin, Aloe vera was introduced to China and southern European countries in the 17th century.[1,2] It also has an important place in the field of traditional medicine in some modern cultures, such as China, Japan, and India.[3] In the United States, Aloe vera first gained popularity in the 1930s, as a consequence of studies indicating efficacy in treating X-ray burns.[4,5]

Aloe vera has commonly been used in the treatment of skin problems. Aloe vera products for topical use are derived from a clear, viscous liquid that appears when the leaves of the plant are cut, and this liquid is frequently an ingredient in cosmetics and alternative medicine products.[6,7] These products are claimed to be effective in the treatment of many dermal and mucosal problems such as wounds, burns, frostbite, xerosis, psoriasis, eczema, genital herpes, aphthous stomatitis, and seborrheic dermatitis.[8,9] However, studies have not found adequate evidence to support claims of effectiveness of Aloe vera treatment. Although some studies have demonstrated promising results in treating burns and abrasions in particular, they have not proven Aloe vera to be superior to standard treatment for these conditions.[10,11] Aloe vera products for oral consumption include capsules made of Aloe leaves, dried latex, and Aloe vera juice.[6] These products are utilized especially in the treatment of constipation because of a laxative effect. However, the US Food and Drug Administration (FDA) has stated that use of aloe as a laxative is not safe. Moreover, the FDA required aloe laxative products to be removed from all sales

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points in the United States in 2002.[10,12] In recent years, Aloe vera has frequently been claimed to have an effect on cancer. In particular, topical use is alleged to be effective in the prevention and treatment of skin irritation after radiotherapy; however, clinical studies do not support these claims.[8,13–16]

Laboratory Studies on the Effects of Aloe Vera on Cancer

In laboratory studies, Aloe vera has been shown to have some anti-oxidant, anti-inflammatory, immunomodulatory, and anti-cancer properties.[17–19] The immunomodulatory properties of Aloe vera, which contains many active components, are attributed to acemannan, while its anti-proliferative properties are attributed to the components anthracene and anthraquinone.[20,21]

In a study published in 2014, Aloe emodin, an anthraquinone component in Aloe vera, inhibited the proliferation and increased the radiosensitivity of HeLa cervical cancer cell lines.[22] In a laboratory study on hepatocellular cancer cell lines, it also inhibited cell proliferation and induced cell apoptosis.[23] In a study on breast cancer cell lines, it once again suppressed proliferation,[24] and in another study on colon cancer cell lines, it induced apoptosis through the activation of caspase-6.[25] Similarly, there are also studies showing that Aloe emodin inhibited cell growth in cell lines of lung cancer, leukemia, and neuroectodermal cancer.[26–28] In another study, Aloin, another anthraquinone component in aloe, inhibited angiogenesis through suppression of vascular endothelial growth factor (VEGF).[29] In an in vitro study carried out on neuroblastoma cells, Aloe vera was found to decrease neuroblastoma cell proliferation by suppressing cyclin D2 transcription.[30] In a study on prostate cancer cell cultures (PC3), Aloe emodin was found to inhibit prostate cancer cell proliferation by acting through mammalian target of rapamycin complex 2 (mTORC2) (Table 1).[31]

Clinical Studies on the Effects of Aloe Vera on Cancer

Despite some positive results obtained from a few studies on the anti-cancer potential of Aloe vera, such results are not adequate to be reflected in clinical practice. The most highlighted and advocated effect of Aloe vera is the prevention and treatment of skin irritation caused by radiotherapy.[32] Clinical studies have produced inconsistent results and have not verified this effect. In a Phase III study carried out on 225 breast cancer patients treated with postoperative adjuvant radiotherapy, it was stated that Aloe vera provided no significant benefit to skin problems caused by radiotherapy.[13] Another study combining 2 separate Phase III randomized clinical studies had similar findings regarding the effect of Aloe vera.[14] Comparable results were also obtained in a review compilation of 7 clinical studies.[15] In another study that enrolled 57 patients with head and neck cancer, Aloe vera was observed to delay the onset of radiotherapy-induced skin lesions and reduce their intensity; however, it was ineffective in the prevention of lesions or reducing their incidence.[16]

In a study that involved the evaluation of the use of Aloe vera in conjunction with chemotherapy, a subset of 240 patients with metastatic tumor was given chemotherapy alone, while the rest also received 10 mg daily oral dose of Aloe vera. Tumor regression rate and 3-year survival rate were found to be significantly higher in the group given chemotherapy plus Aloe vera.[20] In a small epidemiological study, lung cancer incidence was observed to be lower in those using Aloe vera orally on a regular basis; however, the study was not of a level that results might be considered promising.[33]

In a systematic compilation published in 2011, the prevention of oral mucositis due to chemotherapy by using Aloe vera was studied. Despite some positive results, researchers noted that this effect might be specific to a certain chemotherapeutic agent or type of cancer and emphasized the need for well-designed studies with subgroup analyses.[34] In a preliminary study carried out on 20 patients with oral submucous fibrosis, Aloe vera gel provided a benefit in reducing the symptoms.[35] In another study that enrolled 58 patients with head and neck cancer, the oral administration of Aloe vera made no contribution in terms of reducing symptoms or increasing quality of life (Table 1).[36]

Potential Side Effects of Aloe Vera

Although many proponents of alternative medicine claim that Aloe vera has no side effects, it is an herbal treatment about which many toxicity cases have been reported.[37] Moreover, Aloe vera administered by injection resulted in death in 4 reported cases.[38,39]

In a case reported in the literature, a 56-year-old female patient with reticular lichen planus lesion in her mouth declined use of corticosteroid and turned to alternative medicine procedures that included the

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Table 1 Selected laboratory and clinical studies

Reference	Type of study	Type of cancer	Result
Luo J et al.[22]	Laboratory	Cervical cancer	Increased radiosentivity
Kuo PL et al.[23]	Laboratory	Hepatocellular cancer	• Inhibited the cell proliferation • Induced the cell apoptosis
Huang PH et al.[24]	Laboratory	Breast cancer	Suppressed the proliferation
Suboj P et al.[25]	Laboratory	Colon cancer	Induced apoptosis
Lee HZ et al.[26]	Laboratory	Lung carcinoma	Inhibited cell growth in cell lines
Chen HC et al.[27]	Laboratory	Promyelocytic leukemia	Inhibited cell growth in cell lines
Pecere T et al.[28]	Laboratory	Neuroectodermal tumors	Inhibited cell growth in cell lines
Pan Q et al.[29]	Laboratory	Colorektal cancer	Inhibited the angiogenesis through VEGF suppression
Yonehara A et al.[30]	Laboratory	Neuroblastoma	Suppressing the cyclin D2 transcription level
Liu K et al.[31]	Laboratory	Prostate cancer	Inhibit cancer cell proliferation by acting through mammalian target of rapamycin complex 2
Heggie S et al.[13]	Clinical	Breast cancer	No significant benefit in skin problems caused by radiotherapy
Williams MS et al.[14]	Clinical	–	No significant benefit in skin problems caused by radiotherapy
George J et al.[16]	Clinical	Head and neck cancer	Delay the start time of radiotherapy induced skin lesions and reduce their intensity
Lissoni P et al.[20]	Clinical	Metastatic cancers	Tumor regression
Su CK et al.[36]	Clinical	Head and neck cancer	No contribution in terms of reducing the symptoms and increasing quality of life

consumption of Aloe vera juice. Although she used this product for a period of 11 months, there was no improvement in oral lichen planus, and in fact, hypothyroidism developed as well.[40] In another case where Aloe vera was used in conjunction with chemotherapy, serious hypokalemia developed.[41] In a study published in 2010, 3 cases of toxic hepatitis due to use of Aloe vera were reported.[42] There are many other cases of toxic hepatitis associated with Aloe vera reported in the literature.[43,44] There are also cases in which it delayed recovery of postoperative wounds,[45] and caused the development of Henoch-Schonlein purpura.[46]

Abdominal cramps, diarrhea and related electrolyte disorders due to the oral administration of Aloe vera have been reported. In some preliminary studies, Aloe vera was stated to have a blood sugar reducing effect, and diabetic patients using or considering using Aloe vera were warned about the risk of possible hyperglycemia. The National Center for Complementary and Integrative Health (NCCIH) states that there is not adequate scientific evidence supporting the use of Aloe vera for any health problem.[10]

In a study conducted by the US National Toxicology Program (NTP), the carcinogenic potential of the oral administration of Aloe vera in mice was investigated. The results indicated that long-term exposure to Aloe vera might be carcinogenic.[47] Another study carried out on mice showed that Aloe vera taken orally is likely to trigger colon cancer;[48] and another study showed that Aloe vera may increase skin cancer induced by ultraviolet rays.[49]

In the literature, there is also evidence regarding drug interactions with Aloe vera. A laboratory study showed that the plant juice of Aloe vera inhibits the CYP3A4 and CYP2D6 enzymes which may affect the intracellular concentration of drugs metabolized by these enzymes.[50] It has been stated that use of Aloe vera might increase the effects of antiarrhythmics, cardiac glycosides, diuretics, and steroid drugs.[32] In 1 instance, a possible sevoflurane-Aloe vera interaction may be responsible for a women losing approximately 5 liters of blood during surgery.[51]

Conclusion

Aloe vera is a product likely to have certain benefits because of the active components in its content; however, its superiority to standard treatments for any health problem has yet to be shown unequivocally. It is claimed to be effective in a variety of applications, but it is potential effect on cancer has been of particular

interest in recent years. The most advocated benefit of Aloe vera for a cancer patient is its alleged ability to prevent and treat skin lesions caused by radiotherapy. However, clinical studies carried out indicate that Aloe vera is ineffective in this regard. On the other hand, some laboratory studies have indicated certain effects of oral and injected Aloe vera products; however, these results have not been verified in clinical studies. Many side effects as well as related deaths have been reported in the literature. For now, it would be practical to abstain from using these products until a clear benefit of Aloe vera and its active components is demonstrated and a safety profile for use is introduced.

Conflict of interest: None declared.

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