



The use of aloe vera in cancer radiation: An updated comprehensive review

Carrie-Jo E. Farrugia*, Elizabeth Sutton Burke, Mariah E. Haley, Komul T. Bedi, Mona A. Gandhi

St. John Fisher College Wegmans School of Pharmacy, 3690 East Avenue, Rochester, NY, 14618, USA



ARTICLE INFO

Keywords:

Aloe vera
Aloe barbadensis
Cancer
Radiation

ABSTRACT

Introduction: Many cancer patients require radiation therapy and often experience adverse effects including erythema, itching, and pain. Aloe vera has been studied for its potential use in the prevention and treatment of radiation related adverse effects as it possesses a variety of properties and is considered an antioxidant and anti-inflammatory agent. Multiple controlled trials have been performed in order to evaluate the efficacy of aloe vera for the prevention and treatment of radiation side effects. Previous systematic reviews have examined the use of aloe vera for radiation-induced skin reactions, however updated literature now includes the use of aloe vera in proctitis.

Objectives: The aim of this comprehensive review is to summarize and evaluate the use of aloe vera in patients who have undergone radiation therapy for the treatment of cancer.

Results: Aloe vera may not be effective for prophylaxis or treatment of radiation adverse effects in breast cancer patients. Moderate efficacy was seen when aloe vera was used in combination with mild soap versus soap as monotherapy for the treatment of radiation skin reactions. Aloe vera may be effective when cumulative radiation doses are greater than 2,700 cGy and for acute radiation proctitis.

Conclusions: There is contradictory evidence for the use of aloe vera in the setting of radiation in regards to its efficacy in the prevention and treatment of radiation-induced adverse effects.

1. Introduction

Aloe vera, or aloe barbadensis, is a herbal substance that is part of the Liliaceal family, which contains over 300 species [1]. Aloe vera is commonly known for its topical use in the treatment of burn injuries due to anti-inflammatory, antioxidant, and antibacterial properties [2,3]. The mechanism of action for aloe vera is not fully known, however it is speculated that inhibition of cyclooxygenase may play a role [2,4]. Inhibition of cyclooxygenase may contribute to aloe vera's anti-inflammatory and antioxidant properties and as such it has the ability to treat burns and accelerate wound healing [2]. Aloe vera may also play a role in leukocyte and platelet aggregation causing a decrease in vasoconstriction, which also contributes to wound healing [3]. The mechanism of action of aloe vera allows for a variety of pharmacological claims and therefore has a wide range of therapeutic uses which include, but are not limited to, arthritis, asthma, candida, digestive bowel disorders, skin problems, and ulcers [1]. The ability of aloe vera to mitigate the negative impact of radiation is now being evaluated in clinical trials.

Radiation is often a critical addition to chemotherapeutic regimens in order to increase the efficacy of treatment and in some cases may be

used as the sole therapeutic modality. Approximately two-thirds of cancer patients will require the use of radiation [5]. Radiation causes DNA damage, and subsequently the formation of free radicals and anti-inflammatory responses at the site of action [6]. Radiation can have a series of adverse effects including acute reactions that may occur within hours of radiation therapy [7]. Acute reactions are generally defined as cutaneous adverse effects including but not limited to itching or erythema and ranging in severity from mild to exceptionally painful [3]. Acute adverse reactions are caused by damage to the epidermal basal layer of the skin [3]. The squamous cells that are formed in this layer migrate to the outermost layer of the epidermis and are eventually shed at a faster than skin that has not been exposed to radiation [3]. This shedding process causes the skin to become dry and cracked, which may cause pruritus and also pain [3].

Aloe vera is comprised of over 70 active components including anthraquinones, vitamins, nonessential amino acids, essential amino acids, and inorganic compounds [1]. The wide variety of aloe vera constituents allow for aloe vera to penetrate skin tissue and also provide essential nutrients to the skin [1]. It is thought that aloe vera can ameliorate radiation adverse events on the epidermis and dermis due to its wound healing enhancement properties [6]. Aloe vera's ability to

* Corresponding author.

E-mail address: cef08613@sjfc.edu (C.-J.E. Farrugia).

Table 1
Summary of aloe vera products used in patients with breast cancer.

Author and Year	Sample Size	Medium Used	Composition	Volume	Frequency and Duration
Hoopfer et al. (2015)	248	Cream	30 mg of processed aloe (1000–5000 MW fraction) within 100 mL of placebo cream	Approximately 2.5 mLs	Three times a day throughout radiation and for 1 month after radiation
Nyström et al. (2007)	50	Gel	97% aloe barbadensis	0.2 mLs	Twice a day on every treatment day
Heggie et al. (2002)	208	Gel	98% aloe vera	N/R	Three times a day during radiation and for two weeks after radiation completion
Ahmadloo et al. (2017)	100	Gel	Aloe vera and 1% additive materials including pectin, vitamin C, and Natamycin	1–2 mm of thickness on the radiation site	Twice a day in a minimum of 6 h intervals throughout treatment

N/R = not reported by authors.

increase wound oxygenation and minimize the amount of dead tissue at radiation sites allows it to potentially counteract the negative adverse events of radiation therapy [3]. It is important to understand effective prophylactic and treatment regimens in order to manage radiation-induced skin reactions.

To our knowledge there have not been any updated comprehensive or systematic reviews on the use of aloe vera in cancer radiation to date. The aim of this comprehensive review is to summarize and evaluate the current evidence behind the use of aloe vera in patients receiving radiation for the treatment of cancer.

2. Objectives

The primary objective of this article is to review current literature on aloe vera and its potential use for the prevention and treatment of radiation related adverse events when used in the treatment of cancers.

3. Methods

3.1. Database and search strategies

The authors utilized PubMed, Google Scholar, clinicaltrials.gov, and EBSCO as primary literature search tools. The search criteria that was utilized was: (aloe vera) AND (cancer radiation).

3.2. Inclusion criteria

- 1) Controlled trials using aloe vera in cancer radiation
- 2) Patients receiving aloe vera for the prevention or treatment of radiation adverse effects
- 3) English language

3.3. Exclusion criteria

- 1) Non-clinical trials
- 2) Non-human studies
- 3) Aloe vera used in mucositis from cancer radiation
- 4) Co-formulations containing aloe vera

4. Results

4.1. Study selection

We identified and screened 54 papers published in the years 1999–2017 by titles and abstracts. Of these, 42 were excluded because they either did not evaluate aloe vera as monotherapy, did not specifically use aloe vera for radiation adverse effects, or evaluated aloe vera for mucositis caused by radiation. Mucositis was excluded due to pre-existing comprehensive reviews [8,9]. A previous systematic literature review for aloe vera in radiation-induced skin reactions was conducted in 2005, however recent information on proctitis has been published in 2017 [10]. All authors agreed upon the remaining articles that are integrated into this review.

4.2. Results of individual studies

4.2.1. Breast cancer

A 2015 phase III trial evaluated the effects for treatment of skin reactions in patients undergoing radiation treatment for breast cancer [6]. A total of 248 patients were randomized to three comparative arms; placebo (77 patients), aloe cream (81 patients), or powder (79 patients) [6]. High quality aloe cream was extracted to meet International Aloe Science Council standards [6]. The powder arm consisted of nonmetallic baby powder or cornstarch while the placebo cream contained Aquatrix II, Lexamul 561 emulsifier, methyl paraben, dimethicone, isopropyl myristate, propylene glycol, cetyl alcohol and stearic

Table 2
Summary of aloe vera products used in patients with proctitis.

Author and Year	Sample Size	Medium Used	Composition	Volume	Frequency and Duration
Sahebnaasagh et al. (2017)	20	Ointment	9 g of aloe vera powder levigated with 7 g of liquid white paraffin and geometrically mixed with 284 g of vaseline to yield the ointment aloe vera gel powder 3%	1 g	Applied twice a day for four weeks

acid emulsifiers, and triethanolamine [6]. Within one week of receiving radiation treatment, patients in each study arm reported acute skin reactions including erythema, dry and moist desquamation, and skin rashes [6]. The overall mean of the Catterall Skin Scoring Profile (CSSP) groups was 6.27 for the powder arm, 6.96 for the aloe arm ($p = 0.0227$) and 6.99 for the placebo group ($p = 0.127$) [6]. This study showed that aloe cream was not beneficial for skin reactions caused by radiation. The study authors concluded that aloe cream did not help to improve adverse skin reactions [6]. However, there was a statistically significant difference in pain scores from radiation among the study arms. Nine of the sixty-seven patients in the powder group, twenty one of seventy-two in the aloe group, and twenty five of seventy-four patients in the placebo arm had high pain defined by the 6-point Likert tool ($p = 0.0163$) [6]. Aloe vera did not show statistical significance for preventing or decreasing skin reactions from cancer radiation [6].

A 2007 study evaluated 50 females with breast cancer to determine if aloe vera could mitigate the intensity of erythema caused by acute radiation dermatitis [11]. Erythema was evaluated using near infrared spectroscopy, laser doppler, and digital color photography. The three study arms included aloe barbadensis 97% gel, essex lotion, and no lotion. Neither aloe vera gel or essex lotion versus placebo showed statistical significance for any of the methods used [11]. Aloe vera gel and essex lotion did not have any clinical impact on erythema [11].

A 2002 phase III study examined if aloe vera gel had an effect on skin side-effects on irradiated breast tissue. Two hundred and eight patients participated in this study with 107 patients in the 98% aloe vera gel arm and 101 patients in the topical aqueous cream arm [3]. Topical aloe vera gel was not statistically significant for reducing symptoms of itching, pain, erythema, dry or moist desquamation in breast cancer patients undergoing radiation [3].

In a 2017 prospective randomized controlled trial, aloe vera gel lacked prophylactic properties when studied in breast cancer patients who had radiation-induced dermatitis [5]. Fifty patients were enrolled in the aloe vera gel arm while fifty patients did not receive aloe vera treatment for a total of 100 study participants [5]. After five weeks of therapy, 45 patients in the aloe vera arm and 47 patients in the control arm had varying grades of dermatitis [5]. There were no statistical differences seen between either treatment over the five week duration [5]. A summary of aloe vera products used in breast cancer patients can be seen below in Table 1.

4.2.2. Proctitis

Radiation of the pelvic area may cause acute radiation proctitis (ARP) in up to 50% of patients and can present with a variety of symptoms including pain, abdominal cramping, diarrhea, and rectal bleeding [2]. In a 2017 randomized, double-blind, prospective, placebo-controlled trial, the use of aloe vera was evaluated revealing successful treatment of acute radiation proctitis. The study enrolled 20 patients, 9 in the aloe group and 11 in the placebo group, and all experienced ARP [2].

The active arm used was aloe vera 3% gel powder in white paraffin; patients receiving topical aloe vera greatly improved from a total clinical presentation score of 4.3 (SEM 2.2) to 1.2 (SEM 0.8) by week four of treatment [2]. The placebo group was almost unchanged with a total clinical presentation score of 4.2 (SEM 1.2) to 3.5 (SEM 1.1) by week four of treatment [2]. Total clinical presentation included hemorrhage, abdominal rectal pain, diarrhea, and fecal urgency and the

differences in the two arms were statistically significant ($p = 0.0087$) [2]. Diarrhea was the most commonly prevented ARP symptom ($p = 0.008$) [2]. Patients treated with aloe vera have almost four times higher odds of experiencing a decrease in overall clinical presentation compared to patients not treated with aloe vera (OR 3.97, 95% CI 1.3–11.9) [2].

The Radiation Therapy Oncology Group (RTOG) score showed a similar trend with a score of 2.89 (SEM: 2.1) to 0.89 (SEM: 1.0) in the aloe vera arm [2]. Aloe vera had almost six times higher odds of a decreased RTOG score compared to the placebo arm ($p = 0.0016$, OR 5.9, 95% CI 1.6–21.6) [2]. The authors concluded that topical 3% aloe vera was determined to be safe and effective for proctitis including ARP symptoms in patients undergoing radiation therapy. A summary of aloe vera products used in proctitis can be seen below in Table 2.

4.2.3. Breast, pelvic, head-and-neck cancer combination

A total of 60 patients were evaluated in a 2013 self-controlled clinical trial after receiving five weeks of radiation for head-and-neck, breast and pelvic cancers [12]. Patients were instructed to apply commercially available aloe lotion to only one side of their body twice a day with nothing used on the other half of their body [12]. Dermatitis on the aloe side was grade 1, grade 2, and grade 3 in 42, 32, and 17 people, respectively. The control side of the body showed a grade 1, grade 2, and grade 3 in 32, 17, and 1 person, respectively [12]. The RTOG acute radiation morbidity scoring criteria was used for dermatitis grading [12]. Overall, aloe vera showed statistical significance in week four ($p < 0.000$), week five ($p < 0.000$) and week six ($p < 0.006$) [12]. It was concluded that aloe vera lotion has protective properties against radiation-induced dermatitis [12].

A 2001 randomized, prospective, blinded trial included seventy-three patients who had cancer of the head/neck, chest, abdomen/pelvis, or in the extremities. Patients were randomized to receive 100% pure aloe vera gel ($n = 33$) or placebo ($n = 40$) and all patients were instructed to wash with mild soap. There was no statistical differences in skin changes when looking at variables including chemotherapy, skin texture, erythema, itching, and skin tanning [13]. There was also no statistical significance when evaluating the skin change in correlation to the dose toxicity of radiation ($p = 0.189$) [13]. Nineteen of twenty two patients (86%) in the aloe vera/soap arm showed moderate skin changes [13]. Cumulative radiation doses greater than 2,700 cGy showed statistical significance ($p = 0.0130$) [13]. Forty-four percent of patients in the aloe/soap arm went four weeks before any skin changes occurred compared to the soap alone arm, this pattern was not seen at cumulative radiation doses less than 2,700 cGy ($p = 0.4336$) [13]. The trial showed the benefits of using 100% pure aloe vera gel to protect patients from radiation dermatitis, especially with cumulative radiation doses over 2,700 cGy [13]. A summary of aloe vera products used in breast, pelvic, head-and-neck cancer combinations can be seen below in Table 3.

5. Discussion

Seven studies were included in this comprehensive literature review of aloe vera in the prevention and treatment of radiation-induced adverse effects. Four studies specifically looked at breast cancer patients undergoing radiation. All four suggest that aloe vera is not useful for radiation adverse effects in breast cancer patients [3,5,6,11]. One

Table 3
Summary of aloe vera products used in patients with breast, pelvic, head-and-neck cancer combinations.

Author and Year	Sample Size	Medium Used	Composition	Volume	Frequency and Duration
Haddad et al. (2013)	60	Commercially-available lotion	Aloe vera along with additives such as lanolin oil, glyceryl stearate, diluted collagen, tocopherol, allantoin, and paraben	On one half of the body	Twice daily from the beginning of radiation and for two weeks after radiation
Olsen et al. (2001)	73	Gel	100% pure aloe vera	Applied the gel liberally	Each day following radiation treatment

controlled trial showed success for treatment of acute radiation proctitis with aloe vera [2]. Two studies evaluated a variety of radiation sites including head/neck, chest, and abdomen. One study showed that aloe vera gel used with mild soap may be effective, especially with cumulative radiation doses over 2,700 cGy [13]. The second study also showed that aloe vera can reduce radiation-induced dermatitis when used prophylactically [12]. A major limitation of the reviewed studies is their small sample size. Future large randomized clinical trials would be useful in determining if aloe vera is consistently useful in preventing and treating radiation adverse effects. Another limitation is that the authors did not identify how they decided on the amount of aloe vera that should be used in order to have proper absorption at radiation sites.

6. Conclusions

Based on the trials found in this review, there is conflicting evidence as to whether or not aloe vera can prevent or treat radiation-induced adverse effects. Aloe vera was not found to be consistently effective for radiation effects in breast cancer patients. Conversely, aloe vera seems to be effective for acute radiation proctitis, but further large randomized controlled trials will be necessary to make a more definitive recommendation.

Conflicts of interest

None.

Financial Support and sponsorship

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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