

Table 1: Controlled clinical trials of *Aloe vera*

Source: Lorenc A, CAM-Cancer Consortium. [Aloe vera. \[online document\]](#), September 2018.

Type of cancer	First author Year (ref)	Study design	Participants	Interventions	Main outcome measures	Main results	Comments
Radiation-induced skin problems							
Head and neck cancer	Rao 2017 (36)	RCT	60 head and neck cancer patients undergoing radiotherapy/chemoradiotherapy of more than 66Gy	Topical <i>Aloe vera</i> cream 5x/day vs baby oil	Grading of acute skin reaction using Radiation Therapy Oncology Group (RTOG) four-point rating scale	Statistically significant delay in the incidence of dermatitis at week three in the <i>Aloe vera</i> group. <i>Aloe vera</i> reduced the incidence of grade 1, 2, and 3 dermatitis at subsequent time points (grade 4 dermatitis not seen in either group). Continued application of <i>Aloe vera</i> two weeks after radiotherapy statistically significantly reduced the average grade of dermatitis.	Patients/caregivers were not blinded to treatment allocation, but outcome assessors were. Attrition bias is unlikely as there were no withdrawals (one patient died). Random sequence generation method is not described but groups appear comparable. No sample size calculation.
Breast cancer	Ahmadloo 2017 (37)	RCT	100 newly diagnosed breast cancer patients undergoing radiotherapy	Topical <i>Aloe vera</i> gel throughout treatment, vs radiotherapy only	Prevalence and/or severity of radiotherapy-induced dermatitis using Acute Radiation Morbidity Scoring Criteria	No significant differences in the grade of dermatitis between the two groups in any week.	No details of randomisation process so selection bias may be present. Study was not blinded. There was no loss to follow up. No sample size calculation.
	Hoopfer 2015 (38)	RCT	248 breast cancer patients.	(3 arm trial) Topical <i>Aloe vera</i> cream, vs dry powder (baby powder/cornstarch) or placebo cream	Acute skin toxicity measured using a modified 10-point Catterall skin scoring profile	<i>Aloe vera</i> did not reduce acute skin toxicity or symptom severity. <i>Aloe vera</i> and placebo cream both increased the skin reaction on both univariate and multivariate analyses. Similar pattern of increased skin reaction toxicity occurred with both creams compared with the dry powder.	Patients and outcome assessors were blinded to treatment allocation. Creams were quality tested. Powered sample size and intention-to-treat analysis.

Various cancers	Haddad 2013 (39)	Self-controlled trial	60 patients with head and neck/breast/pelvic cancer undergoing radiotherapy of more than 40Gy	Topical <i>Aloe vera</i> lotion on one half of irradiated area vs no medication on other half.	Dermatitis grade using Radiation Therapy Oncology Group acute radiation morbidity scoring criteria	No significant difference between the halves of the irradiated area until the end of the 3rd week of radiotherapy. From week 4 to week 6 of radiotherapy and then at weeks 2 and 4 after radiotherapy, the mean grade of dermatitis was significantly lower for the <i>aloe vera</i> treated halves.	Study was self-controlled so not randomised. No blinding was used which may introduce bias. No details regarding attrition (53/60 patients were followed up).
Oral mucositis							
Head and neck cancer	Puataweepong 2009 (41)	RCT	61 head and neck cancer patients	Oral <i>Aloe vera</i> juice vs placebo, in addition to usual care	Onset and incidence of the severe mucositis (RTOG grade 2, 3, and 4)	The incidence of severe mucositis was significantly lower (53%) in the <i>Aloe vera</i> group compared to the placebo group (87%). No difference in the duration of mucositis.	Triple-blind study. Sample size did not reach the required calculated size. No loss to follow up. Some baseline differences between groups.
	Sahebjamee 2015 (42)	RCT	26 head and neck cancer patients	5ml <i>Aloe vera</i> mouthwash vs benzydamine mouthwash	Mucositis severity using the WHO grading system	No difference between <i>Aloe vera</i> and benzydamine in mucositis onset or severity.	Triple-blind study but small sample size.
	Su 2004 (30)	RCT	58 head and neck cancer patients	Oral <i>Aloe vera</i> (20ml juice) or placebo in addition to usual care.	Incidence and duration of mucositis	No statistically significant inter-group differences in terms of quality of life, mucositis, pain, weight loss and other endpoints	Double blinded but small sample size due to recruitment difficulties.
Leukaemia	Mansouri 2016 (43)	RCT	64 patients with chemotherapy-induced stomatitis	5ml <i>Aloe vera</i> solution mouthwash three times a day for 14 days vs standard care (ordinary recommended mouthwashes)	WHO stomatitis intensity checklists and Visual Analog Scale for pain.	<i>Aloe vera</i> mouthwash significantly reduced the intensity of stomatitis and its pain in the intervention group compared to the control group	They had no loss to follow up, outcome assessors were blind to treatment allocation

Oral Submucosal Fibrosis (OSMF)							
OSMF	Sudarshan 2012 (44)	RCT	20 subjects with OSMF	5 mg of <i>Aloe vera</i> gel applied topically 3 times daily for 3 months. vs antioxidant capsules twice daily for 3 months	VAS for burning sensation. Measurement of mouth opening, tongue protrusion and cheek flexibility	<i>Aloe vera</i> patients responded better in terms of symptoms and early-stage histopathology. <i>Aloe vera</i> generated a statistically significant relative reduction in burning sensation, improvement in mouth opening, and cheek flexibility	The study was small and not powered, although there was no loss to follow-up. Only participants were blinded.
	Patil 2014 (45)	RCT	120 subjects with OSMF	5mg <i>Aloe vera</i> gel 3 times a day, vs two oxtard capsules (a polyherbal formulation) twice daily for 3 months	Measurement of mouth opening, tongue protrusion. Presence, absence or reduction of other clinical parameters	Statistically significant improvements in mouth opening and tongue protrusion, pain, difficulty in swallowing and speech in the oxtard group, no difference in burning sensation.	Although this study is single blinded, it is unclear who was blinded. The randomisation process is not explained.
	Singh 2016 (46)	RCT	40 patients with OSMF	<i>Aloe vera</i> gel applied to the oral mucosa 3 times daily vs Antoxid tm capsules twice daily for 3 months. Both groups also did physiotherapy exercises (ice-cream stick exercise) four times a day	VAS for burning sensation. Measurement of mouth opening, tongue protrusion and cheek flexibility	Significant improvement in the <i>Aloe vera</i> group for burning sensation compared to Antoxid group. For mouth opening and tongue protrusion the % change was significantly different between groups, but the follow up scores were not. There were no differences in cheek flexibility.	This study is subject to several limitations including poor reporting, no details of randomisation or attrition and no blinding
	Anuradha 2016 (47)	RCT	74 patients with OSMF	30 ml <i>Aloe vera</i> juice (orally) twice a day and 5mg gel (topically) three times a day, vs intralesional injection of hydrocortisone and hyaluronidase	VAS for burning sensation. Measurement of mouth opening, tongue protrusion and cheek flexibility	Results shows that both groups showed statistically significant improvements in all study parameters at the end of the study and <i>Aloe vera</i> results were comparable to the control group.	Randomisation process is not described and there was 31% loss to follow up, but outcome assessors were blinded.

				for 6 weeks with antioxidant supplements for 3 months.			
Other outcomes							
Pelvic malignancies	Sahebnasagh 2017 (48)	RCT	20 patients with proctitis caused by radiotherapy of pelvic malignancies.	3% <i>Aloe vera</i> vs placebo ointment 1g twice daily for 4 weeks (both groups also received sulfasalazine).		Significant improvement in the symptom index for diarrhoea, faecal urgency, clinical presentation total, Radiation Therapy Oncology Group total and lifestyle. Haemorrhage and abdominal/rectal pain did not improve significantly.	Triple-blinded and had a powered sample size with no loss to follow-up.
Various cancers	Lisoni 2009 (49)	RCT	240 patients with mixed metastatic solid tumours	chemotherapy vs chemotherapy plus oral <i>Aloe vera</i> (extract of 300g fresh leaves 3x/day).	Clinical responses radiologically evaluated	Tumour regression, 3-year survival times and subjective symptoms were both better in the <i>Aloe</i> group.	This study seems well-conducted and its results are encouraging. However, independent replication seems necessary.
	Lisoni 1998 (31)	RCT	50 patients with advanced mixed cancers	melatonin vs melatonin plus oral <i>Aloe vera</i> tincture (1ml, 2x/day).	Clinical responses (tumour regression, stable disease, progression) 1-year survival	Significantly higher % of non-progressing patients in <i>Aloe</i> group. The percent 1-year survival was significantly higher in <i>aloe</i> group.	These findings are preliminary at best.