Table 1: Controlled clinical trials of *Aloe vera* for cancer

Source: Lorenc A, CAM-Cancer Consortium. *Aloe vera*. [online document]. http://cam-cancer.org/en/aloe-vera. December 12, 2020.

Type of cancer	First author Year	Study design	Participants	Interventions	Main outcome measures	Main results	Comments
Radiation-induced skin problems							
Head and neck cancer	Rao 2017	RCT	60 head and neck cancer patients undergoing radiotherapy/ chemoradio-therapy of more than 66Gy	1) Topical *Aloe vera* cream 5x/day 2) Baby oil	1) 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 *Aloe vera* group. *Aloe vera* 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 *Aloe vera* 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	RCT	100 newly diagnosed breast cancer patients undergoing radiotherapy	1) Topical *Aloe vera* gel throughout treatment 2)Radiotherapy only	1)Prevalence and/or 2) 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.
Oral mucositis							
Head and neck cancer	Puatawee-pong 2009	RCT	61 head and neck cancer patients	1) Oral *Aloe vera* juice 2) Placebo	1) Onset and incidence of the severe mucositis (RTOG grade 2, 3, and 4)	The incidence of severe mucositis was significantly lower (53%) in the *Aloe vera* 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.

	Su 2004 (30)	RCT	58 head and neck cancer patients	1) Oral *Aloe vera* (20ml juice) 2) Placebo	1) 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	1) 5ml *Aloe vera* solution mouthwash three times a day for 14 days 2) Standard care (ordinary recommended mouthwashes)	1) WHO stomatitis intensity checklists 2) VAS for pain.	*Aloe vera* 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
	Alkhouli 2020	RCT	26 children with acute lymphoblastic leukaemia	1) Aloe vera 2) Sodium bicarbonate	1) Assessment of oral mucosa using WHO grading system weekly for 2 months.	No significant differences in frequency of mucositis but Aloe vera group had significantly reduced severity compared to control in the 2^{nd} ($p=0.001$), 3^{rd}($p<0.001$), 4^{th} ($p=0.025$) and 7^{th} ($p=0.036$) week, and delayed onset ($p = .001$).	Small sample size which may be underpowered. Little detail on randomisation. Triple-blinded. Reliant on parents administering the intervention correctly.

Proctitis							
Pelvic cancer	Sahebnasagh 2020	RCT	42 patients with pelvic malignancies receiving radiotherapy	1) *Aloe vera* 3% 2) Placebo topical ointment Twice daily for 6 weeks	1) Rectal bleeding severity (0-4) 2) Abdominal/rectal pain severity (0-4) 3) Diarrhoea severity (0-4) 4) Fecal urgency severity (0-4) 5) RTOG acute toxicity 6) Psychosocial status 7) Lifestyle impact 8) Inflammation (CRP)	Significant improvements in Aloe vera group compared to control for diarrhoea ($p < 0.001$), rectal bleeding ($p < 0.001$), and fecal urgency ($p = 0.001$), lifestyle score ($p < 0.001$) and inflammation ($p=0.009$).	Very well conducted study. Triple blinded. Powered sample size and well randomised.
	Sahebnasagh 2017	RCT	20 patients with proctitis caused by radiotherapy of pelvic malignancies.	1) 3% *Aloe vera* 2) Placebo ointment 1g Twice daily for 4 weeks (both groups also received sulfasalazine).	1) Rectal bleeding severity (0-4) 2) Abdominal/rectal pain severity (0-4) 3) Diarrhoea severity (0-4) 4) Fecal urgency severity (0-4) 5) RTOG acute toxicity 6) Psychosocial status 7) Lifestyle impact	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.

Antitumour treatment							
Various cancers	Lissoni 2009	RCT	240 patients with mixed metastic solid tumours	1) Chemotherapy plus oral *Aloe vera* (extract of 300g fresh leaves 3x/day). 2) Chemotherapy only	Clinical responses radiologically evaluated	Tumour regression, 3-year survival times and subjective symptoms were both better in the *Aloe* group.	This study seems well-conducted and its results are encouraging. However, independent replication seems necessary.
	Lissoni 1998	RCT	50 patients with advanced mixed cancers	1) Melatonin plus oral *Aloe vera* tincture (1ml, 2x/day). 2) Melatonin only	1) Clinical responses (tumour regression, stable disease, progression) 2) 1-year survival	Significantly higher % of non-progressing patients in *Aloe* group. The percent 1-year survival was significantly higher in *aloe* group.	These findings are preliminary at best.
Prevention: Oral Submucosal Fibrosis (OSMF)							
OSMF	Sudarshan 2012	RCT	20 subjects with with OSMF	1) 5 mg of *Aloe vera* gel applied topically 3 times daily for 3 months. 2) Antioxidant capsules twice daily for 3 months	1) VAS for burning sensation. 2) Measurement of mouth opening, tongue protrusion and cheek flexibility	*Aloe vera* patients responded better in terms of symptoms and early-stage histopathology. *Aloe vera* 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	RCT	120 subjects with OSMF	1) 5mg *Aloe vera* gel 3 times a day 2) Two oxitard capsules (a polyherbal formulation) twice daily for 3 months	1) Measurement of mouth opening, tongue protrusion. 2) 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 oxitard 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	RCT	40 patients with OSMF	1) *Aloe vera* gel applied to the oral mucosa 3 times daily 2) Antoxid[tm] capsules twice daily for 3 months. Both groups also did physiotherapy exercises (ice-cream stick exercise) four times a day	1) VAS for burning sensation. 2) Measurement of mouth opening, tongue protrusion and cheek flexibility	Significant improvement in the *Aloe vera* 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	**RCT**	74 patients with OSMF	1) 30 ml *Aloe vera* juice (orally) twice a day and 5mg gel (topically) three times a day 2) Intralesional injection of hydrocortisone and hyaluronidase for 6 weeks with antioxidant supplements for 3 months.	1) VAS for burning sensation. 2) 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 *Aloe vera* 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.