Volume 13, No 3 | International Journal of Radiation Research, July 2015

The effect of "Curcuma Longa" topical gel on radiation -induced oral mucositis in patients with head and neck cancer

A. Mansourian[1], M. Amanlou[2], Sh. Shirazian[1*], Z. Moosavian Jahromi[3], A. Amirian[4]

[1]*Department of Oral Medicine and Dental Research Center, Faculty of Dentistry, Tehran University of Medical Sciences, Tehran, Iran*
[2]*Department of Medicinal Chemistry, Faculty of Pharmacy and Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran, Iran*
[3]*Department of Oral Medicine, Dental Branch of Tehran, Islamic Azad University, Tehran, Iran*
[4]*Department of Oral Medicine, Dental School, Tehran University of Medical Sciences, Tehran, Iran*

► ***Short report***

**** Corresponding author:***
Dr. Shiva Shirazian,
Fax: *+98 21 88015801*
E-mail:
shiraziansh@gmail.com

Revised: Dec. 2014
Accepted: Jan. 2015

Int. J. Radiat. Res., July 2015; 13(3): 269-274

DOI: 10.7508/ijrr.2015.03.011

ABSTRACT

Background: Different treatment and protective approaches for radiation-induced oral mucositis have been practiced and have varieties of success. Of which, radioprotective agents, synthetic or natural, have been of great interest for researchers. This study aims to evaluate the effect of curcuma longa topical gel as a herbal production on mucositis induced by radiation therapy of head and neck cancers. ***Materials and Methods:*** Thirty seven patients with head and neck cancer admitted for radiation therapy were selected. The patients were given curcuma longa or placebo topical gel for 8 weeks since the initiation of the radiotherapy, and were evaluated weekly for the presence and the extent of oral mucositis. ***Results:*** No grade-3 mucositis was observed in patients who used curcuma longa topical gel, and the grade of the mucositis was significantly different between the two groups with better effects found in case group compared to controls. No significant difference between the case and control groups was observed when comparing the time of appearing the first signs of mucositis. Oral lesions in case group were significantly smaller than that of control group. ***Conclusion:*** This study showed that the topical gel, containing curcuma longa's derivate, can effectively reduce the oral symptoms of mucositis in patients undergoing head and neck cancer radiotherapy. This herbal drug improves the grade of mucositis and reduces the size of oral lesions resulting from radiotherapy to the head and neck region.

Keywords: *Curcuma longa, oral mucositis, radiotherapy.*

INTRODUCTION

Oral mucositis is a debilitating condition following cancer therapy and its severity depends on several factors like dosage or duration of radiotherapy or target organ in radiated area [(1)]. Complications of mucositis such as infection, difficulty in swallowing or eating can lead to weight loss, nutrient deficiency or limitation in treatment protocols [(2)].

Oral mucositis occurs in about 80% of patients with head and neck cancer who receive radiotherapy or chemotherapy [(3)]. Although several protocols were used for protection of normal tissue from radiation-induced

[Downloaded from ijrr.com on 2026-09-13]

[DOI: 10.7508/ijrr.2015.03.011]

lesions,these agents only act symptomatically and do not solve the problem [4].

The recommendations for management of oral mucositis include regular assessment of oral pain, regular and systematic oral hygiene care using a standard protocol, dental examinations, and treatment. Currently, there is no successful intervention to prevent or treat oral mucositis. Among agents studied,

special attention is towards some plant and natural products [5].

Radioprotective agents are synthetic compounds or natural products that are administred immediately before irradiation to reduce injuries caused by ionizing radiation [6]. An ideal radioprotector is better tod be cheap, non-toxic in a wide range of doses, orally administered, rapidly absorbed, with a reasonably good dose reduction factor that can act through multiple mechanisms. Some plant and natural products have been reported to have these qualities [7].

For many years, different herbal materials have been investigated for their radioprotective activity. Of which, ethanolic extract of propolise [8], zingiber officinale [9], menthe arvensis linn [10], topical honey [5,11], and many other herbal derivates, like abana, Triphala, Hippophae rhamnoides, Mangifera indica, Panax ginseng, Mentha piperita, Tinospora cordifolia, Aegle marmelos, Amaranthus paniculatus and Ageratum conyzoides[6], have shown promises in reducing radiation-induced pathoses.

The turmeric (*Curcuma longa*) plant, a perennial herb belonging to the ginger family, is cultivated extensively in south and southeast tropical Asia. The rhizome of this plant is also referred to as the "root" and is the most useful part of the plant for culinary and medicinal purposes. The most active component of turmeric is curcumin, which makes up 2–5% of the spice [12].

Oral or topical use of curcumin has been reported to be effective in wound repair in normal and diabetic-individuals. It has inhibitory activity against hydrogen peroxide–induced oxidative damage in human keratinocytes and fibroblasts. Curcumin has also been reported to have potent antioxidant activity and to confer protection against radiation *in-vitro* and *in-vivo*. The other attractive feature of curcumin to explore as a vulnerary agent is that it is nontoxic and has been consumed daily for centuries in Asian countries [13].

The aim of this study was evaluating the effect of curcuma longa topical gel as a radioprotective agent on radiation-induced oral mucositis in patients with head and neck cancer.

MATERIALS AND METHODS

This double-blind, placebo-controlled randomized clinical trial was approved by Tehran University of Medical Sciences' ethics committee (reference number 9170) and was registered in the Iranian Registry of Clinical Trials (IRCT), with registration ID of IRCT 138904064255N1. Before the initiation of the study, the whole process of the research was explained to each patient and all questions of patients were answered.

All participants signed an informed consent and they could refuse to cooperate in the study at each phase. Thirty-seven patients presented to the Cancer Institute of Imam Khomeini Hospital (Tehran University of Medical Sciences) for radiation therapy were selected for this trial. Type of head and neck cancer and radiation dose in addition to the demographic data was recorded in separate forms.

The inclusion criteria were: minimum age of 18 years, presence of head and neck cancer, minimum radiation dose of 50 Gy (the least dose resulting in mucositis), the ability of patient to use topical gel (by his/her or examiner's report), minimally 50% of patient's oral cavity in radiation field (according to the radiotherapist's opinion), and signing the informed consent.

The exclusion criteria were: history of radiation therapy or chemotherapy in previous year, chemotherapy protocol in addition to radiotherapy, any allergy to condiments, especially "Turmeric root", any complications due to the use of topical gel during the study, suffering from any kind of oral disease such as active oral infection, ulcer, having any systemic disease or taking any medication.

[Downloaded from ijrr.com on 2026-09-13]

[DOI: 10.7508/ijrr.2015.03.011]

Study design

Balanced block randomization method using random number table was used for randomization of the patients. This information was secret until data analysis.

Each patient was given a container of a gel with a written instruction for use; application of the gel to the whole oral cavity was as follows: the patients had to avoid eating or drinking for 15 minutes before the initiation of radiotherapy and they had to cover the whole mouth with a thin layer of the gel by a cotton applicator. Gel was applied for all radiotherapy duration (21 days) 3 times a day.

Preparation of the drug

500 gr of fresh curcuma powder was shed in a percolation device, 2500 ml ethanol (75ºC) was added, and then it was kept in a room temperature for 24 hours. Extract was separated and filtered. This procedure was repeated three times. Filtered extract was distilled in a vacuum rotary in a distiller. The mixture was put in the refrigerator away from the direct light.

One-hundred gr Sodium carboxymethyl cellulose was mixed with 900 ml boiling water with a magnetic stirrer until a stable gel was made as a placebo. At the end, 10 gr of the prepared extract added to 990 gr of the prepared gel and stirred vigorously for 4 h.

In the case group, patients used curcuma longa topical gel (dried hydroalcohol derivative of curcuma Longa, 0.5% gel), and in the control group, a yellowish ineffective inert placebo in the form of gel, with the same appearance as the curcuma longa topical gel was used. The instructions for use was the same in both groups.

During radiotherapy, all patients were evaluated at days 7, 14 and 21 after the initiation of therapy. Oral cavity was examined by an oral medicine specialist in the hospital for any existing sign of mucositis.

Burning mouth sensation which is defined as a subjective burning feeling in the oral mucosa was measured by the visual analysis scale (VAS) in each appointment,

Oral mucosal erythema, was measured in each visit by a checkered transparent paper.

Mucositis grade according to WHO guideline (table 1) was recorded in subjects' files during each visit.

Data analysis methods

Data analysis was carried out by the Statistical Package for the Social Sciences (SPSS) ver 16. Chi-Square and T Test were used to analyze data between the two groups. Normal distribution of continuous data like age and size of lesions were tested by Kolmogrov- Smirnov and Shapiro. Significance of P value in all statistical tests was set at $P<0.05$.

RESULTS

Thirty seven patients with different types of head and neck cancers were selected from the Cancer Institute of Imam Khomeini Hospital (Tehran University of Medical Sciences) between February and May 2010.

Out of 37 patients (19 patients in intervention group and 18 patients in control group), 6 (16.22%) were female and 31(83.78%) were male (table 2). The mean age (*t-test*, $P>0.05$) and gender ratio (chi-square, $P>0.05$) had no significant differences between the two groups. In the intervention group, 12 patients (63.2%) received radiation dose of 50 Gy and 7 (36.8%) patients received 60 Gy and in the control group 10 (55.6%), 7 (38.9%) and 1 (5.6%) patients received radiation doses of 50, 60, 65 Gy, respectively. There was no significant differences between the two groups in the received radiation dose (*t*-test, $P>0.05$) .

Table 1. Patients' oral mucositis grading, adapted from WHO oral toxicity scale [1].

Oral Mucositis				
Grade 1	**Grade 2**	**Grade 3**	**Grade 4**	**Grade 5**
None	Erythema±Soreness	Erythema, ulcers, Patient can swallow solid diet	Ulcers, extensive erythema. Patient cannot swallow solid diet	Mucositis to the extent that alimentation is not possible

[Downloaded from ijrr.com on 2026-09-13]

[DOI: 10.7508/ijrr.2015.03.011]

The diagnosis of patients was as follows: 10 (27.1%) with Larynx squamous cell carcinoma (SCC), 6 (16.2%) with tongue SCC, 6 (16.2%) with lip cancer (1 with lip sarcoma, 3 with lip SCC, 1 with lip BCC and 1 with lip papillary carcinoma diagnosis), 3 (8.1%) with hypopharynx SCC, 3 (8.1%) with neck cancer (2 with Neck SCC and 1 with plasmocytoma neck mass diagnosis), 3 (8.1%) with buccal SCC, 2 (5.4%) with ear SCC, 2 (5.4%) with nasopharynx SCC and 2 (5.4%) with nose SCC. According to random allocation of the subjects, 19 (51.4%) patients were randomized to the intervention group and 18 (48.6%) patients to the control group.

Maximum grade of mucositis is shown in table 3. There was no grade3 mucositis in the intervention group but 7 (38.9%) patients were in grade 3 mucositis in the control group. Grade 4 mucositis was not observed in any of the patients. There was a significant difference in the frequency of different grades of mucositis in the two groups (chi-square P<0.001).

The two groups had no significant differences in the time between treatment initiation and maximum grade of mucositis (chi-square P=0.315), but the time the symptoms started was significantly longer in the intervention group (table 4).

The mean size of oral lesions, oral erythema and burning mouth sensation in the intervention group was significantly lower than the control group (P<0.001, T test) (table 5).

Table 2. Demographic characteristics of the patients.

Gender	Intervention group (n=19)	Control group (n=18)
Male Female	4 15	2 16
Age (Yr) ± SD	47.3±9.7	55.6±14.6

Table 3. The maximum grade of mucositis.

Study groups	Grade-1 mucositis N (%)	Grade-2 mucositis N (%)	Grade-3 mucositis N (%)
Case	15 (78.9%)	4 (21.1%)	0 (0%)
Control	3 (16.7%)	8 (44.4%)	7 (38.9%)
Total	18 (48.6%)	12 (32.4%)	7 (18.9%)

DISCUSSION

Curcumin, as a traditional herbal drug, has been used in many countries for a wide variety of inflammatory diseases including sprains and swellings caused by injury, wound healing, and abdominal problems [13]. Curcuma longa rhizome is widely used in Indian cuisine as well as in traditional medicine. Pharmacological properties include anti-inflammatory, anti-HIV, antibacteria, antitumour and antioxidant effects. Curcumin (diferuloylmethane) has been reported to render radioprotective effect [14].

Up to now, many studies have been conducted to reveal the tissue protective effects the curcumin against radiation. Curcumin has been reported to scavenge oxygen free radicals and inhibit lipid peroxidation and protect the cellular macromolecules, including DNA from oxidative damage [5]. Curcumin can inhibit generation of superoxide anion and hydroxyl radicals [15].

In the present study, a gel, containing turmeric derivate was used for protecting the mucosa against radiation-induced mucositis in patients with head and neck cancer, and its effects were compared with the placebo gel. To the knowledge of the authors, it was the first study to evaluate the effects of Curcumin Longa gel on the mucositis. We found that this herbal gel could reduce the signs of oral mucositis and burning mouth feeling, but it could not be

Table 4. The incidence of the maximum intensity of the mucositis by the days after initiation of the therapy.

Mucositis (day)	7	14	21
Intervention group	4 (21.1%)	6 (31.6%)	9 (47.4%)
Control group	8 (44.4%)	4 (22.2%)	6 (33.3%)
Total	12 (32.4%)	10 (27.0%)	15 (40.5%)

Table 5. The results of examining patients for oral erythema, burning mouth and oral ulcers.

	Case group N=19	Control group N=18
Max. size of oral erythema (mm)	4.9±2.2	8.9±2.7
Max. size of oral ulcer (mm)	1.3±2.7	6.4±4.2
VAS analysis	3.7±2.1	7.9±2.0

[Downloaded from ijrr.com on 2026-09-13]

[DOI: 10.7508/ijrr.2015.03.011]

considered as a preventing agent in such radiation-induced conditions. The intensity of mucositis in the intervention group was milder than the control group. No patient in treatment group experienced, grade-3 mucositis, and only 4 patients had grade-2 mucositis and 15 patients had grade1 mucositis.

It is mentioned by Shishodia *et al.* that the antioxidant activity of curcumin could be mediated through antioxidant enzymes such as superoxide dismutase, catalase, and glutathione peroxidase. Curcumin has been shown to serve as a Michael acceptor reacting with glutathione and thioredoxin. Reaction of curcumin with these agents reduces intracellular GSH in the cells. The suppression of lipid peroxidation by curcumin could lead to suppression of inflammation [12]. Study of Shishodia *et al.* supports our finding of reducing inflammation in patients under curcumin radioprotection in contrast to patients studied by placebo gel.

Jagetia and colleagues, evaluated the role of curcumin in accelerating the repair of excision wound in mice, whole body exposed to various doses of gamma-radiation [13]. By this research, they concluded that pretreatment with curcumin significantly enhanced the rate of wound contraction, decreased mean wound healing time, increased synthesis of collagen, hexosamine, DNA, and nitric oxide and improved fibroblast and vascular densities. Hence, the reduction of the size of oral lesions in our study could be due to the effect of this drug on wound contraction and the synthesis of collagen.

Burning mouth factor in the present study, which was analyzed by VAS, was significantly lower in the interventional group compared to the control group. This finding can be due to the anti-inflammatory and wound healing properties of curcuma longa. Actually, when this drug reduces the oral lesions, it lessens the burning sensation of the mouth (may be due to the oral ulcer and erythema) indirectly.

Additionally, comparison of the two groups of study revealed delayed occurrence of mucositis in the intervention group in contrast to the controls.

Kakoei *et al.* [3] compared the effect of cryotherapy and standard oral care on radiation-induced oral mucositis. They showed that the severity of pain and symptoms of mucositis was reduced in the case group, but the signs of mucositis didn't improve. Their patients who received cryotherapy reported feeling more comfort in their mouth. In our study, patients in the intervention group experienced milder signs of oral mucositis, burning mouth sensation and intensity of mucositis. Gorgu *et al.* [2] showed that prophylaxis using of zinc sulfate didn't have effects on oral mucositis and incidence of mucositis and esophagitis. They used different scales for assessing oral mucositis and mentioned that the level of zinc before the initiation of treatment was not similar between two groups that could have affected their results

Henke *et al.* reported the efficacy of Palifermin to reduce the severity of oral mucositis in patients with head and neck cancer against placebo who received postoperative radiochemotherapy. They showed that Palifermin decreased the duration of severe mucositis [16]. Similar to our study, their patients didn't report any mouth or throat soreness. Leborgne *et al*. found that prescription of 40 mg/day prednisone in patients with head and neck cancer under radiotherapy could reduce the treatment interruptions but the intensity and duration of mucositis wasn't reduced [17].

Curcumin is remarkably tolerated well, but its bioavailability is poor. It does not appear to be toxic to animals or humans even at high doses [18].

In the present study, patients who had used curcuma longa topical gel, did not demonstrate any side effects, except for two reports of feeling nausea after applying the gel which had been completely resolved after two weeks of application.

To conclude, this study showed that the topical gel, containing curcuma longa's derivate, can effectively reduce the oral symptoms of mucositis in patients undergoing head and neck cancer radiotherapy because of its anti-inflammatory and antioxidant effects. This herbal drug not only lessens the grade of mucositis, but also reduces the size of oral

[Downloaded from ijrr.com on 2026-09-13]

[DOI: 10.7508/ijrr.2015.03.011]

lesions resulted from radiotherapy to the head and neck region.

Conflicts of interest: *none to declare.*

REFERENCES

1. Sahebjamee M, Mansourian A, Mohammad MH, Zadeh MT, Bekhradi R, Kazemian A,et al. (2015) Comparative Efficacy of Aloe vera and Benzydamine Mouthwashes on Radiation-induced Oral Mucositis: A Triple-blind, Randomised, Controlled Clinical Trial. *Oral Health Prev Dent,* ***13(4):*** *309-15*
2. Gorgu SZ, Ilknur AF, Sercan O, Rahsan H, Nalan A (2013) The effect of zinc sulfate in the prevention of radiation induced oral mucositis in patients with head and neck cancer. *Int J Radiat Res,* ***11(2):*** *111-116.*
3. Kakoei S, Ghassemi A, Nakhaee N (2013) Effect of cryotherapy on oral mucositis in patients with head and neck cancers receiving radiotherapy. *Int J Radiat Res,* ***11 (2):*** *117-120.*
4. Rezvani M (2003) Treatment of radiation-induced normal tissue lesions. *Iran J Radiat Res,* ***1(2):*** *63-78.*
5. Rashad UM, Al-Gezawy SM, El-Gezawy E, Azzaz AN (2009 Honey as topical prophylaxis against radiochemotherapy-induced mucositis in head and neck cancer. *J Laryngol Otol,* ***123(2):*** *223-228.*
6. Hosseinimehr SJ (2007) Trends in the development of radioprotective agents. *Drug Discov Today,* ***12(19-20):*** *794-805.*
7. Jagetia GC (2007) Radioprotective potential of plants and herbs against the effects of ionizing radiation. *J Clin Biochem Nutr,* ***40(2):****74-81.*
8. Ghassemi L, Zabihi E, Mahdavi R, Seyed Majidi M, Akram S, Motallebnejad M (2010) The effect of ethanolic extract of propolis on radiation-induced mucositis in rats. *Saudi Med J,* ***31(6):****622-626.*
9. Sharma A, Haksar A, Chawla R, Kumar R, Arora R, Singh S (2005) Zingiber officinale Rosc. modulates gamma radiation-induced conditioned taste aversion. *Pharmacol Biochem Behav,* ***81(4):****864-870.*
10. Jagetia GC and Baliga MS (2002) Influence of the leaf extract of Mentha arvensis Linn. (mint) on the survival of mice exposed to different doses of gamma radiation. *Strahlenther Onkol,* ***178(2):*** *91-98.*
11. Khanal B, Baliga M, Uppal N (2010) Effect of topical honey on limitation of radiation-induced oral mucositis: an intervention study. *Int J Oral Maxillofac Surg,* ***39(12):*** *1181-1185.*
12. Shishodia S, Sethi G, Aggarwal BB (2005) Curcumin: getting back to the roots. *Ann N Y Acad Sci,* ***1056:*** *206-217.*
13. Jagetia GC and Rajanikant GK (2004) Role of curcumin, a naturally occurring phenolic compound of turmeric in accelerating the repair of excision wound, in mice whole-body exposed to various doses of gamma-radiation. *J Surg Res,* ***120(1):*** *127-138.*
14. Arora R, Gupta D, Chawla R, Sagar R, Sharma A, Kumar R (2005) Radioprotection by plant products: present status and future prospects. *Phytother Res,* ***19(1):*** *1-22.*
15. Reddy AC and Lokesh BR(1994) Studies on the inhibitory effects of curcumin and eugenol on the formation of reactive oxygen species and the oxidation of ferrous iron. *Mol Cell Biochem,* ***137(1):*** *1-8.*
16. Henke M, Alfonsi M, Foa P, Giralt J, Bardet E, Cerezo L, *et al.*(2011) Palifermin decreases severe oral mucositis of patients undergoing postoperative radiochemotherapy for head and neck cancer: A Randomized, Placebo-Controlled Trial. *J Clin Oncol* ***29(20):*** *2815-2820.*
17. Leborgne JH, Leborgne F, Zubizarreta E, Ortega B, Mezzera J (1997) Corticosteroids and radiation mucositis in head and neck cancer. A double-blind placebo-controlled randomized trial. *Radiotherapy and Oncology,* ***47(2):*** *145–148.*

[Downloaded from ijrr.com on 2026-09-13]

[DOI: 10.7508/ijrr.2015.03.011]