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Curcumin Oral Gel and its Relation to Salivary Tumor Necrosis Factor-Alpha and Interleukin-6 that Treated Oral Mucositis in Head and Neck Cancer Patients Undergoing Concurrent Chemoradiation

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Abstract

Background: Curcumin oral gel is one example of a traditional herbal medication, it has shown potential in several pharmaceutical uses. Oral mucositis is commonly prevent and treat using magic solution, a mouthwash that contains a combination of pharmaceuticals. Tumor necrosis factor- α and Interleukin-6 are salivary cytokines stimulates the immune response and promotes inflammation during infection or other tissue damage causes inflammation.

Objective: To determine the effect of curcumin oral gel on salivary tumor necrosis factor-α and interleukin-6 levels in head and neck cancer patients under concurrent chemoradiation induced oral mucositis.

Patients and Methods: Two groups of forty-five patients each, with a total of ninety head and neck cancer patients receiving concurrent chemoradiation. Enzyme-linked immunosorbent assay measured salivary tumor necrosis factor-alpha and interleukin-6 levels. Oral mucositis was assessed by WHO scale.

Results: Patients who took oral curcumin gel had less severe oral mucositis and lower salivary levels of tumor necrosis factor-alpha and interleukin-6. WHO scale between the two groups showed significant differences at 2 weeks (P = 0.041) and 6 weeks (P=0.02).

Conclusion: Study concludes that curcumin oral gel might reduced salivary tumor necrosis factor-alpha and interleukin-6 levels and may serve as an alternative treatment for oral mucositis resulting from chemoradiation.

Keywords: Head and neck cancer, Concurrent chemoradiotherapy, Oral mucositis, Curcumin, Tumor necrosis factor-alpha, Interleukin-6.

Introduction

Curcumin goes under another name, The Zingiberaceae family includes turmeric. One to two percent curcuminoids and three to twelve percent volatile oil are the two main components of the root. A phenolic compound with possible health benefits, dimethylsulfoxide is also known as curcumin. (1, 2). Numerous clinical investigations have shown the extensive variety of pharmacologic capabilities exhibited by Curcumin oral gel. These features include the ability to

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enhance wound healing, anti-inflammatory, antifungal, antibacterial, and anticarcinogenic actions (3, 4). Curcumin improves epithelialization and wound healing by protecting and activating keratinocytes while scavenging reactive oxygen species and serving as an antioxidant (5, 6). Curcumin may potentially increase the effectiveness of morphine by decreasing pain transmission channels and promoting the production of serotonin, dopamine, and noradrenaline at large dosage (7). Head and neck cancers(HNC) involve a wide range of malignancies that may develop in salivary glands, paranasal sinuses, the larynx, pharynx, and oral cavity (8). When head and neck cancer has spread locally, first line of treatment choice is a chemotherapy combined with radiotherapy (9). Cytotoxic concurrent chemoradiotherapy causes oral mucositis (OM), an inflammatory condition of the mouth and throat that is a major problem in oncology (10). Oral mucositis may progress to deep, confluent ulcers if left untreated.The level of functioning and the standard of living of a patient are often compromised by pain caused by mucositis (11, 12). In cells such as macrophages, epithelial, endothelial, and mesenchymal cells, the transcription nuclear factor-κB(NF-κB) is made active by concurrent chemotherapy and radiation (CCRT). The result is an increase in genes that are upregulated and the generation of cytokines that promote inflammation, like tumour necrosis factor-α (TNF-α) and interleukin-6 (IL-6). The transcription of genes encoding cyclooxygenase 2 (COX2), mitogen-activated protein kinase (MAPK) and tyrosine-kinase signaling molecules is induced by cytokines that enhance the main signal or activate nuclear factor-κB in other cells. In the cell epithelium and lamina propria, matrix metalloproteinase (MMP-1 and MMP-3), is activated by both TNF-α and IL-6, leading to tissue injury (13, 14).

Aim of this study: To determine the effect of curcumin oral gel on salivary tumor necrosis factor-α and interleukin-6 levels in head and neck cancer patients under concurrent chemoradiation induced oral mucositis.

Patients and Methods

From March 2023 to June 2024, this study was carried out. Protocol number: 934724 indicates that the study was given the go light by the Research Ethics Committee of the University of Baghdad, College of Dentistry. There were 90 HNC patients that took part in the research. There were two groups created: the experimental group and the comparison group.

Subjects: For the trial, 45 patients were given oral gel containing curcumin, whereas 45 patients were given magic-solution as a control**.**

Inclusion criteria: included being between the ages of 30 and 70, diagnosed with cancer of the head and neck and being scheduled for concurrent chemoradiotherapy. Patients were also required to wear mask of head and neck during radiation therapy, and their oral cavity mucosa had to be within the radiation range. Chemotherapy was cisplatin 40 mg/m2 administered weekly, and radiotherapy consisted of 33 fractions scheduled 5 times a week for 6 weeks with 50 and 70 Gray (Gy).

Exclusion criteria: were individuals receiving only radiation and those having palliative radiotherapy.

Assessment of oral mucositis Clinical: On the 2nd week of chemoradiation and the last day of the chemoradiation treatments, patients were examined and scored on a scale from 0 to 4 developed by the World Health Organization WHO. With a score of 0, no symptoms are present; with a score of 1, the oral mucosa is red and uncomfortable; and a score of 2 indicates that the mouth is ulcerous and makes it hard to eat normally. At 3, the ulcer has already developed, and the patient is limited to drinking fluids; at 4, the patient is unable to eat or drink anything (15).

Curcuma longa oral gel: The subjects in the

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curcumin group were given Curenext®, a product made by (Abbott Healthcare, India) which includes 10 milligrams of Curcuma longa root extract (rhizome) per gram of gel. Patients were told to use a cotton swab or finger to apply the gel three times a day beginning with the initial saliva sample collection until their chemoradiotherapy treatment was finished. A standard mouthwash consisting of nystatin, dexamethasone, lidocaine, and tetracycline was administered to patients in the magic-solution group (16, 17).

Saliva sample collection and storage: Each of the 90 patients had three complete saliva samples taken: once before chemoradiation, once after the second week of treatment, and again at the six-week chemoradiation. Patients spat into a plastic tube that was marked with their name, group, and visit date in order to collect their unstimulated saliva. The next step was to place it in an icebox and freeze it stored at a temperature of -80°C till the time of analysis comes.

Laboratory analysis: Salivary TNF-α and IL6 levels were examined using the enzyme-linked immunosorbent test (ELISA). (ELISA) is a type of solid phase immunoassay in which antigens or antibodies are covalently bound with suitable enzymes that can catalyze the change of substrates into dyed products. It is an approved technique to investigate different biological markers Commercial quantitative sandwich assay (ELISA) kits from Cloud-clone Corp (CCC, USA) were used in compliance with the manufacturer's recommendations (18). To find the levels of TNF-α and IL6, saliva samples were taken, using phosphate-buffered saline as a negative control and a manufacturer-supplied standard curve.

Statistical analysis

The data was handled in an Excel spreadsheet. Analysis was carried out using SPSS version 22. Statistical tests were used: a paired t-test, an independent t-test, a Bonferroni test, a Wilcoxon Signed Ranks test, and chi-square ($\chi 2$) test. A P-value below 0.05 was defined significant.

Results

When comparing the two groups according to age and sex, no statistically significant differences were found.

Salivary tumor necrosis factor-α (TNF- α):

The comparison between the two studied groups with respect to TNF- α marker, along different of an experimental periods, results shows that mean values are decreases clearly over the time periods, and at a lower levels with respect to treated with curcumin group (Table 1 , Figure 1).

Table 1. Summary statistics of TNF- α (pg/ml) marker along different periods of the studied groups.

Periods	Groups	No.	Mean	Std. D.	Std. E.	95% C. I. for Mean		Min.	Max.
						L.b.	U.b.		
Initiation period	Curcumin	45	208.0	34.95	5.21	197.51	218.52	113.29	282.61
	Magic Solution	45	266.4	77.50	11.55	243.08	289.64	135.99	391.84
After 2 weeks	Curcumin	45	142.6	27.73	4.13	134.26	150.92	104	216.96
	Magic Solution	45	218.3	47.78	7.12	203.91	232.62	100.45	295.76
After 6 weeks	Curcumin	45	88.95	9.44	1.41	86.12	91.79	74.49	111.6
	Magic Solution	45	182.8	55.76	8.31	166.05	199.56	116.17	324.32

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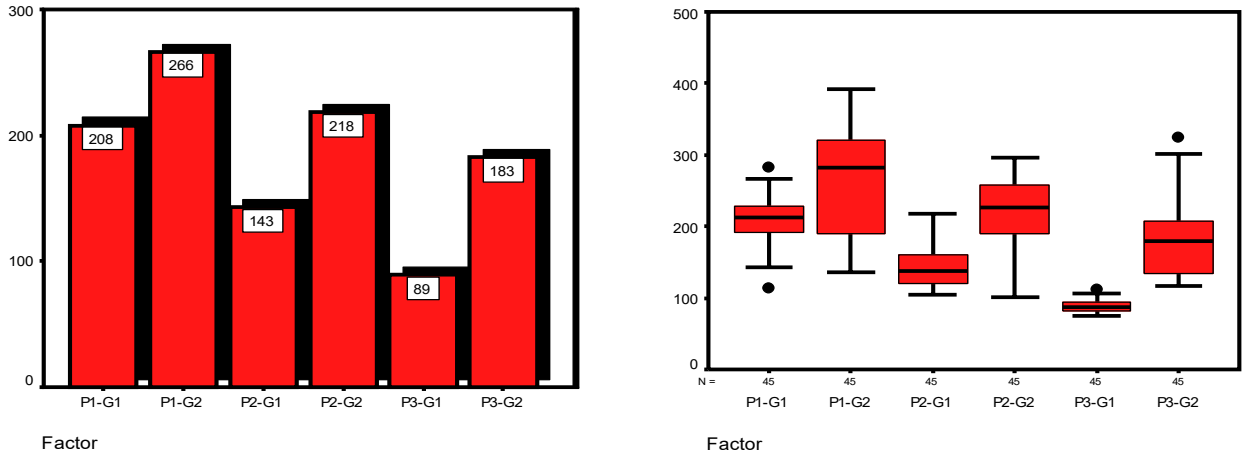

Figure 1. Stem-leaf plot and Bar Chart for exploring behavior of TNF-α marker reading's distribution along the study of the sequential periods in each group.

Means salivary TNF- α were highly significantly (P = 0.000) decreased two and six weeks after chemoradiotherapy compared to that before chemoradiotherapy and six weeks after chemoradiotherapy compared to that at two weeks after chemoradiotherapy in both study groups. The decrement in TNF- α two and six weeks after chemoradiotherapy was considerably significantly higher in the curcumin group than that treated with magic solution compared to that before chemoradiotherapy (P < 0.05) in Table 2.

Salivary interleukin 6 (IL-6): The comparison between the two studied groups concerning the "IL6" marker along different experimental periods. The results show that mean values decrease clearly over the periods and at lower levels concerning the curcumin group (Table 3, Figure 2).

Table 4 shows the means salivary IL-6 were highly significantly (P = 0.000) decreased two and six weeks after chemoradiotherapy compared to that before chemoradiotherapy and six weeks after chemoradiotherapy compared to that at two weeks after chemoradiotherapy in both study groups. The decrement in IL-6 two and six weeks after chemoradiotherapy group treated with curcumin had a significantly higher than that treated with magic solution compared to that before chemoradiotherapy (P < 0.05).

Table 2. Significant levels for testing covariate of TNF- α (pg/ml) marker's readings in each group independently over the sequential periods.

Groups	Pairwise Comparisons		Mean Diff. (I-J)	Std. lkError	Sig. (*) Level	95% C. I. for Diff.	
	(I) TNF- α	(J) TNF- α				L.b.	U.b.
Curcumin	Initiation	After 2 w.	-20.02	4.416	0.000	-28.92	-11.1
		After 6 w.	33.62	2.211	0.000	29.17	38.1
	After 2 w.	After 6 w.	53.64	4.129	0.000	45.32	62.0
Magic Solution	Initiation	After 2 w.	-147.78	11.471	0.000	-170.90	-124.7
		After 6 w.	-64.23	8.381	0.000	-81.12	-47.3
	After 2 w.	After 6 w.	83.55	10.036	0.000	63.33	103.8
(*) HS: Highly Sig. at P<0.01; S: Sig. at P<0.05; Testing is based on repeated measurers of several related groups, through using adjustment for multiple comparisons by "Bonferroni" test.							

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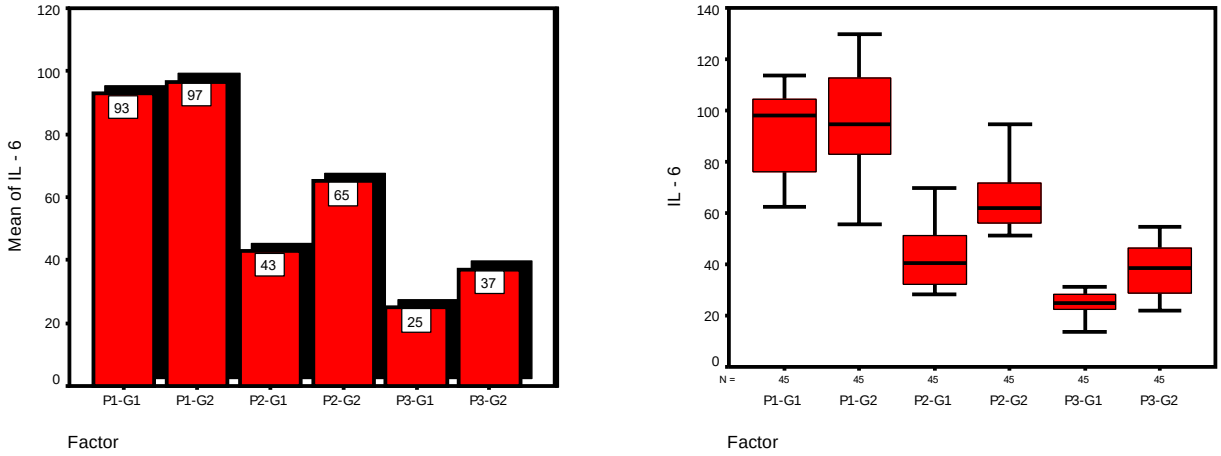

Figure 2. Bar Chart, and stem-leaf plot for explore behavior of IL-6 marker reading's distribution along the studied of sequential periods in each group.

Table 3. Summary Statistics of IL-6 (pg/ml) marker along different periods of the studied groups.

Periods	Groups	No.	Mean	Std. D.	Std. E.	95% C. I. for Mean		Min.	Max.
						L.b.	U.b.		
Initiation period	Curcumin	45	92.88	15.39	2.29	88.26	97.51	62.27	113.75
	Magic Solution	45	96.69	19.60	2.92	90.80	102.58	55.71	129.76
After 2 weeks	Curcumin	45	42.80	12.42	1.85	39.07	46.53	28.30	69.65
	Magic Solution	45	65.17	11.89	1.77	61.60	68.74	51.03	94.79
After 6 weeks	Curcumin	45	24.99	3.90	0.58	23.82	26.16	13.68	31.00
	Magic Solution	45	37.15	9.43	1.41	34.31	39.98	21.89	54.87

Table 4. Significant levels for testing covariate of IL-6 (pg/ml) marker readings in each group independently over the sequential periods.

Groups	Pairwise Comparisons		Mean Diff. (I-J)	Std. Error	Sig. Level	95% C. I. for Diff.	
	(I) IL-6	(J) IL-6				L.b.	U.b.
Curcumin	Initiation	After 2 w.	50.086	2.570	0.000	43.69	56.48
		After 6 w.	67.895	2.167	0.000	62.50	73.29
	After 2 w.	After 6 w.	17.809	1.741	0.000	13.48	22.14
Non Curcumin	Initiation	After 2 w.	31.515	3.089	0.000	23.83	39.20
		After 6 w.	59.540	3.624	0.000	50.52	68.56
	After 2 w.	After 6 w.	28.025	2.261	0.000	22.40	33.65
(*) HS: Highly Sig. at P<0.01; Testing are based on repeated measurers of several related groups, through using adjustment for multiple comparisons by "Bonferroni" test.							

Clinical evaluation of oral mucositis

world health organization scale: Table 5 and Figure 3 at both the two-week and six-week chemoradiation evaluations, the curcumin group had a significantly lower mean WHO score than the magic-solution group. Results in Table 6 demonstrate WHO score readings that too highly significant differences are accounted at P<0.01 concerning all probable pairwise comparisons grade of mucositis GOM , either for curcumin or magic solution groups % independently.

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Table 5. Summary Statistics of Grade of Mucositis WHO score along different periods of the studied groups.

Groups	Statistics	Periods		
		Initiation	After 2 weeks	After 6 weeks
Curcumin	Mean of Score	0.000	1.667	1.178
	Interquartile Range	0.000	1.000	1.000
	Minimum score	0.000	1.000	1.000
	Maximum score	0.000	3.000	2.000
Magic solution	Mean of Score	0.000	1.689	1,378
	Interquartile Range	0.000	0.000	1.000
	Minimum score	0.000	1.000	1.000
	Maximum score	0.000	3.000	3.000

Table 6. Significant levels for testing of GOM score's readings in each group independently over the sequential periods.

Groups	Pairwise Comparisons		Z-value	Sig. Level
	(I) GOM	(J) GOM		
Curcumin	Initiation	After 2 w.	-5.964	0.000
		After 6 w.	-6.283	0.000
	After 2 w.	After 6 w.	-4.491	0.000
Magic Solution	Initiation	After 2 w.	-5.970	0.000
		After 6 w.	-6.081	0.000
	After 2 w.	After 6 w.	-3.300	0.001
(*) HS: Highly Sig. at P<0.01; Testing are based on the "Wilcoxon Signed Ranks" test.				

Grade of mucositis between study groups:

Table 7 shows the comparison in grade of mucositis between study groups after chemoradiotherapy. After two weeks, 66.7% of patients in curcumin group were graded I compared to 42.3% in magic solution group; with statistical significance p-value = 0.041. After six weeks, 82.2% of patients in the curcumin group were graded I compared to 60% in the magic solution the group, a statistically significant difference (P=0.02) was seen.

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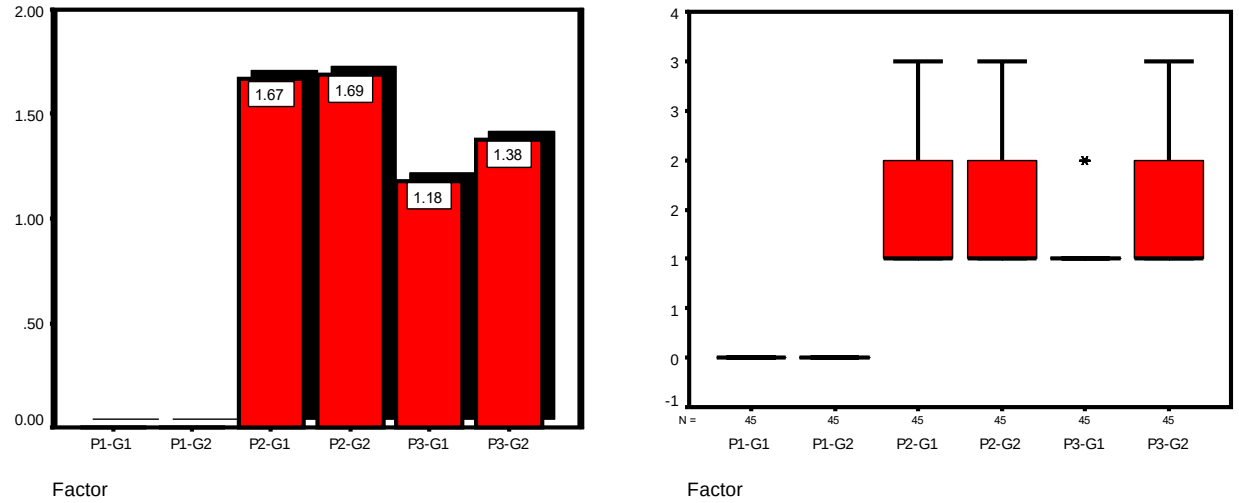

Figure 3. Bar Chart, and stem-leaf plot for exploring behavior of GOM Score reading's distribution along the studied of sequential periods in each group.

Table 7. Comparison between study groups by grade of mucositis.

Grade of mucositis (WHO)	Study group		X^2 test	P - Value
	Curcumin (%) n= 45	Magic Solution (%) n= 45		
Two weeks after chemoradiotherapy				
1	30 (66.7)	19 (42.3)	6.351	0.041
2	11 (24.4)	15 (33.3)		
3	4 (8.9)	11 (24.4)		
Six weeks after chemoradiotherapy				
1	37 (82.2)	27 (60.0)	7.75	0.02
2	8 (17.8)	13 (28.9)		
3	0 (0)	5 (11.1)		
WHO: World Health Organization. X^2: chi-square test.				

Discussion

Since it is simpler to apply, absorbs quickly, topical curcumin treatment, in the form of an oral gel, offers several benefits over systemic curcumin because it interacts with surrounding tissues, prolonging the contact period that increases its benefits, and because it has fewer evident bad effects. For individuals suffering from dysphagia or gastrointestinal issues, oral gel formulations may be helpful in reducing side effects (15-17,19). Concurrent chemoradiotherapy causes basal epithelial cell death, which may occur as a result of free radical production.

The activation of second messengers by these free radicals transmits signals from surface receptors on cells to their inner surroundings, leading to an increase in inflammatory cytokines, harm to tissues, and cell death. Macrophages secrete cytokines that promote inflammation, including TNF-α and IL-6, intensify mucosal damage; moreover, a superimposed infection of the ulcerated mucosa might trigger the generation of these pro-inflammatory cytokines (20-22).

TNF-α is a cytokine that promotes inflammation released by macrophages, endothelial cells, and fibroblasts. It is plays an important in the formation and development of OM in in patients with head and neck cancer receiving CCRT. Typically, it goes

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undetected in healthy people. However, in cases of inflammation or infection, it is found to be highly concentrated in both serum and tissues. The severity of an infection is correlated with the salivary and serum levels. A wide range of cells have the ability to create TNF-α, such as monocyte/macrophage, neutrophils, natural killer cells (NK),T and B lymphocytes, smooth and cardiac muscle cells , osteoclasts, endothelial cells, fibroblasts (23, 24). Patients with oral cancer had significantly higher

levels of salivary TNF-α, according to Deepthi's research (25). IL-6 is a cytokine that promotes inflammation and an anti-inflammatory myokine secreted by T cells and macrophages when an infection or other kind of tissue injury causes inflammation (26). After chemotherapy drugs have been administered, many investigations showed that nuclear factor NF-κB and pro-inflammatory cytokines (TNF-α, interleukin IL-6 and IL-1β) are altered in both blood and tissue expression (27, 28). Study by Alburgaiba et al. showed patients with HNC had a significant increase in salivary TNF-α and IL-6 levels, after completing radiation (29). This study demonstrates that the salivary TNF-α and IL-6 levels are much lower after chemoradiotherapy compared to before, and that the severity of OM is reduced when curcumin oral gel is used, which is in accordance with Sufiawati et al. study indicated that cancer patients receiving chemotherapy induced oral mucositis may benefit from using a magic mouthwash containing curcuma xanthorrhiza, as it dramatically reduced salivary TNF-α levels (30). Curcumin may be able to suppress NF-κB, according to Aggarwal et al. reported that curcumin inhibits the expression of several genes controlled by nuclear factor (NF-κB)

(31). These include nitric oxide synthase (NOS), chemokines, cell surface adhesion molecules, TNF, IL-6, matrix metalloproteinase-9, and cyclooxygenase-2. The anti-inflammatory actions of curcumin are explained by lowering the expression of these genes, which are essential regulators of inflammation (32, 33). Also, in this study the majority of participants using curcumin experienced only mild mucositis grade1 at the end of the chemoradiotherapy sessions; a few had grades 2 but none had severe mucositis (grades 3 and 4) whereas patients in magic solution group experienced grade 2 and grade 3 mucositis. These findings are in agreement with those of Alsalim et al.,2024 reported that after the completion of radiation treatments, most patients treated with curcumin had no mucositis (grade 0), mild

mucositis (grades 1 and 2) occurred in a few of individuals in this group, but severe mucositis (grades 3 and 4) did not (34). And results are consistent with those of the Shah study shown that grade 3 mucositis did not occur in the curcumin group, unlike the control group (1). In addition, Patil's research demonstrated significantly difference between two groups in WHO grades (33). When it comes to reducing the severity of chemoradiotherapy-induced oral mucositis in HNC patients, curcuma long a gel outperformed both chlorhexidine gel (17) and placebo gel (16). Also, results are coincided with the study done by Arun et al., 2020 that the majority of patients in the curcumin group experienced only grade 1 mucositis after four weeks of treatment (35).

Conclusions

Using topical curcumin oral gel compared to magic solution significantly reduced levels of TNF-α and IL-6 in saliva from patients with HNC undergoing concurrent chemoradiotherapy, suggesting that it effectively prevents and manages oral mucositis caused by concurrent chemoradiation, and could be used as an alternative treatment for this condition.

Recommendations

It was recommended that head and neck cancer patients use curcumin oral gel as a preventive agent

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for chemoradiation-induced oral mucositis before concurrent chemoradiotherapy. In addition, a multicenter study is essential to achieve a sufficient sample size and increase the likelihood of obtaining reliable evidence for evaluating biomarkers that assist in treating mucositis. Furthermore, it was recommended that each oncology center should establish a dental unit staffed by highly trained dentists to provide adequate care for patients with oral mucositis and other dental-related disorders during cancer therapy.

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Ethical clearance: Approved by a protocol number 934724 by the Research Ethics Committee of the University of Baghdad, College of Dentistry.

Conflict of interest: None

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References

1. Shah S, Rath H, Sharma G, Senapati SN, Mishra E. Effectiveness of curcumin mouthwash on radiation-induced oral mucositis among head and neck cancer patients: A triple-blind, pilot randomised controlled trial. Indian J Dent Res. 2020Sep-Oct;31(5):718-727. https://doi.org/10.4103/ijdr.IJDR_822_18

2. Liu Z, Smart JD, Pannala AS. Recent developments in formulation design for improving oral bioavailability of curcumin: A review. Journal of Drug Delivery Science and Technology. 2020;60:102082. https://doi.org/10.1016/j.jddst.2020.102082

3. Jagiełło K, Uchańska O, Matyja K, Jackowski M, Wiatrak B, Kubasiewicz-Ross P, et al. Supporting the Wound Healing Process-Curcumin, Resveratrol and Baicalin in In Vitro Wound Healing Studies. Pharmaceuticals (Basel). 2023 Jan6;16(1):82. https://doi.org/10.3390/ph16010082

4. Jaafar NS, Jaafar IS. Natural Products as A Promising Therapy for SARS COV-2; An Overview. Iraqi J Pharm Sci. 2021;30(1):29-40. https://doi.org/10.31351/vol30iss1pp29-40

5. Ghani BA. Histological evaluation of the effect of topical application of Curcumin powder and essential oil on skin wound healing. Journal of Baghdad College of Dentistry. 2015;27(3):58-63. https://jbcd.uobaghdad.edu.iq/index.php/jbcd/article/view/807

6. Shamash MSA, Zaidan TF. Effect of topical curcumin on the healing of major oral mucosal ulceration. EurAsian Journal of BioSciences. 2020;14(2):4653-4660.

7. Ramezani V, Ghadirian S, Shabani M, Boroumand MA, Daneshvar R, Saghafi F. Efficacy of curcumin for amelioration of radiotherapy-induced oral mucositis: a preliminary randomized controlled clinical trial. BMC Cancer. 2023 Apr 17;23(1):354. https://doi.org/10.1186/s12885-023-10730-8

8. Idan HM, Motib AS. Incidence of head and neck cancer among Baquba Teaching Hospital Patients. Diyala Journal of Medicine. 2024 Oct 25;27(1):86-96. https://doi.org/10.26505/djm.v27i1.1144

9. Du C, Ying H, Zhou J, Hu C, Zhang Y. Experience with combination of docetaxel, cisplatin plus 5-fluorouracil chemotherapy, and intensity-modulated radiotherapy for locoregionally advanced nasopharyngeal carcinoma. International Journal of Clinical Oncology.2013;18:464–71. https://doi.org/10.1007/s10147-012-0403-y

10. Baydar M, Dikilitas M, Sevinc A, Aydogdu I. Prevention of Oral Mucositis Due to 5-Fluorouracil Treatment with Oral Cryotherap. J Natl Med Assoc. 2005; 97(8): 1161–1164. https://pmc.ncbi.nlm.nih.gov/articles/PMC2575965/

11. Al-Ansari S, Zecha J a. EM, Barasch A, de Lange J, Rozema FR, Raber-Durlacher JE. Oral

ORIGINAL RESEARCH
Published: 25 April 2025
DOI: 10.26505/djm.v28i1.1211

Mucositis Induced By Anticancer Therapies. Curr Oral Heal Reports. 2015; 2(4):202–211. https://doi.org/10.1007/s40496-015-0069-4

12. Muhammad RT, Alzubaidee AF. Oral complications of cancer medication in hemato-oncologic patients. Diyala Journal of Medicine. 2020 Dec.

13. Sonis ST. The pathobiology of mucositis. Nat Rev Cancer. 2004; 4(4): 277–84. https://doi.org/10.1038/nrc1318

14. Ben Salem M, Affes H, Athmouni K, Ksouda K, Dhouibi R, Sahnoun Z, Hammami S, Zeghal KM. Chemicals Compositions, Antioxidant and Anti-Inflammatory Activity of Cynara scolymus Leaves Extracts, and Analysis of Major Bioactive Polyphenols by HPLC. Evidence-based Complement Altern Med. 2017; 2017. https://doi.org/10.1155/2017/4951937

15. Zhang L, Tang G, Wei Z. Prophylactic and Therapeutic Effects of Curcumin on Treatment- Induced Oral Mucositis in Patients with Head and Neck Cancer: A Meta-Analysis of Randomized Controlled Trials. Nutr Cancer. 2021; 73(5): 740-749. https://doi.org/10.1080/01635581.2020.1776884

16. Charantimath S. Use of curcumin in radiochemotherapy induced oral mucositis patients: A control trial study. International Journal of Medical and Health Sciences. 2016; 10(3): 147-52. https://pubmed.ncbi.nlm.nih.gov/26436049/

17. Mansourian A, Amanlou M, Shirazian S, Moosavian JZ, Amirian A. The effect of “Curcuma Longa” topical gel on radiation-induced oral mucositis in patients with head and neck cancer. Int J Radiat Res. 2015;13(3):269-74. https://doi.org/10.5339/jemtac.2024.uncidc.4

18. Hussein, A.A., Motib, A.S., & Hadi, L.M. "Evaluation of ELISA and HBsAg Rapid Test Cassette Assay in Detection of Hepatitis B Virus." Journal of Pharmaceutical Sciences and Research 10.12 (2018): 3157.

19. Budi HS, Anitasari S, Ulfa NM, Juliastuti WS, Aljunaid M, Ramadan DE, Muzari K, Shen YK. Topical Medicine Potency of Musa paradisiaca var. sapientum (L.) kuntze as Oral Gel for Wound Healing: An In Vitro, In Vivo Study. Eur J Dent. 2022 Oct;16(4):848-855. https://doi.org/10.1055/s-0041-1740226

20. Trucci VM, Veeck EB, Morosolli AR. Current strategies for the management of oral mucositis induced by radiotherapy or chemotherapy. Rev Odonto Cienc. 2009;24(3):309–314. https://revistaseletronicas.pucrs.br/fo/article/view/4854

21. Sultani M, Stringer AM, Bowen JM, Gibson RJ. Anti-Inflammatory Cytokines: Important Immunoregulatory Factors Contributing to Chemotherapy-Induced Gastrointestinal Mucositis. Chemother Res Pract.2012;2012:1–11. https://doi.org/10.1155/2012/490804

22. Lalla R V., Sonis ST, Peterson DE. Management of Oral Mucositis in Patients with Cancer. Dent Clin North Am. 2008; 52(1):1–17. https://doi.org/10.1016/j.cden.2007.10.002

23. Bradley J. TNF-mediated inflammatory disease. J Pathol. 2008; 214: 149–160. https://doi.org/10.1002/path.2287

24. Aggarwal BB, Kohr WJ, Hass PE, Moffat B, Spencer SA, Henzel WJ, et al. Human tumor necrosis factor. Production, purification, and characterization. J Biol Chem. 1985; 260(4): 2345–2354. https://pubmed.ncbi.nlm.nih.gov/3871770/

25. Deepthi G, S R K Nandan, Pavan G Kulkarni. Salivary Tumour Necrosis Factor-α as a Biomarker in Oral Leukoplakia and Oral Squamous Cell Carcinoma. Asian Pac J Cancer Prev. 2019;20(7):2087-2093. Published 2019 Jul 1. https://pubmed.ncbi.nlm.nih.gov/31350970/

26. Rincon M. Interleukin-6: from an inflammatory marker to a target for inflammatory diseases. Trends Immunol 2012: 33: 571-577.

ORIGINAL RESEARCH
Published: 25 April 2025
DOI: 10.26505/djm.v28i1.1211

https://doi.org/10.1016/j.it.2012.07.003

27. Sakamoto K, Takeda S, Kanekiyo S, Nishiyama M, Kitahara M, Ueno T, Yamamoto S, Yoshino S, Hazama S, Okayama N, Nagano H. Association of tumor necrosis factor-α polymorphism with chemotherapy-induced oral mucositis in patients with esophageal cancer. Mol Clin Oncol. 2017;6(1):125–129. https://doi.org/10.3892/mco.2016.1081

28. Steer JH, Kroeger KM, Abraham LJ, Joyce DA. Glucocorticoids Suppress Tumor Necrosis Factor-Alpha Expression By Human Monocytic THP-1 Cells By Suppressing Transactivation Through Adjacent NF-κB And C-Jun-Activating Transcription Factor- 2 Binding Sites İn The Promoter. J Biol Chem. 2000;275(24):18432–18440.

https://doi.org/10.1074/jbc.m906304199

29. Mohammed H. Alburgaiba, Fawaz D. Al-Aswad, Haider N. Salh. Salivary tumor necrosis factor-α and interleukin-6 in patients with head and neck cancer before and after radiotherapy. SRP. (2019), [cited March 29, 2021]; 10(1): 146-150. https://dx.doi.org/10.5530/srp.2019.1.27

30. Sufiawati Irna, Indra Gunawan, Indra Wijaya, Taofik Rusdiana and Anas Subarnas. “Reduction of salivary tumor necrosis factor alpha levels in response to magic mouthwash with Curcuma xanthorriza in cancer patients undergoing chemotherapy.” Journal of Research in Pharmacy (2018): n. pag. https://doi.org/10.12991/jrp.2018.00

31. Aggarwal BB. Anticancer Potential Of Curcumin: preclinical and clinical studies. Anticancer Res. 2003; 23(1A): 363– 398. https://pubmed.ncbi.nlm.nih.gov/12680238/

32. van’t Land B, Blijlevens NM a, Marteijn J, Timal S, Donnelly JP, de Witte TJ,
M'Rabet L. Role of curcumin and the inhibition of TNF-kappaB in the onset of chemotherapy-induced mucosal barrier injury. Leukemia. 2004;18(2):

http://dx.doi.org/10.1177/09636897221086969

33. Patil K, Guledgud MV, Kulkarni PK, Keshari D, Tayal S. Use of Curcumin Mouthrinse in Radio-Chemotherapy Induced Oral Mucositis Patients: A Pilot Study. J Clin Diagn Res. 2015;9(8): ZC59–ZC62. https://doi.org/10.7860/JCDR/2015/13034.6345

34. Alsalim SA, Diajil AR. The effect of curcumin oral gel on radiation- induced oral mucositis in relation to salivary epidermal growth factor. Journal of Emergency Medicine, Trauma & Acute Care. 2024(2):4 http://dx.doi.org/10.5339/jemtac.2024.uncidc.4

35. Arun P, Sagayaraj A, Azeem Mohiyuddin SM, Santosh D. Role of turmeric extract in minimising mucositis in patients receiving radiotherapy for head and neck squamous cell cancer: a randomised, placebo-controlled trial. J Laryngol Otol. Published online February 7, 2020. https://doi.org/10.1017/s0022215120000316

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جل الكركمين الفموي وعلاقته بعامل نخر الورم اللعابي ألفا وإنترلوكين ٦ المستخدم في علاج التهاب الغشاء المخاطي الفموي لدى مرضى سرطان الرأس والرقبة الذين يخضعون للعلاج الكيميائي الإشعاعي المتزامن

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الملخص

الخلفية: يُعد هلام الكركمين الفموي أحد الأمثلة على الأدوية العشبية التقليدية، وقد أظهر إمكانات في العديد من الاستخدامات الصيدلانية. التهاب الغشاء المخاطي للفم عادة ما يمنع ويعالج باستخدام المحلول السحري ، وهو غسول للفم يحتوي على مزيج من الأدوية. عامل نخر الورم ألفا والإنترلوكين-٦، هما سايتوكينات لعابية، تحفز الاستجابة المناعية وتعزز الالتهاب أثناء العدوى أو تلف الأنسجة الأخرى الذي يسبب الالتهاب

الأهداف: تحديد تأثير هلام الكركمين الفموي على مستويات عامل نخر الورم ألفا والإنترلوكين-٦ في اللعاب لدى مرضى سرطان الرأس والرقبة الذين يتلقون العلاج الكيميائي الإشعاعي المتزامن الناجم عنه التهاب الغشاء المخاطي الفموي.

المرضى والطرق: أجريت الدراسة على مجموعتين، كل مجموعة تضم خمسة وأربعين مريضًا، بإجمالي تسعين مريضًا بسرطان الرأس والرقبة يتلقون العلاج الكيميائي الإشعاعي المتزامن. مقايسة الممتز المناعي المرتبط بالإنزيم قاس مستويات عامل نخر الورم ألفا والإنترلوكين-٦ في اللعاب. قُيّم التهاب الغشاء المخاطي الفموي وفقًا لمقياس منظمة الصحة العالمية.

النتائج: أظهر المرضى الذين تناولوا جل الكركمين الفموي التهابًا أقل حدة في الغشاء المخاطي الفموي، ومستويات أقل من عامل نخر الورم ألفا والإنترلوكين-٦ في اللعاب. أظهر مقياس منظمة الصحة العالمية بين المجموعتين اختلافات كبيرة عند أسبوعين **(P = 0.041)** و ٦ أسابيع **(P = 0.02)**.

الاستنتاج: خلصت الدراسة إلى أن جل الكركمين الفموي قد يخفض مستويات عامل نخر الورم ألفا والإنترلوكين-٦ في اللعاب، وقد يُستخدم كعلاج بديل لالتهاب الغشاء المخاطي الفموي الناتج عن العلاج الكيميائي والإشعاعي.

الكلمات المفتاحية: سرطان الرأس والرقبة، العلاج الكيميائي والإشعاعي المتزامن، التهاب الغشاء المخاطي الفموي، الكركمين، عامل نخر الورم ألفا، الإنترلوكين-٦.

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