

## Review Article

# Therapeutic potency of curcumin on radiodermatitis: A systematic review

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### Abstract

**Objective:** Radiodermatitis (RD) is a frequent adverse event of radiotherapy (RT). Currently, there is no consensus and approved protocol for the treatment of RD. Curcumin (CUR) is a natural polyphenol obtained from turmeric and it has low intrinsic toxicity in humans. The aim of this systematic review was to explore the efficacy of CUR for prevention and treatment of RD.

**Materials and Methods:** A systematic literature review was performed in the following online databases: Cochrane library, PubMed, Scopus, Web of Science, MEDLINE, and EMBASE. Among the 5 selected records, 3 had a randomized clinical trial (RCT)-design and the other had a pilot and controlled study designed. The included studies were performed on breast cancer (N=3), head and neck cancers (N=1) and different types of cancer (N=1).

**Results:** Four of the studies reported that the application of curcumin in cancer patients undergoing radiotherapy is associated with decreased intensity of radiodermatitis. However, one study did not report any significant effect of CUR on radiodermatitis. This review provides substantial evidence which confirm the clinical value of CUR in cancer supportive care.

**Conclusion:** Further prospective clinical trials in larger scales are warranted in order to determine the " supplemental form and dose of CUR" for RD prevention and treatment in patients receiving radiotherapy.

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## Introduction

Radiodermatitis (RD) is a frequent adverse event of radiotherapy (RT) (Ryan *et al.*, 2013). RD results from damage to DNA, and modifications in the structure of proteins, lipids, or carbohydrates. Accumulation of these changes leads to injury and destruction of epidermal basal cells (Zhang *et al.*, 2013). The clinical presentations of RD include a wide range including erythema, xeroderma, hyperhidrosis, dyspigmentation, telangiectasias, hair loss, deep ulcers, fibrosis and necrosis (McQuestion, 2006). Acute RD influences the quality of life. In patients with severe forms of RD, unplanned gaps may occur during treatment and interfere with treatment plan (Bataini *et al.*, 1988).

Management of severe forms of RD is very vital in cancer patients requiring curative radiotherapy. Currently, there is no consensus and approved protocol for the treatment of RD except using lukewarm water and lenient soap (Campbell and Illingworth, 1992; Roy *et al.*, 2001; Lavery, 1995). Recently, moisturizing creams, anti-inflammatory agents, silymarin, *Aloe vera* gel, marigold, and curcumin (CUR) have been investigated for their therapeutic potencies. Results of previous studies suggest these agents as palliative treatment of RD (Falkowski *et al.*, 2011; Heggie *et al.*, 2002; Pommier *et al.*, 2004).

Considerable efforts have been performed to investigate the efficiency of topical compounds in the treatment of RD (Tables 1 and 2). Results of a meta-analysis study that performed in 2013 demonstrated the therapeutic and prophylactic efficacy of several agents such as corticosteroids trolamine, gentian violet, sucralfate, *Aloe vera*, biafine, urea, mixture of oil and aqueous, vitamin C, and hyaluronic acid on treatment of radiodermatitis (Zhang *et al.*, 2013).

CUR (1,7-bis(4-hydroxy-3-methoxyphenyl)1,6-heptadiene-3,5-dione) is a natural polyphenol obtained from

turmeric (*Curcuma longa* L.), with low intrinsic toxicity in humans (Hosseini *et al.*, 2017). CUR is known for its antimicrobial, anti-cancer, anti-inflammatory, and chemotherapeutic properties (Tajbakhsh *et al.*, 2017; Sahebkar, 2014; Shafiee *et al.*, 2017; Najafi *et al.*, 2015; Arshami *et al.*, 2013; Amini *et al.*, 2023). Interestingly, CUR is able to suppress enzymes mediating the production of reactive oxygen species (ROS), inflammatory lipids, pro-inflammatory transcription factors, at both protein and gene levels and upregulates the expression level of anti-oxidant enzymes (Ryan *et al.*, 2013).

CUR inhibits amyloid fibril formation. Due to this property, CUR is utilized for the treatment of common skin diseases including eczema, acne, and skin crease. Also, a number of experimental studies have approved its prophylactic role in UV-induced skin tumorigenesis (Dwivedi and Abu-Ghazaleh, 1997; Dwivedi *et al.*, 2003; Dwivedi *et al.*, 2005). However, the therapeutic properties of CUR in humans is still inconsistent and without a general agreement (Palatty *et al.*, 2014; Wolf *et al.*, 2017).

This study aims to explore the efficacy of CUR for prevention and treatment of RD by searching for evidence through a systematic review. Considering the multi-functional and strategic role of CUR in reduction of inflammation and oxidation, utilizing this agent in RD treatment may improve clinical management and patient-related outcomes.

## Materials and Methods

### Search strategy and study selection

We employed multiple databases to find literature on the effect of purified CUR or curcumin-containing mixtures or standardized *Curcuma spp.* extracts on RD. Human interventional studies which investigated radiation dermatitis severity or intensity in both intervention and comparator groups at basal level and the

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end of intervention, were eligible for inclusion.

The systematic literature review restricted to English language was performed in the following online data bases: Cochrane library, PubMed, Scopus, Web of Science, MEDLINE, and EMBASE. The following keywords were applied for the search: 'curcumin', 'curcuma', 'turmeric', 'curcuma domestica', 'Curcuma longa L', 'radiotherapy', 'dermatitis', 'radiodermatitis' and 'radiation dermatitis'. Figure 1 shows the summary of systematic search with details. Also, a manual search through the reference lists of the included articles and relevant papers was performed. The articles with irrelevant titles, review papers, conference abstracts, case reports, and experimental studies were excluded. Screening and selection of articles to be entered in the systematic review were independently performed by 2 expert reviewers. Discrepancies in the included papers were resolved by discussion with supervisors.

### Data extraction

Our favorable outcomes were Radiation Dermatitis Severity (RDS), signs of skin damage, and the incidence of side effects. The following information was retrieved from the included studies: year of publication, country, type of study, type of cancer, mean dose of radiation, number of patients, age, dose and duration of treatment with CUR. Furthermore, mean±SD of RD manifestation degree (RDS score or incidence and number of side effects) at basal time and at the end of intervention were gathered.

## Results

### Literature review

A total of 438 papers were recognized. About 91% of these papers were omitted after deleting duplicates and screening of the titles and abstracts. After reviewing the full text of the remaining articles, five articles were obtained for analysis (Figure 1).

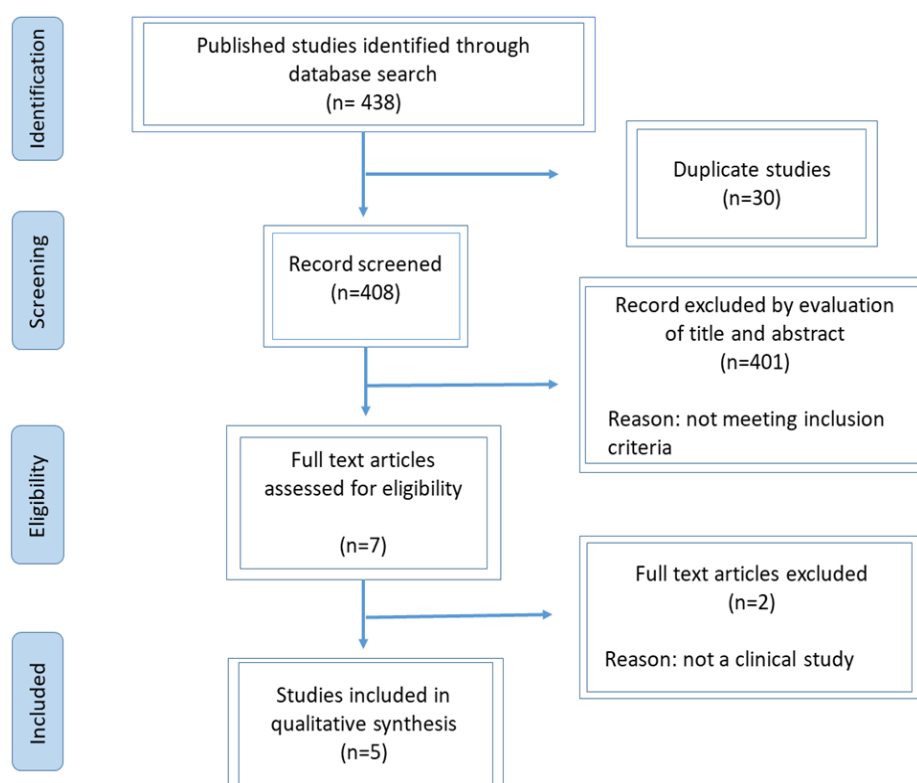


Figure 1. Flowchart of literature search and selection process

Among the 5 selected records, 3 had a randomized clinical trial (RCT)-design (Ryan *et al.*, 2013; Rao *et al.*, 2017; Wolf *et al.*, 2017) and two others had a pilot and controlled study design (Palatty *et al.*, 2014; Belcaro *et al.*, 2014). Three studies were conducted among breast cancer patients (Ryan *et al.*, 2013; Rao *et al.*, 2017; Wolf *et al.*, 2017), one study examined head and neck cancer patients (Palatty *et al.*, 2014), and the other one was conducted on different cancers (Belcaro *et al.*, 2014).

Duration of treatment among the studies ranged between 5 to 7 weeks. There was a wide spectrum of radiation doses (30-66 Gy). Only one study used purified CUR for supplementation (Ryan *et al.*, 2013). Two studies utilized curcuminoids (containing CUR, demethoxy CUR, and bisdemethoxy CUR) (Belcaro *et al.*, 2014; Wolf *et al.*, 2017) and the remaining two studies utilized Vicco turmeric cream (VTC), containing turmeric and sandal wood oil (*Santalum album* L) (Palatty *et al.*, 2014; Rao *et al.*, 2017). Three articles administered placebo (Ryan *et al.*, 2013; Belcaro *et al.*, 2014; Wolf *et al.*, 2017). In two studies moisturizing cream or Johnsons Baby Oil (JBO) (Palatty *et al.*, 2014; Rao *et al.*, 2017) were prescribed as the comparator group.

Results of Rao and colleagues showed that the usage of CUR-based cream among breast cancer patients led to delay and mitigation in radiodermatitis (Rao *et al.*, 2017). In line with this, Palatty *et al.* (Palatty *et al.*, 2014) and Ryan *et al.* (Ryan *et al.*, 2013) found that CUR reduced the intensity of RD. In contrast with this, Wolf and colleagues showed that CUR could not reduce RD severity (Ryan Wolf *et al.*, 2018). Belcaro and colleagues reported that CUR could successfully reduced the radiotherapy-related side effects in different types of cancer (Belcaro *et al.*, 2014).

## Discussion

Finding from the current systematic review could provide evidence of the beneficial effect of CUR on the improvement of RD in cancer patients receiving RT. Consistently, preclinical and experimental studies have shown that CUR supplementation therapy was associated with improved outcomes in the treatment of ulcer, dermatitis and papilloma formation in mice with radiation exposure. The pathogenesis of RD includes production of ROS and damage to DNA (Stone *et al.*, 2003; Schaeue *et al.*, 2012). CUR increases the expression of enzymes like catalase, superoxide dismutase, glutathione transferase, and glutathione-peroxidase, at both protein and mRNAs levels. A great body of evidence has indicated that CUR can scavenge reactive oxygen and nitrogen species (Baliga *et al.*, 2013; Gupta *et al.*, 2013; Najafi *et al.*, 2015). Also, results obtained from *in vivo* and *in vitro* studies supported CUR's antioxidant functions and its critical role in prevention of lipid peroxidation and DNA degradation (Jelveh *et al.*, 2013; Parshad *et al.*, 1998; Ghasemi *et al.*, 2022). CUR enhanced the repair and regeneration of wounds and re-epithelialization of the epidermis, decreased mean healing duration, increased neovascularization, and upregulated production and deposition of collagen at the injury site (López-Jornet *et al.*, 2011; Jagetia and Rajanikant, 2004; Jagetia and Rajanikant, 2005).

Moreover, CUR has shown significant anti-inflammatory effects in cutaneous tissues (Huang *et al.*, 1997). According to the literature, CUR inhibits ornithine decarboxylase responses, DNA synthesis, epidermal lipoxygenase and cyclooxygenase (COX) activity, and activation of inflammatory pathways including extracellular signal-related kinase (ERK) and nuclear factor kB (NF-kB) signaling pathways in stimulated cells (Chun *et al.*, 2003; Baliga *et al.*, 2013; Thangapazham *et al.*, 2013; Gupta *et al.*, 2013; Ghasemi *et al.*, 2022; Shojaei *et al.*,

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2023). Furthermore, CUR significantly downregulates both acute and chronic skin inflammatory reactions and induces protective effects by decreasing early-releasing cytokines and interleukins including tissue necrosis factor- $\alpha$  (TNF- $\alpha$ ), lymphotoxin- $\beta$ , transforming growth factor beta (TGF- $\beta$ ), hypoxia-inducible growth factor-1 $\alpha$ , transcription factor Egr-1(Egr-1), stromal cell-derived growth factor-1 $\alpha$ , and hemeoxygenase-1 in epidermis (Okunieff et al., 2006). Previous studies demonstrated that CUR suppresses

the induction of immediate early response genes in endothelial cells fibroblasts (Pendurthi and Rao, 2000; Chen et al., 2006).

The current systematic review has several limitations. There were few eligible records, and most had small sample sizes (<40 subjects). In spite of small number of patients in the included studies, the ongoing trials (Table 1), have recruited large number of patients which may produce more reliable results.

Table 1. A review of clinical trials investigating therapeutic role of curcumin in radiodermatitis

Study (Year)	Registration number	Phase	Subjects enrolled	Type of cancer	Location	Follow up period	Status
Morrow (2015)	NCT02556632	II	191	Non-inflammatory breast cancer	University of Rochester	1 week	Completed
Ryan (2010)	NCT01246973	II	686	Breast cancer	University of Rochester	6 weeks	Completed
Heydari (2019)	IRCT20181208041882N3	III	52	Breast cancer	Yazd University of Medical Sciences	4 weeks	Ongoing

Table 2. Characteristics of included studies

Author, year	Ryan 2013 (Ryan et al. 2013)		Palatty 2018 (Palatty et al. 2014)		Stone 2003 (Belcaro et al. 2014)		Ryan wolf 2018 (Rao et al. 2017)		Wolf 2017 (Wolf et al. 2017)	
Country	USA		India		Italy		India		USA	
Design	Double Blind RCT		Pilot		Controlled study		Investigator-blinded RCT		Double-blinded RCT	
Duration of trial	7 weeks		7 weeks		60 days		5 weeks		During course of RT until one-week post RT	
Type of cancer	Breast		Head/Neck		All types		Breast		Breast	
Intervention	Case	Curcumin (2.0 grams, 3 times daily)	Case	VTC (2 g, 5 times daily)	Case	Curcuminoids (100 mg, 3 times daily)	Case	VTC (5 gr, 5 times daily)	Case	Curcuminoids (500 mg, 3 times daily)
	Control	Placebo	Control	Moisturizing cream, JBO (2 ml, daily)	Control	Placebo	Control	Moisturizing cream, JBO (5ml, 5 times daily)	Control	Placebo
Sample size	case	14	case	22	case	40	case	20	case	283
	control	16	control	24	control	40	control	20	control	295
Age (year)	58.1 $\pm$ 2.2		56.9 $\pm$ 7.21		55.8 $\pm$ 3.3		50.93 $\pm$ 9.52		57.6 $\pm$ 0.4	
Race	White/Caucasian, Black/African American, Multiracial		NR		NR		NR		White/Caucasian, Black/African American, Multiracial	
Administration route	Oral		Topical		Oral		Topical		Oral	
Mean radiation dose (Gy)	46.51 $\pm$ 3.48		66.0 $\pm$ 5.70		30-50		50		48.34 $\pm$ 0.14	
Assessed measurements	RDS score		Signs of skin damage		The incidence of side effects		Dermatological analysis based on the criteria of (RTOG/EORTC)		RDS score	

Abbreviations: RT (radiation therapy), JBO (Johnsons Baby Oil), VTC (Vicco Turmeric Cream), RDS (Radiation Dermatitis Severity), RTOG/EORTC (Radiation Therapy Oncology Group/ European Organization for Research and Treatment Cancer), NR (Not reported).

Furthermore, there were significant variations among the included studies in terms of study type, demographic characteristics, tumor types, mean radiation dose, supplement form, dose, and duration. However, evaluation of the therapeutic potential of CUR in healing dermatitis following radiation therapy in patients with breast cancer is an issue that has received much attention. The majority of the published data and ongoing trials are focused on this topic. Regarding the considerable number of breast cancer patients, the effect of CUR on RD in these patients may present valuable findings.

The included clinical trials did not mention CUR dose, which can be considered as an important limitation of this study can be since the “effective dose” of CUR for severe RD is not identifiable. However, the 6.0 g daily dose of CUR certainly reduced the rate of adverse reactions and detection of circulating CUR. Although 6.0 g of CUR is an accepted and routine dose, it is plausible that a megadose of CUR (up to 8 grams daily), may act more efficiently against RD severity. None of the selected studies administrated bioavailability-improved formulations of CUR, except one study in which CUR was co-administered with lecithin as an absorption enhancer (Belcaro *et al.*, 2014). One major problem of CUR, is its miserably low oral bioavailability, particularly from non-dietary pharmaceutical complexes, with the need to increase its concentration in patients. Therefore, the development of better formulations of CUR could have an exciting effect on compliance, making it easy to systematically evaluate the clinical importance of this compound in cancer best supportive care.

In conclusion, our systematic review of the evidence of eligible studies presented that CUR supplementation has significant beneficial effects on RD severity. This review provides substantial evidence confirming the clinical value of CUR in cancer supportive care. Further prospective

clinical trials in larger scales are warranted in order to determine the "real effective extract, supplemental form and dose of CUR" for RD prevention and treatment in patients receiving radiotherapy.

### Conflicts of interest

The authors have declared that there is no conflict of interest.

### References

- Amini S, Sahebkar A, Dehghani A, Iraj B, Rezaeian-Ramsheh A, Askari G, Majeed M, Bagherniya M. 2023. The effect of curcumin-piperine on cardiometabolic, inflammatory and oxidative stress factors and macular vascular density in optical coherence tomography angiography (OCTA) in patients with non-proliferative diabetic retinopathy: Study protocol for a randomized, double-blind controlled trial. *Avicenna J Phytomed*, 13: 153-164.
- Arshami J, Pilevar M, Aami Azghadi M, Raji AR. 2013. Hypolipidemic and antioxidative effects of curcumin on blood parameters, humoral immunity, and jejunum histology in Hy-line hens. *Avicenna J Phytomed*, 3: 178-185.
- Baliga S, Venkatesh S, Mrinal S, Bala N, Palatty PL. 2013. Turmeric (*Curcuma longa* L.) the Indian Golden Curry Spice as a Skin Care Agent: Validation of the Traditional Uses. In: *Bioactive Dietary Factors and Plant Extracts in Dermatology*, pp.93-102, Springer.
- Bataini JP, Bernier J, Asselain B, Lave C, Jaulerry C, Brunin F, Pontvert D. 1988. Primary radiotherapy of squamous cell carcinoma of the oropharynx and pharyngolarynx: tentative multivariate modelling system to predict the radiocurability of neck nodes. *Int J Radiat Oncol Biol Phys*, 14: 635-642.
- Belcaro G, Hosoi M, Pellegrini M, Appendino G, Ippolito E, Ricci A, Ledda A, Dugall M, Cesarone MR, Maione C. 2014. A controlled study of a lecithinized delivery system of curcumin (Meriva®) to alleviate the adverse effects of cancer treatment. *Phytother Res*, 28: 444-450.
- Campbell IR, Illingworth MH. 1992. Can patients wash during radiotherapy to the

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- breast or chest wall? A randomized controlled trial. *J Clin Oncol*, 4: 78-82.
- Chen A, J Xu, Johnson AC. 2006. Curcumin inhibits human colon cancer cell growth by suppressing gene expression of epidermal growth factor receptor through reducing the activity of the transcription factor Egr-1. *Oncogene*, 25: 278-287.
- Chun KS, Keum YS, Han SS, Song YS, Kim S H, Surh YJ. 2003. Curcumin inhibits phorbol ester-induced expression of cyclooxygenase-2 in mouse skin through suppression of extracellular signal-regulated kinase activity and NF- $\kappa$ B activation. *J Carcinog*, 24: 1515-1524.
- Dwivedi C, Abu-Ghazaleh A. 1997. Chemopreventive effects of sandalwood oil on skin papillomas in mice. *Eur J Cancer*, 6: 399-401.
- Dwivedi C, Guann X, Harmsen WL, Voss A L, Goetz-Parten DE, Koopman EM, Johnson KM, Valluri HB, Matthees DP. 2003. Chemopreventive effects of  $\alpha$ -santalol on skin tumor development in CD-1 and SENCAR mice. *Cancer Epidemiol Biomarkers Prev*, 12: 151-156.
- Dwivedi C, Maydew ER, Hora JJ, Ramaeker DM, Guan X. 2005. Chemopreventive effects of various concentrations of  $\alpha$ -santalol on skin cancer development in CD-1 mice. *Eur J Cancer*, 14: 473-476.
- Falkowski S, Trouillas P, Duroux JL, Bonnetblanc JM, Clavère P. 2011. Radiodermatitis prevention with sucralfate in breast cancer: fundamental and clinical studies. *Support Care Cancer*, 19: 57-65.
- Ghasemi SZ, Memarzia A, Behrouz S, Gholamnezhad Z, Boskabady MH. 2022. Comparative effects of Curcuma longa and curcumin on paraquat-induced systemic and lung oxidative stress and inflammation in rats. *Avicenna J Phytomed*, 12: 414-424.
- Gupta SC, Patchva S, Aggarwal BB. 2013. Therapeutic roles of curcumin: lessons learned from clinical trials. *AAPS J*, 15: 195-218.
- Heggie S, Bryant GP, Tripcony L, Keller J, Rose P, Glendenning M, Heath J. 2002. A phase III study on the efficacy of topical aloe vera gel on irradiated breast tissue. *Cancer Nurs.*, 25: 442-451.
- Hosseini M, Hassanian SM, Mohammadzadeh E, ShahidSales S, Maftouh M, Fayazbakhsh H, Khazaei M, Avan A. 2017. Therapeutic potential of curcumin in treatment of pancreatic cancer: Current status and future perspectives. *J Cell Biochem*, 118: 1634-1638.
- Huang MT, Newmark HL, Frenkel K. 1997. Inhibitory effects of curcumin on tumorigenesis in mice. *J Cell Biochem*, 27: 26-34.
- Jagetia GC, 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: 127-138.
- Jagetia GC, Rajanikant GK. 2005. Curcumin treatment enhances the repair and regeneration of wounds in mice exposed to hemibody  $\gamma$ -irradiation. *Plast Reconstr Surg*, 115: 515-528.
- Jelveh S, Kaspler P, Bhogal N, Mahmood J, Lindsay PE, Okunieff P, Doctrow SR, Bristow RG, Hill RP. 2013. Investigations of antioxidant-mediated protection and mitigation of radiation-induced DNA damage and lipid peroxidation in murine skin. *Int J Radiat Biol*, 89: 618-627.
- Lavery BA. 1995. Skin care during radiotherapy: a survey of UK practice. *Clin Oncol*, 7: 184-187.
- López-Jornet P, Camacho-Alonso F, Jiménez-Torres MJ, Orduña-Domingo A, Gómez-García F. 2011. Topical curcumin for the healing of carbon dioxide laser skin wounds in mice. *Photomed Laser Surg*, 29: 809-814.
- McQuestion M. 2006. Evidence-based skin care management in radiation therapy. *Semin Oncol Nurs*, 22: 163-173.
- Najafi H, Changizi Ashtiyani S, Sayedzadeh SA, Mohammadi Y, Arijani Z, Fakhri S. 2015. Therapeutic effects of curcumin on the functional disturbances and oxidative stress induced by renal ischemia/reperfusion in rats. *Avicenna J Phytomed*, 5: 576-586.
- Okunieff P, Xu J, Hu D, Liu W, Zhang L, Morrow G, Pentland A, Ryan JL, Ding I. 2006. Curcumin protects against radiation-induced acute and chronic cutaneous toxicity in mice and decreases mRNA expression of inflammatory and fibrogenic cytokines. *Int J Radiat Oncol Biol Phys*, 65: 890-898.
- Palatty PL, Azmidah A, Rao S, Jayachander D, Thilakchand KR, Rai MP, Haniadka R, Simon P, Ravi R, Jimmy R. 2014. Topical

- application of a sandal wood oil and turmeric based cream prevents radiodermatitis in head and neck cancer patients undergoing external beam radiotherapy: a pilot study. *Brit J Radiol*, 87: 20130490.
- Parshad R, Sanford KK, Price FM, Steele VE, Tarone RE, Kelloff GJ, Boone CW. 1998. Protective action of plant polyphenols on radiation-induced chromatid breaks in cultured human cells. *Anticancer Res*, 18: 3263-3266.
- Pendurthi UR, Rao LV. 2000. Suppression of transcription factor Egr-1 by curcumin. *Thromb Res*, 97: 179-189.
- Pommier P, Gomez F, Sunyach MP, Dhombres A, Carrie C, Montbarbon X. 2004. Phase III randomized trial of *Calendula officinalis* compared with trolamine for the prevention of acute dermatitis during irradiation for breast cancer. *J Clin Oncol*, 22: 1447-1453.
- Rao S, Hegde SK, Baliga-Rao MP, Lobo J, Palatty PL, George T, Baliga MS. 2017. Sandalwood oil and turmeric-based cream prevents ionizing radiation-induced dermatitis in breast cancer patients: Clinical study. *Medicines (Basel)*, 4: 43.
- Roy I, Fortin A, Larochelle M. 2001. The impact of skin washing with water and soap during breast irradiation: a randomized study. *Radiat Oncol J*, 58: 333-339.
- Ryan JL, Heckler CE, Ling M, Katz A, Williams JP, Pentland AP, Morrow GR. 2013. Curcumin for radiation dermatitis: a randomized, double-blind, placebo-controlled clinical trial of thirty breast cancer patients. *Radiat Res*, 180: 34-43.
- Sahebkar A. 2014. A systematic review and meta-analysis of randomized controlled trials investigating the effects of curcumin on blood lipid levels. *Clin Nutr*, 33: 406-414.
- Schae D, Kachikwu EL, McBride WH. 2012. Cytokines in radiobiological responses: a review. *Radiat Res*, 178: 505-523.
- Shafiee M, Mohamadzade E, ShahidSales S, Khakpouri S, Maftouh M, Parizadeh SA, Hasanian SM, Avan A. 2017. Current status and perspectives regarding the therapeutic potential of targeting EGFR pathway by curcumin in lung cancer. *Curr Pharm*, 23: 2002-2008.
- Shojaei M, Sahebkar A, Khorvash F, Fallahpour S, Askari G, Bagherniya M. 2023. The effects of phytosomal curcumin supplementation on clinical symptoms, and inflammatory and oxidative stress biomarkers in patients with migraine: A protocol for a randomized double-blind placebo-controlled trial. *Avicenna J Phytomed*, 13: 45-57.
- Stone HB, Coleman CN, Anscher MS, McBride WH. 2003. Effects of radiation on normal tissue: consequences and mechanisms. *Lancet Oncol*, 4: 529-536.
- Tajbakhsh A, Hasanzadeh M, Rezaee M, Khedri M, Khazaei M, Shahid Sales S, Ferns GA, Hassanian SM, Avan A. 2017. Therapeutic potential of novel formulated forms of curcumin in the treatment of breast cancer by the targeting of cellular and physiological dysregulated pathways. *J Cell Physiol*, 3: 2183-2192.
- Thangapazham RL, Sharad S, Maheshwari R K. 2013. Skin regenerative potentials of curcumin. *Biofactors*, 39: 141-149.
- Wolf JR, Heckler CE, Guido JJ, Peoples AR, Gewandter JS, Ling M, Vinciguerra VP, Anderson T, Evans L, Wade J, Pentland A P, Morrow GR. 2017. Oral curcumin for radiation dermatitis: a URCC NCORP study of 686 breast cancer patients. *Support Care Cancer*, 26: 1543-1552.
- Wolf JR, Heckler CE, Guido JJ, Peoples AR, Gewandter JS, Ling M, Vinciguerra VP, Anderson T, Evans L, Wade J. 2018. Oral curcumin for radiation dermatitis: A URCC NCORP study of 686 breast cancer patients. *Support Care Cancer*, 26: 1543-1552.
- Zhang Y, Zhang S, Shao X. 2012. Topical agent therapy for prevention and treatment of radiodermatitis: a meta-analysis. *Support Care Cancer*, 21: 1025-1031.