International Journal of Science and Research (IJSR)
ISSN (Online): 2319-7064
Index Copernicus Value (2015): 78.96 | Impact Factor (2015): 6.391

Curcumin- Nature's Remedy for Oral Diseases

Chaya M David[1], Kanaparthi Alekhya[2], Mahesh D R[3], Soujanya LK[4], Garima[5], Raunaque Saba[6]

[1]Professor and HOD, Department of Oral Medicine and Radiology, Dayananda Sagar College of Dental Sciences, Bangalore-560078

[2]Postgraduate Student, Department of Oral Medicine and Radiology, Dayananda Sagar College of Dental Sciences, Bangalore-560078,

[3]Reader, Department of Oral Medicine and Radiology, Dayananda Sagar College of Dental Sciences, Bangalore-560078

[4]Postgraduate Student, Department of Oral Medicine and Radiology, Dayananda Sagar College of Dental Sciences, Bangalore-560078

[5]Postgraduate Student, Department of Oral Medicine and Radiology, Dayananda Sagar College of Dental Sciences, Bangalore-560078

[6]Postgraduate Student, Department of Oral Medicine and Radiology, Dayananda Sagar College of Dental Sciences, Bangalore-560078

Abstract: ***Turmeric is a spice, used in India and other Asian countries for centuries because of its medicinal properties.[1] It is derived from the roots of the plant Curcuma longa, which is a member of the Zingiberaceae family.[1-4] Curcumin, the principal Curcuminoids found in Turmeric, is generally considered as the most active constituent responsible for its therapeutic benefits. In addition to Curcumin, the turmeric is also composed of other Curcuminoids like demethoxycurcumin, bisdemethoxycurcumin and essential oils that have been responsible for the therapeutic effects.[1-3]Recent, evidences suggested that Curcumin has multiple mechanisms of actions like anti-inflammatory, antioxidant, antimicrobial and anticancer activities. This, lead to the renewed scientific interest in this ancient spice to prevent and treat various oral diseases including oral cancer.[1] The aim of this article is to review the pharmacological actions and therapeutic benefits of Curcumin in the treatment of oral diseases.***

Keywords: Curcumin, Curcuminoids, Oral diseases, anti inflammatory, antioxidant

1. Introduction

Nature has gifted mankind with various natural plant resources; many of these natural products derived from plants have played a pivotal role in the health care both in ancient and modern society. Though the mechanisms of action of traditional medicines are shrouded in mystery; man has relied upon them for their medicinal values and beneficial effects for the treatment of various ailments. Great Healers, in one form or another are sought out by us as a part of our daily diet .One such regularly used culinary spice in the house hold eaten throughout Asia as a food both in raw and cooked forms is Turmeric. Curcumin is derived from the rhizome (underground stem), and is an active component of plant Curcuma longa.[1]

Ever since its historical discovery, Curcumin has assayed an extremely crucial role. It was used in ancient Indian medicine for the treatment of illnesses due to its antiseptic, antifungal, anti-inflammatory and antioxidant properties. [1,2]A need for a newer, safer, cheaper and effective therapy to enhance people's health made a way for this natural medicinal spice with innumerable healing properties into modern medicine. This review is an attempt to provide a much deeper understanding of Curcumin and its therapeutic potentials for various oral diseases.

2. History of Curcumin

Curcumin is considered as one of the most beneficial compounds due to its medicinal properties. It is extracted from the turmeric plant (Curcuma longa); the history of which dates back to about 5,000 years as a principal healing agent in traditional system of medicine.[1,2] Sushruta's Ayurvedic Compendium, dating back to 250 BC, recommends use of turmeric to relieve the effects of poisoned food.[3]

The advancements in the field of medicine lead to the discovery of Curcumin, two centuries ago when Vogel and Pelletier reported the isolation of "yellow coloring material" from the rhizomes of *Curcuma longa* and named it as Curcumin in 1842.[1,2,6] In the decades that followed, several chemists reported possible structures of Curcumin. Milobedzka and Lampe in 1910 identified the chemical structure of Curcumin as diferuloylmethane.[1-3] Further work by the same group in 1913 resulted in the synthesis of the compound.[11] Subsequently, Srinivasan separated and quantified the components of Curcumin by chromatography.[1,3] From there on, more than 100 components, including the volatile oils that have the therapeutic properties have been isolated from turmeric and the research still continues.[1,2]

3. Composition

Curcumin occurs naturally in the rhizome of Curcuma longa, which is grown commercially and sold as turmeric.[1] Curcumin is the phytochemical that gives turmeric its yellow color and is now recognized as being responsible for most of the therapeutic effects. Curcumin isolated from turmeric plant, once believed to be a single component later found to have three closely related species.[1,2]

The Curcuminoids constitute approximately 5% of most turmeric preparations are a mixture of three principal compounds: Curcumin (Curcumin I), demethoxycurcumin (Curcumin II), and bisdemethoxycurcumin (Curcumin III).[1-6] All the three Curcuminoids are equipotent in exhibiting the therapeutic actions. Hence, most of the studies refer Curcumin as a whole component rather than individual

components.The turmeric also contains several volatile oils like germacrone; termerone; β-termerones; β-bisabolene; α-curcumene; zingiberene bisacurone; alkaloids and sterols. These Curcuminoids and essential oils have been reported to be the main components responsible for eliciting the medicinal properties.[1-2]

4. Mechanisms of Action of Curcumin

Over the decades several studies have identified various molecular mechanisms of action of Curcumin. It modulates numerous molecular targets by altering their gene expression, signaling pathways or through direct interaction.

Anti inflammatory action:
Curcumin act via single or combination of any of the mechanism involving inhibition of arachidonic acid metabolism, inhibition of cyclooxygenase (COX), inhibition of the prostaglandin synthesis, inhibition of lipoxygenase (LOX), inhibition of cytokines (IL, TNF) release of steroidal hormones from the adrenals and stabilization of lysosomal membrane.[1-3,6]

A study conducted by Srivastava et al demonstrated that Curcumin inhibited the incorporation of arachidonic acid into platelet phospholipids and inhibited the deacylation of phospholipids. Thus inhibits synthesis of prostaglandins through inhibition of COX enzyme.[6] Ramsewak et al demonstrated that Curcumin I–III were active against COX-I enzyme with 125 µg/ml and showed 32%, 38.5% and 39.2% inhibition of the enzyme, respectively. They suggested that Curcumin reduces pro-inflammatory cytokine synthesis via inhibition of LOX enzyme.[6]

Recent studies have demonstrated that nuclear factor κB (NF-κ B) was involved in regulation of COX-2 & iNOS expression. Surh suggested that Curcumin down-regulated the levels of COX-2 and iNOS through suppression of NF-κ B.[6]

Stabilization of lysosomal enzymes by Curcumin is also one of the mode in which Curcumin shows its anti-inflammatory action. A Study conducted by Srivastava R et al comparing Curcumin and ibuprofen showed Serum phosphatase activity increased from 7.26 to 15.4 units due to inflammation. They concluded that Curcumin prevented the increase by 50% and hence, showed lysosomal membrane stabilization effect .[6]

Antioxidative effect
Curcumin is a unique antioxidant, the presence of the hydroxyl groups in the chemical structure of all the Curcuminoids ensures antioxidant activity. Curcumin, shows free radicals scavenging action and also inhibits the formation of reactive oxygen species (ROS) like hydroxyl radicals, superoxide radicals, peroxyl radicals and peroxynitrite.[7]

Curcumin contains two electrophilic unsaturated carbonyl groups, which can react with nucleophiles such as glutathione. Curcumin and its compounds have been recently demonstrated to induce the activities of detox system.[1-3] Curcumin was found to generate hydroxyl radicals through the Fenton reaction by reducing Fe3+ to Fe2+. Reddy ACP et al conducted a study on the effect of Curcumin and eugenol on the generation of reactive oxygen species in model systems were investigated. Both Curcumin and eugenol inhibited superoxide anion generation in xanthine-oxidase system to an extent of 40% and 50% respectively. The $^{\cdot}OH$-radical formation was inhibited to an extent of 66% and 46%, respectively, by Curcumin and eugenol. They concluded that Curcumin prevented the oxidation of Fe^{2+} in Fentons reaction which generates $^{\cdot}OH$ radicals.[7]

Curcumin through ROS-dependent mechanism perturbs multiple cell signaling molecules is known to exert its anticancer effect either by scavenging or by generating reactive oxygen species (ROS). They also reported a better correlation between anti-inflammatory activity and superoxide scavenging property.[7] Balasubramanyam et al demonstrated that Curcumin abolished ROS generation in cells from control and diabetic subjects. The pattern of these ROS inhibitory effect by Curcumin proves it to be a potent antioxidant.[7]

Curcumin is capable of scavenging oxygen free radicals, such as superoxide anions and hydroxyl radicals, which are the initiators of lipid peroxidation. The lipid peroxidation has a main role in the inflammation, in heart diseases, and in cancer.[7,9] Jayaprakasha et al demonstrated the protective effect of Curcumin against the cytotoxic effects of ethanol by measuring lipid peroxidation in terms of thiobarbituric acid reactive substances of malondialdehyde formed/100gm tissue. They found that the amount of lipid peroxidation was increased by ethanol only by two folds compared to control, but with liver cells pretreated with Curcumin the level of lipid peroxidation lowered to reach control level.[6,7]Priyadarsini et al evaluated the antioxidant mechanism of Curcumin and dimethoxy Curcumin by radiation-induced lipid peroxidation in rat liver microsomes.They concluded that at equal concentration, the efficiency to inhibit lipid peroxidation is changed from 82% with Curcumin to 24% with dimethoxy Curcumin.[6]

5. Antimicrobial Action

Studies have reported that Curcumin show a broad-spectrum of antimicrobial activity that includes antibacterial, antiviral and antifungal activities.[8]

a. Anti bacterial
One of the probable antibacterial mechanisms of actions is by inhibition of the cell dynamics.Curcumin via inhibition of assembly dynamics of FtsZ in the Z-ring can possibly suppress the bacterial cell proliferation. Kaur S et al conducted a study to evaluate the inhibitory effect against FtsZ on E. coli and B. subtilis. They concluded that Curcumin could suppress the FtsZ assembly leading to disruption of both the prokaryotic cell division causing the bacterial cell death.[8]

A study conducted by Niamsa N et al to asses the antibacterial activity of C. longa rhizome extract and they demonstrated that Curcumin is a potent bacterial agent with minimum inhibitory concentration value of 4 to 16 g/L and minimum bactericidal concentration value of 16 to 32 g/L

against S. epidermis ATCC 12228, Staph aureus ATCC 25923, Klebsiella pneumoniae ATCC 10031 and E. coli ATCC 25922 .[8]

b. Anti viral

It has been demonstrated that Curcumin as a plant derivative has a wide range of antiviral activity against different viruses. Therapeutic target for antiviral activity of Curcumin is by reduction of viral RNA expression, protein synthesis, and virus proteasus. In addition, it was found to have a protective effect on cells against virus-induced apoptosis and cytopathic activity.[8]

The clinical trial conducted by Ungphaiboon S on HIV patients using clear liquid soap containing 0.5% w/v ethanol extract of C. longa rhizome demonstrated reduced the wound infections and 100% decrease in itching symptom and it also affected the abscess to convert to dryness scabs (78.6%).[8]

Chen DY et al conducted a study on the anti-influenza activity of Curcumin against influenza viruses PR8, H1N1, and H6N1. The results showed more than 90% reduction in virus yield in cell culture using 30 μM of Curcumin against influenza viruses.[8] Divya CS et al conducted a study to evaluate Antitumor action of Curcumin in human papillomavirus. They concluded that Curcumin showed inhibitory activity against the expression of E6 and E7 genes of HPV-16 and HPV-18 that are highly oncogenic human papilloma viruses.[8]

c. Antifungal activity

Traditionally turmeric was used in food products, as it prevented fungal related spoilage of food. Extensive research on has been carried out proving Curcumin, a derivative of turmeric as a natural antifungal agent. [8]

The mechanism demonstrating antifungal effect of curcumin was found to be down regulation of desaturase leading to significant reduction in ergosterol of fungal cell. Reduction in ergosterol results in accumulations of biosynthetic precursors of ergosterol causing cell death via generation of ROS and reduction in proteinase secretion are other possible critical factors for antifungal activity of Curcumin.[8]

Ungphaiboon S et al conducted a study using the methanol extract of turmeric and demonstrated antifungal activity against Cryptococcus neoformans and Candida albicans with MIC values of 128 and 256 μg/mL, respectively.[8]

A study conducted by Neelofar K et al to evaluate efficacy of Curcumin against 14 strains of Candida isolates proved that Curcumin is a potent fungicide compound against Candida species with MIC values range from 250 to 2000 μg/mL .[8]

A study by Khan N et al demonstated anti-Candida activity of Curcumin against 38 different strains of Candida including some fluconazole resistant strains and clinical isolates of C. albicans, C. glabrata, C. krusei, C. tropicalis, and C. guilliermondii. The MIC_{90} values for sensitive and resistant strains were 250–650 and 250–500 μg/mL, respectively. Further more they suggested that possible mechanism for cell death of Candida species was through intracellular acidification via inhibition of H^+extrusion.[8]

Tsao SM et al studied antifungal activity of Curcumin on 200 clinical isolates of Candida species. They demonstrated fungicidal activity for Curcumin with MIC value of 32–128 μg/mL. Combination of Curcumin with amphotericin exhibited synergistic activity, suggesting that combination treatment of Curcumin with existing fungicidal agents provided significant effect against systemic fungal infections.[8]

d. Anti carcinogenic

Curcumin as an anticarcinogenic is one of the most common agent under extensive medical research .various in vitro and in vivo studies have reported that there are several pathways and molecular targets that play an active role in the stages those relating to invasion, growth, metastasis, inflammation, angiogenesis and survival of cancer cells.[9]

A wide variety of effects of Curcumin are mediated by its capability to act as a free radical scavenger, to alter gene expression of various stress protein and genes involved in angiogenesis, and to inhibit activity of many important transcription factors, an anti-inflammatory, as there is suggestive evidence that inflammation may have an active role in the three phases of carcinogenesis by its ability to selectively modify various cell signalling molecules.[9]

Curcumin regulates the expression of inflammatory cytokines (*e.g* Tumor Necrosis Factor-alpha (TNF-α) and Interleukins(IL-1), growth factors (*e.g*. VEGF, EGF), growth factor receptors (*e.g*., EGFR, HER-2, AR), enzymes (*e.g*., Cyclooxygenase-2 (COX-2), Lipooxygenase (LOX), matrix metallopeptidase 9 (MMP9), adhesion molecules (*e.g*., intracellular adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule-1 (VCAM-1), and endothelial leukocyte adhesion molecule-1 (ELAM-1) ,apoptosis related proteins (*e.g*. Bcl-2, caspases) cell cycle proteins (*e.g* cyclin D1). Curcumin modulates the activity of several transcription factors (*e.g* NF-κB, AP-1, STAT) and their signalling pathways.[9] However, detailed review in this regard is beyond the scope of this article.

6. Curcumin in Oral Diseases

Curcumin, the most active polyphenolic constituent shows a wide range of beneficial properties. Evidence on the diversified therapeutic approaches of Curcumin for most of the diseases makes it a potential agent to be used in various oral diseases.

1) Aphthous ulcers:

Aphthous ulcers are among the most common oral lesions in the general population. Due to the undetermined etiology of ulcer formation, there is no definite treatment and mainly treatment aimed at relieving the symptoms. It has been observed in various studies that Curcumin showed effective relief of these symptoms due to its anti inflammatory activity (Table 1).

Table 1

Author	Year	Curcumin dosage	Patients	Outcome
Halim DS [10] et al	1994	Curcumin powder.	20	Both Curcumin and triamcinolone had similar efficiency in treatment of RAS
Antharjanm R[11] et al	2009	Curcumin oil	10	The ulcers started healing earlier & there was also early reduction in pain in Curcumin group.
Manifar S [12] et al	2012	Curcumin gel (2%Curcumin)	29	Curcumin gel significantly reduced pain intensity.
Deshmuk RA[13] et al	2014	Cure next oral gel (10mg/1gm of C.longa)	60	Both Curcumin and triamcinolone had similar efficiency in treatment of oral RAS

2) Gingival and Periodontal disease

The clinical signs of gingivitis and periodontitis include changes in the morphology of the affected gingival tissue, which causes loss of teeth. Gingival & Periodontal treatment aims to cure inflamed tissue and reduce the number of pathogenic bacteria. various studies in this regard suggested Curcumin through its anti-inflammatory, antimicrobial properties make it a favorable agent in the treatment of gingival and periodontal diseases(Table 2).[4,5]

Table 2

Mouth wash				
Author	Year	Curcumin dosage	Patients	Outcome
Waghmare P[14] et al	2011	Turmeric mouthwash (10 mg/ 100 ml of water)	100	Reduction in total microbial count was observed in both the groups
Mali AM [15] et al	2012	Curcumin mouthwash (0.1%turmeric mouthwash)	60	Curcumin mouthwash can be effectively used as an adjunct to mechanical plaque control
Muglikar S[16] et al	2013	Curcumin mouthwash	30	They concluded that both Curcumin and chlorexidine showed significant improvement in clinical features.

Local drug delivery system				
Suhag A[17] et al	2007	Subgingival irrigation Curcumin (1% solution)	20	The results indicated that Curcumin group showed significant reduction in bleeding on probing (100%) and redness (96%).
Behal R[18] et al	2011	2% whole turmeric gel	30	The was a significant reduction in plaque index, gingival index, sulcus bleeding index, probing pocket depth, and gain in attachment loss
Gottumukala SN[19] et al	2014	Curcumin based collagen(50mg/cm^2)	60	The results demonstrated that, both the groups (chlorexidine and Curcumin) produced significant reduction in clinical & microbiological parameters
Farjana HN et al[20]	2014	Curcuma gel (10gms of curcuma extract)	10	They concluded that application of oral curcuma gel thrice daily for a period of three weeks showed decrease in gingival inflammation.
Anitha V[21] et al	2015	Curcumin gel (250gm Curcumin+95ml glycerol)	30	They concluded that Curcumin showed a significant difference over chlorhexidine in reducing the microbial & clinical parameters evaluated
Anuradha B et al [22]	2015	Curcumin gel (Cure next). Each gram contains10mg *C. longa* extract	30	Significant reduction clinical parameters and gain in clinical attachment level were demonstrated in both the groups.
Shama V[23] et al	2016	Curcumin gel (Cure next). Each gram contains10mg *C. longa* extract	20	The concluded that topical application of *C. longa* extract was effective in the treatment of gingivitis/mild periodontitis.
Roopa DA[24] et al	2016	Curcumin gel (Cure next). Each gram contains10mg *C. longa* extract	30	They concluded that the gel containing curcuma longa extract was efficient in treating gingivitis due to its anti-inflammatory property

3) Potentially malignant oral disease

Oral Potentially malignant disorders are a group of disorders of varying etiologies, usually tobacco, characterized by mutagen associated spontaneous or heredity alterations or mutations in the genetic material of oral epithelial cells with or without clinical and histomorphological alterations that may lead to oral squamous cell carcinoma transformation.[25] Due to its antioxidant, an anticancerous & anti-inflammatory property Curcumin plays a key role in the treatment of these diseases(Table:3)

Table 3

Leukoplakia				
Author	Year	Curcumin dosage	Patients	Outcome
Rai B [25]et al	2010	Curcumin caplets (900mg Curcumin, 80gm demethoxycurcumin, 20mg bidemethoxycurcumin)	25	The patients with oral Leukoplakia, showed significant symptomatic relief and also reduction in clinical size of the lesion by treatment with Curcumin.
Oral lichen planus (OLP)				

Chainani-Wu N[26] et al	2007	Curcumin- 2000mg/day In addition, all subjects received prednisone at 60 mg/day for the first 1 week.	33	They concluded that Curcumin at this dose was tolerable. Further they suggested future studies with a larger sample size, higher dose of Curcuminoids without an initial course of prednisone.
Rai B [25]et al	2010	Curcumin caplets (900mg Curcumin, 80gm demethoxycurcumin, 20mg bidemethoxycurcumin)	25	It was noted that the markers in saliva, serum and vitamin level increased in patients suffering from lichen planus.
Chainani Wu [27] et al	2012	Curcumin (up to 6,000 mg/day	100	They concluded that higher dosages of Curcumin (up to 6,000 mg/day) helped a significant number of OLP patients symptomatic relief
Singh V [28]et al	2013	Turmeric ointment (turmeric + glycerin)	10	Curcumin showed positive results both in terms of symptomatic relief and decrease in size of the lesion.
Keshari D [29]et al	2015	cure next oral gel (10mg/1gm of C longa)	27	They have concluded that Curcumin can be used as a safe alternative Furthermore there were no side effects in study group proving antifungal activity of Curcumin
Kia SJ[30] et al	2015	5% Curcumin oral paste	50	They concluded that Curcumin is a safe alternative & the combination strategies are more efficient in treatment of early periodontitis
Amirchaghmaghi M et al [31]	2016	Curcumin tablets (2000 mg/day)	20	They demonstrated no significant difference between the Curcumin and control groups.
Oral Submucous Fibrosis (OSMF)				
Hastak K [32] et al	1997	Turmeric in any of the three form i.e. Alcoholic extracts of turmeric, turmeric oil and turmeric oleoresin	58	It was found to be effective in decreasing the number of micronucleated cells both in exfoliated oral mucosal cells and in circulating lymphocytes
Deepa DA [33] et al	2010	Curcumin capsule , turmeric oil(9gm oil)	48	The results were almost equal by use of either of the form of Curcumin.
Rai B[24] et al	2010	Curcumin caplets (900mg Curcumin, 80gm demethoxycurcumin, 20mg bisdemethoxyc- urcumin)	25	Curcumin showed significant decrease in burning sensation and improvement in mouth opening
Agarwal N[34] et al	2014	Turmix (*C. longa* 300 mg, Piperine 5 mg)	30	They concluded that there was significant decrease in burning sensation but mouth opening was not significantly improved.
Karthik PM [35] et al	2014	Ground mixture of Turmeric+ jaggery	30	It was found that jaggery & turmeric application showed a very good prognosis in the inter incisal mouth opening recorded.
Yadav M [36] et al	2014	Turmix (*C. longa* 300 mg, Piperine 5 mg)	40	They inferred that Turmix proved to be beneficial and effective in the management of early OSMF
Hazarey VK[37] et al	2015	Curcumin lozenges (400mg Curcumin)	33	They concluded that Curcumin proved to be beneficial and effective in the management of OSMF
Srivastava A [38]et al	2015	Paste of 1 gm of turmeric powder & tulsi powder in glycerine .	45	They results showed decrease in burning sensation and significant increase in the mouth opening.
Devaraju RR[39] et al	2017	4% Curcumin orabase	30	The improvement in mouth opening and the decrease in burning sensation were statistically significant

4) Head and neck cancer:

Anticarcinogenic activity of Curcumin is multifaceted. In head and neck cancers the use of Curcumin is still in the stage of invitro studies. Lo Tempio MM et al demonstrated that Curcumin caused Growth suppression of HNSCC cell lines with decreased NF-kB activation.[40] Cohen AN demonstrated Suppression of Interleukin 6 and 8 production in head and neck cancer cells with Curcumin via inhibition of Ikappa beta kinase invitro.[41]

5) Radiation mucositis

Mucositis is the painful inflammation and ulceration of the mucous membrane, usually as an adverse effect of chemotherapy and radiotherapy for cancer. Curcumin showed remarkable results in the management of mucositis (Table:4)

Table 4

Author	Year	Curcumin dosage	Patients	Outcome
Elad S [42]et al	2013	Curcumall mouthwash	7	Reduction in compliance criteria for Curcumin mouthwash group
Saldanha SP[43] et al	2014	Curcumin mouthwash	29	The authors concluded that both mouth washes were individually effective but on comparison turmeric mouth wash was better than saline.
Rao S [44]et al	2014	Turmeric solution (400mg Curcumin in 80 ml water)	80	They concluded that turmeric solution provided significant benefit by reducing the severity of mucositis
Patil K[45] et al	2015	Curcumin mouthwash	20	The authors concluded that turmeric mouth wash was better than chlorexidine gel and there was better patient compliance
Charantimath S [46] et al	2016	Cure next oral gel (10mg/1gm of C.longa)	40	They concluded that Curcumin gel is effective and safer alternative in treatment of oral mucositis.

7. Miscellaneous

a. Pit and fissure sealant: Curcumin through its anti microbial property causes reduction of caries. This sealant can be produced from a composition comprising a polymerizable resin system containing acrylic monomer and group consisting of Annatto extract, turmeric extract and Apo-8-Carotenal.[4]

b. Intracanal medicament: It has been reported that E. faecalis is the predominant microbe seen in root canal of the infected teeth.[47] Curcumin through its anti microbial activity, acts as an intra canal medicament in the endodontic treatment. Neelakantan P [47]et al conducted an invitro study on 30 extracted teeth using Turmeric extract(5% turmeric powder in 10 ml water) and concluded that Curcumin showed antibacterial activity against E. faecalis.simillarly, Prabhakar A [48] et al in 2013 conducted an invitro study in 40 extracted tooth and reported 54% inhibition of E. faecalis using Turmeric extract(200gms in 500ml water),proving it to be an efficacious intracanal medicament

8. Adverse Effects

Generally considered safe, but may cause nausea, stomach upset, gastric irritation, diarrhoea & allergic reaction. Singh B et al in 2015 reported allergic contact mucositis in a patient using Curcumin gel, however they concluded that it may be due to the dyes like erythrosine used in the preparation .[49]

9. Future Challenges

The major concerns with Curcumin are low oral bioavailability that can be attributed to its poor absorption, high rate of metabolism and rapid elimination from the body.[47] Therefore, novel strategies using the nanotechnology in drug delivery, Curcumin with other combinations like turmeric oil, piperine & metal complex are being aggressively explored to enhance the bioavailability.[50]

10. Conclusion

Throughout the human history, there has been a conspicuous concern for health care and the cure of the disease, even though the concepts themselves took a very long time to develop into a body of knowledge.[1]From time immemorial, we have been using Curcumin, in the form of turmeric to attain the state of well-being. Currently, several proven studies clearly suggest that Curcumin has an edge over conventional allopathic treatment that suffer the limitation of low benefit to high risk ratio.[1,2] However, there is less information and research in this field. Therefore, further research is required to determine the optimal dosage, bioavailability, and bio-efficacy of Curcumin drugs.

References

[1] Aggarwal BB, Sundaram C, Malani N, Ichikawa H. Curcumin: the Indian solid gold. Adv Exp Med Biol. 2007;595:1–75.
[2] Aggarwal BB, Surh YJ, Shishodia S, editors. The molecular targets and therapeutic uses of curcumin in health and disease. Springer Science & Business Media; 2007.
[3] Lal J. Turmeric, Curcumin and our life: a review. Bull Environ Pharmacol Life Sci 2012;1(7):11–7.
[4] Chaturvedi T P. Uses of turmeric in dentistry: An update. Indian J Dent Res 2009;20:107-9
[5] Rastogi P, Anand V, Gulati M, Nandlal, Dixit J, Singhal R. A review of curcumin in reference to its use in oral diseases. Annals Ayurvedic Med .2012; 1(4):140-143.
[6] Kohli K, Ali J, Ansari M J, Raheman Z. Curcumin: A natural antiinflammatory agent. Indian J Pharmacol 2005;37:141-7
[7] Menon V P, Sudheer AR. Antioxidant and anti-inflammatory properties of curcumin. Adv. Exp. Med. Biol. 2007; 595, 105–125.
[8] Moghadamtousi SZ, Kadir HA, Hassandarvish P, Tajik H, Abubakar S, Zandi K. A review on antibacterial, antiviral, and antifungal activity of curcumin. BioMed Res Int. 2014;2014:186864.
[9] Shanmugam MK, Rane G, Kanchi MM, Arfuso F, Chinnathambi A, Zayed ME et al. The multifaceted role of curcumin in cancer prevention and treatment. Molecules. 2015 Feb 5;20(2):2728-69.
[10] Halim D, Binti N, Khalik B. Novel Material in the Treatment of Minor Oral Recurrent Aphthous Stomatitis. Int Med J,1994:0(3):392-394.
[11] Antharjanm, R. and Anita, B., Curcumin as a treatment modality in recurrent aphthous stomatitis. Case Report. Kerala Dental Journal. 2009.32 (4); 206-208.
[12] Manifar S, Obwaller A, Gharehgozloo A, Kordi H, Akhondzadeh S. Curcumin gel in the treatment of minor aphthous ulcer: A randomized, placebo-controlled trial. Journal of Medicinal Plants. 2012; 1 (41):40-45
[13] Deshmukh RA, Bagewadi AS. Comparison of effectiveness of curcumin with triamcinolone acetonide in the gel form in treatment of minor recurrent aphthous stomatitis: A randomized clinical trial. Int J of Pharm Investig . 2014;4(3):138-141.
[14] Waghmare P, Chaudhari A, Karhadkar V et al . Comparative Evaluation of Turmeric and ChlorhexidineGluconate Mouthwash in Prevention of Plaque Formation and Gingivitis: A Clinical and Microbiological Study. J Contemp Dent Pract.2011;12 (4): 221-224.
[15] Mali AM, Behal R, Gilda SS. Comparative evaluation of 0.1% turmeric mouthwash with 0.2% chlorhexidine gluconate in prevention of plaque and gingivitis: A clinical and microbiological study. J Ind Soc Peri.2012;16 (3): 386.
[16] Muglikar S, Patil KC, Shivswami S, Hegde R. Efficacy of. curcumin in the treatment of chronic gingivitis: A pilot. study. Oral Health Prev Dent 2013;11:81-86
[17] Suhag A, Dixit J, Dhan P. Role of curcumin as a subgingival irrigant: A pilot study. Perio.2007;4 (2):115-121
[18] Behal R, Mali AM, Gilda SS, Paradkar AR. Evaluation of local drug-delivery system containing 2% whole turmeric gel used as an adjunct to scaling and root planing in chronic periodontitis: A clinical and

microbiological study. J Indian Soc Periodontol 2011;15:35-8.
[19] Gottumukkala SN, Sudarshan S, Mantena SR. Comparative evaluation of the efficacy of two controlled release devices: Chlorhexidine chips and indigenous curcumin based collagen as local drug delivery systems. Contemp Clini Dent.2014; 5 (2): 175.
[20] Farjana HN, Chandrasekaran SC, Gita B. Effect of Oral Curcuma Gel in Gingivitis Management - A Pilot Study. J Clin Diagn Res.2014;8(12):ZC08-ZC10.
[21] Anitha V, Rajesh P, Shanmugam M, Priya BM, Prabhu S, Shivakumar V. Comparative evaluation of natural curcumin and synthetic chlorhexidine in the management of chronic periodontitis as a local drug delivery: A clinical and microbiological study. Indian J Dent Res 2015;26:53-6.
[22] Anuradha B, Bai YD, Sailaja S et al . Evaluation of AntiInflammatory Effects of Curcumin Gel as an Adjunct to Scaling and Root Planing: A Clinical Study. *J Int Oral Health*. *2015* Jul; *7(7): 90*–93.
[23] Sharma V, Kalsi DS. Effects of topical application of *Curcuma longa* extract in the treatment of early periodontal diseases. Indian J Dent Sci 2016;8:118-23
[24] Roopa DA, Singh S, Gupta S, Pandey YN, Goswami A, Johari S. Curcumin: A Herbal Approach in the Management Of Gingivitis.Rama Univ J Dent Sci .2016 Mar;3(1):1-5.
[25] Rai B, Kaur J, Jacobs R, Singh J. Possible action mechanism for curcumin in precancerous lesions based on serum and salivary markers of oxidative stress. J oral sci. 2010;52(2): 251-256.
[26] Chainani-Wu , Silverman S Jr, Reingold A, Bostrom A, Mc Culloch C, Lozada-Nur F et al. A randomized, placebo-controlled, double-blind clinical trial of curcuminoids in oral lichen planus. Phytomedicine. 2007;14(7-8):437-46.
[27] Chainani-Wu N, Madden E, Lozada NF, Silverman SJ. High-dose curcuminoids are efficacious in the reduction in symptoms and signs of oral lichen planus. J Am Acad Dermatol 2012;66(5):752-760.
[28] Singh V, Pal M, Gupta S, Tiwari SK, Malkunje L, Das S. Turmeric – a new treatment option for lichen planus: A pilot study. Natl J Maxillofac Surg, 4, 2013, 198-201.
[29] Keshari D, Patil K Efficacy of topical curcumin in the management of oral lichen planus: A randomized controlled trial. J Adv Clin Res Insights2015; 2:197-203.
[30] Kia SJ, Shirazian S, Mansourian A, Khodadadi Fard L, Ashnagar S. Comparative Efficacy of Topical Curcumin and Triamcinolone for Oral Lichen Planus: A Randomized, Controlled Clinical Trial. *J Dent (Tehran, Iran)*. 2015;12(11):789-796.
[31] Amirchaghmaghi M, Pakfetrat A, Delavarian Z et al. Evaluation of the Efficacy of Curcumin in the Treatment of Oral Lichen Planus: A Randomized Controlled trial.J Clin Diagn Res. 2016;10(5):ZC134-ZC137.
[32] Hastak K, Lubri N, Jakhi SD et al. Effect of turmeric oil and turmeric oleoresin on cytogenetic damage in patients suffering from oral Submucous fibrosis. Cancer Lett. 1997;116: 265-269.
[33] Deepa DA, Balan A, Sreelatha KT. Comparative study of the efficacy of curcumin and turmeric oil as chemopreventive agents in oral submucous fibrosis: A clinical and histopathological evaluation. J Indian Acad Oral Med Radiol.2010; 22(2): 88-92
[34] Agarwal N, et al. Evaluation of efficacy of turmeric in management of oral submucous fibrosis. J Indian Acad Oral Med Radiol. 2014;26(3):260–63
[35] Karthik PM, Sande A, Ashwinirani SR et al. Comparison of Mouth Opening with Different Non-Surgical Treatment Modalities in Oral Submucous Fibrosis. Amer J Drug Deli Therap. 2015; 2(3):072-7.
[36] Yadav M, Aravinda K, Saxena VS, Ratnakar P, Gupta J et al . Comparison of curcumin with intralesional steroid injections in oral submucous fibrosis -a randomized, open-label interventional study. J Oral Biol Craniofac Res. 2014;4(3):169–73.
[37] Hazarey VK, Sakrikar AR, Ganvir SM. Efficacy of curcumin in the treatment for oral submucous fibrosis - A randomized clinical trial. J Oral Maxillofac Pathol. 2015;19:145-52.
[38] Srivastava A, Agarwal R, Chaturvedi TP, Chandra A, Singh OP. Clinical evaluation of the role of tulsi and turmeric in the management of oral submucous fibrosis: A pilot, prospective observational study. J Ayurveda Integr Med. 2015 Jan;6(1):45.
[39] Devaraju RR, Aitha H, Gotoor S, Muppirala AV, Katne T. Curcumin orabase in the management of oral submucous fibrosis: a novel approach. International journal of scientific research. 2017;6(6):12-15.
[40] LoTempio MM, Veena MS, Steele HL et al Curcumin suppresses growth of head and neck squamous cell carcinoma. Clin Cancer Res. 2005; 11: 6994-7002.
[41] Cohen EE, Lingen MW, Vokes EE: The expanding role of systemic therapy in head and neck cancer. J Clin Oncol. 2004; 22: 1743-1752.
[42] Elad S, Meidan I, Sellam G et al. Topical curcumin for the prevention of oral mucositis in paediatric patients: case series. Altern Ther Health Med. 2013; 19(3):21-24
[43] Saldanha SP, Almeida VD. A Comparative Study to Assess the Effectiveness of Turmeric Mouth Wash versus Saline Mouth Wash on Treatment Induced Oral Mucositis (Tiom) in a Selected Hospital at Mangalore. J Clin Res Bioeth .2014;5 (6): 1.
[44] Rao S, Dinkar C, Vaishnav LK, Rao P, Rai MP, Fayad Ret al The Indian Spice Turmeric Delays and Mitigates Radiation-Induced Oral Mucositis in Patients Undergoing Treatment for Head and Neck Cancer: An Investigational Study. Integr Cancer Ther. 2014;13:201–210.
[45] 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:ZC59–ZC62.
[46] Charantimath S. Use of Curcumin in Radiochemotherapy Induced Oral Mucositis Patients: A Control Trial Study. World Academy of Science, Engineering and Technology, International Journal of Medical, Health, Biomedical, Bioengineering and Pharmaceutical Engineering. 2016 Mar 1;10(3):147-52.
[47] Neelakantan P, Jagannathan N, Nazar N. Ethnopharmacological approach in endodontic treatment: A focused review. Int J Drug Dev Res. 2011;3:68-77

[48] Prabhakar A, Taur S, Hadakar S, Sugandhan S. Comparison of Antibacterial Efficacy of Calcium Hydroxide Paste, 2% Chlorhexidine Gel and Turmeric Extract as an Intracanal Medicament and their Effect on Microhardness of Root Dentin: An in vitro Study. Int J of Clinii Pedi Dent. 2013;6(3):171-177
[49] Singh B, Sharma A, Garg A. Herbal oral gel induced contact stomatitis along with desquamative gingivitis due to a coloring agent. J Indian Soc Periodontol.2015;19(5):569-57.
[50] Anand P, Kunnumakkara AB, Newman RA, Aggarwal BB. Bioavailability of curcumin: problems and promises. Molecular Pharm.2007; 4: 807-818