TPM Vol. 32, No. S5, 2025
ISSN: 1972-6325
https://www.tpmap.org/

Open Access

ROLE OF HERBAL DERIVATIVES IN THE MANAGEMENT OF ORAL SUBMUCOUS FIBROSIS

SHRUTHI R.P
POST GRADUATE STUDENT, DEPARTMENT OF ORAL MEDICINE AND RADIOLOGY, SREE BALAJI DENTAL COLLEGE AND HOSPITAL, CHENNAI, TAMIL NADU, INDIA

AMUDHAN A
ASSISTANT PROFESSOR, DEPARTMENT OF ORAL MEDICINE AND RADIOLOGY, SREE BALAJI DENTAL COLLEGE AND HOSPITAL, CHENNAI, TAMIL NADU, INDIA

AAFREEN FATHIMA.H
SAVEETHA MEDICAL COLLEGE, SAVEETHA INSTITUTE OF MEDICAL AND TECHNICAL SCIENCES

ABSTRACT:
Oral submucous fibrosis (OSMF) is a cancerous condition affecting oral cavity with a higher rate of malignant transformation. It is a chronic debilitating disease affecting the oral mucosa as well as oropharynx. There are numerous therapy options available, such as antioxidants, corticosteroids, nutritional supplements to surgical management in advance stages of OSMF. The utilization of medicinal and aromatic plants has gained increasing attention in recent years, with new concepts as they have demonstrated a wide range of therapeutic potential, including anti-inflammatory, immunomodulatory, and antioxidant properties. Herbal medicines include the crude or unrefined products of plants, or herbal medicines produced from plants containing concentrated or purified herbal ingredients The properties of herbal derivative medicine such as antioxidant, anti-inflammatory and analgesic effects that may be crucial in mitigating the underlying inflammatory and fibrotic processes associated with oral submucous fibrosis.
This narrative review will elaborate on the various traditionally used herbal medicines and their role in the management of OSMF

keywords: Oral Submucous Fibrosis, Oral potential malignant disorder, conservative management, herbal medicine

INTRODUCTION

Oral Submucous fibrosis refers to a long-term illness that can impact any area of the mouth and occasionally the throat. It is invariably connected to a juxta-epithelial inflammatory response, which is either preceded by or connected to vesicle formation. Subsequently, there is a fibro-elastic modification of the lamina propria and epithelial atrophy, resulting in the stiffening of the oral mucosa, trismus, and difficulty eating[(1)]. Clinical features include a burning feeling in the mouth cavity, blanching to a leathery texture with pale mucosa visible, giving the impression of marbles, and, in more advanced stages of the condition, fibrotic bands, trismus, and shrinking uvula. Oral submucous fibrosis affects 2.5 million people worldwide, with a higher incidence in the Indian subcontinent, according to estimates[(1)].
It appears that OSMF management is difficult. Though many herbal remedies, surgical techniques, and medical therapy have been tried, there isn't a single, universally recognized cure. For the treatment of OSMF, herbal derivative medicine is found to be a cautious approach. Aloe vera, spirulina, tulasi, oxitard, nigella sativa, curcumin, and many more herbal items are among them[(2)].

METHOD OF LITERATURE SEARCH:

Scholarly searches in Pubmed, Pubmed Central, google, and google scholar was done with the keywords OSMF, Herbal medicines, Lycopene, Tulasi, Spirulina, curcumin, and conservative management

HERBAL DERIVATIVES:

Curcumin

A polyphenol chemical called curcumin (diferuloylmethane) was taken from the Curcuma longa L. plant's crushed rhizomes (Zingiberaceae family). In South Asia, curcumin is frequently utilized in traditional medicine. The primary component of turmeric that provides fibrinolytic activity is curcumin, a yellow pigment that occurs

naturally and has a variety of biological uses. It offers a large variety of therapeutic properties, such as antiseptic, antiviral, antibacterial, anti-inflammatory, chemopreventive, analgesic, anticarcinogenic, and antifungal properties. Turmeric's main polyphenolic compound, curcumin, also goes by the names 1, 6-heptadiene3,5-dione ,7-bis (hydroxyl-3-methoxyphenyl) -1. It was initially taken out of the medicine in 1815. Curcumin is soluble in acetone and ethanol but insoluble in water. The ratios of curcuminoids in curcumin are around 5 percent bisdemethoxycurcumin, 15 percent demethoxycurcumin, and 80 percent curcumin. Curcumin works to lessen inflammation by blocking histamine and increasing the production of cortisol. It has an anti-inflammatory impact via inhibiting nuclear factor kappa B, which in turn reduces the inflammatory response of TNF-α-stimulated human endothelial cells[3]. Moreover, platelet-derived growth factors can be inhibited.

Table 1: Chemical composition of curcumin

Curcumin derivatives	Properties
Curcumin	Antioxidant, Anti-ischemic, Antileukemic, Antilymphatic, Antiprostaglandin, Antithrombaxane, Antitumor agent, Metal chelator, protease inhibitor, Cox-2 inhibitor. Fibrinolytic, Protein kinase inhibitor
Bis- desmethoxycurcuminn	Antiangiogenic, Antiinflammatory, Cytotoxic
Desmethoxy curcumin	Antiangiogenic, Antiinflammatory, Anticancer
Tetrahydro Curcumin	Antioxidant, Antiinflammatory
Alpha curcumene	Antitumour, Antinflammatory
Ar- tumerone	Anti-inflammatory, Antitumor, Cox-2 inhibitor
Curcumol	Anticancer, Antitumor, Anti-saarcomic
Curdione	Anti-leukopenic, Antisarcoma, Antitumor, Anti X-radiation
Dehdrocurdione	Analagesic, Antipyeritic, Calcium channel blocker
Zingiberene	Antirhinoviral, Antiulcer, Carminative

Agarwal N et al. conducted a research investigation to assess the efficiency of turmeric in 30 cases of OSMF. There was a development in the burning feeling and mouth opening. Curcumin's anti-inflammatory properties were proposed to be caused by its inhibition of many molecules involved in the inflammatory process. Additionally, they can prevent cellular growth and limit lipid peroxidation, which lowers the rate of collagen synthesis and results in fibrinolytic activity[4].

Deepa DA et al. carried out a second trial to assess the usefulness of curcumin and turmeric in 48 patients with osmf when given as turmeric oil and curcumin capsules. Patients treated with turmeric oil saw a notable improvement in their symptoms, and curcumin also exhibited fibrinolytic and anti-inflammatory qualities[5] [6].

Yadav M et al. studied the effects of intralesional steroid injections against curcumin in individuals with osmf. When the tongue protrusion, interincisal distance and burning sensation were assessed weekly, it was discovered that the study's characteristics had significantly improved.

Balwant Rai studied oxidative stress indicators found in serum as well as saliva to determine curcumin's potential mechanism of action in premalignant disease. It was shown that curcumin increases lipid peroxidase activity, vitamin E and C levels, and DNA damage to mediate its anti-pre-cancer properties. This may be because curcumin reduces oxidative stress and produces vitamins C and E, which shield DNA from damage. This implies that curcumin's anti-precancerous properties are mediated via antioxidant processes[7]. Curcumin has been shown by Zhang SS et al. to have potential therapeutic efficacy in patients with osmf because it disturbs the cell cycle, slows cell proliferation, promotes apoptosis, and lowers collagen types I & III levels. According to a different study, curcumin treatment dramatically decreases the growth factor for connective tissue, it has a connection to the development and course of osmf. Consequently, curcumin's anti-inflammatory, antioxidant, and fibrinolytic characteristics are helpful for treating OSMF cautiously.

Aloevera

Aloe vera gel contains polysaccharides that promote wound healing. The adaptogenic substance enhances immunity by homeostasis. The various components include vitamins (A and C), enzymes (bradykinase, peroxidase, amylase, catalase), sugars (mono and disaccharides) and minerals (zinc and copper). Bradykinin, histamine, and TNF-a are examples of chemical mediators whose synthesis is inhibited by enzymes, which have anti-inflammatory qualities. These mediators provide the skin and mucous membranes flexibility by inducing the granulation tissue of healing wounds to produce hyaluronic acid as well as dermatan sulfate. According to a study by Singh et al., Aloe vera gel reduces burning when used in conjunction with physical therapy. promotes mouth opening, and enhances oral mucosa flexibility. Aloe vera gel thus offers an excellent cure when combined with quitting habits. Similar outcomes were noted in a Singh et al. investigation that contrasted lycopene and aloe

vera[8]. Anuradha et al. found that using systemic and topical aloe vera for three months increased mouth opening, cheek flexibility, and decreased burning, all of which are equivalent to intralesional injections of hyaluronidase and hydrocortisone combined with supplements containing antioxidants[9]. When compared to aloe vera, Patil et al's study shown better outcomes utilizing spirulina, lycopene, & oxitrid. While treating OSMF, aloe vera is a cost-effective, non-invasive topical treatment that works well [10].

Spirulina

Spirulina is a cyanobacteria biomass that contains minerals, carotenoids, phycocyanin, and vitamins A and B12. Although it lowers cholesterol, its popularity has grown due to its antioxidant properties. A decrease in IL-6 and an increase in IL-2 indicate the antioxidant impact. The chemopreventive effect is produced by carotenoids and superoxide dismutase, which also help treat oral precancerous lesions. When compared to the group treated with spirulina alone, patients who received mouth stretching devices combined with 500 mg of spirulina shown good clinical results, including decreased Flexibility "of the oral mucosa, burning sensation, and opening of the mouth (Kanjani et al., 2013)[11]. In 42 subjects with OSMF, Patil S et al. assessed the effectiveness of spirulina along with aloe vera. Patients' mouth opening and oral ulcers improved clinically when they received spirulina. Nonetheless, neither group's burning sensation nor discomfort significantly improved. They came to the conclusion that spirulina seems to have more promising results for managing OSMF than aloe vera[10]. The initial investigation to assess the combined effects of PTX and spirulina in 40 OSMF patients was Mulk BS et al. Regarding mouth opening and tongue protrusion, there was no discernible" difference between the two groups. However, it was discovered that Spirulina was better than PTX since it reduced burning feeling effectively and had no negative side effects. While the Spirulina group did not have any unfavorable side effects at all, the PTX group did experience nausea, gastritis, and bloating in the stomach[12]. Shetty et al. distinguished the effectiveness of Adding intralesional beta-methasone along with spirulina to the group receiving a placebo a steroid injection in an intervention research including 40 OSMF patients. The burning feeling and tongue opening significantly improved in the spirulina group[12]. Spirulina is a useful adjunct therapy for OSMF in its early phases.

Tulasi

Tulasi (Ocimum sanctum Linn) exhibits anti-inflammatory, antioxidant, and immunomodulatory action which boosts immunity. The chemical components include polyphenol rosmarinic acid which exhibit antioxidant effect. In order to suppress the activation of NF-kappa B caused by carcinogens like TNF, phorbol ester, okadaic acid, and hydrogen peroxide, oleanolic acid, ursolic acid, a pentacyclic triterpene acid, and hydrogen peroxide are used. These compounds also inhibit NF-kappa B p65 nuclear translocation, and p65 phosphorylation, are dependent gene expression. Ultimately, they prevent cell proliferation, cell accumulation during the G1-G0 phase of the cell phase and the death of cells. The anti-inflammatory is exhibited by certain enzymes. The antistress property is exhibited by reducing the cortisol effect[2].

In a study of 41 OSMF cases, Srivastava A et al. investigated the therapeutic usefulness of combining turmeric and Tulasi in a glycerine basis[13]. The combination of these two drugs produced a clinically considerable reduction in mouth opening as well as burning feeling. They came to the conclusion that Tulasi and Turmeric provided a safe, affordable, and effective therapy option in all grades of OSMF when combined with a change in lifestyle. After using 500 mg of Tulasi paste in 20 OSMF cases, Madulatha et al. saw a considerable decrease in mouth opening and burning sensation, leading them to conclude that Tulasi can be utilized as a conservative tretment option for symptomatic features of OSMF[14].

Lycopene

Lycopene is a non-provitamin A carotenoid and a potent antioxidant. It is a tetraterpene molecule that contains eleven double linear bonds and eight isoprene. It exhibits antioxidant, anticancer, "and anti-inflammatory action. Its therapeutic qualities have been proven in several in vitro along with in vivo experiments investigations. Lycopene has antioxidative properties since it lowers NO levels, TNF-α, and downregulates the activity of the iNOS gene in addition to lowering MPO activity, HO-1 mRNA gene expression is upregulated, TNF-α and lipopolysaccharide stimulated COX-2(cyclooxygenase-2), NOS2 (nitric oxide synthase 2"), inhibited COX-2, along with NF-κB are suppressed. decreased leukocyte movement, demonstrating its anti-inflammatory characteristics. This investigation demonstrated the anticancer impact of lycopene by showing a significant improvement in the expression of LC3-I & p-ERK (phosphorylated extracellular signal-regulated kinase) proteins in HGC-27 cells treated with lycopene. Lycopene is commonly utilized in the treatment of OPMD since it has been demonstrated to modify the dysplastic alterations[15]. Karemore et al. treated 92 OSMF patients by comparing the impact of lycopene that is antioxidant along with placebo in regards to habit cessation. When compared to a placebo, lycopene performed better on all the OSMF metrics. The study found that mouth opening had improved[16]. St. Beena Kumary et al. discovered that hyaluronidase and dexamethasone were more effective than lycopene in treating the 60 OSMF cases. In the lycopene group, "there was also a discernible decrease in burning sensation and a noticeable increase in mouth opening. When medical comorbidities limit the use of dexamethasone, lycopene has been demonstrated to be an effective alternative[17]. In treating 45 patients with OSMF, Johnny et al. assessed the effectiveness of lycopene along with the lycopene-hyaluronidase combination

versus placebo. In the therapy of OSMF, lycopene and lycopene & hyaluronidase combination showed a substantial improvement above the placebo group in terms of mouth opening and burning feeling but when in contrast to lycopene alone, the lycopene hyaluronidase combination did not demonstrate any discernible variation. In 60cases with OSMF, Saran et al. assessed the effectiveness of curcumin along with lycopene. When it came to improving mouth opening, lycopene outperformed" curcumin, and both medications successfully reduced the burning feeling experienced by OSMF patients[18].One promising antioxidant for the treatment of OSMF is lycopene. since it lessens both subjective and objective symptoms.

Oxitard

Oxitard is a herbal "antioxidant made from a combination of Withania somnifera, Daucus carota, Glycyrrhiza glabra, Vitis vinifera, powders of Emblica Officinalis and Yashada bhasma, and oils of Triticum sativum and Mangifera indica" with extracts demonstrating antibacterial and antiviral action. Withania somnifera reduces inflammation, stress, and anxiety while boosting immunity. Vitamin A can be found in daucus carota. Glycyrrhiza glabra is an immunostimulant that also lowers inflammation. Vitis vinifera is a caustic that has anti-inflammatory properties that lessen burning pain. Zinc in Yashada bhasma and vitamin C in Emblica Officinalis promote wound healing and cell renewal, respectively. Minerals included in Triticum sativum improve its antioxidant qualities.

Patil S et al. compared the effectiveness of Oxitard medicine versus a placebo in treating OSMF. The group of Oxitard shown a noticeable enhancement of the indicators and signs, according to the authors conclusion. Oxitard is a useful medication that can help in OSMF management [19].

Colchicine

Colchicine is derived from the plant colchicum autumnale. By blocking the creation of microtubules and fibroblasts ability to secrete collagen, colchicine lowers the amount of collagen produced. In the underlying submucosa, collagenase activity is increased and fibroblast overproduction is suppressed. TGF-β, IL-4, and IL-6—cytokines that produce collagen—are neutralized.

In order to treat OSMF, Krishnamoorthy B et al. investigated the effectiveness and side effects of injecting 0.5 ml of hyaluronidase intralesionally and taking 500 mg of colchicine orally. Colchicine demonstrated better outcomes in easing OSMF symptoms When assessing the effectiveness of systemic colchicine in conjunction with intralesional injections of hyaluronidase and triamcinolone acetonide in patients with Stage II OSMF, the Daga et al trial produced contraindicating results. The sensation of burning were lessened and the mouth opening was improved in the patients undergoing injectable therapy[20]. The mucosa's blanching outcomes were better in both groups. Given the negative consequences, comprehensive monitoring is necessary. Colchicine is contraindicated in liver problems and should be used cautiously because greater doses have been associated with harmful consequences.

Salvianolic acid

China uses a herbal remedy called Salvia miltiorrhiza bage, or Radix Salviae miltiorrhizae (danshen), made from desiccated root. Danshen contains Sal-B (salvianolic acid B), which is derived from salvia miltiorrhizae and is a powerful biological active component[21]. Sal-B is made up of seven antioxidant-active phenolic hydroxyls. Jiang et al. assessed the efficacy of using intralesional triamcinolone acetonide together with SA-B to treat OSMF. During the treatment phase, the mouth opening of the SA-B group improved more than that of the other group, but during the follow-up, it declined [22].

Nigella sativa

The family Ranunculaceae includes Nigella sativa. Most people refer to it as black seed. Thymol, α-pinene, carvacrol, dithymoquinone, p-cymene, 4-terpineol, t-anethol, thymohydroquinone, sesquiterpene longifolene, and Thymoquinone are among the chemical constituents. Isoquinoline alkaloids are present in it. Additionally, it contains the powerful anticancer drug saponin as well as the pentacyclic triterpene alpha hederin[23].

The ability to fight bacteria Several crude N. sativa extracts were tested for their antibacterial activity against 16 gram negative as well as 6 gram positive bacterial isolates. Multiple antibiotic resistances, particularly against gram-negative drugs, were demonstrated by these isolates. Several studies have demonstrated the antioxidant property's capacity to reduce agents of inflammation such as IL-6, TN-alpha, and PGE while increasing IL-10. Investigations were conducted on the anticancer & counter-angiogenic properties of nigella extract osteogenic sarcoma both in vitro and in vivo[24]. The human osteosarcoma cells exhibited a higher percentage of apoptosis and growth inhibition, according to the results. In animal models, Nigella sativa aqueous extract was discovered to possess anti-inflammatory properties and analgesic properties; on the other hand, an investigation was conducted into the anti-inflammatory properties of Nigella sativa alcoholic extracts and callus on mixed glial cells of rats. These attributes demonstrated an efficacious treatment in OSMF. In 40 OSMF cases, Papalia PR et al. examined the effectiveness of Nigella sativa and turmeric combined with black pepper. They also measured the levels of superoxide dismutase both prior to and following the therapy, which increased mouth opening, decreased a scorching feeling, and raised level of SOD[25].

Tea pigments

Tea pigments are created when the polyphenols in the tea leaves oxidize. Flavons, which have anti-inflammatory, anti-tumor, and antioxidant qualities, are present in the tea pigments. Nuclear factor-kappa B (NF-kappaB) is inhibited by polyphenols and flavonoids, which in turn controls the release of molecules that cause inflammation, such as cytokines. In addition, pigments of tea reduce the viscosity of blood., enhance micro-circulation, and block the activities of superoxide dismutase these properties exhibit their application in OSMF. The initial study by Li XM et al found that mouth opening improved in the initial phases of OSMF patients with haematinic deficiencies [(26)].

CONCLUSION:

The management of OSMF involves no single treatment modality. Triple therapy has been shown to be effective. Herbal remedies hold great promise for treating a wide range of potentially fatal illnesses. They can be used for a longer duration in medically compromised patients without any major systemic adverse effects. Although herbal products showed promising results there are only a few studies have been conducted in the managing of OSMF. The effectiveness of herbal products has been found to have lower efficacy or similar efficacy when compared to conventional modalities. However, these are used as an adjuvant modality or as conjugation to enhance the therapeutic effect of other treatment modalities.

Conflict of interest: : Nil
Funding source:: Nil

REFERENCE:

1. Pindborg JJ, Sirsat SM. Oral submucous fibrosis. Oral Surg Oral Med Oral Pathol. 1966;22:765–779
2. Sanjay C J, Shilpa Padar Shastry, Karthikeya Patil, Nagabhushana Doggalli, Naveen Kumar, Swathi Sharma, Herbal therapy in Oral Submucous Fibrosis: A Short Review Indian Journal of Forensic Medicine & Toxicology, July-September 2021,15,(3) 509-513
3. Chandramani B. Morea, Deepa Jatti Patila, Naman R. Rao, Medicinal management of oral submucous fibrosis in the past decade- A systematic review Journal of Oral Biology and Craniofacial Research 10(2020) 552-568
4. Agarwal, S.; Rao, A. Carotenoids and chronic diseases. Drug Metab. Drug Interact. 2000, 17, 189–210
5. Abhijeet Alok et al., Curcumin – Pharmacological Actions and its Role in Oral Submucous Fibrosis: A Review, Journal of Clinical and Diagnostic Research. 2015 Oct, Vol-9(10): ZE01-ZE03
6. 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.
7. Dwivedi N, Agarwal A. Aloe vera: magic or myth. SRM J res dent sci 2013; 4: 119 Fujita K, teradaira R. Bradykininase activity of aloe extract. Biochem Pharmacol. 1976:25–205
8. Singh N, Hebbale M, Mhapuskar A, Ul Nisa S, Thopte S, Singh S. Effectiveness of aloe vera and antioxidant along with physiotherapy in the management of oral submucous fibrosis. J Contemp Dent Pract. 2016;17(1):78–84.
9. Anuradha A, Patil B, Asha VR. Evaluation of efficacy of aloe vera in the treatment of oral submucous fibrosis - a clinical study. J Oral Pathol Med. 2017;46(1):50–55
10.Patil S, Al-Zarea BK, Maheshwari S, Sahu R. Comparative evaluation of natural antioxidants spirulina and aloe vera for the treatment of oral submucous fibrosis. Journal of oral biology and craniofacial research 5 (2015)11e15
11. Kanjani V, Annigeri RG, Revanappa MM, Rani A. Efficacy of spirulina along with different physiotherapeutic modalities in the management of oral submucous fibrosis. Ann Maxillofac Surg. 2019;9(1):23–27.
12. Mulk BS, Deshpande PS, Velpula N, Chappidi V, Chintamaneni RL, Goyal S. Spirulina and Indian Journal of Forensic Medicine & Toxicology, July-September 2021, Vol. 15, No. 3 513 Pentoxyfilline – A Novel Approach
13. Shetty P, Shenai P, Chatra L, Rao PK. Efficacy of spirulina as an antioxidant adjuvant to corticosteroid injection in management of oral submucous fibrosis. Indian J Dent Res. 2013;24:347e350.
14. Srivastava A, Agarwal R, Chaturvedi TP, Chandra A, Singh OP Clinical evaluation of the role of tulasi and turmeric in the management of oral submucous fibrosis: A pilot, prospective observational study. J Ayurveda Integr Med. 2015;6(1):45-9.
15. G. Madhulatha, N. Vijayalaxmi, T. Harshavardhan Tulasi a magical herb and a boon for management of oral submucous fibrosis: a clinical study. International Journal of Research in Medical Sciences Madhulatha G et al. Int J Res Med Sci. 2017 Nov;5(11):4719-4723

16. Karemore TV, Motwani M. Evaluation of the effect of newer antioxidant lycopene in the treatment of oral submucous fibrosis. Indian J Dent Res. 2012;23:524-8.
17. Muhammad Imran, Fereshteh Ghorat, Iahtisham Ul-Haq, Habib Ur-Rehman Farhan Aslam , Mojtaba Heydari , Mohammad Ali Shariati , Eleonora Okuskhanova , Zhanibek Yessimbekov , Muthu Thiruvengadam , Mohammad Hashem Hashempur and Maksim Rebezov- Lycopene as a Natural Antioxidant Used to Prevent Human Health Disorders antioxidants 2020, 9, 706
18. Saran G, Umapathy D, Misra N, et al. A comparative study to evaluate the efficacy of lycopene and curcumin in oral submucous fibrosis patients: a randomized clinical trial. Indian J Dent Res. 2018;29(3):303–312. 53.
19. Patil S, Halgatti V, Maheshwari S, Santosh BS. Comparative study of the efficacy of herbal antioxdants oxitard and aloe vera in the treatment of oral submucous fibrosis. J Clin Exp Dent. 2014;6(3):e265-70
20. Daga D, Singh RK, Pal US, Gurung T, Gangwar S. Efficacy of oral colchicine with intralesional hyaluronidase or triamcinolone acetonide in the Grade II oral submucous fibrosis. Natl J Maxillofac Surg. 2017;8(1):50–54.
21. Zhao Y, Guo Y, Gu X. Salvianolic Acid B, a potential chemopreventive agent, for head and neck squamous cell cancer. J Oncol. 2011:534548 2011
22. Xiao-Wen Jiang, DDS, PhD,a,b Yi Zhang, MD,c Shou-Kang Yang, MD,a Hao Zhang, MD,a Kun Lu, MD,a and Guo-Liang Sun, MD, a- Efficacy of salvianolic acid B combined with triamcinolone acetonide in the treatment of oral submucous fibrosis 115(3) 339-344
23. Aftab Ahmad, Asif Husain, Mohd Mujeeb, Shah Alam Khan, Abul Kalam Najmi, Nasir Ali Siddique, Zoheir A. Damanhouri, Firoz Anwar A review on therapeutic potential of Nigella sativa: A miracle herb Asian Pacific Journal of Tropical Biomedicine
24. Atta-Ur-Rahman. Nigellidine-a new indazole alkaloid from the seed of Nigella sativa. Tetrahedron Lett 1995; 36(12): 1993-
25. Papalia PR, Annigeri RG, Mehta R.Clinico biochemical evaluation of turmeric with black pepper and nigella sativa in management of oral submucous fibrosis-a double blind, randomized preliminary study Oral Surg Oral Med Oral Pathol Oral Radiol. 2016 Dec;122(6):705-712.
26. Li X, Tang J, Hua Xi, Kou Qiang, Xue Yi, Zhi Za. Clinical treatment observation of tea pigment for oral submucous fibrosis. 1998;16(1):50–52.