WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
Coden USA: WJPRAP Impact Factor 8.63
Volume 15, Issue 21, 157-170. Review Article ISSN 2277–7105

CANCER TREATMENT- ASSOCIATED ULCERATIVE ORAL MUCOSITIS: CONTEMPORARY UNDERSTANDING AND AYURVEDIC MANAGEMENT STRATEGIES - A NARRATIVE REVIEW

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Article Received on 02 Oct. 2026,
Article Revised on 22 Oct. 2026,
Article Published on 01 Nov. 2026,

https://doi.org/10.5281/zenodo.23757109

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How to cite this Article: *1Dr. Prinsitha K. A., 2Rejani H MD (Ay). (2026). Cancer Treatment-Associated Ulcerative Oral Mucositis: Contemporary Understanding And Ayurvedic Management Strategies - A Narrative Review. World Journal of Pharmaceutical Research, 15(21), 157–170.
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ABSTRACT

Ulcerative Oral Mucositis (UOM) is a common and debilitating complication of chemotherapy, radiotherapy, chemoradiotherapy, and hematopoietic stem cell transplantation. It is characterized by erythema, ulceration, severe pain, and impaired oral functions, leading to reduced quality of life and interruption of cancer treatment.. In Ayurveda, UOM can be correlated *with Sarvasara Mukhapaka*, a *Pitta-pradhana Tridoshaja* condition affecting the oral mucosa. *Kabala* (therapeutic gargling) with *Dugdhika Kera Tailam* has been used in clinical practice for its *Pitta-shamana*, *Vrana-ropana*, and *Daha-shamana* properties. The medicated oil provides prolonged contact with the oral mucosa, promoting local healing, reducing inflammation, pain, and burning sensation, and restoring mucosal integrity. This may potentially support mucosal healing and provide relief from symptoms such as pain and burning sensation. Therefore, *Kabala* with *Dugdhikā Kera Taila* may have potential as a complementary and cost-effective intervention in the supportive management of UOM, warranting further clinical evaluation, while supporting continuity of cancer therapy and improving patients' quality of life.

INTRODUCTION

Cancer treatment involves a range of therapeutic modalities aimed at controlling tumour growth, reducing tumour burden, preventing disease progression, and improving survival and quality of life. Non-surgical cancer therapies include chemotherapy, radiotherapy, targeted therapy, immunotherapy, hormone therapy, and selected local ablative modalities.[1] Although these treatments have significantly improved cancer outcomes, their effects are not limited to malignant cells and may cause considerable toxicity to normal tissues. Chemotherapy particularly affects rapidly proliferating tissues such as the oral and gastrointestinal mucosa, bone marrow, and hair follicles, while radiotherapy involving the head and neck can produce significant local oral complications. Targeted therapy and immunotherapy may also be associated with oral and systemic adverse effects. High-risk chemotherapeutic agents associated with oral mucositis include 5-Fluorouracil (5-FU), methotrexate, cytarabine, anthracyclines, alkylating agents, antimetabolites, and mTOR inhibitor.[2,3]

Ulcerative Oral Mucositis (UOM) is one of the important and debilitating complications of cancer therapy, particularly following chemotherapy, head and neck radiotherapy, concurrent chemoradiotherapy, and hematopoietic stem cell transplantation. It is characterized by mucosal erythema, inflammation, epithelial breakdown, and painful ulceration resulting from direct epithelial injury, oxidative stress, inflammatory mediator release, and impaired mucosal repair. Non-keratinized oral mucosa is particularly vulnerable because of its high cellular turnover and limited protective keratin layer.[4] Severe UOM may result in significant pain, burning sensation, difficulty in eating, chewing and swallowing, increased risk of secondary infection, nutritional impairment, interruption of anticancer treatment, and deterioration in quality of life.[5] Therefore, effective management of UOM is an important component of supportive cancer care, highlighting the need for safe and effective therapeutic approaches to reduce mucosal injury and promote healing.

Epidemiology

Oral mucositis occurs in approximately 20–40% of patients receiving conventional chemotherapy, while its incidence may exceed 75–90% among patients undergoing high-dose chemotherapy, head and neck radiotherapy, concurrent chemoradiotherapy, or hematopoietic stem cell transplantation (HSCT). It usually develops within 5–14 days after chemotherapy. its severity is influenced by the treatment regimen and dose, as well as oral hygiene, nutritional status, and individual patient-related factors.[6,7]

Risk Factors

The risk and severity of oral mucositis are influenced by several patient-, tumour-, and treatment-related factors. Patient-related factors include extremes of age, female sex, poor oral hygiene, reduced salivary flow or xerostomia, malnutrition or low body mass index, impaired renal function, smoking, previous episodes of oral mucositis, and genetic susceptibility. Tumour-related factors include the site and stage of the tumour, particularly when the radiation field involves the oral cavity. Treatment-related factors include high-dose chemotherapy, head and neck radiotherapy, altered radiation fractionation, concurrent chemoradiotherapy, the type and dosage of chemotherapeutic agents, and the use of targeted therapy or immunotherapy.[8]

Pathophysiology (Five-Phase Model)

The pathogenesis of oral mucositis occurs through five interconnected phases. Phase 1 – Initiation begins with cytotoxic therapy-induced damage to basal epithelial cells and DNA, accompanied by the generation of reactive oxygen species (ROS). In Phase 2 – Upregulation, transcription factors are activated, resulting in the release of pro-inflammatory cytokines such as TNF-α, IL-1, and IL-6. During Phase 3 – Signal Amplification, the cytokine cascade further amplifies tissue injury, leading to increased apoptosis and progressive mucosal destruction. Phase 4 – Ulceration is characterized by the development of painful oral ulcers, which may undergo secondary bacterial colonization, further increasing inflammation and the risk of systemic infection. Finally, during Phase 5 – Healing, epithelial cells proliferate and differentiate, resulting in gradual restoration of mucosal integrity and normal oral function.[9]

Clinical Features

Oral mucositis commonly presents with erythema of the oral mucosa, burning sensation, and pain, which may progress to white desquamative patches followed by painful ulcers with pseudomembrane formation. Patients may experience difficulty in chewing and swallowing (dysphagia), difficulty in speech, and reduced oral intake. The commonly affected sites include the buccal and labial mucosa, ventral surface of the tongue, floor of the mouth, and soft palate. In most cases, the lesions heal within 2–3 weeks after completion of cancer therapy, provided there is no further mucosal injury.[10]

History and Physical Examination

Radiation-induced OM: Appears around the 3rd week of radiotherapy, lasts 7–98 days; affects soft palate, floor of mouth, cheeks, tongue, and lips. Symptoms include severe pain, difficulty eating/speaking, and occasional bleeding.[2]

Chemotherapy-induced OM: Develops 5–14 days after chemotherapy; starts with erythema, progresses to ulceration with pseudomembrane, mainly involving non-keratinized mucosa. Healing occurs with neutrophil recovery.[1]

Evaluation[11]

The diagnosis of oral mucositis is based mainly on clinical history and thorough oral examination, with assessment of the timing of onset, symptoms, and appearance of the oral lesions in relation to cancer therapy. Microbiological culture or biopsy may be considered when lesions occur on the hard palate, attached gingiva, or dorsal surface of the tongue, particularly to exclude infectious or other pathological conditions. The severity of mucositis is assessed using standardized clinical grading scales, which help to determine the extent of mucosal involvement and guide management.

CTCAE Grading

Functional

Grade 1: Mild/no symptoms, normal diet.

Grade 2: Moderate pain, modified diet.

Grade 3: Severe pain, limits oral intake.

Grade 4: Life-threatening.

Grade 5: Death.

Clinical

Grade 1: Erythema.

Grade 2: Patchy ulcers/pseudomembranes.

Grade 3: Confluent ulcers with bleeding.

Grade 4: Tissue necrosis/spontaneous bleeding.

Grade 5: Death.

WHO Oral Mucositis Scale

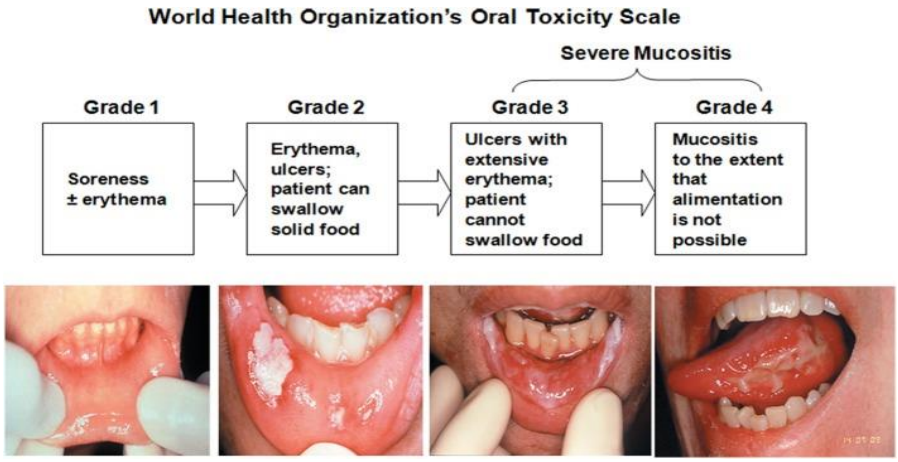
Grade 0: No mucositis.

Grade 1: Erythema and soreness.

Grade 2: Ulcers, able to eat solids.

Grade 3: Ulcers, liquid diet only.

Grade 4: Extensive ulcers, oral feeding impossible.



Differential Diagnosis

The differential diagnosis of oral mucositis includes oral candidiasis, herpes simplex virus (HSV) infection, bacterial infections, drug-induced mucosal reactions, erythema multiforme, and Stevens–Johnson syndrome. These conditions should be considered when oral lesions show atypical features, unusual distribution, prolonged duration, or inadequate response to supportive management.[12]

Management

The management of oral mucositis is primarily supportive and includes maintaining good oral hygiene and standardized oral care protocols**,** adequate pain control using topical agents such as lidocaine and systemic analgesics, and the use of benzydamine mouthwash and mucosal coating agents where appropriate[4,5] Oral cryotherapy may be used during selected chemotherapy regimens, while low-level laser therapy (photobiomodulation**)** may help reduce the severity and duration of mucositis[4,13] Secondary infections should be identified and treated with appropriate antifungal or antimicrobial agents. Adequate nutritional support**,** including a soft or liquid diet and nutritional supplements, is important to maintain oral intake and prevent nutritional deterioration. Severe oral mucositis also imposes a substantial economic burden, as it may increase hospital admissions, length of hospital stay, emergency visits, and the need for nutritional support, opioid analgesics, and antimicrobial therapy. Consequently, severe mucositis can significantly increase treatment-related healthcare costs,

particularly among patients undergoing intensive chemoradiotherapy or hematopoietic stem cell transplantation.[4]

Ayurvedic View of Oral Side Effects of Non surgical cancer treatments

Oral side effects of non surgical cancer therapies do not match exactly with any single *Mukharoga* described in Ayurveda. However, they can be considered under *Anukta Vyadhi* (conditions not specifically mentioned in texts) and treated using the principles laid down by Acharya Charaka.[14] Symptoms resembling oral side effects —such as difficulty opening the mouth (*Krichchhen Vivrinoti Mukham*), burning sensation (*Ushna),* intolerance to spicy foods (*Tikshna Asaha),* dryness of mouth (*Mukhashosha*), altered taste (*Virasa jnana),* and ulceration or mucosal breaks (*Mukhantargata Vrana, Vranavasthu, Durudha Vrana*)—are scattered across classical Ayurvedic literature.[15,16,17] Because of these symptoms, oral side effects of non surgical cancer therapies can be viewed as a *Pitta-dominant Tridoshaja Sarvasara Mukharoga,* meaning a disorder affecting the entire oral cavity.[16]

Ayurvedic Review – Sarvasara Mukhapāka

Mukhapaka, also termed *Sarvasara Roga,* refers to diseases of the oral cavity where the mucosa undergoes inflammation and ulceration. Acharya Kashyapa and Acharya Charaka described this condition as *Mukhapaka*[16,18], while Acharya Susruta and Vagbhata referred to it as *Sarvasara Roga.*[16,17] Charaka linked its symptoms to *Pittaja Nānātmaja Roga*, and Susruta classified *Sarvasara Mukharoga* under *Vataja, Pittaja, Kaphaja*, and *Raktaja* types.[15,16] Dalhana, in his commentary on *Susruta Samhita*, considered *Mukhapaka* as a *Pittaja Vikara.*[19]

***Nidana* (Causes)**

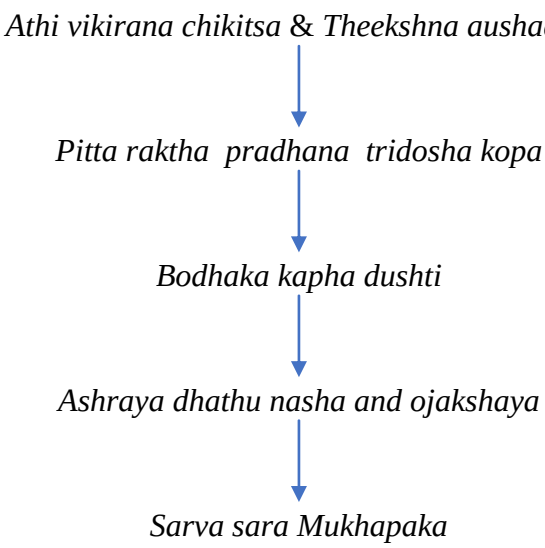
The causes of chemo-radiation–induced oral side effects relate to the *Agantuja Nidana* (external causes) of *Sarva-sara Mukharoga*—primarily *agni* (radiation) and *Tikshna Aushadhi* (strong chemotherapeutic drugs).[20]

***Samprapti* (Pathogenesis)**

The mucosal injury produced by chemotherapy and radiotherapy may be correlated with an *Abhighātajanya* factor, wherein direct cytotoxic and radiation-induced tissue injury acts as a local insult to the oral mucosa. The excessive heat and tissue-damaging effects of radiotherapy, together with the potent actions of chemotherapy and targeted therapies, may be

conceptually correlated with *Tīkṣṇa Agni* and *Tīkṣṇa Auṣadha*, leading to the aggravation of *Pitta* and *Rakta Doṣas*.

The vitiated *Pitta–Rakta* subsequently affects the oral mucosa, a *Kapha*-dominant region, resulting in disturbance and impairment of *Bodhaka Kapha* and its normal protective functions. This manifests as *dāha, vedanā, śotha* and *pāka*, resembling the clinical features described under *Sarvasara mukha pāka*. With continued exposure to the causative factors, persistent *Doṣa* aggravation and mucosal injury may lead to *Dhātu Kṣaya* (tissue depletion) and *Ojas Kṣaya* (reduced vitality), further compromising tissue integrity and healing.



***Roopa* (Clinical Features)**

The aggravation of *Pitta*-dominant *Tridosha* produces symptoms such as mucosal ulceration, dryness, burning, redness, discoloration, inflammation, increased heat, debility, and ulcer formation. These signs closely resemble *Sarvasara Mukhapaka*, as described in the *Mukharoga Vigjnaneeya* chapter of *Ashtanga Hridaya Uttarasthana.* The condition may gradually affect the lips, tongue, teeth, gums, and throat, eventually making mouth opening difficult. This interferes with proper food intake, leading to impaired formation of *rasa* and subsequent *dhatus*. If untreated, the entire body may suffer, and *ojas* can become depleted.[17]

***Roopa* According to *Dosha* Predominance[17]**

Vata	***Pitta***	***kapha***	***Rakta***
Aruna Ruksha vrana *Tamra oshta* *Sphutita Mukham*	*Daha* *Oosha* *Tiktha Vakrata* *Ksharokshitha sama vrana*	*Pichila vrana*	*Daha* *Oosha* *Tikta vakrata* *Ksharokshitha sama vrana*

Krichrena Vivrunothi			

***Sarva Sara Mukhapaka Chikitsa* According to Classical Texts**

Avoiding causative factors (*nidāna parivarjana*) and adopting pacifying therapies (*saṃśamana*) are the primary lines of treatment for *Mukhapāka.* Acharya Charaka has described several purification procedures (*śodhana karma*) such as *virechana*, *śirovirechana*, and various local treatments including *kavala*, *gandusha*, *pratiśāraṇa*, *charvana*, and *kāshayapāna.*[21]

Kabala, mentioned as an important therapy for *Mukharoga*, can be recommended as the main line of treatment.[22] The technique of *kabala* may help prevent possible drug interactions from other internal medications used during non surgical cancer therapies. Among the four types of *kabala* described in Ayurveda, *ropana kabala*—especially when prepared with substances having *kashaya*, *tikta*, and *madhura rasa*—is most suitable for this condition. Besides its wound-healing (*ropana*) action, *kabala* also helps manage diseases related to the neck, ears, oral cavity, eyes, throat, and lips. It improves strength of the jaw, enhances speech, strengthens teeth, promotes oral hygiene, improves taste perception, and increases appetite. Most of these problems correspond to the side effects of non surgical cancer therapies. Therefore, the proposed *Pitta-Pradhana Tridosha Shāmaka* formulation used in *kabala* form could be effective in reducing these oral side effects.[23]

Dugdhika kera thaila

Sl no	Drug	Scientific name
1	*Dugdhika*	*Euphorbia thymifolia*
2	*Narikela*	*Coccos Nucifera*

DISCUSSION

From an Ayurvedic perspective, the oral complications produced by chemotherapy and radiotherapy cannot be directly equated with a single classical *Mukharoga*. However, based on the principles described *Sushruta Samhita*, and *Ashtanga Hridaya*, the clinical presentation of ulcerative oral mucositis closely resembles *Sarvasara Mukharoga* which is described as a predominantly *Pitta*-dominant *Tridoṣaja* disorder affecting the entire oral cavity.[16,17]

The etiological factors responsible for the development of oral mucositis can be correlated with *Āgantujā Nidāna — Ativikiraṇa Cikitsā*, particularly *Atitīkṣṇa Agni* in the form of

radiation exposure and *Tīkṣṇa Auṣadhi* in the form of chemotherapeutic agents. These factors produce excessive aggravation of *Pitta* and *Rakta Doṣas*, leading to inflammation, ulceration, and tissue damage within the oral mucosa. Simultaneously, vitiation of *Bodhaka Kapha* impairs normal oral functions such as taste perception, lubrication, and maintenance of mucosal integrity, resulting in symptoms including burning sensation, dryness, altered taste, pain, and difficulty in mastication and swallowing. Persistent exposure to these aggressive therapeutic modalities causes progressive tissue destruction and impaired healing, ultimately leading to *Dhātu Kṣaya* and *Ojas Kṣaya*, reflecting systemic weakness and reduced vitality. Clinically, manifestations such as erythema, ulceration, increased local heat, tenderness, and restricted mouth opening closely resemble the features described for *Sarvasara Mukhapāka* in *susrutha samhitha.*[16] If left inadequately managed, the condition may interfere with food intake and nutrition, resulting in impaired tissue nourishment and deterioration of overall systemic health and quality of life.

During the inflammatory phase of ulcerative oral mucositis, erythema, burning sensation, edema, and ulcer formation occur due to epithelial injury and inflammatory cytokine release,[25] *Dugdhikā* (*Euphorbia thymifolia*) contains flavonoids, tannins, triterpenoids, and phenolic compounds which exhibit anti-inflammatory[26], antioxidant[27], analgesic[28], antimicrobial activities[29] and anti ulcerogenic activities thereby reducing oxidative stress, pain, and microbial invasion. *Cocos nucifera* contains lauric acid, capric acid, vitamin E, and polyphenols that help reduce inflammation and protect damaged mucosa from secondary infection.[30] It possesses immunomodulatory, antimicrobial, anti-inflammatory, mucosal protective, antiulcerogenic, and wound-healing properties, which collectively support oral mucosal protection, ulcer healing, tissue regeneration, and reduction in the severity of oral mucositis.[31]

In Ayurveda, these actions correlate with *Tikta* and *Kaṣāya rasa*, producing Pitta śamana, *Śothahara*, and *Vraṇa śodhana* effects that reduce burning sensation, swelling, and ulcer contamination. The tannins and flavonoids present in *Dugdhikā* exert antimicrobial and astringent actions that help cleanse the wound and reduce exudation. Lauric acid and monolaurin present in coconut possess potent antibacterial and antifungal properties, helping maintain oral hygiene and prevent opportunistic infection. These pharmacological actions correspond to *Vaktra śodhana, Saṅgrāhaka*, and the cleansing and contracting effects of *Kaṣāya rasa* described in Ayurveda.[24]

Actions On Wound Healing[24]

Rasa / Guna	Karma	Properties
Kaṭu	*Vraṇān Avasādayati, Śvayathu Nāśanam, Vaktra Śodhana*	Defloration and preparation of wound bed; cleansing of oral cavity
Kaṣāya	*Saṅgrāhaka, Pīḍana, Stambhana, Ropaṇa*	Controls discharge, contracts tissues, stabilizes ulcer surface and promotes healing
Tikta	*Pitta–Śleṣmaharam, Piyopaśoṣaṇam*	Reduces inflammation, dries excessive moisture and pus
Madhura	*Bṛṃhaṇa, Balya, Ropaṇa*	Nourishes tissues, promotes healing and strength
Śīta & Snigdha	*Dāha Praśamanam*	Soothes burning, relieves irritation, maintains lubrication

In the proliferative phase, fibroblast proliferation, collagen synthesis, angiogenesis, and granulation tissue formation occur. Flavonoids and triterpenoids in *Dugdhikā* promote fibroblast activity and collagen deposition, thereby accelerating tissue repair. Coconut lipids, amino acids, and micronutrients maintain moisture balance and provide nutritional support essential for cellular regeneration and epithelial growth. The antioxidant components also protect newly formed tissues from oxidative injury. In Ayurvedic terms, these effects are attributed to *Madhura rasa*, *Bṛṃhaṇa*, and *Vraṇa ropaṇa*, which nourish tissues and promote healing and regeneration.

During the re-epithelialization phase, closure of the ulcer surface and restoration of mucosal integrity take place. Phenolic compounds and flavonoids in *Dugdhikā* support epithelial cell migration and tissue remodeling, while vitamin E and essential fatty acids in coconut enhance mucosal barrier restoration and membrane stability. The moisturizing property of coconut also prevents dryness and irritation of healing mucosa. These actions correlate with *Ropaṇa karma*, and *Pitta-vāta śamana*, which restore normal mucosal structure and function.

In the remodeling or maturation phase, collagen fibers reorganize and the healed mucosa gains strength and stability. The antioxidant phytoconstituents of *Dugdhikā* and coconut reduce oxidative stress and prevent recurrent tissue injury, while the nutritive fatty acids and micronutrients improve tissue resilience and mucosal integrity. This helps reduce fibrosis, pain, and recurrence of ulceration.

Pharmacological Research Supporting Role In Ulcerative Oral Mucositis

According to *Sushruta Samhita Sūtra Sthāna*, “□□□□□□□□□□□□□□□□□□□ □□□□□□□□”□indicates the use of *Kabala* with drugs possessing *Kaṣāya, Tikta*, and *Madhura rasa* for *Vraṇa Ropaṇa* in *Mukhāntargata vraṇa* (oral ulcers). *Kabala* with *Dugdhikā* (*Euphorbia thymifolia*) and *Narikela* (*Cocos nucifera*) exerts significant wound-healing action through both pharmacological and local therapeutic effects. Flavonoids, tannins, and phenolic compounds in *Dugdhikā* promote fibroblast proliferation, collagen synthesis, granulation tissue formation, and epithelial regeneration, thereby accelerating ulcer healing, while the unctuous and soothing nature of *Narikela* reduces dryness, irritation, and friction and supports mucosal repair. Through repeated contact with the oral mucosa, *Kabala* cleanses oral debris, microorganisms, and inflammatory secretions, thereby reducing irritation and microbial load. It also stimulates salivary secretion through neuro-salivary reflexes, improving mucosal hydration and natural antimicrobial defense. The lipid-rich formulation forms a protective coating over the ulcerated mucosa, minimizing friction and facilitating re-epithelialization, while the rich vascularity of the oral mucosa enhances local absorption of active constituents and promotes faster tissue repair and *Vrana Ropaṇa*.

CONCLUSION

Kabala with *Dugdhikā Kera Taila* appears to be a safe and effective therapeutic approach for the management of ulcerative oral mucositis induced by non-surgical cancer therapies. It demonstrated beneficial effects in reducing ulcer severity and associated symptoms while improving oral health–related quality of life. The intervention was well tolerated, with no adverse effects reported, supporting its safety and clinical acceptability.

These findings highlight the potential of *Kabala* with *Dugdhikā Kera Taila* as a supportive therapeutic modality for promoting mucosal healing, alleviating oral discomfort, and improving oral health outcomes in patients undergoing non-surgical cancer therapies.

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