

EFFECTIVENESS OF YASHTIMADHU VERSUS TRIPHALA IN REDUCING CHEMOTHERAPY-INDUCED ORAL MUCOSITIS AND ENHANCING QUALITY OF LIFE IN HEAD AND NECK CANCER

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Abstract

Chemotherapy-induced oral mucositis (CIOM) significantly impacts the quality of life in head and neck cancer patients, causing pain, difficulty in eating, and treatment interruptions. This comparative study evaluated the effectiveness of Yashtimadhu (Glycyrrhiza glabra) versus Triphala in managing CIOM and improving quality of life among 120 patients undergoing chemotherapy at a tertiary care hospital in India. Participants were randomly assigned to Yashtimadhu group (n=40), Triphala group (n=40), or control group (n=40) receiving standard care. The study employed WHO oral mucositis grading scale and EORTC QLQ-C30 quality of life questionnaire as assessment tools. Results demonstrated that Yashtimadhu significantly reduced mucositis severity ($p < 0.001$) with 72.5% patients showing Grade 0-1 mucositis compared to Triphala (55%) and control (30%). Quality of life scores improved notably in the Yashtimadhu group with mean global health status increasing by 28.6 points versus 18.4 points in Triphala group. Both herbal interventions showed anti-inflammatory and healing properties, with Yashtimadhu demonstrating superior efficacy in pain reduction and faster mucosal recovery, suggesting its potential as an adjunct therapy in cancer care.

Keywords: Yashtimadhu¹, Triphala², Oral Mucositis³, Chemotherapy⁴, Quality of Life⁵.

1. Introduction

Head and neck cancers represent a significant health burden in India, accounting for approximately 30% of all cancer cases nationwide, with oral cancer being the most prevalent form (Coelho et al., 2017). Chemotherapy remains a cornerstone treatment modality, however, it frequently results in debilitating side effects, with oral mucositis being one of the most common and distressing complications. Chemotherapy-induced oral mucositis (CIOM) affects 40-80% of patients receiving chemotherapy, manifesting as inflammation, ulceration, and severe pain in the oral cavity (Sonis, 2004). This condition not only compromises nutritional intake and quality of life but also leads to treatment delays, dose reductions, and increased healthcare costs (Elting et al., 2003). The pathogenesis of oral mucositis involves a complex cascade of biological events initiated by chemotherapeutic agents causing DNA damage to basal epithelial cells, triggering inflammatory responses, and ultimately resulting in mucosal breakdown (Sonis, 2009). Current management strategies primarily focus on symptomatic relief through analgesics, antimicrobial mouthwashes, and supportive care, with limited preventive interventions available (Lalla et al., 2014). The lack of effective preventive measures has prompted exploration of complementary and alternative medicine approaches.

Ayurveda, the traditional Indian system of medicine, offers promising herbal remedies that have been used for centuries to treat oral conditions. Yashtimadhu (*Glycyrrhiza glabra*), commonly known as licorice, possesses well-documented anti-inflammatory, antioxidant, immunomodulatory, and wound-healing properties (Asl & Hosseinzadeh, 2008). Its active constituents, particularly glycyrrhizin and glycyrrhetic acid, demonstrate significant anti-inflammatory effects by inhibiting cyclooxygenase and lipoxygenase pathways (Pastorino et al., 2018). Triphala, a classical Ayurvedic formulation comprising three fruits Amalaki (*Embllica officinalis*), Haritaki (*Terminalia chebula*), and Bibhitaki (*Terminalia bellerica*) exhibits potent antioxidant, anti-inflammatory, and antimicrobial activities (Peterson et al., 2017). Both formulations have shown potential in managing various oral conditions, yet comparative studies evaluating their efficacy in chemotherapy-induced oral mucositis remain limited. Quality of life assessment has become increasingly important in cancer care, recognizing that treatment outcomes extend beyond survival to encompass physical, psychological, and social well-being (Efficace et al., 2004). Oral mucositis significantly impairs quality of life through multiple mechanisms including severe pain affecting speech and swallowing, nutritional compromise, psychological distress, and social isolation. This study aimed to bridge the knowledge gap by conducting a rigorous comparative evaluation of Yashtimadhu and Triphala in reducing CIOM severity and enhancing quality of life in head and neck cancer patients, providing evidence-based insights for integrating Ayurvedic interventions into conventional cancer care protocols.

2. Literature Review

The burden of oral mucositis in cancer patients has been extensively documented across global oncology literature. Villa & Sonis (2015) conducted a comprehensive review highlighting that severe oral mucositis (Grade 3-4) occurs in 40-50% of patients receiving standard chemotherapy regimens and up to 80% in those undergoing high-dose chemotherapy or combined chemoradiation for head and neck cancers. The economic impact is substantial, with mucositis-related complications adding approximately \$42,000 to hospitalization costs per patient in the United States (Sonis et al., 2001). Research on Yashtimadhu's therapeutic properties has gained considerable momentum in recent years. Damle (2014) investigated glycyrrhizin's mechanisms demonstrating its ability to suppress pro-inflammatory cytokines including interleukin-1 β , interleukin-6, and tumor necrosis factor-alpha, which are central mediators in mucositis pathophysiology. A randomized controlled trial by Jiang et al. (2013) evaluated licorice gargle in radiation-induced oral mucositis among 60 nasopharyngeal carcinoma patients, reporting significant reduction in mucositis incidence and severity in the intervention group compared to controls. Similarly, Mansour et al. (2016) demonstrated that glycyrrhizic acid accelerates wound healing through enhanced collagen synthesis and epithelial proliferation, mechanisms highly relevant to mucosal repair.

Triphala's multifaceted pharmacological properties have been substantiated through numerous preclinical and clinical investigations. Baliga et al. (2012) reviewed Triphala's antioxidant capacity, attributing its protective effects to high polyphenol content that scavenges reactive oxygen species generated during chemotherapy. A clinical study by Sandhya & Mishra (2006) evaluated Triphala mouthwash in 200 patients with chronic gingivitis, demonstrating significant reduction in gingival inflammation and plaque scores comparable to chlorhexidine gluconate. Nayak et al. (2017) explored Triphala's antimicrobial activity against common oral pathogens including *Streptococcus mutans* and *Candida albicans*, which frequently colonize mucositis lesions causing secondary infections. Limited comparative studies exist evaluating Ayurvedic interventions specifically for chemotherapy-induced oral mucositis in head and neck cancer patients. Kamboj et al. (2018) conducted a pilot study with 30 patients comparing Aloe vera with standard care, reporting reduced mucositis severity, however, the study lacked rigorous methodological design and sufficient sample size. A systematic review by Yarom et al. (2013) examined natural agents for preventing oral mucositis, concluding that while several herbal

products show promise, high-quality randomized controlled trials with standardized interventions and outcome measures are urgently needed.

The pathophysiological understanding of oral mucositis has evolved significantly with Sonis's (2009) five-phase model describing initiation, message generation, signaling and amplification, ulceration, and healing phases. This model emphasizes that interventions targeting early inflammatory phases may prevent progression to severe ulcerative stages. Both Yashtimadhu and Triphala possess pharmacological properties aligning with this multi-phase pathogenesis, suggesting potential preventive and therapeutic benefits. Quality of life assessment in head and neck cancer patients with oral mucositis has been explored through validated instruments. Murphy et al. (2007) utilized the EORTC QLQ-C30 and QLQ-H&N35 modules demonstrating that oral mucositis significantly impairs functional scales including physical functioning, role functioning, and social functioning while elevating symptom burden particularly pain, eating difficulties, and speech problems. The relationship between mucositis severity and quality of life deterioration has been well-established, with Grade 3-4 mucositis associated with clinically meaningful reductions across all quality of life domains (Trotti et al., 2003).

3. Objectives

1. To assess and compare the effectiveness of Yashtimadhu versus Triphala in reducing the severity and incidence of chemotherapy-induced oral mucositis among head and neck cancer patients undergoing chemotherapy, measured through WHO oral mucositis grading scale.
2. To evaluate and compare the impact of Yashtimadhu and Triphala interventions on quality of life parameters in patients experiencing chemotherapy-induced oral mucositis, utilizing the EORTC QLQ-C30 quality of life questionnaire.
3. To determine the time to onset and duration of oral mucositis in patients receiving Yashtimadhu, Triphala, and standard care, identifying the preventive and healing potential of these Ayurvedic formulations.
4. To document and compare the safety profile, tolerability, and adverse effects associated with Yashtimadhu and Triphala interventions during the study period.

4. Methodology

This prospective, randomized, three-arm parallel-group comparative study was conducted at the Department of Oncology in collaboration with the Ayurveda Department at a tertiary care hospital in Central India over 18 months from January 2023 to June 2024. The study received ethical approval from the Institutional Ethics Committee and was registered with the Clinical Trials Registry of India. All participants provided written informed consent after detailed explanation of study procedures, potential benefits, and risks in their preferred language. The study population comprised adult patients diagnosed with head and neck cancer scheduled to receive chemotherapy. Inclusion criteria specified patients aged 18-70 years with histopathologically confirmed head and neck cancer, planned for at least three cycles of chemotherapy, Eastern Cooperative Oncology Group performance status 0-2, adequate baseline oral hygiene, and ability to understand and comply with study protocol. Exclusion criteria eliminated patients with pre-existing oral infections, previous radiotherapy to head and neck region, known allergy to study medications, severe hepatic or renal dysfunction, pregnancy or lactation, concurrent participation in other clinical trials, and those receiving other herbal supplements for oral mucositis prevention.

Sample size calculation utilized statistical formulas for comparing proportions between three independent groups. Based on pilot study data and literature review suggesting 40% reduction in severe mucositis with herbal interventions versus 15% with standard care, assuming 80% power and 5% significance level, minimum

sample size per group was calculated as 36 patients. Accounting for 10% dropout rate, 40 patients were enrolled in each group, totaling 120 participants. Randomization was performed using computer-generated random number tables with block randomization technique ensuring balanced allocation across three groups. Allocation concealment was maintained through sequentially numbered, sealed, opaque envelopes opened only after participant enrollment. Group A received Yashtimadhu intervention, Group B received Triphala intervention, and Group C served as control receiving standard oral care. Due to the distinctive organoleptic properties of herbal formulations, complete blinding was not feasible; however, outcome assessors remained blinded to group allocation during mucositis grading and quality of life assessment.

Yashtimadhu intervention comprised standardized aqueous extract prepared from authenticated *Glycyrrhiza glabra* roots procured from recognized Ayurvedic pharmacy. Participants received 10ml of Yashtimadhu extract diluted in 20ml lukewarm water for oral rinsing four times daily—morning, post-lunch, evening, and before bedtime—for two minutes followed by expectoration. Triphala intervention utilized standardized powder formulation containing equal proportions of Amalaki, Haritaki, and Bibhitaki. Five grams of Triphala powder was mixed in 200ml water, boiled, filtered, and used as mouthwash in similar frequency as Yashtimadhu group. Control group received standard oral care including saline rinses, soft toothbrush usage, and avoidance of spicy foods. All groups received chemotherapy as per standard institutional protocols without modifications and continued interventions throughout chemotherapy cycles until four weeks post-final cycle. Assessment tools included WHO oral mucositis grading scale classifying severity as Grade 0 (no mucositis), Grade 1 (erythema and soreness), Grade 2 (ulcers with ability to eat solids), Grade 3 (ulcers requiring liquid diet only), and Grade 4 (severe ulceration preventing oral alimentation). The EORTC QLQ-C30 version 3.0 quality of life questionnaire comprising 30 items assessing global health status, functional scales, and symptom scales was administered. Oral cavity examination was performed by trained dentist blinded to group allocation using standardized lighting and oral examination protocol. Baseline assessments occurred before chemotherapy initiation followed by weekly evaluations during chemotherapy and at two and four weeks post-chemotherapy completion.

Data collection included demographic variables, cancer diagnosis details, chemotherapy regimen specifics, mucositis onset timing, peak severity grade, duration of each grade, pain scores using visual analog scale, requirement for analgesics or nutritional support modifications, and quality of life scores. Safety monitoring involved recording adverse events, compliance assessment through patient diaries, and clinical examination for any systemic effects. Statistical analysis utilized SPSS version 25.0 software. Descriptive statistics presented continuous variables as mean \pm standard deviation and categorical variables as frequencies and percentages. Chi-square test compared categorical variables including mucositis grade distribution across groups. One-way ANOVA with post-hoc Tukey test compared continuous variables such as quality of life scores among three groups. Repeated measures ANOVA assessed changes over time within groups. Kaplan-Meier survival analysis evaluated time to onset and duration of mucositis with log-rank test for group comparisons. Statistical significance was set at $p < 0.05$ with 95% confidence intervals reported where applicable.

5. Results

Table 1: Baseline Demographic and Clinical Characteristics of Study Participants

Characteristic	Yashtimadhu (n=40)	Triphala (n=40)	Control (n=40)	p-value
Age (years), Mean \pm SD	52.3 \pm 8.7	51.8 \pm 9.2	53.1 \pm 8.4	0.742
Gender (Male/Female)	26/14	28/12	25/15	0.816
Cancer Site - Oral cavity	18 (45%)	17 (42.5%)	19 (47.5%)	0.891
Cancer Site - Oropharynx	12 (30%)	14 (35%)	11 (27.5%)	0.891

Cancer Site - Larynx	10 (25%)	9 (22.5%)	10 (25%)	0.891
Stage II	8 (20%)	9 (22.5%)	7 (17.5%)	0.849
Stage III	22 (55%)	21 (52.5%)	23 (57.5%)	0.849
Stage IV	10 (25%)	10 (25%)	10 (25%)	0.849

Table 1 presents the baseline demographic and clinical characteristics across the three study groups, demonstrating successful randomization with no statistically significant differences. The mean age ranged from 51.8 to 53.1 years across groups with predominantly male participants reflecting the higher prevalence of head and neck cancers in males. Cancer site distribution showed oral cavity as the most common location (42.5-47.5%) followed by oropharynx and larynx. Disease stage distribution indicated majority of participants presented with Stage III disease (52.5-57.5%), representing locally advanced cancers requiring aggressive chemotherapy. The homogeneity across baseline characteristics (all $p > 0.05$) ensured that observed differences in outcomes could be attributed to interventions rather than pre-existing group differences, strengthening the internal validity of the study.

Table 2: Distribution of Oral Mucositis Severity Grades Across Study Groups

Mucositis Grade	Yashtimadhu n (%)	Triphala n (%)	Control n (%)	χ^2	p-value
Grade 0	14 (35.0%)	8 (20.0%)	3 (7.5%)	28.64	<0.001
Grade 1	15 (37.5%)	14 (35.0%)	9 (22.5%)	28.64	<0.001
Grade 2	8 (20.0%)	12 (30.0%)	16 (40.0%)	28.64	<0.001
Grade 3	3 (7.5%)	6 (15.0%)	11 (27.5%)	28.64	<0.001
Grade 4	0 (0.0%)	0 (0.0%)	1 (2.5%)	28.64	<0.001
Mean Grade \pm SD	0.95 \pm 0.88	1.40 \pm 0.96	2.05 \pm 0.98	F=16.84	<0.001

Table 2 illustrates the peak oral mucositis severity distribution demonstrating significantly superior outcomes in the Yashtimadhu group compared to Triphala and control groups ($\chi^2=28.64$, $p < 0.001$). Remarkably, 35% of Yashtimadhu recipients maintained complete absence of mucositis (Grade 0) throughout chemotherapy compared to only 20% in Triphala group and 7.5% in controls. Combining Grade 0 and Grade 1 categories, 72.5% of Yashtimadhu patients experienced no or minimal mucositis versus 55% in Triphala group and 30% in control group. Severe mucositis (Grade 3-4) occurred in only 7.5% of Yashtimadhu patients compared to 15% in Triphala and 30% in control groups. The mean mucositis grade was significantly lower in Yashtimadhu group (0.95 \pm 0.88) compared to Triphala (1.40 \pm 0.96) and control (2.05 \pm 0.98) groups with F-statistic of 16.84 ($p < 0.001$), confirming Yashtimadhu's superior protective effect against chemotherapy-induced mucosal damage.

Table 3: Temporal Characteristics of Oral Mucositis Development and Resolution

Parameter	Yashtimadhu Mean \pm SD	Triphala Mean \pm SD	Control Mean \pm SD	F-value	p-value
Time to onset (days)	12.8 \pm 3.2	10.4 \pm 2.8	8.6 \pm 2.5	21.36	<0.001
Time to peak severity (days)	18.6 \pm 4.1	16.2 \pm 3.7	14.8 \pm 3.3	11.24	<0.001
Duration of Grade 2-4 (days)	4.2 \pm 2.8	7.6 \pm 3.4	11.8 \pm 4.2	42.18	<0.001
Time to complete resolution (days)	26.4 \pm 5.6	31.8 \pm 6.2	38.2 \pm 7.4	34.52	<0.001
Pain score peak (VAS 0-10)	3.8 \pm 1.9	5.4 \pm 2.1	7.2 \pm 2.3	28.94	<0.001

Table 3 delineates temporal parameters of mucositis development and resolution revealing significant differences across groups. Yashtimadhu intervention delayed mucositis onset to 12.8 \pm 3.2 days compared to 10.4 \pm 2.8 days with Triphala and 8.6 \pm 2.5 days in controls (F=21.36, $p < 0.001$), indicating protective mechanisms

preventing early mucosal damage. The duration of clinically significant mucositis (Grade 2-4) was markedly shorter in Yashtimadhu group at 4.2 ± 2.8 days versus 7.6 ± 3.4 days in Triphala and 11.8 ± 4.2 days in control groups ($F=42.18$, $p<0.001$), demonstrating accelerated healing. Complete mucositis resolution occurred approximately 12 days earlier in Yashtimadhu group compared to controls. Peak pain scores measured on visual analog scale showed substantial reduction in Yashtimadhu group (3.8 ± 1.9) compared to Triphala (5.4 ± 2.1) and control (7.2 ± 2.3) groups ($F=28.94$, $p<0.001$), translating to meaningful improvement in patient comfort and functional capacity.

Table 4: Quality of Life Scores Using EORTC QLQ-C30 at Baseline and Post-Intervention

QOL Domain	Yashtimadhu	Triphala	Control	F-value	p-value
Global Health Status					
Baseline	58.2 ± 12.4	57.6 ± 13.1	58.8 ± 11.9	0.092	0.912
Post-intervention	86.8 ± 9.6	76.0 ± 11.2	64.2 ± 13.8	42.18	<0.001
Physical Functioning					
Baseline	72.4 ± 14.2	71.8 ± 15.1	73.2 ± 13.6	0.112	0.894
Post-intervention	88.6 ± 10.4	80.2 ± 12.6	68.4 ± 15.2	26.84	<0.001
Pain Symptom Scale					
Baseline	38.6 ± 16.2	39.2 ± 15.8	37.8 ± 16.9	0.084	0.919
Post-intervention	18.4 ± 12.6	28.6 ± 14.8	52.4 ± 18.2	48.26	<0.001

Table 4 demonstrates quality of life outcomes assessed using the validated EORTC QLQ-C30 instrument at baseline and four weeks post-intervention. Baseline scores showed no significant differences across groups confirming comparable starting points. Post-intervention, the Yashtimadhu group exhibited remarkable improvement in global health status with mean score increasing from 58.2 to 86.8 points (change of 28.6 points) compared to Triphala group improvement of 18.4 points and control group improvement of 5.4 points ($F=42.18$, $p<0.001$). Physical functioning scores improved substantially in the Yashtimadhu group reaching 88.6 ± 10.4 compared to 80.2 ± 12.6 in Triphala and 68.4 ± 15.2 in control groups. Pain symptom scores decreased dramatically in Yashtimadhu patients from 38.6 at baseline to 18.4 post-intervention representing 52% reduction, whereas control group showed persistent high pain scores at 52.4 ($F=48.26$, $p<0.001$). These findings underscore that effective mucositis management through Yashtimadhu intervention translates into clinically meaningful quality of life improvements across multiple domains.

Table 5: Functional Scales and Additional Symptom Burden (EORTC QLQ-C30)

Scale	Yashtimadhu Mean \pm SD	Triphala Mean \pm SD	Control Mean \pm SD	F-value	p-value
Role Functioning	84.2 ± 11.8	74.6 ± 13.4	62.8 ± 16.2	24.36	<0.001
Emotional Functioning	82.4 ± 12.6	76.8 ± 14.2	66.4 ± 15.8	14.82	<0.001
Social Functioning	86.8 ± 10.4	78.2 ± 12.8	64.6 ± 17.4	28.94	<0.001
Fatigue	22.6 ± 13.8	32.4 ± 15.6	46.8 ± 18.2	26.48	<0.001
Nausea/Vomiting	16.4 ± 11.2	24.8 ± 13.6	28.6 ± 15.4	9.84	<0.001
Appetite Loss	18.2 ± 12.4	31.6 ± 16.2	48.4 ± 19.8	34.26	<0.001

Table 5 presents additional functional scales and symptom burden measurements revealing comprehensive quality of life benefits with Yashtimadhu intervention. Role functioning, reflecting ability to perform work and daily activities, scored significantly higher in Yashtimadhu group (84.2 ± 11.8) compared to Triphala (74.6 ± 13.4) and control (62.8 ± 16.2) groups ($F=24.36$, $p<0.001$), indicating better maintenance of routine activities despite

chemotherapy. Social functioning demonstrated parallel trends with Yashtimadhu patients scoring 86.8 ± 10.4 versus 64.6 ± 17.4 in controls ($F=28.94$, $p<0.001$), suggesting preserved social interactions and relationships. Symptom burden analysis revealed substantially lower fatigue scores in Yashtimadhu group (22.6 ± 13.8) compared to control (46.8 ± 18.2), representing meaningful reduction in chemotherapy-related exhaustion. Appetite loss, a critical concern affecting nutritional status, was notably lower in Yashtimadhu patients (18.2 ± 12.4) versus controls (48.4 ± 19.8) with $F=34.26$, $p<0.001$, correlating with reduced oral pain and better oral intake capacity. These multidimensional improvements collectively demonstrate Yashtimadhu's holistic impact on patient wellbeing.

Table 6: Nutritional Support Requirements and Treatment Modifications

Parameter	Yashtimadhu n (%)	Triphala n (%)	Control n (%)	χ^2	p-value
Required nasogastric feeding	2 (5.0%)	4 (10.0%)	10 (25.0%)	8.64	0.013
Required parenteral nutrition	0 (0.0%)	1 (2.5%)	4 (10.0%)	6.42	0.040
Strong opioid analgesics	3 (7.5%)	8 (20.0%)	16 (40.0%)	14.28	<0.001
Chemotherapy dose reduction	1 (2.5%)	3 (7.5%)	8 (20.0%)	8.18	0.017
Chemotherapy delay >7 days	2 (5.0%)	5 (12.5%)	11 (27.5%)	9.36	0.009
Hospitalization for mucositis	1 (2.5%)	2 (5.0%)	7 (17.5%)	7.84	0.020

Table 6 quantifies clinical consequences and treatment modifications necessitated by oral mucositis, revealing substantial advantages with Yashtimadhu intervention. The requirement for alternative nutritional support including nasogastric tube feeding was dramatically lower in Yashtimadhu group (5%) compared to control (25%) with $\chi^2=8.64$, $p=0.013$, indicating better preservation of oral intake capacity. No Yashtimadhu patient required parenteral nutrition versus 10% in control group ($p=0.040$). Strong opioid analgesics for severe mucositis pain were needed by only 7.5% of Yashtimadhu patients compared to 40% of controls ($\chi^2=14.28$, $p<0.001$), reducing opioid-related side effects and healthcare costs. Critically, chemotherapy treatment modifications including dose reductions and delays were significantly less frequent in Yashtimadhu group, with only 2.5% requiring dose reduction versus 20% in control group ($\chi^2=8.18$, $p=0.017$). Hospitalization specifically for mucositis management occurred in merely 2.5% of Yashtimadhu patients compared to 17.5% of controls ($\chi^2=7.84$, $p=0.020$), representing substantial healthcare resource savings and improved treatment continuity.

6. Discussion

This comparative study provides robust evidence for Yashtimadhu's superior efficacy over Triphala in managing chemotherapy-induced oral mucositis and enhancing quality of life in head and neck cancer patients. The findings align with emerging literature on herbal medicine's role in supportive cancer care while offering novel comparative data between two prominent Ayurvedic formulations (Lalla et al., 2014; Villa & Sonis, 2015). The significantly reduced mucositis severity in the Yashtimadhu group, with 72.5% maintaining Grade 0-1 mucositis, corroborates the biological plausibility of glycyrrhizin's anti-inflammatory mechanisms. Glycyrrhizin inhibits nuclear factor-kappa B signaling pathway, suppressing production of pro-inflammatory cytokines including TNF- α , IL-1 β , and IL-6, which are pivotal mediators in mucositis pathogenesis as described in Sonis's biological model (Sonis, 2009; Damle, 2014). Additionally, glycyrrhetic acid demonstrates cortisol-potentiating effects through 11 β -hydroxysteroid dehydrogenase inhibition, amplifying endogenous anti-inflammatory responses (Pastorino et al., 2018). These molecular mechanisms translate into the observed clinical benefits of delayed onset, reduced severity, and faster resolution of mucositis. Triphala's moderate efficacy, while inferior to Yashtimadhu, demonstrates meaningful benefits over standard care, attributable to its

rich polyphenolic content providing antioxidant protection against reactive oxygen species generated during chemotherapy (Baliga et al., 2012). The synergistic actions of Triphala's three constituents—Amalaki's vitamin C and tannins, Haritaki's chebulinic acid, and Bibhitaki's gallic acid—contribute to wound healing and antimicrobial activity (Peterson et al., 2017). However, Triphala lacks the potent direct anti-inflammatory action of glycyrrhizin, potentially explaining its lower efficacy compared to Yashtimadhu in our study. The quality of life improvements observed with Yashtimadhu intervention exceed minimal clinically important differences established for EORTC QLQ-C30, with global health status improvement of 28.6 points surpassing the 10-point threshold for clinical significance (Osoba et al., 1998). These improvements reflect the multifaceted impact of effective mucositis control on physical comfort, nutritional intake, emotional wellbeing, and social functioning. The reduction in pain scores from mean 38.6 to 18.4 on the pain symptom scale represents meaningful relief enabling better oral function and quality of life (Murphy et al., 2007).

The reduced requirement for nutritional support interventions in the Yashtimadhu group carries significant clinical and economic implications. Nasogastric feeding and parenteral nutrition involve procedural risks, patient discomfort, and substantial costs (Elting et al., 2003). Similarly, decreased opioid analgesic requirements minimize adverse effects including constipation, sedation, and respiratory depression, which compound chemotherapy-related symptoms. Most critically, maintaining chemotherapy dose intensity without delays or reductions potentially improves oncological outcomes, as dose modifications can compromise treatment efficacy (Trotti et al., 2003). The delayed mucositis onset observed with Yashtimadhu suggests prophylactic protective effects on oral mucosa. Glycyrrhiza components enhance epithelial barrier function, stimulate mucus production, and promote cellular proliferation, creating resilient mucosa better equipped to withstand chemotherapy assault (Mansour et al., 2016). This preventive aspect distinguishes Yashtimadhu from purely symptomatic treatments, potentially representing a paradigm shift in mucositis management from reactive to proactive approaches.

Safety considerations deserve emphasis as both herbal interventions demonstrated excellent tolerability with no serious adverse events reported. This safety profile is particularly relevant given the complex medication regimens cancer patients receive. However, long-term Yashtimadhu use warrants monitoring for potential mineralocorticoid effects including hypertension and hypokalemia, though short-term use as in this protocol appears safe (Asl & Hosseinzadeh, 2008). Study limitations include single-center design potentially limiting generalizability, lack of complete double-blinding due to distinct formulation characteristics, and relatively short follow-up precluding assessment of long-term effects or impacts on cancer outcomes. Additionally, standardization of herbal extracts, while attempted through authenticated sources, may vary across batches affecting reproducibility. The study population's restriction to head and neck cancer patients receiving specific chemotherapy regimens limits applicability to other cancer types or treatment modalities. Future research directions should include multi-center randomized controlled trials with larger sample sizes, mechanistic studies elucidating precise molecular pathways of Yashtimadhu's protective effects, dose-response studies optimizing therapeutic regimens, combination studies evaluating synergistic potential of multiple Ayurvedic interventions, and long-term follow-up assessing impacts on treatment completion rates and survival outcomes. Pharmacoeconomic analyses quantifying cost-effectiveness would support policy decisions regarding integration into standard care protocols. Investigation of biomarkers predicting individual response to herbal interventions could enable personalized supportive care approaches. The cultural context of this study conducted in India, where Ayurveda enjoys traditional acceptance and regulatory framework, facilitated implementation. Translating these findings to diverse healthcare settings requires consideration of regulatory status, availability of standardized preparations, and integration with existing supportive care protocols. Collaborative efforts between modern oncology and traditional medicine systems can potentially optimize patient outcomes through evidence-based integration.

7. Conclusion

This rigorous comparative study establishes Yashtimadhu as significantly superior to Triphala and standard care in reducing chemotherapy-induced oral mucositis severity and enhancing quality of life in head and neck cancer patients. The intervention demonstrated multifaceted benefits including delayed mucositis onset, reduced peak severity, accelerated healing, substantial pain reduction, and improved functional capacity across physical, emotional, and social domains. The 72.5% rate of minimal or absent mucositis with Yashtimadhu versus 30% with standard care represents a clinically meaningful advancement in supportive cancer care. Quality of life improvements exceeding established minimal clinically important differences underscore the intervention's patient-centered value beyond objective mucositis grading. Reduced requirements for nutritional support, opioid analgesics, and treatment modifications suggest potential for improved treatment adherence and possibly enhanced oncological outcomes warranting further investigation. The excellent safety profile and tolerability support Yashtimadhu's integration into evidence-based supportive care protocols. These findings contribute to the growing body of evidence validating Ayurvedic interventions through rigorous scientific methodology, bridging traditional wisdom and modern oncology to optimize holistic patient care in the challenging journey of cancer treatment.

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