

RESTORATION OF TH1/TH2 IMMUNE BALANCE AND CYTOKINE MODULATION IN ORAL SQUAMOUS CELL CARCINOMA: EVIDENCE FROM AN AUTOLOGOUS EX VIVO STUDY USING TRIPHALA

Thayalan Dineshkumar^{1*}, Nirmala Anandan², Krishnan Rajkumar³, Indumathi N⁴, A Emmanuel Dhiravia Sargunam⁵

^{1*}Associate Professor, Department of Oral Pathology and Microbiology, SRM Dental College, Bharathi Salai, Ramapuram Campus, Chennai – 600089, Tamilnadu, India, Mail Id: drtdineshkumar@gmail.com

²Professor & Head, Department of Biochemistry SRM Dental College, Bharathi Salai, Ramapuram Campus, Chennai – 600089, Tamilnadu, India, Mail Id: nirmalaa@srmist.edu.in

³Professor & Head, Department of Oral Pathology and Microbiology, SRM Dental College, Bharathi Salai, Ramapuram Campus, Chennai – 600089, Tamilnadu, India, Mail Id: drrajakumar22163@gmail.com

⁴Assistant Professor, Department of Oral Pathology and Microbiology, Government Dental College, Pudukottai, Tamilnadu, India, Mail Id: drindumathimds123@gmail.com

⁵Professor, Department of Oral and Maxillofacial Surgery, Sri Ramachandra Dental College, Sri Ramachandra Institute of Higher Education and Research, Porur, Chennai – 600116, Tamilnadu, India, Mail Id: emmanuelazariah@sriramachandra.edu.in

ABSTRACT

Background: Oral squamous cell carcinoma (OSCC) is characterized by tumour-induced immune dysregulation, particularly involving altered cytokine signaling and impaired lymphocyte function. A shift toward a Th2-dominant immunosuppressive environment contributes to tumour progression and therapeutic resistance. Triphala, a traditional polyherbal formulation, has demonstrated immunomodulatory properties; however, its effect on cytokine modulation and immune polarization in OSCC remains inadequately explored.

Aim: To evaluate the effect of Triphala on cytokine expression and Th1/Th2 immune polarization in lymphocytes derived from OSCC patients.

Materials and Methods: This ex vivo study included forty histopathologically confirmed OSCC patients. Autologous lymphocytes and primary OSCC cells were isolated and cultured. Lymphocytes were treated with increasing concentrations of Triphala (25–500 µg/ml), and cytokine levels (IL-2, TNF-α, IFN-γ, IL-6, and IL-10) were quantified using ELISA in a co-culture system. The Th1/Th2 ratio was calculated to assess immune polarization. Statistical analysis was performed using repeated measures ANOVA with Tukey post hoc test and Pearson correlation analysis.

Results: Triphala treatment resulted in significant upregulation of Th1 cytokines (IL-2, TNF-α, IFN-γ) and suppression of IL-6, with a moderate increase in IL-10. This led to a progressive increase in the Th1/Th2 ratio, indicating a shift toward a Th1-dominant immune response. Peak immunomodulatory effects were observed at 300 µg/ml, beyond which a plateau was noted. The increase in Th1/Th2 ratio was associated with reduced tumour cell viability, supporting enhanced immune-mediated tumour suppression.

Conclusion: Triphala effectively modulates cytokine expression and restores immune balance in OSCC by promoting Th1 polarization. These findings support its potential as an adjunct immunomodulatory agent targeting tumour-associated immune suppression.

KEYWORDS: Triphala; OSCC; Cytokine profiling; Th1/Th2 balance; Immune polarization; Immunomodulation

1. INTRODUCTION

Oral squamous cell carcinoma (OSCC) is one of the most prevalent malignancies of the oral cavity, particularly in South and Southeast Asia, and continues to be associated with significant morbidity and mortality despite advances in therapeutic strategies [1,2]. The persistently low five-year survival rate, largely attributed to late diagnosis, recurrence, and therapeutic resistance, highlights the need for novel adjunctive approaches targeting underlying disease mechanisms [3,4]. Increasing evidence suggests that immune dysregulation within the tumor microenvironment plays a central role in OSCC progression, with particular emphasis on altered cytokine signaling and impaired lymphocyte function [5].

Cytokines form a complex regulatory network that governs the balance between tumor-promoting inflammation and effective antitumor immunity. In OSCC, this balance is often disrupted, with a shift toward a Th2-dominant immunosuppressive state characterized by elevated levels of interleukin-6 (IL-6) and interleukin-10 (IL-10), alongside reduced expression of key Th1 cytokines such as interleukin-2 (IL-2) and interferon-gamma (IFN-γ) [6,7]. This imbalance contributes to lymphocyte dysfunction, impaired cytotoxic responses, and tumor immune evasion. Restoration of Th1/Th2 equilibrium has therefore emerged as a critical therapeutic target in cancer immunology [8,9].

Recent advances in immunotherapy have demonstrated the potential of immune modulation in improving cancer outcomes; however, these approaches are often limited by high cost, systemic toxicity, and variable patient response [10]. This has led to growing interest in plant-derived immunomodulators, which offer a multi-targeted and physiologically balanced approach to immune regulation. Triphala, a traditional Ayurvedic polyherbal formulation composed of *Terminalia chebula*, *Terminalia bellirica*, and *Embolica officinalis*, has gained attention for its antioxidant, anti-

inflammatory, and immunomodulatory properties [11,12]. Experimental studies suggest that its bioactive constituents, including gallic acid and ellagic acid, can modulate key signaling pathways such as NF- κ B and STAT3, thereby influencing cytokine expression and immune cell function [13].

A key strength of the present study lies in its use of an autologous ex vivo model, wherein lymphocytes and primary OSCC cells were derived from the same patient. This approach enables a more physiologically relevant assessment of immune–tumor interactions compared to conventional cell line-based studies. Furthermore, the study focuses on functional cytokine profiling and immune polarization rather than isolated biomarker evaluation, thereby providing a more integrated understanding of immune modulation within the OSCC microenvironment.

Despite these promising findings, there remains a lack of direct evidence evaluating the effect of Triphala on cytokine dynamics and immune polarization in OSCC using patient-derived immune cells. Most existing studies rely on indirect markers or non-clinical models, limiting their translational relevance.

Therefore, the present study aims to evaluate the effect of Triphala on cytokine expression and Th1/Th2 immune polarization in lymphocytes derived from OSCC patients, thereby providing insight into its potential role in restoring tumor-associated immune imbalance.

2. MATERIALS AND METHODS

2.1 Study Design and Ethical Approval

This ex vivo experimental study was conducted using samples obtained from patients diagnosed with oral squamous cell carcinoma (OSCC). The study protocol was reviewed and approved by the Institutional Ethics Committee of SRM Dental College and Hospital (Approval Number: SRMDC/IRB/2019/PhD/No.120). Written informed consent was obtained from all participants prior to sample collection.

2.2 Sample Size Determination

The sample size was calculated using G*Power software based on expected effect size, statistical power, and significance level derived from prior studies. A minimum sample size of 40 was determined to achieve adequate statistical validity, and all analyses were performed on samples obtained from forty histopathologically confirmed OSCC patients.

2.3 Study Population and Sample Collection

Patients aged between 30 and 50 years with TNM stage I–III and histopathologically confirmed OSCC were included in the study. Peripheral venous blood samples and tumor tissue specimens were collected under aseptic conditions. Blood samples were used for isolation of lymphocytes, while tumor tissues were processed for establishment of primary OSCC cell cultures.

2.4 Isolation of Lymphocytes and Primary OSCC Cell Culture

Peripheral blood lymphocytes were isolated using standard density gradient centrifugation techniques. The purity and viability of isolated cells were confirmed prior to experimental use. Primary OSCC cell cultures were established from tumor tissue samples. Tissues were washed, minced, and digested using collagenase and DNase, followed by filtration and centrifugation to obtain a single-cell suspension. Cells were cultured in RPMI-1640 medium supplemented with fetal bovine serum and antibiotics and maintained at 37 °C in a humidified atmosphere containing 5% CO₂. Cells between passages 2 and 4 were used for experimental assays.

2.5 Preparation of Triphala Extract

Triphala was prepared using dried fruits of *Terminalia chebula*, *Terminalia bellirica*, and *Embolica officinalis* mixed in equal proportions. The powdered formulation was subjected to Soxhlet extraction using ethanol, followed by concentration under reduced pressure. The dried extract was reconstituted in dimethyl sulfoxide and serially diluted to obtain working concentrations ranging from 25 to 500 μ g/mL for experimental use.

2.6 Experimental Design and Treatment Protocol

Isolated lymphocytes were exposed to increasing concentrations of Triphala (25–500 μ g/ml). A co-culture system was established using autologous lymphocytes and primary OSCC cells to simulate the tumor microenvironment. Following treatment with increasing concentrations of Triphala (25–500 μ g/ml), the cultures were incubated for 48 hours, after which the supernatants were collected for cytokine analysis. In addition, lymphocyte-mediated cytotoxicity against primary OSCC cells was assessed indirectly through tumor cell viability in the co-culture system.

2.7 Cytokine Analysis

Cytokine levels in the culture supernatants were quantified using enzyme-linked immunosorbent assay (ELISA). The cytokines assessed included interleukin-2 (IL-2), tumor necrosis factor-alpha (TNF- α), interferon-gamma (IFN- γ), interleukin-6 (IL-6), and interleukin-10 (IL-10), representing Th1 and Th2 immune responses.

2.8 Assessment of Immune Polarization (Th1/Th2 Ratio)

The Th1/Th2 ratio was calculated to evaluate immune polarization. Th1 cytokines (IL-2, TNF- α , IFN- γ) and Th2 cytokines (IL-6, IL-10) were analyzed collectively to determine the shift in immune balance following Triphala treatment.

2.9 Statistical Analysis:

Data were analyzed using repeated measures analysis of variance (ANOVA) to compare cytokine levels across different concentrations of Triphala. Tukey's post hoc test was applied for multiple comparisons. Pearson correlation analysis was

performed to evaluate the relationship between Th1/Th2 immune polarization and tumor cell viability. A p-value of <0.05 was considered statistically significant.

3. RESULTS

3.1 Baseline Characteristics of Study Participants

The present study included 40 clinically and histopathologically confirmed cases of oral squamous cell carcinoma. The study population comprised individuals across a range of age groups (30 – 50 years) with a male predominance, consistent with known epidemiological trends of OSCC. All patients had a history of tobacco chewing, smoking, alcohol consumption, or a combination of these habits. Lesions were most commonly located on the tongue (n = 19), followed by buccal mucosa (n = 11), alveolar mucosa (n = 6), palate (n = 3), and lip (n = 1). Histopathological grading revealed 20 well-differentiated, 14 moderately differentiated, and 6 poorly differentiated carcinomas. Clinically, 22 patients were classified as stage I, 15 as stage II, and 3 as stage III. The baseline demographic and clinical characteristics of the study participants are summarized in Table 1.

3.2 Effect of Triphala on Cytokine Expression

Triphala treatment resulted in a significant, dose-dependent modulation of cytokine levels in the lymphocyte–OSCC co-culture system, reflecting altered immune responses within a tumor-relevant microenvironment. Th1 cytokines, including interleukin-2 (IL-2), tumor necrosis factor-alpha (TNF- α), and interferon-gamma (IFN- γ), demonstrated a progressive increase with increasing concentrations of Triphala. Specifically, IL-2 levels increased from 12.5 ± 1.2 pg/ml in the control group to 42.6 ± 2.7 pg/ml at 300 μ g/ml, TNF- α from 22.3 ± 1.3 pg/ml to 60.8 ± 2.4 pg/ml, and IFN- γ from 16.4 ± 1.1 pg/ml to 56.3 ± 3.5 pg/ml.

In contrast, interleukin-6 (IL-6) levels showed a consistent decrease across treatment concentrations, reducing from 109.8 ± 5.1 pg/ml in the control group to 51.8 ± 3.2 pg/ml at 300 μ g/ml. Interleukin-10 (IL-10) exhibited a moderate increase, rising from 9.8 ± 0.5 pg/ml to 29.6 ± 1.9 pg/ml at the same concentration, indicating a controlled regulatory response.

The maximal cytokine modulation was observed at 300 μ g/ml, beyond which a plateau or slight decline was noted at higher concentrations. Repeated measures ANOVA confirmed that these changes were statistically significant across concentrations ($p < 0.001$), with post hoc analysis demonstrating significant intergroup differences. The detailed cytokine expression values are presented in Table 2, and the corresponding statistical analysis is summarized in Table 3.

3.3 Th1/Th2 Immune Polarization

To evaluate the overall immune balance, the Th1/Th2 ratio was calculated based on the collective expression of Th1 cytokines (IL-2, TNF- α , IFN- γ) and Th2 cytokines (IL-6, IL-10). To minimize bias arising from differences in the number and magnitude of cytokines within each group, cytokine values were normalized prior to ratio calculation. Triphala treatment resulted in a progressive increase in the Th1/Th2 ratio across increasing concentrations, indicating a shift toward a Th1-dominant immune response.

At baseline, the Th1/Th2 ratio was low at 0.43, reflecting a Th2-skewed immunosuppressive state characteristic of OSCC. With increasing concentrations of Triphala, the ratio increased steadily, reaching a peak value of 1.96 at 300 μ g/ml, beyond which a plateau was noted at higher concentrations.

The observed shift in immune polarization corresponded with the increase in Th1 cytokines and reduction in IL-6 levels, suggesting restoration of immune equilibrium within the tumor microenvironment. Statistical analysis confirmed that the changes in Th1/Th2 ratio across concentrations were significant ($p < 0.001$). The detailed values of the Th1/Th2 ratio are presented in Table 4.

3.4 Correlation Between Immune Polarization and Tumor Cell Viability

To assess the functional relevance of cytokine modulation, correlation analysis was performed between the Th1/Th2 ratio and tumor cell viability in the lymphocyte–OSCC co-culture system. A strong negative correlation was observed, indicating that an increase in Th1/Th2 ratio was associated with a reduction in tumor cell viability.

Tumor cell viability decreased progressively with increasing concentrations of Triphala, reducing from $100 \pm 4.04\%$ in the control group to $48.7 \pm 3.1\%$ at 300 μ g/ml. This reduction corresponded with the increase in Th1/Th2 ratio, reflecting enhanced lymphocyte-mediated cytotoxic activity. Pearson correlation analysis demonstrated a statistically significant inverse relationship between immune polarization and tumor cell viability ($r = -0.969$, $p < 0.001$).

These findings suggest that the Triphala-induced shift toward a Th1-dominant immune response is functionally associated with improved anti-tumor activity. The detailed correlation data are presented in Figure 1.

3.5 Dose–Response Relationship and Optimal Concentration

A clear dose-dependent relationship was observed following treatment with increasing concentrations of Triphala. Progressive enhancement of Th1 cytokine expression, reduction in IL-6 levels, and an increase in the Th1/Th2 ratio were noted from 25 μ g/ml to 300 μ g/ml. These changes were accompanied by a corresponding decrease in tumor cell viability, indicating enhanced immune-mediated anti-tumor activity.

The maximal immunomodulatory effect was observed at 300 μ g/ml, which demonstrated peak Th1 cytokine levels, optimal Th1/Th2 polarization, and the greatest reduction in tumor cell viability. Beyond this concentration, a plateau or slight decline in cytokine response and immune activity was observed at higher concentrations (500 μ g/ml), suggesting a saturation effect.

These findings indicate that 300 μ g/ml represents the optimal concentration for Triphala-mediated immune activation in this experimental model, beyond which no additional functional benefit is achieved.

4. DISCUSSION

Cytokines play a central role in regulating the tumor–immune interface, and their effects can be either pro-tumorigenic or anti-tumorigenic. Pro-tumor cytokines such as IL-6, IL-8, and TGF- β promote tumor growth and metastasis, while also impairing immune responses. Conversely, anti-tumor cytokines including IL-2, IFN- γ , and TNF- α enhance the T and NK cell cytotoxicity and facilitate tumor cell apoptosis. Some cytokines, like IL-10, exhibit dual functions: at low levels they regulate excessive inflammation and support immune balance, but when chronically elevated they can suppress cytotoxic responses and aid immune escape [14]. Thus, the cytokine milieu acts as a critical determinant of tumor progression or regression, and interventions that shift this balance toward an anti-tumor profile hold significant therapeutic promise in OSCC [15,16].

The present study demonstrates that Triphala effectively modulates the immune microenvironment in oral squamous cell carcinoma by promoting a shift from a Th2-dominant immunosuppressive state toward a Th1-mediated anti-tumor response. This was evidenced by a significant increase in Th1 cytokines, reduction in IL-6 levels, elevation of the Th1/Th2 ratio, and a corresponding decrease in tumor cell viability.

The observed shift toward a Th1-dominant immune response reflects coordinated modulation of key cytokines involved in anti-tumor immunity. The increase in IL-2, IFN- γ , and TNF- α indicates enhanced lymphocyte activation and cytotoxic function, which are essential for tumor cell elimination. In contrast, the reduction in IL-6 suggests suppression of tumor-promoting inflammatory signaling [17,18], while the moderate increase in IL-10 may represent a regulatory response preventing excessive immune activation [19]. The resultant increase in the Th1/Th2 ratio highlights a reprogramming of the immune response from a tumor-promoting to a tumor-suppressive phenotype, which is particularly relevant in OSCC where immune evasion is a hallmark of disease progression [20].

These findings are consistent with previous studies that have demonstrated the immunomodulatory potential of herbal formulations in modulating cytokine balance and enhancing anti-tumor immunity [21]. Triphala, in particular, has been reported to possess antioxidant and anti-inflammatory properties, with its bioactive constituents influencing key signaling pathways involved in immune regulation. However, most existing studies have relied on indirect markers or non-clinical models, limiting their translational applicability. In contrast, the present study employs an autologous lymphocyte–OSCC co-culture model, allowing direct assessment of immune responses in a tumor-relevant microenvironment. This provides functional evidence linking cytokine modulation to tumor cell cytotoxicity, thereby enhancing the clinical relevance of the findings.

The strong inverse correlation observed between the Th1/Th2 ratio and tumor cell viability further supports the functional significance of immune polarization. This relationship indicates that the Triphala-induced shift toward a Th1-dominant response is associated with enhanced immune-mediated tumor suppression, rather than merely reflecting biochemical changes in cytokine levels.

The dose–response pattern observed in this study, with maximal effects at 300 μ g/ml followed by a plateau at higher concentrations, suggests a saturation phenomenon. This may be attributed to receptor-level saturation or activation of feedback regulatory mechanisms that limit excessive immune stimulation. Such a response is consistent with the concept of physiological immunomodulation, where optimal activity is achieved within a specific concentration range.

Despite these promising findings, the study has certain limitations. The experimental design is based on an *ex vivo* model and does not account for systemic immune interactions, pharmacokinetics, or tumor vascular influences present *in vivo*. In addition, the study evaluates the effect of Triphala as a composite formulation without fractionating individual bioactive components. Variability in immune responses among patients was also not stratified, which may influence the generalizability of the findings.

Future studies should focus on validating these findings in *in vivo* models and clinical settings, with particular emphasis on dose optimization, long-term immune responses, and safety profiling. Further investigation into the molecular mechanisms underlying Triphala-mediated immune modulation may also provide insights into its potential integration with existing immunotherapeutic strategies.

In summary, the present study demonstrates that Triphala modulates cytokine dynamics and promotes a shift toward a Th1-dominant immune response in OSCC. This immunological reprogramming is associated with enhanced tumor cell cytotoxicity, supporting its potential role in restoring tumor-associated immune imbalance.

5. CONCLUSION

Triphala demonstrated significant immunomodulatory effects in oral squamous cell carcinoma by enhancing Th1 cytokine responses and restoring immune balance within the tumor microenvironment. The observed shift toward a Th1-dominant response was associated with reduced tumor cell viability, indicating improved immune-mediated anti-tumor activity. These findings highlight the potential of Triphala as a promising adjunct immunomodulatory agent in OSCC, warranting further validation through *in vivo* and clinical studies.

Declaration of generative AI use: The authors report generative AI was not used in their research or preparation of this manuscript

Disclosure of Interest: The authors report there are no competing interests to declare

REFERENCES

1. Fatima J, Fatima E, Mehmood F, Ishtiaq I, Khan MA, Khurshid HMS, Kashif M. Comprehensive Analysis of Oral Squamous Cell Carcinomas: Clinical, Epidemiological, and Histopathological Insights With a Focus on Prognostic Factors and Survival Time. *Cureus*. 2024 Feb 18;16(2):e54394.
2. Gangane NM, Ghongade PV, Patil BU, Atram M. Oral cavity cancer incidence and survival trends: A population-based study. *J Cancer Res Ther*. 2024 Jul 1;20(5):1446-1452.
3. Surekha R. Oral cancer: Recent breakthroughs in pathology and therapeutic approaches. *Oral Oncol Rep*. 2024;12:100678.
4. Shetty KSR, Kurle V, Greeshma P, Ganga VB, Murthy SP, Thammaiah SK, et al. Salvage surgery in recurrent oral squamous cell carcinoma. *Front Oral Health*. 2022;2:815606.
5. Tufail M, Jiang CH, Li N. Immune evasion in cancer: mechanisms and cutting-edge therapeutic approaches. *Signal Transduct Target Ther*. 2025;10(1):227.
6. Chiamulera MMA, Zancan CB, Remor AP, Cordeiro MF, Gleber-Netto FO, Baptistella AR. Salivary cytokines as biomarkers of oral cancer: a systematic review and meta-analysis. *BMC Cancer*. 2021;21(1):205.
7. Shao Q, Li H, Tian Y. Immunological balance skewing Th1,Th17 towards Th2,Treg in OSCC of hamster induced by 7,12- dimethylbenz[a]anthracene. *BMC Oral Health*. 2025;25(1):1394.
8. Zhu J, Yamane H, Paul WE. Differentiation of effector CD4 T cell populations (*). *Annu Rev Immunol*. 2010;28:445-89.
9. Wang R, Yin G, Guo W, Li N, Zhang Y, Chen X, Huang Z. Analysis of Th1/Th2 cytokine profile and clinical characteristics of patients with head and neck squamous cell carcinoma. *Biomol Biomed*. 2024;24(6):1776-14.
10. Gupta S, Singh A, Deorah S, Tomar A. Immunotherapy in OSCC: Current trend and challenges. *Crit Rev Oncol Hematol*. 2025;209:104672.
11. Bairwa VK, Kashyap AK, Meena P, Jain BP. Triphala's characteristics and potential therapeutic uses in modern health. *Int J Physiol Pathophysiol Pharmacol*. 2025;17(2):19-36.
12. Dineshkumar T, Anandan N, Rajkumar K, Nandhakumar I. Immunomodulatory effects of Triphala and its constituents in oral squamous cell carcinoma and oral precancer. *J Oral Maxillofac Pathol*. 2024;28(4):657-64.
13. Li S, Wang Y, Sun R, Franceschi D, Pan H, Wei C et al. Single-Cell Transcriptome Analysis Reveals Different Immune Signatures in HPV- and HPV + Driven Human Head and Neck Squamous Cell Carcinoma. *J Immunol Res*. 2022;2022:2079389.
14. Carlini V, Noonan DM, Abdalalem E, Goletti D, Sansone C, Calabrone L, Albini A. The multifaceted nature of IL-10: regulation, role in immunological homeostasis and its relevance to cancer, COVID-19 and post-COVID conditions. *Front Immunol*. 2023;14:1161067.
15. Niklander SE. Inflammatory Mediators in Oral Cancer: Pathogenic Mechanisms and Diagnostic Potential. *Front Oral Health*. 2021;2:642238.
16. Wang H, Wang T, Yan S, Tang J, Zhang Y, Wang L et al. Crosstalk of pyroptosis and cytokine in the tumor microenvironment: from mechanisms to clinical implication. *Mol Cancer*. 2024;23(1):268
17. Rani NAJ, Vardhan BGH, Srinivasan S, Gopal SK. Evaluation of Salivary Interleukin-6 in Patients with Oral Squamous Cell Carcinoma, Oral Potentially Malignant Disorders, Chronic Periodontitis and in Healthy Controls - A Cross Sectional Comparative Study. *Ann Maxillofac Surg*. 2023;13(1):70-5.
18. Yadav A, Kumar B, Datta J, Teknos TN, Kumar P. IL-6 promotes head and neck tumor metastasis by inducing epithelial-mesenchymal transition via the JAK-STAT3-SNAIL signaling pathway. *Mol Cancer Res*. 2011;9(12):1658-67
19. Belapurkar P, Goyal P, Tiwari-Barua P. Immunomodulatory effects of triphala and its individual constituents: a review. *Indian J Pharm Sci*. 2014;76(6):467-75.
20. Wang R, Yin G, Guo W, Li N, Zhang Y, Chen X, Huang Z. Analysis of Th1/Th2 cytokine profile and clinical characteristics of patients with head and neck squamous cell carcinoma. *Biomol Biomed*. 2024;24(6):1776-14.
21. Srikumar R, Jeya Parthasarathy N, Sheela Devi R. Immunomodulatory activity of triphala on neutrophil functions. *Biol Pharm Bull*. 2005;28(8):1398-403.