Published Online: 2024 November 20

Research Article



The Effect of *Cordia myxa* Mouthwash on the Incidence and Severity of Stomatitis in Leukemia Patients Undergoing Chemotherapy: A Protocol Study

Mostafa Javadi (**b**¹, Shahram Molavynejad (**b**^{2,*}, Bayan Saberipoor (**b**², Ahmad Ahmadzadeh Deilami³, Amir Siahpoosh (**b**⁴, Seyed Ali Mousavi⁵, Masoomeh Salehi Kambo⁵

¹ Department of Nursing, School of Nursing and Midwifery, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

² Nursing Care Research Center in Chronic Diseases, School of Nursing and Midwifery, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

³ Thalassemia and Hemoglobinopathy Research Center, Health Research Institute, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

⁴ Medicinal Plant Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

⁵ Shoushtar Faculty of Medical Sciences, Shoushtar, Iran

* Corresponding Author: Nursing Care Research Center in Chronic Diseases, School of Nursing and Midwifery, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran. Email: shahrambaraz@ajums.ac.ir

Received: 28 April, 2024; Revised: 20 September, 2024; Accepted: 15 October, 2024

Abstract

Background: Stomatitis, or oral inflammation, is one of the common complications in patients undergoing chemotherapy, causing pain, discomfort, infection, and prolonged hospitalization.

Objectives: The purpose of this study is to investigate the effect of *Cordia myxa* mouthwash on preventing stomatitis in patients undergoing chemotherapy.

Methods and Result: This study will be a double-blind, single-center, randomized controlled clinical trial focusing on 60 patients undergoing chemotherapy. The samples will be randomly divided into intervention and control groups. In addition to receiving the routine Betadine mouthwash, participants in the intervention group will receive a solution of 30 drops of 5% *C. myxa* formulation in 20 cc of water, and they will be asked to put the solution in their mouth, swirl it for a minute, and then spit it out. In the control group, in addition to Betadine mouthwash, a sterile water placebo (with the same taste and smell) will be used. The data will be analyzed based on statistical tests using SPSS version 22.

Conclusions: If this intervention proves effective in improving access and adherence to treatment, it would represent a step forward in addressing a chronic health problem common among leukemia patients undergoing chemotherapy. Given its natural essence and the fact that it is not associated with any complications, *C. myxa* mouthwash can be used safely alongside the main treatment to prevent and reduce the severity of mouth ulcers caused by chemotherapy.

Keywords: Stomatitis, Chemotherapy, Mouthwash, Cordia myxa, Nursing

1. Background

Leukemia is a type of blood cancer caused by the excessive production of white blood cell-forming tissues, leading to a significant increase in premature or abnormal WBCs in the blood circulation (1, 2). Chemotherapy is a systemic and common method to treat leukemia. However, the side effects of chemotherapy result in adverse anatomical and functional conditions, such as dysphagia, vomiting,

diarrhea, malnutrition, arthralgia, bleeding, anemia, and mucositis (stomatitis) (3).

Oral mucositis is one of the most common complications, occurring in almost 40% of patients undergoing chemotherapy (4). Chemotherapy induces inflammation and ulceration through tissue damage caused by a sequence of chemical, metabolic, and biological events that occur in several stages. Stomatitis typically begins within the first week of treatment and peaks in the second week (3). These oral ulcers can cause

Copyright © 2025, Javadi et al. This open-access article is available under the Creative Commons Attribution 4.0 (CC BY 4.0) International License (https://creativecommons.org/licenses/by/4.0/), which allows for unrestricted use, distribution, and reproduction in any medium, provided that the original work is properly cited.

pain, dysphagia, difficulties in eating, swallowing, speaking, increased hospitalizations (5), weight loss, local infection (6), physical limitations, psychological

discomfort, and impaired quality of life for patients (7). Moreover, the disrupted oral mucosa caused by stomatitis can be fatal for patients, as it provides a pathway for the entry of pathogenic microorganisms, leading to various infections, including life-threatening septicemia (8). Additionally, patients with high-grade mucositis often need to reduce their chemotherapy regimen, resulting in delays in cancer treatment and a worsened prognosis (9).

Despite the devastating clinical consequences of oral mucositis, there is no effective treatment to prevent or reduce it in patients. Oral and gastrointestinal mucositis remains a significant challenge for individuals undergoing cancer treatment. The few interventions supported by solid evidence are not universally applicable to all types of oral mucositis, nor are their effects on tissues fully understood. This lack of clarity leads to varied and often arbitrary protocols with significant differences between medical centers (9). Although some complementary and alternative medicines, such as medicinal herbs, have been used to prevent and treat stomatitis, their therapeutic effects have not been conclusively confirmed (10).

One medicinal plant with a long history of proven therapeutic effects is the Assyrian plum, scientifically known as Cordia myxa L. It is the most common species within the genus Cordia, belonging to the Boraginaceae family, and is generally found in tropical and semi-arid regions. C. myxa grows in tropical, dry, and moist deciduous forests. In traditional (ancient) medicine, it is used to treat throat and chest ailments, relieve gallbladder issues, quench thirst, relieve hoarseness, and treat heartburn, as well as bladder and intestinal ulcers (11). Different parts of the plant, such as the fruit, bark, leaves, and seeds, are utilized for their anti-fever, antioxidant, anti-diabetic, anti-ulcer, immunemodulating, and anti-cancer properties. Additionally, this plant has been used as a remedy for impotence, stomach pain, asthma, oral ulcers, bronchitis, diarrhea, cardiovascular diseases, rheumatism, and tooth decay (12-15).

The fruit, leaves, seeds, and bark of this plant contain pyrrolizidine alkaloids, flavonoids, saponins, terpenes, and sterols (16, 17). Recently, the presence of rutin, along with p-coumaric acid or caffeic acid, has been identified in C. myxa. Rosmarinic acid, which is also present, exhibits various biological activities such as antioxidant, anti-inflammatory, and neuroprotective effects (18). Cordia myxa possesses antimicrobial, anti-inflammatory, analgesic, and diuretic effects and is used to treat disorders of the digestive, respiratory, genitourinary, cardiac, vascular, and blood systems (19). Both in acute and chronic phases, the hydro-alcoholic extract of C. myxa fruit has demonstrated analgesic and antiinflammatory properties (20). In 2001, Al-Awadi et al. showed that experimental colitis could be treated using the C. myxa fruit preparation 170, which possesses antiinflammatory qualities. The dichloromethane and ethyl acetate fractions of C. myxa showed notable antiinflammatory effectiveness, with inhibition percentages of 45.16% and 40.26%, respectively, which were relatively close to that of indomethacin (51.61%) when comparing the complete ethanol extract and various fractions of C. *myxa* leaves (21).

In Iran, *C. myxa* L. grows in tropical and subtropical regions, particularly in the south and southwest of the country (22). The fruit and leaves of this plant are readily available at an affordable price in these regions.

2. Objectives

Since no similar research has been conducted on the effects of this fruit on the prevention of oral ulcers, this study aims to investigate the effect of *C. myxa* mouthwash on the incidence and severity of stomatitis in leukemia patients undergoing chemotherapy.

3. Methods and Results

3.1. Design and Setting

The present study is a double-blind, randomized controlled clinical trial conducted on leukemia patients undergoing chemotherapy in the oncology departments of Baqaei 2 Hospital, affiliated with Ahvaz Jundishapur University of Medical Sciences in Ahvaz.

3.2. Participants

Using the following statistical formula and assuming parameters ($P_1 = 0.73$), ($P_2 = 0.38$), ($\alpha = 0.05$), ($\beta = 0.20$), and an anticipated attrition rate of 15%, the sample size has been set at (n = 60) for both the intervention and control groups.

$$n = \frac{\left(z_{1-\frac{\alpha}{2}+} z_{1-\beta+P_2}\right)^2 \left[P_1(1-P_1) + P_2\left(1-P_2\right)\right]}{\left(P_1-P_2\right)^2}$$
(1)

Patients meeting the following criteria will be eligible to participate in this study: Aged 18 or older, recently diagnosed with acute leukemia, receiving a consistent chemotherapy regimen for two weeks, fully conscious, without ulcers in the mouth area, and without conditions such as asthma, diabetes, allergies, or other allergic diseases. Additional criteria include not using narcotic drugs or other mouthwash solutions and not receiving radiotherapy. Withdrawal criteria will include any change in chemotherapy regimen or occurrence of systemic infection during the study.

3.3. Randomization and Blinding/Masking

Patients who meet the inclusion criteria will be assigned to either the intervention or control group using the permutation block randomization method. A randomization list will be prepared by a statistician and provided to the first author. In this list, patients will be randomly assigned to the intervention and control groups, labeled as codes A and B, and made available to the first author. The sequence of assignments will be concealed in consecutively numbered opaque envelopes, with each envelope opened only at the time of intervention.

3.4. Control of Bias

In this study, both the researcher (first author) and the patients will be blinded to group allocation. Patients will remain unaware of their group assignment. A pharmacologist will label the primary drug and placebo with codes C and D, respectively, and will then provide them to the first author for intervention. The physician responsible for assessing oral stomatitis will also be blinded to the group assignments.

3.5. Intervention Protocol

Both groups will be provided with soft toothbrushes and instructed on proper brushing techniques. Additionally, both groups will be taught the correct way to use the mouthwash. In the oncology departments where this study will be conducted, a 1% Betadine mouthwash solution (5 cc of Betadine in 500 cc of saline) is routinely used to prevent stomatitis.

In the intervention group, in addition to the routine 1% Betadine mouthwash, patients will be instructed to add 30 drops of a 5% mucilage formulation of *C. myxa* to 20 cc of water. They will then place this solution in their mouths, swirl it for one minute, and spit it out. Patients will be advised to avoid eating or drinking anything for 1 hour after using the mouthwash.

In the control group, in addition to the Betadine mouthwash, patients will receive a placebo—sterile water with the same taste and smell—delivered in a glass with a dropper.

For a period of 14 days, patients in both groups will brush their teeth using a soft toothbrush and the same toothpaste three times daily, after breakfast, lunch, and dinner, followed by the designated mouthwash. On days one, seven, and fourteen, an attending physician will examine the mouths of all patients individually, recording findings using the World Health Organization (WHO) stomatitis checklist.

3.6. Ethical Considerations

This study will be approved by the Ethics Committee of Ahvaz Jundishapur University of Medical Sciences (Ref ID: IR.AJUMS.REC.1398.752). Before assignment to study groups, patients will be briefed on the study objectives, and informed consent will be obtained from each participant. They will be assured of their anonymity throughout the study, that all personal information will remain confidential, and that they may withdraw from the study at any time if they wish. Patients who are not part of the intervention group will continue to receive all essential hospital services and treatments. Additionally, the study will be registered in Iranian Registry of Clinical Trials the (IRCT20180511039610N2, Registration date: 2018-10-24). Outcome Assessment: Variables and Measurement Instruments

To evaluate the study objectives, a specialist doctor will assess the oral area for signs of mucositis on days one, seven, and fourteen in both the intervention and control groups.

3.7. Independent Variables

- Condition or group: Use of mouthwash with a 5% *C. myxa* mucilage formulation in addition to a 1% Betadine mouthwash (intervention group) or a sterile water

placebo mouthwash in addition to a 1% Betadine mouthwash (control group).

- Demographic data: Age, sex, marital status, educational attainment, chemotherapy regimen, and use of painkillers.

3.8. Dependent Variable

- Evaluation of oral mucositis: The primary dependent variable is the severity of oral mucositis.

3.9. Oral Mucositis Evaluation

The severity of oral mucositis (stomatitis) will be assessed using a checklist based on criteria from the WHO and the National Cancer Institute (NCI) (23). According to WHO criteria, stomatitis is classified as follows: Grade 0: No stomatitis; grade I: Erythema and soreness of the oral mucosa, potentially involving the inner cheeks, but without ulceration; grade II: Presence of ulcers in the mouth; however, the patient is still able to eat; grade III: Ulcers accompanied by extensive erythema; the patient is unable to eat solid foods and requires a liquid diet; grade IV: Severe inflammation and ulcers that make oral feeding impossible; the patient is limited to liquid intake only.

This grading will help objectively assess the severity and progression of oral mucositis in each patient.

The NCI Scale is a graded scale for assessing oral mucositis severity as follows: Zero indicates no visible change, 1 indicates the presence of erythema, 2 denotes patchy ulcers up to 1.5 cm in diameter, 3 indicates patchy ulcers larger than 1.5 cm in diameter, and 4 represents ulcers with necrosis and bleeding. In this study, oral mucositis will be considered severe if classified as Grade 3 or 4 on either the NCI or WHO Scales.

The secondary outcomes include the difference in the score between the initial and final evaluations on the HADS survey (Hospital Anxiety and Depression Scale), a 14-question survey assessing anxiety and depression. Additionally, another secondary outcome is the difference in the quality of life score, as defined by the EQ-5D survey, between the initial evaluation and the assessment conducted three months post-surgery.

Data will be expressed as mean and standard deviation for continuous quantitative variables with a normal distribution, as median and interquartile range for quantitative variables with a non-normal distribution, and as frequency and percentage for qualitative variables. The normality of data distribution will be assessed using the Shapiro-Wilk test, while homoscedasticity will be checked using the Fisher-Snedecor test. Comparisons between independent groups will be analyzed using the χ^2 or Fisher's exact test for categorical variables. Baseline outcomes on the first, seventh, and fourteenth days will be compared between the control and intervention groups using the *t*-test or the Mann-Whitney test, depending on data distribution.

To evaluate the trend of oral ulcer presentation on the first, seventh, and fourteenth days, Friedman's repeated measures analysis or generalized estimating equations (GEE) will be employed, based on data normality. The significance level is set at 0.95 to identify significant differences between variables; thus, P-values less than 0.05 will be considered statistically significant. Data analysis will be conducted using SPSS 23.0 statistical software. If the frequency of missing data exceeds 5%, additional analyses will be performed using imputation methods.

4. Discussion

The expected result is to prevent the occurrence of stomatitis or to reduce its incidence through an intervention using C. myxa mouthwash as a complementary treatment. The C. myxa mouthwash is safe, easy to use, and does not interfere with other treatments or interventions, making it feasible for incorporation into routine nursing care for patients undergoing chemotherapy, both in hospital and at home. The use of this mouthwash could potentially lower the costs associated with treating oral stomatitis. However, its effects and cost-effectiveness remain largely unstudied, and it is not yet supported by the Ministry of Health and Medical Education of Iran. This study aims to expand our knowledge about the benefits of C. myxa mouthwash, providing evidence for its effectiveness against stomatitis. These findings could have significant implications for public policymakers as well as oncologists.

The results of Hemati et al. indicated that the mucilage of *C. myxa* significantly inhibited the growth of eight strains of gram-negative and gram-positive pathogenic bacteria under laboratory conditions (24). Similarly, Nariya et al. investigated the antibacterial and antifungal effects of the bark of a *C. myxa* species, demonstrating that the bark possesses both antifungal and antibacterial properties (25).

One limitation of the present study is the potential for genetic variability in patients' susceptibility to nausea and vomiting, which is beyond the researcher's control. Another limitation is the small sample size, as the study was conducted in only one hospital. Additionally, factors such as psychological stress, genetics, nutritional imbalances, immune and hormonal changes, and allergies are all recognized as important contributors to the etiology of mouth ulcerations.

Footnotes

Authors' Contribution: Research conception and design: M. J., S. M., B. S., A. A. D., and A. S.; data collection: B. S. S. A. M., and M. S. K.; analysis and interpretation of data: S. M., B. S. S., A. M., and M. S. K.; drafting of the manuscript: M. J., S. M., B. S., A. A. D., A. S., S. A. M., and M. S. K.; review and editing: M. J., S. M., B. S., A. A. D., and A. S. All authors contributed to the article and approved the submitted version.

Clinical Trial Registration Code: The author will observe the ethical principles of research work of the Declaration of Helsinki. This investigation was registered in the Iranian Registry of Clinical Trials Center (IRCT20180511039610N2).

Conflict of Interests Statement: The authors declare that they have no conflict of interest about this working.

Data Availability: The dataset presented in the study is available on request from the corresponding author during submission or after publication.

Ethical Approval: At first, a written permit will obtain to conduct the research, and the proposal was approved under the code IR.AJUMS.REC.1397.110 by the Ethics Committee of Ahvaz Jundishapur University of Medical Sciences.

Funding/Support: This study was drawn from a research project (NCRCCD-9703) sponsored by deputy of research and technology of AJUMS. The payment was spent on the design and implementation of the study.

Informed Consent: Written informed consents will also obtain from the participants.

References

- Shysh AC, Nguyen LT, Guo M, Vaska M, Naugler C, Rashid-Kolvear F. The incidence of acute myeloid leukemia in Calgary, Alberta, Canada: a retrospective cohort study. *BMC Public Health J.* 2017;**18**(1):94. [PubMed ID: 28774275]. [PubMed Central ID: PMC5543578]. https://doi.org/10.1186/s12889-017-4644-6.
- Whiteley AE, Price TT, Cantelli G, Sipkins DA. Leukaemia: a model metastatic disease. *Nat Rev Cancer J.* 2021;21(7):461-75. [PubMed ID: 33953370]. [PubMed Central ID: PMC8722462]. https://doi.org/10.1038/s41568-021-00355-z.
- Lee YH, Hong J, Kim I, Choi Y, Park HK. Prospective evaluation of clinical symptoms of chemotherapy-induced oral mucositis in adult patients with acute leukemia: A preliminary study. *Clin Exp Dent Res J.* 2020;6(1):90-9. [PubMed ID: 32067405]. [PubMed Central ID: PMC7025998]. https://doi.org/10.1002/cre2.253.
- Ribeiro ILA, Limeira RRT, Dias de Castro R, Ferreti Bonan PR, Valenca AMG. Oral Mucositis in Pediatric Patients in Treatment for Acute Lymphoblastic Leukemia. *Int J Environ Res Public Health*. 2017;**14**(12). [PubMed ID: 29182564]. [PubMed Central ID: PMC5750887]. https://doi.org/10.3390/ijerph14121468.
- Rambod M, Pasyar N, Ramzi M. The effect of zinc sulfate on prevention, incidence, and severity of mucositis in leukemia patients undergoing chemotherapy. *Eur J Oncol Nurs.* 2018;**33**:14-21. [PubMed ID: 29551172]. https://doi.org/10.1016/j.ejon.2018.01.007.
- Pulito C, Cristaudo A, Porta C, Zapperi S, Blandino G, Morrone A, et al. Oral mucositis: the hidden side of cancer therapy. *J Exp Clin Cancer Res.* 2020;**39**(1):210. [PubMed ID: 33028357]. [PubMed Central ID: PMC7542970]. https://doi.org/10.1186/s13046-020-01715-7.
- Martinez JM, Pereira D, Chacim S, Mesquita E, Sousa I, Martins A, et al. Mucositis care in acute leukemia and non-Hodgkin lymphoma patients undergoing high-dose chemotherapy. *Support Care Cancer J*. 2014;22(9):2563-9. [PubMed ID: 24743853]. https://doi.org/10.1007/s00520-014-2199-y.
- Costa RC, Bezerra PMM, Damascena LCL, Ribeiro ILA, Bonan PRF, de Sousa SA, et al. Impact of Saliva and Cariogenic Microbiota on the Chemotherapy-Induced Oral Mucositis in Oncopediatric Patients: A Preliminary Longitudinal Study. Int J Dent. 2020;2020:1243953.
 [PubMed ID: 33163075]. [PubMed Central ID: PMC7605952]. https://doi.org/10.1155/2020/1243953.
- Elad S, Yarom N, Zadik Y, Kuten-Shorrer M, Sonis ST. The broadening scope of oral mucositis and oral ulcerative mucosal toxicities of anticancer therapies. *CA Cancer J Clin*. 2022;**72**(1):57-77. [PubMed ID: 34714553]. https://doi.org/10.3322/caac.21704.
- Meyer-Hamme G, Beckmann K, Radtke J, Efferth T, Greten HJ, Rostock M, et al. A survey of chinese medicinal herbal treatment for chemotherapy-induced oral mucositis. *Evid Based Complement Alternat Med.* 2013;2013:284959. [PubMed ID: 24285975]. [PubMed Central ID: PMC3830834]. https://doi.org/10.1155/2013/284959.
- Jamkhande PG, Barde SR, Patwekar SL, Tidke PS. Plant profile, phytochemistry and pharmacology of Cordia dichotoma (Indian cherry): a review. *Asian Pac J Trop Biomed*. 2013;3(12):1009-16. [PubMed ID: 24093795]. [PubMed Central ID: PMC3805104]. https://doi.org/10.1016/S2221-1691(13)60194-X.
- El-Newary SA, Sulieman AM, El-Attar SR, Sitohy MZ. Hypolipidemic and antioxidant activity of the aqueous extract from the uneaten pulp of the fruit from Cordia dichotoma in healthy and hyperlipidemic Wistar albino rats. J Nat Med. 2016;70(3):539-53. [PubMed ID: 26968538]. https://doi.org/10.1007/s11418-016-0973-5.
- 13. Hatware KV, Sharma S, Patil K, Shete M, Karri S, Gupta G. Evidence for gastroprotective, anti-inflammatory and antioxidant potential of

methanolic extract of Cordia dichotoma leaves on indomethacin and stress induced gastric lesions in Wistar rats. *Biomed Pharmacother*. 2018;**103**:317-25. [PubMed ID: 29660650]. https://doi.org/10.1016/j.biopha.2018.04.007.

- Ozbayer C, Kurt H, Ozdemir Z, Tuncel T, Moheb Saadat S, Burukoglu D, et al. Gastroprotective, cytoprotective and antioxidant effects of Oleum cinnamomi on ethanol induced damage. *Cytotechnol J.* 2014;66(3):431-41. [PubMed ID: 23868387]. [PubMed Central ID: PMC3973792]. https://doi.org/10.1007/s10616-013-9594-y.
- Saeed SMG, Ali SA, Faheem K, Ali R, Giuffre AM. The Impact of Innovative Plant Sources (Cordia myxa L. Fruit (Assyrian Plum) and Phoenix dactylifera L. Biowaste (Date Pit)) on the Physicochemical, Microstructural, Nutritional, and Sensorial Properties of Gluten-Free Biscuits. *Food J.* 2022;11(15). [PubMed ID: 35954112]. [PubMed Central ID: PMC9368538]. https://doi.org/10.3390/foods11152346.
- Oza MJ, Kulkarni YA. Traditional uses, phytochemistry and pharmacology of the medicinal species of the genus Cordia (Boraginaceae). J Pharm Pharmacol. 2017;69(7):755-89. [PubMed ID: 28266011]. https://doi.org/10.1111/jphp.12715.
- Rahman MA, Sahabjada AJ. Evaluation of anticancer activity of Cordia dichotoma leaves against a human prostate carcinoma cell line, PC3. J Tradit Complement Med. 2017;7(3):315-21. [PubMed ID: 28725626]. [PubMed Central ID: PMC5506664]. https://doi.org/10.1016/j.jtcme.2016.11.002.
- Kendir G, Bae HJ, Kim J, Jeong Y, Bae HJ, Park K, et al. The effects of the ethanol extract of Cordia myxa leaves on the cognitive function in mice. *BMC Complement Med Ther*. 2022;**22**(1):215. [PubMed ID: 35948926]. [PubMed Central ID: PMC9367120]. https://doi.org/10.1186/s12906-022-03693-z.

- Matias EFF, Alves EF, do Nascimento Silva MK, de Alencar Carvalho VR, Coutinho HDM, da Costa JGM. The genus Cordia: botanists, ethno, chemical and pharmacological aspects. *Brazil J Pharmacogn*. 2015;25(5):542-52. https://doi.org/10.1016/j.bjp.2015.05.012.
- Ranjbar M, Varzi HN, Sabbagh A, Bolooki A, Sazmand A. Study on analgesic and anti-inflammatory properties of Cordia myxa fruit hydro-alcoholic extract. *Pak J Biol Sci.* 2013;16(24):2066-9. [PubMed ID: 24517032]. https://doi.org/10.3923/pibs.2013.2066.2069.
- Al-Awadi FM, Srikumar TS, Anim JT, Khan I. Antiinflammatory effects of Cordia myxa fruit on experimentally induced colitis in rats. *Nutr J.* 2001;17(5):391-6. https://doi.org/10.1016/s0899-9007(01)00517-2.
- 22. Saki J, Khademvatan S, Pazyar N, Eskandari A, Tamoradi A, Nazari P. In Vitro Activity of Cordia myxa Mucilage Extract Against Leishmania major and L. infantum Promastigotes. *Jundishapur J Microbiol.* 2015;**8**(3). https://doi.org/10.5812/jjm.19640.
- Martins AFL, Nogueira TE, Morais MO, Oton-Leite AF, Valadares MC, Batista AC, et al. Effect of photobiomodulation on the severity of oral mucositis and molecular changes in head and neck cancer patients undergoing radiotherapy: a study protocol for a cost-effectiveness randomized clinical trial. *Trial J.* 2019;**20**(1):97. [PubMed ID: 30709370]. [PubMed Central ID: PMC6359861]. https://doi.org/10.1186/s13063-019-3196-8.
- Hemati E, Jooyandeh H, Alizadeh Behbahani B, Noshad M. Antimicrobial potential of Cordia myxa fruit on pathogenic bacteria: A study "in vitro" laboratory conditions. *Food Sci Tech J.* 2020;**17**(101):71-80. https://doi.org/10.52547/fsct.17.101.71.
- Nariya PB, Bhalodia NR, Shukla VJ, Acharya RN. Antimicrobial and antifungal activities of Cordia dichotoma (Forster F.) bark extracts. *Ayu J.* 2011;32(4):585-9. [PubMed ID: 22661859]. [PubMed Central ID: PMC3361940]. https://doi.org/10.4103/0974-8520.96138.