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Evaluation of pharmaceutical use of chamomile in dentistry: A review

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ABSTRACT

Introduction: Oral mucosa is one of the body's most sensitive tissues. Due to the prevalence of oral ulcers and the effect of cancers on the oral mucosa, treating oral lesions is particularly important. Matricaria chamomilla is widely used in traditional medicine. Chamomile compounds have antibacterial، antiviral, anti-inflammatory and accelerate epithelialization. However no systematic study has been undertaken on the application of chamomile in treating oral lesions. Therefore this study aims to determine the medicinal use of chamomile in dentistry.

Materials and Methods: This systematic review searched major international electronic databases, including PubMed, ISI and Scopus, from August 1998 to August 2021. The articles included in this review were clinical trials in which the participants used chamomile as a mouthwash or gel.

Results: In this study, the therapeutic effects of chamomile were evaluated in 14 clinical trial studies. Most of the studies reviewed in the articles referred to the properties of flavonoid compounds with anti-inflammatory and analgesic properties of chamomile.

Conclusion: Today, medicinal plants are used in treatment and one of the most common plants used for medicinal purposes is chamomile. It is used in dentistry, and its positive effects on plaque, gingivitis, caries, mucositis and its antibacterial effects have been reported.

Keywords: Chamomilla; Oral mucosa; Systematic review.

Introduction

Ulcers are the most common lesions in the oral mucosa. Oral ulcers are defined as discontinuities of the oral mucosa caused by damage to the epithelium and lamina propria, which might be accompanied by pain and difficulty swallowing in the form of erythematous patches, erosions, and ulcers [1-3]. Available treatments to improve and reduce the symptoms of wounds include corticosteroids, Chlorhexidine, Curcumin, honey, and herbs such as chamomile, aloe vera, licorice, etc. [4-7]. Unfortunately, due to the spread of head and neck cancers and the use of radiation therapy and chemotherapy, which are the main strategies for treating head and neck cancers, there is an increase in side effects such as dry mouth and mouth ulcers [8-10]. Oral mucositis is one of the most common side effects of chemotherapy and radiotherapy.

The mucosa usually reaches its peak 3-5 days after the start of chemotherapy, starting from 7-14 days, when the tongue, sublingual folds, and soft palate exhibit a milky white layer. In these patients, oral mucositis (OM) symptoms include erythema, pain and edema, and difficulty swallowing, which can lead to wounds. Severe OM can lead to serious complications such as systemic infection, fever, sores, and painful inflammation, leading to malnutrition. Oral ulcers can be infected by bacteria and can be life-threatening for patients [11-13]. Young people are at high risk for oral mucositis due to their high cell count and rapid proliferation rate. Other complications such as dry mouth, multiple caries due to inability to maintain oral hygiene, plaque, and gingivitis are the problems in these patients [14-20].

The Food and Drug Administration has approved no oral medication to prevent mucositis. Benefiting from the protective effects of natural products is probably one of the most promising preventive strategies against radiation toxicity or anti-cancer agents. Treatment can be symptomatic or sedative: local anesthesia and anti-inflammatory and systemic analgesics are used to relieve discomfort. Antimicrobial agents are prescribed to prevent infection. However, there is no consensus on any of them. Chamomile flower extract (Matricaria recutita) has important therapeutic properties, including antioxidant properties. It also has antimicrobial, anti-inflammatory, hypocholesterolemic, antigenotoxic, and anti-platelet aggregation activity. This medicinal plant is widely used in traditional medicine for various dermatologic, gastrointestinal, and even neurologic disorders [21-24]. The use of chamomile products as toothpaste or mouthwash has also shown beneficial effects on oral health and mucosal treatment due to radiation and chemotherapy [15,25]. This study aimed to provide an overview of the therapeutic uses of chamomile in dentistry concerning the reduction or prevention of mucositis, plaque, gingivitis, and caries using a systematic search in international databases.

Materials and Methods

In the preliminary study, according to the keywords medicinal plants, chamomile, plaque, and gingivitis, mucositis-related articles were obtained from three main databases, including PubMed, ISI Web of Science, Scopus, and Google scholar. From August 1998 to the end of August 2021, more than 148 studies were obtained. First, all the identified articles from various sources were collected by one of the researchers using Endnote software. After merging the articles obtained from all the mentioned databases and removing the duplicate articles, the two researchers independently reviewed all these articles. Based on the inclusion criteria, all the studies examining the preventive and therapeutic applications of chamomile in dentistry were included in the study, regardless of the language and status of their publication: all studies that mentioned the outcomes of the study, including the properties of chamomile in medical and dental fields. Exclusion criteria: qualitative studies, letters to the editor, and review studies. The remaining abstracts, which included 14 articles, were studied independently by two researchers.

The full texts of the related articles were reviewed by two researchers, and the articles were identified as fully complying with the inclusion criteria. Using articles in forward and backward citations, other articles were added to the collection of references. The data collection form was designed and used to extract data electronically in STATA 14 software, which included the name of the first author, year of publication, country, how to use the independent variable, the average age of the subjects, sample size, and drug effects. The data collection form was designed and used to extract data electronically in STATA 14 software, which included the name of the first author, year of publication, country, how to use the independent variable, the average age of the subjects, sample size, and drug effects.

Results

In general, 148 articles were obtained, of which 95 articles were obtained from the search of electronic databases until August 2021, and 53 were obtained from the review of the list of sources of selected articles. Twenty-one duplicate articles were identified and removed using EndNote software, and 50 articles were removed after reviewing their titles and abstracts due to lack of relevance to the objectives of this study. In this way, 23 articles were selected to read their full texts, of which 9 articles did not meet the inclusion criteria of this structured review and meta-analysis and were excluded. Finally, 14 articles were selected and included in the meta-analysis, which included 13 clinical trials and one case-control study comprising 695 participants. The tables show the names of the authors and their year of publication, country, type of study, how they used chamomile, sample sizes, the characteristics of the people studied, and the results. The quality of the studies included in the meta-analysis was evaluated using the NOS scale in the range of 7 to 8. Based on the results of this scale, the quality of all studies was high.

Discussion

The oral mucosa is one of the body's most sensitive tissues due to the prevalence of oral ulcers, periodontal diseases, and gingivitis and the effects of systemic diseases and cancers on the oral mucosa, and the prevalence of head and neck cancers and other body organisms. Therefore, the need for chemotherapy and radiotherapy has increased, resulting in complications such as oral mucositis, increased plaque and gingivitis, frequent lesions, and increased tooth decay in these patients. As a result, treating oral wounds and lesions is particularly important. Medicinal plants have been a topic of interest for researchers in recent decades due to less toxic and natural factors in medicine and dentistry. The effect of plants on human health has been shown for thousands of years [26-29].

Plants are inseparable from both traditional and non-traditional medicine, which date back to at least 5000 years ago [30-32]. One of the most common plants used for medicinal purposes is chamomile, from which tea and standard herbal extracts are prepared using dried flowers of Matricaria species. Chamomile is one of the oldest, most widely used and documented medicinal plants in the world, and it is recommended for all kinds of treatments in medicine and dentistry. And the development of new oral care products based on the composition of plant extracts has grown steadily. Chamomile compounds include chamazulene, (-alpha-bisabolol), bisabolol oxides A and B, flavonoids, and spiroethers. These compounds have different medicinal activities, such as antibacterial, antifungal, antiviral, and anti-inflammatory effects. They also accelerate wound healing and epithelialization.

Therefore, due to the need for treatment with fewer side effects, the use of traditional medicine is studied, considering the properties of chamomile and the fact that no systematic study has evaluated the application of chamomile flowers; therefore, the present study was undertaken. Mucositis in the form of oral ulcers is a common disease with various causes [33,34]. Stomatitis is a dose-dependent limitation caused by bolus (5-fluorouracil) in the chemotherapy regimen. Wound healing is one of the effects of topical use of chamomile, which was investigated in a double-blind experimental study on 14 patients who underwent dermabrasion tattooing. The effects of chamomile on wound drying and rapid epithelialization showed a significant difference from the group that did not use chamomile [35,36]. Recent studies have shown that chamomile causes faster wound healing than corticosteroids [37,38]. However, further studies are needed before it can be considered for clinical use. In the studies reviewed in this systematic review regarding the anti-inflammatory and analgesic effects of chamomile, 8 articles investigated the effect of chamomile on mucositis and complications of chemotherapy and radiotherapy "Table 3". Of these studies, 6 articles showed a significant effect of chamomile on reducing the severity of wounds, pain, and the period of mucositis. Fidler et al and Holmes et al did not find a preventive effect on the onset of mucositis, but they found differences in reducing the intensity of pain and the period of infection, which were not statistically significant [39,40]. Chamomile flowers contain 1-2% volatile oils, including α-bisabolol and anti-inflammatory and antiphlogistic properties. α-bisabolol oxides A and B and matricin are usually converted to camazolin and other flavonoids that have anti-inflammatory and antiphlogistic effects [41-44].

Considering the anti-inflammatory properties of chamomile, the effect of chamomile mouthwash on plaque and gingivitis was investigated in two articles. Both articles showed the significant impact of chamomile on reducing the number of these cases [15,16]. The antimicrobial activity of chamomile extract against different types of microorganisms was also evaluated. On the 15th day, the test group had a more significant reduction in the extent of the wound area compared to the control (61 vs. 48%), with faster epithelialization, and the increase in the speed of wound healing was significantly higher [45]. Concerning the antimicrobial effect of chamomile, in the 3 reviewed articles, 2 articles stated the great effect of chamomile on reducing microbial counts and inflammation "Tabel 4". However, in Azimi's article, no difference was found in bacterial colon counts in the oral cavity compared to normal saline solution "Tabel 2". Regarding the effect of chamomile on plaque and gingivitis in the 3 articles reviewed, all the three articles found a significant effect of chamomile on reducing the number of these cases [46-48]. In relation to the effect of chamomile on dental caries, in the two reviewed articles, one article mentioned the positive effect of chamomile on preventing dental caries by reducing Lactobacillus and Streptococcus counts and reducing demineralization "Tabel 1". In another article, Barga et al (2021) mentioned the effect of the chamomile plant on preventing dental caries. It did not affect dental caries [49,50].

Table 1. Effects of chamomile in enamel caries prevention.

First author	Year	Country	Study design	Consumption method	No. of patients	Result
Barga et al.	2021	Brazil		Solution		Ineffective
M.A. Adil Ahmed et al.	2017	Iran	Clinical trial	Mouthwash	30	Consumption of green tea and chamomile tea inhibits salivary Streptococcus mutans count and causes a reduction in salivary pH

Table 2. Effects of chamomile on gingivitis and plaque.

First author	Year	Country	Study design	Consumption method	No. of patients	Patient characteristic feature	Result
Paula Goes et al.	2016	Brazil	Clinical trial	Mouthwash	30	Patients undergoing orthodontic treatment with fixed appliances	MTC significantly reduced biofilm accumulation and gingival bleeding in patients with gingivitis
Pourabbas et al.	2010	Iran	Clinical trial	Mouthwash	25	Gingivitis patients	Using GC mouthwash offers benefits in plaque and gingival reduction without any significant adverse effects on tooth staining

Table 3. Effects of chamomile on mucositis.

First author	Year	Country	Study design	Consumption method	No. of patients	Patient characteristic feature	Result
Azar Aghamohamadi et al.	2016	Iran	Clinical trial	Mouthwash	66	head and neck cancer	Kamillosan liquid oral rinse delayed the onset of radiation mucositis and, in most patients, reduced its intensity
Ardakani et al.	2016	Iran	Clinical trial	Topical	60	Patients undergoing hematopoietic stem cell transplantation (HSCT).	Maximum and average daily grades of OM were significantly reduced
Barga et al.	2015	Brazil	Clinical trial	Mouthwash	40		Delayed the onset of radiation mucositis and its duration and intensity
Elhadad et al.	2020	Egypt	Clinical trial	Topical gel	45	Patients who were undergoing chemotherapy.	Significantly decreased the severity of the mucositis with lower pain scores

First author	Year	Country	Study design	Consumption method	No. of patients	Patient characteristic feature	Result
Fidler et al.	1996	Nebraska	Clinical trial	Mouthwash	164	from bolus 5-fluoro-uracil-based (5-FU) chemotherapy regimens	Did not support the present study hypothesis
Tatiana Stuart Vieira Holmesa et al.	2018	Brazil	Clinical trial	Mouthwash	22	Patients undergoing hematopoietic stem cell transplantation	Chamomile had no prophylactic effects on the onset of oral mucositis, but it was proven to be effective in decreasing the severity of this condition
Pourdeghatkar et al.	2017	Iran	Clinical trial	Mouthwash	62	Acute lymphoblastic leukemia under chemotherapy	Effective and significant compound in preventing oral mucositis

Table 4. Antimicrobial effects of chamomile.

First author	Year	Country	Study design	Consumption method	No. of patients	Patient characteristic feature	Result
Khezri et al	2013	Iran	Clinical trial	Mouthwash	80	The third or fourth day of ICU stay	Matricaria mouthwash also showed a significant difference in decreasing S. pneumoniae and S. aureus
Maryam Azimi et al.	2016	Iran	Clinical trial	Mouthwash	39	patients with endotracheal tubes	Prevented the growth of bacterial colonies in the mouth, similar to saline solution and Matricaria mouthwashes
M., Paknejad et al.	2006	Iran	Clinical trial	Mouthwash	32	patients with chronic periodontitis	Matricaria was more effective in eliminating inflammation and PBI.

Conclusions

According to the results of this review, currently, medicinal plants are used in the field of treatment. From the ancient periods until now, chamomile has been one of the most commonly used plants in medicine and dentistry due to its medicinal effects and the presence of photochemical substances. Chamomile has been mentioned in the reviewed articles in the field of dentistry due to its positive effects on plaque and gingivitis, reduction of cariogenic microorganisms, improvement and reduction of the course and severity of mucositis, acceleration of wound healing, and antibacterial effect. There exist several other reviews, although previous reviews have focused on fewer interventions. The most important difference between our systematic review, and previously published reviews is that we have a more stringent assessment of the risk of bias and quality of included trials. This is important because the strength of recommendations (eg, in future

guidelines) will be based on the quality of the evidence. 'We planned threshold analysis as a quantitative means to assess the robustness of network meta-analysis recommendations to potential limitations in the evidence. We were unable to use this approach because of substantial overlap in credible intervals from the network meta-analysis. Due to overlap in the intervals, no recommendations could be made, which is a fundamental prerequisite to performing a valid threshold analysis. To comply with our protocol, we report threshold results in (supplementary Web appendix), but chose to use GRADE to interpret the evidence. We were not able to evaluate small study bias due to too low number of trials. We found three completed trials in trial registers; two are under review, and the publication status of one trial is unknown.

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Conflict of Interest

There is no conflict of interest to declare.

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