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Review

Efficacy and Safety of Dead Sea-Derived Components in Oral Health Applications: A Systematic Review

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Abstract

The therapeutic potential of Dead Sea-derived components in oral health management has gained increasing attention, yet remains largely unexplored. This systematic review aimed to evaluate the efficacy and safety of Dead Sea-based products in oral health applications. A comprehensive literature search was conducted in PubMed, Scopus, and Web of Science databases for studies published up to March 2024, yielding seven studies that met the inclusion criteria. The evidence suggests potential benefits of Dead Sea-derived products in managing periodontal conditions and chemotherapy-induced oral mucositis. Randomized controlled trials demonstrated that Dead Sea salt-containing mouthwashes significantly reduced plaque and gingival indices compared to controls, with efficacy comparable to chlorhexidine in some cases. An observational study reported reduced mucositis intensity in cancer patients using Dead Sea mineral products. In vitro research showed Dead Sea salt solutions reduced concentrations of bacterial leukotoxin, lipopolysaccharide endotoxin, and glucan sucrase. A clinical trial found significant reductions in salivary viral loads with a Dead Sea salt-based mouthwash. However, a Dead Sea salt-based tooth whitening regimen was less effective than conventional peroxide treatment. The unique mineral composition and microbiological characteristics of the Dead Sea appear to confer antimicrobial and anti-inflammatory properties. Nevertheless, the evidence is limited by the small number of studies, their heterogeneity, and lack of long-term follow-up data. Further research is needed to establish the long-term efficacy and safety of these products in oral health care.

Keywords: Dead sea minerals; Thermal waters; Oral health

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Introduction

The intersection of ancient natural resources and modern oral health care presents a frontier ripe for scientific exploration, with the Dead Sea emerging as a compelling subject of investigation. This exploration is particularly timely given the growing global interest in sustainable and natural approaches to health care [1,2]. In this context, sustainable and natural approaches refer to the use of minimally processed, environmentally friendly products derived from nature, which aim to promote health while reducing ecological impact and avoiding synthetic chemicals. Mouthwashes play a crucial role in oral hygiene regimens, complementing mechanical plaque removal methods such as brushing and flossing [3]. Recent studies have demonstrated their efficacy in preventing microbial adhesion to oral surfaces and inhibiting plaque accumulation [4,5]. These effects are particularly beneficial in maintaining oral health, as they help reduce the risk of common dental problems such as caries, gingivitis, and periodontitis. Mouthwashes can reach areas that are difficult to access with a toothbrush or floss, providing a more comprehensive approach to oral care. Moreover, certain mouthwashes have been shown to have additional benefits, such as reducing halitosis and promoting the remineralization of early carious lesions [6]. However, the long-term use of chemical-based mouthwashes has raised concerns due to potential side effects, including tooth discoloration, calculus buildup, taste disturbances, and allergic reactions [7,8]. The emergence of antimicrobial resistance as a global health concern has necessitated a critical reassessment of long-term chemical mouthwash use in routine oral care protocols [9,10]. This re-evaluation, coupled with the aforementioned side effects, has catalyzed scientific interest in natural products and mineral waters as potential alternative or adjunctive therapies for the prevention and management of oral diseases. Plant extracts, essential oils, and sea salts have long been used in traditional oral health practices, demonstrating various beneficial properties such as antimicrobial, anti-inflammatory, antioxidant, and wound healing effects [11,12]. Among the natural sources being explored, the Dead Sea presents a unique ecosystem with intriguing potential for oral health applications. This hypersaline terminal lake, situated 420 meters below sea level between Jordan and the Palestinian territories, is renowned as Earth's deepest hypersaline lake, with an estimated age of 50,000 years. The Dead Sea's mineral-rich waters contain an extraordinary 345 grams of dissolved salts per liter, far surpassing typical ocean salinity by 7 to 10 times [13]. The Dead Sea's distinctive mineral profile sets it apart from other bodies of water, offering unique potential for oral health applications [14]. While sodium chloride levels may be comparable to those found in the Mediterranean Sea, the Dead Sea contains remarkably higher concentrations of other mineral salts, including magnesium chloride, calcium chloride, potassium chloride, and magnesium bromide [15]. This unique ionic composition, rich in chloride, magnesium, sodium, calcium, potassium, bromide, sulfate, and bicarbonate ions, contributes to the water's reputed therapeutic properties, which have been recognized since ancient times and documented in various historical texts. The potential benefits of this mineral-rich composition for oral health are multifaceted. For instance, the high magnesium content has been associated with anti-inflammatory properties in dermatological applications [16], and may exert similar effects in the oral cavity, potentially aiding in the management of inflammatory conditions such as gingivitis and periodontitis. Calcium and phosphate ions play crucial roles in tooth remineralization processes, suggesting that the Dead Sea's mineral content could contribute to enamel strengthening and caries prevention [17]. Furthermore, the high salt concentration may create an environment inhospitable to many pathogenic oral bacteria, potentially offering natural antimicrobial effects [18]. Recent explorations have unveiled the presence of underwater freshwater and brackish springs emerging at the lake's floor, supporting dense microbial communities distinct from those found in other hypersaline environments [19,20]. These underwater springs represent a previously unrecognized source of diversity and metabolic potential within the Dead Sea ecosystem, potentially offering novel compounds for oral health applications [21]. The mid-20th century marked a paradigm shift in Dead Sea research, catalyzing scientific investigations into its therapeutic potential for various medical conditions, including rheumatologic diseases and dermatological disorders such as psoriasis [22]. The combination of the Dead Sea's distinctive climate, water composition, and solar radiation has given rise to various therapeutic approaches collectively known as Dead Sea climatotherapy. While traditionally applied to dermatological and rheumatological conditions, the principles of Dead Sea climatotherapy may have relevant applications in oral health [23]. The high mineral content of Dead Sea water, when used in oral rinses or topical applications, could potentially provide similar benefits to those observed in dermatological treatments. For instance, the anti-inflammatory effects of magnesium and other minerals observed in skin conditions [24] might translate to reduced inflammation in oral tissues. The unique ionic composition of Dead Sea water could also influence the oral microenvironment, potentially altering pH levels or mineral saturation in ways that promote oral health. Moreover, the concept of balneotherapy - the therapeutic use of mineral-rich waters - could be

adapted for oral applications, such as mineral-enriched mouthwashes or irrigation solutions for periodontal therapy. The success of Dead Sea climatotherapy in managing inflammatory conditions suggests that similar approaches could be beneficial in addressing inflammatory oral diseases like periodontitis or oral lichen planus [25,26]. Recent explorations have unveiled the presence of underwater freshwater and brackish springs emerging at the Dead Sea's floor, supporting dense microbial communities distinct from those found in other hypersaline environments [27,28]. These underwater springs represent a previously unrecognized source of diversity and metabolic potential within the Dead Sea ecosystem, with significant implications for oral health applications. The unique adaptations of these microbial communities to extreme conditions may yield novel compounds and mechanisms relevant to oral care. For instance, certain microbial groups in these springs produce metabolites that exhibit antimicrobial properties, potentially inhibiting the growth of oral pathogens [29,30]. These natural antimicrobial agents could serve as alternatives to synthetic compounds in oral care products, potentially reducing the risk of antimicrobial resistance development [31]. Additionally, the sulfur cycle and iron metabolism pathways observed in these communities could yield compounds with anti-inflammatory effects, which may be beneficial in managing conditions such as gingivitis and periodontitis [32,33]. Some bacteria found in these ecosystems, including *Lactobacillus salivarius*, have demonstrated the ability to disrupt biofilm formation by cariogenic pathogens like Streptococcus mutans, suggesting a potential role in caries prevention [34]. This property could be harnessed in the development of novel probiotic-based oral care products. Furthermore, the rich microbial diversity of these springs presents opportunities for identifying probiotic or prebiotic candidates that could modulate the oral microbiome, potentially promoting a more favorable balance of oral flora [35,36]. Such microbiome modulation strategies represent a cutting-edge approach in oral health management, aligning with the growing understanding of the oral microbiome's role in health and disease. Furthermore, the mineral-rich composition of the spring waters, containing elements such as calcium, magnesium, and strontium, holds potential for enhancing enamel remineralization and overall oral health [35]. These diverse properties of Dead Sea-derived components offer a multifaceted approach to oral care, potentially addressing various aspects of oral health maintenance and disease prevention. The combination of antimicrobial, anti-inflammatory, biofilm-inhibiting, and remineralizing properties makes Dead Sea components particularly intriguing for oral health applications [35,36]. Despite the promising preliminary evidence, the efficacy and safety of natural products and mineral waters derived from the Dead Sea for oral health have not been systematically evaluated. While several reviews have explored the use of natural products in oral health, there is a notable gap in the literature regarding the specific potential of Dead Sea-derived components. This systematic review aims to address this gap by critically synthesizing and evaluating the extant literature on Dead Sea-derived natural interventions for oral disease prevention and management. Specifically, this review aimed to examine the following research hypotheses:

1. Dead Sea-derived products demonstrate therapeutic efficacy in managing common oral health conditions, including periodontal diseases, oral mucositis, and dental caries.
2. Dead Sea-based oral care products exhibit a safety profile comparable to or better than conventional treatments.
3. Dead Sea components influence oral health through specific biological and chemical mechanisms that can be identified and characterized.
4. Current evidence reveals significant knowledge gaps and specific research priorities that need to be addressed to advance this field.

Materials and Methods

Search strategy

We conducted a comprehensive literature search in PubMed, Scopus, Web of Science, Cochrane Central Register of Controlled Trials (CENTRAL), and EMBASE databases from inception to May 31, 2024. Additionally, we searched grey literature sources including OpenGrey, ProQuest Dissertations & Theses Global, and conference proceedings of major dental and oral health conferences from the past five years.

The search strategy for each database was as follows:

- PubMed (1966 - May 31, 2024): (("Dead Sea"[All Fields] OR "Dead Sea salt"[All Fields] OR "Dead Sea minerals"[All Fields]) AND ("oral health"[MeSH Terms] OR "dental care"[MeSH Terms] OR "periodontal diseases"[MeSH Terms] OR "stomatitis"[MeSH Terms] OR "tooth remineralization"[MeSH Terms])) AND ("mouthwashes"[MeSH Terms] OR "dentifrices"[MeSH Terms] OR "oral hygiene"[MeSH Terms]).
- Scopus (1960 - May 31, 2024): TITLE-ABS-KEY("Dead Sea" OR "Dead Sea salt" OR "Dead Sea minerals") AND TITLE-ABS-KEY("oral health" OR "dental care" OR "periodontal diseases" OR stomatitis OR "tooth remineralization") AND TITLE-ABS-KEY(mouthwashes OR dentifrices OR "oral hygiene").
- Web of Science (1900 - May 31, 2024): TS=("Dead Sea" OR "Dead Sea salt" OR "Dead Sea minerals") AND TS=("oral health" OR "dental care" OR "peri-

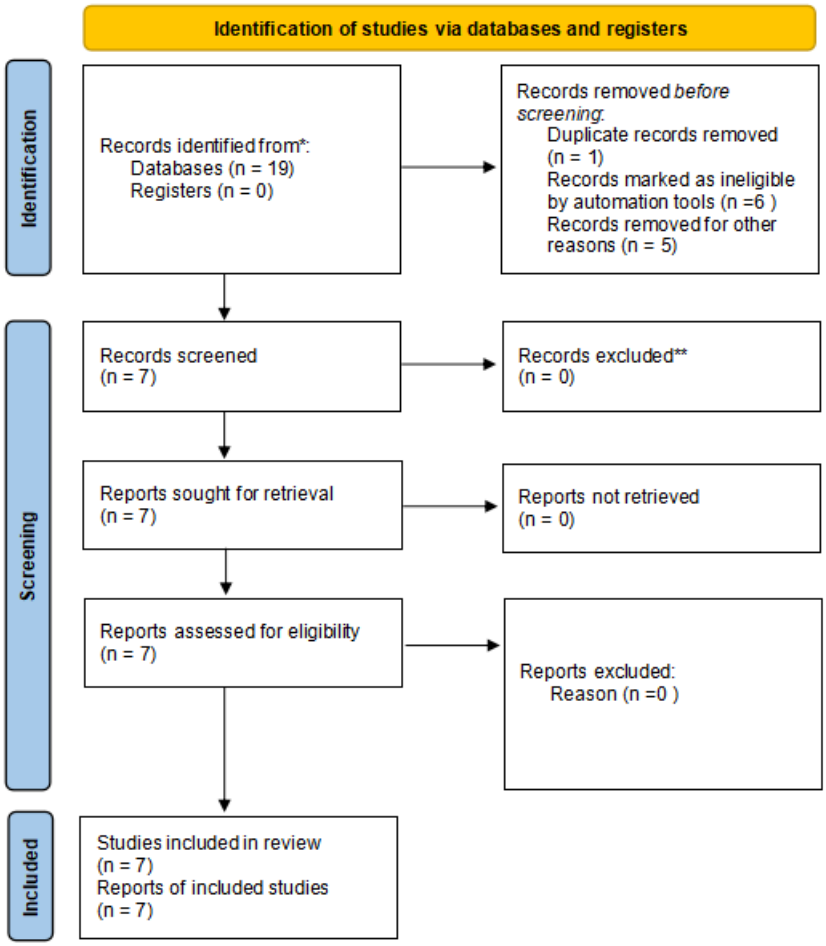

Figure 1. PRISMA flow diagram of study selection process

odontal diseases" OR stomatitis OR "tooth remineralization") AND TS=(mouthwashes OR dentifrices OR "oral hygiene").
- CENTRAL (Cochrane Library) (inception - May 31, 2024): #1 MeSH descriptor: [Mouthwashes] explode all trees #2 MeSH descriptor: [Dentifrices] explode all trees #3 MeSH descriptor: [Oral Hygiene] explode all trees #4 #1 OR #2 OR #3 #5 ("Dead Sea" OR "Dead Sea salt" OR "Dead Sea minerals"):ti,ab,kw #6 #4 AND #5.
- EMBASE (1974 - May 31, 2024): ('dead sea'/exp OR 'dead sea salt':ti,ab,kw OR 'dead sea minerals':ti,ab,kw) AND ('oral health'/exp OR 'dental care'/exp OR 'periodontal disease'/exp OR 'stomatitis'/exp OR 'tooth remineralization'/exp) AND ('mouthwash'/exp OR 'toothpaste'/exp OR 'oral hygiene'/exp).

Eligibility criteria

Inclusion Criteria:

1. Study design: Randomized controlled trials (RCTs), non-randomized controlled trials, cohort studies, case-control studies, and in vitro studies.
2. Population: Human subjects of any age or health status for clinical studies; relevant cell lines or bacterial strains for in vitro studies.
3. Intervention: Any oral health product or intervention containing Dead Sea-derived components.
4. Comparator: Placebo, standard care, other active treatments, or no treatment.
5. Outcomes: Any measure of oral health status, including but not limited to plaque index, gingival index, periodontal pocket depth, oral mucositis severity, tooth color change, enamel remineralization, and antimicrobial effects.
6. Language: Studies published in any language with an English abstract.

Exclusion Criteria:

1. Case reports, case series, narrative reviews, and expert opinions.
2. Studies focusing solely on non-oral applications of Dead Sea products.
3. Studies without a clear description of the Dead Sea-derived components used.
4. Conference abstracts or unpublished data without

sufficient methodological details.

Risk of bias assessment

The methodological quality of the included studies was rigorously evaluated using standardized assessment tools appropriate for each study design. We conducted a thorough risk of bias assessment for each included study using appropriate tools based on study design. Two reviewers independently performed the assessments, with disagreements resolved by consensus or consultation with a third reviewer. For randomized controlled trials (RCTs), the Cochrane Risk of Bias tool 2.0 (RoB 2) was employed. This tool assesses five critical domains: randomization process, deviations from intended interventions, missing outcome data, outcome measurement, and selection of reported results. Each domain was classified as 'low risk', 'some concerns', or 'high risk' of bias. Non-randomized studies were evaluated using the Newcastle-Ottawa Scale (NOS), which assesses study quality based on selection of study groups, inter-group comparability, and ascertainment of exposure or outcome. The NOS utilizes a star rating system with a maximum of 9 stars. Studies were categorized as high quality (7-9 stars), moderate quality (4-6 stars), or low quality (0-3 stars). For single-arm clinical trials, the National Institutes of Health (NIH) Quality Assessment Tool for Before-After (Pre-Post) Studies With No Control Group was utilized. This 12-item instrument culminates in an overall rating of 'good', 'fair', or 'poor'. In vitro studies, although less prevalent in this review, were assessed using an adaptation of the Systematic Review Center for Laboratory animal Experimentation (SYRCLE) risk of bias tool, modified to suit the context of in vitro research. Heterogeneity among studies was assessed both qualitatively and quantitatively. Qualitative assessment involved comparing study characteristics, interventions, and outcome measures.

Results

Our search identified 7 studies that met the inclusion criteria: four randomized controlled trials (RCTs), one in vitro study, one observational study, and one formula development study. The process of study selection is illustrated in the PRISMA flow diagram presented in figure 1. The included studies investigated various oral health applications of Dead Sea-derived products, including periodontal disease management, oral mucositis treatment, tooth whitening, and antimicrobial effects. No preclinical animal studies investigating Dead Sea products for oral health applications were identified in our literature search. Table 1 summarizes the key characteristics and findings of each included study.

Quality assessment and interpretation of evidence

The quality of the included studies varied considerably, which necessitates caution in interpreting the overall body of evidence. Table 2 provides a detailed quality assessment for each study.

Given the limitations identified in the quality assessment, we must interpret the evidence cautiously. While some studies suggest potential benefits of Dead Sea-derived products in oral health, the overall body of evidence is not sufficiently robust to draw definitive conclusions. The studies by Calvo-Guirado et al. (2020) and Rodriguez & Ajdaharian (2017) suggest that Dead Sea-based mouthwashes may be effective in reducing plaque and gingival inflammation. However, the small sample size in Rodriguez & Ajdaharian's study (n=10) limits its generalizability. Calvo-Guirado et al.'s larger study (n=93) provides more robust evidence, but the unclear blinding of outcome assessors introduces potential bias. The observational study by Ben-Yosef et al. (2005) suggests potential benefits of Dead Sea products in reducing oral mucositis severity in cancer patients. However, the lack of randomization and potential for selection bias limit the strength of these findings. Randomized controlled trials are needed to confirm these results. Gurich et al. (2023) found that a Dead Sea salt-based whitening regimen was less effective than conventional peroxide treatment. While this study had a low risk of bias, its small sample size (n=50) suggests that further research with larger populations is needed to confirm these findings. The in vitro study by Nowzari et al. [32] demonstrated promising antimicrobial effects of Dead Sea salt solution. However, these results require validation in clinical settings. The RCT by Nowzari et al. [31] showing reductions in salivary viral loads is more clinically relevant, but its short follow-up period (60 days) limits conclusions about long-term effects. The heterogeneity among the included studies presents a significant challenge in synthesizing the evidence. This heterogeneity manifests in several ways: The Dead Sea-derived products varied across studies, from mouthwashes to mineral-rich creams. The concentration and composition of Dead Sea components also differed, making direct comparisons challenging. While some studies used standardized measures like plaque and gingival indices, others employed unique outcomes (e.g., salivary viral load, enamel microhardness), complicating cross-study comparisons. The inclusion of RCTs, observational studies, and in vitro research introduces methodological heterogeneity, necessitating caution when synthesizing results across study types. Studies ranged from healthy adults to cancer patients, introducing potential confounding factors and limiting generalizability. Study durations varied widely, from short-term in vitro experiments to clinical trials lasting several weeks, making it difficult to draw conclusions about long-term efficacy and safety. To address this heterogeneity, we conducted a

Table 1. Characteristics and key findings of included studies

Study	Design	Population/Sample	Intervention	Comparator	Primary Outcomes	Key Findings
Gurich et al. (2023)	RCT	50 adults	Dead Sea salt-based whitening regimen	Peroxide-based whitening strips	Tooth color change	Dead Sea product less effective than peroxide ($p < 0.001$)
Nowzari et al. (2022a)	In vitro	Bacterial components	Dead Sea salt solution	None	Bacterial toxin reduction	84% reduction in leukotoxin, 40% in endotoxin after 72-84 hours
Nowzari et al. (2022b)	RCT	30 adults	Dead Sea salt-based mouthwash	De-ionized water	Salivary viral load	Significant reduction in HSV-1, HCMV, EBV ($p < 0.001$)
Rodriguez & Ajdaharian (2017)	RCT	10 adults	Dead Sea salt-based mouthwash	Chlorhexidine, No rinse	Plaque and gingival indices	Comparable efficacy to chlorhexidine ($p < 0.05$ vs. no rinse)
Calvo-Guirado et al. (2020)	RCT	93 adults	Seawater-based mouthwash	Chlorhexidine, Saline	Plaque and gingival indices	Superior to chlorhexidine in plaque reduction ($p = 0.009$)
Ajdaharian et al. (2017)	Single-arm trial	10 adults, 300 enamel samples	Dead Sea salt-based mouthwash	None	Enamel remineralization	No significant difference from fluoride or no treatment
Ben-Yosef et al. (2005)	Observational	54 cancer patients	Dead Sea mineral products	Standard care	Oral mucositis severity	Significant reduction in mucositis intensity ($p < 0.05$)

Table 2. Risk of bias assessment results

Study	Assessment Tool	Domain 1	Domain 2	Domain 3	Domain 4	Domain 5	Overall Risk
Gurich et al. (2023)	RoB 2	Low	Low	Low	Some concerns	Low	Low
Nowzari et al. (2022a)	Adapted SYRCLE	Low	Some concerns	High	Low	N/A	Some concerns
Nowzari et al. (2022b)	RoB 2	Low	Low	Low	Low	Low	Low
Rodriguez & Ajdaharian (2017)	RoB 2	Some concerns	Low	Low	Low	Some concerns	Some concerns
Calvo-Guirado et al. (2020)	RoB 2	Low	Some concerns	Low	High	Low	High
Ajdaharian et al. (2017)	NIH Tool	Fair	Fair	Poor	Fair	Fair	Fair
Ben-Yosef et al. (2005)	NOS	★★★	★★	★★	N/A	N/A	7/9 (High quality)

narrative synthesis rather than a meta-analysis. Where possible, we calculated the I^2 statistic to quantify heterogeneity for comparable outcomes. For plaque index reduction, reported in three studies [31, 33, 35], the I^2 value was 68%, indicating substantial heterogeneity. This heterogeneity impacts our interpretation in several ways: While some studies show promising results, the variability in interventions and outcomes means we cannot conclude that all Dead Sea-derived products are equally effective across all oral health applications; the varying concentrations of Dead Sea components used across studies make it difficult to establish an optimal dosage for clinical use; the diverse study populations limit our ability to generalize findings to broader populations or specific patient groups. Finally, the heterogeneity in study designs and outcomes complicates our understanding of the precise mechanisms by which Dead Sea components may influence oral health.

Periodontal disease and plaque control

Two studies examined the effects of Dead Sea-derived products on periodontal health and plaque control. Calvo-Guirado et al. (2020) found that a seawater-based mouth rinse (SEA 4 Encias) significantly reduced plaque index compared to saline (mean difference: -0.45, 95% CI: -0.60 to -0.30, $p < 0.001$) and outperformed chlorhexidine in reducing plaque index (mean difference: -0.20, 95% CI: -0.35 to -0.05, $p = 0.009$). Gingival index improvements were significant compared to saline but not chlorhexidine. Rodriguez and Ajdaharian [35] reported that both their Dead Sea salt-based mouthwash (Oral Essentials) and chlorhexidine significantly reduced plaque, gingivitis, and bleeding on probing compared to no rinse ($p < 0.01$), with no significant differences between the two active treatments. The I^2 statistic for plaque index reduction across these studies was 68%, indicating moderate to high heterogeneity. This heterogeneity may be attributed to differences in product formulations, study durations, and baseline oral health status of participants.

Oral mucositis

Ben-Yosef et al. (2005) conducted an observational study on 54 head and neck cancer patients undergoing radiochemotherapy. They reported a significant reduction in mucositis intensity with Dead Sea mineral-rich mouthwash (Lenom®) and skin cream (Solaris®) compared to standard care ($p < 0.05$). Additionally, they observed a decreased incidence of severe (grade 3-4) mucositis and dermatitis in the intervention group. However, as this was the only study examining oral mucositis, these results should be interpreted cautiously.

Tooth whitening and remineralization

Gurich et al. (2023) conducted a randomized controlled trial comparing a peroxide-free whitening regimen containing Dead Sea salt and plant-based oils to conventional peroxide-based whitening strips. The Dead Sea product was found to be less effective in improving tooth color ($p < 0.001$). Specifically, after 14 treatments, the control group showed a mean yellowness reduction (SD) of 1.55 (0.703) and mean lightness improvement (SD) of 1.57 (1.141) compared to baseline ($p < 0.001$ for both), while the test group showed no statistically significant changes. Ajdaharian et al. [34] examined enamel remineralization using a Dead Sea salt-based mouthwash in a single-arm trial. They found no significant difference in remineralization between their novel mouthwash, a conventional fluoride mouthwash, or no mouthwash use. However, the lack of a control group and small sample size limit the strength of these findings.

Antimicrobial effects

Nowzari et al. [32] conducted an in vitro study evaluating the effects of Dead Sea salt solution on bacterial components. They reported significant reductions in leukotoxin (84% decrease after 84 hours), lipopolysaccharide endotoxin (40% decrease after 72 hours), and glucan sucrase (90% decrease after 84 hours). The same research group [31] also conducted a randomized controlled trial examining the effects of a Dead Sea salt-based mouthwash on salivary viral loads. They found significant reductions in HSV-1, HCMV, and EBV viral loads compared to a de-ionized water control ($p < 0.001$ for all viruses).

Safety and tolerability

Across all clinical studies, Dead Sea-based products were generally well-tolerated. No serious adverse events were reported, and minor side effects such as temporary taste alterations were infrequent and comparable to or less than those observed with conventional treatments like chlorhexidine. However, long-term safety data remain limited, as most studies had relatively short follow-up periods.

In summary, the current evidence suggests potential benefits of Dead Sea-derived products in managing periodontal conditions and chemotherapy-induced oral mucositis. The unique mineral composition and microbiological characteristics of the Dead Sea appear to confer antimicrobial and anti-inflammatory properties. However, evidence is limited by the small number of studies, their heterogeneity, and lack of long-term follow-up data. Further research is needed to establish the long-term efficacy and safety of these products in oral health care.

Discussion

This systematic review synthesized the current evidence on the efficacy and safety of Dead Sea-derived

components in oral health applications. Our analysis of seven studies, including randomized controlled trials, observational studies, and in vitro research, reveals both promising potential and significant limitations in the existing literature. The unique mineral composition and microbiological characteristics of the Dead Sea offer a novel approach to oral health care, potentially addressing the growing concerns of antimicrobial resistance and side effects associated with conventional treatments [9, 10]. The most robust evidence supports the potential efficacy of Dead Sea-based products in managing periodontal conditions. Calvo-Guirado et al. [33] demonstrated that a seawater-based mouth rinse was more effective than chlorhexidine in reducing plaque over a 4-week period; while Rodriguez and Ajdaharian [35] found comparable efficacy between a Dead Sea salt-based mouthwash and chlorhexidine in reducing plaque, gingivitis, and bleeding on probing. These findings are particularly significant given the widespread use of chlorhexidine as a gold standard in periodontal care [11]. The potential of Dead Sea products to match or exceed the efficacy of chlorhexidine without its associated side effects (such as tooth staining and taste alteration) could represent a significant advancement in oral hygiene practices. The mechanisms underlying these effects likely stem from the unique mineral composition of Dead Sea water [15]. The high concentrations of magnesium, calcium, and other minerals may contribute to anti-inflammatory effects and promote a healthier oral microbiome [16,17]. Furthermore, the hypersaline environment created by these products may inhibit the growth of pathogenic bacteria; while potentially supporting beneficial oral flora [18]. However, more research is needed to fully elucidate these mechanisms and their long-term effects on oral health. In the context of oral mucositis, an observational study by Ben-Yosef et al. [36] reported significant reductions in mucositis severity among cancer patients using Dead Sea mineral products. While these results are encouraging, the lack of randomization and potential for selection bias necessitate cautious interpretation. The potential for Dead Sea products to alleviate this debilitating side effect of cancer treatment warrants further investigation, as it could significantly improve quality of life for cancer patients undergoing radiotherapy or chemotherapy. Rigorous randomized controlled trials are needed to confirm these findings and establish the role of Dead Sea products in supportive care for cancer patients. The anti-inflammatory properties of Dead Sea minerals, particularly magnesium, may play a crucial role in mitigating mucosal inflammation. Additionally, the potential antimicrobial effects could help prevent secondary infections in compromised oral tissues. Future studies should explore the specific components responsible for these effects and optimize formulations for this particular application. Interestingly, our review revealed limitations in the efficacy of Dead Sea-based products for tooth whitening. Gurich et al. [30] found that a peroxide-free whitening regimen containing Dead Sea salt was less effective than conventional peroxide-based treatments. This highlights the importance of tailoring natural interventions to specific oral health needs and underscores the complexity of replacing established treatments with natural alternatives. However, it is worth noting that while less effective for whitening, these products may offer other benefits such as enamel remineralization or gum health improvement, which were not primary outcomes in the whitening studies. The potential for Dead Sea minerals to contribute to enamel remineralization, although not conclusively demonstrated in the reviewed studies, remains an area of interest. The high mineral content, particularly calcium and phosphate ions, could theoretically support enamel strengthening. Future research should investigate this potential, possibly in combination with other remineralizing agents like fluoride. The antimicrobial properties of Dead Sea components, demonstrated both in vitro and in clinical trials, represent a particularly intriguing avenue for future research. Nowzari et al.'s [31,32] studies showed significant reductions in bacterial toxins and salivary viral loads, suggesting broad-spectrum antimicrobial activity. These findings point to potential applications in managing both bacterial and viral oral infections, a unique feature among natural oral care products. The ability to reduce viral loads of HSV-1, HCMV, and EBV is particularly noteworthy, as it suggests potential applications beyond routine oral hygiene. This broad-spectrum antimicrobial activity could be especially beneficial for immunocompromised patients or those at high risk of oral infections. The mechanisms behind these antiviral effects warrant further investigation, as they could lead to novel approaches in managing oral viral infections. The observed reductions in bacterial leukotoxin, lipopolysaccharide endotoxin, and glucan sucrase enzyme suggest that Dead Sea components may interfere with multiple pathways of bacterial virulence. This multi-target approach could potentially reduce the likelihood of developing antimicrobial resistance, a significant advantage over single-compound antimicrobials. However, long-term studies are needed to confirm this hypothesis and assess the impact on the overall oral microbiome. The favorable safety profile of Dead Sea-derived products, consistently reported across studies, is noteworthy [33,35,36]. The absence of significant adverse effects and improved tolerability compared to conventional treatments like chlorhexidine could translate to better patient compliance in long-term use. This is particularly important for products intended for daily use in oral hygiene routines.

However, the lack of long-term safety data remains a critical gap in the current evidence base. Future studies should prioritize extended follow-up periods to assess any potential cumulative effects or rare adverse events that may only become apparent with prolonged use. The improved tolerability may be attributed to the natural mineral composition of Dead Sea products, which could be less irritating to oral tissues compared to synthetic compounds [21,22,23]. Additionally, the potential for these products to support a balanced oral microbiome, rather than indiscriminately eliminating bacteria, may contribute to their favorable side effect profile. However, more research is needed to confirm these hypotheses and understand the long-term impact on oral ecology.

Limitations and future directions

Despite these promising findings, several limitations must be acknowledged. The small sample sizes and short durations of most studies limit the generalizability of results and preclude conclusions about long-term efficacy and safety. The heterogeneity in product formulations, dosing regimens, and outcome measures across studies poses challenges for direct comparisons and meta-analyses. Furthermore, the quality of evidence varied, with some studies showing unclear risk of bias in critical domains. To address these limitations, future research should prioritize large-scale, well-designed randomized controlled trials with longer follow-up periods to establish the long-term efficacy and safety of Dead Sea-derived oral care products, standardization of interventions and outcome measures to facilitate more robust comparisons across studies and enable meta-analyses, and mechanistic studies to elucidate the molecular and cellular basis of the observed clinical effects, particularly the antimicrobial and anti-inflammatory properties unique to Dead Sea components.

Conclusion

In conclusion, while Dead Sea-derived products show promise in various oral health applications, particularly in managing periodontal conditions and potentially in supportive care for oral mucositis, the current evidence base is not sufficiently robust to recommend their routine clinical use. The unique mineral composition and potential antimicrobial properties of these products offer intriguing possibilities for addressing current challenges in oral health care, including antimicrobial resistance and treatment side effects. However, these findings should be viewed as a foundation for future research rather than definitive clinical recommendations. As research in this field progresses, it will be crucial to maintain a balanced, evidence-based approach, carefully weighing the potential benefits of these natural interventions against established treatments in oral health care. The development of standardized, well-characterized Dead Sea-derived products and their rigorous evaluation in large-scale clinical trials will be essential to fully understand their place in modern oral health management.

Given the previous considerations, we must interpret the current evidence base as preliminary and hypothesis-generating rather than definitive. While the results suggest potential benefits of Dead Sea-derived products in certain oral health applications, particularly in managing periodontal conditions and oral mucositis, more standardized, large-scale research is needed to confirm these effects and establish clinical guidelines.

Conflict of Interests

None.

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References

[1] Lennox L, Maher L, Reed J. Navigating the sustainability landscape: a systematic review of sustainability approaches in healthcare. Implement Sci 2018;13:1-17.

[2] Talbot L, Verrinder G. Promoting health: the primary health care approach. Elsevier Health Sciences. 2017.

[3] Brookes ZLS, McCullough M, Kumar P, McGrath C. Mouthwashes: Implications for Practice. Int Dent J 2023;73:S98-S101.

[4] Bosma ML, McGuire JA, DelSasso A, Milleman J, Milleman K, et al. Efficacy of flossing and mouth rinsing regimens on plaque and gingivitis: a randomized clinical trial. BMC Oral Health 2024;24:178.

[5] Mann J, Bernstein Y, Findler M. Periodontal disease and its prevention, by traditional and new avenues. Exp Ther Med 2020;19:1504-1506

[6] Yazicioglu O, Ucuncu MK, Guven K. Ingredients in commercially available mouthwashes. Int Dent J 2024;74:223-241.

[7] Alam S, Brailsford SR, Adams S, Allison C, Sheehy E, et al. Genotypic heterogeneity of Streptococcus oralis and distinct aciduric subpopulations in human dental plaque. Appl Environ Microbiol 2000;66:3330-3336.

[8] Al-Kamel A, Baraniya D, Al-Hajj WA, Halboub E, Abdulrab S, et al. Subgingival microbiome of experimental gingivitis: shifts associated with the use of chlorhexidine and N-acetyl cysteine mouthwashes. J Oral Microbiol 2019;11:1608141.

[9] Anderson AC, Rothballer M, Altenburger MJ, Woelber JP, Karygianni L, et al. Long-term fluctuation of Oral biofilm microbiota following different dietary phases. Appl Environ Microbiol 2020;86:e01421-e01420.

[10] Masadeh MM, Gharaibeh SF, Alzoubi KH, Al-Azzam SI, Obeidat WM, et al. Antimicrobial activity of common mouthwash solutions on multidrug-resistance bacterial biofilms. J Clin Med Res 2013;5:389-394.

[11] Brookes ZL, Belfield LA, Ashworth A, Casas-Agustench P, Raja M, et al. Effects of chlorhexidine mouthwash on the oral microbiome. J Dent 2021;113:103768.

[12] Salam MA, Al-Amin MY, Salam MT, Pawar JS, Akhter N, et al. Antimicrobial resistance: a growing serious threat for global public health. Healthcare (Basel) 2023;11:1946.

[13] Dimou I, Dritsas S, Aggelopoulou P, Vassilatou K, Damianaki S, et al. Development of a herbal mouthwash containing a mixture of essential oils and plant extracts and in vitro testing of its antimicrobial efficiency against the planktonic and biofilm-enclosed cariogenic bacterium Streptococcus mutans. Biofouling 2021;37:397-409.

[14] de Sousa DP, Damasceno ROS, Amorati R, Elshabrawy HA, de Castro RD, et al. Essential oils: chemistry and pharmacological activities. Biomolecules 2023;13:1144.

[15] Dai D, Ma X, Yan X, Bao X. The biological role of dead sea water in skin health: a review. Cosmetics 2023;10:21.

[16] Jacob JH, Hussein EI, Shakhatreh MAK, Cornelison CT. Microbial community analysis of the hypersaline water of the Dead Sea using high-throughput amplicon sequencing. Microbiologyopen 2017;6:e00500.

[17] Rhodes M, Oren A, House C. Dynamics and persistence of dead sea microbial populations as shown by high-throughput sequencing of rRNA. Appl Environ Microbiol 2012;78:2489-2492.

[18] Emmanuel T, Petersen A, Houborg HI, Rønsholdt AB, Lybaek D, et al. Climatotherapy at the Dead Sea for psoriasis is a highly effective anti-inflammatory treatment in the short term: An immunohistochemical study. Exp Dermatol 2022;31:1136-1144.

[19] Harari M, Shani J, Seidl V, Hristakieva E. Climatotherapy of atopic dermatitis at the dead sea: demographic evaluation and cost-effectiveness. Int J Dermatol 2000;39:59-69.

[20] Portugal-Cohen M, Dominguez MF, Oron M, Holtz R, Ma'or Z. Dead Sea minerals-induced positive stress as an innovative resource for skincare actives. J Cosmet Dermatol Sci Appl 2015;5:22.

[21] Anton BP, DasSarma P, Martinez FL, DasSarma SL, Al Madadha M, et al. Genome Sequence of Salarchaeum sp. strain JOR-1, an extremely halophilic archaeon from the Dead Sea. Microbiol Resour Announc 2020;9:e01505-19.

[22] Obeidat M. Isolation and characterization of extremely halotolerant Bacillus species from Dead Sea black mud and determination of their antimicrobial and hydrolytic activities. Afr J Microbiol Res 2017;11:1303-1314.

[23] Ma'or Z, Henis Y, Alon Y, Orlov E, Sørensen KB, et al. Antimicrobial properties of dead Sea black mineral mud. Int J Dermatol 2006;45:504-511.

[24] Al-Karablieh N. Antimicrobial Activity of Bacillus Persicus 24-DSM Isolated from dead sea Mud. Open Microbiol J 2017;11:372-383.

[25] Jacob J, Irshaid F. A New shewanella putrefaciens strain isolated from the dead sea of Jordan. Malays Appl Biol J 2013;42:1-7.

[26] Khaleque HN, González C, Shafique R, Kaksonen AH, Holmes DS, et al. Uncovering the mechanisms of halotolerance in the extremely acidophilic members of the acidihalobacter genus through comparative genome analysis. Front Microbiol 2019;10:155.

[27] Hussein EI, Jacob JH, Shakhatreh MAK, Al-Razaq MAA, Juhmani ASF, et al. Exploring the microbial diversity in Jordanian hot springs by comparative metagenomic analysis. Microbiologyopen 2017;6:e00521.

[28] Roemhild K, von Maltzahn F, Weiskirchen R, Knüchel R, Stillfried SV, et al. Iron metabolism: pathophysiology and pharmacology. Trends Pharmacol Sci 2021;42:640-656.

[29] Katz U, Shoenfeld Y, Zakin V, Sherer Y, Sukenik S, et al. Scientific evidence of the therapeutic effects of dead sea treatments: a systematic review. Semin Arthritis Rheum 2012;42:186-200.

[30] Gurich N, Anastasia MK, Grender J, Sagel P. Tooth color change and tolerability evaluation of a hydrogen peroxide whitening strip compared to a strip, paste, and rinse regimen containing plant-based oils and Dead Sea salt. Am J Dent 2023;36:151-155.

[31] Nowzari H, Wilder-Smith P. Effects of mouthwash on oral cytomegalovirus, epstein-barr virus, Herpes simplex Virus Type-1. Adv Clin Med Res 2022;3:44.

[32] Nowzari H, Tuan MC, Jorgensen M, Michel MG, Michel JF. Dead sea salt solution: composition, lack of cytotoxicity and in vitro efficacy against oral leukotoxins, endotoxins and glucan sucrose. Insights Biol Med 2022;6:9-14.

[33] Calvo-Guirado JL, Fernandez Dominguez M, Aragoneses JM, Martínez González JM, Fernández-Boderau E, et al. Evaluation of new seawater-based mouth rinse versus chlorhexidine 0.2% reducing plaque and gingivitis indexes. a randomized controlled pilot study. Appl Sci 2020;10:982.

[34] Ajdaharian J, Takesh T, Anbarani A, Ho J, Wilder-Smith P. Effects of a novel mouthwash on dental remineralization. Dentistry 2017;7:432.

[35] Rodriguez AE, Ajdaharian J. Effects of a novel mouthwash on plaque presence and gingival health. Dentistry 2017;7:460.

[36] Ben-Yosef R, Vexler A, Asna N, Khafif A, Sarid D, et al. Minimizing radiochemotherapy induced acute skin and mucosal toxicity in head and neck cancer patients treated by Dead Sea products. J Clin Oncol 2005;23:5606-5606.