

The Efficacy Of Probiotics And Lactoferrin In The Treatment Of Black Stain: A Systematic Review Of The Literature

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ABSTRACT

Introduction: In the context of daily practice, the dental hygienist and the dental team often find themselves treating patients with black stain, a common condition characterized by stains on the tooth surfaces of chromogenic origin. This work analyzes the efficacy of using lactoferrin and probiotics in the treatment of black stain.

Objective: The purpose of this research is to conduct a systematic review of the scientific literature to investigate the efficacy of probiotics and lactoferrin in the prevention and treatment of black stains. The review intends to offer a detailed and impartial synthesis of current knowledge, evaluating whether the available evidence is sufficient to confirm the usefulness of these therapeutic approaches.

Materials and Methods: A systematic review of the literature was performed by consulting several scientific databases, including PubMed/MEDLINE, Embase, and Cochrane. The methodology adopted was based on the PRISMA 2020 protocol, which led to the selection of four articles that met the defined inclusion criteria.

Results: The analysis of the literature highlighted that both examined treatments contribute significantly to reducing the formation of black stains. Lactoferrin acts by sequestering iron ions, responsible for pigmentation, while probiotics support the rebalancing of the oral microbiota, creating an environment less favorable to the proliferation of chromogenic bacteria. The evidence suggests that the combination of lactoferrin and probiotics could constitute an innovative and promising approach in the management of this condition.

Conclusions: The analysis conducted reveals that the currently available information on the treatment of black stain with lactoferrin and probiotics is still limited. Greater attention to research in this area is needed, evaluating the association of lactoferrin and probiotics as a potentially effective therapeutic option to tackle black stains.

Keywords Black stain; Lactoferrin; Probiotics; Oral microbiota; Combination therapy.

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INTRODUCTION

Black stain represents a frequent aesthetic and clinical problem in pediatric and adolescent dentistry. These dental stains, often associated with the presence of chromogenic bacteria, accumulate on the tooth surface, causing dyschromia that can negatively influence patients' self-esteem and motivation towards proper oral hygiene. (1, 2)

In recent years, interest in alternative therapeutic approaches has led to the exploration of the use of lactoferrin and probiotics in combined treatments. Lactoferrin is a glycoprotein present in milk and other biological fluids, known for its antimicrobial and anti-inflammatory properties. It acts by sequestering iron ions, which are fundamental for the growth of microorganisms, including those responsible for black stain, thus reducing bacterial colonization and promoting a favorable balance of the oral microbiota. (3)



Fig. 1 The image shows an example of black stain affecting the anterior dental arches (Partynia, CC BY-SA 4.0, via Wikimedia Commons).

Probiotics, on the other hand, are live microorganisms that provide health benefits to the host by modulating the microbiota. Strains such as *Streptococcus salivarius* M18 and *Lactobacillus reuteri* have demonstrated potential in reducing bacterial plaque and preventing periodontal diseases. However, despite their promising properties, the literature is lacking regarding the combined use of lactoferrin and probiotics in the treatment of black stain. (4) The objective of this study is to examine the available evidence on the efficacy of lactoferrin and probiotics, both as single and potentially combined therapies, for the treatment of black stain.

MATERIALS AND METHODS

A systematic review of the literature was conducted using

the PubMed/MEDLINE, Embase, and Cochrane databases, following the PRISMA method (5). The search was completed on October 18, 2024, and included the search strings in table 1.

The search strings were developed using the PICO protocol.

The inclusion criteria comprised are shown in table 2. While the exclusion criteria were are shown in table 3.

RESULTS

A total of 100 articles were found, 42 for the first search string and 54 for the second string. The third query yielded no results on any database searched. After eliminating duplicates, 42 articles for lactoferrin and 48 for probiotics were analyzed. Of these, four studies were selected for the

Search String		
First search string	Second search string	Third search string
"Chromogenic bacteria teeth OR black stain AND lactoferrin"	"Chromogenic bacteria teeth OR black stain AND probiotics"	"Chromogenic bacteria AND black stain AND probiotics AND lactoferrin"

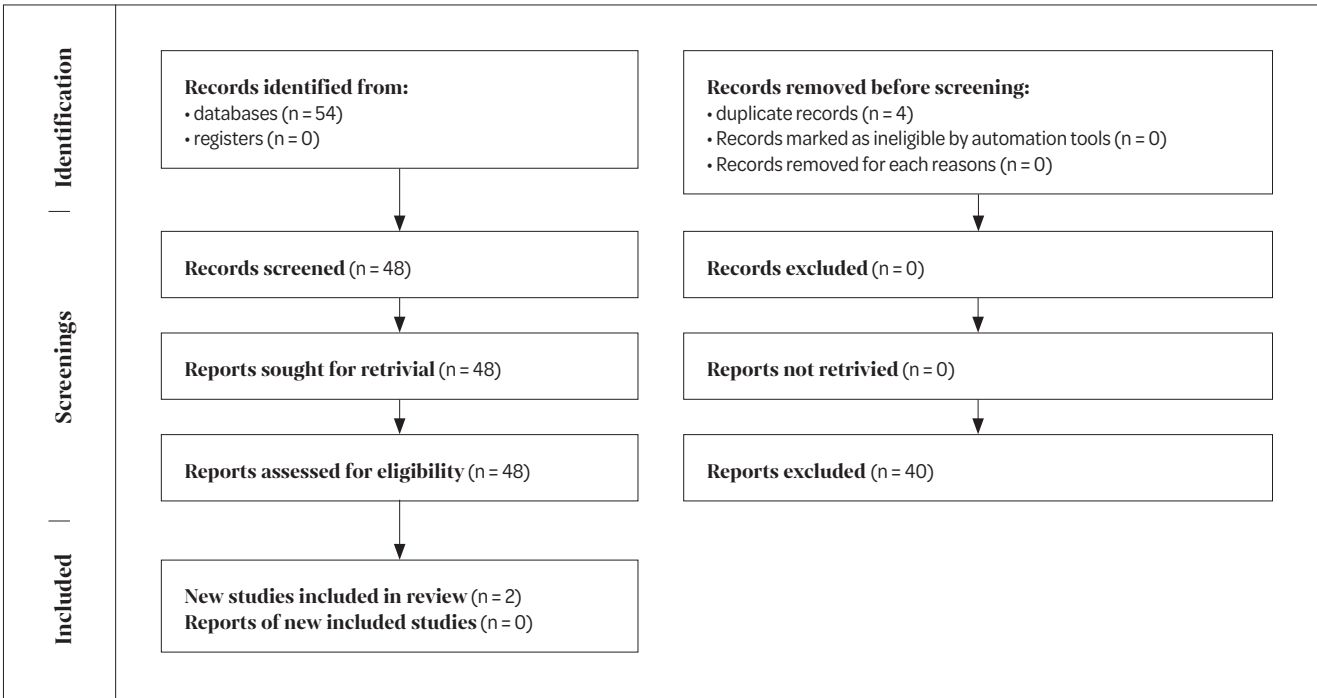
Tab. 1

Inclusion criteria
Availability of the full text
Complete articles
Articles in the English language
Clinical studies
Randomized controlled trials
Systematic reviews and meta-analyses

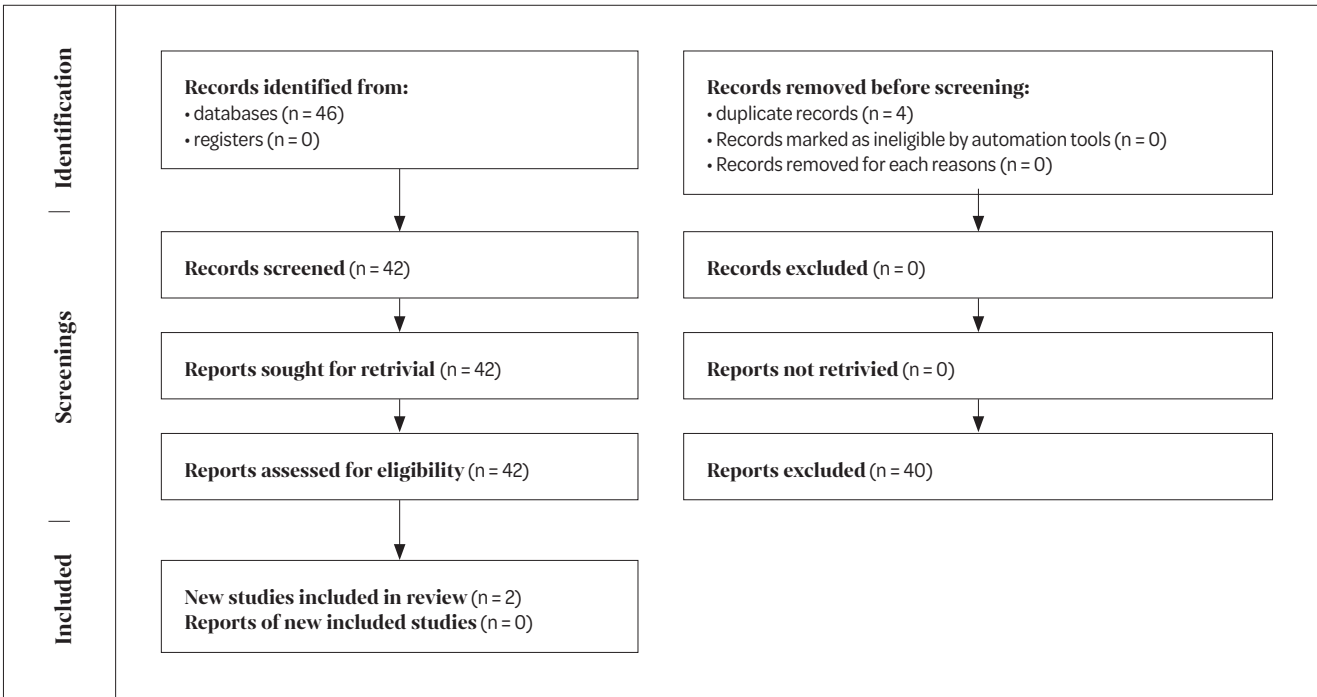
Tab. 2

Exclusion criteria
Inability to access the full text
Incomplete articles
Studies not pertinent to the research question
Incomplete results
Unclear research methodology
Articles not available in the English language

Tab. 3



Tab. 4 PRISMA Flow Diagram of the First Search String



Tab. 5 PRISMA Table for the Second Search String

review after applying the inclusion and exclusion criteria (table 4 and 5). The tables 6 and 7 report the articles that were included in the review.

Lactoferrin

The study by Sangermano R. et al. (6) is observational in nature and involved subjects affected by black stain. The

protocol involved the oral administration of two tablets of Lactoferrin (Lf) (containing 50 mg of Lf and 50 mg of D-Biotin) twice a day, after thorough oral hygiene. The results obtained demonstrate that Lf represents an effective and innovative treatment for counteracting black stain, as it is able to sequester the excess iron ions present in saliva.

The study by Rosa L. et al. (7) describes the complexity of

“Chromogenic bacteria teeth OR black stain AND lactoferrin”

Sangermano R, et al., *The treatment of black stain associated with of iron metabolism disorders with lactoferrin: a literature search and two case studies.* Clin Ter. 2019 Sep-Oct;170(5):e373-e381.

Rosa L, et al., *Lactoferrin: A Natural Glycoprotein Involved in Iron and Inflammatory Homeostasis.* Int J Mol Sci. 2017 Sep 15;18(9):1985.

Tab. 6

“Chromogenic bacteria teeth OR black stain AND probiotics”

Gobbi E, et al., *In vitro inhibitory effect of two commercial probiotics on chromogenic actinomycetes.* Eur Arch Paediatr Dent. 2020 Dec;21(6):673-677.

Bardellini E, et al., *Does Streptococcus Salivarius Strain M18 Assumption Make Black Stains Disappear in Children?* Oral Health Prev Dent. 2020 Apr 3;18(2):161-164.

Tab. 7

the oral microbiota and evaluates the efficacy of lactoferrin through an observational study, in which Lf tablets were administered twice a day for a period of 90 days. The data collected highlight that the availability of iron in saliva is a determining factor for the formation of black stain. In particular, lactoferrin is able to chelate two ferric ions per molecule and establish bonds with anionic surfaces, demonstrating antioxidant, bacteriostatic, bactericidal, anti-biofilm, anti-adhesive, anti-invasive, and anti-inflammatory properties.

Probiotics

The article by Gobbi E. et al. (8) analyzes the inhibitory effect of two commercial probiotics, *Streptococcus salivarius* M18 and *Lactobacillus reuteri* Prodentis, against the microorganisms associated with black stain. The results indicate that both probiotics are able to reduce the presence of pathogens related to black stain, in particular *Aggregatibacter actinomycetemcomitans* and *Actinomyces naeslundii*, in a dose-dependent manner. In detail, *Streptococcus salivarius* M18 showed superior antimicrobial activity compared to *Lactobacillus reuteri* Prodentis. Furthermore, *Actinomyces naeslundii* is less susceptible to the action of probiotics compared to *Aggregatibacter actinomycetemcomitans*. These results highlight the ability of probiotics to inhibit the growth of microorganisms associated with black stain, suggesting that such strains could be evaluated for therapeutic use in the treatment of this condition.

In the randomized study by Bardellini E. et al. (9), the efficacy of the oral probiotic *Streptococcus salivarius* M18 is evaluated in children affected by black stain. 58 children aged between 4 and 10 years were involved, randomly divided into two groups: group A received the product containing *Streptococcus salivarius* M18 once a day for 3 months, while group B received no treatment. The evaluation of black stain was performed after 3 and 6 months. The results show that, after 3 months, black stain was present in 6 of the 28 children in group A and in 13 of the

26 children in group B. After 6 months, black stain was found in 9 of the 28 children in group A and in 14 of the 26 children in group B. Therefore, the administration of *Streptococcus salivarius* M18 via oral tablets seems to contribute to slowing the growth of black stain in children.

DISCUSSION

The results confirm that both lactoferrin and probiotics have significant potential in the treatment of black stain, but independently. Lactoferrin acts primarily by sequestering iron, a key element for the growth of chromogenic bacteria, while probiotics modulate the oral microbiota, favoring an environment less prone to the formation of black stains.

However, the combination of these two therapies remains unexplored. The association of lactoferrin and probiotics could theoretically offer a synergistic effect, combining iron sequestration with the promotion of beneficial bacteria. This hypothesis, if confirmed, could lead to more effective therapeutic protocols. Controlled clinical trials



Fig. 2 The image below illustrates an example of black stain on the posterior teeth.

are needed to evaluate the safety, efficacy, and optimal doses of this combination.

A further aspect to consider is the need to evaluate the efficacy of home treatments compared to professional ones, in particular to improve patient adherence and long-term results.

CONCLUSIONS

The review highlights that lactoferrin and probiotics represent promising approaches for the management of black stain. However, the absence of studies on the combined use of these agents represents a significant gap in the literature.

The combination of lactoferrin and probiotics could potentially revolutionize the treatment of black stain, but further research is needed to evaluate its efficacy and define standardized protocols. Investing in future studies on this topic is essential to improve the quality of care and optimize the management of this widespread dental condition.

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