

INPLASY

Effects of D-Tagatose on the bacterial growth of *Streptococcus mutans* and oral biofilms. Systematic review

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Preliminary searches.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY2023120121

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 31 December 2023 and was last updated on 31 December 2023.

INTRODUCTION

Review question / Objective To analyze the effect of D-tagatose on the proliferation of oral bacteria related to carious lesions.

Condition being studied It is currently known that dental caries is one of the most common chronic noncommunicable diseases (NCD) worldwide, defined as a localized process of multifactorial origin that begins after tooth eruption, the result of which determines the softening and formation of cavities in the dental hard tissue, affecting health and quality of life.

Regarding this pathology, its etiology is commonly attributed to a dysbiosis on the oral biofilm, characterized by the presence of thousands of microorganisms, among which *Streptococcus Mutans* stands out as a determining factor of the cariogenic process, both for its adhesion capacity generated from the fermentation of sugars and carbohydrates from the diet and for the demineralization processes caused by low

concentrations of hydrogen ions. In this context, it is known that an extracellular environment rich in polysaccharides (EPS) allows the synthesis of glucan polymers related to glucosyltransferase enzymes (Gtfs), whose interactions favor the development of the extracellular matrix, transport capacity and carbohydrate metabolism.

In this sense, as D-Tagatose have traditionally been attributed sweetness properties and low or no caloric value, compared to sucrose, in addition to potential effects on the concentration of hydrogen ions related to the prevention of various NCDs, while currently the United States Food and Drug Administration (FDA) has approved since 2003 the use of D-tagatose for daily consumption because it does not generate health complications, This has led the European Union (EU) to designate it as a food ingredient free of restrictions for its use, whose characteristics include an antihyperglycemic potential at postprandial serum level, as well as a preventive capacity on the formation of dental caries and other oral diseases related to the acidogenesis of glucan from the

enzymatic process of GTFs in the presence of sucrose. Similarly, D-tagatose, when compared with other sweeteners such as Xylitol, has been shown to be a much more potent anticariogenic as it does not lose its acid suppressive capacity when combined with sucrose.

METHODS

Participant or population Healthy adults.

Intervention The intervention will consider the administration of any D-tagatose protocol.

Comparator Sucrose as positive control or water as negative control.

Study designs to be included Original articles (experimental and/or observational).

Eligibility criteria All "in vitro" models will be eliminated from this review. In addition to any methodological design other than an original study such as synopses, reviews, editorials and books.

Information sources A search will be carried out in the databases; Virtual Health Library, Europe PMC, Medline (PubMed), Scopus and Cochrane Central. In all databases, the years 2013 to 2023 were applied as a temporal filter, while for the Scopus databases the methodological filter "article" was used. The strategy constructed based on the terms Medical Subject Headings (MeSH): "Tagatose", "D-tagatose" and "Dental caries" together with the Boolean operator "OR" and "AND" so that the following strategy was used for all searches: "Tagatose OR D-tagatose AND Dental Caries".

Main outcome(s) Count of salivary bacteria of the genus *Streptococcus*. In addition, the phenotype, gene expression and bacterial metabolic profiles over time.

Quality assessment / Risk of bias analysis The studies included in this review will be evaluated according to the recommendation of the "Guidelines for the critical review of qualitative studies." This tool consists of 16 questions that evaluate; purpose or objective of the study (item 1), relevance of bibliographic background (item 2), suitability of the study design (item 3), the sample studied (items 4 and 5), use of informed consent (item 6), outcome measures (items 7 and 8), description of the methodology (item 9), significance of the results (item 10), statistical analysis (item 11), practical importance (item 12), description of dropouts (item 13), conclusions

(item 14), practical implications (item 15) and limitations (item 16). These 16 quality criteria were rated on a binary scale (0/1), with the exception of items 6 and 13, where option 3 "not applicable" is added. This tool allows a comparison of the methodological quality of different designs by calculating the percentage score, where the result allows classifying the methodological quality as; (A) Excellent methodological quality, with a score >75, (B) Good methodological quality, with a score between 51 and 74.99, and (C) Low methodological quality, with a score <50.99.

Strategy of data synthesis The search, review and data extraction process will focus on the acronym P.I.C.O (population, intervention, comparison and results of interest), where the following information will be searched; primary author; qualification; keywords; study design; year of publication; population; ethical considerations; intervention, comparisons; results of interest; and conclusions of the work. The search, review and data extraction of each article will be processed independently by two researchers, and any disagreement regarding eligibility will be determined by a third independent researcher.

Subgroup analysis Analysis subgroups will be sought based on the main bacterial genera of the Streptococcaceae family (*mutans*, *gordonii* and *oralis*). As well as attempts will also be made to create subgroups based on the dose of D-tagatose.

Sensitivity analysis The sensitivity of the analysis will consider the weighting of the p value ($p < 0.05$), Confidence Interval (CI: 95%), effect size, in addition to any central tendency and dispersion statistics.

Language restriction None.

Country(ies) involved Chile and Russia.

Keywords Tagatose; Dental Caries; *Streptococcus* Mutans. Biofilms.

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