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Clinical effectiveness of salivary substitutes for patients suffering from Xerostomia - A Systematic review.

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ABSTRACT

Background - Saliva play pivotal role in many systemic activities such as swallowing, speech, digestion and taste perception. Therefore decrease in salivary flow can disrupt such activities and lead to conditions such as dysphagia , taste disorders, malnutrition and halitosis etc. [1]Xerostomia refers to a subjective symptom of dryness of mouth. [2]Hyposalivation refers to a condition when stimulated salivary flow and non stimulated flow are 0.7 ml/min and 0.1- 0.2 ml/min respectively. [3]Xerostomia occurs 5% - 46% of population, elderly people are mostly affected, females are more affected than male. [4]Numerous co-existing systemic as well as environmental condition leads to xerostomia. Xerostomia can be classified as true xerostomia and pseudoxerostomia. True xerostomia refers to a condition where salivary gland dysfunction occur in contrast term pseudoxerostomia consider a condition where hyposalivation occurs without salivary gland dysfunction.[5] Additionally there is a lack of consensus on the optimal formulation, dosage and long term impact of salivary substitutes. Current research has yielded insights into the potential benefits of salivary substitutes including short-term relief of dry mouth symptoms and improved oral comfort.

Material and method - In this review, preferred reporting items for systematic reviews and meta-analyses and Cochrane Collaboration criteria are used as guideline to formulate review question, identify studies and assess their quality of selected studies, data extraction, and reporting. A protocol was developed before starting the search process for this review.

Results -The electronic search identified a total of 438 potential records. A total of 207 articles in PubMed, 229 articles in CENTRAL, and 2 articles were found in Embase. 53 duplicate articles were found and removed. The same two reviewers who performed electronic search, independently screened titles and abstracts of identified records and selected 33 articles on the basis of inclusion–exclusion criteria. Later, articles published before 2009 were excluded from the study and 17 articles were selected. Full-text copies of these reports were obtained. Of these 17 articles. Full text of two articles could not be obtained. Corresponding authors of these two papers were contacted for obtaining full texts but they failed to reply. A total of 15 trials were included for qualitative analysis.

Conclusion - It could be concluded that xerostomia affects the quality of life and studies included in this presented paper were carried out the different artificial salivary substitute therefore it is challenging to reach in definite conclusion. Oral7® Mouthwash (Contains natural enzymes glucose oxidase, lactoperoxidase, lysozyme and lactoferrin) was more effective in case of radiation induce xerostomia, in other hand herbal products were more effective in case of idiopathic xerostomia ,whereas use of Aldiamed® spray more effective in case of type I and type II diabetes mellitus. However, in case of drug induced xerostomia topical application of lycopene enriched virgin olive oil was more effective.

INTRODUCTION

Saliva plays a pivotal role in many systemic activities such as swallowing, speech, digestion and taste perception. Therefore decrease in salivary leads to conditions such as dysphagia , taste disorders, malnutrition and halitosis etc. [1]Xerostomia refers to subjective symptoms of dryness of the mouth. [2]Hyposalivation refers to a condition when stimulated salivary flow and non stimulated flow are 0.7 ml/min and 0.1- 0.2 ml/min respectively. [3]Xerostomia occurs 5% - 46% of population, elderly people are mostly affected, females are more affected than male. [4]Numerous co-existing systemic as well as environmental condition leads to xerostomia. Xerostomia can be classified as true xerostomia and pseudoxerostomia. True xerostomia refers to a condition where salivary gland dysfunction occurs in contrast term pseudoxerostomia consider a condition where hyposalivation

occurs without salivary gland dysfunction. [5]Xerostomia can be caused by various factors. Use of xerogenic medications are primary etiological factor in elderly patients. Medications with anticholinergic activity have potent inhibitory action on salivary glands thus it causes xerostomia. [6]Hyposalivation plays moderate role in condition of microflora, which varies accordance to the condition of the xerostomia. [7]Patients with radiation therapy , type II diabetes , sjogren syndrome are more prone to xerostomia.Preventive measures should be followed by the patients of the xerostomia, maintains of the good oral hygiene and regular oral check up are essential preventive measure of xerostomia. The treatment of xerostomia is difficult and unsatisfactory most of the times. Various treatment modalities have been implicated in eradication of xerostomia. [10]Symptomatic relief can be achieved by the sipping of water, discontinue of xerogenic drugs, quit the habit of tobacco and alcohol consumption, use of salivary stimulator such as chewing gum, and use of artificial salivary substitute. However, the available evidence is often heterogenous with variations in study designs, participant characteristics and outcome measures. Additionally there is a lack of consensus on the optimal formulation, dosage and long term impact of salivary substitutes. Current research has yielded insights into the potential benefits of salivary substitutes including short-term relief of dry mouth symptoms and improved oral comfort.

2. Methodology

In this review, preferred reporting items for systematic reviews and meta-analyses and Cochrane Collaboration criteria are used as guidelines to formulate review question, identify studies, assess the quality of selected studies, extract data, and report. A protocol was developed before starting the search process for this review. The present systematic review was registered at the National Institute for Health Research PROSPERO International Prospective Register of Systematic Reviews (reg.no.: CRD42023477548). This research protocol is designed according to the Preferred Reporting Items for Systematic Review and Meta-Analyses guidelines (PRISMA) 2021.

Review Question:

Which is a better salivary substitute for patients suffering from Xerostomia?

Identification and selection of relevant studies

A literature search was carried out in electronic databases in September 2023. The Cochrane Central Register of Controlled Trials (CENTRAL), PubMed, and Embase were the electronic databases used to retrieve the primary studies. In PubMed, filters were used to limit the search to clinical trials conducted on humans published during the past 10 years (from 2013 to 2022).

To obtain additional data, a manual search was performed using the reference lists of the included articles. Inclusion and exclusion criteria were also considered in hand-searched articles.

Search Strategy:

- The search strategy was based on controlled vocabulary [Mesh Terms] of the Pubmed database along with free keywords that were combined with the Boolean operators.
- The "participant" and intervention concepts from the PICO question was combined with Boolean operators [AND] and [OR].
- Different key words/search terms were used to access studies from the databases. The search terms used to retrieve studies include "Saliva substitutes", "Mouthwash ", "toothpaste", "Xerostomia", "combination therapy", "Randomized Controlled Trials" "meta-analysis", "systematic review".

The selection criteria were as follows:

Inclusion criteria

The following criteria were included in the study:

1. Parallel group and crossover clinical trials.
2. Articles written in English only.
3. Studies on humans only.
4. Studies published after 2012.
5. Studies that investigate the use of salivary substitutes as a primary intervention for xerostomia.
6. Salivary substitutes can include artificial saliva, oral lubricants, or other products designed to mimic the properties of natural saliva.

Exclusion criteria

The following criteria were excluded from the study:

1. Review articles.
2. Letter to editor.
3. Observational studies.
4. Studies conducted on animals.
5. Articles related to interaction of artificial saliva with different dental restorations and metals.
6. Trials related to systemic medication or sialogogues.
7. Trials that compared topical treatments with systemic treatments such as oral pilocarpine or oral cevimeline.
8. Studies with inadequate information on the intervention or outcomes.

Duplicate articles were removed. Articles were initially screened by reading the titles and abstracts. The remaining articles were screened in the final stage by reading the full text, and those not meeting inclusion criteria were excluded from the study.

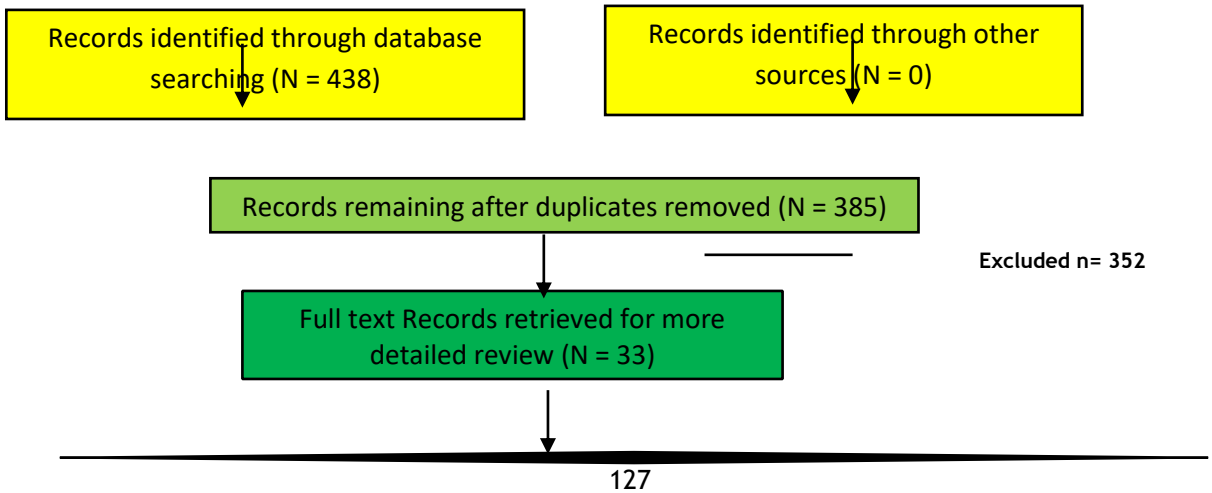
Data extraction

All randomized controlled trials that seemed to fit the reviewer's inclusion requirements were evaluated by the review author and a research assistant in order to determine eligibility, evaluate bias risk and gather data using a data extraction form.

3 - Results

Result of electronic search performed

The electronic search identified a total of 438 potential records. A total of 207 articles in PubMed, 229 articles in CENTRAL, and 2 articles were found in Embase. 53 duplicate articles were found and removed. The same two reviewers who performed electronic search, independently screened titles and abstracts of identified records and selected 33 articles on the basis of inclusion-exclusion criteria. Subsequently, 17 publications were chosen after papers released prior to 2009 were removed from the analysis. Copies of these reports in full texts were acquired. Two of these 17 articles' entire texts could not be retrieved. We reached out to the corresponding authors of these two papers to request full texts, but they did not answer.



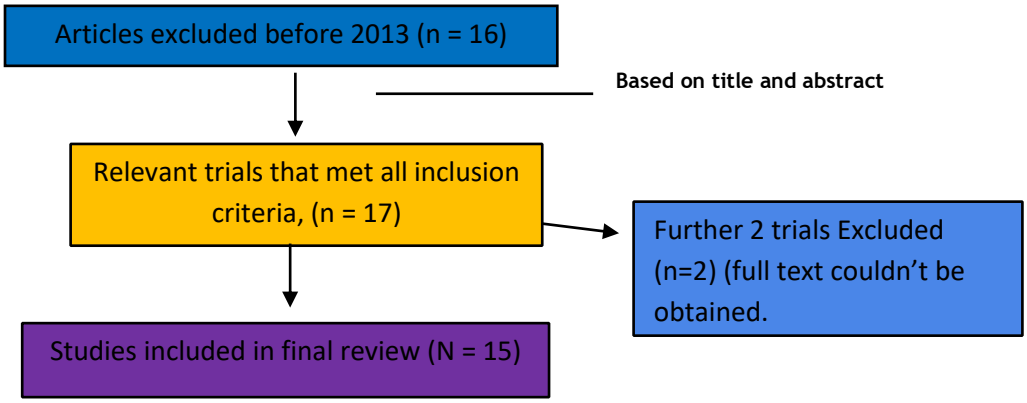


Figure 1: Retrieval and selection of eligible Randomized controlled trials of saliva substitutes for treatment of Xerostomia

CHARACTERISTICS OF INCLUDED STUDIES:

Reference	Year	Country	Design	Participants (N)	Interventions	Comparator/ Control group	Primary Outcome	Author's Conclusion
Balyan V. et al.	2022	India	RCT	30 patients with dry mouth symptoms. (N= 30)	Spray made from peppermint oil (1ml) Propolis (1.5ml), Xylitol and water (50ml)	Ethyl alcohol (10ml), Xylitol (700mg4) and water	Gingival index, plaque index and visual analog scale(VAS) decreases in both groups	Essential oil and propolis spray are effective in improving oral health of patients suffering from dry mouth and dentinal hypersensitivity.
Lam-ubol A et al.	2021	Thailand	RCT	Xerostomic post-radiotherapy head and neck cancer patients. (30 in OMJ group and 26 in GC group) (N=56)	Oral moisturizing jelly (OMJ) (lactoperoxidase enzyme, lactoferrin and lyzozyme)	A topical commercial gel (GC dry mouth gel) (ethyl p-hydroxybenzoate)	Both OMJ and GC saliva gels could improve saliva pH and decrease the number of Candida species	OMJ is superior to GC in its buffering capacity, while GC may better improve salivary flow rate.
Monsen RE et al.	2021		Block RCT	Adult patients with late-stage cancer in an inpatient hospice unit patients. (N=88)	Salvia officinalis (SO) based herbal mouth rinse. (sage)	Normal saline	Salvia officinalis mouth rinse (herbal) intervention was as good as, but not significantly better than normal saline rinsing for reducing oral symptoms.	Both mouth rinses improved oral health parameters, indicating that systematic assessment and oral care may reduce oral discomfort
Marimuthu D et al.	2021	Malaysia	RCT	Nasopharyngeal cancer (NPC) survivors having xerostomia (N=47)	Immunologically active saliva substitute (IASS) (lactoperoxidase, lyzozymes, glucose oxidase, lactoferrin)	Non-immunologically active mouthwash as placebo.	IASS mouthwash significantly reduce summated xerostomia inventory (SXI) and improves unstimulated whole saliva (UWS)	IASS mouthwash significantly reduces subjective xerostomia scores measured using SXI and improves objective measurement of salivary flow using UWS among nasopharyngeal cancer survivors with xerostomia.
Marin C et al.	2021	Chile	RCT	51 participants with drug induced or idiopathic xerostomia (17 in each group) (N= 51)	1. Intervention 1: 1% malic acid salivary stimulant spray 2. Intervention 2:1.33% betaine-based saliva substitute mouthwash	Placebo	Both tested agents are comparable in improving the dry mouth sensation and OHRQoL of patients	Both tested agents are comparable in improving the dry mouth sensation and OHRQoL of patients with drug induced and idiopathic xerostomia.
Nuchit S et al.	2020	Thailand	RCT	Post-radiation head and neck cancer patients with xerostomia divided equally between two groups. (N=62)	Oral moisturizing jelly (OMJ) (lactoperoxidase enzyme, lactoferrin and lyzozyme)	Topical saliva gel (GC) (ethyl p-hydroxybenzoate)	Subjective and objective dry mouth scores, subjective swallowing problem scores, swallowing times, and clinical nutritional status in both groups were significantly improved	Continuous uses of saliva substitutes (OMJ or GC) for at least a month improved signs and symptoms of dry mouth and enhanced swallowing ability.

Morton L et al.	2020	New Zealand	Block RCT	Pre-operative elective surgical patients (N=101)	Saliva substitute (Biotene oral rinse) (phosphate, cetylpyridinium chloride, disodiumphosphate)	Water	The proportion of patients who had improved dry mouth increased from 52% for water to 62% for saliva substitutes.	IM DRY successfully achieved its primary feasibility aims: recruitment rate, completeness of these, acceptability and protocol adherence.
Sinjari B et al.	2020	Italy	RCT	Diabetic Xerostomia (ASDIX) Sixty patients of both genders were randomized into two groups of 30 subjects each (N=60)	AS group (test) :Aldiamed® spray (water, xylitol, propyleneglycol, aloe vera, lyzozyme, lactoferrin)	Placebo Spray	Aldiamed® spray was shown to be more effective than a placebo in the treatment.	The use of Aldiamed® spray was shown to be more effective than a placebo in the treatment of xerostomia in type 1 and type 2 diabetes, confirming the data of a previous short-term study
BardelliniE et al.	2019	Italy	RCT	28 patients with xerostomia due to chronic Graft versus Host Disease (cGVHD) (N=28)	14 patientsreceived a topical sialagogue spray containing malic acid 1% (SalivAktive®)	Second group, 14 patients received a placebo	Dry Mouth Questionnaire (DMQ) scores and unstimulated salivary flows rate showed significant improvement in group I	Malic acid 1% spray can be considered effective in the treatment of GVHD induced xerostomia.
Jose AG et al.	2018	Spain	Placebo-Controlled Crossover Trial	Elderly individuals (16 women and 4 Men) with dry mouth. (N=20)	Mouthwash Biotene and the Oral Balance gel (glyceryl polymethacrylatepolyglycitol, xylitol, hydroxyethylcellulose, sodium phosphate, aloe vera gel, potassium thiocynate)	Placebo after a 20-day washout period, the second phase of the study was started and the products was reversed	Improvement was observed in OHIP values, the presence of dry mouth, and the need to drink fluids to swallow.	The findings of a subjective questionnaire showed that an experimental moisturizing mouthwash provided greater relief than water only from dry mouth symptoms over 8 days.
Bachok N et al.	2017	Malaysia	RCT	Histopathologically diagnosed head and neck cancers patients (N=30)	Oral7® Mouthwash (Contains natural enzymes glucose oxidase,lactoperoxidase, lysozyme and lactoferrin)	Salt-soda Mouthwash (contains sodiumchloride + sodium bicarbonate + water)	No significant decrease in DMFT, Quality of life better in Oral 7® Mouthwash	Oral7® showed advantages over salt-soda solution in relation to reducing xerostomia, easing radiation-induced mucositis, and improving quality of life, despite the non significant difference in the dental caries assessment.
Mardani H et al.	2017	Iran	RCT	Xerostomia in patients with type II diabetes (N=20)	Ginger root (Zingiberofficinale) mouthwash	Oral spray that contained1/3 edible glycerin, and 2/3 distilled water	The mean amount of saliva after using the ginger plant spray increased significantly.	Herbal spray in rapidly increasing the patients' saliva and satisfaction as well as the acceptability of this type of medicine to treat dry mouths
Donath F et al.	2016	Germany	RCT	Male and female subjects (18 years and older) having drug-induced xerostomia and documented Hyposalivation Male =17, Female =7 (N=24)	DC161-DP0292 oral spray (glycerol, povidine K30, xanthan gum, potassium chloride, xylitol, potassium dihydrogen phosphate, benzylic alcohol, water, macroglycerol 40 hydroxysterate)	uasyal oral spray .4% triesters of glycerol oxidized fatty acids of vegetal origin)	DC161-DP0292 provides fast and long-acting symptomatic relief and is a relevant new treatment for drug-induced xerostomia.	DC1661-DP0292, is therefore considered to be a relevant treatment for drug-induced xerostomia, providing fast and long-acting symptomatic relief while potentially improving patient compliance.
Anabel NM et al.	2016	Spain	Randomized Placebo controlled trial	The study included 60 elderly subjects with drug-induced xerostomia (N=60)	Extra virgin olive oil with lycopene 300 ppm in a 250-ml spray container	Placebo (Water+dye)	topical application improve the xerostomia-related symptoms	The topical application of lycopene enriched virgin olive oil and its placebo counterpart improved xerostomia-related symptoms significantly (but not salivary flow rate) in patients with drug-induced xerostomia.
Jose AG et al.	2016	Spain	RCT	Eligible subjects were stratified by dry mouth severity (mild, moderate or severe) and randomized to receive one of	1.Oral gel 2.Oral rinse 3.Mouth spray (glycerin, xylitol, sorbitol, propylene glycol)	ter	Dry mouth-related QoL scores were statistically significant in favor of the active treatments versus water. All the dry mouth management	Dry mouth-related QoL scores were statistically significant in favor of the active treatments versus water

				the study treatments. (N=396)			strategies in this trial were well tolerated.	

Table 2: Risk of Bias Assessment

Reference	Year of Publication	Random Sequence Generation	Allocation concealment	Blinding	Incomplete outcome data
Balyan V et al.	2022	High risk .	High risk	Moderate risk (Single blind study).	Unclear risk Loss to follow up not reported .
Lam-ubol A et al.	2021	Low risk participants were randomly allocated to OMJ or commercially available GC dry mouth gel using a minimization method to match age, sex, and baseline subjective dry mouth score between groups.	High risk Not reported	Moderate risk Single blind study. no further information provided	Low risk Loss to follow up in study group was reported as 18.9% and in control group as 25.7%
Monsen RE et al.	2021	Low risk web-based randomization service in three blocks of 20 subjects and a final block of 28 subjects	Low risk Allocation sequence was concealed from the researchers enrolling participants by sequential numbered, opaque sealed envelopes.	Moderate risk Single Blind study " information provided	Low risk 25% in Intervention group and 9% in control group loss to follow up reported Primary and Secondary outcome both reported
Marimuthu D et al.	2021	Low risk A randomization list was generated from the statistics website http://www.graphpad.com/quickcalcs/index.cfm	Low risk, The researcher assigning the participants to intervention arms did not know the allocation sequence until the moment of assignment Not reported	Low risk Double blind study Both the researcher and patient are blinded to the type of intervention they received. The randomization list was not known to the researcher measuring the study outcome measures until data was analyzed.	Low risk 4% loss to follow up reported in both the groups.
Marin C et al.	2021	Low risk Randomization was done by an investigator not involved in the study through a specific web page (http://www.randomization.com/) using the method of randomly permuted blocks.	Low risk, Each formulation was placed into identical opaque flasks (with atomizer) and labelled according to randomization by personnel unrelated to the study	High risk Not reported	Unclear risk
Nuchit S et al.	2020	Low risk Participants were randomized to each group using minimization by matching age, sex, baseline subjective dry mouth score, and body mass index (BMI)	High risk, Not reported	High risk Open label	Low risk 16.2% loss to follow up in study group and 13.8% in control group.
Morton L et al.	2020	Low risk Block randomisation in groups of eight with an intervention ratio of 1:1 using a computer generated random number	Low risk, Sealed opaque envelopes.	Moderate risk single-blind study	Low risk Loss to follow up reported , 1.96% in control group whereas 0% in study group.
Sinjari B et al.	2020	Low risk was obtained using computer generated random numbers, centralized with sequentially sealed opaque envelopes provided by the study advisor as previously performed	Low risk sealed opaque envelopes	Low risk "in a double-blind manner," Both the patient and scientific experts were “blind” for what concerns the group they were assigned to. In addition, the AS and PS packages were identical in appearance	Low risk 3.3% loss to follow up in study group and 0% in control group
Bardellini E et al.	2019	Low risk, Automatically generated list in a 1:1 block size for two patients.	Low risk Patients codes where inserted into closed envelopes.	Low risk “Double Blinded” Both patients and researchers were blinded throughout the study.	High risk Not reported

Jose AG et al.	2018	Unclear risk, Parallel group Study No further information provided	High risk Not reported	Unclear risk "Single Blinded" but no further information provided	High risk, Not reported
Bachok N et al.	2017	Low risk Quasi-clinical trial Random allocation to treatment was attempted using the random numbers generated at www.randomization.com website.	High risk, Not reported	High risk, Not reported	High risk, Not reported
Mardani H et al.	2017	High risk, Not reported	High risk, Not reported	High risk, Not reported	High risk, Not reported
Donath F et al.	2016	Low risk, Computer generated randomization list provided by the Institute de Recherche Pierre Fabre.	High risk, Not reported	High risk Open label	High risk, Not reported
Anabel NM et al.	2016	Low risk, Randomization was performed using random numbers generated by specialized software (http://www.randomization . com)	Low risk The products were coded by an operator (external to the study) in identical opaque containers (without any brand name).	Low risk Double blind study Both patients and researchers were blinded to group assignment (treatment/placebo)	Low risk Loss to follow up in study group = 16.6% Loss to follow up in control group = 30%
Jose AG et al.	2016	Low risk Multicenter, randomized, parallel group study	Unclear risk	Unclear risk	Unclear risk

DISCUSSION

The study included in this review evaluated a range of the intervention used in treatment of the xerostomia. Different interventions were found to be at high or unclear risk of bias. Therefore, it was difficult to conclude the most effective intervention. However, the findings of all studies included in this study were summarized. The selected studies were categorized as:-

(A) Studies conducted on subjects with drug induced xerostomia
(B) Studies conducted on subjects with radiation induced xerostomia
(C) Studies conducted on subjects with systemic disease
(D) Studies conducted on subjects with idiopathic xerostomia

(A) Drug-induced xerostomia

Three studies were conducted on drug induced xerostomia. A study by **Martin C et al. (2021)**[13] included 1% malic acid salivary mouthwash, 33% betaine-based saliva substitute mouthwash, and a placebo control group. The study's findings indicated that the two tested agents are similar in terms of enhancing patients' subjective experience of dry mouth and overall health-related quality of life in cases of drug-induced and idiopathic xerostomia. **Donath F et al.(2016)**[14]conducted a study all selected interventions were DC161 oral spray, saliva substitute and comparator and concluded that DC161-DP0292 provides fast and long-acting symptomatic relief and is a relevant new treatment for drug-induced xerostomia. **Anabel NM et al.(2016)**[3]conducted a study all selected interventions were extra virgin olive oil with lycopene 300 ppm in a 250-ml spray container and placebo (water+dye) and concluded that the topical application of lycopene enriched virgin olive oil and its placebo counterpart improved xerostomia-related symptoms significantly.

(B) Radiation induced xerostomia

Five studies conducted on radiation induced xerostomia. **Lamubol A et al.(2021)**[12] conducted a study all selected interventions were oral moisturizing jelly (OMJ), a topical commercial gel(GC dry mouth gel) author concluded that OMJ is superior to GC in its buffering capacity, while GC may better improve salivary flow rate.**Monsen RE et al.(2021)**[15] conducted a study where all selected interventions were salvia officinalis (SO) based herbal mouth rinse, normal saline and concluded that both mouth rinses improved oral health parameters, indicating that systematic assessment and oral care may decrease oral discomfort. **Marimuthu D et al.(2021)**[16]conducted a study all selected interventions were immunologically active saliva substitute (IASS) and non-immunologically active mouthwash as placebo, and concluded that IASS mouthwash significantly reduces subjective xerostomia scores measured using SXI and improves measurement of salivary flow using UWS objective among nasopharyngeal cancer survivors with xerostomia.**Nuchit S et al.(2020)**[1]conducted a study all selected intervention were oral moisturizing jelly (OMJ) and topical saliva gel (GC) and concluded that continuous uses of saliva substitutes (OMJ or GC) for at least a month improved signs and symptoms of dry mouth and enhanced swallowing ability. **Bachok N et al(2017)**[17] conducted a study all selected interventions were Oral7® Mouthwash (Contains natural enzymes glucose oxidase,lactoperoxidase, lysozyme and lactoferrin) and salt - sodaMouthwash (contains sodiumchloride + sodium bicarbonate + water) and concluded that Oral7® showed advantages over salt-soda solution in relation to reducing xerostomia easing radiation induced mucositis and improving quality of life despite non significant difference in dental caries assessment.

(C) Systemic disease induced xerostomia

Two studies conducted for systemic disease induced xerostomia. **Sinjari B et al.(2020)**[18]conducted a study all selected interventions were AS group Aldiamed® spray and PS group placebo spray and found that The use of Aldiamed® spray more effective than placebo spray in the treatment of xerostomia of type I and II diabetes mellitus. **Mardani H et al.(2017)**[19] conducted a study all selected interventions were Ginger root (Zingiberofficinale) mouthwash and Oral spray that contained1/3 edible glycerin, and 2/3 distilled water and summarized that the use of herbal spray to treat dry mouths has been shown to quickly increase patient satisfaction and salivary flow.

(D) Idiopathic xerostomia

Five studies conducted for idiopathic xerostomia. **Balyan V et al.(2022)**[20]conducted a study all selected interventions were spray made from peppermint oil Propolis, Xylitol and Ethyl alcohol, Xylitol and water at found that essential oil and propolis spray are effective in improving oral health of patients suffering from dry mouth and dentinal hypersensitivity. **Morton L et al.(2020)**[21] conducted a study where all selected interventions were saliva substitute (Biotene oral rinse) and water and

concluded that patients who had improved dry mouth increased from 52% for water to 62% for saliva substitute.**BardelliniEet al.(2019)**[22] conducted a study all selected interventions were topical sialagogue spray containing malic acid 1% (SalivAktive®) and placebo and concluded that malic acid 1% spray can be considered effective in the treatment of GVHD induced xerostomia. **Jose AG et al. (2018)**[23] conducted a study where all selected interventions were mouthwash biotene and the oral balance gel and placebo and concluded that experimental moisturizing mouthwash provided greater relief than water only from dry mouth symptoms over 8 days.

CONCLUSION

It could be concluded that xerostomia affects the quality of life and studies included in this presented paper were carried out with different artificial salivary substitutes therefore it is challenging to reach a definite conclusion. Oral7® Mouthwash (Contains natural enzymes glucose oxidase,lactoperoxidase, lysozyme and lactoferrin) was more effective in case of radiation induced xerostomia, in other hand herbal products were more effective in case of idiopathic xerostomia, whereas use of Aldiamed® spray more effective in case of type I and type II diabetes mellitus. However, in case of drug induced xerostomia topical application of lycopene enriched virgin olive oil was more effective.

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