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Literature Review

Fluoride Varnish with Antibacterial Agents for Dental Caries Prevention: A Short Review on Its Fabrication

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ABSTRACT

Introduction: In recent years, the medical field has begun to use medicinal plant in the manufacture of modern medicines. Most of the medicinal plants used have antibacterial properties such as cinnamon, clove, betel, and holy basil. These medicinal plants could be used in the manufacture of fluoride varnish to support antibacterial properties in preventing the development of dental caries. **Objective:** This study aimed to provide update review of medicinal plant used as antibacterial agent in the fabrication of fluoride varnish to prevent dental caries. **Method:** Data collection were carried out by searching the literature on article search sites, namely PubMed and Scopus which were published from 2017 to 2022. Data searches were carried out systematically using the keywords fluoride varnish, dental caries, antibacterial, and fabrication. The author performs data search, data selection, and data extraction. **Results:** Only nine articles were found after a thorough selection process and database search using search terms and keywords. Seven of the studies were in vitro study and two was randomized clinical trial (RCT). In the overall fluoride varnish efficacy study, adding medicinal plant as an antibacterial agent showed strong antibacterial action against *S. mutans* with great bacterial inhibition zone. Together with its constituent parts, the fabricating method, such as the temperature and stirring rate, influence the optimal result of fluoride varnish. **Conclusion:** The addition of medicinal plants and method modification in the fabrication of fluoride varnish showed potential antibacterial properties that enhance higher fluoride release.

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INTRODUCTION

Fluoride varnish (FV) is one of the methods for applying topical fluoride, which can effectively prevent dental caries.[1] Several studies have been carried out to improve the remineralization ability of tooth structure by modifying the FV fabrication procedure. The procedure used in the previous study was a modification of the rotational speed and temperature when FV was stirred.[2,3] It was reported that high stirring speed and temperature can increase the release of fluoride ions in FV. In addition, flavoring oil and antibacterial agents were also reported to increase the rate of release of fluoride ions from FV.[4]

Lately, FV is fabricated with the aim of preventing the growth of bacteria that can cause dental caries, such as chlorhexidine and silver diamine.[5,6] Despite adding antibacterial properties, several studies claimed that it should not be used for extended periods of time since it can cause unpleasant side effects including discoloration of teeth, mucosal peeling, and altered taste.[7,8] Due of these negative consequences, research is being done to create FV with antibacterial agents from natural sources with higher safety profiles.

The "Return to Nature" idea refers to a recent change in the direction of the universal health movement, which previously used synthetic materials instead of medicinal plants.[9,10] Known for thousands of years as a rich source of therapeutic compounds for illness prevention, medicinal plants are well-known on a global scale.[10,11] The purpose of this review is to provide an updated overview of the development of medicinal plant using as antibacterial agent for fabricate fluoride varnish, as well as its effect on adding antibacterial properties for dental caries prevention.

MATERIALS AND METHODS

The author followed the criteria established in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[9] guidelines for this review, and using PICO as seen in Table 1. A systematic search was performed on PubMed and Scopus in August and September 2022 using the following search terms as shown in Table 2.

Based on the findings, an additional manual search considering the references of the included studies was executed. Only English full-text articles that were published after 2017 until 2022 were properly considered. Moreover, only papers that specifically mention fluoride varnish with antibacterial agent from medicinal plant content and its fabrication are included. Two reviewers independently evaluated and chose the literature for this review. The results of the analysis of the two reviewers were then discussed together so that they were included as material to the review's content.

Table 1. Description of the PICO (P = Population, I = Intervention, C = Comparison, O = Outcome) elements

Research Question	**How is the fabrication of FV with the addition of antibacterial agents from medicinal plants?**
Population	High-caries-risk teeth.
Intervention	Fluoride varnish with medicinal plant content as an antibacterial agent.
Comparison	Conventional fluoride varnish.
Outcome	Bacterial inhibition zone and fluoride ions release.

Table 2. Search terms used for database

No	**Database**	**Search Terms**
1	PubMed	(((fluoride varnish) AND (dental caries)) AND (antibacterial agent)) Filters: in the last 5 years
2	Scopus	(TITLE-ABS-KEY (varnish AND caries)) AND ((antibacterial)) AND (plant) AND (LIMIT-TO (PUBYEAR, 2022) OR LIMIT-TO (PUBYEAR, 2021) OR LIMIT-TO (PUBYEAR, 2020) OR LIMIT-TO (PUBYEAR, 2019) OR LIMIT-TO (PUBYEAR, 2018))

RESULTS

The systematic research revealed 1173 articles, and 373 duplicate records were then eliminated. 752 of the 800 articles were omitted because of not using fluoride varnish as the topical fluoride and lack of antibacterial ingredient. Thirty-nine studies were not using medicinal plants as an antibacterial agent also not retrieved. Only nine in total were chosen for this review, as shown in Fig. 1. A brief description of each of the seven entire manuscripts was provided in Table 3. Each full text used an antibacterial agent from different medicinal plants.

DISCUSSION

Based on the findings of a systematic search, nine publications were found that really studied the fabrication of fluoride varnish (FV) with addition of an antibacterial agents of medicinal plant to prevent the growth of S. mutans. Several researchers stated that some medicinal plants extract may contain secondary metabolites like essential oils, flavonoids, alkaloids, triterpenoids, and phenolic compounds which can be effective against *S. mutans*, a microorganism involved in the development of dental caries.[2–4,10,11,15] The variations in chemical

Table 3. Advantage of medicinal plant extract as an antibacterial agent in the fabrication of fluoride varnish.

Author, Year (Type of Study)	Subject	Advantage Finding / Claims
Sankeshwari et al, 2018[10] (*In vitro* study)	The fabrication of a novel fluoride varnish containing licorice (*Glycyrrhiza glabra*) extract to prevent the growth of *Streptococcus mutans*.	Licorice extract, 2 mg/mL, along in fluoride varnish showed positive antibacterial activity against *Streptococcus mutans*.
Elgamily et al, 2019[11] (*In vitro* study)	In comparison to MI varnish, methanolic extractions of five plants (cinnamon, turmeric, ginger, clove, and black seed) were examined for their ability to inhibit the development of *Streptococcus mutans* and *Lactobacillus acidophilus*.	The antibacterial activity of cinnamon and clove extract against *S. mutans* and *L. acidophilus* was extremely good. Ginger and black seed extracts showed no antibacterial action, whereas turmeric only has the potential to be antibacterial against *L. acidophilus.*
Valadas et al, 2019[12] (Randomized Clinical Trial)	24 caries-free children between the ages of 3 and 6 years old is given a copaiba (*Copaifera langsdorffii*) dental varnish to observe the reduction of *Streptococcus mutans*.	The amount of *S. mutans* bacteria might be reduced more effectively using a 1% copaiba dental varnish concentration.
Son et al, 2020[13] (*In vitro* study)	The components of *Psoralea corylifolia*, such as bakuchiol, bavachalcone, isobavachromene, and bavachromene, in comparison to xanthorrhizol, the components isolated from java turmeric (*Curcuma xanthorrhiza* Roxb.), to inhibit oral microorganisms.	All antibacterial agents were effective against *S. mutans*, bavachalcone was the most effective agent.
Valadas et al, 2021[14] (Randomized Clinical Trial)	Ninety second deciduous molars caries-free were randomly divided into three groups: copaiba (*Copaifera langsdorffii*), chlorhexidine, and fluoride. The varnishes were applied for three times: baseline (D0), after 90 days (D90), and after 180 days (D180).	Copaiba varnish showed strong antibacterial action against *S. mutans* for up to 12 months in children with a high risk of caries after three annual applications.
Souza et al, 2021 [15] (*In vitro* study)	Chitosan films containing distilled pyroligneous extracts of *Eucalyptus grandis* (DPEC) were evaluated for antimicrobial activity against *Candida albicans, Streptococcus mutans,* and *Lactobacillus acidophilus* by direct contact test.	All DPEC film formulations showed promising results in good antimicrobial potential against the main bacterial strains related to cariogenesis.
Geraldine et al, 2021[4] (*In vitro* study)	Fluoride varnish formulation using addition of LorAnn Oils flavor oils with the flavors strawberry-kiwi, cinnamon roll, and marshmallow, and also natural antibacterial agents from extracts of pomegranate (*Punica granatum*) fruit, betle (*Piper crocatum*) leaves, and soursop (*Annona muricata*) leaves to inhibit *Streptococcus mutans*.	The addition of 0.1 g/mL red betel leaves extract as antibacterial agent offers higher bacterial inhibition zone when compared to red pomegranate or soursop leaves extract with the same concentration.
Gabriella et al, 2022[3] (*In vitro* study)	*Streptococcus mutans* growth suppression caused by the addition of red betel leaf and wuluh starfruit leaf extracts to a fluoride varnish fabrication.	The optimal stirring temperature was 90^{o}C and the largest *S. mutans* inhibition zone was produced from fluoride varnish with addition of 0.1 g/mL red betel leaf extract.
Alviora et al, 2022[2] (*In vitro* study)	The leaves extracts of ruku (Ocimum sanctum) and wungu leaves (*Graptophyllum pictum* L. Griff) has the ability to inhibit bacteria *Streptococcus mutans*.	Stirring with rotational speed of 280 rpm can accelerate the release of fluoride ions during the first 4 hours. Fluoride varnish with the addition of ruku leaf extract provided a better inhibition zone for *S. mutans* than the addition of wungu leaves.

structure and molecular weight for each compound might be the cause of the different antibacterial effects. The amount of hydroxyl groups and the length of the hydrocarbon chain vary among aromatic hydrocarbons. The efficiency of the inhibition of *S. mutans* appears to increase with the amount of hydroxyl groups and hydrocarbon length.[13]

Phenolic compounds have beneficial properties as fungicides, antiseptics, and disinfectants with activity against a variety of pathogens, including a number of viruses.[16] By rearranging the amino acid chains in bacterial DNA, the high concentration of flavonoids, ethanol, and saponin disrupt the genetic equilibrium and cause bacterial DNA damage that results in lysis and death of cells.[17] Other ingredients in medicinal plants

extract such as β-caryophyllene, sesquiterpenes, and diterpenes are effective against a number of pathogens, particularly gram-positive bacteria including *Staphylococcus spp.* and *Streptococcus spp.* Moreover, it has been suggested that the β-caryophyllene can stops plaque-forming bacteria from proliferating by preventing adhesion of bacteria.[18,19]

According to earlier investigations, the FV manufacturing process can also affect fluoride ion released. Alviora et al. found that the fluoride ion release increased with FV agitation speed of 280 rpm.[2] Bae and Son used 240 rpm for stirring the production of FV.20 High stirring rates will cause the dissolved particles to disintegrate more quickly and reduce their size. The contact surface area between the solute and solvent increases with decreasing solute particle size.[21] As a result, the ions in the solute will be liberated and dispersed in the solvent more quickly.

Gabriella et al. reported that the effect of temperature on the fabrication of fluoride varnish can also affect the rate of release of fluoride ions.[3] This is because the higher the temperature used, the substances dissolved in the solvent will be more active and collide with each other. As a result, the ions in the solution will start to come out in greater numbers.[22]

It is possible to halt the demineralization process in tooth enamel caused by *S. mutans* by adding antibacterial properties to fluoride varnish using phenolic compounds derived from medicinal plants. Researchers have also shown that the use of medicinal plants with modification of its fabrication may increase the release of fluoride ions from fluoride varnish. Due to the demineralization process, the released fluoride will bond to the dissolved calcium ions to produce CaF_2 as a fluoride reservoir and will also bind to the enamel structure to create the more acid-resistant fluorapatite structure.[23] Over time, this may encourage the remineralization of tooth enamel.

CONCLUSION

This review demonstrates that the fabrication of FV with antibacterial characteristics from medicinal plants can be explored to be used in preventing caries from S. mutans and increase the fluoride ion release from fluoride varnish. Apart from the constituent components of fluoride varnish, it is also necessary to consider the procedural process of fluoride varnish fabrication. This evaluation reveals that there is still little information on the possible usage of medicinal plants to fabricate fluoride varnish with added antibacterial properties. Authors believe there is room for more research into the use of different kind of medicinal plants as antibacterial agents in the fabrication of fluoride varnish.

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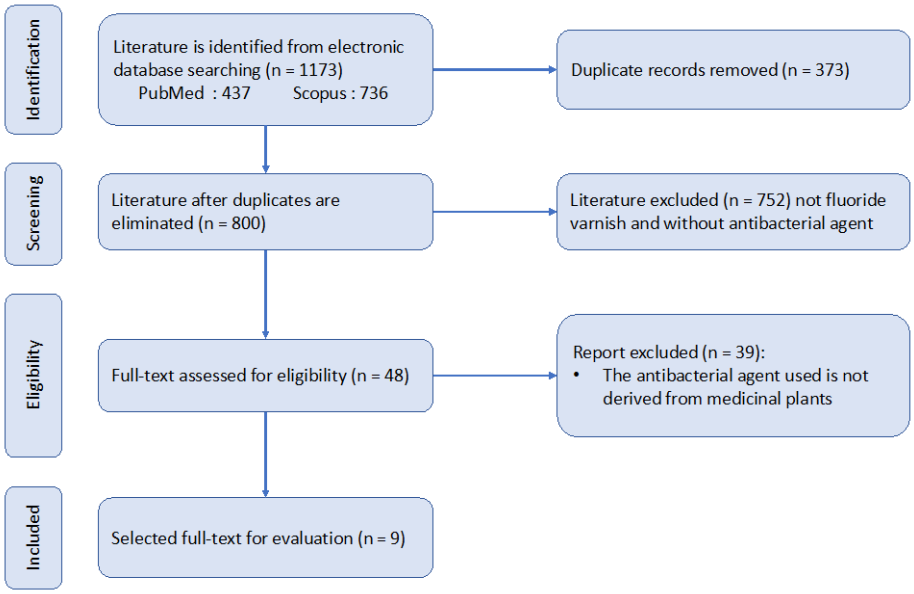

Figure 1. Identification of studies via databases and registers.

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