Review Article

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Remineralisation of Enamel using Natural and Plant Products: A Narrative Review

Dentistry Section

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ABSTRACT

Preventive approaches towards dental caries have been the focus of research in dentistry since the last century. Fluoride and various non fluoride remineralising products are already in the market. Despite this, in the last two decades, the scientific community has increased its exploration of alternative caries prevention solutions, including herbal remedies. The primary objective of this article was to review the current status and developments in the field of remineralisation using natural products, ethnopharmacological agents, and their active compounds. It could be concluded from the current review that natural phytochemicals have considerable promise as supplementary anticariogenic therapies for the prevention and treatment of dental caries. However, the ultimate efficacy of therapeutic solutions containing cariostatic natural substances depends on their capacity to demonstrate a significant reduction in individual caries progression. To establish the effectiveness of natural products in preventing dental caries or promoting remineralisation, well-designed Randomised Controlled Trials (RCTs) are necessary. In addition, additional research is required to discover the precise cariostatic modes of action and effective dosage of natural substances.

Keywords: Dental caries, Early childhood caries, Natural products, Phytochemicals

INTRODUCTION

Caries of the teeth are an epidemic problem worldwide that affects the teeth and is characterised by the dissolution of minerals and cavitation, ultimately causing pain and agony, and impacting both function and facial attractiveness [1,2]. In its 2003 report on oral health, the World Health Organisation (WHO) presents a summary of worldwide caries epidemiology that validates its global pandemic dispersion [3]. Tooth decay affects of all races, ethnicities, nationalities, and sexes. The infection will destroy the tooth's pulp and surrounding tissues if left untreated. Caries is a cyclical demineralisation and remineralisation of the mineral phase of tooth [4]. Cavitation occurs when demineralisation dominates.

The demineralisation process entails the loss of minerals underneath the surface of the enamel at the leading edge of the lesion mineral ions are transferred from the plaque to the advancing front and from the advancing front to the plaque [1]. The process of remineralisation is a natural repairing mechanism that restores the elements to the crystal structure of Hydroxyapatite (HAP) [5]. Under neutral pH, calcium and phosphate ions are redeposited in the caries lesion from saliva and plaque fluid, causing the growth of bigger, more acid-resistant HAP crystals [6]. Enamel, dentin, and cementum all have the same chemical base for the demineralisation-remineralisation process. However, the various mineral and organic tissue architectures and concentrations in each tooth component cause significant variances and carious lesions [2].

It is proven that fluoride can prevent caries lesions by remineralising demineralised enamel, thereby controlling caries lesions. In 2013, Amaechi BT and Van Loveren C, stated that fluoride forms fluorapatite crystals by becoming permanently bound to the enamel crystal [7]. Also, the decreased acid dissolution of fluorapatite can be associated with its low carbonate content and high amounts of fluoride in toothpaste. Systemic fluorides were harmful, leading to the development of non toxic fluoride substitutes that are effective remineralising agents [1]. Fluorosis can be caused by the unsupervised administration of fluoride containing dental products to children during tooth development. Polyphenolic compounds with remineralisation and antibacterial properties have been identified as active compounds in natural plant products [8].

Recent attention has been focused on the health benefits of natural products. Alternative non fluoride toothpaste that has herbal products or enzymes with antiseptic and antimicrobial properties are in use [9,10]. Natural ingredients have been used as folk medicines for millennia, and using them to develop new drugs has been quite fruitful [11]. Plant-derived antibacterial compounds may serve as an alternative to chemical treatments for plaque control and demineralisation [12]. Recent research has shown that polyphenol components in plants have anticariogenic and oral disease preventive properties [13]. Currently, research is being conducted on various foods and beverages, including tea, coffee, grapes, propolis, shiitake (Lentinula edodes) mushrooms, and traditional herbs [8].

The primary objective of this article was to review the current status and developments in the field of remineralisation using natural products, ethnopharmacological agents, and their active compounds.

NATURAL REMINERALISING PRODUCTS

Grape Seed Extract

The grape (*Vitis vinifera L.*) is among the most widely consumed fruits in the world [14]. It contains numerous bioactive compounds, including phenolic acids, flavonols, anthocyanins, proanthocyanidins, and stilbenes, the concentrations can differ between grape pulp, seed, and skin [15]. Reports have shown that grapes has numerous health advantages, such as anti-inflammatory, antioxidant, anticancer, gut-microbiome-modulating, and cardioprotective properties. Grapefruit is consumed as a fresh fruit in addition to being a raw material for manufacturing, wine, grape juice, and raisins. Moreover, grape byproducts such as grape seed and grape pomace have food sector applications [16].

In recent years, the use of grape seeds in alternative medicine has been on the rise to treat a variety of diseases, due to their high phenolic and antioxidant content [17]. Grape seeds have many applications in dentistry for restorative procedures and caries prevention. Grape seeds effects on dental pathologies are attributable to the proanthocyanidin group [18]. It inhibits the colonisation of *S. mutans*, responsible for dental caries [19]. In addition, numerous

scientific studies have emphasised the role of extract from grape seeds in dental remineralisation [20], averts tooth erosion [21], and affects tooth tensile strength [22]. Such mechanisms are caused by grape extract's phytocompounds, which bind to enzymes that break down tooth enamel and stimulate crosslinking of collagen-rich dentin surfaces, both of which are beneficial to oral health [18]. Comparative studies on remineralisation using Grape Seed Extract (GSE) have been tabulated in [Table/Fig-1] [23-28].

Galla Chinensis

Galla Chinensis, the result of the Chinese sumac aphid, which parasitises on Rhus Chinensis Mill leaves is a fascinating non toxic natural Chinese traditional medicine. After removing the larvae, the plant is gathered in autumn and fried dried into a traditional remedy. It has antibacterial, antiviral, and antifungal characteristics, as well as to speed blood coagulation [29].

G.Chinensis suppresses the growth, adhesion, and acid generation of cariogenic microorganisms [30,31]. In contrast to other natural products, G.Chinensis appears to possess low antibacterial activity. It is the only traditional medication proven to influence the process of hard tissue mineralisation, setting it apart from other naturally occurring anticaries compounds. G.Chinensis crude aqueous extract has been proven to suppress the demineralisation of enamel [32]. In addition, it has been shown that under pH-cycling conditions, it results in a net rehardening of artificial carious lesions [33,34].

In recent years, it has been demonstrated that an extract of Galla Chinensis that is rich in polyphenols was found to reduce the proliferation and metabolism of caries pathogens, as well as promote remineralisation and prevent demineralisation of enamel [35]. Comparative studies on remineralisation using Galla Chinensis extract have been tabulated in [Table/Fig-2] [36,37].

Propolis

The word propolis is derived from the Greek words "pro," which means defense, and "polis," which means city. Therefore, propolis protects the hive (city) [38]. Bees collect propolis, a resinous hive byproduct. According to records, the ancient Egyptians (about 1300 BC) used propolis to heal many diseases [39]. Propolis was exploited by the Romans and Greeks for its wound-healing powers [40].

Active natural elements such as plant balsams, volatile oils, flavonoids, phenolic acids, fatty acids, aromatic alcohols, mineral salts, vitamins, and beeswax are all found in propolis, which is a black, dense, and sticky mixture of resin and wax [38]. It's a natural compound with a variety of therapeutic uses. Several studies demonstrate propolis's pharmacological activity in the pharmaceutical, medicinal, veterinary, and dentistry domains. Propolis is beneficial to health in many ways. It is effective against *S.mutans*, facultative anaerobes, and Gram+ve cocci in the mouth [39-41]. To capitalise on this enormous opportunity, numerous firms have included propolis in their toothpaste and mouthwashes to prevent tooth decay and gingivitis [42]. It has been shown that toothpaste, dentifrices, and mouthwashes containing propolis, in addition to enabling biofilm clearance and prevention, possess remarkable anti-inflammatory characteristics [42]. Comparative studies on remineralisation using propolis have been tabulated in [Table/Fig- 3] [43-47].

Aloe Vera

Aloe Vera is a monoecious perennial plant with shallow roots. It grows easily in the dry climates of Asia [48]. It is a small fleshy herb that resembles a cactus, with green dagger-shaped succulent, spiky, and leaflets with a transparent, viscous gel along their margins that possesses significant antibacterial, antiviral, and antifungal activities [49]. Aloe vera contains numerous active compounds, such as amino acids, anthraquinone, polysaccharides, monosaccharides, hormones, vitamins, enzymes, minerals, salicylic acid, saponins, lignin, tannins, lectin, and sterols [50]. The phenolic molecule anthraquinone can suppress bacterial growth by triggering bacterial cell lysis at low doses. It's also rich in enzymes such as oxidases, amylase, and catalase, but so are inorganic ones like potassium, calcium, and magnesium [51]. For the above reasons, it has been used to inhibit caries-promoting microorganisms.

Several studies have reported the use of aloe vera in dentistry for its antimycotic effect on *Candida albicans* and treatment of aphthous stomatitis [52]. It's an ingredient in dentifrices and

S. No.	Authors name and year	Place of study	Type of study	Products compared	Parameter assessed	Conclusions
1	Desai S et al., [23], 2022	Udaipur, India	In-vitro	Casein Phosphopeptide--Amarphous Calcium Phosphate (CPP-ACP), tricalcium phosphate and grape seed extract	Scannng Electron Microscopy,(SEM), Energy Dispersive X-ray Analysis, (EDAX), and microhardness test	Grape Seed Extract (GSE) showed significantly greater remineralisation compared to the CPP-ACPF and tricalcium phosphate.
2	Senthil Kumar V and Ramesh S, [24], 2021	Chennai, India	In-vitro	CPP-ACP, ginger-honey and grape seed extract	Microhardness test, fluorescence spectroscopy	The GSE was significantly better in remineralisation than other agents.
3	Nagi SM et al., [25], 2019	GIZA, Egypt	In-vitro	Grape seed extract 6%, 10%, and fluoride	Microhardness and energy-dispersive X-ray and ultra-morphological examination	GSE hydrogels have positive effects on the remineralisation process.
4	Hussein F et al., [26], 2019	Cairo, Egypt	In-vitro	Artificial saliva grape seed extract and Silver diamine fluoride (SDF)+Potassium iodide (KI)	Microhardness	SDF applications after GSE improved the microhardness of demineralised dentin when compared to the monotherapy of each treatment.
5	Vural S and Ökte Z, [27], 2023	Turkey	In-vitro	Sodium fluoride 6.5% and grape seed extract	Elastic modulus microhardness surface topography	GSE is a natural promoter of dentin remineralisation that was more effective than fluoride application.
6	Amin RA et al., [28], 2019	Cairo, Egypt	In-vitro	Sodium fluoride and grape seed extract	Microhardness surface topography	GSE enhanced the remineralisation process of artificial enamel lesions of primary teeth.

[Table/Fig-1]: Summary and comparison of studies on remineralisation using grape seed extract.

S. No.	Authors name and year	Place of study	Type of study	Products compared	Parameter assessed	Conclusions
1	Abdel-Azem HM et al., [36], 2020	Ismailia, Egypt,	In-vitro	Galla chinensis extract and sodium fluoride.	Surface microhardness, elemental analysis, micromorphological appearance	Galla chinensis extract could be used as an effective natural alternative for dentin remineralisation.
2	Xia Y et al., [37], 2020	Chongqing, China	In-vitro	Galla Chinensis extract and sodium fluoride	Dentinal tubule sealing by Scanning Electron Microscopy (SEM),	Galla chinensis extract reduced the symptoms of dentin hypersensitivity by sealing the dentinal tubules.

[Table/Fig-2]: Summary and comparison of studies on remineralisation using Galla Chinensis.

S. No.	Authors name and year	Place of study	Type of study	Products compared	Parameter assessed	Conclusions
1	Ali S et al., [43], 2021	Dammam, Kingdom of Saudi Arabia	In-vitro	Artificial oil and propolis oil	Surface microhardness	Propolis has good remineralisation potential.
2	Hosseinpour-Nader A et al., [44], 2023	Tehran, IRAN	Ex-vivo	Artificial saliva, sodium fluoride, propolis quantum dots, nisin, and quercetin nanoparticles	Surface changes, microhardness, and surface topography and anti-biofilm effects on *S. mutans*	Propolis quantum dots can be used for the eradication of *S.mutans* biofilms and remineralisation of white spot lesions.
3	Gargouri W et al., [45], 2020	Tunisia	In-vitro	Xylitol, Xylitol+CPP_ACP, Xylitol+Propolis and artificial saliva	Mineral content by SEM and EDAX, surface morphology, microhardness	Xylitol with propolis showed dentinal tubules occlusion, improvement of microhardness, and decrease in roughness.
4	Zaleh AA et al., [46], 2022	Tehran, IRAN	Ex-vivo	Artificial saliva sodium fluoride, nano curcumin propolis and nanoparticles	Microhardness surface changes surface topography	Nanoproolis combined with nanocurcumin with photodynamic therapy had better enamel remineralisation efficacy.
5	Soekanto SA et al., [47], 2019	Indonesia	In-vitro	Silver diamine fluoride and propolis fluoride	Inhibition of biofilm	Both had same inhibition effects against biofilm formation with *S Mutans*.

[Table/Fig-3]: Summary and comparison of studies on remineralisation using propolis.

mouthrinses for the treatment of gingivitis [53]. However, only a small number of studies [54] have examined the effect of aloe vera on the remineralisation of initial carious lesions [55]. Aloe vera is biocompatible and non toxic for periodontal tissues even with continuous use [56]. A study concluded that aloe vera gel when applied in the proper concentration, aided in the creation of a dentin bridge while preserving the vitality of the pulp [57]. Ions like sodium, potassium, magnesium, and calcium can flow through the porous mineralised enamel surface, Therefore, the remineralising potential of the 35% pure aloe vera gel-based dentifrice could be related to the deposition of arginine coupled with calcium on the enamel surface [58]. Comparative studies on remineralisation using Aloe vera have been tabulated in [Table/Fig-4] [59-63].

Ginger

Ginger (*Zingiber Officinale*) is the most widely used herb in India, and it has antimicrobial and antifungal properties [64]. Bioactive components of ginger rhizome oleoresin include 1-(4′-hydroxy-3′- methoxyphenyl)-5-hydroxy-3-deconone, {1-(4′-hydroxy-3′- methoxyphenyl)-5-hydroxy-3-deconone}), the principal pungent ingredient believed to exert various pharmacological and physiological activities [65].

In India, honey is traditionally combined with herbal remedies like ginger [24]. It is effective against oral pathogenic bacteria [65,66]. Gingerol and shagelol, bioactive components derived from ethanolic extracts of ginger, exhibit antifungal and antibacterial activity. Ginger's remineralisation capacity is attributable to its antimicrobial properties and high fluoride content [65]. Comparative studies on remineralisation using ginger have been tabulated in [Table/Fig-5] [24,67,68].

Hesperidin

Hesperidin is a citrus-derived flavonoid glycoside with antimicrobial and remineralising properties. French chemist Lebreton was the first to isolate hesperidin (C28H34O15), a flavonoid glycoside, from citrus peel [69]. This has also been identified in the genus *Rutaceae*, bergamot fruit, lemon peel, lemon fruit, and banana fruit among others [70]. It could also exist in the airborne section of the *Rubiaceae genus* and the Cruciferous plant leeks, as well as in the roots and entire grasses. In its structure hesperidin contains an aglycon (hesperetin or methyl eriodictyol) bonded to rutinose {6-O-(-l-Rhamnopyranosyl)-D-glucopyranose} and/or {6-O-(-l-Rhamnosyl)-D-glucose} [71]. It is used to treat type 2 diabetes, cancer, cardiovascular disease, neurological

S. No.	Authors name and year	Place of study	Type of study	Products compared	Parameter assessed	Conclusions
1	Gandhi R et al., [59], 2022	Chennai, India	In-vitro	Flaxseed paste, aloe vera gel, and fluoride toothpaste	Microhardness surface topography	Aloe vera gel showed promising results by significantly remineralising white spot lesions.
2	Nassar D et al., [60], 2022	Egypt	In-vitro	Aloe vera and sodium fluoride	Mineral composition surface topography	Aloe vera gel could be an acceptable alternative to fluoride.
3	Al Haddad T et al., [61], 2021	Beirut, Lebanon	In-vitro	Non fluoridated toothpaste, fluoridated toothpaste and aloe vera gel	Mineral composition surface topography	The aloe vera gel demonstrated a remineralisation capacity equal to fluoride toothpaste.
4	Yikici C and Ozcan S, [62], 2022	Ankara, Turkey	In-vitro	Fluoride-free toothpaste, Fluoride Toothpaste with 1100 ppm fluoride, Fluoride Toothpaste with 1450 ppm fluoride, Aloe vera gel, Aloe vera gel+1100 ppm Fluoride, Aloe vera gel+1450 ppm Fluoride	Surface microhardness	Toothpaste containing 1450 ppm fluoride and aloe vera provides an effective remineralisation.
5	Moustafa NM et al., [63], 2020	Egypt	In-vitro	Green tea, aloe vera and chlorhexidine	Microhardness	Chlorhexidine could be substituted by natural safe herbal sources like aloe vera.

[Table/Fig-4]: Summary and comparison of studies on Remineralisation using Aloe Vera.

S. No.	Authors name and year	Place of study	Type of study	Products compared	Parameter assessed	Conclusions
1	Senthil Kumar V and Ramesh S., [24], 2021	Chennai, India	In-vitro	CPP-ACP, ginger-honey and grape seed extract	Microhardness test, fluorescence spectroscopy	The grape seed extract was significantly better in remineralisation than other agents.
2	Kaul S et al., [67], 2020	India	In-vitro	Ginger, honey and chitosan	Lesion depth(ΔF), Maximum βfluorescence loss (ΔF Max), and lesion volume (ΔQ) using QLF	Ginger honey showed significant remineralisation between 2nd and 3rd week.
3	Eliwa M, [68], 2023	Egypt	In-vitro	Ginger extract, rosemary extract and sodium fluoride	Colour	Natural agent extracts could be effective in remineralising white spot lesions.

[Table/Fig-5]: Summary and comparison of studies on remineralisation using Ginger.

and psychiatric disorders, and as a radioprotectant. Hesperidin administration can benefit a variety of cutaneous functions in both healthy and diseased skin [72].

Hesperidin can remineralise both superficial and subsurface lesions, according to a study that induced artificial caries on bovine dentin using pH cycling. It has also been suggested that hesperidin's ability to induce dentin remineralisation may be due to its interaction with collagen proteins [73]. It appears that a stable organic matrix is important for the remineralisation process since it facilitates calcium and phosphorus ion deposition and limits their further release from tooth tissues [73]. Comparative studies on remineralisation using Hesperidin have been tabulated in [Table/Fig-6] [74].

S. No.	Authors name and year	Place of study	Type of study	Products compared	Parameter assessed	Conclusions
1	Elasser DM et al., [74], 2022	Cairo, Egypt	In-vivo	Hesperidin, Propolis, SDF+KI	Mineral density using digital radiograph	Silver diamine fluoride had a higher significant remineralising effect than control, propolis, or hesperidin.

[Table/Fig-6]: Summary and comparison of studies on Remineralisation using Hesperidin.

Honey is expected to promote the demineralisation process due to its composition. Several investigations have revealed a low demineralisation effect. A study to compare the enamel demineralisation depth of five sweeteners (sucrose, sucralose, fructose, palm sugar, and honey) revealed that artificial (sucralose) and natural (honey) sweeteners have an inferior cariogenic potential than sucrose [82]. Previous research has also demonstrated that honey has a lesser demineralisation effect than fructose and glucose and even less than sucrose [83]. In contrast according to two recent research [24,84], natural honey can remineralise the enamel surface in-vitro. Comparative studies on remineralisation using honey have been tabulated in [Table/Fig-7] [24,67,85,86].

S. No.	Authors name and year	Place of study	Type of study	Products compared	Parameter assessed	Conclusions
1	Senthil Kumar V and Ramesh S, [24], 2021	Chennai, India	In-vitro	CPP-ACP, ginger-honey and grape seed extract	Microhardness test, fluorescence spectroscopy	The grape seed extract was significantly better in remineralisation than other agents.
2	Kaul S et al., [67], 2020	India	In-vitro	Ginger, honey and chitosan	Lesion depth(ΔF), maximum βfluorescence loss (ΔF Max), and lesion volume (ΔQ) using QLF	Ginger and honey showed significant remineralisation between 2nd and 3rd week.
3	Deglovic J et al., [85], 2022	Bratislava, Slovakia	Microbiological	Honey	Antimicrobial/antibiofilm	The most beneficial property of honey is antibacterial/ antibiofilm activity.
4	Jamil WE and El Sharkawy DA, [86], 2022	Cairo, Egypt	In-vitro	Sodium fluoride, Ginger honey extract and Rosemary Extract	Colour change	Ginger and honey mixture enhances remineralisation.

[Table/Fig-7]: Summary and comparison of studies on remineralisation using honey.

Honey

Bees make honey from blossom nectar. Honeybees visit several blooms and ingest nectar in their honey stomachs, where digestive enzymes break sucrose into glucose and fructose. The bees spit raw honey onto the hives, flap their wings to dry it, and then seal the honey with wax [75]. Chemically, 17-20% of honey is made of water, and other constituents including flavour, and colour [76], all contribute to its uniqueness. The chemical composition of honey has been extensively examined, and it is estimated that the natural product contains more than 200 components [77]. Sugar accounts for approximately 90-95% of honey's dry matter, followed by water, mineral components, and organic acids [76]. According to a report, manuka honey is efficient in inhibiting plaque formation, by preventing the growth of biofilm and thereby decreasing acid production [78].

Honey's antibacterial characteristics are primarily determined by its low pH, high sugar content, hydrogen peroxide, low water activity, gluconic acid, and antimicrobial proteins/peptides [79]. Manuka honey contains phytochemicals such as methylglyoxal and flavonoids such as polyphenols, which improve the antibacterial capabilities of honey. Recent research indicates that hydrogen peroxide has a substantial role in antibacterial activity. Polyphenols, which are commonly present in honey, contribute to antibacterial activity by directly producing H_2O_2 and by converting $Fe^{3+}$to Fe^{2+}, which initiates the fenton reaction and generates more powerful reactive hydroxyl radicals. Even while studies have suggested that honey's efficiency against *S. mutans* is limited, a relatively recent experiment employing various Greek honey kinds and manuka honey showed that all honey samples were extremely effective against *S. mutans* [80], at concentrations ranging from 12.5% to 50% [81].

Theobromines

Theobromine is the main alkaloid that comes from the cacao plant. Its chemical name is 3,7- dimethylxanthine. Chocolate, tea, and other foods contain this water-soluble, crystalline, bitter powder. Chocolate, a food made from cacao beans, has been linked to an increased risk of dental caries [87]. However, in recent years, there have been arguments made for the use of theobromine as an efficient remineralising agent. Theobromine may cause calcium and phosphate to form bigger HAP crystals. These crystallites strengthen enamel and prevent acid attacks. In addition, research indicates that cocoa bean husk is excellent at reducing mutant streptococci and has less toxicity than fluoride [88]. Theobromine-containing toothpaste is commonly accessible in the US but less popular abroad than other remineralising agents. Manufacturers' statements about the effectiveness of theobromine-containing dentifrices are based on scant research [87], and nothing is known about how theobromine works as a remineralisation agent. According to current research, a substantial reduction in lesion depth was detected in (increased remineralisation) [88] specimens treated with theobromine. Comparative studies on remineralisation using theobromine have been tabulated in [Table/Fig-8] [89-95].

Gum Arabica (GA)

Gum Arabica has shown promising results in the search for novel antimicrobial agents against pathogenic microorganisms responsible for plaque and tooth decay. GA has derived from the branches and stem of the species *Acacia*. GA has been found to improve gastrointestinal distress, decrease intestinal mucosal inflammation, and play a role in the treatment of chronic renal failure and diabetes. As an oral care agent, GA's high calcium concentration may promote the remineralisation of caries and inhibit the early formation

S. No.	Authors name and year	Place of study	Type of study	Products compared	Parameter assessed	Conclusions
1	Premnath P et al., [89], 2019	India	In-vitro	Sodium fluoride, amine fluoride and theobromine,	The initial and final size of each lesion using confocal Laser microscopy	Theobromine demonstrated less remineralisation potential in comparison to dentifrices containing NaF+f-(TCP) and amine fluoride.
2	Shawky R et al., [90], 2021	Egypt	In-vitro	Theobromine toothpaste and fluoride toothpaste,	SEM analysis for surface topography	Theobromine could be a suitable alternative to fluoride for caries prevention.
3	Thomas NA et al., [91], 2021	India	In-vitro	Sodium fluoride and theobromine	SEM and EDAX for surface topography and mineral analysis	Theobromine can be used as an alternative to the conventional fluoride-containing agents in remineralising white spot lesions.
4	Taneja V et al., [92], 2019	India	In-vitro	Theobromine novamin nano Hydroxyapatite (HAP),	SEM and EDAX for surface topography and elemental mineral analysis	Theobromine can be used as an effective novel remineralising agent alternative to the already-available agents.
5	Farhad F et al., [93], 2021	Iran	In-vitro	Theobromine and sodium fluoride gels	Microhardness elemental mineral analysis	Theobromine was more effective at a lower concentration and may serve as a safe and effective alternative to fluoride.
6	Durhan MA et al., [94], 2021	Turkey	In-vivo	Fluoridated toothpaste and Theobromine toothpaste	Salivary pH, buffering capacity, S Mutans Level	Theobromine-containing toothpaste can be considered an effective agent in remineralising white spot lesions.
7	Elsherbini MS, [95], 2020	Egypt	In-vitro	Sodium fluoride gel theobromine gel	SEM and EDAX for surface topography and elemental mineral analysis	Theobromine gel had more effective remineralising potential than fluoride gel.

[Table/Fig-8]: Summary and comparison of studies on remineralisation using theobromine.

of dental plaque. In addition, GA inhibits the growth of certain oral microorganisms [96]. The antimicrobial effect is attributable to the presence of cyanogenic glycosides and various enzymes, including oxidases, peroxidases, and others [97]. GA's antibacterial, anti-inflammatory, fungicidal, and anticoagulant properties may help maintain oral health by reducing plaque and gingival irritation when added to dentifrices [96].

Additionally, minerals including calcium, magnesium, and potassium can be found in it [96], which may promote tooth remineralisation. The calcium ion concentration in gum arabica can replenish Ca^{2+} ions that have been removed from hydroxyapatite crystals, avoiding further demineralisation of enamel. Onishi T et al., demonstrated that the concentration of insoluble Ca^{2+} and PO_4^- ions in gum arabic facilitates tooth remineralisation [98]. GA inhibits acid-dependent demineralisation and maintains remineralisation even in fluoride-free environments [97]. Currently, remineralisation agents produced from gum arabic are not commonly used, especially in gel formulations. One such study involving gel prepared using gum arabica showed an enhancement in tooth enamel hardness following the application of gel [99]. Comparative studies on remineralisation using honey have been tabulated in [Table/Fig-9] [96,100-101].

products are not chemically stable, deteriorating in the presence of heat, humidity, light, or oxygen, diminishing their clinical value [102]. Similarly, several natural compounds have bitter or alkaloid flavours or after taste, necessitating the use of powerful sweets.

Improving the retention duration of natural substances that are administered to the oral mucosa is another significant difficulty. For dental plaque biofilms to be able to affect the microbial ecology and/or demineralisation-remineralisation equilibrium, they must be exposed to effective concentrations of the chemoprophylactic chemical for an extended period. Micellar drug delivery methods and different polymeric delivery systems have been found to boost retention times [103] and may be utilised in oral care products containing natural ingredients. Nanotechnology could prevent caries using nano sized calcium phosphate particles containing tea polyphenols [104].

Geographical and seasonal influences on phytochemical make-up must be considered when using natural products for caries control. Due to the heterogeneity of natural products, natural agents used for caries prevention must have well-documented origins and composition, and the active components must be identified and standardised as much as feasible [105].

S. No.	Authors name and year	Place of study	Type of study	Products compared	Parameter assessed	Conclusions
1	Hassan RR et al., [100], 2022	Cairo, Egypt	In-vitro	Gum Arabica, CPP-ACP and GumArabica+CPP-ACP	Microhardness, Surface Topography	Gum arabic could be a promising remineralising agent although it had a limited initial remineralising potential.
2	Nassir S et al., [101], 2019	Sudan	In-vitro	Aqueous of Gum Arabic, Hashab (*Acacia Senegal*) and Talha (*Acacia Seyal*)	Antimicrobial property	Gum arabic inhibited the growth of *Streptococcus mutans.*
3	Ahmed O et al., [96], 2022	South Africa	Microbiological study	Gum Arabica-Silver and Nanoparticles	Biofilm Inhibition	GA-AgNPs can be used as an additive to dental products, particularly because they can attach themselves to enamel and prevent bacterial biofilm formation on the teeth.

[Table/Fig-9]: Summary and comparison of studies on remineralisation using gumarabica.

DISCUSSION

Natural products have a potent effect in preventing dental caries, albeit with some disadvantages. First, their effectiveness is inferior to that of standard antimicrobials and fluoride containing or non fluoride chemotherapeutic agents.

To turn a natural product into a promising clinically relevant anticaries medicine, various obstacles must be addressed. Formulating lipophilic natural products to solve concerns such as phase separation and stability is a significant difficulty. Natural

The safety profile of natural dental care products is an additional issue that is sometimes disregarded. Although many food-derived phytochemicals have been categorised as generally recognised as safe compounds and are not anticipated to cause acute toxicological problems [106,107], this does not imply that all-natural products are fully safe for human consumption. Concerning the natural items indicated for use in dentistry, very little is known about their quality, safety, and probable combinations with other medications [106]. Before recommending the widespread use of

natural products for dental care, comprehensive animal and human safety studies evaluating acute, sub-chronic, and chronic toxicity, especially concerning brief daily exposures in topical treatments, are necessary [106].

CONCLUSION(S)

The final effectiveness of therapeutic solutions incorporating cariostatic natural ingredients is contingent on their ability to demonstrate a significant reduction in individual caries increment. Well-designed RCTs are required to determine the effectiveness of natural products in reducing dental caries or promoting remineralisation. In addition, additional research is necessary to determine the precise cariostatic modes of action of natural compounds and their optimal dosage regimen.

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