Journal of Materials Science Research and Reviews

Volume 7, Issue 1, Page 80-101, 2024; Article no.JMSRR.112975

Overview of the Skeleton Significance of Toothpaste Formulation, Evaluation and Historical Perspectives: Insights from Bangladesh's Toothpaste Industry

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/112975

Received: 11/12/2023
Accepted: 16/02/2024
Published: 19/02/2024

Review Article

ABSTRACT

Toothpaste plays an important role in maintaining and improving oral health and aesthetics. Over time, toothpaste recipes have evolved from simple suspensions of broken eggshells or ashes to complex formulations containing up to twenty different chemicals. Toothpaste is designed to combat various dental issues such as cavities, gum disease, bad breath, calculus, erosion and

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dentin hypersensitivity. It contains abrasives to clean and whiten teeth, flavours to freshen breath and dyes to improve its cosmetic appeal. The right toothpaste is formulated to maximize the bioavailability of its active ingredients. For instance, the permissible theoretical fluoride concentration range is between 850.0-1150.0 ppm. The most scientifically supported anti-plaque agent in toothpaste is Triclosan. Toothpaste must have a pH level between 05.50 and 10.50. Condensed phosphates are mainly used as chemical whitening agents in toothpaste. However, developing toothpaste is a complex process because numerous separate activities must come together in a single phase. Toothpaste development is still ongoing as there are several challenges including the low oral substantivity of most active ingredients which must be overcome. This present study states that a systematic review is a vital research piece that provides insights into the future of Bangladesh. This review conducts a thorough analysis of the country's potentials and opportunities, presenting a comprehensive understanding of its development. Using the toothpaste skeleton as a metaphor for the foundation of Bangladesh's growth, this overview examines its significance in detail.

Keywords: Aspartame; calcium oxide; fluoride; foaming power; sodium lauryl sulfate (SLS).

1. INTRODUCTION

1.1 Literature Drawback

Toothpaste is a paste or gel used with a toothbrush to maintain and improve oral health, appearance, and tooth well-being. Toothpaste is an abrasive that aids in the removal of oral calculus and meal from the teeth, aids in the suppression of halitosis, and delivers active ingredients to help prevent tooth decay and gum disease [1]. Salt and sodium bicarbonate are two ingredients that can be used in place of commercial toothpaste. Toothpaste is typically beneficial for oral hygiene and avoidance of dental issues such as cavities and aids in the control and removal of plaque accumulation [2]. Aids in the prevention and destruction of germ buildup in teeth and the maintenance of gum health. However, using toothpaste while brushing the teeth does not affect the extent of plaque clearance. Toothpaste is becoming more popular as a dentifrice as a result of urbanization and increased public awareness of dental care [3,9]. To date, the growth, creation and advertising of toothpaste have been mostly narrowed to organized companies, especially Binaca, Signal, Forhans as well as Colgate but toothpaste is currently being manufactured on an enormous scale for small-scale units due to the straightforward method involved and minimal expenditure. It mostly includes abrasives and ingredients for cleaning [4]. Sugar substitutes, flavours, preservatives, disinfectants, binders and water are used as surface active agents. Toothpaste, dental floss and mouthwash are the most commonly used dental hygiene items [5]. There are numerous varieties of toothpaste in the marketplace. Traditional herbal toothpaste is currently supplied to the Middle Eastern region, West German nations and East European countries [6-9]. Gels are more popular today than traditional pastes. Gels do not contain fluoride, a highly valued chemical for preventing tooth decay. Gels contain Silica gel, whereas pastes include Sodium Laurel Sulphate and an additive [10,87-89]. From the perspective of this review manuscript, we distinguished the parameters and performance of the toothpaste skeleton.

1.2 Classification of Toothpaste

A summary of toothpaste classification can be found below, which reviews notable sources with significant formulation ingredients. In Table 1, classifications are described.

1.3 History of Toothpaste

This section will give an outline of the history of toothpastes and their far older cousin, toothpowders. A summary of information obtained from several sources [3, 6, 11] will be shown. Toothpowders and other types of toothpaste are not new inventions. Ancient Egyptians originally produced a dental cream containing powdered ashes from oxen hooves, myrrh, egg shells and pumice around 3,000-5,000 BC [4, 7, 11], largely to remove dirt from teeth [5, 73]. Water was most likely only added at the time of use. Around 1,000 BC, Persians included charred shells of snails and oysters, as well as gypsum, herbs, and honey Greeks and Romans added extra abrasives to the powder combination 1,000 years later, such as broken bones and oyster shells [6, 11]. The Romans appear to have been the first to add flavours, most likely to assist with unpleasant breath and to render their paste more appealing. This flavouring was essentially crushed charcoal and bark distant cousins of modern flavours [7]. China and India were both utilizing a powder/paste at an identical time. The Chinese, in particular, were treating their toothpastes with ginseng, herbal mints, and salt, resulting in toothpastes that are not identical to the ones used today. The most prevalent problems with previous toothpaste were abrasiveness, poor flavour, and excessive expense, making it, not the economical mass-market commodity toothpaste today. Fig 1, shows an ancient Egypt toothpaste sketch [73,74,84].

Doctors, dentists, and chemists were in charge of developing toothpowders with the sole aim of cleaning teeth [8]. Dr. Washington Sheffield of Connecticut was the first to package toothpaste in a collapsible tube in 1892 [9].

The first usage of fluoride in 1914 was one of the most significant achievements in the history of teeth. British Patent GB 3,034 (filed in 1914, patented in 1915) describes "improvements in or relating to dentifrices and toothpaste formulations containing sodium fluoride, among other things." However, it is unknown when the first fluoridated toothpaste was sold [10]. This announcement occurred after more than ten years of caries study, partly because of a collaborative research project led by Dr. Joseph Muhler of Indiana University [11]. A novel toothpaste was produced that contains 1,000 ppm fluoride as stannous fluoride and heat-treated calcium phosphate as an abrasive. In a clinical investigation, this toothpaste was reported to result in a significant reduction in caries occurrence in children [12,85].

Table 1. Listed below are the ingredients that make up toothpaste pastes

Classification of toothpaste			
(a) Herbal Toothpaste		(b) Commercial Brand	(c) The Gel Craze
i. Neem toothpaste	ii. Ayurvedic Toothpaste		
The medicinal benefits of neem, which is derived from a tree called neem in southern Asia. Neem has the inherent capacity to avert bacterial growth in the oral cavity. [8, 86].	Ayurvedic toothpaste Orohyi is a potent oral hygiene and health product comprised of rare herbs and fruits. The medicinal qualities of these herbs indicate the essence of Ayurveda [8, 86].	There are plenty of toothpaste brands as Forhans, Binnaca, Signal, Fresh Gel, Aromatic, Colgate, and other special toothpaste brands available [9, 87].	Gels are being offered more than normal pastes recently. Several gels lack fluoride which is suggested for tooth decay prevention. Gels comprise Silica gel, and pastes comprise Sodium Laurel Sulphate. [10, 87].

Fig. 1. The oldest known recipe for toothpaste comes from ancient Egypt

This was not, however, the first known caries trial using fluoride toothpaste. An earlier study by Bibby [13] failed to show a cariostatic advantage of numerous 500-ppm fluoride as sodium fluoride-containing dental micro-pastes in kids and teens. However, the ADA approved the use of fluoride salts in toothpaste in 1960, paving the way for a global roll-out of fluoride toothpaste [14,15].

2. INGREDIENTS OF TOOTHPASTE

2.1 Active Ingredients

2.1.1 Fluorides

Several fluoride compounds, in varying proportions, can be used depending on the specific legislation of the country or region. Because law differs greatly between nations, only data from the EU [16] and the United States [17], two key dental care markets, are included here. Fluoride compounds are regulated as cosmetics in the EU, and a total of 20 distinct chemicals are permitted in Table 2 [74]. Mixtures of several fluoride derivatives are permitted, as long as the maximum fluoride concentration does not exceed 1,500 ppm. Surprisingly, several of the permitted fluoride compounds are only marginally soluble. Fluoride compounds are regulated as drugs in the United States, with much fewer molecules permitted (Table 3) [75].

The differences in the least concentrations across fluoride compounds are most likely due to historical factors abrasives were of lower quality than today and used to contain a particular amount of metal impurities which will decrease the concentration of soluble fluoride in manufacturing over time, particularly in formulations including NaF.

Pharmacopoeia reference standard in animal caries reduction testing, enamel solubility reduction tests, and fluoride enamel uptake tests. While these tests provide a degree of confidence in estimated clinical efficacy, their scientific merit is now being questioned, and they should be switched with more precise surrogate evaluations of clinical utility, such as laboratory pH cycling models with the ability to demonstrate a fluoride dose-response as a minimum standard. There are legal distinctions between the maximum allowable levels of fluoride in toothpaste for adult users and kids under the age of six. In the EU, the latter can include up to 1,500 ppm fluoride, albeit fluoride concentrations vary significantly amongst toothpastes (250-1,500 ppm fluoride) designed for children aged 6 and under. The following three fluoride compounds can be found in toothpaste in practically all other countries of the world (Table 3): NaF, Na_2PO_3F, or SnF_2; probably due to the same corporations dominating most marketplaces as in the EU and USA.

2.1.2 Antiplaque/antigingivitis agents

Triclosan, stannous chloride/fluoride, and zinc citrate/chloride are the most frequently utilized and scientifically proven antiplaque/antigingivitic compounds in toothpaste. Triclosan was released in conjunction with Gantrez (copolymer of methyl vinyl ether and maleic acid), with the latter claiming to improve triclosan intraoral substantivity [18]. It is commonly used at a level of 0.3% w/w and Gantrez at a level of 2% w/w. According to The Globally Harmonized System of Classification and Labeling of Chemicals, triclosan is defined as ' very hazardous to marine life with long-term effects' and has, as a result, come under increased attention in recent times [19].

2.1.3 Antimalodor agents

Chemical reactions with volatile sulfur compounds (VSCs) such as methyl mercaptan and hydrogen sulfide are commonly used in anti-malodor products. The zinc salts described earlier are the most widely utilized because zinc has antimicrobial characteristics [20].

2.1.4 Antitartar/anticalculus agents

Calculus is defined as "a concretion usually of mineral salts around organic material found especially in hollow organs or ducts" [21], whereas tartar is defined as "an incrustation on the teeth composed of plaque that has solidified due to mineral salt formation" [22]. Condensed inorganic and organic phosphates with linear or cyclic structures are the most frequent [23].

2.1.5 Whitening agents

According to their mechanism of action, formulation elements for increased extrinsic stain removal and prevention can be classified as mechanical, chemical, or optical whitening agents [24-27].

Table 2. Fluoride compounds approved for use in cosmetic/ toothpaste products in the EU

Substance	Linear formula	INCI	IUPAC
Amine fluoride 3- (N-hexadecyl-N-2-hydroxyethyl-ammonio) propylbis (2-hydroxy-ethyl) ammonium dihydrofluoride[2]	$C_{27}H_{59}N_2O_3F_2$	olaflur	Olaflur
Aluminium fluoride[2]	AlF_3		
Ammonium mono-fluoro-phosphate	$(NH_4)_2PO_3F$	not listed	
Ammonium fluoride	NH_4F		
Ammonium fluorosilicate	$(NH_4)_2SiF_6$		Ammonium hexa-fluorosilicate
Calcium fluoride	CaF_2		
Calcium mono-fluoro-phosphate	$CaPO_3F$		Calcium fluorophosphate
Hexadecyl ammonium fluoride	$C_{16}H_{35}NHF$	Cetyl amine hydrofluoride	Hetaflur
Magnesium fluoride	MgF_2		
Magnesium fluorosilicate	$MgSiF_6$		Magnesium hexafluorosilicate
N, N´, N ´-tris(polyoxyethylene)-N-hexadecyl-propylene diamine dihydrochloride	n/a	not listed	
Nico-methanol hydrofluoride[2]	C_6H_8FNO	not listed	
Octadecenyl-ammonium fluoride	n/a	not listed	
Potassium fluoride[2]	KF		
Potassium fluorosilicate	K_2SiF_6		di-potassium hexafluorosilicate
Potassium mono-fluoro-phosphate	K_2PO_3F		di-potassium fluorophosphate
Sodium fluoride[2]	NaF		
Sodium fluorosilicate	Na_2SiF_6		di-sodium hexa-fluorosilicate
Sodium mono-fluoro-phosphate	Na_2PO_3F		di-sodium mono-fluoro-phosphate
Tin difluoride	SnF_2	stannous fluoride	

Table 3. Fluoride compounds approved for use in toothpaste in the USA

Sl. No.	Substance	Permissible theoretical fluoride concentration, ppm	Minimum available fluoride concentration, ppm	Reference
1	Sodium fluoride	850.0-1,150	650.0	[75]
2	Sodium mono-fluoro-phosphate	850.0-1,150	800 or 1275	[75]
3	Stannous fluoride	850.0-1,150	700 or 290 for products containing calcium phosphate	[75]

2.1.6 Agents for the relief of dentin hypersensitivity

Dentin hypersensitivity can be relieved in a variety of ways, including nerve de-sensitization and physical obstruction of dentinal tubules [28]. Potassium salts, such as citrate and nitrate, can be used to desensitize nerves. These salts are usually employed in quite high quantities (about 5% w/w), which has a detrimental impact on the flavour of toothpaste bitterness [29-33].

2.1.7 Erosion prevention agents

Toothpaste claiming to counteract enamel loss has only lately been developed. Because there were no good clinical indices to monitor the progress of erosion in vivo, such toothpastes were created primarily utilizing in vitro and in situ models with highly regulated, standardized, and sometimes biased conditions [34]. Some claim that optimizing the injection of sodium fluoride to promote regeneration of an early corrosive lesion is the best approach [34,35], whereas other manufacturers use the response of stannous fluoride and/or chloride with the enamel and dentin surfaces to create a protective coating on the dental hard tissues [36-38].

2.1.8 Noteworthy active ingredients

Several ostensibly antiracial substances have been and continue to be used in toothpaste. These include calcium glycerophosphate (CaGP) [39], xylitol [40], isomalt [41], nano-hydroxyapatite (mainly in Japan) [42], sodium trimeta-phosphate [43], and so-called re-mineralizing agents (CPP-ACP) [44, 45].

2.2 Formulation EXCIPIENTS

While the active compounds indicated above are mostly liable for the therapeutic advantages of toothpaste, toothpaste could not be called toothpaste without the excipients described below [46, 76]

2.2.1 Abrasives

Abrasives are the most common toothpaste excipient and only play a minor role in toothpaste consistency. Abrasive particles can become caught between toothbrush bristles when brushing. The stain can be eliminated without inflicting considerable harm to the tooth's exterior because these granules are tougher than the stain but milder than sound enamel [46].

2.2.2 Surfactants

Surfactants are accountable not only for the foaming characteristic of toothpaste but also for the intraoral dispersal of toothpaste and the micellization of hydrophobic components such as taste compounds and organic antiplaque/antigingivitic actives (e.g., triclosan) [47]. Nonionic surfactants are currently employed in mouthwash formulations rather than toothpaste due to their limited foaming power [48].

2.2.3 Viscosity and rheology modifiers

The major goal of viscosity and rheology modifiers is to create a gel phase with a uniform distribution of all toothpaste constituents and to keep the constituents from separating over lengthy periods of storage [49].

2.2.4 Humectants

Humectants (hydrating agents) are used to prevent water separation and evaporation, as well as to give a shiny and smooth surface and a homogeneous delivery system. Glycerin and sorbitol are the most commonly utilized compounds for this purpose, owing to their consistency with other excipients in formulations and low raw material costs [46,49].

2.2.5 Flavors

Flavors are mainly offered for cosmetic and pleasant purposes. They give breath freshening and sensory cues such as chilling, heating, or tingling, based on the flavor ingredient employed. Flavors are a particularly costly and volatile excipient, and they can be employed at quantities ranging from 0.3 to 2.0% w/w. Surfactants are principally liable for flavor distribution in toothpaste [49].

2.2.6 Sweeteners

To enhance the taste of toothpaste, sweeteners are included. All commonly utilized sweeteners are synthetic, and the vast majority of toothpaste makers employ sodium saccharin or, less frequently, sucralose. Sweeteners usually appear in concentrations less than 0.5% w/w. Whereas xylitol (10% w/w) can be regarded as a sweetener, its primary and still debated aim is caries prevention [49].

2.2.7 Colouring

The colour of toothpaste is critical for consumer acceptance. The majority of corporations want a white paste that may be blended with other coloured stripes to represent a variety of benefits. Whiteness is accomplished by adding titanium dioxide (1% w/w), whereas coloured striping or a coloured centre can be achieved by applying synthetic colourants (approx. 0.1% w/w) [49].

2.2.8 Preservatives

To avoid bacterial development during prolonged storage, toothpaste formulas that are free of an ionic surfactant are frequently prepared with preservatives (approx. 0.2% w/w). Sodium benzoate, ethyl and methylparaben are the most often used preservatives [49].

2.2.9 Water

Water is a crucial solvent for inorganic active chemicals, particularly fluorides, and is certainly the cheapest excipient that manufacturers try to optimize in toothpaste formulation. To eliminate calcium and trace impurities that may reduce the stability and bioavailability of active substances, water must first be filtered [49].

2.2.10 Other excipients

Mica is used in toothpaste for its shine and cleaning properties. pH is adjusted with sodium hydroxide, ethanol serves as a solvent, and polyethylene and polypropylene glycols are utilized as humectants, dispersants, and to maintain xanthan gum evenly distributed in toothpaste. Excipients of significance include vitamins C and E as antioxidants, allantoin for 'gum health,' enzymes to reduce plaque formation, and herbal extracts for their antibacterial qualities [49].

2.3 Delivery Formats

The tube is a particularly common method of toothpaste delivery. Toothpaste in pumps is also accessible, however, due to higher formulation and production costs, as well as the increased possibility of 'capping-off,' producers avoid using pumps. Lesser viscosity formulations are offered in stand-up tubes for simpler distribution. One firm recently developed gel-to-foam solutions in a can. The formulations include isopentane, which reportedly assists in the intra-oral distribution of actives due to its low boiling point [49].

3. FORMULA AND MANUFACTURE OF TOOTHPASTE

The significant formula of the toothpaste is reviewed in detail.

3.1 Drawback of Formulation of Toothpaste

The formulation known as toothpaste is used to increase the appearance and health of teeth [50]. For washing the teeth, toothpaste is a popular preparation [51]. A toothbrush is used to perform the essential task of cleaning. The goal of using toothpaste is to give preventative and therapeutically active substances such as fluoride, metal salts, and pyrophosphate. As a result, there is a current demand for safe, effective, and well-formulated dentifrices [52].

3.1.1 Formulation of toothpaste by *Aloe vera*

Aloe vera is the earliest known medical plant and the most widely used herbal remedy in the world [53]. The existence of organic anthraquinones in the Aloe vera plant confers antimicrobial activity: aloe emodin, aloetic acid, aloin, anthracene,ethanol, barbaloin, chrysophanic acid, ethereal oil, an ester of cinnamonic acid, isobarbaloin, and resistannol [54]. Because Leptotrichae is the coating around the teeth that absorbs colours, the paste with a high concentration of sodium chloride content inhibits the creation of the coat described in Table 4. It is quite difficult for a dentist to remove such a layer without causing harm to the enamel. To avoid the creation of such layers and their spread, an excessive amount of sodium chloride may be utilized [55].

Aloe plant leaves were obtained from a medical garden and carefully cleansed. The pulp was then extracted by using an incisor on the leaves. The pulp was carefully mixed with a juicer and filtered through a cotton cloth to eliminate any undesired material. The conventional method was used to determine the concentration of various substances. The variables chosen were antibacterial activity and foaming power, with degrees of low (-1), medium (0), and high (+1) as shown in Table 5. The creation of various formulations was carried out in keeping with the formula shown in Table 6.

As shown in Table 6, substances were employed for each formulation according to their proper scales and measurements. The powder ingredients were all sieved via sieve 60. All of the water-soluble chemicals, such as sodium chloride, saccharine, methylparaben, and propylparaben, were mixed to make a solution. According to geometry, di-calcium phosphate, calcium carbonate, sodium lauryl sulphate, and gum tragacanth were combined and placed into a clean Mortar Pestle. The fresh juice of aloe was then added to this mixture, and the paste was made by progressively adding the aforesaid solution of water-soluble components. The main composition of the batches is described in Table 7 [77].

3.1.1.1 Evaluation of formulations

For a week, all of the formulated batches were assessed for their drying tendency at room temperature. Table 6 summarizes the observations. Table 6 shows how the organoleptic characteristics of the formulated batches were tested.

3.1.1.2 Physicochemical parameters

Extruding a 15 to 20 mm length paste from a collapsible tube of sample on butter paper and then pressing it along its whole length with a finger was used to assess the presence of hard, sharp-edged abrasive particles.5 gram of correctly weighed sample was transferred to a 100 ml cleaned beaker. To this, freshly boiling and cooled water was added and thoroughly mixed to get a homogeneous suspension. A pH meter was used to measure the pH in less than 5 minutes. Results were tabulated in Table 7.

Table 4. Several uses of *Aloe vera* in dental practice

Sl. No.	Uses	Reference
1	In dental implants	[56]
2	In periodontal surgery	[57]
3	Can be applied to gum tissues when they are scratched by a toothbrush, sharp foods or toothpick injury.	[58]
4	Chemical burns from aspirin.	[59]
5	Application in extraction sockets.	[60]
6	It can be directly applied at the site of periodontal surgery.	[61]
7	Its application around dental implants are to control inflammation caused by bacterial contamination.	[62]
8	Acute mouth lesion is known as a hepatic viral lesion, aphthous ulcers, cancer cracks and cracks arising at the corners of our lips.	[63]

Table 5. Factorial design

Level	Concentration of Aloe	The concentration of Sodium Lauryl Sulphate	Reference
Low	-1(3%)	-1(1%)	[77]
Medium	0(4%)	0(1.5%)	[77]
High	1(5%)	1(2%)	[77]

Table 6. Developed batches from F1 to F9 as per factorial design

Batch	Concentration of Aloe	The concentration of Sodium Lauryl Sulphate	Reference
F1	0	1	[77]
F2	0	0	[77]
F3	1	0	[77]
F4	0	-1	[77]
F5	1	1	[77]
F6	1	-1	[77]
F7	-1	-1	[77]
F8	-1	0	[77]
F9	-1	1	[77]

Table 7. Composition of the batches (% w/w)

S. no.	Ingredients	All quantities are expressed in gm/ 100 gm								
		F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
1	Aloe	4	4	5	4	5	5	3	3	3
2	Sodium Chloride	1	1	1	1	1	1	1	1	1
3	Dicalcium Phosphate	23	24	23	25	22	24	26	25	24
4	Calcium Carbonate	21	20	20	20	21	20	20	20	21
5	Glycerine	30	30	30	30	30	30	30	30	30
6	Gum Tragacanth	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2
7	Saccharine	0.75	0.75	0.75	0.75	0.75	0.75	0.75	0.75	0.75
8	Sodium Lauryl Sulphate	2	1.5	1.5	1	2	1	1	1.5	2
9	Methyl Paraben	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25
10	Propyl Paraben	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
11	Distilled Water	16.3	16.8	16.8	16.3	16.3	16.3	16.3	16.8	16.3

3.1.1.3 Microbial study

The modified agar well diffusion method was employed to test the antibacterial activity of the formulation, with nutrient agar plates seeded with 0.2 ml of S. aureus 24.0 hours broth culture. After the agar plates had solidified, wells were cut at identical distances in each plate with a sterile 8 mm borer. Plate wells were filled with approximately 0.5 ml of formulation. The plates were then incubated for 24 hours at 37 degrees Celsius. Zones of inhibition (in cm) were used to assess antibacterial activity. Table 8, demonstrated how produced toothpaste formulations were assessed based on a range of assessment criteria, including texture, extrudability, appearance, colour, drying tendency, and aftertaste [77].

The performance-based evaluation of the foaming power and microbial study was completed, as indicated in Table 8 [77]. Depending on the sodium lauryl sulphate content, the foaming power ranges from 28 to 42 millilitres. The produced formulations have pH values between 5.87 and 6.54 in *Table 9*. By calculating the Zone of Inhibition on nutrient agar plates seeded with S. aureus culture broth, the microbiological investigation was assessed [77].

3.1.1.4 Effect of the independent variable on foaming power and zone of inhibition

The selected cubic model was determined to be significant after using experimental design, with a model F value of 916.43, a p-value less than 0.05, and an R2 value of 0.99. The likelihood that noise might produce the F value is only 2.54%. A contour graph in Fig. 3(a) displays the correlation between several foaming power-related parameters. The selected cubic model was determined to be significant after using experimental design, with a model F value of 887.29, a p-value less than 0.05, and an R^2 = 0.99. The likelihood of the F value being large, which could be caused by noise, is only 2.58%. The contour graph in Fig. 3(b) displays a correlation between the variables related to the zone of inhibition.

Several dental publications have found that *Aloe vera* has several positive uses. Additionally, sodium chloride has been utilised in dentistry since ancient times. As a result, numerous global corporations have attempted to promote toothpaste that contains sodium chloride in the modern era. In the current study, we combined these two components to look for potential antibacterial action. Following completion of the task and analysis of the data gathered, we concluded that the current combination exhibited antibacterial activity against S. aureus [77].

3.1.2 Formulation of toothpaste according to the invention and comparison with the prior art

By concentrating a sorbitol syrup (NEOSORBR 70/70), several sorbitol syrups are created as humectants with dry matter contents (DM) of 70%, 86.8% (prior art) and 74% and 78% (innovation). These syrups are used to produce different kinds of toothpaste with the same amount of Sorbitol described in Table 10, 11 [78].

After the discovery, the time required for a homogenous dispersion of the silicas was significantly shortened by sorbitol syrups. According to the invention's formulations, it is noticed that increasing the amount of water available up to 12% of water improves the solubilization and/or dispersion of the other constituents [78]. Better viscosities result in a paste texture that is better and a reduced mixing time for silica. The silicas in paste 4, which is made with sorbitol syrup with an 86.8% dry matter concentration, are not sufficiently dispersed. Therefore, the invention's use of sorbitol syrups in the production of toothpaste is highly advantageous both economically and technically [78].

Table 8. Preliminary evaluation of the toothpaste

Batches	Evaluation Parameters						
	Dryness test	Colour	Appearance	Extra durability	Texture	After taste	Reference
F1	Not dried	Cream white	Paste-like	Easy	Smooth	Slightly sweet and salty	[77]
F2	Not dried	Cream white	Paste-like	Easy	Smooth	Slightly sweet and salty	[77]
F3	Not dried	Cream white	Paste-like	Easy	Smooth	Slightly sweet and salty	[77]
F4	Not dried	Cream white	Paste-like	Easy	Smooth	Slightly sweet and salty	[77]
F5	Not dried	Cream white	Paste-like	Easy	Smooth	Slightly sweet and salty	[77]
F6	Not dried	Cream white	Paste-like	Easy	Smooth	Slightly sweet and salty	[77]
F7	Not dried	Cream white	Paste-like	Easy	Smooth	Slightly sweet and salty	[77]
F8	Not dried	Cream white	Paste-like	Easy	Smooth	Slightly sweet and salty	[77]
F9	Not dried	Cream white	Paste-like	Easy	Smooth	Slightly sweet and salty	[77]

Table 9. Determination of foaming power, pH and zone of inhibition

Batches	Evaluation Parameters			
	Foaming power	pH	Zone of inhibition (cm)	Reference
F1	35	5.93	3.2	[77]
F2	32	6.13	3.5	[77]
F3	40	6.43	5.0	[77]
F4	31	6.37	3.5	[77]
F5	42	6.24	4.8	[77]
F6	29	6.54	4.6	[77]
F7	33	5.87	2.5	[77]
F8	30	6.33	2.8	[77]
F9	39	6.22	2.9	[77]

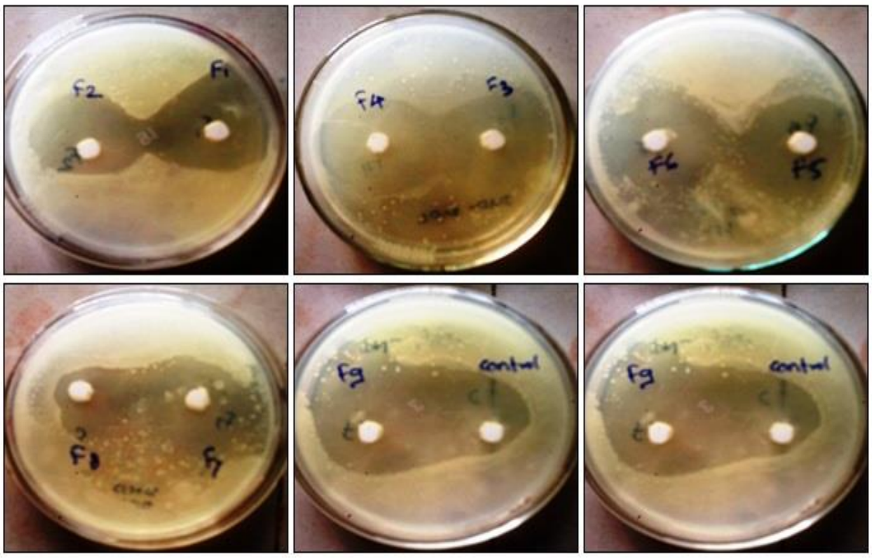

Fig. 2. Microbial study of *s. aureus* of toothpaste

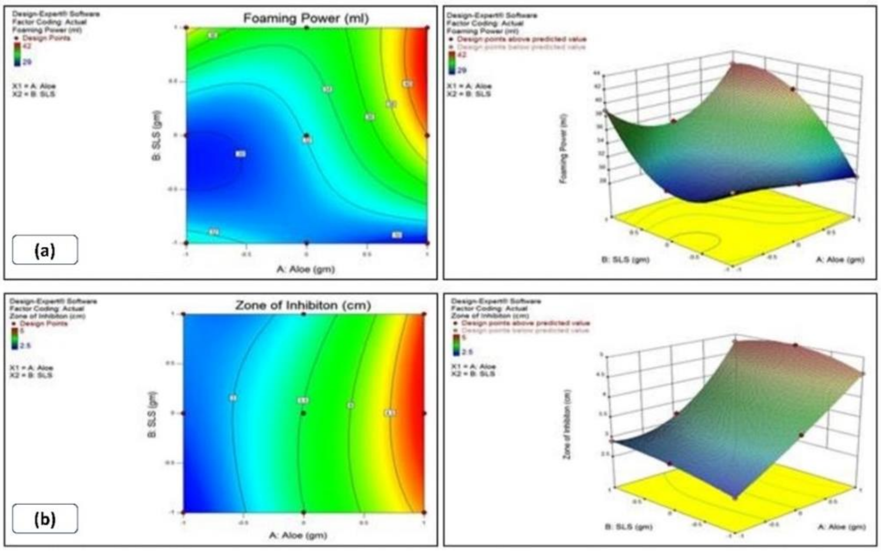

Fig. 3. (a) Correlation of factor and 3D graph with respect to foaming power (b) correlation of factor and 3D graph with respect to zone of inhibition

3.1.3 Formulation of Toothpaste with Calcium Carbonate

These findings show that using the Sorbitol syrups developed after the innovation significantly improves the abrasive mixing times. This has the benefit of cutting down on the overall time needed to manufacture toothpaste [78].

3.1.4 Formulation of toothpastes with sodium bicarbonate

The sorbitol syrup is composed of 88.0 % hydrogenated mono-and/or disaccharides with the remaining 100.00 containing oligo- and polysaccharides (NEOSORB.R. 70/70 SB) [78]. These syrups were used to create a variety of sodium bicarbonate toothpastes with the same dry sorbitol concentration (31.5%) are described in Table 14, 15 [78].

The only way each paste is made differently is whether or not an extra mixing time is applied. The purpose of this extra mixing time is to potentially remove any remaining grains from the mixture.

Table 10. The formula for each toothpaste (percentages expressed by weight)

		Reference
Silica (TDXOSIL 43)	9.0%	[78]
Detergent (SIPON LCSV95, 30% DM)	4.16%	[78]
Silesia mint flavor	0.80%	[78]
Sodium mono-fluoro-phosphate	0.76%	[78]
Carboxymethylcellulose (BLANOSE 7 MXF)	0.70%	[78]
Green colorant (0.5% DM)	0.50%	[78]
Sodium saccharinate	0.20%	[78]
Preservative (methylparaben)	0.18%	[78]
Preservative (propylparaben)	0.02%	[78]
		[78]
Paste 1: NEOSORB 70/70 containing 70% DM	64.0%	[78]
Water	5.68%	[78]
Paste 2: NEOSORB containing 74% DM	60.54%	[78]
Water	9.14%	[78]
Paste 3: NEOSORB containing 78% DM	57.44%	[78]
Water	12.24%	[78]
Paste 4: NEOSORB containing 86.8% DM	51.61%	[78]
Water	18.07%	[78]

Table 11. The results of PASTE

Parameters	PASTE 1	PASTE 2	PASTE 3
Total time	30 min 30 s	28 min 30 s	21 min 30s
Time for T to mix the silicas	21 min 30 s	19 min 30 s	12 min 30s
Viscosity atT0 (cps)	360.0	360.0	460.0
Viscosity at 24 h (cps)	440.0	460.0	520.0
Reference	[78]	[78]	[78]

Table 12. The formula is the following

Sl No.			Reference
	Calcium carbonate (SOCAL 90A):	45.0%	[78]
	Sipon LCSV95 (3.0% DM):	5.66%	[78]
	Blanose 7MXF:	1.20%	[78]
	Silesia mint flavour:	1.00%	[78]
	Sodium monofluorophosphate	0.80%	[78]
	Sodium saccharinate:	0.20%	[78]
	Methylparaben:	0.18%	[78]
	Propylparaben:	0.02%	[78]
	Paste 1: NEOSORB 70/70 containing 70% DM:	35.7%	[78]
	Water	10.29%	[78]
	Paste 2: NEOSORB containing 75% DM:	33.32%	[78]
	Water	12.67%	[78]
	Paste 3: NEOSORB containing 80% DM:	31.34%	[78]
	Water	14.75%	[78]

Table 13. The results are presented formulated PASTE

Parameters	Formulation		
	Paste 1	Paste 2	Paste 3
Total manufacturing time	15min	13min 30s	12min
Carbonate mixing time T	6min	4min 30s	3min
Reference	[78]	[78]	[78]

Table 14. The formula for each toothpaste (percentages expressed by weight)

Sl. No.			Reference
	NEOSORB (R 70.70 SB.:	45.0%	[78]
	Water	16.94%	[78]
	Sodium bicarbonate:	10.0%	[78]
	Thickening silica Tixosil 43:	10.0%	[78]
	Abrasive silica Tixosil 73:	9.0%	[78]
	Sodium lauryl sulfate Sipon LCSV95 (3.0% DM):	5.66%	[78]
	Mint flavor	1.0%	[78]
	Sodium monofluorophosphate:	0.8%	[78]
	Sodium carboxymethylcelluloseBlanose 7MXF:	0.7%	[78]
	Titanium dioxide	0.7%	[78]
	Sodium saccharinate:	0.2%	[78]

Table 15. The results are presented by Ingredient

Sl. No.						Reference
1	Dry matter content of the sorbitol syrup (%)	70.0	74.0	78.0	81.6	[78]
2	Additional mixing T(min)	9.0	6.0	3.0	0.0	[78]
3	Total mixing time (min)	27.0	24.0	21.0	18.0	[78]
4	Paste viscosity after manufacture (cP)	230	310	230	320	[78]
5	Paste viscosity after cooling (cP)	380	500	580	560	[78]

Similar to the previous examples, these results show that the Sorbitol syrups developed after the invention have the advantage of allowing for reduced mixing times, increased dry matter contents, improved silica dispersion, and flawless carboxymethylcellulose hydration. This leads to an increased paste viscosity once manufactured. A sorbitol syrup with a dry matter content of 74–81.6%, a reducing sugar content of less than 500 ppm, and a D-sorbitol concentration of 72%–77% by weight on a dry basis that is non-crystallizable at 20° C. The dry matter content of the Sorbitol syrup, as stated in claim 1, ranges from 74 to 80% [78].

4. PHYSICOCHEMICAL CHARACTERISTICS OF TOOTHPASTES AND NATURAL POWDER

4.1 Drawback

In vitro studies have examined the physical-chemical properties of several toothpaste varieties and natural powder samples, as well as their antibacterial efficacy against *Viridans streptococci* bacteria. The quality of toothpaste and natural powder products is determined by X-ray diffraction in addition to physical-chemical analytical measures like pH, conductivity, moisture content, and fluoride concentration. Antimicrobial agents, such as zinc oxide, titanium oxide, tin oxide, and their composites, have been added to toothpaste ingredients to improve their composition [64]. This is done to prevent and suppress microbial development, which is the primary cause of tooth decay and other oral disorders [65]. Furthermore, fluoride is one of the most important active elements in toothpaste and is useful in cleaning teeth that are not yet fully developed [66, 90-94]. Fluoride in dentistry functions by breaking down the cell walls of bacteria and reducing their enzymatic activity to prevent them from fermenting carbohydrates in the oral cavity and from aggregating. [67-69]. Excessive fluoride of more than 1500 ppm can cause poisoning, bone fragility, liver, and kidney damage [70].

4.1.1 Antimicrobial assay and significant parameters

Following Kirby-Bauer's instructions, the disc diffusion method was used to conduct the antimicrobial assay on the samples. After being injected into chocolate agar, loop-full growths from the bacterial isolate were cultured for eighteen hours at 37 °C. [71]. The entire Blood agar and Chocolate agar adjustment suspensions were streaked with a cotton swab that had been dipped in the solution. Sample discs or pleats were gently pressed onto the agar's surface. As the antibiotic seeped into the agar from the disc, the plates were incubated at 37°C for the entire night. The plates were inspected to check for inhibitory zones after incubation [72]. Because fluorides can prevent tooth decay, they are one of the most significant elements in toothpaste products for oral hygiene. Fig. 4(a) displays the fluoride concentration of the study samples. S6 had a lower number of fluorides than the other samples, however S1, S2, and S4 had greater levels than the reported level, while S3 and S5 had lower levels than the claimed level. The amount of fluoride in toothpaste directly affects dental hygiene; higher and lower concentrations result in dental fluorosis.

In Fig.4, Floride concertation pH measurement for toothpaste and powder samples, pH of the mouth at different brushing times are illustrated [71,72]. Toothpaste's pH level is crucial in maintaining the mouth's basic pH level and preventing the growth of germs that could harm teeth and lead to gum disease, cavities, and tooth decay. As a result, the toothpaste sample pH is determined as indicated in Fig. 4(b). It shows that all save S1 have basic pH levels; S1 has a neutral pH.[71,72]. However, some acidic foods that are, have a pH of less than 7, cause saliva to become more acidic in the mouth and reduce pH. Depending on the food type consumed, saliva may need from minutes to hours to neutralise the pH of the mouth in this situation. Consequently, to keep the mouth medium at the basic pH as indicated in Fig. 4(c), brushing your teeth for at least two minutes after each meal is essential. Also, proper brushing and the type of toothpaste have an effect on the medium of the mouth as shown in Fig. 4(c), except for example 6, most samples show that brushing and keeping the mouth in the basic medium for two minutes after eating lowers the pH of the mouth in an acidic medium, which is likely to create an environment more favourable for dangerous bacteria that cause tooth decay. [71, 72, 79].

4.1.2 Conductivity, moisture content of toothpaste and natural powder samples

Fig. 5 (a), displays a sample's conductivity at room temperature. Because S4 has more active ions than any other sample, it has a higher conductivity than any other sample, while S6 has a lower conductivity than any other sample because it contains fewer active ions [72, 79].

The physical characteristics and quality of toothpaste are influenced by its moisture content. The toothpaste's moisture content aids in preventing dry mouth. Except for S6, which has lower moisture contents, the S3 has higher moisture contents than the other samples as shown in Fig. 5 (b) [72, 79]. Toothpaste is given texture by humectants, which also aid in retaining moisture to prevent drying out. Three common humectants include water, sorbitol, and glycerin. The best humectant is xylitol since it has so many advantages. It increases salivary flow, which helps avoid dry mouth, and it has been found in preliminary studies to help reduce dental decay [79].

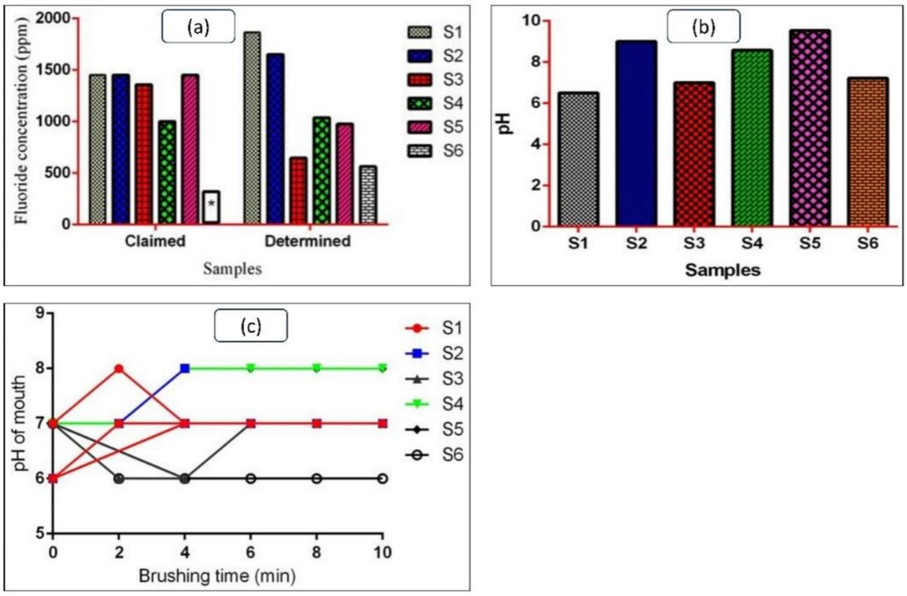

Fig. 4. (a) Floride concertation in toothpaste sample (b) pH measurement for toothpaste and powder sample (c) pH of the mouth different brushing time

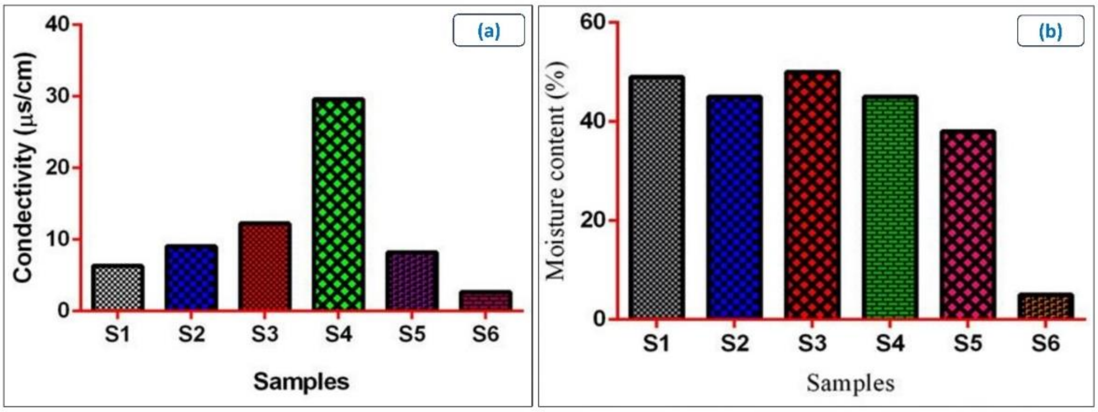

Fig. 5. (a) Conductivity of toothpaste and natural powder samples at room temperature (b) moisture percentage of toothpaste and natural powder samples

4.1.2.1 X-ray diffraction of toothpaste and natural powder samples

As indicated in Tables 16 and 17, the toothpaste and natural powder underwent X-ray diffraction examination. The XRD identified numerous elements in both samples with varied percentages [92, 95-101]. However, compared to toothpaste samples, the natural powder had a higher percentage of heavy elements, and the ratio of hazardous heavy elements including nickel and lead was noted in the powder at varying percentages. [72, 79].

The fluoride concentration of natural powder is too low, and there are discrepancies between the estimated and stated fluoride concentrations, according to the physical-chemical study of toothpaste and powder samples. The samples' pH ranged from 6.5 to 9.8, which is crucial for maintaining a healthy oral environment. [72,79]. To determine the ideal brushing time to keep the mouth in the basic medium, the brushing time was tested on all samples at various intervals ranging from 2 to 10 minutes. Except for S6, the active ions in the samples being measured by the conductometer and the samples' moisture % were not in the proper ratio to prevent mouth drying during brushing. The toothpaste and natural powder samples' XRD analyses revealed the various elemental percentages in the samples as well as the presence of hazardous heavy elements in the natural powder sample. [79].

Table 16. Quantitative analysis of the natural powder sample by X-ray diffractometer

Element oxides	Mass%	Reference
SiO2	47.10	[71, 72, 79]
CaO	24.20	[71, 72, 79]
Al2O3	10.60	[71, 72, 79]
MgO	7.22	[71, 72, 79]
Fe2O3	6.55	[71, 72, 79]
K2O	2.08	[71, 72, 79]
TiO2	0.96	[71, 72, 79]
SO3	0.374	[71, 72, 79]
P2O5	0.312	[71, 72, 79]
MnO	0.124	[71, 72, 79]
ZnO	0.01	[71, 72, 79]
NiO	0.032	[71, 72, 79]
SnO2	0.0138	[71, 72, 79]
PbO	0.0017	[71, 72, 79]

Table 17. Quantitative analysis of toothpaste samples by X-ray diffractometer

Element oxides	mass%	Reference
SiO2	28.90	[71, 72, 79]
CaO	59.30	[71, 72, 79]
Al2O3	0.962	[71, 72, 79]
MgO	0.476	[71, 72, 79]
Fe2O3	0.116	[71, 72, 79]
K2O	0.839	[71, 72, 79]
TiO2	2.16	[71, 72, 79]
SO3	3.00	[71, 72, 79]
P2O5	3.68	[71, 72, 79]
MnO	0.0138	[71, 72, 79]
ZnO	2.71	[71, 72, 79]
NiO	0.00	[71, 72, 79]
SnO2	0.123	[71, 72, 79]
PbO	0.00	[71, 72, 79]

4.2 The Features of Good Toothpaste in Dentists' Ideas

When it comes to toothpaste, dentists have their rationales. These are the things that make good toothpaste, according to our emergency dental clinic are highlighted in Table 18 [80].

4.3 Quality of Toothpaste

Standing in the hygiene aisle is not the most complicated or overwhelming part of the day. This is especially true if all we want to do is quickly pick up a toothpaste tube and go. Fortunately, we don't need to worry about this experience taking too long if we know some useful tips for selecting toothpaste that works well for our oral health are pointed out in Table 19. Let us provide some insight so we can quickly enter and exit the pharmacy [81].

5. TOOTHPASTE INDUSTRY PROSPECTS IN BANGLADESH

The toothpaste product is the blooming sector now a days in the Bangladesh consumer market.

Table 18. The factor of good toothpaste

Sl. No.		Reference
1	To achieve a more radiant, glossy, and whiter smile	[80]
2	smelling and tasting fantastic	[80]
3	Avoid damaging the enamel.	[80]
4	creating more salvia in the oral cavity	[80]
5	Stop dental decay	[80]
6	Stop tartar from accumulating on your teeth.	[80]
7	Being reasonably priced	[80]
8	obtaining a standard organization certification	[80]
9	Making use of appropriate packaging	[80]
10	Diminished sensitivity of teeth	[80]

Table 19. Quality of Toothpaste

Sl. No.	Quality	Significance	Reference
1	Fluoride	When selecting toothpaste, be sure it contains fluoride by looking at the packaging. This mineral, which is found naturally, guarantees that your oral hygiene is quite good. In the early stages of tooth decay, fluoride "re-mineralizes" your teeth by frequently replenishing missing minerals that could otherwise result in cavities.	[81]
2	Smooth not gritty	Selecting an abrasive toothpaste is never a good idea. Rather, you need a cleaning solution that will remove stains from your teeth without harming the enamel which is their outermost layer.	[81]

Table 20. Toothpaste Industry of Bangladesh

Name of the Company	Description	Ingredient	Brand	Marketed Brand
Unilever Bangladesh Ltd.	Unilever is a British multinational consumer goods company headquartered in London. The Factory location is Kalurghat, Chittagong, BD.	Calcium Carbonate, Aqua, Sorbitol, Sodium Lauryl Sulphate, Hydrated Silica, Flavour, CI 73360, Sodium mono-fluoro-phosphate, Tri potassium Citrate, CI 77891, Sodium Silicate, Cellulose gum, Sodium Saccharine, Triclosan. [82, 83].	Pepsodent	i.Pepsodent Germi-check ii. Sensitive expert iii. Pepsodent Charcoal white
		Sorbitol, Water, Hydrated Silica, Sodium Lauryl Sulphate, PEG-32, Flavor, Cellulose gum, Sodium Saccharin, Sodium Fluoride, Zinc Sulphate, CI 77019, Sodium Hydroxide, CI 42090, CI 77891[82, 83].	Closeup	i.Eucalyptus Mint ii. Fresh Attraction iii.Nature Rush iv. Menthol Fresh v.Pepper mint Splash vi.Red Hot vii. White Attraction viii.Natural Smile
Square Toiletries Ltd.	Square Toiletries Ltd. is one of the fast-moving consumer goods companies in Bangladesh and is a subsidiary of Square Group.	Calcium carbonate, Silica, Sodium Carboxymethyl cellulose, Sodium saccharin, Sodium mono-fluoro-phosphate, Sodium lauryl sulfate, Glycerine, Sorbitol, Aqua, PEG, Triclosan, Benzyl Alcohol, Frescolat, Peppermint and Spearmint oil, Clove Bud Oil [82, 83].	White Plus	i.White Plus Toothpaste ii.Meril Baby Gel Toothpaste (Orange) iii.Meril Baby Gel Toothpaste (Strawberry)

6. CONCLUSION

In our nation, toothpaste manufacturing and exporting are major industries with several sectors. Due to the availability, quality, and affordability of raw materials, the majority of industries are operating profitably. Every year, a significant amount of high-quality toothpaste is imported due to strong demand. It is well known that toothpaste intended for medical use is not made in our nation, although this fact seems to be unimportant to everyone. Toothpaste is crucial for both oral health and daily living. It shields our teeth from a range of illnesses, cavities, and microbes. The permissible theoretical Fluoride concentration range is between (850-1150) ppm. The most scientifically supported antiplaque agent in toothpaste is Triclosan. The toothpaste needs to have a pH between 5.5 and 10.5. Condensed phosphates are used mostly as chemical whitening agents in toothpaste. Our nation's products are excellent and exceptional. Bangladesh's toothpaste manufacturing sector has a promising and prosperous future.

ACKNOWLEDGEMENT

We have cited as many references as permitted and apologize to the authors of those publications that we have not cited due to limitation of references. We apologize to other authors who have worked on several aspects of toothpaste but whom we have unintentionally overlooked.

COMPETING INTERESTS

Authors have declared that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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