

Research Article

Physicochemical characteristics evaluation of commercial artificial saliva based on hydroxyethyl cellulose: Study experimental

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ABSTRACT

Introduction: Artificial saliva is used to manage xerostomia, a medical disorder primarily caused by impaired salivary gland function, by serving as a substitute for natural saliva. Because of its favorable viscosity and stability, hydroxyethyl cellulose (HEC) is frequently used as a thickening agent and lubricant in artificial saliva. Artificial saliva should be evaluated for its physicochemical characteristics to ensure that the formulation closely mimics natural saliva. This study aimed to evaluate the physicochemical characteristics of HEC-based artificial saliva commercially available in Indonesia. **Methods:** Based on market availability, two artificial saliva products in liquid formulations were obtained and analyzed. Sample 1 was an HEC-based formulation with a combination of polyethylene glycol (PEG) and methylparaben, whereas sample 2 was an HEC-based formulation with Aloe vera and cetylpyridinium chloride (CPC). The physicochemical characteristics of the samples were evaluated based on chemical properties (pH and buffer capacity) and physical properties (viscosity, density, and surface tension). **Results:** The results showed that sample 1 had an average pH of 6.81 ± 0.32 , a buffer capacity of $0.288 \text{ mmol H}^+/\text{L}$, a viscosity of 10.33 mPa.s , a density of 1.065 g/cm^3 , and a surface tension of 44.8 mN/m . Meanwhile, sample 2 had an average pH of 5.08 ± 0.52 , a buffer capacity of $0.158 \text{ mmol H}^+/\text{L}$, a viscosity of 2.50 mPa.s , a density of 1.113 g/cm^3 , and a surface tension of 45.6 mN/m . **Conclusion:** This study found that sample 1 demonstrated chemical and physical characteristics more similar to natural saliva, whereas sample 2 had a lower pH, buffer capacity, and viscosity but a slightly higher density and surface tension.

KEYWORDS: Hydroxyethyl cellulose, artificial saliva, saliva substitute, physicochemical characteristics.

Evaluasi karakteristik fisikokimia air liur buatan komersial berbasis hidroksietil selulosa: Studi eksperimental

ABSTRAK

Pendahuluan: Air liur buatan digunakan untuk mengobati xerostomia, suatu gangguan medis yang terutama disebabkan oleh gangguan kelenjar ludah, dengan menggantikan air liur alami. Karena viskositas dan stabilitasnya yang menguntungkan, hidroksietil selulosa (HEC) sering digunakan sebagai pengental dan pelumas dalam air liur buatan. Air liur buatan perlu dievaluasi dari segi karakteristik fisikokimia untuk memastikan bahwa formulasi tersebut menyerupai air liur alami. Penelitian ini bertujuan untuk mengevaluasi karakteristik fisikokimia air liur buatan berbasis HEC yang tersedia secara komersial di Indonesia. **Metode:** Berdasarkan ketersediaan di pasaran, dua air liur buatan dalam formulasi cair diperoleh dan dianalisis. Sampel 1 adalah formulasi berbasis HEC dengan kombinasi polietilen glikol (PEG) dan metilparaben, sedangkan sampel 2 adalah formulasi berbasis HEC dengan lidah buaya dan setilpiridinium klorida (CPC). Karakteristik fisikokimia sampel diukur, baik sifat kimia (pH, kapasitas buffer) maupun sifat fisik (viskositas, densitas, tegangan permukaan) dievaluasi. (3) **Hasil:** Hasil penelitian menunjukkan bahwa sampel 1 memiliki pH rata-rata $6,81 \pm 0,32$, kapasitas buffer $0,288 \text{ mmol H}^+/\text{L}$, viskositas $10,33 \text{ mPa.s}$, densitas $1,065 \text{ g/cm}^3$, dan tegangan permukaan $44,8 \text{ mN/m}$. Sementara itu, sampel 2 memiliki pH rata-rata $5,08 \pm 0,52$, kapasitas buffer $0,158 \text{ mmol H}^+/\text{L}$, viskositas $2,50 \text{ mPa.s}$, densitas $1,113 \text{ g/cm}^3$, dan tegangan permukaan $45,6 \text{ mN/m}$. **Simpulan:** Penelitian ini menemukan bahwa sampel 1 menunjukkan karakteristik kimia dan fisik yang lebih mirip dengan air liur alami, sedangkan sampel 2 memiliki pH, kapasitas buffer, dan viskositas yang lebih rendah tetapi densitas dan tegangan permukaan yang sedikit lebih tinggi.

KATA KUNCI: Hidroksietil selulosa, air liur buatan, pengganti air liur, karakteristik fisikokimia.

INTRODUCTION

Saliva is a biological fluid secreted by the major and minor salivary glands. The major salivary glands include the parotid, submandibular, and sublingual glands, while the minor salivary glands are distributed throughout the oral cavity. Saliva functions as a lubricant that maintains oral health and facilitates chewing, swallowing, and speaking.^{1,2} In healthy individuals, normal saliva production is approximately 1–1.5 L/day, with an unstimulated salivary flow rate of 0.3–0.4 mL/min and a stimulated flow rate of 1.5–2.0 mL/min³. Hyposalivation is defined as an unstimulated salivary flow rate of ≤ 0.1 mL/min and a stimulated flow rate of ≤ 0.5 –0.7 mL/min. A decrease in saliva secretion may be associated with reduced buffering capacity, increased viscosity, and a decrease in salivary pH (normal range: 6.0–7.0).^{4,5}

Saliva secretion is influenced by both physiological and pathological factors. Physiological factors include hydration status, sex, age, smoking habits, circadian and circannual cycles, mechanical stimulation (e.g., chewing), and sensory stimulation (e.g., taste and food aroma). The parasympathetic nervous system plays a dominant role in saliva secretion under physiological conditions, stimulating the production of a large volume of watery saliva during eating. In contrast, the sympathetic nervous system becomes more active under pathological conditions, producing thicker saliva in response to stress.^{6,7} Pathological factors involve conditions that impair saliva production, such as autoimmune diseases and infections such as human immunodeficiency virus (HIV) infection and acquired immunodeficiency syndrome (AIDS), which can reduce salivary flow. Side effects of anticholinergic drugs and radiation therapy in patients with head and neck cancer can also damage the acinar cells of the salivary glands, leading to impaired saliva production and progressive glandular dysfunction, which ultimately may contribute to hyposalivation and xerostomia.^{6,8}

Xerostomia is characterized by the subjective sensation of dry mouth and may be associated with reduced saliva production, with unstimulated salivary flow rates of ≤ 0.1 mL/min. This condition affects approximately 10–46% of the global population, with a higher prevalence in women and individuals over 60 years of age.^{9,10} Xerostomia can cause difficulties in speaking and swallowing, leading to discomfort that negatively impacts both health and quality of life.¹¹ Muller et al. reported that xerostomia increases the risk of dental caries and oral infections, highlighting the need for effective management to improve patients' quality of life, including the use of artificial saliva as a treatment option.^{12–14}

Artificial saliva serves as a substitute for natural saliva, and is designed to mimic selected physicochemical and lubricating properties of natural saliva. This product is developed as a therapeutic option for patients with xerostomia and impaired salivary production. A study conducted by Kuswandani et al. found that artificial saliva effectively alleviates xerostomia due to its lubricating properties, buffering stability, antibacterial activity, and ability to moisten the oral mucosa.^{14–16} Hydroxyethyl cellulose (HEC) is frequently used in artificial saliva as a thickening and lubricating agent due to its ability to increase viscosity and provide lubrication, thereby helping to mimic the properties of natural saliva and alleviate oral discomfort.^{17,18} A study by Park et al. demonstrated that HEC is advantageous for drug and gene delivery due to its high biocompatibility and water solubility.¹⁹ This finding was supported by research conducted by Ciekot et al. that highlighted HEC's excellent thickening and stabilizing properties due to its chemical stability and biocompatibility.²⁰

HEC-based artificial saliva products, including those containing polyethylene glycol (PEG)-methylparaben and Aloe vera-cetylpyridinium chloride (CPC), have been reported as safe and effective for xerostomia management by regulatory and professional organizations, including Health Canada, the American Dental Association (ADA), and the United States Food and Drug Administration (FDA). Despite being available online in Indonesia, these products have not yet received official distribution approval from the Indonesian Food and Drug Authority (BPOM), raising concerns regarding their quality and safety, particularly for long-term use.

Although previous studies have demonstrated the advantages of hydroxyethyl cellulose (HEC) as a formulation component for artificial saliva, these studies have primarily focused on the properties of HEC itself rather than on commercially available artificial saliva products. In addition, information

regarding the physicochemical characteristics of commercial products, including pH, buffering capacity, viscosity, density, and surface tension, is generally not comprehensively reported or independently evaluated in the scientific literature. To date, no study has specifically evaluated these physicochemical characteristics of commercially available HEC-based artificial saliva marketed in Indonesia, highlighting the need for an independent laboratory-based evaluation. Therefore, characterizing these chemical characteristics (pH and buffering capacity) and physical characteristics (viscosity, density, and surface tension) is important for assessing the extent to which commercially available HEC-based artificial saliva products reproduce selected characteristics of natural saliva. The findings of this evaluation may provide preliminary information on product quality and can contribute to the further development and optimization of affordable, physiologically appropriate HEC-based artificial saliva formulations. This study aimed to evaluate physicochemical characteristics of HEC-based artificial saliva commercially available in Indonesia.

METHODS

This study was a quantitative laboratory-based experimental study. Two commercially available hydroxyethyl cellulose (HEC)-based artificial saliva products marketed in Indonesia were selected as the study samples. Sample 1 was an HEC-based artificial saliva containing polyethylene glycol (PEG) and methylparaben, whereas Sample 2 was an HEC-based artificial saliva containing Aloe vera and cetylpyridinium chloride (CPC). This study was conducted from October 2024 to February 2025 at the Pharmaceutics Laboratory, Faculty of Pharmacy, Padjadjaran University. The evaluated parameters included pH, buffering capacity, viscosity, density, and surface tension.

The pH was determined using the potentiometric method with a pH meter equipped with a pH electrode (Ohaus, USA).²¹ Buffering capacity was measured using the incremental acid-base titration method.²² Viscosity was assessed using the rotational method with a Brookfield viscometer (ATO NDJ-8S, China).²³ Density was determined using the pycnometric method with a pycnometer (Gau-Lussac, France).²⁴ Surface tension was measured using the capillary rise method with a capillary tube and a manual tensiometer.²⁵ Each measurement was repeated three times to ensure data validity and reliability. The research data were analyzed descriptively and presented in tabular form, and compared with the physicochemical characteristics of natural saliva to evaluate the extent to which the artificial saliva products reproduced selected characteristics of natural saliva (Table 2).

Table 1. Formulation of commercial artificial saliva based on HEC

Ingredient	Formulation of sample 1	Formulation of sample 2	Function
Glycerin	20 g	20 g	Humectant
Xylitol	5 g	5 g	Sweetener and saliva-stimulating agent
Hydroxyethyl cellulose	1 g	1 g	Viscosity-increasing agent
Aloe vera	-	3 g	Soothing agent to help relieve irritation
Sorbitol	-	8 g	Humectant and additional sweetener
PEG-40			
hydrogenated castor oil	1 g	-	Surfactant and solubilizer
Methylparaben	0.1 g	-	Preservative
Hydrogenated starch hydrolysate	-	5 g	Humectant
Sodium benzoate	0.2 g	0.2 g	Preservative to prevent microbial growth
Cetylpyridinium chloride	-	0.1 g	Antimicrobial agent
Sodium phosphate	0.1 g	0.1 g	Buffering agent
Purified water	Up to 100 mL	Up to 100 mL	Main solvent

RESULTS

The physicochemical characteristics of the two commercially available HEC-based artificial saliva products (Sample 1 and Sample 2) evaluated based on pH, buffering capacity, viscosity, density, and surface tension. The results were analyzed descriptively and compared with the physicochemical characteristics of natural saliva to assess the extent to which the artificial saliva products resembled natural saliva. The results of this study are presented in Table 2.

Table 2. Summary of commercial artificial saliva characterization based on HEC

Sample	pH	Buffer Capacity (mmol H ⁺ /L)	Viscosity (mPa.s)	Density (g/cm ³)	Surface Tension (mN/m)
1	6.81±0.32	0.288	10.33	1.065	44.8
2	5.08±0.52	0.158	2.50	1.113	45.6
Natural saliva (reference range)	6.0-7.0	0.50-4.90	2.75-15.5	1.002-1.012	44.9-68.7

DISCUSSION

This study evaluated the pH, buffering capacity, viscosity, density, and surface tension of two commercially available HEC-based artificial saliva products and compared these parameters descriptively with reported physicochemical characteristics of natural saliva to assess the extent to which the products resemble natural saliva.

According to Table 2, the average pH value of Sample 1 is 6.81±0.32, whereas the product containing Aloe vera-CPC (Sample 2) had an average pH of 5.08±0.52. Based on the mean pH values of both samples, Sample 1 fell within the reported physiological pH range of natural saliva, whereas Sample 2 had a lower pH. This finding is consistent with the study by Kubala E et al., which reported that the pH range of human saliva is 6.0–7.0.5 In contrast, Sample 2 had a lower and more acidic pH than the reported range of natural saliva.

Although both artificial saliva products share similar formulations, differences exist in their compositions. Sample 2 contains additional Aloe vera, an herbal plant known for its antibacterial and antifungal properties.²⁶ Forouzande B et al. reported that Aloe vera helps protect oral tissues and reduces the risk of dental caries and periodontal disease through its antimicrobial and anti-inflammatory effects.²⁷ Additionally, this product contains cetylpyridinium chloride (CPC), an antimicrobial agent with activity against oral microorganisms. CPC may contribute to antimicrobial activity in oral-care formulations and enhance user comfort.²⁸ From a formulation perspective, Sample 2 contains additional ingredients that may provide therapeutic benefits beyond its primary function as artificial saliva. The presence of Aloe vera in the formulation may contribute to the lower pH of Sample 2, as Safitri et al. found that Aloe vera exhibits acidic properties with a pH of approximately 4.8. Meanwhile, Nasila K et al., reported that CPC has a neutral pH and does not significantly affect the final product's acidity.^{29,30}

Human saliva is secreted by the salivary glands, including the parotid, submandibular, and sublingual glands. The parotid gland, the largest salivary gland, produces secretions that contribute to oral fluid composition and pH regulation.³¹ Artificial saliva is designed to mimic selected characteristics of natural saliva. However, the present study demonstrated that the two commercially available HEC-based artificial saliva products exhibited different physicochemical properties. In particular, Sample 2 showed a pH below reported range of human saliva, indicating that not all commercially available HEC-based artificial saliva products closely replicate the physiological pH of natural saliva. Pandey P et al., reported that human saliva pH is influenced by various factors, including secretion rate, diet, and bicarbonate ion content. A lower-pH saliva substitute, such as Sample 2, may contribute to a more acidic oral environment, potentially increasing the risk of enamel demineralization.³² Enamel demineralization can occur when the enamel is exposed to an environment with a pH below 5.5, as explained in the study by Panigoro et al.³³ Based on this study, Sample 2 had a pH of 5.08, and this finding warrants consideration when evaluating the formulation.

Although this value falls below the physiological pH range of normal saliva (6.0–7.0), it remains safe for short-term use when applied as directed, thereby minimizing the risk of enamel demineralization.

Buffering capacity determines the extent to which artificial saliva can neutralize acids and maintain pH balance. Based on Table 2, the mean buffering capacity of Sample 1 was 0.288 mmol H⁺/L, while that of Sample 2 was 0.158 mmol H⁺/L. These findings demonstrate that both products had lower buffering capacities than the reported range for human saliva. This finding is consistent with the report by Kubala E et al., which indicated that the buffer capacity of natural human saliva ranges from 0.50 to 4.9 mmol H⁺/L.⁵

The study by Chen J et al. reported that natural saliva contains components such as bicarbonate ions, phosphate, and proteins, which play crucial roles in buffering capacity.³⁴ The lower or absence of these components in artificial saliva may limit its buffering efficiency compared to natural saliva. Furthermore, Pandey P et al. reported that low buffer capacity may increase the risk of enamel demineralization, particularly in individuals with a low salivary flow rate or medical conditions affecting saliva production.³²

The buffering capacity of artificial saliva is essential in managing xerostomia and medical conditions that cause hyposalivation, such as Sjögren's syndrome or the side effects of radiation therapy to the head and neck. Artificial saliva with adequate buffering capacity can potentially help reduce the risk of dental caries, enamel erosion, and discomfort caused by pH fluctuations in the oral cavity. Therefore, improving artificial saliva formulations with more optimal buffering components may provide greater clinical benefits for patients with xerostomia and hyposalivation.¹⁸

Viscosity is one of the key characteristics that plays a crucial role in assessing how closely a product resembles natural saliva, particularly in terms of thickness. Table 2 shows that the mean viscosity of Sample 1 was 10.33 mPa.s, whereas Sample 2 had an average viscosity of 2.50 mPa.s. In line with this study, Kuswandani et al. reported that the reported viscosity range for human saliva is 2.75–15.5 mPa.s.³⁵ Based on these findings, sample 1 fell within the reported viscosity range of natural saliva, whereas Sample 2 was slightly below this range.

The viscosity difference between these two artificial saliva products may be due to variations in the composition of active ingredients in their formulations. Previous studies have suggested that although both products use hydroxyethyl cellulose as the primary thickening agent, other dissolved substances in the formulation, such as electrolytes or additional excipients, may significantly alter viscosity values. Furthermore, Ekta N reported that artificial saliva with better dental protective capabilities tends to have higher viscosity due to the presence of thickening agents such as glycerol and cellulose in the formulation.¹⁸

The viscosity of artificial saliva has clinical relevance in maintaining oral cavity lubrication, enhancing patient comfort, and supporting physiological functions such as speaking, swallowing, and protecting the mucosa from irritation. Artificial saliva with appropriate viscosity can help individuals with xerostomia or hyposalivation by reducing the sensation of oral dryness, improving fluid adhesion to mucosal tissues, and slowing water evaporation, thereby enhancing hydration effects in the oral cavity. Selecting an appropriate viscosity for artificial saliva is crucial for improving its effectiveness in patients with impaired saliva production.⁶

The density of artificial saliva provides insight into its physical characteristics, which can affect both comfort and effectiveness in the oral cavity. As shown in Table 2, the mean density of Sample 1 was 1.065 g/cm³, while Sample 2 had a slightly higher density of 1.113 g/cm³. Both samples exhibited higher densities compared to natural saliva, which typically ranges from 1.002 to 1.012 g/cm³.³⁶

According to the study by Foglio Bonda et al., although there is a density difference between artificial and natural saliva, this difference is not significant, considering that both primarily consist of water. The higher density may be due to thickening agents such as hydroxyethyl cellulose or other components absent in natural saliva.³⁶ Furthermore, the study by Jirapornchai S et al. reported that artificial saliva may not function optimally if its density is too high or too low, as this can affect its suitability for specific treatments or its ability to maintain optimal oral health.³⁷

An appropriate density may contribute to the appropriate distribution and handling of the product within the oral cavity, optimize lubrication, and enhance adhesion to the mucosa. Therefore, density

should be considered as one of the physicochemical parameters during artificial saliva formulation development.³⁷

Surface tension is a key factor influencing how artificial saliva spreads and coats oral tissues. Table 2 shows that the average surface tension of Sample 1 was 44.8 mN/m, whereas Sample 2 had a mean value of 45.6 mN/m. These results align with previous studies indicating that natural saliva has a surface tension ranging from 44.9 to 68.7 mN/m.³⁷

Lower surface tension can facilitate spreading and lubrication, which is essential for oral comfort and health. The study by Jirapornchai S et al. reported that lower surface tension contributes to the comfort and protective function of artificial saliva in the oral cavity. Optimal surface tension allows artificial saliva to spread evenly across the mucosal surface, retain moisture, and facilitate the delivery of active ingredients such as enzymes or antimicrobial agents. This improves its effectiveness in alleviating xerostomia and protecting oral tissues.³⁷

Overall, sample 1 showed greater agreement with the reported physicochemical characteristics of natural saliva than Sample 2, particularly in terms of pH, buffer capacity, viscosity, density, and surface tension. The natural enzyme content in Sample 1 also helps maintain microbial balance in the mouth. However, improvements in buffer capacity are needed to enhance its ability to mimic natural saliva more effectively.

Sample 2 has different physicochemical characteristics from Sample 1 and contains additional ingredients with reported antimicrobial and anti-inflammatory properties. A recent study suggested that replacing CPC with mucin may improve its physicochemical properties and increase its similarity to natural saliva. Mucin, the primary glycoprotein in natural saliva, plays a crucial role in enhancing viscosity, buffering capacity, and lubrication.³⁸ Its addition to an artificial saliva formulation may improve lubrication and furthermore protect oral tissues. Mucin can be found naturally in both plants and animals. An in vitro study by Yoretina et al., found that catfish mucus (*Clarias batrachus*) contains mucopolysaccharides and bioactive proteins that improve mucosal hydration and exhibit antimicrobial activities, making it a potential ingredient in artificial saliva formulations for xerostomia treatment.³⁹

Previous clinical studies have also demonstrated that artificial saliva can improve oral lubrication, relieve xerostomia symptoms, and enhance patient comfort, although its effectiveness varies depending on the product formulation. Therefore, further research on artificial saliva is necessary to improve its quality and effectiveness in supporting the physiological functions of natural saliva. The differences observed between Sample 1 and Sample 2 in several physicochemical characteristics may influence their performance and user experience.⁴⁰ This study was limited to the physicochemical characterization of two commercially available HEC-based artificial saliva products, and therefore their clinical effectiveness was not evaluated. Differences in the chemical composition between artificial and natural saliva may influence product performance. Future research involving a larger sample size and a broader variety of artificial saliva products should be considered to further evaluate and improve their effectiveness in maintaining optimal oral health.

CONCLUSION

The evaluation of the physicochemical characteristics of commercially available HEC-based artificial saliva demonstrated that Sample 1 had greater overall agreement with the reported physicochemical characteristics of natural saliva than Sample 2, particularly in terms of pH, buffering capacity, viscosity, density, and surface tension. In contrast, Sample 2 had a lower pH, lower buffering capacity, lower viscosity, slightly higher density, and higher surface tension. These differences may affect the comfort and functionality of artificial saliva in supporting oral health and lubrication. The implication of this research is that it provides useful information for the selection of commercially available artificial saliva products and may serve as a reference for the future development and improvement of HEC-based artificial saliva formulations with physicochemical properties that more closely resemble those of natural saliva.

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