International Journal of Applied Pharmaceutics

ISSN- 0975-7058 Vol 17, Special Issue 1, 2025

Original Article

FORMULATION AND *IN VITRO* EVALUATION OF ANTIBACTERIAL POTENTIAL OF PINEAPPLE (*ANANAS COMOSUS* (L) MERR*)* PEELS EXTRACT MOUTHWASH

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Received: 04 Oct 2024, Revised and Accepted: 20 Nov 2024

ABSTRACT

Objective: Pineapple peel is a byproduct of pineapple commonly found in Indonesia. Its abundant metabolites are promising as a natural antibacterial agent and developed as a mouth care product. This research aimed to formulate a mouthwash product using pineapple peel extract, evaluate the formula according to internationally accepted regulation standards, and investigate its antibacterial activity.

Methods: The pineapple peel extract is obtained by ethanol maceration process and then went through filtration and evaporation. The extract was incorporated into mouthwash using co-solvation techniques and evaluated for its physicochemical properties and antibacterial activity towards *Streptococcus mutans, Porphyromonas gingivalis*, and *Lactobacillus acidophilus*.

Results: The formulation met the regulation standard criteria according to these parameters: microbial test, metal impurities, and alcohol content. The formulation also shows antibacterial properties towards *S. mutans*, *P. gingivalis*, and *L. acidophilus* with zones of inhibition were 10.17± 1.25 mm, 11.75±0.54 mm, and 7.25±0.54 mm, respectively.

Conclusion: The physicochemical and microbiological evaluation confirmed the formula's compliance with the Indonesian Food and Drug Regulatory Body and antibacterial properties toward *S. aureus, P. gingivalis,* and *L. acidophilus.*

Keywords: Pineapple peel extract, Mouthwash formulation, Antibacterial activity

DOI: https://dx.doi.org/10.22159/ijap.2025.v17s1.13 Journal homepage: https://innovareacademics.in/journals/index.php/ijap

INTRODUCTION

According to the World Health Organization (WHO), approximately 3.5 million people globally are affected by oral health issues. These conditions are more prevalent in many low and middle-income countries because of the inadequate resources to manage and prevent these conditions [1]. Periodontal disease such as periodontitis involves inflammation and manifests through symptoms such as gingivitis and sometimes bad breath. Severe periodontitis, identified as the sixth most common chronic disease worldwide, affects approximately 750 million people, significantly impacting their quality of life [2].

Pineapple (*Ananas comosus* l Merr) grow widely as a tropical fruit in Indonesia, renowned for its distinctive flavour and versatility in culinary applications. However, beyond its culinary appeal, pineapple presents an opportunity for further utilization, particularly its peel, which is often considered a waste byproduct. Pineapple peel harbours significant concentrations of flavonoids and bromelain [3]. Flavonoids are recognized for their antibacterial properties, while bromelain, a proteolytic enzyme, exhibits the ability to hydrolyse bacterial protein bonds, thereby inhibiting bacterial growth [4]. Bioactive compounds in pineapple peel extract, such as flavonoids, tannins, saponins, and bromelain, inhibit bacterial growth that causes gingivitis and contributes to plaque formation. The plaque is considered an immune response towards inflammation of microbiological origin and using mouth rinse as chemical plaque control for 6 mo can reduce plaque significantly [5, 6]. Pineapple peel extract that contains flavonoid and bromelain would induce bacterial cell lysis and prevent plaque formation [7, 8].

Mouthwash serves as a product for maintaining oral hygiene and combating oral issues such as gum inflammation and bad breath [9]. Mouthwashes can inhibit the growth of pathogenic microbes when used adjunctively and manage key oral diseases, namely caries, gingivitis, and periodontal disease [10]. The optimal formulation of mouthwash allowed the active ingredients to reach parts that were unable reached by a toothbrush or dental floss. Several herbs are considered good alternatives for oral health problems [11]. Innovations in herbal mouthwash formulations continuously seek effective components to enhance efficacy with quality that meets both regulatory standards and consumer preferences. Herbal mouthwash can reduce the grade and pain of oral mucositis [12]. Continuous use of natural mouthwash also can improve and maintain oral health status, becoming an effective and safe intervention as a nonpharmacological treatment option for protecting the oral mucosa [13].

Considering the antimicrobial potential of pineapple peel extract, it emerges as a promising candidate for incorporation into mouthwash formulations. With its natural antimicrobial compounds, including bromelain and other bioactive components, pineapple peel extract has potential in mouthwash formulations aimed at promoting oral health. However, because the pineapple peel extract did not dissolve in water easily, there must be some adjustments added to the mouthwash formulation. Many other substances are needed to create a formula while not necessarily having medical benefits. Due to the lack of studies on the components of mouthwash, it was advised to carefully designate the novelty of mouthwash formulas according to each medical and pharmaceutical necessity [14]. Therefore, the mouthwash product should meet the quality requirements, and the efficacy should be evident.

While the previous study examines and confirms the effectiveness of mouthwash formula from pineapple peel extracts in reducing the plaque index of orthodontic fixed appliance patients, this study aims to develop a formula that is designed to meet regulatory standards. This ensures the safety and quality of the formulation, which is crucial for commercial applications. This research also endeavours to harness the antimicrobial potential towards specific bacterial growth of pineapple peel extract in a mouthwash formulation. This study aims to advance the creation of innovative oral herbal mouthwash by examining the evidence of its quality standard and its specific antimicrobial properties, thereby promoting overall oral health and well-being.

MATERIAL AND METHODS

Material

Pineapple peel collected from Padang and Bukittinggi in West Sumatera, Glycerin (Bratachem, Indonesia), Stevia (Nutrifood,

Indonesia), Sodium Benzoate (Bratachem, Indonesia), Peppermint Oil (Bratachem, Indonesia), Water Purified.

Pineapple peel extraction

The pineapple peel was chopped and contained in a clean container and soaked in ethanol for 3-5 d. The ethanol extract was filtered and evaporated using a rotary evaporator (Buchi). The choice of maceration for extraction considering not only the method was simple and cheap, previous research confirmed the effectivity of this extraction method [15, 16].

Formulation

The mouthwash was prepared according to the master formula (table 1). The pineapple peel extract was set to 10% in the formula as the antimicrobial activities of pineapple peel extract that we studied before showed that the 10% extract carried antimicrobial properties toward tooth decay bacteria *S. sanguinis* and *S. mutans* [16, 17].

Evaluation

- **Physical evaluation**

The physical evaluation of the mouthwash formulation, including odour, taste, and color, was conducted through sensory feel and visual inspection.

- **Microbial growth**

The enumeration of aerobic organisms was determined by total plate count methods and most probable number methods by USP 43 NF 38 Standard. The specific microbial growth study was tested towards *E. coli, Salmonella sp, Shigella sp, and Clostridia* [18]

- **Alcohol content**

The alcohol content was determined using gas chromatography-FID Head Space. Control and sample were placed on the headspace vials, then sealed, heated and shaken vials to allow any ethanol present to equilibrate between sample and headspace [19, 20].

- **Water content**

The water content of the formulation was determined using thermogravimetric analysis by USP 43 NF 38 standard [21].

- **Metal impurities**

The formulation was tested using ICP-OES (Inductively Coupled Plasma – Optical Emission Spectrometry) [22].

***In vitro* antibacterial activity**

In vitro, antibacterial activity was performed on isolated colonies of *Streptococcus mutans, Porphyromonas gingivalis*, and *Lactobacillus acidophilus*. Three wells with approximately 2 mm diameter were punched in each blood media agar and the mouthwash solution with a similar volume (approximately 20-50 µl) was introduced into the media. The plates were incubated at 37 °C for 24 h and the zone of inhibition was observed. Sodium chloride 0.9% was used as the negative control, and three commercial mouthwash products (Brand A®, Brand B®, and Brand C®) were used as positive controls. Negative and positive control antibacterial activity was performed triple on isolated colonies of *S. mutans.* The zone of inhibition of growth was measured in millimetres [16, 23].

Statistical analysis

The difference in the mean values of inhibition diameter from mouthwash formulation and three commercial brands toward *S. mutans* was analyzed using one-way ANOVA with a significance level (p-value) of 0.05, p-valued less than 0.05 considered statistically significant.

RESULTS

The evaluation of the formulation of pineapple peel extract mouthwash was done simplo and duplo with the result shown in table 2, and the antibacterial study was conducted using agar diffusion methods. The diameters of the inhibition zones of the mouthwash formulation on three bacteria showed notable antimicrobial activities against the bacteria tested with the result shown in table 3. The product demonstrated zones of inhibition ranging from 7.25±0.54 mm to 11.75±0.54 mm (table 3), while the zones of inhibition of negative control (sodium chloride 0.9 % solution) was 0 nm (fig. 2). The zones of positive control towards *S. mutans* were 4 mm, 2 mm, and 0 mm (fig. 3).

Table 1: Formulation of pineapple peel extract mouthwash

Composition		Formula (%)
Pineapple peel extract	Active ingredients	10
Glycerin	Co-solvent	10
Tropicana slim stevia®	Sweetener	5
Sodium Benzoate	Preservative	0.10
Peppermint Oil	Flavouring agent	0.005
Water purified up		100

Table 2: Evaluation of pineapple peel extract mouthwash

Parameter		Unit	Simplo	Duplo
Organoleptic	Odour	-	Acceptable	Acceptable
	Taste	-	bittersweet	bittersweet
	Visual appearance	-	Brown	Brown
Water Content	Water Content	%	76.36	76.10
Alcohol content	Alcohol content	mg/l	458.91	468.41
Impurities	Arsen	mg/kg	Not detected	Not detected
	Cadmium	mg/kg	Not detected	Not detected
	Mercury	mg/kg	Not detected	Not detected
	Lead	mg/kg	Not detected	Not detected
Microbial test	Plate Count Number	colony/g	1 x 10^1	1 x 10^1
	E. coly	colony/g	<10	<10
	Salmonella sp.	/g	negative	negative
	Shigella sp.	/g	negative	negative
	Most Probable Number	colony/g	<10	<10
	Enterobacteriaceae count	colony/g	<10	<10
	Clostridia	/g	negative	Negative
	Aflatoxin B1	mcg/kg	Not detected	Not detected
	Aflatoxin B2	mcg/kg	Not detected	Not detected
	Aflatoxin G1	mcg/kg	Not detected	Not detected
	Aflatoxin G2	mcg/kg	Not detected	Not detected
	Aflatoxin Total	mcg/kg	Not detected	Not detected

Table 3: Diameter of inhibition from pineapple peel extract mouthwash towards *S. mutans, P. gingivalis*, and *L. acidophilus*

Microorganism	Diameter inhibition (mm)
Streptococcus mutans	10.17±1.25
Porphyromonas gingivalis	11.75±0.54
Lactobacillus acidophilus	7.25±0.54

Data are given as mean±SD.

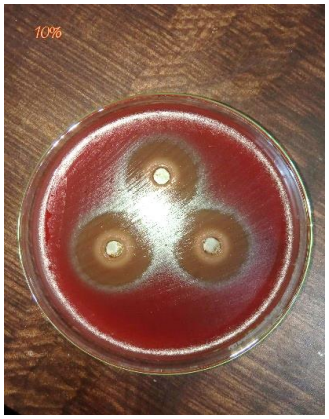

Fig. 1: The diameter inhibition from pineapple peel extract mouthwash towards *S. mutans, P. gingivalis*, and *L. acidophilus* using the disc diffusion method on blood media agar. The zones of inhibition were measured in millimeters

Fig. 2: The diameter inhibition from negative control (sodium chloride 0.9 %) towards *S. mutans.* Examined using the disc diffusion method on blood media agar. The zones of inhibition were measured in millimetres

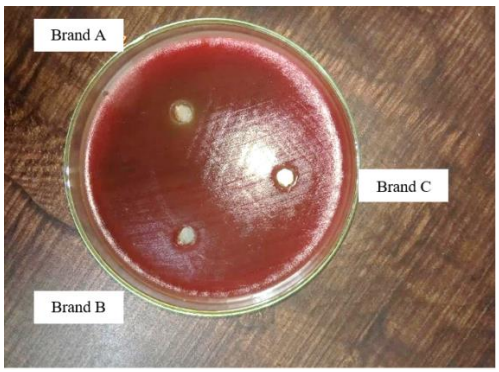

Fig. 3: Petri disc of diameter inhibition from positive control towards *S. mutans.* Diameter inhibition was measured in mm and analyzed using one-way ANOVA (analysis of variance) with a significance level (p-value) of 0.05; p-value less than 0.05 is considered statistically significant.

DISCUSSION

From the organoleptic study, the color, odor, and taste of the formula were brown liquid with a distinctive mint smell and sweet taste which were stated as acceptable by 27 volunteers. This is important because the product was going to be given orally and stay in the oral cavity, thus palatability is critical. The water content of this formula, with 76.35 % and 76.10% of total composition, indicate that the formula prone to microbial growth; thus, the enumeration study was needed to keep the stability of the product checked. According to Indonesian regulations, the microbial quality standard for this type of product is less than 105 cfu/ml and less than 102 cfu/ml. Thus, the enumeration study of the mouthwash formula followed this standard. Specific bacteria growth, such as *Escherichia coli, Salmonella*, *Shigella* and *Aflatoxin,* were also not detected during the study. The investigation into metal and biological impurities that showed negative findings gives this product safety assurance.

While the alcohol content of this formula was determined because of the probability of alcohol residue from the extraction process of pineapple peel, the maximum alcohol content requirement was 1 % or less [24]. With 458.91 and 468.41 mg/l of alcohol content in the product showed that the minimum alcohol content standard was met. The alcohol detected was not a part of the formulation but the regulatory acceptance level standard of herbal pharmaceutical products considering there was a trace amount of alcohol that couldn't be avoided during the extraction process. Despite being minimal, the presence of alcohol may still influence both antibacterial efficacy and consumer acceptance. Its presence may be undesirable for certain populations due to sensitivity or contraindication to its presence or personal religious beliefs or cultural norms preference [25]. Developing and comparing to alternative alcohol-free bromelain content mouthwash formula is advisable to ensure its efficacy and address consumer concerns.

The antibacterial study showed that the mouthwash formula effectively inhibited the growth of *S. mutans, P. gingivalis*, and *L. acidophilus* and had the potential to prevent oral plaque and other oral problems. The mouthwash exhibited the greatest inhibitory effect against *P. gingivalis* with a diameter of inhibition 11.75±0.544 mm, suggesting its efficacy against this periodontal pathogen. The relatively high activity against P. gingivalis highlights the potential of the formulation in managing periodontal diseases. Against *S. mutans* (a key contributor to dental caries), the inhibition zone was 10.17±1.25 mm, reflecting good antibacterial potential for reducing dental plaque and cavities. While no antibacterial activity was shown by the negative control (sodium chloride 0,9 % solution), the greater number of zones of inhibition from the formula *towards S. mutans* compared to three other positive controls showed potential antibacterial activity of this product. This result, supported by some previous studies, highlighted the effectiveness of bromelain as an antibacterial towards *Staphylococcus aureus* and *Propionibacterium acnes* and oral products from pineapple peels against periodontal pathogens such as *Enterococci Faecalis*, *Aggregatibacter actinomycetemcomitans, Treponema denticola*, and *Fusobacterium nucleatum* biofilm growth [6, 7, 26]. The p-values from statistical analysis of mean diameter between mouthwash formulation and branded products one-way ANOVA show p-values 2.3578e-7, indicating there was a significant difference between diameters of inhibition observed. We suggest that our formulation has a distinct antimicrobial effect and further investigation is needed to confirm its efficacy. The larger inhibition zone observed with our formulation could be attributed to the unique active compounds in the pineapple peel extract, such as bromelain and flavonoids.

The mechanism of antimicrobial action of bromelain enzyme remains unclear, although it is suspected that bromelain may inhibit

bacterial growth by hydrolyzing some peptide bonds and digesting protein in the bacteria cell wall, therefore causing the cell wall to be damaged. Flavonoids are polar phenolic compounds that can penetrate the bacterial peptidoglycan layer in the cell wall bacteria and damage the cytoplasmic membrane, leading to cell death. Pineapple peel extract that contains flavonoid and bromelain would induce bacterial cell lysis, prevent plaque formation, and prevent periodontal disease [23, 27, 28]. Some antimicrobial activity showed the dependence of the structure of the antimicrobial towards specific bacteria [29]. While the three bacteria examined in this study are g-positive bacteria, the difference in their unique wall structure and characteristics likely contribute to the observed variation inhibition zones.

Although the mouthwash was confirmed to have antibacterial activity, the lack of *in vivo* studies or clinical trials limits the ability to confirm its efficacy. Further study must be done to ensure the stability of the formula. Other research should also focus on conducting clinical evaluations to assess the mouthwash's impact on oral health parameters such as a quantitative study on its effectiveness against plaque.

CONCLUSION

A formulation of liquid mouthwash from ethanol extract from pineapple peel was developed and evaluated according to Indonesian regulation standards. The physicochemical and biological evaluation confirms the formulation met with regulation quality standards. The antibacterial study showed that this product was effective towards inhibition of *S. mutans, P. gingivalis*, and *L. acidophilus* and had the potential to prevent oral plaque and other periodontal problems. The antibacterial study has shown that the formula's potential antibacterial activities were three times higher than positive controls. However, further optimization and clinical trials are necessary prior to commercial scale-up.

ACKNOWLEDGEMENT

We acknowledge all the authors listed contributed to this. We would also like to thank Mesa Irna Suryani from the Faculty of Pharmacy, Universitas Andalas for assisting with the production process of the product involved in this research and SIG Laboratory (West Java, Indonesia) for some of the data acquisition.

SOURCE OF FUNDING

Hibah Penelitian Terapan Unggulan Perguran Tinggi Politeknik Kesehatan Kementerian Kesehatan Padang, Number: HK.02.03/00534/2022

AUTHORS CONTRIBUTIONS

The research was developed based on the idea of Minarni, while the product formulation and quality product target were developed by Azhoma Gumala and the writing concept was reviewed by Susi. All of the authors contributed equally in this study and approved the final version of this manuscript.

CONFLICT OF INTERESTS

There was no conflict of interest in this study.

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