Cerdika: Jurnal Ilmiah Indonesia, Juli 2022, 2 (7), 671-676
p-ISSN: 2774-6291 e-ISSN: 2774-6534

Available online at http://cerdika.publikasiindonesia.id/index.php/cerdika/index

A Combination of 10% Gambier Extract and 0.0048% Fluoride Toothpaste as An Alternative Antifungal Therapy

Pudji Handayani[1*], Muhammad Naufal Denhari Aflah[2], Siti Rusdiana Puspa Dewi[3]
Medical Faculty of Universitas Sriwijaya, Palembang, Indonesia[1, 2, 3]
pudji.handayani@fk.unsri.ac.id[1], naufal.Denhari16@gmail.com[2], sitrus.pd@gmail.com[3]

Received: 04-07-2022
Revised : 08-07-2022
Approved: 25-07-2022

Abstract

Poor oral hygiene might lead to Candida albicans infection. Since long term used of synthetics antifungal therapy could lead to fungal resistance, an alternative of antifungal therapy was needed. It has been reported that Gambier (Uncaria gambir ROXB) contains catechins and tannins which have antifungal effects invitro, but research using Gambier extract as a toothpaste for daily oral hygiene maintenance has not established. This study was done to determine the antifungal effect and the synergy of the combination of 10% gambier and fluorides in toothpaste preparation against Candida albicans. A true experimental laboratory study with a post-test-only design group was established. Three groups namely 10% gambier extract toothpaste, the combination of 10% gambier extract and 0.0048% fluorides toothpaste, lastly the 0.0048% fluoride toothpaste were tested. Gambier extract was obtained using the soxhletation method and the separation of the solvent from the extract was carried out by the distillation method. Agar Well method antifungal test was used to measure the inhibition zone value of tested groups. Data were analyzed using one-way Anova. Inhibition test of tested groups showed that only combination of gambier and fluorides toothpaste was effective in inhibiting Candida albicans with an average inhibition zone value of 8.35 mm. Toothpaste preparation of 10% Gambier extract and 0.0048% fluorides combination produce a synergistic therapeutic effect in antifungal therapy.

Keywords: antifungal agents; candida albicans; fluorides; toothpastes.

**Correspondence Author: Pudji Handayani*
Email: pudji.handayani@fk.unsri.ac.id

INTRODUCTION

Oral candidiasis is the most common infection of the oral cavity caused by *Candida sp* especially *Candida albicans (C. albicans)* (Millsop & Fazel, 2016). Oral Candidiasis usually found in very young, very old, and very ill persons (Glick, 2015). *World Health Organization* (WHO) reported that the incidence of oral candidiasis was about 5,8% to 98,3% with predisposing factors, such as local (bad oral hygiene, uncleaned dentures) and systemic (long term use of steroids or antibiotics, uncontrolled systemic diseases) factors (Apriliana Puspitasari et al., 2019).

Basically, *C. albicans* is a normal oral microflora that could become pathogens if there are changes in host defence mechanism caused by predisposing factors that previously mentioned (Glick, 2015). It has been previously reported that maintaining oral hygiene leads to prevention of oral candidiasis. Lack of oral hygiene increased the *C. albicans* colonization, thus lead oral candidiasis (Nur'aenya et al., 2017). There many evidence of oral candidiasis and predisposing factors published but less about its relation with oral

hygiene. Since the prevention of oral candidiasis can be done through managing oral hygiene, research of antifungal for daily oral hygiene needs to be established.

Toothpaste is usually required in managing daily oral hygiene. Toothpaste has active components (that has therapeutic effect) and non-active components (such as toothpaste consistence, taste, and others non-therapeutic components) (Ambar Puspitasaria et al., 2018). Fluorides as an active components in toothpaste have the ability in inhibiting *Candida albicans* growth by inhibits the synthesis of enolase enzyme that formed the energy for Candida itself. This condition caused Phosphate Enol Pyruvate (PEP) declined to be synthesized, with the result that Carbohydrate transport from the Candida's' cell wall to cytoplasm disrupted and the *Candida albicans* colonization decreased (Sukanto, 2012).

Gambier (Uncaria gambir ROXB*)* extract also can inhibit the growth of *Candida albicans* invitro in the work of bioactive (Ismail et al., 2021) and antioxidant on it. (Widiyarti et al., 2014) *Gambier* consist of bioactive agents such as catechin (Marlindaa, 2018), quercetin, gallic acid, ellagic acid, and catechol. (Rahmana et al., 2018) *Gambier* also has an antioxidant effect from tannin, catechin dan gambiriin (Achmad et al., 2021). Since *Gambier* extract in toothpaste form have not been tested invitro, this study was done to verify whether *Gambier* extract could be an alternative for herbal toothpaste in maintaining oral hygiene and preventing oral candidiasis (Suraini et al., 2015).

RESEARCH METHODE

The study was held with the approval of Ethical Committee, Medical Faculty of Universitas Sriwijaya with protocol number: 065-2021.

Extracting 10% *Gambier* extract

The dry *Gambier (Uncaria gambir* ROXB*)* extracted plants were obtained from Kebun Babat Toman Sekayu, South Sumatera-Indonesia. The dry extracted gambier then processed to make a 10% *Gambier* extract using soxhletation method.

Production of the Tested toothpaste (The Combination of 10% Gambier extract and fluoride toothpaste, the Fluoride toothpaste, and the 10% extract toothpaste)

The tested toothpastes were made with almost the same steps but using different active agents. The material used in every step in making toothpastes were the same. For instance, steps in making 10% Gambier extract toothpaste were made by combining 2.5% *carboxy methyl cellulose* (CMC) with 5% glycerine until it well-mixed (Phase A). After that, made a combination of water and 0.12% sodium saccharine (Phase B) until it became homogenic. Continued to phase C, by combining the active component, 10% gambier extract with 44% calcium carbonate ($CaCo_3$), Phase A, and Phase B preparation then stir until it became homogeneous once again. After all the components were well-mixed, the paste was made. Add 2% sodium lauryl sulphate (Phase D) with the previous made paste until it became homogeneous.

The steps in making the Combination of 10% **Gambier** extract-fluoride and fluoride toothpastes were the same (Phase A, B, and D) but in phase C, the active agents were substituted with each of the toothpaste material. For instance, the active agents in Combination of 10% **Gambier** extract-fluoride toothpaste were 10% **Gambier** extract and 0.0048% fluoride and the active agent in fluoride toothpastes was 0.0048% fluoride. Each toothpaste active agents then added to each phase C steps.

Preparation of *Candida albicans* suspension

C. albicans ATCC 10231 used in this study was obtained from the Balai Besar Laboraturium Kesehatan (BBLK) Palembang-South Sumatera. *C. albicans* cultures on

Sabouraud Dextrose Agar (SDA) medium were incubated at room temperature for two days. *C. albicans* cultures were collected using an inoculation needle and suspended in a test tube containing 0.9 percent NaCl. The fungal suspension in the test tube is homogenized. The turbidity is then adjusted to 0.5 Standard MacFarland (1-5 x 10^6 CFU/ml) using a densitometer.

Growth inhibition test

The well-diffusion method was used to evaluate the inhibition of these toothpaste. Sabouraud Dextrose Agar (SDA) medium containing C. albicans colony culture was injected with cork holes 6 mm in diameter to create wells. Each well is filled with one type of toothpaste formulation (Gambier toothpaste 10%, fluoride, and combination fluoride-gambir extract 10%). The agar media was then incubated for 48 hours at 37°C. The diameter of the vertical and horizontal clear zones is determined by measuring the clear zone surrounding the well using a calliper (Figure 1). Each group received eight replications. The measurement data are added together and then averaged.

Data Analysis

Data were analysed with software Statistical Package For Social Sciences (SPSS) to test the normality distribution with Saphiro-Wilk test and followed by homogeneity with Levene's Test.

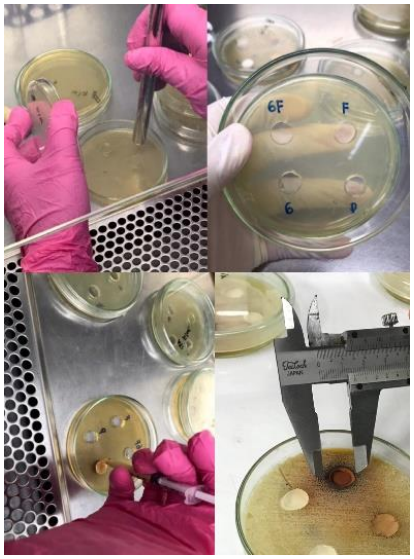

Figure 1. Inhibition zones of *C. albicans* were tested using agar well-method

RESULTS AND DISCUSSION

The zone of inhibition was only observed in the 10% gambier fluoride-extract combination toothpaste group stated in Table 1 below.

Table 1. The inhibition zone measurement results

	10% gambier extract toothpaste	0.0048% fluoride toothpaste	10% gambier fluoride-extract toothpaste
1	0	0	9,7
2	0	0	8,7
3	0	0	5,6
4	0	0	8,7

5	0	0	8,7
6	0	0	7,8
7	0	0	9,6
8	0	0	8
Total	**0**	**0**	**66.8**
Average	**0**	**0**	**8,35**

These study findings revealed that a concentration of 10% gambier extract in toothpaste formulations was ineffective in preventing the development of Candida albicans. The concentration of gambier extract in the toothpaste in this study was lower than that of Suraini et al., who used a higher concentration of gambier extract. This might be one of the reasons why the gambier extract toothpaste used in this study had no antifungal effects (Suraini et al., 2015).

The quantity of abrasive material in toothpaste, particularly $CaCO_3$, might have affected the study's findings. A previous study by Lucida et al. stated that the content could diminish the efficacy of the active components and influence the viscosity of the toothpaste (Lucida et al., 2010). The decrease in active component efficacy was caused by a reduction in the action of catechins and tannins in gambier extract. Any substantial variations in toothpaste viscosity will affect the activity of phenolic compounds produced from gambier extract. Meanwhile, 44% $CaCO_3$ was employed in this investigation. As a result, its viscosity may impact the inhibitory test results (Lucida et al., 2010).

This study's fluoride concentration was lower than in the prior study. The results of this investigation revealed that toothpaste with a fluoride concentration of 0.0048% was ineffective in preventing the development of Candida albicans compared to an earlier study conducted by Ajeng et al., who utilized toothpaste with a fluoride concentration of 1,12%. A greater fluoride concentration in toothpaste can prevent the development of Candida albicans (Fitranti et al., 2011).

The toothpaste in this study, containing 10% gambier extract and 0.0048 percent fluoride, showed synergism in suppressing Candida albicans growth. This was because the major active ingredient in gambier, i.e., phenolic compounds (catechins and tannins), when coupled with fluoride, increases the permeability of Candida albicans cell walls. It disrupts the transfer of Candida cell wall polysaccharides. Based on this description, it was possible to deduce that the presence of phenol and fluoride compounds had a synergistic impact, reducing Candida albicans colonization.

The limitation of this study was that the extract with 10% concentration is more prone to clump, requiring periodic stirring to ensure that the extract does not clump (homogeneous). This study also modified the research methods. Modifications included gambier extraction using the distillation method as the solvent evaporation procedure. This method was found to be more effective in separating the extract from the solvent. It is faster and may prevent the extract from being easily oxidized.

Since no purification of gambier extract was performed in this investigation, the proportion of active components in gambier in the form of catechins and tannins was unknown with certainty. Purification is required to acquire more catechins and tannins in gambier so that the mechanism of action of these compounds could function effectively.

This study observed that a toothpaste combining gambier extract and fluoride could inhibit the development of Candida albicans compared to gambier toothpaste or fluoride toothpaste individually. This might be an alternative to herbal-based toothpaste to decrease Candida albicans colonies. The improvement on toothpaste formulation by altering the concentration used may support the toothpaste optimally. The addition of chemicals to enhance toothpaste storage time is also required so that the toothpaste may be used for an extended period.

CONCLUSION

Toothpaste containing 10% gambier extract and fluoride was found to exhibit antifungal action against Candida albicans, making it a potential choice for maintaining oral hygiene and preventing Candida infection.

BIBLIOGRAPHY

Achmad, H., Edith, I., Irawaty, A., Riyanti, E., & Saptarini, R. (2021). Gambier Extract (Uncaria gambier Roxb .) as Herbal Treatment for the Oral Cavity : A Systematic Review. *Sys Rev Pharm*, *12*(2), 414–419.

Bintari, N. W. D., Setyapurwanti, I., Devhy, N. L. P., Widana, A. A. O., & Prihatiningsih, D. (2020). Screening Candida Albicans Penyebab Kandidiasis Oral dan Edukasi Oral Hygiene Pada Lansia Di Panti Sosial Tresna Werdha Wana Seraya Bali. *Jurnal Pengabdian Kesehatan*, *3*(1), 28–40. https://doi.org/10.31596/jpk.v3i1.65

Dewi, S. R. P., Pratiwi, A., & Teodorus. (2018). The effect of Gambier extracts (Uncaria gambir RoxB.) as antiseptic on gingival wound in rats. *ODONTO : Dental Journal*, *5*(1), 80–88.

Fitranti, A., Sutjiati, R., & Joelijanto, R. (2011). Perbedaan Potensi Pasta Gigi dan Obat Kumur yang Mengandung Fluor terhadap Jumlah Koloni Candida Albicans pada Piranti Ortodonsi Lepasan. *The Effects of Brief Mindfulness Intervention on Acute Pain Experience: An Examination of Individual Difference*, *17*, 21–28.

Glick, M. (2015). *Burket's Oral Medicine* (12th ed.). People's Medical Publishing House-USA.

Hakim, L., & Ramadhian, R. (2016). Oral Candidiasis (Kandidiasis Oral). *Majority*, *4*(November), 53–57.

Inmawaty, J., Sudjarwo, I., & Satari, M. H. (2012). Inhibitory concentrations of gambier (Uncaria gambir Roxb.) catechins extract against Streptococcus mutans. *Padjadjaran Journal of Dentistry*, *24*(3), 161–166. https://doi.org/10.24198/pjd.vol24no3.26832

Ismail, A. S., Rizal, Y., Armenia, & Kasim, A. (2021). Identification of bioactive compounds in gambier (Uncaria gambir) liquid by-product in west Sumatra, Indonesia. *Biodiversitas*, *22*(3), 1474–1480. https://doi.org/10.13057/BIODIV/D220351

Lucida, H., Rustini, Saufitri, D., & Dachriyanus. (2010). Formulation of Anti-Plaque Toothpaste From Standardized Gambir Extract and Its Antimicrobial Activity. *Jurnal Farmasi Indonesia*, *5*(2), 70–77. https://doi.org/10.35617/JFI.V5I2.40

Magdalena, N. V., & Kusnadi, J. (2015). Antibakteri Dari Ekstrak Kasar Daun Gambir (Uncaria gambir var Cubadak) Metode Microwave-Assisted Extraction Terhadap Bakteri Patogen. *Jurnal Pangan Dan Agroindustri*, *3*(1), 124–135.

Marlinda. (2018). Identifikasi kadar katekin pada gambir (Uncaria Gambier Roxb). *Jurnal Optimalisasi*, *4*(1), 47–53.

Millsop, J., & Fazel, N. (2016). Oral candidiasis. *Clinics in Dermatology*, *36*(4), 487–494. https://doi.org/10.1136/pmj.78.922.455

Nur'aeny, N., Hidayat, W., Dewi, T. S., Herawati, E., & Wahyuni, I. S. (2017). Profil oral candidiasis di bagian ilmu penyakit mulut RSHS Bandung periode 2010-2014. *Majalah Kedokteran Gigi Indonesia*, *3*(1), 23. https://doi.org/10.22146/majkedgiind.11320

Puspitasari, Ambar, Balbeid, M., & Adirhesa, A. (2018). Perbedaan Pasta Gigi Herbal dan Non-Herbal terhadap Penurunan Plaque Index Score pada Anak. *E-Prodenta Journal of Dentistry*, *1*(1), 116–123.

Puspitasari, Apriliana, Kawilarang, A. P., Ervianti, E., & Rohiman, A. (2019). Profil Pasien

Baru Kandidiasis. *Berkala Ilmu Kesehatan Kulit Dan Kelamin*, *31*(1), 24–34.

Putra, D. D. A., Astuti, P., & Rochim, A. (2015). Uji Klinis Penggunaan Pasta Gigi Herbal Terhadap Penurunan Indeks Plak Rongga Mulut. *E-Jurnal Pustaka Kesehatanurnal Pustaka Kesehatan*, *3*(2), 224–229.

Rahman, E. D., Sari, E., Burmawi, Frizka, & Endah. (2018). Determination of Extraction Process Conditions of Gambier Catechin (Uncaria Gambier Roxb) from Solok Bio Bio Lima Puluh Kota District - West Sumatera. *IOP Conference Series: Materials Science and Engineering*, *316*(1). https://doi.org/10.1088/1757-899X/316/1/012022

Sukanto. (2012). Takaran Dan Kriteria Pasta Gigi Yang Tepat Untuk Digunakan Pada Anak Usia Dini (Appropriate Amount and Criteria of Tooth Paste Used for Early-Aged Children). *Unej*, *9*(2), 104–109.

Suraini, S., Chairani, C., & Enlita, E. (2015). Uji Aktivitas Antijamur Ekstrak Gambir (UncariagambirRoxb) terhadap Candida albicans secara in Vitro. *Scientia : Jurnal Farmasi Dan Kesehatan*, *5*(2), 62. https://doi.org/10.36434/scientia.v5i2.23

Widiyarti, G., Sundowo, A., & Angelina, M. (2014). Pembuatan Sediaan Oral Nutraceutical d ari Ekstrak Gambir. *Jurnal Ilmu Kefarmasian Indonesia*, *12*(2), 145–153.