Original Article

Effects of Thai *Kaempferia Parviflora* Extract on Human Gingival Fibroblasts: An *in vitro* Study of Wound Healing

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ABSTRACT

Aim: Gingival fibroblasts are key players in oral wound healing as they migrate to the wound and produce extracellular matrix. Although contemporary methods can enhance healing, there is ongoing interest in alternative medicine due to its accessibility. *Kaempferia parviflora*, a traditional Thai herb, has been comprehensively studied for its pharmacological properties; however, its specific roles in wound healing remain to be explored. Thus, our study aimed to investigate the effects of *K. parviflora* extract (KPE) on the proliferation, migration, and collagen production of human gingival fibroblasts (HGFs). **Methods:** HGFs were treated with 0.46–7.5 mg/mL KPE, followed by determination of cell viability using 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay on days 1, 3, 5, and 7, and cell migration was assessed using scratch assay at 12, 24, and 48 h. Collagen production was analyzed by picrosirius red staining and real-time polymerase chain reaction (qRT-PCR) on days 7, 14, and 21. **Results:** At 0.46 mg/mL, KPE induced cell proliferation in HGFs on days 3, 5, and 7, whereas higher concentrations were cytotoxic to HGFs. This concentration also enhanced cell migration at all time points, whereas higher doses hampered this process. KPE at 0.46 mg/mL stimulated collagen production and upregulated the expressions of *COL3A1* and *COL1A1* genes on day 14, although these levels were decreased by day 21. **Conclusions:** KPE could promote proliferation, migration, and collagen production in HGFs, demonstrating its potential use as an adjunctive treatment for oral wounds. Nevertheless, establishing a safety margin is crucial before clinical application due to the possibility of cytotoxicity at higher concentrations.

Keywords: *Cell migration, Cell proliferation, Collagen, Human gingival fibroblast, Kaempferia parviflora*

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Introduction

Delayed wound healing has become a major global concern due to the increasing number of affected individuals and associated treatment costs.[1] Oral wounds located in the periodontal tissue, palate, and tongue can greatly impact abilities to chew, swallow, and speak, eventually leading to a lower quality of life.[2] In addition, chronic periodontal wounds have also been shown to be associated with cardiovascular diseases through increased bacteria and inflammatory processes.[3,4] Furthermore, various factors such as aging, smoking, alcohol consumption, as well as systemic diseases inevitably hinder the

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wound healing process.[2,5] Therefore, promoting oral wound healing is of great importance to alleviate this societal burden.

Wound healing is an intricate process associated with the repair of injured tissue in the skin and other soft tissues. The process comprises four overlapping stages: hemostasis, inflammation, proliferation, and remodeling.[6] In the oral mucosa, gingival fibroblasts serve a vital role in the proliferative and remodeling phases of wound healing.[7] During the proliferative phase, these fibroblasts migrate to the wound area, undergo proliferation, and secrete collagen type III as a provisional matrix. During the remodeling phase, they replace collagen type III with type I, which is more mature and compacted.[7] Thus, enhancing the activities of gingival fibroblasts could potentially be one of the approaches to improve wound healing.

Although various modern approaches have been demonstrated to accelerate the healing process by promoting the functions of the key players or providing the framework and essential components in each phase,[8,9] many of these approaches are difficult to access or raise ethical concerns. Hence, several studies have still focused on use of medicinal plants due to their accessibility and historical use in folk medicine. A diverse array of medicinal plants has been employed in wound healing management,[10] although their bioactive compounds require intensive investigations.

Kaempferia parviflora, also known as Krachaidam, is a native Thai herb belonging to Zingiberaceae, commonly found in tropical countries such as Thailand and Malaysia.[11] The extract from *K. parviflora* has traditionally been used to treat asthma, rheumatoid arthritis, skin diseases, as well as wounds for decades.[12] Recent studies have unveiled the pharmacological properties of *K. parviflora*, which include anticancer, anti-allergy, and anti-inflammatory effects.[12] The major bioactive compound, polymethoxyflavones, which includes 5,7-dimethoxyflavone (DMF), 5,7,4′-trimethoxyflavone (TMF), and 3,5,7,3′,4′-pentamethoxyflavone (PMF), has been shown to have several protective effects, such as mitigating oxidative stress, decreasing cytokine production, and promoting collagen production. These effects have been demonstrated in both *in vivo* and *in vitro* skin models, particularly in dermal fibroblasts.[13-15]

The rationale for our study centers on promoting wound healing in the oral cavity by using *K. parviflora*, a traditional Thai plant, to improve the quality of life for patients with chronic oral wounds, as well as to reduce treatment costs. Due to its potential to protect skin from several conditions,[13-15] we hypothesized that *K. parviflora* could also facilitate wound healing in the oral mucosa, which shares a similar structure to that of the skin. Therefore, our study aimed to investigate the effects of *K. parviflora* rhizome extract (KPE) on an *in vitro* model of wound healing, focusing on the proliferation, migration, and collagen production of human gingival fibroblasts (HGFs).

Materials and Methods

Preparation of the *k. parviflora* rhizome extract

K. parviflora rhizomes were purchased from Phitsanulok province, Thailand. The rhizomes were dried, followed by submerging in 95% ethanol for 3 days at room temperature. The extracted solution was filtered, concentrated, and lyophilized to achieve a crude extract with a 6.39% yield. A stock solution (1 g/mL) of the extract was prepared in 50% DMSO (Sigma-Aldrich, St. Louis, MO, USA) and stored at 4 °C until further use. The concentration of DMSO used to dilute KPE was below 0.4%, which has been shown to have no effect on the proliferation of dermal fibroblasts.[16]

Cell culture

Human gingival fibroblasts (HGFs, 2620, ScienCell Research Laboratories, Carlsbad, CA, USA) were maintained in a culture medium containing Dulbecco's modified Eagle medium (DMEM)-high glucose (Gibco, Thermo Fisher Scientific, Carlsbad, CA, USA) supplemented with 10% fetal bovine serum (FBS, Gibco) and 1% antibiotic–antimycotic solution (Gibco) in a 5% CO_2 at 37°C. HGFs between the 5th and 9th passages were used in the following experiments.

Cell viability assay

HGFs were seeded in 96-well plates (Corning, Inc., Corning, NY, USA) at a density of 2×10^3 cells/well. After incubating for 24 h, cells were treated with various concentrations of KPE (0.46, 0.94, 1.87, 3.75, and 7.5 mg/mL). On days 1, 3, 5, and 7, cells were washed and incubated with 1 mg/mL 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT; Sigma-Aldrich) solution for 2 h. The formazan crystals were then dissolved in dimethyl sulfoxide (DMSO; Sigma-Aldrich) for 30 min. Absorbance at 570 nm was measured using an Epoch microplate spectrophotometer (Biotek®, Shoreline, WA, USA). The concentration that reduced the cell viability by more than 30% compared to the control was considered toxic, as defined by ISO 10993-5.[17]

Wound healing (scratch) assay

HGFs were seeded in 24-well plates (Corning, Inc.) until they reached 100% confluence. The cells in monolayer were scratched using an 80-µm-diameter

Table 1: Primer sequences used in qRT-PCR

Gene		Sequence	Primer size (bp)	GenBank number
COL1A1	(F)	5′-AACATGGAGACTGGTGAGACCT-3′	145	NM_000088.4
	(R)	5′-CGCCATACTCGAACTGGAATC-3′		
COL3A1	(F)	5′-AATGCCTGGAGAAAGAGGAGGT-3′	124	NM_000090.4
	(R)	5′-AATAGGACCAGTAGGACCCCTTG-3′		
GAPDH	(F)	5′-GGAGCGAGATCCCTCCAAAAT-3′	197	NM_001357943.2
	(R)	5′-GGCTGTTGTCATACTTCTCATGG-3′		

pipette tip, followed by washing to remove the detached cells. Subsequently, HGFs were treated with various concentrations of KPE. Cell migration was observed at 12, 24, and 48 h after incubation. Cells were fixed with methanol for 2 min prior to staining with 10% Giemsa solution. Four photographs per well were taken for analysis by using an inverted microscope (CKX53, Olympus, Tokyo, Japan). The number of cells migrating into the scratched area was counted using ImageJ software (NIH, Bethesda, MD, USA). The average number of cells observed to migrate per picture was used to calculate the percentage of cell migration as follows:

$$\text{The percentage of cell migration} = \frac{\text{Average cell migration per picture (sample)}}{\text{Average cell migration per picture (control)}} \times 100.$$

Analysis of collagen production

HGFs were seeded in 24-well plates (Corning, Inc.) at a density of 5×10^3 cells/well. After incubating for 24 h, cells were treated with 0.46 mg/mL of KPE. Collagen production was observed on days 7, 14, and 21. Cells were fixed with 100% methanol for 10 min prior to staining with picrosirius red solution (Bio-Optica, Milano, Italy) according to the manufacturer's instructions. The photographs were taken by using an inverted microscope. To quantify the amount of collagen relatively, the samples were destained with 0.1 M NaOH solution for 5 min. Absorbance at 540 nm was measured by using a microplate spectrophotometer.

Real-time quantitative reverse transcriptase polymerase chain reaction

HGFs were seeded in six-well plates (Costar®, Corning, Inc.) at a density of 1×10^4 cells/well. After incubating for 24 h, cells were treated with 0.46 µg/mL of KPE. The expressions of type I and type III collagen genes (*COL1A1* and *COL3A1*, respectively) were observed on days 7, 14, and 21. Total RNA was extracted using TRIzol reagent (Ambion, USA). In each sample, 1 µg of total RNA was converted into complementary DNA (cDNA) using the iScript™ Reverse Transcription Supermix (Bio-Rad, Hercules, CA, USA). RT-PCR was performed using SYBR Green Supermix (Bio-Rad). The primers for *COL1A1*, *COL3A1*, and *GAPDH* (internal control) are listed in Table 1.

Statistical analysis

Statistical significance was evaluated using GraphPad Prism 10.2.3 for macOS (GraphPad Software, La Jolla, CA, USA). Two-way analysis of variance (ANOVA) followed by Tukey–Kramer's test was performed for intergroup comparison of three or more groups. Multiple unpaired *t* tests with Bonferroni correction were performed to compare two groups. The significance was taken when the *P* value was less than 0.05.

Results

Proliferation of HGFs

To investigate whether KPE could promote cell proliferation, HGFs were exposed to KPE at different concentrations for 1, 3, 5, and 7 days, and the cell viability was determined using the MTT assay. As shown in Figure 1, none of the KPE concentrations significantly affected the cell viability on day 1. On days 3, 5, and 7, KPE at 0.46 mg/mL significantly increased cell viability to 111.61 ± 2.66%, 113.54 ± 4.20%, and 111.76 ± 7.41% respectively, compared to the control. In contrast, higher concentrations of KPE decreased cell viability in a dose- and time-dependent manner. By days 5 and 7, concentrations greater than 0.93 mg/mL decreased cell viability to below 70% and were thereby considered toxic concentrations according to ISO 10993.

Migration of HGFS

To investigate the effect of KPE on cell migration, HGFs at confluence were scratched, and the number of cells migrating into the gap was counted at 12, 24, and 48 h after exposure to different concentrations of KPE. As demonstrated in Figure 2, KPE at 0.46 mg/mL significantly increased the number of migrating cells to 115.01 ± 10.51%, 114.71 ± 6.52%, and 125.66 ± 7.94% at 12, 24, and 48 h, respectively,

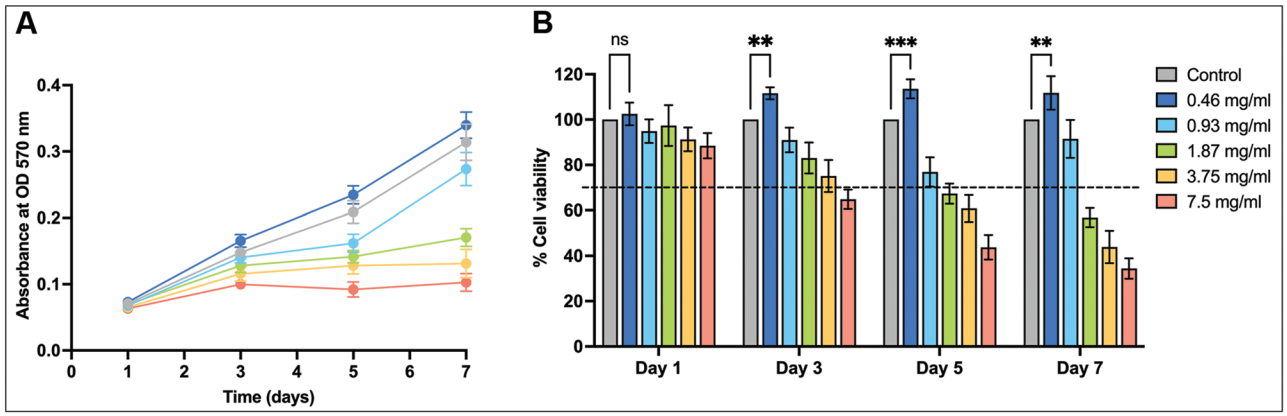

Figure 1: Effect of KPE on the cell viability of human gingival fibroblasts (HGFs). (A) Absorbance at 570 nm showing the proliferation profile of HGFs treated with different concentrations of KPE on days 1, 3, 5, and 7. (B) Percentage of cell viability calculated from the absorbance. HGFs in the culture medium were assigned as the control group. Data represent means with standard deviation (S.D.) of three independent experiments. Significant differences are shown with ** ($P < 0.01$) and *** ($P < 0.001$). The cytotoxicity potential margin (70% cell viability) is shown with a dashed line.

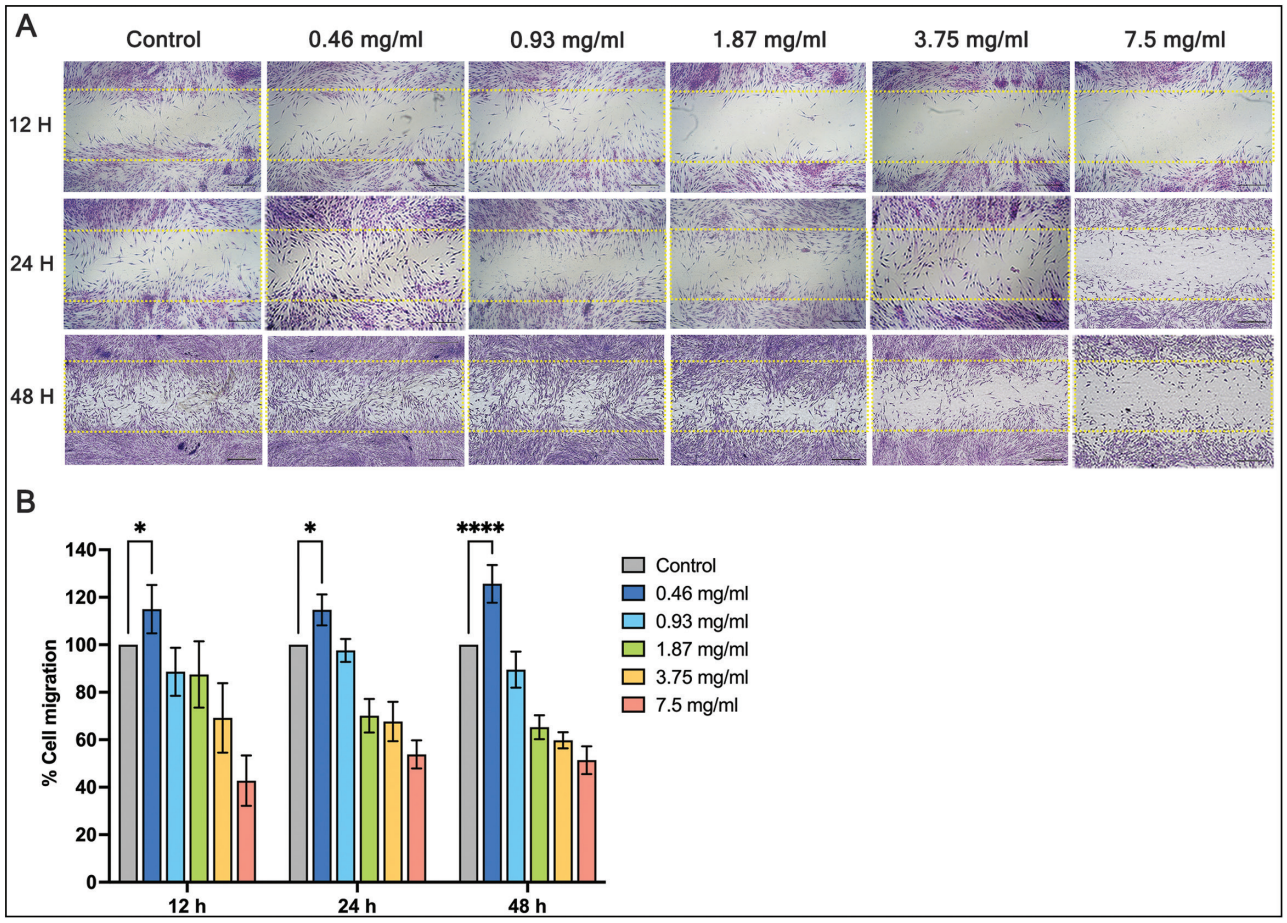

Figure 2: Effect of KPE on the migration of HGFs. (A) Representative images at 40× magnification of HGFs treated with different concentrations of KPE at 12, 24, and 48 h. Scale bar = 500 µm. (B) Percentage of cells migrating into the gap. Data represent means with S.D. of three independent experiments. Significant differences are shown with * ($P < 0.05$) and **** ($P < 0.0001$).

compared to the control. In contrast, concentrations greater than 0.93 mg/mL inhibited cell migration in a dose- and time-dependent manner. Due to its ability to promote the proliferation and migration of HGFs, KPE at 0.46 mg/mL was selected for the subsequent experiments.

Collagen production

To investigate the effect of KPE on collagen production, cells were exposed to 0.46 mg/mL KPE and stained with picrosirius red on days 7, 14, and 21. As shown in Figure 3A, cells treated with 0.46 mg/mL KPE exhibited an increase in both the area and intensity of picrosirius red staining on days 14 and 21 compared to the control. The relative amount of collagen produced was demonstrated by measuring the absorbance at 540 nm [Figure 3B] and calculated as a percentage [Figure 3C]. Both the control and KPE-treated groups displayed an increase in collagen over time. However, the KPE-treated group showed a significantly higher amount of collagen on day 14 (114.27 ± 6.01%), and this increase slightly diminished on day 21 (105.08 ± 5.70%) to a level that was not different from that of the control.

The types of collagen fibers were further investigated at the transcriptional level by qRT-PCR. On day 7, the expression of the *COL3A1* gene, encoding collagen type III, and *COL1A1* gene, encoding collagen type I, was shown to increase, albeit with no statistical difference between the control and the KPE-treated groups [Figure 4]. On day 14, the expression of the *COL3A1* gene was significantly higher in the KPE-treated group (11.29 ± 1.20) compared to the control (3.72 ± 0.72). However, this gene expression was downregulated by day 21. The expression of the *COL1A1* gene also significantly increased on day 14 (3.96 ± 0.39) compared to the control (1.91 ± 0.53), and decreased by day 21. Overall, the expression of the *COL3A1* gene was higher than that of the *COL1A1* gene.

Discussion

Our results indicate that 0.46 mg/mL KPE increased the proliferation and migration of HGFs, whereas higher concentrations reduced cell viability and migration. Additionally, KPE at this concentration was shown to enhance collagen production during the early phase of wound healing, while decreasing collagen levels during the remodeling phase.

The ability of 0.46 mg/mL KPE to promote the proliferation and migration of HGFs would be beneficial for the proliferative phase of wound healing, where gingival fibroblasts migrate to the affected area and proliferate.[7] Consistent with this findings, KPE at 0.46 mg/mL was shown to promote proliferation of human normal oral keratinocytes (NOK).[18] In

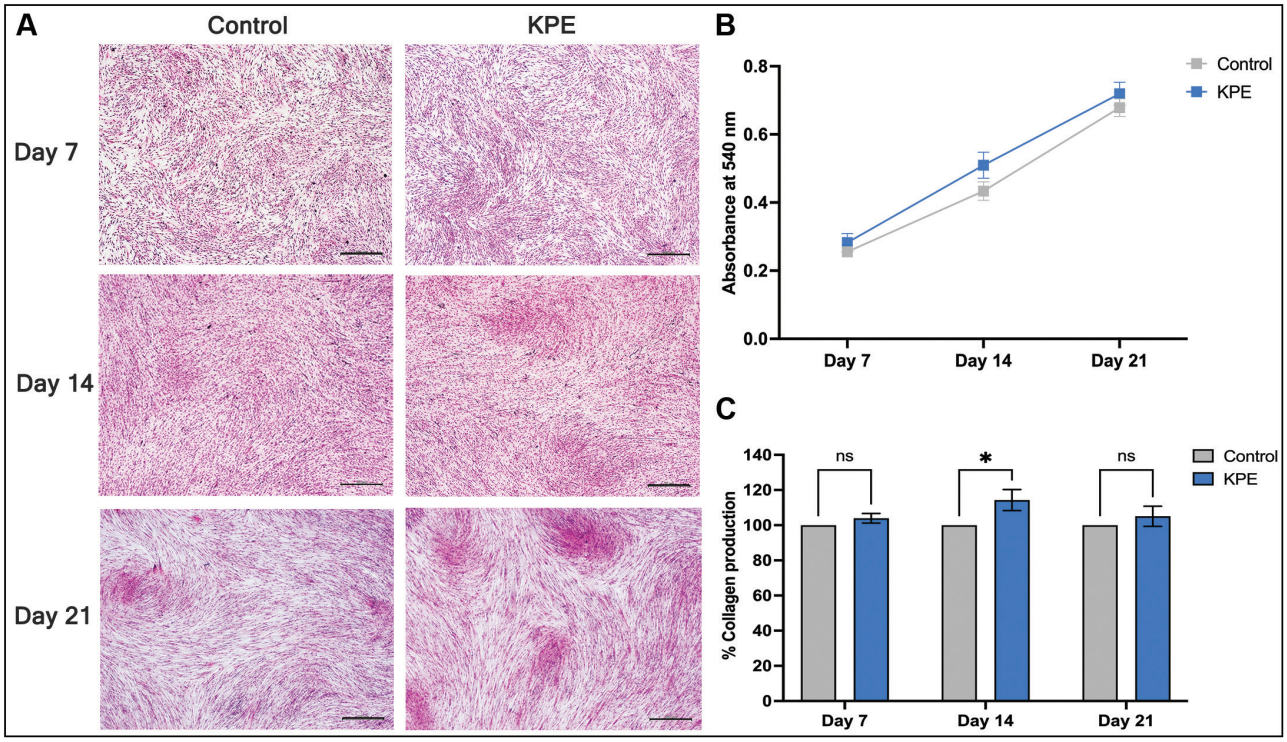

Figure 3: Collagen production of HGFs treated with 0.46 mg/mL KPE. (A) Representative images at 40× magnification of HGFs stained with picrosirius red on days 7, 14, and 21. Scale bar = 500 µm. (B) Absorbance at 540 nm measured after dissolving picrosirius red stain. The absorbance indicates the relative amount of collagen produced at each time point. (C) Percentage of collagen production calculated from the absorbance. Data represent means with S.D. of three independent experiments. A significant difference is shown with * ($P < 0.05$).

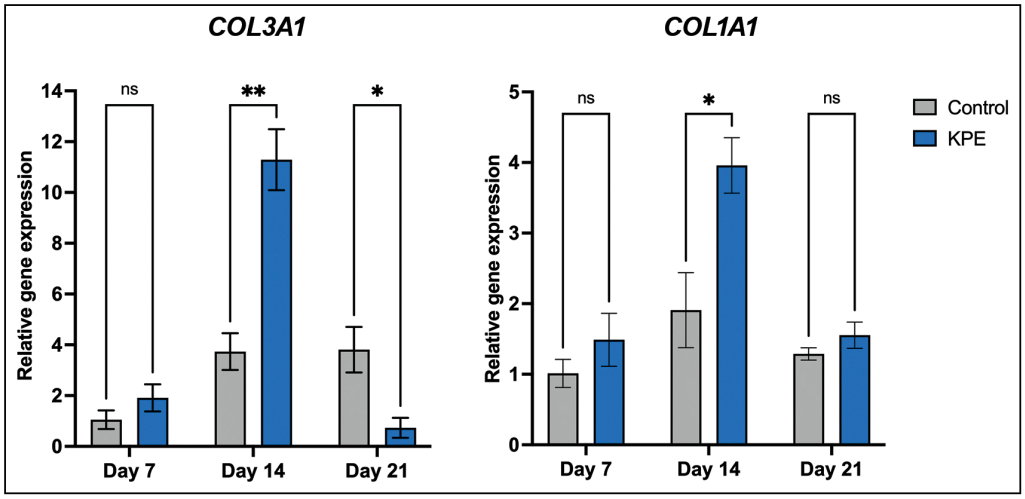

Figure 4: Relative expressions of *COL3A1* and *COL1A1* genes in HGFs treated with 0.46 mg/mL KPE. The *COL3A1* and *COL1A1* mRNA levels were normalized to *GAPDH* mRNA. Data represent means with S.D. of three independent experiments. Significant differences are shown with * ($P < 0.05$) and ** ($P < 0.01$).

addition, polymethoxyflavones, the main ingredients in KPE, were shown to increase the thickness of the epidermis in aged skin explants, probably resulting from an increase in the number of epidermal cells.[15] Currently, there are no studies investigating the effects of KPE or its bioactive ingredients on oral wound healing. The mechanisms through which KPE stimulates cell proliferation and migration require further investigation.

On the contrary, our findings also reveal the cytotoxic effects of KPE on HGFs when applied at higher concentrations, corresponding to the previous study in NOK.[18] The anti-proliferative property of KPE has been highlighted as a potential chemotherapy in numerous studies.[19-21] Although the authors applied KPE at concentrations in the µg/mL range, which were lower than those used in our study, the extract was reported to induce apoptosis in leukemia[19] and cholangiocarcinoma[20] cell lines. In a cervical cancer cell line, KPE was found to suppress cell proliferation and migration toward scratched areas and chemoattractants.[21]

Chemotherapeutic agents typically target rapidly dividing cells, such as cancer cell lines, more than non-cancerous cells, which have slower rates of division.[22] Prolonged treatment or higher doses of chemotherapy can also inevitably damage normal cells.[22,23] It is possible that cancer cell lines are more vulnerable to the toxicity of KPE than primary cells and that KPE may exert varying effects at different concentrations. In our case, KPE at 0.46 mg/mL stimulated the proliferation and migration of HGFs, while these effects were reversed at higher concentrations. Therefore, the application of KPE appears to be a double-edged sword, where its effects depend on its concentration and the condition of the cells to which KPE is applied.

Collagen production and remodeling are another critical process in soft tissue wound healing, continuing from the proliferative phase to provide strength to the newly repaired tissue.[7] In the KPE-treated group, our results show a significant increase in collagen production on day 14, which later declined by day 21. This aligns with the expression of the collagen genes. The gene expressions also confirm the result of picrosirius red staining, suggesting that the increase in the stained areas was not caused by cell proliferation. Consistently, KPE and polymethoxyflavones were also shown to promote collagen type I synthesis in the skin of mice exposed to UVB,[14] as well as aged skin explants and dermal fibroblasts.[15]

In normal wound healing, collagen type III is produced as a provisional matrix during the proliferative phase. Due to its lower stability and smaller size, collagen type III is later replaced by type I during the remodeling phase.[7,24] However, while the study of KPE on the production of collagen type III requires more clarification, our study revealed a gradual increase in production of collagen type III along with type I during the proliferative phase as a result of KPE treatment. The high abundance of collagen type III was previously observed until day 20 in the healing of the tympanic membrane.[25] The authors reasoned that the absence of granulation tissue in the tympanic membrane and different behaviors of the fibroblasts in the membrane could lead to a variation in the healing process. In a related experimental setting to ours, HGFs treated

with the culture medium collected from periodontal ligament stem cells displayed elevated mRNA levels of collagen type III and I on day 7 of culture.[26] This result could be used to exclude the possibility that the increase in collagen type III mRNA on day 14 was because of the absence of a preceding inflammatory response. It is likely that KPE may employ different mechanisms from other substances in inducing collagen production.

Although our findings indicate a higher expression of *COL3A1* than *COL1A1* in the KPE-treated group, the mRNA levels of both genes, particularly *COL3A1,* were eventually decreased by day 21. This reduction in collagen production is crucial for the remodeling phase of wound healing to prevent unfavorable keloid formation.[7] However, this phase also involves collagen degradation by the matrix metalloproteinases and rearrangement of collagen fibers by adhesion proteins in fibroblasts.[7] Further research is needed to determine whether KPE plays a role in other aspects of this phase.

The limitation of our study is that we used the crude extract of the *K. parviflora* rhizome. The effects of KPE displayed in the results are probably caused by the combination of myriad substances in the extract, raising significant challenges for its application in patients due to safety concerns.[27] Our study can be further replicated by applying purified compounds in KPE, such as polymethoxyflavones, to exclude synergistic and antagonistic interactions from other substances. Additionally, due to limited research on the effects of KPE on oral cells, more studies can be performed to explore the underlying mechanisms of KPE on oral wound healing.

Regarding its clinical implications, a recent clinical trial has demonstrated that topical KPE exhibits minimal effects on skin irritation and sensitization, highlighting its promise as an anti-aging product.[28] In the oral cavity, KPE could potentially be applied as an adjunctive treatment alongside conventional oral wound dressings, possibly formulated as a topical gel loaded in a custom-made soft tissue guard. This technique, when used with hyaluronic acid gel, was shown to enhance pain reduction following gingivectomy when combined with photobiomodulation.[29] However, further studies are necessary to examine the effects of KPE when applied in conjunction with modern approaches, and extensive research on animal models should be conducted to establish the safety margin of KPE prior to clinical use.

Conclusion

Collectively, our findings reveal that KPE at a low concentration could increase the proliferation and migration of HGFs. In addition, KPE could not only enhance collagen production in the proliferative phase but also decrease the production when the healing process progresses, thereby reducing the likelihood of hypertrophic scar formation. Thus, KPE can be a promising candidate for adjunctive treatment to promote oral wound healing. However, due to its inherent toxicity, KPE should be used with caution when applied at high concentrations.

Patient declaration of consent

Not applicable.

Acknowledgment

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Authors contributions

Not applicable.

Data availability statement

Available on request from Supaporn Mala, e-mail: Supaporn.mal@mahidol.ac.th.

Ethical policy and institutional review board statement

This study received approval as non-human subject research by the Faculty of Dentistry/Faculty of Pharmacy, Mahidol University, Institutional Review Board (MU-DT/PY-IRB 2023/DT053). Therefore, no consent to participate was required.

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Conflicts of interest

All authors declare no conflict of interest.

Abbreviations

KPE	*Kaempferia parviflora* extract
HGFs	Human gingival fibroblasts
MTT	3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide
qRT-PCR	Real-time polymerase chain reaction
DMEM	Dulbecco's modified Eagle medium
DMSO	Dimethyl sulfoxide
FBS	Fetal bovine serum

References

1. Sen CK. Human Wound and its burden: Updated 2020 compendium of estimates. Adv Wound Care (New Rochelle) 2021;10:281-92.
2. Politis C, Schoenaers J, Jacobs R, Agbaje JO. Wound healing problems in the mouth. Front Physiol 2016;7:507.

3. Sanz M, Marco del Castillo A, Jepsen S, Gonzalez-Juanatey JR, D'Aiuto F, Bouchard P, *et al*. Periodontitis and cardiovascular diseases: Consensus report. J Clin Periodontol 2020;47:268-88.
4. Polizzi A, Nibali L, Tartaglia GM, Isola G. Impact of nonsurgical periodontal treatment on arterial stiffness outcomes related to endothelial dysfunction: A systematic review and meta-analysis. J Periodontol 2024;1:16.
5. Ngeow WC, Tan CC, Goh YC, Deliberador TM, Cheah CW. A narrative review on means to promote oxygenation and angiogenesis in oral wound healing. Bioengineering (Basel) 2022;9:636.
6. Guo S, Dipietro LA. Factors affecting wound healing. J Dent Res 2010;89:219-29.
7. Smith PC, Martínez C, Martínez J, McCulloch CA. Role of fibroblast populations in periodontal wound healing and tissue remodeling. Front Physiol 2019;10:270.
8. Tatarusanu SM, Lupascu FG, Profire BS, Szilagyi A, Gardikiotis I, Iacob AT, *et al*. Modern approaches in wounds management. Polymers (Basel) 2023;15:3648.
9. Nourian Dehkordi A, Mirahmadi Babaheydari F, Chehelgerdi M, Raeisi Dehkordi S. Skin tissue engineering: Wound healing based on stem-cell-based therapeutic strategies. Stem Cell Res Ther 2019;10:111.
10. Shedoeva A, Leavesley D, Upton Z, Fan C. Wound healing and the use of medicinal plants. Evid Based Complement Alternat Med 2019;2019:2684108.
11. Saokaew S, Wilairat P, Raktanyakan P, Dilokthornsakul P, Dhippayom T, Kongkaew C, *et al*. Clinical effects of krachaidum (*Kaempferia parviflora*): A systematic review. J Evid Based Complement Altern Med 2017;22:413-28.
12. Singh A, Singh N, Singh S, Srivastava RP, Singh L, Verma PC, *et al*. The industrially important genus kaempferia: An ethnopharmacological review. Front Pharmacol 2023;14:1099523.
13. Phung HM, Lee S, Hong S, Lee S, Jung K, Kang KS. Protective effect of polymethoxyflavones isolated from *Kaempferia parviflora* against TNF-α-induced human dermal fibroblast damage. Antioxidants (Basel) 2021;10:1609.
14. Park JE, Pyun HB, Woo SW, Jeong JH, Hwang JK. The protective effect of *Kaempferia parviflora* extract on UVB-induced skin photoaging in hairless mice. Photodermatol Photoimmunol Photomed 2014;30:237-45.
15. Klinngam W, Rungkamoltip P, Thongin S, Joothamongkhon J, Khumkhrong P, Khongkow M, *et al*. Polymethoxyflavones from *Kaempferia parviflora* ameliorate skin aging in primary human dermal fibroblasts and *ex vivo* human skin. Biomed Pharmacother 2022;145:112461.
16. Moskot M, Jakóbkiewicz-Banecka J, Kloska A, Piotrowska E, Narajczyk M, Gabig-Cimińska M. The role of dimethyl sulfoxide (DMSO) in gene expression modulation and glycosaminoglycan metabolism in lysosomal storage disorders on an example of mucopolysaccharidosis. Int J Mol Sci 2019;20:304.
17. Biological evaluation of medical devices-Part 5: tests for in vitro cytotoxicity. ISO 10993-5; 2009. Available from: https://www.iso.org/obp/ui#iso:std:iso:10993:-5:en.
18. Thairat S, Srichan R, Mala S. Cytotoxic effect of *Kaempferia parviflora* extract on normal oral keratinocytes and a human squamous carcinoma cell line. M Dent J 2022;42:33-8.
19. Banjerdpongchai R, Suwannachot K, Rattanapanone V, Sripanidkulchai B. Ethanolic rhizome extract from *Kaempferia parviflora* wall. ex. Baker induces apoptosis in HL-60 cells. Asian Pac J Cancer Prev 2008;9:595-600.
20. Leardkamolkarn V, Tiamyuyen S, Sripanidkulchai BO. Pharmacological activity of *Kaempferia parviflora* extract against human bile duct cancer cell lines. Asian Pac J Cancer Prev 2009;10:695-8.
21. Potikanond S, Sookkhee S, Na Takuathung M, Mungkornasawakul P, Wikan N, Smith DR, *et al*. *Kaempferia parviflora* extract exhibits anti-cancer activity against hela cervical cancer Cells. Front Pharmacol 2017;8:630.
22. Bagnyukova TV, Serebriiskii IG, Zhou Y, Hopper-Borge EA, Golemis EA, Astsaturov I, *et al*. Chemotherapy and signaling: How can targeted therapies supercharge cytotoxic agents? Cancer Biol Ther 2010;10:839-53.
23. Tamaki T, Naomoto Y, Kimura S, Kawashima R, Shirakawa Y, Shigemitsu K, *et al*. Apoptosis in normal tissues induced by anti-cancer drugs. J Int Med Res 2003;31:6-16.
24. Singh D, Rai V, Agrawal DK. Regulation of collagen i and collagen III in tissue injury and regeneration. Cardiol Cardiovasc Med 2023;7:5-16.
25. Makuszewska M, Bonda T, Cieślińska M, Bialuk I, Winnicka MM, Niemczyk K. Expression of collagen type III in healing tympanic membrane. Int J Pediatr Otorhinolaryngol 2020;136:110196.
26. Banlue A, Kaewmuangmoon J, Janebodin K, Tansriratanawong K. Induction of migration and collagen synthesis in human gingival fibroblasts using periodontal ligament stem cell conditioned medium. Eur J Dent 2024;18:219-27.
27. Heinrich M, Jalil B, Abdel-Tawab M, Echeverria J, Kulić Z, McGaw LJ, *et al*. Best practice in the chemical characterisation of extracts used in pharmacological and toxicological research-the ConPhyMP-guidelines. Front Pharmacol 2022;13:953205.
28. Klinngam W, Rungkamoltip P, Wongwanakul R, Joothamongkhon J, Du-a-man S, Khongkow M, *et al*. Skin rejuvenation efficacy and safety evaluation of *Kaempferia parviflora* standardized extract (BG100) in human 3D skin models and clinical trial. Biomolecules 2024;14:776.
29. Yakout BK, Kamel FR, Khadr MAE-AA, Heikal LAH, El-Kimary GI. Efficacy of hyaluronic acid gel and photobiomodulation therapy on wound healing after surgical gingivectomy: A randomized controlled clinical trial. BMC Oral Health 2023;23:805.