ORIGINAL ARTICLE Open Access

Evaluating the effect of Tualang honey on the viability and migration of human gingival fibroblasts

Nor Azira Zahadi[1], Zurairah Berahim[2]*, Siti Lailatul Akmar Zainuddin[3]

[1] *Periodontic Specialist Unit, Klinik Pergigian Jalan Sultan Mahmud, 20300, Kuala Terengganu, Terengganu, Ministry of Health Malaysia.*
[2] *School of Dental Sciences, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan.*
[3] *Faculty of Dentistry, Manipal University College Malaysia. Lot 463-1, Jalan Batu Hampar Bukit Baru, 75150 Melaka.*

Abstract

Tualang honey, produced by the wild bee species *Apis dorsata*, is predominantly found in the South Asian region, particularly in Malaysia. Tualang honey has attracted scientific interest for its antimicrobial, anti-inflammatory, and wound-healing properties, highlighting its potential for therapeutic use. The study aimed to assess the effects of Tualang honey on the viability and migration of human gingival fibroblasts (HGFs) using MTT and scratch assays. HGFs were cultured in standard fibroblast medium at 37°C in a 5% CO_2 humidified incubator. Cells were seeded at 5×10^3 cells/well in a 96-well plate and incubated for 24 hours before being treated with varying concentrations of Tualang honey, with the negative control receiving only growth medium. After 24 hours, cell viability was assessed using the MTT assay and absorbance was measured at 570 nm. For the scratch migration assay, cells were seeded at 10×10^3 cells/well in a 24-well plate and incubated for 24 hours. A scratch was made on the cell layer, followed by treatment with Tualang honey at various concentrations, a negative control (untreated cells), and a positive control (0.1% Gengigel mouthwash). Images were captured at 0-, 24-, and 48-hours using Image-Pro Express software. This study demonstrated that Tualang honey at concentrations of 2.5% and below promoted high cell viability (above 88%), while concentrations ≤0.3% significantly enhanced cell migration. These findings indicate that Tualang honey, when applied at appropriate concentrations, is non-cytotoxic and promotes cell proliferation and possesses strong potential for periodontal tissue healing applications. Therefore, it shows potential as a natural agent for enhancing periodontal wound healing.

Keywords: *human gingival fibroblast, Tualang honey, viability and migration, wound healing*

Received:
29 June 2025
Revised:
26 September 2025
Accepted:
29 September 2025
Published Online:
28 February 2026
How to cite this article:
Zahadi, N.A., Berahim, Z., & Zainuddin, S.L.A. (2026). Evaluating the effect of Tualang honey on the viability and migration of human gingival fibroblasts. *IIUM Journal of Orofacial and Health Sciences*, *7*(1), 28–39. https://doi.org/10.31436/ijohs.v7i1.425
Article DOI:
https://doi.org/10.31436/ijohs.v7i1.425
***Corresponding author**
Address:
School of Dental Sciences, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia.

Telephone: +6097675828

Email address:
zurairah@usm.my

Introduction

Honey has long been recognized for its medicinal value and is increasingly studied for its therapeutic potential. Beyond its role as a natural sweetener, honey possesses a range of bioactive compounds, including enzymes, flavonoids, and phenolics, which contribute to its antioxidant, anti-inflammatory, and antimicrobial properties (Abu Bakar *et al.,* 2017). Traditionally, it has been used to manage digestive, hepatic, respiratory and cardiovascular conditions (Ezz El-Arab *et al*., 2006) and is known to enhance immune function and support wound healing (Medhi *et al*., 2008; Molan, 2001; Tonks *et al*., 2003). Recent studies also

highlight its potential anticancer effects, suggesting a promising role in disease prevention and adjunctive therapy (Bansal *et al*., 2005; de Luna *et al*., 2023).

In Malaysia, Tualang honey (TH) stands out among local varieties such as Kelulut and Acacia for its notable antimicrobial and wound-healing properties. Tualang honey, produced by *Apis dorsata* bees from the giant Tualang tree (*Koompassia excelsa*) in the Malaysian rainforest, is a polyfloral honey with a rich composition of phenolic compounds, flavonoids, and other bioactive constituents. It has been shown to possess strong antioxidant, anti-inflammatory, and antimicrobial properties, which contribute to its therapeutic potential (Azman *et al*., 2024). Studies have shown that Tualang honey effectively inhibits wound-infecting bacteria through both bactericidal and bacteriostatic actions (Aspar *et al.,* 2020; Tan *et al.,* 2009). In addition to its antimicrobial properties, TH has been shown to enhance cellular activities essential for wound repair. For instance, Yaacob *et al.* (2012) reported that TH protected keratinocytes from UVB-induced DNA damage and inflammation by reducing oxidative stress markers and suppressing pro-inflammatory cytokines. Additionally, Syazana *et al.* (2011) found that methanolic extracts of TH modulated fibroblast proliferation, particularly in keloid fibroblasts, suggesting its potential to promote balanced tissue regeneration and minimize scarring. These findings support the therapeutic application of TH in wound management, complementing evidence from other medicinal honeys like Manuka, Acacia, and Buckwheat that promote keratinocyte and fibroblast activity (Ranzato *et al.*, 2012; Ranzato *et al.*, 2013).

Cell migration is a crucial step in the wound healing process, where cells such as keratinocytes, fibroblasts, and endothelial cells move toward the wound site to restore tissue integrity. In the in vitro wound healing models, such as the scratch assay, this migration is observed as cells fill the artificially created gap over time. The efficiency of cell migration reflects the wound's ability to heal, and it is influenced by various factors including cytokines, growth factors, and bioactive compounds. Enhancing cell migration is often a key target in developing treatments to accelerate wound closure and tissue repair (Hofmann *et al*., 2023). Human gingival fibroblasts (HGFs), which are abundantly found in the connective tissue of the periodontium, play a crucial role in producing and maintaining the connective tissue matrix (Naruishi, 2022). Previous studies have shown that HGFs play a key role in repairing periodontal tissue, especially during the later stages of inflammation and wound healing. Their ability to migrate is essential for tissue repair, as they move toward the wound site to perform their functions in response to specific signals in the environment (te Boekhorst *et al.,* 2016). Honey application may help enhance HGF migration and support their wound healing ability.

Periodontal tissue healing remains a clinical challenge, with current treatment options often limited by cost or effectiveness. Tualang honey, a natural product with known bioactive properties, may serve as a safe and affordable alternative. This study aims to evaluate the wound-healing potential of honey by assessing its effects on cell viability, proliferation, and wound closure in a scratch assay model relevant to periodontal tissue healing.

Materials and Methods

Study design

This in vitro experimental study investigated the effects of varying concentrations of Tualang honey on human gingival fibroblasts, using MTT and scratch assays to evaluate cytotoxicity, cell migration, and wound closure. The tests were carried out at the School of Dental Sciences, Universiti Sains Malaysia, Malaysia.

Materials

Human gingival fibroblasts (HGF) cells were purchased from American Type Culture Collection (ATCC) Rockville, MA, U.S.A. Tualang honey was purchased from Federal

Agriculture Marketing Authority (FAMA), Malaysia. Fetal bovine serum (FBS), minimum essential medium - α modification, penicillin-streptomycin, phosphate buffered saline, trypan blue, trypLE express and trypsin-EDTA (0.25%) were purchased from Gibco, (USA). GenGiGel® mouthwash was purchased from OralDent U.K. Dimethyl sulfoxide (DMSO) was purchased from Merck, Germany.

Method

Cytoxicity test using MTT assay

Human gingival fibroblasts (HGFs) were thawed and subcultured in fibroblast growth medium until they reached approximately 90% confluence. The cells were then trypsinized and seeded into a 96-well plate at a density of 5,000 cells per well (Yu *et al.,* 2015). Subsequently, the cells were incubated with Tualang honey at predetermined concentrations ranging from 10% to 0.16% (Ranzato *et al*., 2013; Yun, 2021), at 37°C in a 5% CO_2 for 24 hours. After incubation, 10 µL of MTT solution (5 mg/mL in phosphate-buffered saline) was added to each well, followed by a 4-hour incubation period. The medium containing excess MTT was then removed, and 100 µL of dimethyl sulfoxide (DMSO) was added to each well to dissolve the dark blue formazan crystals formed by viable cells. The plate was shaken at 300 rpm for 15 minutes to ensure complete dissolution of the crystals. Absorbance was measured using a spectral scanning multimode reader (Thermo Scientific Varioskan® Flash, Finland) at a wavelength of 570 nm. The experiment was conducted in triplicate, and three independent experiments were performed.

The average of the triplicates from the control and treatment wells was calculated and applied in the following formula to determine cell viability.

Cell Viability (%) =
(Average absorbance of sample wells / Average absorbance of negative control wells) × 100

To find the value of IC_{50}, the percentage concentration of honey was transformed in log10 and analysed with GraphPad Prism 9 software. The inhibition curve was fitted with nonlinear regression (variable slope).

Scratch wound assay model

The scratch or wound healing assay, first introduced by Todaro *et al.* (1965), is a widely established method for studying cell migration on a two-dimensional surface. Human gingival fibroblasts (HGFs) were cultured to 95% confluence in 24-well plates labeled A to F. The assay was performed following the protocol described by Grada *et al.* (2017), with minor modifications. A scratch wound was created using a sterile 100 µL pipette tip (0.57 mm orifice diameter) and a sterile metal ruler to ensure a straight line. The pipette was held at a consistent angle, and uniform pressure was applied to generate a clean, uniform gap with smooth edges and minimal cellular debris. After scratching, the monolayer was washed with PBS to remove detached cells. Each well was then replenished with 2 mL of medium containing different concentrations of Tualang honey (TH): 5%, 1%, 0.3%, and 0.02% for wells A to D, respectively (Liang *et al.,* 2007). Well E received 2 mL of complete medium as a negative control, while well F received 2 mL of medium containing 0.1% Gengigel mouthwash as a positive control. All cultures were incubated at 37°C in a humidified atmosphere with 5% CO_2.

Wound closure measurement

The migration process was documented by capturing sequential digital photographs of the gap using an inverted microscope. A snapshot method was employed, where the wound area was photographed at the beginning, 24 hours, and 48 hours at 10x magnification. Image-Pro Express software Media Cybernetics, Inc. USA was used for image analysis, and cell migration was assessed by measuring the gap size. Five points were measured in each image, and the average wound width was calculated using ImageJ software. The percentage of wound closure was counted by measuring and

calculating the differences between final wound width and initial wound.

Wound Closure Percentage (%) = (Initial wound area - Final wound area) / Initial wound area) × 100

The migration rate can be quantified by dividing the change in wound width by the time spent in migration. The data obtained from these experiments were calculated using Microsoft Excel and the rates of migration (R_M) was calculated using the following formulation:

$$R_M = (Wi - Wf) / t$$

where:
R_M = Rate of cell migration, measured in micrometers per hour (μm/hour)
Wi = Initial wound width, measured in micrometers (μm)
Wf = Final wound width, measured in micrometers (μm)
t = Time taken, measured in hours (h)

Data analysis

Data were analysed using IBM SPSS Statistics Version 26 (IBM Corp., USA). The Kruskal–Wallis test was used for the cytotoxicity data due to non-normal distribution, with significance set at $p < 0.05$. For the migration assay, percentage wound closure and HGF migration rates were plotted over time. As the sample size exceeded 30 ($n > 30$), the central limit theorem was applied. Means and standard deviations were calculated, and a univariate two-way ANOVA was performed. Bonferroni adjustment was used for multiple comparisons. Statistical significance was set at $p < 0.05$ with a 95% confidence interval.

Results

For the cytotoxicity test, a statistically significant difference was observed among the treatment groups ($p = 0.000$), indicating a dose-dependent cytotoxic response. At the highest concentration tested (10%), cell viability was significantly reduced to 16.63% ± 1.52, indicating pronounced cytotoxicity. A moderate reduction in viability was observed at 5%, with a mean value of 69.77% ± 24.46. In contrast, lower concentrations (2.5% and below) maintained high cell viability, exceeding 88%. Notably, 2.5%, 1.25%, and 0.62% concentrations exhibited viability levels above 90%, which is comparable to the control group, suggesting minimal or no cytotoxic effects. The effect of various concentrations of TH on cell viability after 24 hours of exposure is presented in Figure 1.

The inhibition curve demonstrates a clear dose-dependent reduction in cell viability with increasing concentrations of TH after 24 hours of treatment. The curve follows a typical sigmoidal pattern, indicative of a cytotoxic effect. The highest concentration (10%) showed the greatest inhibitory effect, reducing viability to below 20%, while lower concentrations, particularly from 2.5% and below, had minimal impact on cell viability. The IC_{50} (half maximal inhibitory concentration) appears to fall between 2.5% and 5%, suggesting this range is critical for transitioning from non-toxic to cytotoxic effects. The steep slope of the curve between these concentrations highlights a narrow therapeutic window (Figure 2).

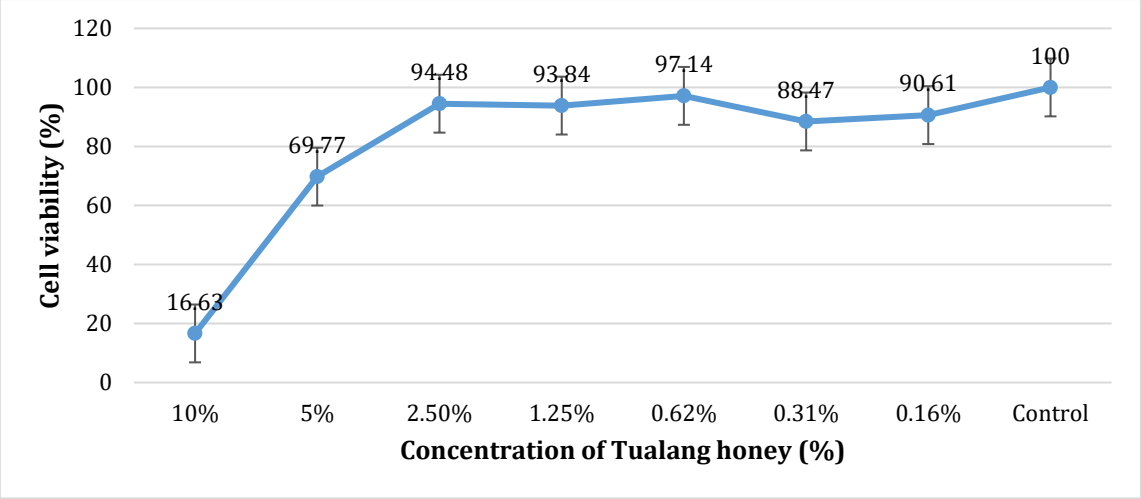

Figure 1. Cell viability of HGFs treated with various concentrations of Tualang honey using MTT assay after 24 hours.

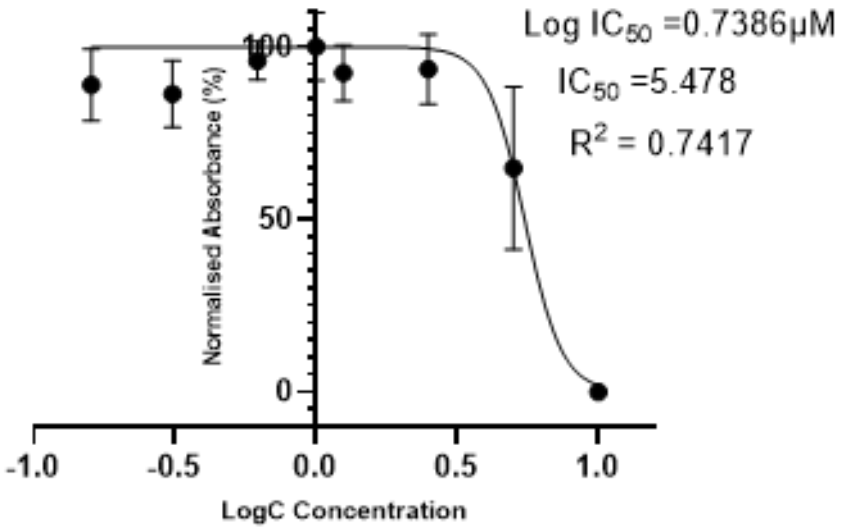

Figure 2. Dose-response inhibition curve of Tualang honey on cell viability.

Pairwise comparisons between each concentration of Tualang honey and the negative control revealed that only the higher concentrations (10% and 5%) caused statistically significant reductions in cell viability (Figure 3). Specifically, the 10% concentration showed a highly significant cytotoxic effect compared to the control ($p = 0.000$), while the 5% concentration also demonstrated a significant difference ($p = 0.027$). In contrast, all lower concentrations (≤2.5%) did not show any statistically significant difference in cell viability when compared to the control group ($p > 0.05$), indicating that these concentrations are non-cytotoxic under the tested conditions. These results further support the concentration-dependent cytotoxicity of Tualang honey, where significant inhibition of cell viability is only evident at concentrations ≥5%.

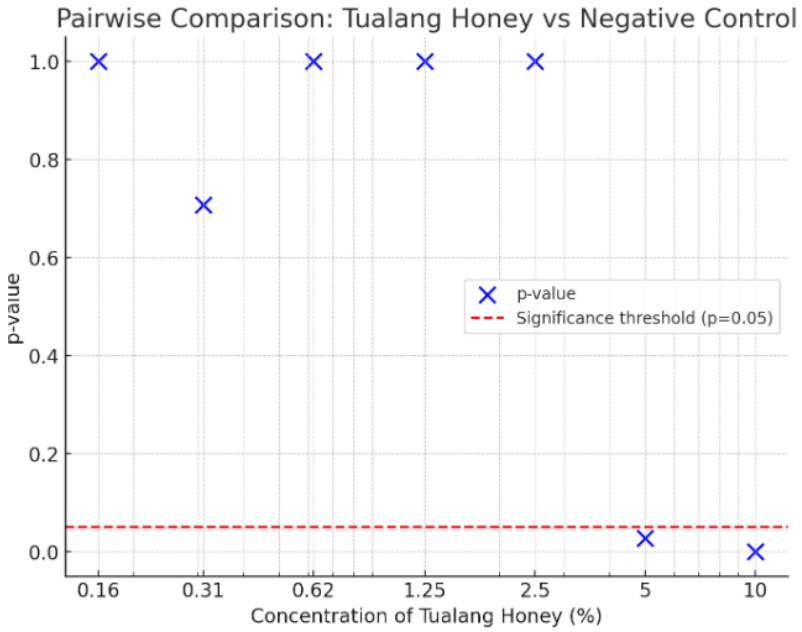

Figure 3. Pairwise comparison of HGF cell viability treated with Tualang honey at 24 hours, assessed by MTT assay.

Effect of Tualang honey on wound closure at 24 and 48 hours

The wound healing potential of Tualang honey was evaluated by measuring the percentage of wound closure at 24- and 48-hours post-treatment. A statistically significant difference was observed among all treatment groups at both time points ($p < 0.001$), indicating a concentration-dependent effect (Figure 4). At the highest concentration tested (5%), a negative wound closure was recorded at both 24 hours (−13.35 ± 0.37%) and 48 hours (−24.93 ± 0.5%), suggesting potential cytotoxicity or impaired cell migration. In contrast, lower concentrations demonstrated improved wound healing outcomes. Treatment with 1% honey yielded moderate wound closure (24.64% at 24 hours and 57.23% at 48 hours). The most effective responses were observed at 0.3% and 0.02% concentrations, with closure exceeding 50% at 24 hours and reaching 79.46% and 85.46% at 48 hours, respectively comparable to both negative and positive controls.

Effect of Tualang honey on the rate of human gingival fibroblasts migration

The migration rate of human gingival fibroblasts (HGFs) in response to various concentrations of TH was assessed at 24 and 48 hours, revealing a clear concentration-dependent trend (Figure 5). At 24 hours, the highest migration rate was observed in the positive control group (3.05 µm/h), followed closely by 0.3% TH (2.80 µm/h), 0.02% TH (2.77 µm/h), and the negative control (2.58 µm/h). In contrast, 1% TH exhibited a reduced migration rate (1.56 µm/h), while 5% TH showed a negative rate (−0.83 µm/h), suggesting a potential inhibitory or cytotoxic effect on cell motility. A similar pattern persisted at 48 hours, where the positive control maintained the highest rate (2.79 µm/h), closely followed by 0.3% TH (2.71 µm/h) and 0.02% TH (2.37 µm/h). The negative control showed a consistent rate (2.14 µm/h), whereas 1% TH remained lower (1.81 µm/h), and 5% TH continued to suppress cell migration (−0.77 µm/h).

Pairwise comparison of Tualang honey concentrations and HGF migration at 24 hours and 48 hours

Pairwise comparisons showed that 5% and 1% TH significantly reduced HGF migration rates compared to both control groups ($p = 0.000$) (Figure 6). In contrast, 0.3% and 0.02% showed no significant difference from the controls ($p = 1.000$). Migration increased significantly over time between 0, 24, and 48 hours ($p = 0.000$), indicating a time-dependent increase in cell movement.

Microscopic evaluation of HGF migration following treatment with Tualang honey

Wound widths measured at 0, 24, and 48 hours revealed a concentration-dependent response to TH (Figure 7). At 5%, wound width increased over time (91.19 µm to 113.99 µm), indicating impaired migration or cytotoxicity. The 1% group showed partial closure (107.54 µm to 46.45 µm), suggesting suboptimal healing. In contrast, 0.3% and 0.02% concentrations significantly reduced wound widths (107.82 µm to 27.09 µm and 123.46 µm to 18.98 µm, respectively), indicating enhanced HGF migration. The negative control also showed substantial closure (115.75 µm to 4.48 µm), with the 0.02% group closely matching this response, supporting its efficacy in promoting wound healing.

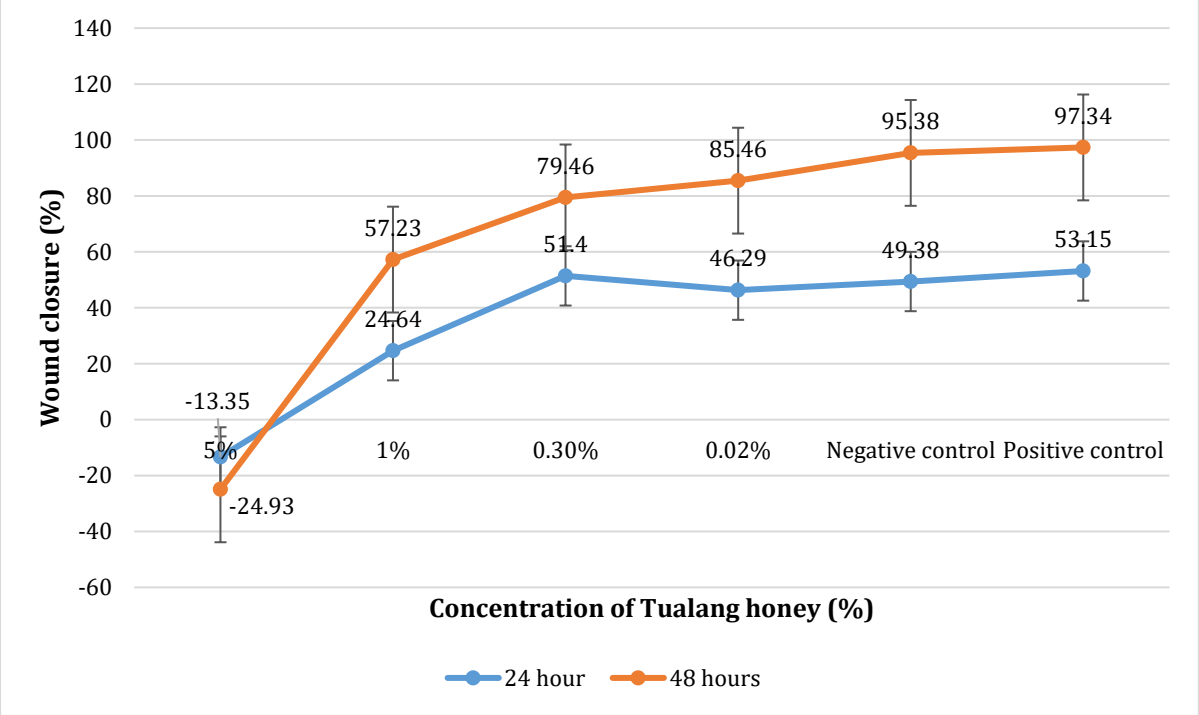

Figure 4. Percentage of wound closure at different concentrations of Tualang honey after 24 and 48 hours, based on scratch wound assay.

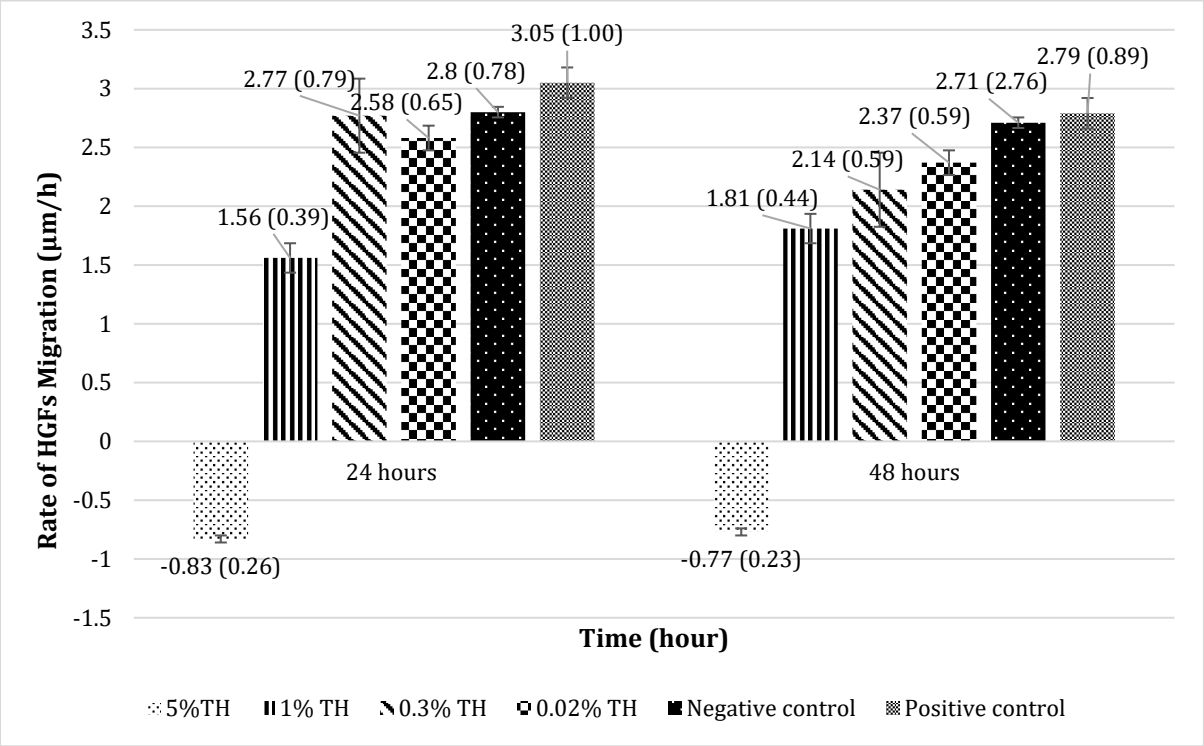

Figure 5. Rate of human gingival fibroblasts migration at various concentrations of Tualang honey at 24- and 48-hour using scratch assay.

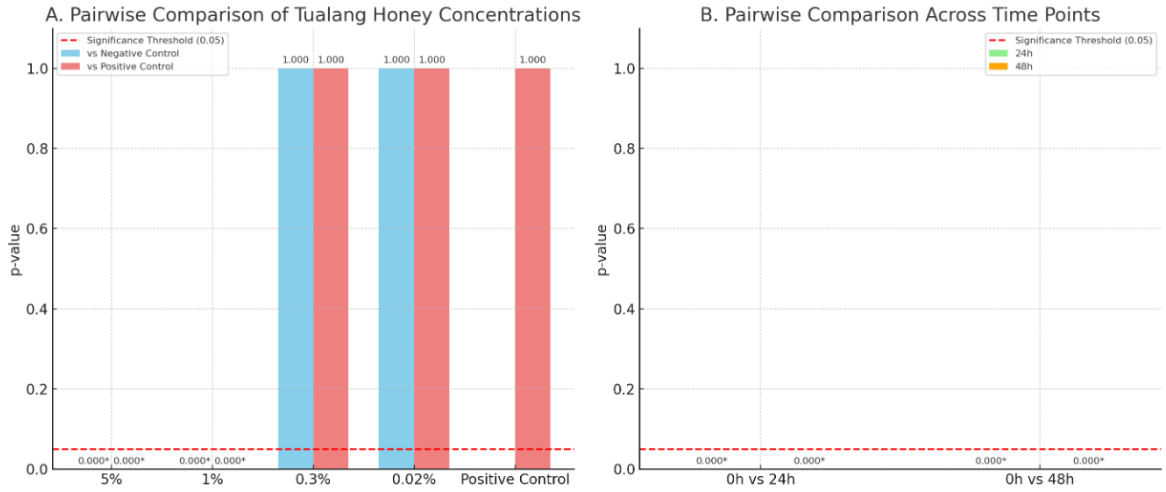

Figure 6. A. Pairwise comparison of Tualang honey concentrations (vs negative & positive controls). B. Pairwise comparison across time points (0h vs 24h, 0h vs 48h) using the scratch migration assay.

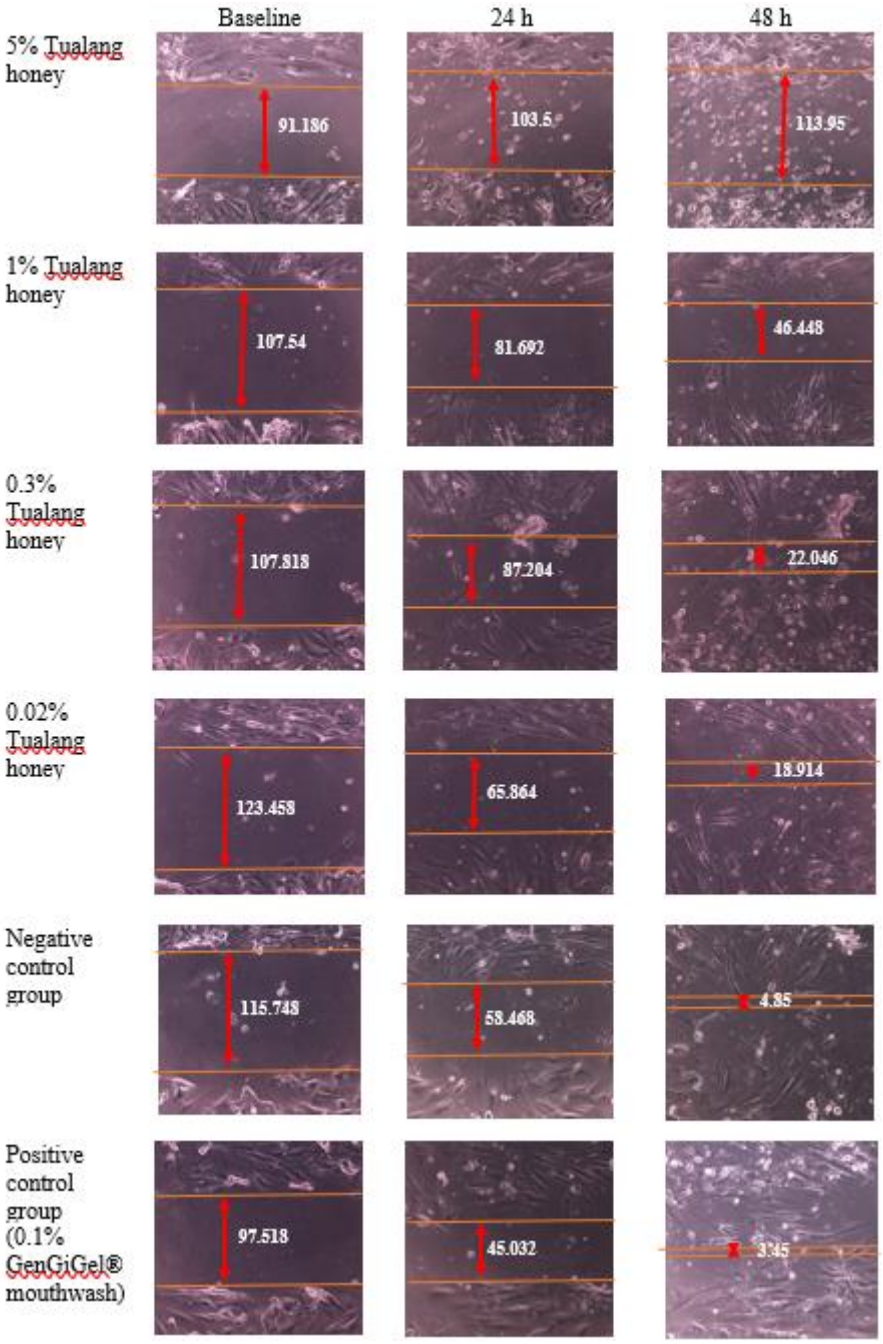

Figure 7. Microscopic images of scratch assays were captured at 100× magnification to evaluate migration of human gingival fibroblasts (HGFs) over 24 and 48 hours at various concentrations of Tualang honey and the control group (without treatment).

Discussion

Manuka honey is widely regarded as the gold standard among medical-grade honeys due to its unique methylglyoxal content and well-established antibacterial efficacy. However, Tualang honey, derived from the Malaysian rainforest, demonstrates a distinct mechanism of action that may complement or even surpass certain aspects of Manuka honey. Unlike Manuka, Tualang honey is exceptionally rich in polyphenols and flavonoids, which confer strong antioxidant properties and play a crucial role in modulating oxidative stress during wound healing. It also enhances fibroblast proliferation, reduces inflammatory cell

infiltration, and promotes tissue remodeling, highlighting a broader bioactive profile that supports wound repair. These findings suggest that while Manuka honey's activity is predominantly antibacterial, Tualang honey offers a multifaceted wound-healing mechanism through combined antioxidant, anti-inflammatory, and pro-proliferative effects (Fauzi *et al*., 2016). The study aimed to assess the effects of TH on the viability, wound closure, and migration of HGFs using MTT and scratch assays.

The results demonstrate that TH exhibits a concentration-dependent cytotoxic effect on HGFs. At the highest concentration tested (10%), a significant reduction in cell viability was observed, indicating strong cytotoxicity, while moderate effects were seen at 5%. High concentrations of honey may induce cytotoxicity in HGFs due to the combined effects of osmotic stress, low pH, hydrogen peroxide, and bioactive compounds (Gharzouli *et al.,* 2002; Molan, 1992). In contrast, concentrations of 2.5% and below did not significantly affect cell viability, suggesting they are non-toxic. These findings are consistent with previous reports demonstrating the biocompatibility of honey. Akmar *et al*. (2022) found that Kelulut and Acacia honey, at concentrations up to 2%, did not significantly reduce fibroblast viability. Similarly, Yun *et al.* (2021) found that Malaysian Kelulut honey maintains cell viability above 70% across a broad range of concentrations (3.125 to 200 mg/ml) and time points (24, 48, and 72 hours).

The IC_{50} values observed in this study range from 2.5% to 5%, indicating a critical concentration threshold for the transition from non-toxic to cytotoxic effects. The steep dose-response curve suggests that TH has a narrow therapeutic window, where slight increases in concentration may shift its effects from beneficial to harmful. This is supported by pairwise comparisons, which demonstrated that concentrations of 5% and above significantly reduced cell viability compared to the negative control, while concentrations below 5% showed no significant difference, indicating a lack of cytotoxicity. As this result was obtained in vitro, where cells are directly exposed to honey, the biological response may significantly differ in a more complex in vivo environment. Factors such as metabolic processes, immune responses, and tissue interactions could influence the actual impact in vivo.

The scratch assay demonstrated a concentration-dependent effect of TH on HGFs migration and wound closure. Lower concentrations of TH (0.3% and 0.02%) effectively promoted wound healing, as evidenced by significant wound closure and improved cell motility over 48 hours. In contrast, higher concentrations (1% and 5%) hindered fibroblast migration, with the 5% concentration showing negative migration, indicating a possible cytotoxic or inhibitory effect. Importantly, this is the first known study to assess the effect of TH on HGFs using a scratch assay, providing new insights into its wound healing potential in an oral context.

These findings are consistent with earlier studies involving various types of honey that support wound healing by enhancing cell migration. For instance, Ranzato *et al.* (2013) showed that acacia, buckwheat, and manuka honeys promoted fibroblast migration and wound closure potentially through distinct mechanisms. Similarly, Chaudhary *et al.* (2020) reported that Jamun honey at a 0.1% concentration significantly accelerated fibroblast migration and wound healing. Supporting this, Ranzato *et al.* (2012) found that low concentrations of honey (0.1%) also stimulated keratinocyte migration and re-epithelialization, highlighting honey's general capacity to enhance cell motility during tissue repair. Although direct studies on Tualang honey's effects on gingival fibroblasts are limited, Tan *et al.* (2014) demonstrated that TH facilitated migration of corneal epithelial progenitor cells, suggesting similar pro-migratory effects may occur in fibroblasts. In addition, Losageanu *et al.* (2024) observed that different types of honey enhanced fibroblast activity, further reinforcing honey's role in supporting wound healing processes.

Notably, Tualang honey at lower concentrations demonstrated comparable effects to a clinically established wound healing agent. When compared with the positive control used in this study, Gengigel mouthwash, which is a hyaluronic acid-based formulation, Tualang honey at concentrations of 0.3% and 0.02% demonstrated similar efficacy in promoting HGF migration. Previous research has confirmed that Gengigel is minimally cytotoxic and supports fibroblast migration, reinforcing its use in oral wound management (Marques *et al.,* 2024; Mercan & Salkin, 2019). These findings suggest that Tualang honey, at appropriately low concentrations, may serve as a natural alternative for enhancing oral wound healing, with effects comparable to a standard commercial product.

Conclusion

Although limited to in vitro conditions, Tualang honey demonstrated dose-dependent effects in both cytotoxicity and wound healing models. Lower concentrations (≤0.3%) were non-cytotoxic to human gingival fibroblasts and promoted cell migration and wound closure, while higher concentrations (≥5%) showed cytotoxicity. The findings contribute to the growing evidence of Tualang honey's therapeutic value in regenerative dentistry. Future studies should investigate the molecular pathways underlying its bioactivity, validate the effects in animal models and three-dimensional culture systems, and explore novel formulations such as hydrogels or scaffolds to optimize its clinical application.

Authors Contributions

Dr Siti Lailatul Akmar Zainuddin was involved in planning the study and supervised the research, Dr Zurairah binti Berahim was involved in planning the study, reviewed and edited the manuscript for clarity and content. Dr. Nor Azira binti Zahadi conducted the data collection and prepared the initial draft of the manuscript. All authors read and approved the final version of the manuscript.

Acknowledgement

The authors wish to express their sincere gratitude to the Universiti Sains Malaysia for the provision of research facilities and materials that made this study possible and to Ministry of Health Malaysia for the generous scholarship support.

Ethical Approval Statement

There is no animal experiment carried out for this study.

Conflict of Interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

Declaration of Generative AI And AI-Assisted Technologies in the Writing Process

ChatGPT (developed by OpenAI) was used to assist with grammar checking, sentence rephrasing, and summarizing during the preparation of this manuscript. All AI-assisted content was carefully reviewed and edited by the authors to ensure accuracy, clarity, and alignment with the intended meaning. The authors take full responsibility for the content of the manuscript.

References

Abu Bakar, M. F., Sanusi, S. B., Abu Bakar, F. I., Cong, O. J., & Mian, Z. (2017). Physicochemical and antioxidant potential of raw unprocessed honey from malaysian stingless bees. *Pakistan Journal of Nutrition*, *16*(11), 888–894. https://doi.org/10.3923/pjn.2017.888.894

Aspar, M. M., Edros, R., & Hamzah, N. A. (2020). Antibacterial evaluation of malaysian kelulut, tualang and acacia honey against wound infecting bacteria. *IOP Conference Series: Materials Science and Engineering*, *991*(1).

https://doi.org/10.1088/1757899X/991/1/012065

Azman, A.S.S., Tan, J.J., Abdullah, M.N.H., *et al*. (2024). *Medicinal activities of Tualang honey: a systematic review. BMC Complementary Medicine and Therapies*, 24 (266).

Bansal, V., Medhi, B., & Pandhi, P. (2005). Honey--a remedy rediscovered and its therapeutic utility. *Kathmandu University Medical Journal (KUMJ)*, *3*(3), 305–309.

de Luna, F. C., Ferreira, W. A., Casseb, S. M., & de Oliveira, E. H. (2023). Anticancer potential of flavonoids: an overview with an emphasis on tangeretin. *Pharmaceuticals*, 16 (9). https://doi.org/10.3390/ph16091229

Ezz El-Arab, A. M., Girgis, S. M., Hegazy, E. M., & Abd El-Khalek, A. B. (2006). Effect of dietary honey on intestinal microflora and toxicity of mycotoxins in mice. *BMC Complementary and Alternative Medicine*, *6*(1), 6. https://doi.org/10.1186/1472-6882-6-6

Fauzi, A.N., Norazmi, M.N., Yaacob, N.S. (2016) Tualang honey promotes apoptotic cell death induced by tamoxifen in breast cancer cell lines. *Evidence-Based Complementary and Alternative Medicine*, 2016:3729051. https://doi.org/10.1155/2016/3729051

Gharzouli, K., Amira, S., Gharzouli, A., & Khennouf, S. (2002). Gastroprotective effects of honey and glucose-fructose-sucrose-maltose mixture against ethanol-, indomethacin-, and acidified aspirin-induced lesions in the rat. *Experimental and Toxicologic Pathology*, *54*(3), 217–221. https://doi.org/10.1078/0940-2993-00255

Hofmann, E., Fink, J., Pignet, A.-L., Schwarz, A., Schellnegger, M., Nischwitz, S. P., Holzer-Geissler, J. C. J., Kamolz, L.-P., & Kotzbeck, P. (2023). Human in vitro skin models for wound healing and wound healing disorders. *Biomedicines*, 11 (4). https://doi.org/10.3390/biomedicines11041056

Liang, C., Park, A. Y., & Guan, J. (2007). In vitro scratch assay : a convenient and inexpensive method for analysis of cell migration in vitro. *Nature Protocols*, *2*(2), 329–333. https://doi.org/10.1038/nprot.2007.30

Mandal, M. D., & Mandal, S. (2011). Honey: its medicinal property and antibacterial activity. *Asian Pacific Journal of Tropical Biomedicine*, *1*(2), 154–160. https://doi.org/10.1016/S2221-1691(11)60016-6

Marques, A. F. S., Silva, N. M., da Cruz, M., Marques, J., & da Mata, A. D. (2024). Hyaluronic acid-based gels for oral application: comparison of in vitro effects on gingival cells and bacteria. *Journal of Oral Biology and Craniofacial Research*, *14*(3), 238–244. https://doi.org/10.1016/j.jobcr.2024.03.001

Medhi, B., Puri, A., Upadhyay, S., & Kaman, L. (2008). Topical application of honey in the treatment of wound healing: a metaanalysis. *JK Science*, *10*(4), 166–169.

Mercan, U., & Salkin, H. (2019). Comparison of the effect of postoperative care agents on human gingival fibroblasts: a preliminary study. *European Oral Research*, *53*(2), 67–73. https://doi.org/10.26650/eor.20197456

Molan, P.C. (2001). The potential of honey to promote oral wellness. *General Dentistry*, *49*(6), 584–589.

Molan, P.C. (1992). The antibacterial activity of honey. *Bee World*, *73*(1), 5–28. https://doi.org/10.1080/0005772X.1992.11099109

Naruishi, K. (2022). Biological roles of fibroblasts in periodontal diseases. *Cells*, *11*(21). https://doi.org/10.3390/cells11213345

Ranzato, E., Martinotti, S., & Burlando, B. (2012). Epithelial mesenchymal transition traits in honey-driven keratinocyte wound healing: comparison among different honeys. *Wound Repair and Regeneration,* *20*(5), 778–785. https://doi.org/10.1111/j.1524475X.2012.00825.x

Ranzato, E., Martinotti, S., & Burlando, B. (2013). Honey exposure stimulates wound repair of human dermal fibroblasts. *Burns & Trauma*, *1*(1), 32–38. https://doi.org/10.4103/2321-3868.113333

Tan, H. T., Rahman, R. A., Gan, S. H., Halim, A. S., Hassan, S. A., Sulaiman, S. A., *et al.* (2009). The antibacterial properties of Malaysian tualang honey against wound and enteric microorganisms in comparison to manuka honey. *BMC Complementary and Alternative Medicine*, *9*, 34. https://doi.org/10.1186/1472-6882-9-34

te Boekhorst, V., Preziosi, L., & Friedl, P. (2016). Plasticity of cell migration in vivo and in silico. *Annual Review of Cell and Developmental Biology*, *32*(1), 491–526. https://doi.org/10.1146/annurev-cellbio-111315-125201

Tonks, A. J., Cooper, R. A., Jones, K. P., Blair, S., Parton, J., & Tonks, A. (2003). Honey stimulates inflammatory cytokine production from monocytes. *Cytokine*, *21*(5), 242–247. https://doi.org/10.1016/s1043-4666(03)00092-9

Yaghoobi, R., Kazerouni, A., & Kazerouni, O. (2013). Evidence for clinical use of honey in wound healing as an anti-bacterial, anti-inflammatory anti-oxidant and anti-viral agent: a review. *Jundishapur Journal of Natural Pharmaceutical Products*, *8*(3), 100–104. https://doi.org/10.17795/jjnpp-9487

Yu, L. X., Taib, H., Berahim, Z., Ahmad, A., & Zainuddin, S. L. A. (2015). The effect of Tualang honey on human periodontal ligament fibroblast proliferation and alkaline phosphatase level. *Sains Malaysiana*, *44*(7), 1021–1025. https://doi.org/10.17576/jsm-2015-4407-14

Yun, C. Z. (2021). Cytotoxic evaluation of malaysian kelulut honey on human gingival fibroblast cell line using mtt assay cytotoxic evaluation of Malaysian kelulut honey on human gingival fibroblast. *Journal of Dentistry Indonesia*, *28*(2), 88–93.