

## Documents

Anuar, M.N.N.<sup>a</sup>, Ibrahim, M.<sup>a</sup>, Zakaria, N.H.<sup>b</sup>, Ichwan, S.J.A.<sup>c</sup>, Isa, M.L.M.<sup>d</sup>, Alewi, N.A.M.<sup>a</sup>, Hagar, A.<sup>a</sup>, Majid, F.A.A.<sup>b</sup>

### The Antioxidant Activity and Induction of Apoptotic Cell Death by *Musa paradisiaca* and *Trigona* sp. Honey Jelly in ORL115 and ORL188 Cells

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<sup>a</sup> Department of Nutrition Sciences, Kulliyyah of Allied Health Sciences, International Islamic University Malaysia, Pahang, Kuantan, 25200, Malaysia

<sup>b</sup> Institute of Marine Biotechnology, Universiti Malaysia Terengganu, Kuala Nerus, Terengganu, Malaysia

<sup>c</sup> PAPRSB Institute of Health Sciences, Universiti Brunei Darussalam, Gadong, Brunei Darussalam

<sup>d</sup> Department of Basic Medical Sciences for Nursing, Kulliyyah of Nursing, International Islamic University Malaysia, Pahang, Malaysia

#### Abstract

**Background:** Head and neck cancer patients usually need nutritional support due to difficulties in swallowing and chewing. Therefore, this study aimed to formulate *Musa paradisiaca* and *Trigona* sp. honey jelly (MTJ) as a convenient functional food. **Methods:** The antioxidant properties were analysed using 2,2'-diphenyl-1-picrylhydrazyl (DPPH), ferric reducing antioxidant potential (FRAP) and 2,2'-azino-di 3-ethylbenthiazolinesulfonate (ABTS) assays. Cytotoxicity was assayed using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) test and the induction of apoptosis was observed via caspase-3/7 activity assay. The identification of phenolic compounds was done via ultra-high-performance-liquid chromatography coupled to mass spectrometer (UHPLC-MS/MS). **Results:** The antioxidant analysis exhibited: the half inhibitory concentration (IC<sub>50</sub>) of DPPH inhibition, 54.10 (SD = 4.51) µg/mL; the FRAP value, 30.07 (SD = 0.93) mM TEQ/100 g; and the ABTS value, 131.79 (SD = 8.73) mg TEQ/100 g. Cinnamic acid was the most abundant phenolic compound, followed by maleic acid and salicylic acid. The IC<sub>50</sub> for ORL115 and ORL188 were 35.51 mg/mL and 43.54 mg/mL, respectively. The cells became rounded and dissymmetrical which reduced in number and size. The apoptotic cell death in ORL115 and ORL188 was deduced as caspase-3/7 activities that significantly increased (P < 0.05). **Conclusion:** The study evidenced that the antioxidant activity of MTJ could influence the induction of apoptosis in ORL115 and ORL188 in future investigations and verifications. © Penerbit Universiti Sains Malaysia, 2023.

#### Author Keywords

antioxidant; apoptosis; head and neck squamous cell carcinoma; *Musa paradisiaca*; stingless bee

#### Index Keywords

antioxidant, caspase 3, caspase 7, cinnamic acid, gallic acid, kaempferol, maleic acid, phenol, phenol derivative, quercetin, salicylic acid, sinapic acid, vanillic acid; ABTS radical scavenging assay, antioxidant activity, apoptosis, Article, cell death, cell proliferation, cell viability, cell viability assay, cytotoxicity, DPPH radical scavenging assay, dysphagia, ferric reducing antioxidant power, ferric reducing antioxidant power assay, functional food, head and neck cancer, head and neck squamous cell carcinoma, honey, human, human cell, IC<sub>50</sub>, mastication, MTT assay, multiple reaction monitoring, *Musa x paradisiaca*, nonhuman, nutritional support, ORL11 cell line, ORL18 cell line, squamous epithelium cell, stingless bee, swallowing, tandem mass spectrometry, ultra performance liquid chromatography

#### Chemicals/CAS

caspase 3, 169592-56-7; caspase 7, 189258-14-8; cinnamic acid, 4151-45-5, 538-42-1, 621-82-9; gallic acid, 149-91-7; kaempferol, 520-18-3; maleic acid, 110-16-7, 18610-42-9; phenol, 108-95-2, 3229-70-7; quercetin, 117-39-5; salicylic acid, 63-36-5, 69-72-7; sinapic acid, 530-59-6; vanillic acid, 121-34-6

#### Manufacturers

Schott, United States

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#### References

- Johnson, DE, Burtness, B, Leemans, CR, Yan Lui, VW, Bauman, JE, Grandis, JR.  
**Head and neck squamous cell carcinoma**  
(2020) *Nat Rev Dis Primers*, 6, p. 92.

- Heijnen, BJ, Speyer, R, Kertscher, B, Cordier, R, Koetsenruijter, KW, Swan, K  
**Dysphagia, speech, voice, and trismus following radiotherapy and/or chemotherapy in patients with head and neck carcinoma: review of the literature**  
(2016) *Biomed Res Int*, pp. 1-24.  
6086894
- Szychowski, KA, Binduga, UE, Rybczyn'ska-Tkaczyk, K, Leja, ML, Gmin'ski, J.  
**Cytotoxic effects of two extracts from garlic (*Allium sativum L.*) cultivars on the human squamous carcinoma cell line SCC-15**  
(2018) *Saudi J Biol Sci*, 25, pp. 1703-1712.
- Ravasco, P.  
**Nutrition in Cancer Patients**  
(2019) *J Clin Med*, 8 (8), p. 1211.
- Handayani, R, Fans, K, Mastuti, TS, Rosa, D.  
**Comparative study of antioxidant activity from three banana leaves extracts**  
(2021) *J Teknol Industri Pangan*, 32 (1), pp. 92-97.
- Mohd Nur Nasyriq, A, Muhammad, I, Badr Eddin, K, Nur Aizura, MA, Ainin Azwani, AR, Norazlanshah, L  
**Response surface optimisation of high antioxidant jelly from *Musa paradisiaca* and *Trigona* sp. honey using central composite design as a convenient functional food**  
(2019) *Int Food Res J*, 26, pp. 1201-1209.
- Mondal, A, Banerjee, S, Bose, S, Das, PP, Sandberg, EN, Atanasov, AG, Bishayee, A.  
**Cancer preventive and therapeutic potential of banana and its bioactive constituents: a systematic, comprehensive, and mechanistic review**  
(2021) *Front Oncol*, 11, p. 697143.
- Hassan, H, Abdul Karim, N.  
**Honey as versatile remedy: a focus on selected honeys**  
(2018) *Int J Food Nutr Sci*, 6 (1), pp. 1-6.
- Machado De-Melo, AA, Almeida-Muradian, LBD, Sancho, MT, Pascual-Maté, A.  
**Composition and properties of *Apis mellifera* honey: a review**  
(2018) *J Apic Res*, 57 (1), pp. 5-37.
- Martinotti, S, Bucekova, M, Majtan, J, Ranzato, E.  
**Honey: an effective regenerative medicine product in wound management**  
(2019) *Curr Med Chem*, 26 (27), pp. 5230-5240.
- Hazirah, H, Yasmin Anum, MY, Nor wahidah, AK.  
**Antioxidant properties of stingless bee honey and its effect on the viability of lymphoblastoid cell line**  
(2019) *Med & Health*, 14 (1), pp. 91-105.
- Siti Norfitrah, MS, Logaraj, R, Fong, CS, Ridhwan, AW, Mohammad Syaiful Bahari, AR.  
**In-vitro cytotoxicity of *Trigona itama* honey against human lung adenocarcinoma epithelial cell line (A549)**  
(2019) *Euro J Integr Med*, 30, p. 100955.
- Kek, SP, Chin, NL, Yusof, YA, Tan, SW, Chua, LS.  
**Total phenolic contents and colour intensity of Malaysian honeys from the *Apis* spp. and *Trigona* spp. bees**  
(2014) *Agric Sci Procedia*, 2, pp. 150-155.
- Freitas, MCJ, Silveira, GE, Veras, LS, Santos, GFF.  
**Honey bread made with flour of different varieties of green banana**  
(2017) *Demetra: Food Nutri Health*, 12 (2), pp. 465-482.

- Mat Alewi, NA, Ibrahim, M, Md Isa, ML, Abdull Rasad, MSB, Abdul Rafa, AA, Anuar, MNN. **Response surface optimisation and antioxidant characterisation of high antioxidant soft jelly prepared from *Baccaurea angulata* fruit juice and *Trigona* sp. honey using central composite design** (2020) *Int Food Res J*, 27 (3), pp. 454-464.
- Leite, IB, Magalhães, CD, Monteiro, M, Fialho, E. **Addition of honey to an apple and passion fruit mixed beverage improves its phenolic compound profile** (2021) *Foods*, 10 (7), p. 1525.
- Serna Thome, G, Castro Eguiluz, D, Tarlovsky, Fuchs, Sanchez Lopez, M, Delgado Olivares, L, Coronel-Martínez, J. **Use of functional foods and oral supplements as adjuvant in cancer treatment** (2018) *Rev Inves Clin*, 70, pp. 136-146.
- Idris, AA, Maryam, AM, Muhammad, I, Norazlanshah, H, Mohammad Syaiful Bahari, AR, Abdul Ghani, R. **Antioxidant activity and phenolic profile of various morphological parts of underutilised *Baccaurea angulata* fruit** (2015) *Food Chem*, 172, pp. 778-787.
- Nurhazni, KJ, Darina, I, Muhammad, I, Mhammad Noor Adros, Y, Norazmir, MN, Khairil Anuar, MI. **Proximate composition and antioxidant activity of dried belimbing dayak (*Baccaurea angulata*) fruits** (2013) *Sains Malay*, 42, pp. 129-134.
- Ilyasov, IR, Beloborodov, VL, Selivanova, IA, Terekhov, RP. **ABTS/PP decolorization assay of antioxidant capacity reaction pathways** (2020) *Int J Mol Sci*, 21 (3), p. 1131.
- Moniruzzaman, M, Yung, AC, Rao, PV, Hawlader, MNI, Mohd Azlan, SA, Sulaiman, SA. **Identification of phenolic acids and flavonoids in monofloral honey from bangladesh by high performance liquid chromatography: determination of antioxidant capacity** (2014) *BioMed Res Int*, pp. 1-11. 737490
- Fadlullah, MZ, Chiang, IK, Dionne, KR, Yee, PS, Gan, CP, Sam, KK. **Genetically-defined novel oral squamous cell carcinoma cell lines for the development of molecular therapies** (2016) *Oncotarget*, 7 (19), pp. 27802-27818.
- Abel, SDA, Baird, SK. **Honey is cytotoxic towards prostate cancer cells but interacts with the MTT reagent: considerations for the choice of cell viability assay** (2018) *Food Chem*, 241, pp. 70-78.
- Buskaran, K, Hussein, MZ, Mohd Moklas, MA, Fakurazi, S. **Morphological changes and cellular uptake of functionalized graphene oxide loaded with protocatechuic acid and folic acid in hepatocellular carcinoma cancer cell** (2020) *Int J Mol Sci*, 21 (16), p. 5874. 16
- Ahmad, F, Seerangan, P, Mustafa, MZ, Osman, ZF, Abdullah, JM, Idris, Z. **Anti-cancer properties of *Heterotrigona itama* sp. honey via induction of apoptosis in malignant glioma cells** (2019) *Malays J Med Sci*, 26 (2), pp. 30-39.

- Kumar, N, Goel, N.  
**Phenolic acids: natural versatile molecules with promising therapeutic applications**  
(2019) *Biotechnol Rep*, 24, p. e00370.
- Lee, EH, Yeom, HJ, Ha, MS, Bae, DH.  
**Development of banana peel jelly and its antioxidant and textural properties**  
(2010) *Food Sci and Biotechnol*, 19 (2), pp. 449-455.
- Shrikanta, A, Kumar, A, Govindaswamy, V.  
**Resveratrol content and antioxidant properties of underutilized fruits**  
(2015) *J Food Sci Technol*, 52 (1), pp. 383-390.
- Abolmaesoomi, M, Azlina, AA, Sarni, MJ, Johari, MA.  
**Ficus deltoidea: effects of solvent polarity on antioxidant and antiproliferative activities in breast and colon cancer cells**  
(2019) *Europe J Integr Med*, 28, pp. 57-67.
- Noor Azwani, MR, Mariam Firdhaus, MN, Kamyar, S.  
**Formulation and evaluation of semisolid jelly produced by Musa acuminata Colla (AAA Group) peels**  
(2016) *Asian Pac J Tropic Biomedic*, 6 (1), pp. 55-59.
- Marina, CL, Calín-Sánchez, Á, Clemente-Villalba, J, Hernández, F, Carbonell-Barrachina, AA, Sendra, E  
**Quality parameters and consumer acceptance of jelly candies based on pomegranate juice “Mollar de Elche”**  
(2020) *Foods*, 9 (4), p. 516.
- Baroni, MV, Gastaminza, J, Podio, NS, Lingua, MS, Wunderlin, DA, Rovasio, JL  
**Changes in the antioxidant properties of quince fruit (*Cydonia oblonga* Miller) during jam production at industrial scale**  
(2018) *J Food Quali*, 2018, pp. 1-9.
- Zhang, J, Xiao, A, Wang, T, Liang, X, Gao, J, Li, P  
**Effect and mechanism of action of cinnamic acid on the proliferation and apoptosis of leukaemia cells**  
(2014) *Biomedic Res*, 25, pp. 405-408.
- Qi, G, Chena, J, Shi, C, Wang, Y, Mi, S, Shao, W  
**Cinnamic acid (CINN) induces apoptosis and proliferation in human nasopharyngeal carcinoma cells**  
(2016) *Cell Physiol Biochem*, 40, pp. 589-596.
- Pfeffer, CM, Singh, ATK.  
**Apoptosis: a target for anticancer therapy**  
(2018) *Int J Mol Sci*, 19 (2), p. 448.
- Khazaei, S, Abdul Hamid, R, Mohd Esa, N, Ramachandran, V, Aalam, GTF, Etemad, A  
**Promotion of HepG2 cell apoptosis by flower of Allium atroviolaceum and the mechanism of action**  
(2017) *BMC Complement Alternat Med*, 17, p. 104.
- Zarith Nameyrra, MN, Nurul Husna, S, Amirah Haziyah, I, Norhaizan, ME, Amin, I, Siti Farah, MT.  
**Induction of endoplasmic reticulum stress pathway by green tea epigallocatechin-3-gallate (EGCG) in colorectal cancer cells: activation of PERK/p-eIF2α/ATF4 and IRE1α**  
(2019) *BioMedic Res Int*, 2019, pp. 1-9.
- Ghafar, SAA, Fikri, IHH, Eshak, Z.  
**Antioxidant activity of Musa paradisiaca (Banana) soft pith and its cytotoxicity**

**against oral squamous carcinoma cell lines**  
(2019) *Malay J Sci Health Technol*, 3, pp. 1-11.

**Correspondence Address**

Ibrahim M.; Department of Nutrition Sciences, Pahang, Malaysia; email: abumaisarah@iium.edu.my

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