

A SHORT REVIEW ON POTENTIAL MALAY MEDICINE IN CONTROLLING OBESITY AND TREATING CANCERS

MUHAMMAD AMEERUL AMIN BAKAR @ OMAR AND WAN IRYANI WAN ISMAIL

Biological Security and Sustainability Research Group, School of Fundamental Science, Universiti Malaysia Terengganu, 21030 Kuala Nerus, Terengganu, Malaysia.

*Corresponding author: waniryani@gmail.com

Abstract: Malay medicine is one of complementary and alternative medicines in preventing and treating many diseases. However, scientific observation on Malay medicine in treating several non-infectious diseases, including obesity and cancer has not been fully documented and may be obsoleted. Thus, this review compiled several data on the potential of Malay medicine practice by consumption of Gelam honey and herb named *Tinospora crispa* in controlling obesity and treating cancer. In obesity study, findings revealed Gelam honey, and *T. crispa* significantly decreased body weight, total cholesterol, triglycerides and the glucose level compared to controls. Meanwhile, in several cancer studies, both Gelam honey and *T. crispa* were found inhibited colon, breast, liver and lung cancer cell growth. Although the results were at the early stage, the reported studies revealed the potential of Gelam honey and *T. crispa*, which are applied in Malay medicine to control obesity and treat cancers effectively in the future. The data is also useful to conserve both native natural products and to promote a significant application of Malay medicine until to date.

Keywords: Cancer, Malay medicine, honey, obesity, sustainability, *Tinospora crispa*.

Introduction

One of the uniqueness of Malay heritage and culture in Malaysia is an application of Malay medicine. It is a complementary and alternative medicine blended from many cultures ranging from the ancient, animistic, ancient Melayu (Hinduism), Royal Malacca Malay (Islamic early era), colonial era, independent era until today (Harun, 2006). The geographical factor plays a significant role in the development of Malay medicine such as hot and humid climate to cause many types of diseases, and abundance of natural sources including medicinal plants and herbs from local Tropical Rain Forest. The fundamental principle of Malay medicine is either to prevent or to treat diseases by using several approaches such as herbal consumption, diet, massages, cupping, shower, kinaesthetic approach, spiritual, wisdom and taboos. Ultimately, it is to ensure human health is at the exceptional condition (Haliza, 2005).

Currently, chronic or non-infectious diseases such as obesity and cancers are the major health problem in Malaysia and worldwide. According

to World Health Organization (WHO), Malaysia has the highest obesity rate in Southern Asia and ranks sixth in Asia Pacific region (Mohamud *et al.*, 2011). The percentage of obese people increased three folds in the past 15 years from 4 % in 1996 to 16 % in 2011 (Mohamud *et al.*, 2011). Furthermore, there are convincing evidence that the obesity epidemic has closely been associated with other chronic diseases, particularly cancers, which are leading to a high risk of fatality (Field, 2013, Kleinert & Horton, 2015, Ogunbode *et al.*, 2011).

Obesity and cancers are multifactorial diseases. However, diet is one major culprit contributing to the disease, particularly in Malaysia, which is known as "foods' heaven" (Mohamud *et al.*, 2011). The unlimited accessibility and availability of foods, particularly unhealthy food contribute to the obesity and cancers. In order to combat the diseases, several modern drugs have been designed. Unfortunately, the medications induced undesirable side effects such as increase blood pressure, cardiac arrhythmias, steatorrhea

and associated with a risk of developing deficiencies in lipid soluble vitamins and essential fatty acids (Korner & Aronne, 2004).

In Malaysia, there are various types of honey are available such as Tualang, Acacia, Pineapple, Gelam honey and Kelulut Honey. These honey harvested from different species of bees and stingless bees (Ismail, 2016). Meanwhile, *Tinospora crispa* is a medicinal plant belong to the genus of *Tinospora* of Menispermaceae family which is found rich of antioxidant and possesses antidiabetic properties. Those findings have attracted researchers to investigate its effect especially in obesity study (Noor & Ashcroft, 1998; Hamid *et al.*, 2008). Due to the said side effects, much attention has been focused on solving the primary factor in selecting the most appropriate diets enriched with antioxidant properties and without causing any impairment to the human body. Thus, this review is to compile and reveal findings from several studies on the consumption of Gelam honey and *T. crispa* in obesity and cancer studies.

Both Gelam honey and *T. crispa* contain a high amount of antioxidant properties. Interestingly, the natural products have been used since ancient time in Malay medicine for many medicinal purposes. For instance, honey was used to maintain a healthy body, to supply energy and to retain ideal body weight either as a 'makjun' or to consume directly (Bogdanov *et al.*, 2012; Kasikam, 2011). Extensive studied on local honey had been conducted by researchers from the Medical School at Universiti Sains Malaysia, Kelantan. From that research, the findings revealed some medicinal values of honey especially for treating menopause syndrome and improving fertility (Mohamed *et al.*, 2011), and also potential for treating diabetes (Erejuwa *et al.*, 2010; Erejuwa *et al.*, 2012) and cancer (Mohamed *et al.*, 2011).

Meanwhile, *T. crispa* is used to control blood glucose level, and as antiproliferative and antimalarial agents (Najib *et al.*, 1999; Noor & Ashcroft, 1998; Tunpradit *et al.*, 2010; Ueda *et al.*, 2002; Zulkhairi *et al.*, 2011). Intriguingly, both natural products are applied as a part of the

diet in Malay community for a long time ago (Batugal *et al.*, 2004; Kasikam, 2011). However, scientific evidence in treating non-infectious diseases, particularly metabolic diseases using the natural products are still at infancy level. Thus, the review focuses documenting the effects of Gelam honey and *T. crispa*, applied to Malay medicine, on obesity and cancers.

Effects of Gelam Honey and *Tinospora crispa* on Obesity Models

Findings from Abu *et al.* (2014) and Samat *et al.* (2014) reported both Gelam honey and *T. crispa* had positive effects in controlling obesity. Their studies used two species of rats, which were Sprague-Dawley and Wistar rats. Rats in a normal control group were fed with normal diet (negative control), while obese induced rats group were fed with high-fat diet (HFD) to elicit induced-diet obesity. Then, for each species of rats were subdivided into four groups consisting of five rats per group with or without treatment. For treatment of experimental group, the induced HFD of Sprague-Dawley rats fed Gelam honey. Meanwhile, the induced HFD of Wistar rats fed *T. crispa*. Rats fed with HFD treated with orlistat (commercial drug to treat obesity), served as positive control.

Both percentages of body weight in rats fed with Gelam honey and *T. crispa*, respectively in the studies were significantly lower compared to rats fed with HFD. These results are almost similar with rats treated with orlistat. The normal rats (untreated high fat diet) showed the lowest percentage of body weight for both of Sprague-Dawley rats fed with Gelam honey and Wistar rats fed with *T. crispa* (Table 1). Overall, the body weight of rats in Gelam honey group was lower than body weight of rats in a *T. crispa* group. Two different species of rats were used in the studies, i.e. Sprague-Dawley rats were used for Gelam honey study, while Wistar rats were used to examine the effects of *T. crispa* in controlling obesity. Regardless of rats' species, both natural products have potential to reduce the excess weight gain and controls obesity. Another study conducted showed that consumption of

Table 1: Effects of Gelam honey and *T. crispa* on body weight of obesity rat models
(Adapted from Abu *et al.*, 2014; Samat *et al.*, 2014)

Parameter Groups	Percent increased body weight of Sprague-Dawley Rats (% increased body weight) fed with GH	Percent increased body weight of Wistar rats (% increased body weight) fed with TC
Normal control	20 ± 0.54	37 ± 1.70
High-fat diet (HFD) rats	33 ± 1.41	48 ± 1.28
HFD rats & fed with GH	22 ± 1.35*	-
HFD rats & fed with TC	-	41 ± 1.40*
HFD rats and fed with Orlistat	22 ± 0.55*	40 ± 1.06*

The results are reported as means ± SEM; * significant at $p < 0.05$ compared to HFD group using one-way ANOVA test. n= 5 rats/group. GH = Gelam honey, TC = *Tinospora crispa*.

Table 2: The level of Gelam honey on glucose, cholesterol, and triglycerides on Sprague-Dawley rats
(Adapted from Abu *et al.*, 2014; Samat *et al.*, 2014)

Parameter Groups	Glucose (mmol/L)	Cholesterol (mmol/L)	Triglycerides (mmol/L)
Normal control	2.86 ± 0.40	58.75 ± 1.18	2.56 ± 0.27
High-fat diet (HFD)	7.55 ± 1.08	71.58 ± 2.22	5.56 ± 0.27
HFD rats & fed with GH	3.72 ± 0.44*	53.25 ± 3.35*	3.97 ± 0.39*
HFD rats and fed with Orlistat	3.43 ± 0.50*	52.32 ± 2.16*	4.50 ± 0.30*

The result are reported as means ± SEM; * significant at $p < 0.05$ compared to HFD group using one-way ANOVA test. n= 5 rats/group. n= 5 Sprague-Dawley rats/group. GH = Gelam honey.

Table 3: Effect of *T. crispa* on glucose, cholesterol, and triglycerides on Wistar rats (Adapted from Abu *et al.*, 2014; Samat *et al.*, 2014)

Parameter Groups	Glucose (mmol/L)	Cholesterol (mmol/L)	Triglycerides (mmol/L)
Normal control	7.25 ± 0.48	14.03 ± 0.50	2.58 ± 0.10
High-fat diet (HFD)	13.75 ± 0.25	23.38 ± 0.23	4.65 ± 0.10
HFD rats & fed with TC	8.50 ± 0.30*	18.55 ± 0.26*	3.70 ± 0.11*
HFD rats and fed with Orlistat	11.50 ± 0.30*	13.00 ± 0.41*	3.58 ± 0.03*

The results are reported as means ± SEM; * significant at $p < 0.05$ compared to HFD group using one-way ANOVA test. n= 5 rats/group. n= 5 Wistar rats/group. TC = *Tinospora crispa*.

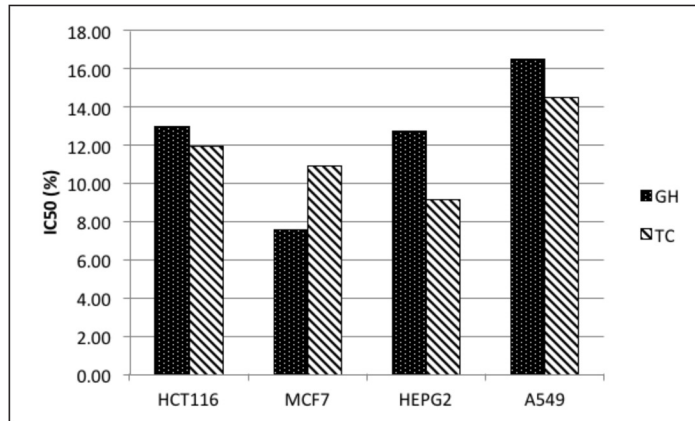


Figure 1: Effect of Gelam honey (GH) and *T. crispa* (TC) on several cancer cell lines. (Adapted from Abu *et al.*, 2011). HCT116 = colon cancer, MCF7 = breast cancer, HepG2 = liver cancer, A549 = lung cancer

Gelam honey on rat could reduce the level of triglycerides significantly if compared to control group (Samat *et al.*, 2017a). Abu *et al.*, (2014) reported that weight of HFD-Wistar rat fed with *T. crispa* could decrease about 5% if compared to untreated group. Thus, Gelam honey and *T. crispa* consumption may have medical benefit in controlling obesity.

Besides of body weight, Samat *et al.* (2014) and Abu *et al.* (2014) revealed that serum analysis from rats fed with Gelam honey and *T. crispa* had a significant decreased in glucose, cholesterol and triglycerides levels compared to rats in HFD and control groups (Tables 2 and 3). Interestingly, the results were comparable with rats treated with orlistat (Abu *et al.*, 2014). This study congruent with an experiment done by Samat *et al.* (2017b), which indicate that the HDF-Sprague Dawley rats fed with Gelam honey were significantly reduced the level of glucose, triglycerides and cholesterol respectively.

Effects of Gelam Honey and *T. crispa* on several cancer cell lines

Besides obesity, a study conducted by Abu *et al.*, (2011) showed that both Gelam honey and *T. crispa* inhibited cancer cell growth of colon (HCT116), breast (MCF7), liver (HepG2) and lung (A549) (Figure 1). The lowest concentration of Gelam honey was 7.57 v/v to inhibit breast cancer cell growth (MCF7). Meanwhile, the most potent concentration of *T. crispa* was 9.13

µg/ml to kill liver cancer cell lines (HepG2). Briefly, all 50% inhibitory concentrations (IC_{50}) were lower than half of sample concentration used in the study disclosed the potential of both natural products to kill the cancer cells even at low level.

Antioxidant Properties of Gelam Honey and *T. crispa*

Effects demonstrated by Gelam honey and *T. crispa* in controlling obesity and inhibit cancer cell growth may come from antioxidant properties. Both Gelam honey and *T. crispa* are rich with antioxidants. These were supported by several studies conducted by Hussein *et al.* (2011), Samat *et al.* (2014) and Abu *et al.* (2014). Phenolic contents, one of the antioxidant properties, were measured through total phenolic contents (TPC) in the honey and the herb. By using Gallic acid as a standard, TPC value for Gelam honey was 37.95 mg GAE/100g. Meanwhile, TPC value for *T. crispa* was 68.69 mgGAE/100g. The results indicated both natural products contained phenolic compounds to display their antioxidant capacity. TPC value for *T. crispa* was higher than Gelam honey because *T. crispa* extract was in concentrated form compared to Gelam honey in liquid form.

Conclusion

Based on the reported data, this short review unveils potentials of Gelam honey, one of Malaysia honey and herb; *T. crispa* reduces the excess weight gain and control obesity, and inhibit cancer cell growth. Even though those reported studies are still at the early stage, the

findings are a stepping-stone to explore more possibilities of Malay medicine to treat many diseases at the similar level of the modern medicine in the future. Moreover, the data can be used to support, protect and transfer this valuable knowledge and heritage to the next generation and to be proud as a part of Malay culture.

Acknowledgments

This research was funded by the Research Acculturation Collaborative Effort (RACE) 600-RMI/RACE 16/6/2 (1/2015) from the Ministry of Higher Education, Malaysia. All authors certify that no actual or potential conflict of interest in relation to this article exists.

References

- Abu, M. N., Samat, S., Kamarapani, N., Nor Hussein, F., & Ismail, W. I. W. (2014). *Tinospora crispa* Ameliorates Insulin Resistance Induced by High-fat Diet in Wistar Rats. *Evidence-based Complementary and Alternative Medicine*, 1-7.
- Abu, M. N., Salleh, M. A. M., Eshak, Z., Hasan, M., Hassan, H. F., & Ismail, W. I. W. (2011). Anti-proliferative Effect of *Tinospora Crispa* (L.) Hook. F. & Thompson and Gelam (*Melaleuca* sp.) Honey on Several Cancer Cell Lines. *Business, Engineering and Industrial Applications (ISBEIA), IEEE Symposium*, 545-548.
- Batugal, P. A., Kanniah, J., Lee, S. Y., & Oliver, J. T. (2004). *Medicinal Plants Research in Asia. Volume 1: The Framework and Project Workplans*. Serdang: International Plant Genetic Resources Institute.
- Bogdanov, S., Jurendic, T., Sieber, R., Gallmann, P., Jasmin, R. F., & Fawcett, K. A. (2012). Honey as Nutrient and Functional Food. *Journal of the American College of Nutrition*, 40(13): 1-37.
- Erejuwa, O. O., Sulaiman, S. A., & Ab Wahab, M. S. (2012). Honey - A Novel Antidiabetic Agent. *International Journal of Biological Sciences*, 17(4): 4400-4423.
- Erejuwa, O. O., Sulaiman, S. A., Wahab, M. S. A., Sirajudeen, K. N. S., Md Salleh, M. S., & Gurtu, S. (2010). Antioxidant Protective Effect of Glibenclamide and Metformin in Combination with Honey in Pancreas of Streptozotocin-induced Diabetic Rats.
- Field, B. C. T. (2013). What's New in Obesity? Neuroendocrinology of Obesity and the Potential for New Treatments, *Medicine*, 41(1): 53-57.
- Haliza, M. R. (2005). *Prinsip dan Amalan dalam Perubatan Melayu*. Kuala Lumpur: Universiti Malaya Press.
- Hamid, M., S. P. M. Bohari, M. S. Bastami, A. M. Ali, N. M. Mustapha, & K. Shari. (2008). "Evaluation of the Insulinotrophic Activity of Malaysian Traditional Plants Extract," *Journal of Biological Sciences*, 8(1): 201-204.
- Harun, M. P. (2006). *Kitab Tib: Ilmu Perubatan Melayu*. Kuala Lumpur: Perpustakaan Negara Malaysia.
- Hussein, S. Z., Kamaruddin, M. Y., Makpol, S., & Yusof, Y. A. M. (2011). Antioxidant Capacities and Total Phenolic Contents Increase with Gamma Irradiation in Two Types of Malaysian honey. *Molecules*, 16: 6378-6395.
- Ismail, W. I. W. (2016). A Review on Beekeeping in Malaysia: History, Importance and Future Directions. *Journal of Sustainability Science and Management*, 11(2): 70-80.
- Kadir, E. A., Sulaiman, S. A., Yahya, N. K., & Othman, N. H. (2013). Inhibitory Effects of Tualang Honey on Experimental Breast Cancer in Rats: A Preliminary Study. *Asian Pacific Journal of Cancer Prevention*, 14(4): 2249-2254.
- Kasikam, K. E. (2011). The Study of Local Wisdom Concerning the Consumption of Native Food and the Utilization of Indigenous Medicinal Vegetables for Health Care in Indonesia. *Potential of Local Knowledge and Practices: A Possibility for Sustainable Development?*, 65-85.

- Kleinert, S., & Horton, R. (2015). Rethinking and Reframing Obesity. *Lancet*, 385(9985): 2326-2328.
- Korner, J., & Aronne, L. J. (2004). Pharmacological Approaches to Weight Reduction: Therapeutic Targets. *The Journal of Clinical Endocrinology & Metabolism*, 89(6): 2616-2621.
- Mohamed, M., Sulaiman, S. A., Jaafar, H., & Salam, K. N. (2011). Antioxidant Protective Effect of Honey in Cigarette Smoke-induced Testicular Damage in Rats. *International Journal of Molecular Sciences*, 12(9): 5508-5521.
- Mohamud, W. N., Musa, K. I., Khir, A. S., Ismail, A. A., Ismail, I. S., Kadir, K. A., Kamaruddin, N. A., Yaacob, N. A., Mustafa, N., Ali, O., Isa, S. H., & Bebakar, W. M. (2011). Prevalence of Overweight and Obesity among Adult Malaysians: An Update". *Asia Pac J Clin Nutr.*, 20(1): 35-41.
- Najib, N. A., Rahman, N., Furuta, T., Kojima, S., Takane, K., & Mohd, M. A. (1999). Antimalarial Activity of Extracts of Malaysian Medicinal Plants". *J. Ethnopharmacol*, 64: 249-254.
- Noor, H., & Ashcroft, S. J. (1998). Pharmacological Characterisation of the Antihyperglycaemic Properties of *Tinospora crispa* Extract. *J. Ethnopharmacol*, 62: 7-13.
- Oqunbode, A. M., Ladipo, M., Ajayi, I. O., & Fatiregun, A. A. (2011). Obesity: An Emerging Disease. *Niger J Clin Pract*, 14(4): 390-394.
- Samat, S., Md Nor, N. A., Hussein, F. N., & Ismail, W. I. W. (2014). Effects of Gelam and Acacia Honey Acute Administration on Some Biochemical Parameters of Sprague-Dawley Rats. *BMC Complementary & Alternative Medicine*, 14: 1-8.
- Samat, S., Hussein, F. N., Eshak, Z., & Ismail, W. I. W. (2017a). Short-term Consumption of Gelam Honey Reduces Triglyceride Level. *International Food Research Journal. In press.*
- Samat, S., Enchang, F. K., Hussein, F. N., & Ismail, W. I. W. (2017b). Four Weeks Consumption of Malaysian Honey Reduces Excess Weight Gain and Improves Obesity-related Parameters in Obese Induced Rats. *Evidence-based Complementary and Alternative Medicine*, 1-10.
- Tungpradit, R., Sinchaikul, S., Phutrakul, S., Wongkham, W., & Chen, S. T. (2010). Anti-cancer Compound Screening and Isolation: *Coscinium fenestratum*, *Tinospora crispa* and *Tinospora cordifolia*. *Chiang Mai J. Sci.*, 37(3): 476-488.
- Ueda, J., Tezuka, Y., Banskota, A. H., Tran, Q. L., Tran, Q. K., Harimaya, Y., Saiki, I., & Kadota, S. (2002). Antiproliferative Activity of Vietnamese Medicinal Plants. *Biol. Pharm. Bull.*, 25: 753-760.