PharmaNutrition 11 (2020) 100180

Contents lists available at ScienceDirect

PharmaNutrition

journal homepage: www.elsevier.com/locate/phanu

Honey and glycemic control: A systematic review

Maryam Zamanian[a], Fatemeh Azizi-Soleiman[b,*]

[a] Department of Epidemiology, School of Health, Arak University of Medical Sciences, Arak, Iran
[b] Department of Nutrition, School of Health, Arak University of Medical Sciences, Arak, Iran

ARTICLE INFO

Keywords:
Honey
Blood glucose
Diabetes

ABSTRACT

Honey has long been reported to have curative effects for a number of diseases. The present review aims to provide the most recent findings regarding the potential role of honey in the management of glycemia. Eight studies met the inclusion criteria and were entered in the systematic review. Blood glucose or HbA1c was significantly reduced after consumption of honey in seven studies. However, blood glucose or HbA1C did not differ significantly in two studies, and significantly increased in two other studies following ingestion of honey. Due to the limited number of studies reviewed, no definite conclusion can be drawn regarding the effects of honey on glycemia in diabetic patients. Therefore, it is necessary to conduct large population-based randomized controlled trials with a sound methodology to verify any beneficial effects of honey on glycemia in humans.

1. Introduction

Diabetes is among the most prevalent chronic disorders across the world. It has been estimated that 451 million adults were afflicted with diabetes in 2017. The number of affected individuals is predicted to reach 693 million by 2045 [1]. According to the definition provided by the world health organization (WHO), hyperglycemia is defined as a fasting blood sugar (FBS) level higher than 126 mg/dL or a random blood glucose level higher than 200 mg/dL [2]. Hyperglycemia is the main diagnostic feature of diabetes and is responsible for diabetes-associated long-term complications including retinopathy, nephropathy, neuropathy, and cardiovascular diseases. Today, diabetes can be managed through appropriate modifications to lifestyle, dietary regimes, and physical activity [3].

Recently, there has been a focus on alternative managemental approaches in diabetes, one of which is the application of complementary supplements such as honey [4]. Honey is a sweet, sticky, yellow substance which is made by bees using the nectar of flowers. Although the main constituents of honey are independent of flower origin, some of the components may vary depending on the type of plants used by bees to make honey. Honey contains carbohydrates (i.e. monosaccharides such as fructose and glucose, disaccharides, trisaccharides, and oligosaccharides), organic acids (mainly gluconic acid), all the essential and non-essential amino acids (except for asparagine and glutamine), some enzymes, vitamins and minerals, flavonoids as well as polyphenols. As a result of these components, honey and its derivatives have been shown to possess remarkable antioxidant, antimicrobial, anti-inflammatory, anti-proliferative, anti-cancer, and anti-metastatic effects [5].

Despite all the beneficial properties of honey, the effects of this compound on blood sugar level are controversial due to its high carbohydrate content. Monosaccharides (including fructose and glucose) comprise about 75 % of the honey sugar content with fructose content being greater than glucose [6]. In fact, the glycemic impacts of honey and its main monosaccharides (i.e. fructose and glucose) have been reported to be 55, 19, and 100 respectively. This is while the glycemic loads of honey, fructose and glucose are 10, 2, and 10 respectively [7].

Beneficial effects have been reported in many studies on animal models of diabetes following consumption of honey. In one study, Rachmat et al. administered either Rambutan honey (0.5, 1 and 2 g/kg b.wt) or glibenclamide (0.065 mg/200 g b.wt.) to alloxan-induced diabetic wistar rats for 21 days [8]. The authors reported a significant reduction in blood glucose level in rats receiving either 0.5 g/kg b.wt honey or 0.065 mg/200 g b.wt glibenclamide. Nevertheless, the effects of honey on glycemia have been controversial in studies on diabetic humans. Therefore it seems critical to rigorously evaluate the effects of honey on human glycemia. For this reason, the primary objective of the present review was to provide the most recent findings regarding the potential role of honey in the management of glycemia.

2. Methods

2.1. Search strategy and study selection criteria

PubMed, Web of knowledge, Scopus and Cochrane Library were

* Corresponding author.
E-mail address: azizi.s@arakmu.ac.ir (F. Azizi-Soleiman).

https://doi.org/10.1016/j.phanu.2020.100180
Received 22 November 2019; Received in revised form 16 January 2020; Accepted 16 January 2020
Available online 23 January 2020
2213-4344/ © 2020 Elsevier B.V. All rights reserved.

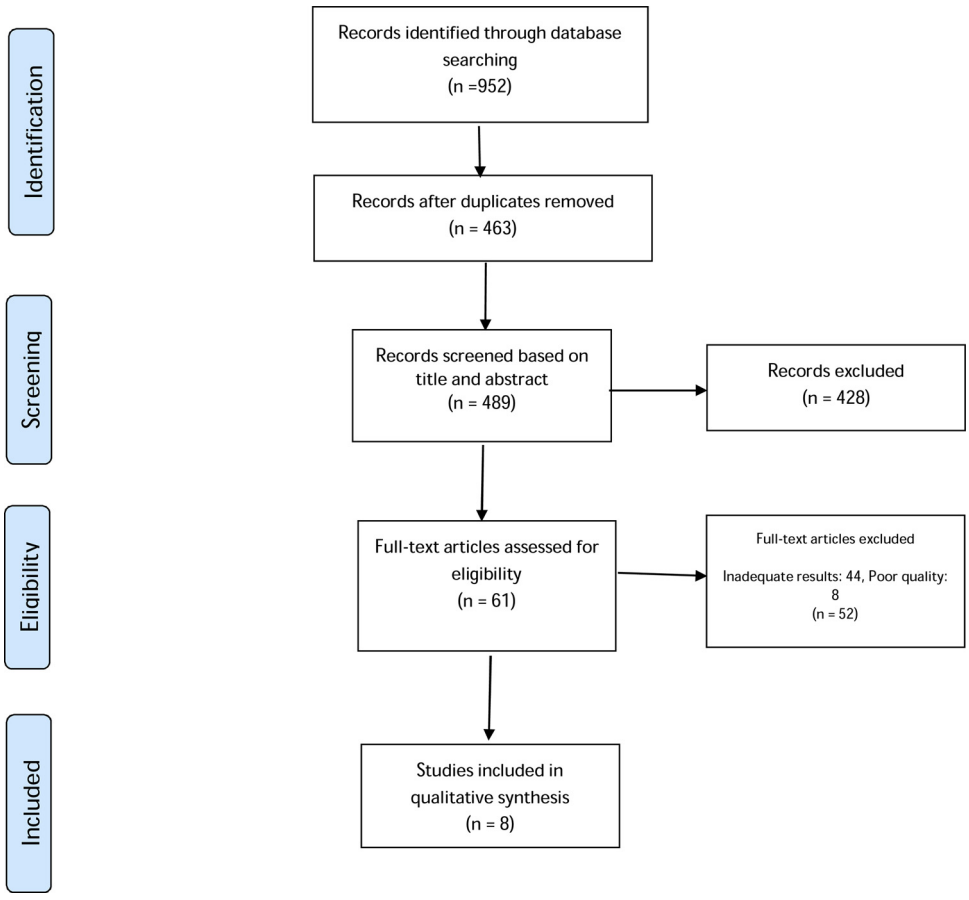

Fig. 1. Study selection process base on PRISMA 2009 Flow Diagram.

systematically searched using the MeSH terms; honey and diabetes. Using Boolean operators and the "*" truncation character, the combinations of ("Honey") AND ("Diabet* OR "Fasting Blood Glucose" OR "Blood glucose" OR "Blood sugar") were applied. All studies published prior to June 2018 were screened.

2.2. Inclusion and exclusion criteria

This was a systematic review of published content reporting the effects of honey supplementation on glycemia. Randomized controlled trials (RCTs), clinical controlled trials (CCTs), clinical trials (CTs) and case reports (CRs) evaluating the effects of honey on blood sugar level were selected. These studies were systematically reviewed to recruit the most relevant works. Animal studies, studies that supplemented honey via inhalation, and those evaluating the short-term impacts of honey on blood sugar were excluded.

2.3. Data extraction and quality assessment

Titles and abstracts were independently screened by both reviewers enlisted as authors in order to identify relevant studies. The eligibility of the studies was independently determined by reading the full texts by the same two reviewers. Disagreements were resolved by discussing the eligibility criteria of the studies. The reference lists of the selected articles were screened in order to find additional relevant studies. The final decision for selecting or omitting the studies was made based on the full-texts.

3. Results

A total of 952 studies were identified after an initial search of the selected databases. Once duplicate publications were removed, 489 studies remained that were screened for relevancy based on their titles and abstracts.

Finally, a total of 61 full-text articles were reviewed, among which 8 studies met the inclusion criteria for being considered in the systematic review (Fig. 1).

The selected studies had been published between 2004 and 2017 and were carried out in Egypt, the United Arab Emirates, Iran, Switzerland, Turkey, Malaysia and New Zealand. The studies had been performed as either cross-over (3 studies) (9–11), parallel (3 studies) (12–14) or before-after designs (2 studies) (15, 16).

The subjects of these studies included both healthy individuals and diabetic patients in non-homogenous populations. The duration of the interventions (i.e. honey administration) varied from 8 days to 4 months in different studies. The types and doses of honey consumed in the different studies have been represented in Table 1.

Honey consumption significantly reduced blood glucose level in four studies [9,10,14,16]. In the cross-over study conducted by Abdul Rahman et al., the mean percentage of FBS changes in the patients receiving honey were −21.94 % and −15.22 % for intervention to control and control to intervention groups, respectively [9]. Honey consumption significantly reduced FBS levels (ranging from 4 to 6 percent) in two out of four studies [14,16]. Furthermore, Despland et al. described that consuming a diet containing 25 % energy (either as honey or pure fructose-glucose) slightly reduced postprandial blood glucose levels [10].

In two other reports assessing relatively long-term (3–4 months) effects of honey on glycemia, the interventions significantly reduced HbA1c levels [9,13]. However, neither blood glucose nor HbA1c changed in the honey-administered groups in two other studies [11,15]. On the contrary, honey consumption was reported to significantly

Table 1
The description of studies that met the eligibility criteria.

Authors	Year	Country	Design	Participants	Sex	Sample size (Intervention/ Control)	Intervention	Duration	Outcomes	Main Findings
Abdulrahman MM, et al	2013	Egypt	Cross-over	Participants with IDDM aged 4–18 years	10 M, 10F	10 patients in each group	0.5 mL/kg body weight per day clover honey	12 w	• -FBS • -PSG • -FCP • -PCP • -HbA1c	Long-term effects of honey: statistically significant reductions in FBS (P = 0.005), PSG (P = 0.000), and HbA1c (P = 0.043), and significant increases in FCP (P = 0.002) and PCP (P = 0.003)
Al-Waili N.S	2004	UAE	Before-after	Healthy subjects	5M, 3F	8	250 mL of water containing 75 g of honey	15 d	FBS	Decreased FBS by 6 %
Bahrami M, et al	2009	Iran	Parallel	Participants with NIDDM [2]	13 M, 35F	25/23	First 2 weeks: 1 g/kg/day; second 2 weeks: 1.5 g/kg/day; third 2 weeks: 2 g/kg/day; and last 2 weeks: 2.5 g/kg/day	8 w	• -FBS • -HbA1c	No significant differences in the FBS between the two groups, after adjustment for the baseline values. Significant increase in HbA1c in honey group (P < 0.01).
Despland C,et al	2017	Switzerland	Cross over	Healthy normal weight males	M	8 patients in each group	1: a control, low sugar, weight maintenance diet 2: a high honey, weight-maintenance diet 3: a high fructose + glucose, weight-maintenance diet	8 d	• -Glucose tolerance • -Postprandial suppression of glucose production	Lower postprandial glucose and insulin concentrations in honey and fructose:glucose mixture groups than control group on day 7. No significant difference in glucose tolerance or postprandial suppression of glucose production between groups on day 8.
Enginyurt O,et al	2017	Turkey	Parallel	Participants with NIDDM and healthy people	Men and women was equally distributed	32/32	Treatment groups (diabetic): receiving 0, 5, 15, or 25 g honey/ day/personControl groups (healthy) receiving 0, 5, 15, or 25 g honey/day/person	4 m	HbA1c	Decreased HbA1c in the group who were given honey.
Husniati L, et al	2013	Malaysia	Before-after	Healthy postmenopausal women	F	40	20 g/day of Tualang honey	4 m	FBS	A significant increase in the FBS level at four months of study.
Whitfield P,et al	2014	New Zealand	Cross-over	Participants with NIDDM	7 M, 5F	12 patients in each group	control: regular kanuka honey, intervention: 53.5 g of a cinnamon-, chromium- and magnesium formulated honey	40 d	• -FBS • -Fasting insulin • -HbA1c	No significant difference in FBS between the two treatments (95 % CI − 2.6 to 0.07). No statistically significant change in HbA1c or fasting insulin.
Yaghoobi N,et al	2008	Iran	Parallel	Overweight or obese subjects aged 20–60 years	24 M,31 F	38/17	Experimental group:70 g/d natural honey Control group: 70 g/d sucrose	30 d	FBS	A mild reduction in FBS (4.2 %) in honey group.

IDDM: Diabetes mellitus type 1; M: Male; F: Female; W: weeks; FBS: Fasting blood glucose; PSG: 2-h postprandial serum glucose; FCP: Fasting C-peptide; PCP: 2-h postprandial C-peptide; HbA1c: Glycosylated hemoglobin; D: days; NIDDM: Diabetes mellitus type 2; M: Months.

increase blood glucose [15] and HbA1c [12] levels.

4. Discussion

There is inconclusive evidence regarding the effects of honey consumption on glycaemia. Most animal studies have reported beneficial dose-dependent effects of honey on blood sugar [17–19]. On the other hand, the number of reliable and well-designed human trials is limited, making it difficult to reach a conclusive verdict. Such controversies may be partly explained by the heterogeneity of the study designs and the participants in the various studies. As mentioned, the studies included in the present systematic review also showed heterogeneity in the health status of the participants, study duration, and the dose and type of administrated honey. These variations may be responsible for the observed differences in obtained results. Particularly, honey composition (such as glucose to fructose ratio or the presence of impurities) can influence the results obtained in trial studies [20].

In the present systematic review, we excluded papers investigating the short-term effects of honey on blood glucose. Multiple studies have evaluated the effects of various intervals of honey consumption on glycemia level in both healthy and diabetic individuals. In comparison with other sugars, honey was shown to profoundly boost glucose level immediately after ingestion [21–25]. Katsilambros et al. reported that both honey and bread increased blood glucose level to a similar extent [26]. Various regulatory effects of honey on glycemic response have been proposed; including lowering carbohydrate absorption, inducing insulin-like activities, as well as promoting antioxidant activities through its bioactive components [27]. The long-term effects of honey consumption (12–16 weeks) on blood glucose level have been promising in some reports [13,15,28]. In contrast, no signifiicant effects were noted for honey on glycemic status in diabetic patients in a study by Husniati et al. [15]. However, Husniati et al. did not measure HbA1c level which is a more reliable indicator of glycaemia than FBS. Furthermore, while Husniati et al. recruited healthy individuals in their study, studies which included diabetic patients reported positive impacts on glycemic status following honey supplementation [13,28]. Nevertheless, we also encountered some limitations in the study conducted by Abdulrahman et al. [28]; namely, small sample size, heterogeneity in the levels of baseline parameters between studied groups, and not considering the effects of dietary regimens, lifestyle, and seasonal variations on glycemia. Furthermore, Enginyurt et al. recruited healthy individuals as a control group in their study which somehow limits the applicability of their results to diabetic patients [13]. Providing a sound judgment on the effects of honey consumption on glycemia level may be difficult considering such variations in methodology and participants across different studies.

Only two studies reported the effects of honey on insulin and C-peptide, with controversial results. Both studies were conducted on diabetic patients. While the effect of honey on C-peptide was favorable after 12 weeks [9], its effect on insulin level was not significant after 40 days [11]. The result of the latter study is in accordance with previous studies evaluating the short-term effect of honey ingestion on C-peptide in diabetic patients [29]. The impact of honey on insulin and C-peptide level still needs more long-term studies to reach better conclusions.

Some of the beneficial effects of honey on blood glucose level can be attributed to fructose functions. Fructose can induce glycogenesis within the liver contributing to glucose biochemical hydrolysis [30]. Accordingly, fructose supplementation in animal models of diabetes has been associated with reduced blood glucose level [31,32]. Aeberli et al. further showed that the administration of fructose (80 g/d) significantly decreased hepatic insulin sensitivity in healthy young men [33]. A systematic review and meta-analysis by Livesey and Taylor demonstrated that the intake of moderate-dose fructose ($\leq$ 50 g/d) improved both HbA1c and triglyceride levels [34]. However, one should be cautious regarding possible long-term complications of such regimens in patients with disorders of glucose and lipid metabolism. Therefore, it is recommended to perform long-term studies to ensure the safety of fructose-based interventions in at-risk populations. Overall, the fructose content of honey may in part explain the variations observed in different studies. The fructose/glucose ratio of honey ranges from 0.4 to 1.6 or even higher [35]. Accordingly, we noted that only three of the eight studies reviewed here reported the fructose/glucose ratio of the supplemented honey in their studies. These were as follows; 30/38 in Al-Waili et al. [16], 45/2 in Bahrami et al. [12], and 23.9/40.9 in Despland et al. [10]. This ratio can also impact the glycemic index of different honeys. Different GIs change glycemia in different manners. This may also explain the conflicting results obtained from different studies.

4.1. Conclusion

Due to the limited number of studies reviewed, no definite conclusion can be drawn regarding the effects of honey on glycemia in diabetic patients. Therefore, it is necessary to conduct large population-based randomized controlled trials with a sound methodology to verify any beneficial effects of honey on glycemia level in humans. It is further advised to conduct long-term trials on the effects of honey supplements with different fructose/glucose ratios in patients with diabetes.

Funding

This work was supported by the School of Health, Arak University of Medical Sciences.

Author's contributions

MZ and FAZ both contributed to the protocol for this review, drafting and revising the draft, approval of the final version of the manuscript, and agreed for all aspects of the work.

Declaration of Competing Interest

None.

Acknowledgment

We are grateful to Dr Zahra Maghsoodi for her suggestions during the drafting of this review.

References

[1] N. Cho, J. Shaw, S. Karuranga, Y. Huang, J. da Rocha Fernandes, A. Ohlrogge, et al., IDF diabetes atlas: global estimates of diabetes prevalence for 2017 and projections for 2045, Diabetes Res. Clin. Pract. 138 (2018) 271–281.
[2] WHO. Diabetes programme, about diabetes, intermediate states of hyperglycemia [Available from: http://www.who.int/diabetes/action_online/basics/en/index2.html.
[3] World Health Organization, Global Health Risks: Mortality and Burden of Disease Attributable to Selected Major Risks, (2009) Geneva: Switzerland. Available from: < http://www.who.int/healthinfo/global_burden_disease/GlobalHealthRisks_report_full.pdf > .
[4] R. Chawla, P. Thakur, A. Chowdhry, S. Jaiswal, A. Sharma, R. Goel, et al., Evidence based herbal drug standardization approach in coping with challenges of holistic management of diabetes: a dreadful lifestyle disorder of 21st century, J. Diabetes Metab. Disord. 12 (1) (2013) 35.
[5] S. Samarghandian, T. Farkhondeh, F. Samini, Honey and health: a review of recent clinical research, Pharmacognosy Res. 9 (2) (2017) 121–127.
[6] P.M. da Silva, C. Gauche, L.V. Gonzaga, A.C.O. Costa, R. Fett, Honey: chemical composition, stability and authenticity, Food Chem. 196 (2016) 309–323.
[7] L.K. Mahan, S. Escott-Stump, J. Raymond, Krause's Food & Nutrition Care Process, Saunders, Philadelphia, PA, 2011.
[8] I.I. Rachmat, E.R. Yuslianti, G.F. Permatasari, T. Koswara, Antihyperglycemic effect of rambutan honey in alloxan-induced diabetic wistar rats, J. Pharmacol. Toxicol. 12 (1) (2017) 42–49.
[9] M.M. Abdulrhman, M.H. El-Hefnawy, R.H. Aly, R.H. Shatla, R.M. Mamdouh, D.M. Mahmoud, et al., Metabolic effects of honey in type 1 diabetes mellitus: a randomized crossover pilot study, J. Med. Food 16 (1) (2013) 66–72.
[10] C. Despland, B. Walther, C. Kast, V. Campos, V. Rey, N. Stefanoni, et al., A

randomized-controlled clinical trial of high fructose diets from either Robinia honey or free fructose and glucose in healthy normal weight males, Clin. Nutr. ESPEN 19 (2017) 16–22.
[11] P. Whitfield, A. Parry-Strong, E. Walsh, M. Weatherall, J.D. Krebs, The effect of a cinnamon-, chromium- and magnesium-formulated honey on glycaemic control, weight loss and lipid parameters in type 2 diabetes: an open-label cross-over randomised controlled trial, Eur. J. Nutr. 55 (3) (2016) 1123–1131.
[12] M. Bahrami, A. Ataie-Jafari, S. Hosseini, M.H. Foruzanfar, M. Rahmani, M. Pajouhi, Effects of natural honey consumption in diabetic patients: an 8-week randomized clinical trial, Int. J. Food Sci. Nutr. 60 (7) (2009) 618–626.
[13] O. Enginyurt, L. Cakir, A. Karatas, S. Cankaya, Y. Kaya, H. Handan Tugcu, et al., The role of pure honey in the treatment of diabetes mellitus, Biomed. Res. (India) 28 (7) (2017) 3305–3312.
[14] N. Yaghoobi, N. Al-Waili, M. Ghayour-Mobarhan, S.M. Parizadeh, Z. Abasalti, Z. Yaghoobi, et al., Natural honey and cardiovascular risk factors; effects on blood glucose, cholesterol, triacylglycerole, CRP, and body weight compared with sucrose, Sci. World J. 8 (2008) 463–469.
[15] Y.L. Husniati, N.H.N. Hazlina, A.K. Azidah, M.N. Norhayati, S.S. Amrah, H.I. Idiana, et al., Safety of honey in postmenopausal women, Int. Med. J. 20 (1) (2013) 25–28.
[16] N.S. Al-Waili, Natural honey lowers plasma glucose, C-reactive protein, homocysteine, and blood lipids in healthy, diabetic, and hyperlipidemic subjects: comparison with dextrose and sucrose, J. Med. Food 7 (1) (2004) 100–107.
[17] N.H. Abou El-Soud, N.A. El-Laithy, E.R. Youness, N.A. Mohamed, A.M.M. Ibrahim, Natural honey lowers plasma glucose, insulin and C-peptide in streptozotocininduced diabetic rats: comparison with metformin, Pharm. Lett. 8 (9) (2016) 141–145.
[18] O. Nasrolahi, R. Heidari, F. Rahmani, F. Farokhi, Effect of natural honey from Ilam and metformin for improving glycemic control in streptozotocin-induced diabetic rats, Avicenna J. Phytomed. 2 (4) (2012) 212–221.
[19] E.O. Omotayo, S. Gurtu, S.A. Sulaiman, M.S. Ab Wahab, K.N.S. Sirajudeen, M.S.M. Salleh, Hypoglycemic and antioxidant effects of honey supplementation in streptozotocin-induced diabetic rats, Int. J. Vitam. Nutr. Res. 80 (1) (2010) 74–82.
[20] M. Miguel, M. Antunes, F. M, Honey as a complementary medicine, Integr. Med. Insights 12 (2017) 1178633717702869.
[21] A. Samanta, A.C. Burden, A.R. Jones, Plasma glucose responses to glucose, sucrose, and honey in patients with diabetes mellitus: an analysis of glycaemic and peak incremental indices, Diabet. Med. 2 (5) (1985) 371–373.
[22] P. Shambaugh, V. Worthington, J.H. Herbert, Differential effects of honey, sucrose, and fructose on blood sugar levels, J. Manipulative Physiol. Ther. 13 (6) (1990) 322–325.
[23] N.S. Al-Waili, A. Haq, Effect of honey on antibody production against thymus-dependent and thymus-independent antigens in primary and secondary immune responses, J. Med. Food 7 (4) (2004) 491–494.
[24] O.P. Agrawal, A. Pachauri, H. Yadav, J. Urmila, H.M. Goswamy, A. Chapperwal, et al., Subjects with impaired glucose tolerance exhibit a high degree of tolerance to honey, J. Med. Food 10 (3) (2007) 473–478.
[25] A. Ahmad, M.K. Azim, M.A. Mesaik, R.A. Khan, Natural honey modulates physiological glycemic response compared to simulated honey and D-glucose, J. Food Sci. 73 (7) (2008) H165–7.
[26] N.L. Katsilambros, P. Philippides, A. Touliatou, K. Georgakopoulos, L. Kofotzouli, D. Frangaki, et al., Metabolic effects of honey (alone or combined with other foods) in type II diabetics, Acta Diabetol. Lat. 25 (3) (1988) 197–203.
[27] M.E. Cortes, P. Vigil, G. Montenegro, The medicinal value of honey: a review on its benefits to human health, with a special focus on its effects on glycemic regulation, Ciencia E Investigacion Agraria. 38 (2) (2011) 303–317.
[28] M. Abdulrhman, M. El Hefnawy, R. Ali, I. Abdel Hamid, A. Abou El-Goud, D. Refai, Effects of honey, sucrose and glucose on blood glucose and C-peptide in patients with type 1 diabetes mellitus, Complement. Ther. Clin. Pract. 19 (1) (2013) 15–19.
[29] M. Abdulrhman, M. El-Hefnawy, R. Hussein, A. Abou El-Goud, The glycemic and peak incremental indices of honey, sucrose and glucose in patients with type 1 diabetes mellitus: effects on C-peptide level-a pilot study, Acta Diabetol. 48 (2) (2011) 89–94.
[30] E. Van Schaftingen, V. A, Stimulation of glucose phosphorylation by fructose in isolated rat hepatocytes, Eur. J. Biochem. 179 (1) (1989) 173–177.
[31] S. Kwon, Y.J. Kim, K. MK, Effect of fructose or sucrose feeding with different levels on oral glucose tolerance test in normal and type 2 diabetic rats, Nutr. Res. Pract. 2 (4) (2008) 252–258.
[32] O.O. Erejuwa, S.A. Sulaiman, M.S. Wahab, Fructose might contribute to the hypoglycemic effect of honey, Molecules 17 (2) (2012) 1900–1915.
[33] I. Aeberli, M. Hochuli, P.A. Gerber, L. Sze, S.B. Murer, L. Tappy, et al., Moderate amounts of fructose consumption impair insulin sensitivity in healthy young men: a randomized controlled trial, Diabetes Care. (2012) DC_120540.
[34] G. Livesey, T. R, Fructose consumption and consequences for glycation, plasma triacylglycerol, and body weight: meta-analyses and meta-regression models of intervention studies, Am J Clin Nutr. 88 (5) (2008) 1419–1437.
[35] O. Bobis, D.S. Dezmirean, A.R. Moise, Honey and diabetes: the importance of natural simple sugars in diet for preventing and treating different type of diabetes, Oxid. Med. Cell. Longev. 2018 (2018) 4757893.