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Evaluation of Anti - Hyperglycaemic activity of *Madhu* (Honey) inHigh fat diet induced diabetes - An Experimental study

Dr. M .Santhyanarayana[1] , K .Sukumar[2]

[1,2]Assistant Professor Department of Cardiology, Guang′anmen Hospital,
China Academy of Chinese Medical Sciences , Community Healthcare Center of Shangzhuang

ABSTRACT

Background: *Madhu (honey) is the only naturally occurring sweetener that has been around for a very long period. It's been used for centuries as both a meal and a medication. For example, Kaphaja Vyadhi (diseases caused by Kapha Dosha) and Sthoulya (obesity owing to Medo Dhatu Vruddhi; an increase in adipocyte bulk) are both conditions for which Madhu is recommended in Ayurvedic literature as a Sarvapramehahara (curer of all forms of Prameha). The purpose of this research is to see whether Madhu has any effect on blood sugar levels. Substances and Techniques: Obese Wistar Albino Rats were fed a high-fat diet (HFD) and given the diabetes-inducing drug streptozotozin (STZ). The dosage conversion formula called for 30 days of treatment with Madhu that had been combined with Triphala Kashaya (Samyoga) and treated with Triphala Kashaya (Samskara). Kevala Madhu (pure honey), Jala Samskaarita Madhu (honey processed with water), and a conventional medicine (Pioglitazone) were compared statistically with a control group, a high-fat diet group, and another group that lost weight. Initial results showed that all treatment groups saw a decrease in body weight and blood glucose levels. Animals given a combination of Triphala Kashaya and Madhu saw their body weights recover and their levels of glucose, cholesterol, and triglycerides drop significantly after treatment. The research found that Madhu combined with Triphala Kashaya (Samyoga group) had significantly more anti-hyperglycaemic and anti-hyper cholestraemic action than Samskaritha Madhu (processed honey group).*

Keywords: *Activity against hyperglycemia, high-fat diet (Honey), Triphala, Samyoga, Samskara, (Streptozotozin), and (STZ)*

Introduction

Lifestyle illnesses, which include diabetes, hypertension, cancer, obesity, and a broad range of metabolic disorders, are the most widely publicized health hazards of the modern period since they are responsible for more deaths than any other condition globally. It is estimated that 79.4 million people in India would have diabetes by 2030, the highest number of any country. Obesity [2] raises the possibility of developing Type 2 Diabetes mellitus. Dyslipedaemia is characteristic of insulin resistance and Type 2 Diabetes mellitus [3, 4], and dysfunctional adipose tissue [3, 4] is associated with obesity. [5] Since both Sthoulya (obesity) and Prameha (diabetes) are Santarpanotthavyadhis (diseases induced owing to excess feeding) [7], and share comparable causal causes, classical Ayurvedic literatures provide thorough narrative regarding the role of Medodhathu in both conditions. Prameha Samprapti is often attributed to abnormal Medodhatu (Bahuabaddhamedas). Sthoola Prameha (obese diabetes) and Krisha Pramehi (lean diabetes) are subcategories of Prameha [8], the former of which requires idiomatic care. Long-term treatment techniques have therapeutic implications that incorporate not just medication but also nutrition and exercise.

Sarvapramehahara, which combines Madhu and Triphala Kashaya, is one of Ayurveda's most often recommended therapeutic

techniques [10]. [11]

Though *Purana Madhu* (old honey) alone has been attributed with *Lekhanakarma* (scrapping), which is indicated in *Sthoulya*, processing with *Dravyas* having similar activities are mentioned in few texts of Ayurveda. Contradictory statements in classical texts regarding heating of *Madhu* necessitate detailed pre-clinical investigations on safety and efficacy. High fat diet along with low dose streptozotocin induced diabetes model in experimental animals is said to mimic type 2 diabetes in human beings. Hence present study was undertaken to evaluate anti - hyperglycaemic activity of honey in processed and unprocessed forms in Streptozotozin/High fat diet induced diabetes in wistar albino rats.

Materials and Methods

Freshly extracted un-processed honey was obtained from the Bhagamandala Honey society, Kodagu district, Karnataka and was stored in dry amber coloured glass bottles for one year to make it *Purana* (aging process). Streptozotozin was procured from SRL chem-company. Deseeded fruits of *Haritaki* (*Terminalia chebula* Retz), *Vibhitaki* (*Terminallia bellerica* Roxb) and *Amalaki* (*Embellica officinalis* Gaertn) were procured from local market. Fruits were pounded to obtain *Yavakuta* (coarse powder) and mixed thoroughly to obtain *Triphala Choorna* (fine powder).

Kashaya (decoction) was prepared as per standard protocol of Sharangadhara Samhita. *Madhupaka Vidhi* (processing honey) was carried out using *Madhu* and *Triphala Kashaya* in equal proportions as per Kaiyadeva Nighantu with minor modifications. [12] *Madhu* and *Triphala Kashaya* were mixed in equal proportions for *Kashaya Samskara* process where as *Madhu* and water was mixed in the ratio of 8:1 for *Jala Samskara*. Instead of heating *Madhu* directly over flame, water bath at (95^0 C) was used during condensation process to avoid charring of honey. [13] Same procedure was adopted for preparation of *Jala Samskaritha Madhu* (honey processed with water).

Table no. 1: Composition of Normal and High FatDiet

Normal Diet requirement per day per rat		High Fat Diet requirement per day per rat	
Constituents	**Weight in gm**	**Constituents**	**Weight in gm**
Whole Wheat	3.24	Whole Wheat	2.72
Yellow Corn	3	Yellow Corn	2.72
Barley	1.8	Barley	1.36
Milk Powder	1.8	Milk Powder	2.04
Bone Meal	0.12	Bone Meal	0.13
Calcium Chloride	0.12	Calcium Chloride	0.13
Salt	0.12	Salt	0.13
Oil	1.8	Oil	1.36
Vit. B12	0.048	Vit. B12	0.054
		Butter	1.363

Preparation of Normal and High fat diet

High fat diet for wistar albino rats was prepared understandard laboratory conditions. Ingredients of diet [14](Table 1) were mixed, converted into pellets, dried in hotair oven and stored in cool and dry container.

Experimental study

Ethical clearance was obtained from Institutional ethics committee, JSS College of Pharmacy, Mysuru (IEAC 210/2016) prior to commencement of the experimental study. Healthy Wistar Albino male rats weighing between 100-150 g were procured from animal breeding facility, department of Pharmacology, JSS College of Pharmacy, Mysuru.

Experimental animals were sorted in 8 groups comprising 6 animals in each group (Table 2). Prior to commencement of experimentation, experimental animals were acclimatised for 15 days under standard laboratory conditions. Regular rat feed and potable water was provided during this period.

Anti-hyperglycaemic study was conducted for 75 days comprising high fat diet administration for 30 days followed by induction of hyperglycaemia with two consecutive doses of Streptozotozin injection (30mg IP) as per standard protocol. [15] After analysing serum glucose concentration, treatment to elicit anti-hyperglycaemic activity was continued for 30 days. Except normal control group animals, other groups received high fat diet ad libitum throughout the study period. After induction of hyperglycaemia test drug was administered simultaneously along with high fat diet. Normal group animals were provided with regular pellets and water.

The standard drug, pioglitazone was administered in the dose of 30 mg/kg. [16] The dose of the test drug (*Kevala Madhu, Jala Samskarita Madhu, Madhu* mixed with *Triphala Kashaya* and *Madhu* processed with *Triphala Kashaya*) was determined and carried out as per the earlier study as *Avaleha Pramana.* [17] Dose for the rat was calculated on the basis of conversion formula. [18] 860mg/200g of honey was fixed as initial dose and calculated periodically based on change in body weight during study period. Distilled water was used as media to administer *Samskaritha Madhu*, whereas group 6 animals received *Madhu* mixed with *Triphala Kashaya* (*Samyoga* group). Group 6 and 8 received *Madhu* mixed with *Triphala Kasaya* and water respectively. Body weight and Blood glucose levels of the animals was recorded before commencement of experiment and on 1st, 2nd, 3rd, 4th, 5th, 6th, 7th, 8th, 9th and 10th weeks. Blood was collected from the retro-orbital area on 76th day and serum was subjected to cholesterol and triglycerides estimation. Data was statistically analysed by ANOVA method using Graph pad prism 6 software for assessing level of significanc

Table no. 2: Showing details of experimental groups

Group 1	Normal diet control group
Group 2	High fat diet –untreated Group
Group 3	High fat diet+streptozotozin - untreated group
Group 4	High fat diet + streptozotozin - treated with pioglitazone
Group 5	High fat diet + streptozotozin - treated with *Triphala Kashaya Samskaritha Madhu*
Group 6	High fat diet + streptozotozin - treated with *Triphala Kashaya* with *Madhu*
Group 7	High fat diet + streptozotozin - treated with *Jala Samskaritha Madhu*
Group 8	High fat diet + streptozotozin - treated with *Purana Madhu*

Observation and Results

All animals pertaining to 8 groups remained healthy with normal food and water intake and no abnormal behaviour was noticed during acclimatisation period.

Body weight: (Graph 1)

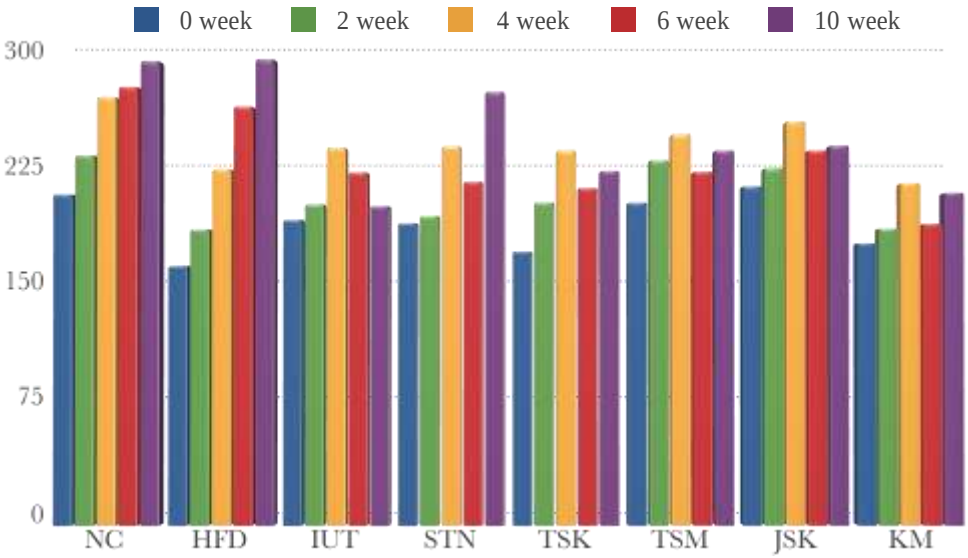
All animals gained weight

till 5th week (before induction of hyperglycaemia) except in control group animals (Normal diet). After administering STZ (except in normal control and HFD group), all other group animals lost weight partially during 5th and 6th week but gained as the treatment continued with different forms of *Madhu* as well as standard drug. Induced untreated group animals continued to loose body weight. Observation made at the end of 10th week (end of experimentation period) revealed gain in the body weight in all treated groups except in induced untreated group. Among treated groups, standard drug treated animals gained bodyweight faster compared to other treated groups and among Madhu treated group, Kevala Madhu (Unprocessed and without mixing with Kashaya) treated group gained relatively more weight of 20-25 gm.

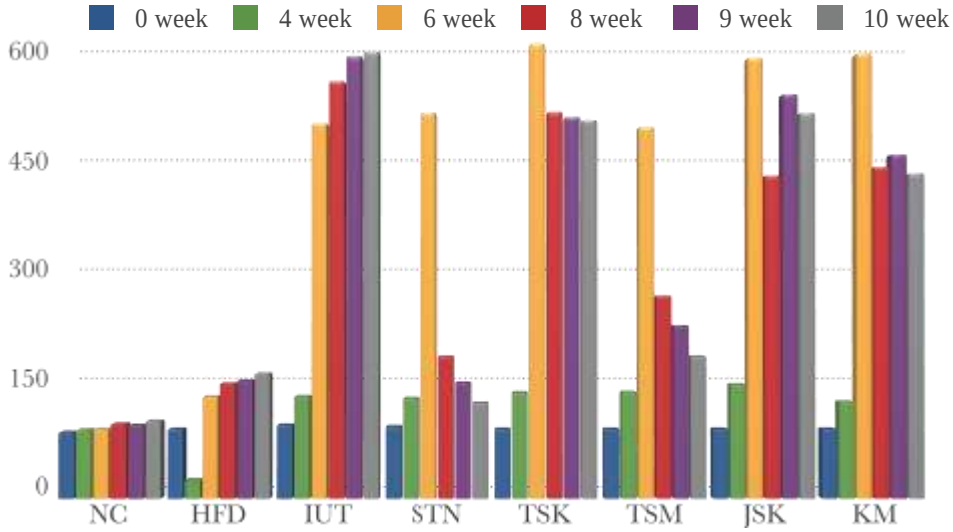
Serum glucose levels: (Graph 2)

After administration of STZ by 5th week, RBS levels of all treated groups as well as induced untreated groups increased considerably and changes were statistically significant compared to control group as well as HFD group (non diabetic). On 7th week, RBS levels reduced marginally in all treated groups. On 8th week, RBS levels among *Triphala Kashaya* + *Madhu* (TSM), *Jala Samskarita Madhu* (JSK), *Kevala Madhu* (KM) and Standard drug (STN) drug treated animals reduced considerably except in *Triphala Kashaya Samskarita Madhu* (TSK) group. When compared between honey treated groups, RBS levels of TSK group remained higher and TSM at comparatively lower point. At the end of 10th week, TSM and s tandard drug treated animals had RBS concentrations at relatively lower point and statistically significant ($p<0.05$) compared to TSK, KM, JSK and untreated group animals.

Graph no.1: Body weight (In grams)



Graph no. 2: RBS of all the group (mg/dl)



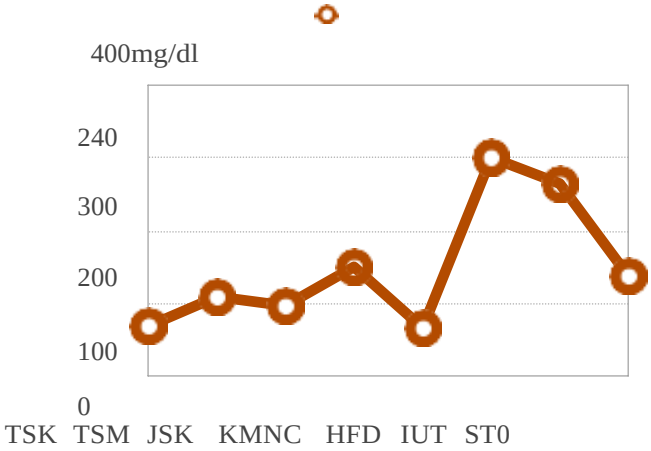
Serum cholesterol: (Graph 3)

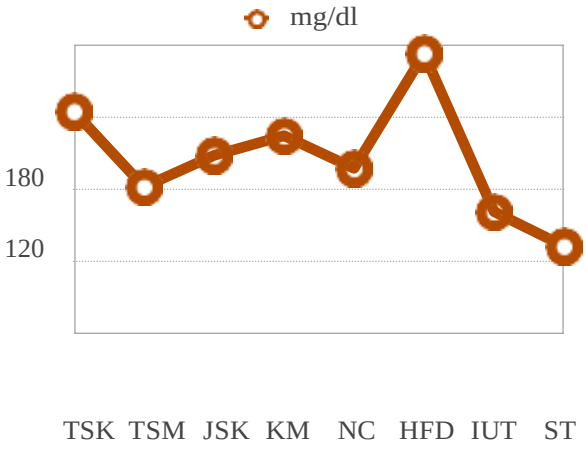
Among all treated groups (including standard drug experimental animals), TSK treated group animals showed very low concentration of cholesterol. Among HFD and induced untreated groups, cholesterol concentration remained relatively higher and statistically significant ($p<0.05$) compared to other treated groups and control group.

Serum Triglycerides: (Graph 4)

Triglycerides level recorded among all treated groups as well as control group animals at the end of experiment remained at low. Increase in triglycerides level was noticed only in HFD group. Among changes observed between all treated groups and control group, STN drug treated experimental animals showed decrease in triglycerides level but was not significant statistically.

Graph no. 3: Effect on S. Cholesterol (mg/dl)Graph no. 4: Effect on S.Triglycerides (mg/dl)





Discussion

Honey bees collect nectar from different sources and presence of harmful microbes including *Clostridium botulinulinum* have been reported in few tested samples.

[19] Probably such incidents might have prompted honey processing during medieval period. Toxicity due to honey is reported to be reduced after processing. [20] Though *Purana Madhu* alone has been attributed with *Lekhanakarma*, which is indicated in *Sthoulya*, processing with dravyas having similar activities may further potentiate desirable effects. Honey is used as an"*Anupana*" with number of other products due to classically specified "*Yogavahi*" nature.60

Heating (processing) method is much debated aspect about honey in both ancient and present eras. Since specific *Madhusamskara* is also mentioned in medieval texts for attaining specific outcomes, testing of processed honey becomes essential over experimental animals to establish safety and efficacy. Earlier studies conducted over effect of different heating temperatures (65^{0}C and 95^{0}C) on HMF content of honey has not revealed much increase of HMF content beyond specified limits. [22]

Pasteurization is carried out to stabilize honey in most of the market samples by using temperature ranging between 72^0–110^{0}c. Heating honey up to 95^{0}c has not caused any change in antioxidant activity as reported earlier [13] and hence same temperature was employed in present study protocol. Milliard reaction is the interaction between proteins and sugars of honey, during storage as well as processing. By-products of Milliard reaction are said to bring desirable therapeutic effects [23-24] as milliard reaction products have been shown more antioxidant property. [25] Dark coloured honey samples have exhibited more noteworthy antioxidant activity [26-27] as mentioned inprevious works. Present study is based on processed honey with *Triphala Kashaya* which is exerted to maximum anti–hyperlipidaemic potential. [28] Since non diabetic rats were used during previous study on hyperlipidaemia, [28] honey has been proved to act more on diabetic conditions rather non diabetic, [29-30] and induction of hyperglycaemia in high fat fed rats was planned as per established protocol.Previous study conducted on *Samskaritha Madhu* (TSK) had revealed significant anti - hyperlipidaemic potential. Considering previous study

findings as well as available facilities and limited time frame, 30 day intervention period was planned [28,22]. Both glucose and fructose have been found playing supportive role with each other i.e. glucose increases absorption of fructose through disaccharide related transport system while fructose enhancing uptake of glucose by liver and muscles resulting in reduction in hyperglycaemia due to activation of enzyme glucokinase, [31-32] which might have played important role in lowering blood sugar in present study. Honey is a complex material having as much as 181 different constituents [33] having maximum amount of oligosaccharides exerting anti-diabetic effect. [34-35] Number of substances like flavonoids, phenolic acids and invert sugar associated with protein enzymes characterise **honey constituents has established antioxidant/anti hyperglycaemic and cytoprotective potential, collectively or individually. Differences in anti-obesity and anti-diabetic potential of processed and unprocessed honey have been observed during study period. This may be linked to activation as well as deactivation of specific molecules during processing phase. Elevation in invert sugar and brown pigment tends to increase by heating thereby increasing anti-oxidant activity. [36] Fructose is reportedly delays gastric emptying and thereby delays food intake. Increased phenolic concentration along with elevated fructose concentration must have caused reduction in body weight in TSK treated groups in which honey sample used was much darker. Fructose is found to be stimulating insulin secretion from beta cells. [37]** This together with enzymes such as glucose oxidase, catalase, ascorbic acid and phenolic compounds exert powerful antioxidant activity. [38-39] Heating of honey though elevates fructose content, deactivates most of protein enzymes leading to shift in its efficacy. This might have caused significant anti-hyperglyceamic effect of unprocessed honey mixed with *Triphala Kashaya*. Diabetes mellitus is characterized by impairment in lipid metabolism associated with elevated LDL levels. [40] Disturbances in lipoprotein synthesis in diabetes mellitus [41] further leads to insulin resistance [42-43] through insulin signalling pathway. Previous studies have established efficacy of honey in improving glycemic control through C-peptide mediated insulin secretion and modulation. [44-45] Honey is said to enhance insulin sensitivity in liver and muscle by increased glucose uptake resulting reduction in glycemic condition, [46] Which may be the primary reason in lowering hyperglycaemic condition in test drug treated groups.

Conclusion

Madhu though stored for one year (*Purana Madhu*) will not lead to significant *Lekhana Karma* (reduction in body weight due to reduction in body mass through Shoshana (Drying/Atrophy) as per Sharangadhara Samhita). *Purana Madhu* mixed with *Triphala Kashay*a is a potential anti-hyperglyceamic agent. *Triphala Kashaya Samskaritha Madhu* can be utilized in dyslipedemia in non diabetic conditions but *Samyoga* (mixing) of honey with *Triphala Kashaya* exerts beneficial activity during diabetes associated with dyslipidaemia. Hence, the present study establishes role of *Samyoga* in obesity induced diabetes.

References

Life style diseases. [Internet]. 2018. [Cited on 20/12/2017]. Available from: http;//www.med-health.net/Life style diseases.html

Wild S S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes - estimates for the year 2000 and projections for 2030. Diabetes Care. 2004;27(3):1047-53

Bleich S, Cutler D, Murray C, Adams A. Why is the developed world obese? Annu Rev Public Health. 2008; 29: 273–95

Bruce K.D, Byrne C.D. The Metabolic Syndrome: Common origins of a multifactorial disorder. postgrad.Med.j. 2009;85:614-621

McGarry J D, Dobbins R L. Fatty acids, lipotoxicity and insulin secretion. Diabetologia. 1990;42:128-138

Agnivesha, Charaka, Chakrapani, Charaka Samhita, edited by Rajeshwar Datt Shastri, Yadunandan Upadhyaya, Gangasahay Pandeya with Vidyothini of Kasinath Pandey, Nidanasthana, chapter 4, 21st ed. Varanasi: Chaukhambha Vishwabharati; 1995;203

Ibidem, Charaka Samhita (6), Sutra sthana, chapter 23, p.296

Ibidem, Charaka Samhita (6), Sutra sthana, chapter 23, p.203

Sushrutha, Susrutha Samhitha with Ayurveda Thatvasandeepika of Srikantamurthy K.R, Chikithsa sthana, chapter 9 1st ed. Varanasi: Choukhambha orientalia:2012

Abdul Sukkur M, Shrikanth P H. Understanding diabesity or school prameha as a lifestyle disorder. Int. J. Res. Ayurveda. Pharm. 2015; 6(5): 580-582

Chakrapanidatta, Chakradatta, edited by PV Sharma, Prameha chikista, Chapter 35, 2nd ed. Varanasi; Chaukhambha Publishers; 1998, p.303

Kaiyyadeva Nighantu of Kaiyyadeva, edited by PV Sharma, Guruprasad Sharma, / 211, 1st ed. Varanasi; Chaukamba Orientalia, 1979; p.42

S Aric G, Markovic K, Vukicevic D, Hruskar M, Vahcic N. Changes of antioxidant activity in honey after heat treatment. Czech J. Food sci. 2013;31:601-06

Vijaimohan K, Jainu K, Sabitha K. E Subramaniyam S, Anandhan C, Devi S C S,. Beneficial effects of alpha linolenic acid rich flaxseed oil on growth performance and hepatic cholesterol metabolism in high fat diet fed rats. Life Sciences. 2006; 79:448–454

Furman, B.L. Streptozotocin-induced diabetic models in mice and rats. Curr. Protoc. Pharmacol. 2015; 70(5):47.1-5.47.20

Takamura T, Ando H, Nagai Y, Yamashita H, Nohara E, Kobayashi K. Pioglitazone prevents mice from multiple low-dose streptozotocin- induced insulitis and diabetes. Diabetes Research and Clinical Practice. 1999; (44);107–114

Annapoorani A, Anilkumar K R, Farhath Khanam, Anjaneya Murthy N, Bawa A.S. Studies on the physicochemical characteristics of heated honey, honey mixed with ghee and their food consumption pattern by rats. AYU. 2010;31(2): 141-146

Jang - Woo Shin, In-Chan Seol, Chang-Gue Son. Interpretation of Animal Dose and Human Equivalent Dose for Drug Development. The Journal of Korean Oriental Medicine. 2010;31(3): 1-7

Microorganism in Honey. [Internet]. The National Honey Board: Frequently Asked Questions. 2017. [Cited on 20/12/2017]. Available from: https:// www.honey.com/faq

Selway JW. Antiviral activity of flavones and flavans; Progclin Bio Res. 1986; 213:521-536

Alvarez-Suarez J.M, Tulipani S, Romandini S, Bertoli E, Battino M. Contribution of Honey in nutrition and human health :A review. Mediterr. J. Nutr. Metab. 2010;3:15-23

Nargis Ravi NR. Evaluation of Medohara Karma of Madhu with

Special Reference to Samyoga and Samskara- An Experimental Study [MD Thesis]. Mysore: RGUHS; 2015
Yeboah K.F, Alli I, Yaylayan A.V. Reactivity of D-glucose and D-fructose during glycation of bovine serum album. Journal of Agricultural and Food Chemistry. 1999;67: 415-20
Jing, H, Kitts D.D. Comparison of ant oxidative and cytotoxic properties of glucose-lysine and Fructose - lysine Maillard reaction products. Food Research International. 2002; 33: 509-16
Rao M S, Chawla S P, Chander R, Sharma A. Antioxidant potential of Maillard reaction products formed by irradiation of Chitosan glucose solution. Carbohydrate Polymers. 2011;83: 714-19
Bertoncel J, Dobersek U, Jamnik M, Golob T. Evaluation of the phenolic content,Antioxidant activity and colour of Slovenian honey. Food Chemistry. 2007;105(2): 822-28
Escuredo O, Miguez M, Fernandez-Gonzalez M, Carmen Seijo M. NutritionalValue and antioxidant activity of honeys produced in a European Atlantic area. Food Chemistry. 2013;138(2-3): 851-56
Erejuwa OO, Sulaiman SA, Wahab MS. Oligosaccharides might contribute to the anti diabetic effect of honey: a review of the literature. Molecules. 2012;17:248-66
Cani PD, Knauf C, Iglesias MA, et al. Improvement of glucose tolerance and hepatic insulin sensitivity by oligo fructose requires a functional glucagon-like peptide 1 receptor. Diabetes. 2006; 55: 1484-90
Turkmen N, Sari, F, Poyrazoglu E S, Velioglu Y S. Effects of prolonged heating on antioxidant activityand colour of honey. Food Chemistry. 2006; 95 (4):653-657
Hibault L. Dietary carbohydrates: self-selection, plasma g lucose and insulin, and brain indoleaminergic systems in rat. Appetite. 1994; 23:275-286
Hadjmohammadi MR, Nazari SS. Pai S, Nargis R, Manjula S N. Role of Samyoga and Samskara on Anti-hyperlipeadaemic/Anti-Obesity activity of Honey –An Experimental Study.J. Res. Tradit. Med. 2015; 1(1):16-22
Erejuwa OO, Gurtu S, Sulaiman SA, et al. Hypoglycaemic and antioxidant effects of honey supplementation in streptozotozin-induced diabetic rats. Int J Vitam Nutr Res. 2010; 80: 74-82
Erejuwa OO, Sulaiman SA, Wahab MS, et al. Comparison of antioxidant effects of honey, glibenclamide, metformin, and their combinations in the kidneys of streptozotozin-induced diabetic rats. Int J Mol Sci. 2011; 12: 829-43
Mayes PA. Intermediary metabolism of fructose. AMJ Clin Nutr. 1993;58: 754S-765S
Kellett GL, Brot - Laroche E, Mace OJ, Leturque
A. Sugar absorption in the intestine: the role of GLUT2. Annu Rev Nutr 2008;28: 35-54
Gheldof N, Wang XH, Engeseth NJ. Identification and quantification of antioxidant components of honeys from various floral sources. J Agric Food Chem. 2002; 50: 5870-7
Separation optimization of quercetin, hesperetin and chrysin in honey by micellar liquid chromatography and experimental design. J Sep Sci. 2010; 33: 3144-51
Krpan M, Markovic K, Šaric G, Skoko B, Hruškar M, et al. Antioxidant Activities and Total Phenolicsof Acacia Honey. Czech Journal of Food Sciences. 2009; 27: S245-S247
Penckofer S, Schwertz D, Florczak K. Oxidative stress and cardiovascular disease in type 2 diabetes: the role of antioxidants and pro-oxidants. J Cardiovasc Nurs. 2002; 16: 68-85
Kokil GR, Rewatkar PV, Verma A, et al. Pharmacology and chemistry of diabetes mellitus and anti diabetic drugs: a critical review. Curr Med Chem. 2010;17:4405-23

Chang YC, Chuang LM. The role of oxidative stress in the pathogenesis of type 2 diabetes: from molecular mechanism to clinical implication. Am J Transl Res. 2010;2:316-31

Talior I, Yarkoni M, Bashan N, et al. Increased glucose uptake promotes oxidative stress and PKC- delta activation in adipocytes of obese, insulin-resistant mice. Am J Physiol Endocrinol Metab. 2003; 285: E295-302

Erejuwa OO, Sulaiman SA, Wahab MS, et al. Glibenclamide or metformin combined with honey improves glycemic control in streptozotozin- induced diabetic rats. Int J Biol Sci. 2011;7: 244-52

Abdulrhman M, El - Hefnawy M, Ali R, et al. Honey and type 1 diabetes mellitus. In: Liu CP, ed. Type 1 diabetes - complications, pathogenesis, and alternative treatments. Croatia: In Tech. 2011: 228-33

Erejuwa OO, Sulaiman SA, Wahab MS. Honey: a novel antioxidant. Molecules. 2012; 17: 4400-23