Significance of Review of Literature

Any scientific investigation starts with a review of the literature. In fact, working with the literature is an essential part of the research process which generates the idea, helps in developing significant questions and is regarded as instrumental in the process of research design. Reviews are short articles that give brief information regarding the work done in a particular area over a period of time.

3.1 Honey

Honey, a wonderfully rich golden liquid is a naturally delicious alternative to white sugar. The honey is the complex substance made when the nectar and sweet deposits from plant are gathered, modified and stored in the honeycomb by honeybees. The use of natural honey as a nutraceutical agent is associated with nutritional benefits and therapeutic promises. Natural honey is widely accepted as food and medicine by all generations, traditions and civilizations, both ancient and modern. The nutritional profiles including its use in infant and children feeding has been reported in different literatures as well as health indices and biomarkers (Ajibola et al., 2012).

Honey is one of the oldest and widely used food products. It contains approximately 400 compounds. The main ingredients of honey are sugars (fructose 38 %, glucose 31 % and sucrose not more than 5 %), water amount is less than 20 %, while the acids are approximately 0.08 %, and the content of mineral substances are approximately 0.18 %. Honey also contains a wide variety of other substances in small concentrations. These include various phenol acids, flavonoids, aminoacids, enzymes, proteins, etc. Content of honey components varies depending on many factors, such as pollen in honey and also from
climate, environment and honey processing (Belitz et al., 2009; Kaskoniene et al., 2009; Ouchemoukh et al., 2007).

Honey differs in appearance, sensory perception and composition because of the variation of botanical origin. The main nutritional and health relevant components are carbohydrates, mainly fructose and glucose but also about 25 different oligosaccharides. Although honey is a high carbohydrate food, its glycemic index varies within a wide range from 32 to 85, depending on the botanical source. It shows that honey has a variety of positive nutritional and health effects, if consumed at higher doses of 50 to 80 g per intake (Bogdanov et al., 2008).

Due to its high carbohydrate content honey is an excellent energy source and possesses some functional effects. It is especially valuable for children and sportsmen. The glycemic index of honey varies from 32 to 91 depending on botanical origin. Honey also contains a great number of other constituents in small and trace amounts, thus possesses numerous nutritional and biological effects, antimicrobial, antioxidant, prebiotic, immunomodulating activities (Bogdanov, 2010). Honey is used in the day to day life as natural sweetener. Importantly, it contains varieties of enzymes such as oxidase, invertase, amylase, catalase etc (Sato et al., 2000).

Manuka honey is obtained from the plant Leptospermum scoparium (family myrtaceae) and used therapeutically for its antibacterial properties. Recent studies suggest that Manuka honey has ameliorative properties in wound healing, fungal infections, ophthalmic disorders, diabetes, gastrointestinal track disorders, skin ulcers and infections (Bansal et al., 2005; Molan, 2006). Documentation on use of honey in treatment for peptic
Review of Literature

Ulcers and gastritis comes from traditional folklore and from numerous reports in modern times (Molan, 2001).

Honey contains a variety of phytochemicals (as well as other substances such as organic acids, vitamins, and enzymes) that may serve as source of dietary antioxidants. The amount and type of these antioxidant compounds depends largely upon the floral source variety of the honey. In general, darker honeys have been shown to be higher in antioxidant content than lighter honeys (Ghelfof et al., 2002).

The antibacterial and antioxidative and other properties in honey mainly depend on content of antioxidants, phenolic compounds, amino acids and vitamins in honey. Mainly antioxidative properties of honey are defined by the content of pollen, propolis and wax in honey. Pollen, propolis and wax are basic sources of phenol compounds in honey (Meda et al., 2005; Bertoncelj et al., 2007).

Phenolic compounds present in honey are classified into two groups-simple phenols and polyphenols. The simple phenols in honey are various phenol acids, but polyphenols are various flavonoids (Kaskoniene et al., 2009; Viuda-Martos et al., 2008; Mariniova et al., 2005).

3.2 Nutrient Composition of Honey

17 honey samples, 11 organic and six non-organic Apis mellifera honey were analysed. The samples were analyzed for moisture, hydroxymethylfurfural, diastase index, water activity, color, total sugar, reducing sugar, sucrose, ash, viscosity, electrical conductivity, pH, acidity. With the exception of acidity, reducing sugar and diastase index, the averages of other parameters were different between the two groups. All samples of
Review of Literature

organic honey presented moisture values between 23.50 and 24.40%. Among the nonorganic honey samples, two samples presented apparent sucrose amount upper the maximum limit established by the Brazilian Legislation. (Sereia et al., 2011).

40 honey samples (harvest 2006), which came from various locations of the Czech Republic and varied in their origins, were evaluated spectrophotometrically for their total polyphenol content, total flavonoids and 3’,4’-dihydroxyflavones and flavonols and major antioxidants were identified by HPLC-DAD and GC-MS. The kind of honey, location, and date of the honey harvest were shown to have a significant effect on the contents of phenolic antioxidants (average content 11.02 mg gallic acid equivalents/100 g), total flavonoids (0.66 mg quercetin equivalents/100 g), and 3’,4’-dihydroxyflavones and flavonols (4.32 µg quercetin equivalents/100 g). In the Czech honey, ferulic acid (0.11 mg/100 g) and chrysin (0.06 mg/100 g) and other minority phenolics and flavonoids were identified and quantified as honey phenolic antioxidants contained (Lachman et al., 2010).

In a study using HPLC a fraction of New Zealand manuka honey was isolated, which exhibited the non-peroxide antibacterial activity. This fraction proved to be methylglyoxal, a highly reactive precursor in the formation of advanced glycation end products (AGEs). Methylglyoxal concentrations in 49 manuka and 34 non-manuka honey samples were determined using a direct detection method and compared with values obtained using standard o-phenylenediamine derivatisation. Concentrations obtained using both the methods were similar and varied from 38 to 828 mg/kg (Christopher et al., 2008).

Honey is a supersaturated solution of sugars, mainly composed of fructose (38%) and glucose (31%), containing also minerals, proteins, free amino acids, enzymes, vitamins and polyphenols. Among polyphenols, flavonoids are the most abundant and are closely related
to its biological functions. Honey positively affects risk factors for cardiovascular diseases by inhibiting inflammation, improving endothelial function, as well as the plasma lipid profile, and increasing low-density lipoprotein resistance to oxidation. Moreover, honey positively modulates the glycemic response by reducing blood glucose, serum fructosamine or glycosylated hemoglobin concentrations and exerts antibacterial properties caused by its consistent amount of hydrogen peroxide and non-peroxide factors as flavonoids, methylglyoxal and defensin-1 peptide (Alvarez-Suarez et al., 2013).

The quality of six types of honey from Slovakia was evaluated. Carbohydrate composition was determined by ion-exchange chromatographic method with refractive index detection. The method was able to resolve glucose, fructose, saccharose and other ingredients in the honey. The limit of detection for sugars was 0.1 mg/ml (S/N=3). The total analysis time was 13 minute. The kinetic study documented that the ratio of fructose/glucose was not significantly changed in time at temperature 80 °C (Cizmarik et al., 2004).

A study determined the fructose, glucose and the minor oligosaccharide content of seven monofloral willow honeys by gas chromatography. Fructose, glucose, sucrose, maltose, isomaltose, turanose, trehalose, palatinose, cellobiose, raffinose and panose were identified and quantified in all samples. Glucose was predominant in 6 out of 7 samples. The mean values of fructose and glucose varied from 32.92 to 38.88 and from 35.27 to 42.29% respectively. The ratio of fructose/glucose varied from 0.78 to 1.10. The amount of sucrose was 0.12–0.25%. It was found that the characteristics of monofloral willow honeys in most cases meet international requirements for natural honey (Kaskoniene et al., 2008).
Content of P, Fe, Al, Mn, Zn, Cu, Ca, Mg, Na and K trace elements, as well as moisture, pH, free acidity, lactone, reducing sugar, sucrose, diastase activity, ashes and hidroxi methylfurfural, were analyzed in 38 samples of natural honey from different places of the centre of Argentina. The mean values for element content were (in µg g⁻¹): P: 28.80, Fe: 3.91, Al: 2.57, Mn: 0.33, Zn: 1.08, Cu: 0.19, Ca: 56.35, Mg: 23.38, Na: 25.56, K: 482.75. Chemical content shows the following media results: moisture 16.24 %, pH 3.85, free acidity 30.15 mg g⁻¹, total acidity 31.65 mg g⁻¹, reducing sugar 68.08 %, sucrose 4.05 %, diastase number 19.73, ashes 0.11 % and hidroxi methylfurfural: 8.98 mg kg⁻¹ (Cantarelli et al., 2008).

A study was conducted to compare the total antioxidant content of natural sweeteners as alternatives to refined sugar. Substantial differences in total antioxidant content of different sweeteners were found. Refined sugar, corn sugar, and agave nectar contained minimal antioxidant activity (<0.01 mmol FRAP/100g); raw cane sugar had a higher FRAP (The ferric-reducing ability of plasma) (0.1 mmol/100 g). Dark and blackstrap molasses had the highest FRAP (4.6 to 4.9 mmol/100g), while maple syrup, brown sugar and honey showed intermediate antioxidant capacity (0.2 to 0.7 mmol FRAP/100g) (Katherine et al., 2009).

The antioxidant activity of 4 honey samples from different floral sources (Acacia, Coriander, Sider and Palm) were evaluated with three different assays, DPPH free radical scavenging assay, superoxide anion generated in xanthine oxidase (XOD) system and low density lipoprotein (LDL) peroxidation assay. The dark Palm and Sider honeys had the highest antioxidant activity in the DPPH assay. But all the honey samples exhibited more or
less the same highly significant antioxidant activity within the concentration of 1mg honey/1 ml in XOD system and LDL peroxidation assays. The chemical composition of these samples was investigated by GC/MS and HPLC analysis, 11 compounds being new to honey. The GC/MS revealed the presence of 90 compounds, mainly aliphatic acids (37 compounds), which represent 54.73, 8.72, 22.87 and 64.10% and phenolic acids (15 compound) 2.3, 1.02, 2.07 and 11.68% for Acacia, Coriander, Sider and Palm honeys (Ahmed et al., 2009).

The anti-oxidant activity may be partly responsible for its anti-inflammatory action because oxygen free radicals are involved in various aspects of inflammation (Henriques et al., 2006). Even when the antioxidants in honey do not directly suppress the inflammatory process, they can be expected to scavenge free radicals in order to reduce the amount of damage that would otherwise have resulted.

Honey is rich in phenolic compounds, which act as natural antioxidants and are becoming increasingly popular because of their potential role in contributing to human health. Many epidemiological studies have shown that regular intake of phenolic compounds is associated with reduced risk of heart diseases. It is suggested that flavonoids decrease the risk of coronary heart disease by three major actions: improving coronary vasodilatation, decreasing the ability of platelets in the blood to clot, and preventing low-density lipoproteins from oxidizing (Khalil et al., 2010).

3.3 Therapeutic Effects of Honey

The global prevalence of chronic diseases such as diabetes mellitus, hypertension, atherosclerosis, cancer disease is on the rise. These diseases, which constitute the major causes of death globally, are associated with oxidative stress. Oxidative stress is defined as
an "imbalance between oxidants and antioxidants in favor of the oxidants, potentially leading to damage". Individuals with chronic diseases are more susceptible to oxidative stress and damage because they have elevated levels of oxidants and reduced antioxidants. This, therefore, necessitates supplementation with antioxidants so as to delay, prevent or remove oxidative damage. Honey is a natural substance with many medicinal effects such as antibacterial, hepatoprotective, hypoglycemic, antihypertensive and antioxidant effects (Erejuwa et al., 2012).

Honey exerts its antioxidant action by inhibiting the formation of free radicals, catalyzed by metal ions such as iron and copper. Flavonoids and other polyphenols, common constituents of honey have the potential to impound these metal ions in complexes, preventing the formation of free radicals (Makawi et al., 2009).

Evidence shows that honey improves glycemic control in diabetes mellitus. Besides its hypoglycemic effect, studies indicate that honey ameliorates lipid abnormalities in rats and humans with diabetes. Based on the similarities of some of these findings with those of honey, together with the evidence that honey contains oligosaccharides, we hypothesize that oligosaccharides present in honey might contribute to the antidiabetic and other health-related beneficial effects of honey. We anticipate that the possibility of oligosaccharides in honey contributing to the antidiabetic and other health-related effects of honey will stimulate a renewed research interest in this field (Erejuwa et al., 2011).

Honey is a natural substance produced by bees from nectar. Several evidence-based health benefits have been ascribed to honey in the recent years. In healthy subjects or patients with impaired glucose tolerance or diabetes mellitus, various studies revealed
Review of Literature

that honey reduced blood glucose or was more tolerable than most common sugars or sweeteners. Based on the key constituents of honey, the possible mechanisms of action of antidiabetic effect of honey are proposed. It’s also highlighted that the potential impacts and future perspectives on the use of honey as an antidiabetic agent. It makes recommendations for further clinical studies on the potential antidiabetic effect of honey. This review provided insight on the potential use of honey, especially as a complementary agent, in the management of diabetes mellitus. Hence, it is very important to have well-designed, randomized controlled clinical trials that investigate the reproducibility (or otherwise) of these experimental data in diabetic human subjects (Erejuwa et al., 2012).

Honey reduces hyperglycemia in diabetic rats and humans. Honey comprises many constituents, making it difficult to ascertain which component(s) contribute(s) to its hypoglycemic effect. It indicates that fructose exerts a hypoglycemic effect. Studies indicate that fructose enhances hepatic glucose uptake and glycogen synthesis and storage via activation of hepatic glucokinase and glycogen synthase, respectively. The data also demonstrate the beneficial effects of fructose on glycemic control, glucose and appetite regulating hormones, body weight, food intake and oxidation of carbohydrate and energy expenditure (Erejuwa et al., 2012).

Several alternate therapies include honey as an important component in the management of diabetes but the mechanism for its hypoglycaemic effect has not been clearly understood. Elevation of plasma insulin levels and lowering of blood glucose levels have been observed in patients with diabetes after administration of honey (Al-Waili, 2003; Al-Waili, 2004).
Few studies have demonstrated that honey may be important in reduction of some biochemical markers that are linked to an increased risk of heart disease (Shambaugh et al., 1990). Hyperlipidaemia and insulin resistance have also been shown to be better after consumption of honey (Katsilambros et al., 1988).

Honey was found to be associated with significantly lower glycemic index than with glucose or sucrose in normal as well as type 1 diabetes in a investigation. Type 2 diabetics had values similar for honey, glucose and sucrose. Honey compared with dextrose caused a significantly lower rise in plasma glucose levels in diabetic subjects. It also caused reduction of blood lipids, homocysteine levels and CRP (C reactive protein) levels in normal and hyperlipidemic subjects (Al-Waili, 2004).

In a study 400 patients were interviewed. The mean age of the respondents was 33 years, having an equal gender distribution, a majority with above grade X education and consisting of labourers, student or housewives. 327 (82%) responds believed in the use of natural products for their medicinal properties, and honey has medicinal uses according to 370 (92.5%). 327 (81.8%) respondents favoured use of honey due to religious reasons, and honey was used in disease prevention and treatment according to a respective 202 (50.5%) and 326 (81.5%) (Qidwai et al., 2009).

There is a need for sweeteners in the diabetic diet to improve overall dietary compliance of diabetic people. Given that honey has a gentler effect on blood sugar levels on a per gram basis, and tastes sweeter than sucrose so that fewer grams would be consumed, it would seem prudent to recommend honey over sucrose (Kiovisto, 1978).
Consumption of honey decreases the concentrations of prostaglandins in the plasma of normal individuals and increases antioxidant agents, serum iron, and blood indices (Al-Waili et al., 2003). Honey increases insulin secretion and decreases blood glucose levels (Al-Waili, 1999; Al-Waili, 2003; Al-Waili, 2004). Al-Waili found that natural honey also improves lipid profile, lowers normal and elevated C-reactive protein (CRP), lowers homocysteine, and decreases triacylglycerole in patients with hypertriglyceridemia (Al-Waili, 2004).

The role of Helicobacter pylori as a causative factor in peptic ulcers led to research on the antibacterial activity of honey as the explanation for its therapeutic action. Research confirmed that Helicobacter pylori was sensitive to honey with a median level of antibacterial activity due to hydrogen peroxide at concentrations of 20% and to Manuka honey with non peroxide antibacterial activity at a concentration of 5% (Molan, 2001; Sato et al., 2000).

Honey compared with dextrose reduced plasma glucose level (PGL) and insulin in normal subjects. Therefore, with use of honey we might avoid development of hyperinsulinemia, as encountered with other sources of carbohydrates. Honey contains fructose in addition to various minerals and antioxidants. Small amounts of fructose could increase hepatic glucose uptake and glycogen storage and reduce glycemia and insulin levels (Watford, 2002).

Pure natural honeys in low doses might be recommended as sources of carbohydrates and even as sweetening agents in place of sucrose to diabetic patients. Natural honey decreased total cholesterol and LDL-C in healthy and hyperlipidemic subjects. Increasing
dietary fructose from 3% to 20% of calories at the expense of starch increased total cholesterol by 9% and LDL-C by 11% (Swanson et al., 1992).

In a study on Streptozocin induced diabetic rats, it was found that the mad honey caused significant decreases in blood glucose and lipid (cholesterol, triglyceride and VLDL) levels in both groups. These decreases may be due to grayanotoxins in the mad honey. It can be stated that grayanotoxins or mad honey decrease the blood glucose and lipids by secreting insulin from the islets of Langerhans in the pancreas by stimulating the parasympathetic nervous system or M2-muscarinic receptors (Nuray Oztasan et al., 2005).

Honey lowers prostaglandins and elevates nitric oxide (NO) in various biological fluids in normal persons. The study was designed to assess the effect of natural honey on prostaglandins and NO levels, blood indices and biochemical tests in a 40 year old woman with AIDS. This presentation is a case story of a 40 year-old women with a long history of AIDS treated with 80 g of natural honey. Plasma and urinary prostaglandin F2 alpha and thromboxane B2 levels, plasma, urine and saliva content of NO-end product (total nitrite) and hematological tests were estimated before and 3 hours after oral consumption of 80 g of natural honey. These variables, in addition to biochemical tests, were re-estimated after 21 days of daily consumption of 80 g of natural honey. Natural honey decreased prostaglandins levels and elevated NO end product, improved hematological and biochemical tests in a patient with a long history of AIDS (Noori et al., 2006).

In another study to determine whether honey and sucrose would have differential effects on weight gain during long term feeding, 45, 2 month old Sprague Dawley rats were fed a powdered diet that was either sugar-free or contained 7.9% sucrose or 10% honey ad
libitum for 52 week (honey is 21% water). Weight gain was assessed every 1 to 2 week and food intake was measured every 2 month. At the completion of the study blood samples were removed for measurement of blood sugar (HbA1c) and a fasting lipid profile. DEXA analyses were then performed to determine body composition and bone mineral densities. Overall weight gain and body fat levels were significantly higher in sucrose-fed rats and similar for those fed honey or a sugar-free diet. HbA1c levels were significantly reduced, and HDL-C significantly increased, in honey-fed compared with rats fed sucrose or a sugar free diet but no other differences in lipid profiles were found (Chepulis et al., 2008).

A study determined the effect of natural honey on total cholesterol, LDL-C, HDL-C, triacylglycerole, C-reactive protein, FBG and body weight in overweight individuals. Patients in the control group received 70 g of sucrose daily for a maximum of 30 days and patients in the experimental group received 70 g of natural honey for the same period. In the control and experimental groups, body weight, BMI, body fat weight, total cholesterol, LDL-C, HDL-C, triacylglycerole, FBG and CRP were measured before treatment and at day 31 after the commencement of treatment. Results showed that honey caused a mild reduction in body weight (1.3%) and body fat (1.1%). Honey reduced total cholesterol (3%), LDL-C (5.8), triacylglycerole (11%), FBG (4.2%), and CRP (3.2%), and increased HDL-C (3.3%) in subjects with normal values, while in patients with elevated variables, honey caused reduction in total cholesterol by 3.3%, LDL-C by 4.3%, triacylglycerole by 19%, and CRP by 3.3% (p < 0.05) (Yaghoobi et al., 2008).

A study was conducted to determine whether honey and sucrose would have differential effects on levels of neutrophil phagocytosis after long-term feeding 36, 2 month old Sprague Dawley rats were fed a powdered diet that was either sugar-free or contained
7.9% sucrose or 10% honey (honey is 21% water) ad libitum for 52 weeks. The percent of neutrophils exhibiting phagocytosis, and the percentage of leukocytes that were lymphocytes were then measured by flow cytometry after 52 weeks. Neutrophil phagocytosis was similar between sucrose- and honey fed rats, and lower in rats fed the sugar-free diet (79.2%, 74.7% and 51.7%, respectively). The percentage of leukocytes that were lymphocytes differed significantly between all three treatments, the levels being highest in honey-fed rats (53% vs 40.1% and 29.5% for sucrose and sugar-free fed rats) (Chepulis, 2007).

A research study determined whether the common antidiabetic drugs glibenclamide and metformin, in combination with tualang honey, offer additional protection for the pancreas of streptozotocin (STZ) induced diabetic rats against oxidative stress and damage. Diabetes was induced in male Sprague Dawley rats by a single dose of STZ (60 mg/kg; ip). Diabetic rats had significantly elevated levels of lipid peroxidation (TBARS), up-regulated activities of superoxide dismutase (SOD) and glutathione peroxidase (GPx) while catalase (CAT) activity was significantly reduced. Glibenclamide and metformin produced no significant effects on TBARS and antioxidant enzymes except GPx in diabetic rats. In contrast, the combination of glibenclamide, metformin and honey significantly up-regulated CAT activity and down-regulated GPx activity while TBARS levels were significantly reduced (Erejuwa et al., 2010).

Volatile organic compounds (VOCs) in honey are obtained from diverse biosynthetic pathways and extracted by using various methods associated with varying degrees of selectivity and effectiveness. These compounds are grouped into chemical categories such as aldehyde, ketone, acid, alcohol, hydrocarbon, norisoprenoids, terpenes and benzene compounds and their derivatives, furan and pyran derivatives. They represent a fingerprint of
a specific honey and therefore could be used to differentiate between monofloral honeys from different floral sources, thus providing valuable information concerning the honey's botanical and geographical origin. However, only plant derived compounds and their metabolites (terpenes, norisoprenoids and benzene compounds and their derivatives) must be employed to discriminate among floral origins of honey. Notwithstanding, many authors have reported different floral markers for honey of the same floral origin, consequently sensory analysis, in conjunction with analysis of VOCs could help to clear this ambiguity. Furthermore, VOCs influence honey's aroma described as sweet, citrus, floral, almond, rancid, etc. Clearly, the contribution of a volatile compound to honey aroma is determined by its odor activity value. Elucidation of the aroma compounds along with floral origins of a particular honey can help to standardize its quality and avoid fraudulent labeling of the product. Although only present in low concentrations, VOCS could contribute to biomedical activities of honey, especially the antioxidant effect due to their natural radical scavenging potential (Manyi-Loh et al., 2011).

In this report, the authors examine the potential impact of climate change on honey bee behaviour, physiology and distribution, as well as on the evolution of the honey bee's interaction with diseases. The European honey bee, Apis mellifera, is the most economically valuable pollinator of agricultural crops worldwide. Bees are also crucial in maintaining biodiversity by pollinating numerous plant species whose fertilisation requires an obligatory pollinator. Apis mellifera is a species that has shown great adaptive potential, as it is found almost everywhere in the world and in highly diverse climates. In a context of climate change, the variability of the honey bee's life-history traits as regards temperature and
the environment shows that the species possess such plasticity and genetic variability that this could give rise to the selection of development cycles suited to new environmental conditions. Although we do not know the precise impact of potential environmental changes on honey bees as a result of climate change, there is a large body of data at our disposal indicating that environmental changes have a direct influence on honey bee development. Conservation measures will be needed to prevent the loss of this rich genetic diversity of honey bees and to preserve ecotypes that are so valuable for world biodiversity (Le Conte et al., 2008).

Honey is not only used as nutrition but also used in wound healing and as an alternative treatment for clinical conditions ranging from gastrointestinal tract problems to ophthalmic conditions. It has been used as wound barrier against tumour implantation in laparoscopic oncological surgery. It has a potential therapeutic role in the treatment of gingivitis and periodontal disease. Based on these facts, the use of honey in the surgical wards is highly recommended and patients about to undergo surgery should ask their surgeons if they could apply honey to their wounds post operation (Khan et al., 2007).

The hyperglycemic effect of the carbohydrate of glucose, sucrose, and honey equivalent to 20g in twelve normal volunteers, eight patients with insulin-dependent diabetes mellitus (IDDM), and six patients with non-insulin-dependent diabetes mellitus (NIDDM) was evaluated. Honey produced an attenuated postprandial glycemic response in normal volunteers (glucose p<0.005, sucrose p<0.05) and IDDMs (glucose p<0.005, sucrose p<0.05). The glycemic index (GI) showed considerable variability within each subject group. Combined with a peak incremental index (PI), the two indices appear to be
more valuable in predicting the glycemic effects of carbohydrates rather than either one alone. We suggest that honey may prove to be a valuable sugar substitute in diabetics, and that both the GI and PI should be used in the analysis of food (Samanta et al., 1985).

Honey contains a high concentration of fructose, a monosaccharide, capable of raising blood sugar level after oral ingestion. It is thus a paradox that nutritional experts have advocated its use as a nutrition supplement in patients with diabetes mellitus. It has also been used, over the years, as a sweetener by those who wish to avoid the use of sugar. Glycemic effect of honey on alloxan-induced diabetes and with concomitant administration of fructose was studied in male rats of the Wistar strain. At the end of three weeks it was found that daily ingestion of honey for three weeks progressively and effectively reduced blood glucose level in rats with alloxan-induced diabetes. Honey also caused a reduction in hyperglycemia induced by long-term ingestion of fructose, albeit to a lesser degree than its effect on alloxan-induced hyperglycemia. Honey could not reduce blood glucose in controlled rats that received neither alloxan treatment nor fructose ingestion, even though it caused an increase in body weight, irrespective of other substances concomitantly administered to the rats. It is thus apparent that honey may be a useful adjunct in the management of diabetes, while serving as a sweetener, especially if taken in moderate quantities (Adesoji et al., 2008).

Honey is reported to have a lower glycemic index compared to many other carbohydrates (Abdulrhman et al., 2011). Honey is being used since long time both in medical and domestic needs, but only recently its antioxidant property has come to limelight. With increasing demand for antioxidant supply in the food, honey is becoming popular as a source of antioxidant since it is rich in phenolic acids and flavonoids. The antioxidants have
several preventative effects against different diseases like cancer, cardiovascular diseases, inflammatory disorders, neurological degeneration, wound healing, infectious diseases and aging, which led to search for foods rich in antioxidants (Kerian et al., 2010).

3.4 Beneficial Effects of Honey on Food Preparations

Meals containing low GI foods reduce both postprandial blood glucose and insulin responses. Animal studies suggest that incorporating slowly digested starch into the diet delays the onset of insulin resistance. Some epidemiologic studies suggest that a low GI diet is associated with reduced risk of developing non-insulin diabetes in men and women. Clinical trials in normal, diabetic and hyperlipidemic subjects show that low GI diets reduce mean blood glucose concentrations, reduce insulin secretion and reduce serum triglycerides in individuals with hypertriglyceridemia. In addition, the digestibility of the carbohydrate in low GI foods is generally less than that of high GI foods. Thus, low GI foods increase the amount of carbohydrate entering the colon and increase colonic fermentation and short chain fatty acid production. This has implications for systemic nitrogen and lipid metabolism, and for local events within the colon (Frost et al., 1996).

A study compared the relative tolerance to honey and glucose by subjects with impaired glucose tolerance or mild diabetes. Twenty five persons in age group of 35 to 60 years, who have a proven parental (mother or father) history of type II diabetes mellitus were subjected to oral glucose tolerance test (GTT) as well as honey tolerance test (HTT) simultaneously. The glucose tolerance was found impaired in 18 subjects while 5 of the subjects were diagnosed mild diabetic. All subjects with impaired glucose tolerance exhibited significantly lower levels of plasma glucose after consumption of honey at all points of
monitoring in comparison to oral glucose. The plasma glucose level in response to honey peaked at 30 to 60 minutes and showed rapid decline as compared to that of oral glucose. Significantly high degree of tolerance to honey was recorded in subjects with diabetes as well, indicating the lower glycemic index of honey. Thus, it is evident from present investigation that honey may prove to be a valuable sugar substitute for subjects with impaired glucose tolerance or mild diabetes (Agrawal et al., 2007).

Food and beverages developed today search the association of pleasant flavor with functional claims, offering consumers healthier products. In this sense, the objective of this work was to develop a ready-to-drink cashew apple juice sweetened with honey in substitution to sucrose and to evaluate its chemical, physicochemical, sensory and microbiological stability during 180 days storage at a temperature of 28±2 °C. In the development of the product, four formulations (A, B, C and D) with different amounts of cashew apple juice (15 and 20%) associated to different amounts of honey in soluble solids (10 and 11 Brix) were evaluated through sensory analysis (flavor and overall acceptability). The best accepted formulation was processed and evaluated after processing and every 45 days until the end of the storage period. Among the formulations tested, the favorite was formulation D, with 20% cashew apple juice and 11 Brix. In the stability studies, the product maintained good acceptability until the end of the storage period, regarding the attributes color, flavor, overall acceptability and purchase intention. The product maintained satisfactory microbiological quality, in agreement with the current Brazilian legislation. The chemical and physicochemical changes did not characterize lack of stability of the product, except for the content of vitamin C that presented an accentuated decrease at the end of
Review of Literature

storage. The product developed can be considered an interesting alternative for the fruit beverage market (Silva et al., 2008).

A research revitalizes the traditional system of medicine in order to achieve self reliance in health care and health for all by analyzing the antimicrobial property of aqueous extracts of aloevera (Aloevera barbedensis), carrot (Daucus carota), Indian gooseberry (Emblica officinalis), honey and pomegranate (Punica granatum), and to assess the reason for inhibition of growth of pathogenic organisms by DNA and protein analysis. Various aqueous extracts showed inhibition to microrganisms like Escherichia coli, Pseudomonas aeruginosa, Salmonella typhi, Shigella flexineri and Staphylococcus aureus. This study also formulated and standardized a nourishing health drink and salad using the tested foods and estimated their shelf life and nutritive value. The health drink and salad had a low protein, low fat and moderate carbohydrate content. Therapeutically this drink and salad can be used to treat obesity (Philip et al., 2012).

A study was carried out to establish the best product “Candy” was prepared with 3 different combinations of honey and carrot by using 750 g honey+1,000 g carrot (T1), 1,000 g honey+1,000 g carrot (T2) and 1,250 g honey + 1,000 g carrot (T3) and sensory evaluation was done on 9 point Hedonic scale. T1 was found to be most preferred candy. Further the T1 candy was assessed for overall quality during storage at room temperature (25–30 °C) for 6 months. Candy can be preserved safely for 6 months in both glass and LDPE packaging materials (Durrani et al., 2011).

The study was undertaken to determine acceptability, glycemic response (GR) and GI of honey incorporated traditional sweet preparation ladoo. It was observed that there was a significant reduction (p<0.001) in GR of honey incorporated ladoo compared to glucose and
ladoo prepared with cane sugar. Honey incorporated ladoo fell into low GI category with almost the same acceptability as cane sugar ladoo (Katare et al., 2013).

Another study was conducted to determine the glycemic index of food products made with different natural sweeteners including honey. Normal healthy subjects (n=10) and subjects with impaired glucose tolerance (n=10) were included in the study and administered with equicarbohydrate quantity of glucose and a food preparation ‘sweet roll’ containing different sweeteners at fasted state on various days. Monitoring of blood glucose in normal healthy subjects and subjects with impaired glucose tolerance at 0, 30, 60, 90 and 120 minutes indicated a significant difference in incremental area under the curve (IAUC) of glucose and food preparations made with different sweeteners. The mean incremental area under the curve of food preparations was significantly lower (p=<0.01) than that of glucose in subjects with impaired glucose tolerance as well as normal healthy subjects. At the same time honey incorporated sweet rolls were found to have lower glycemic index when compared to rolls prepared with cane sugar and jaggery (Rana et al., 2013).

The study was conducted to determine the glycemic index (GI) of products made with different natural sweeteners. Normal healthy subjects (n=9) and impaired glucose tolerant (IGT) subjects (n=9) were included in the study. Blood glucose curves at 0, 30, 60, 90 and 120 minutes indicated significant difference in incremental area under the curve (IAUC) of glucose and nutribar made with different sweeteners in subjects with IGT as well as in normal healthy subjects. The mean IAUC of nutribar was significantly lower (p=<0.01) than that of glucose in subjects with IGT as well as in normal healthy subjects (Rana et al., 2012).
Besides these health benefits and nutritional constituents, honey is also reported to have low glyemic index. A study, reported that honey had a lower GI when compared with sucrose in patients with type 1 diabetes mellitus (Abdulrhman et al., 2011).

3.5 Glycemic Index

There are important differences between glycemic indices of the monosaccharides in honey, notably glucose and fructose levels. Fructose has a glycemic index of only about 23. The Glycemic Index of a sugar can be predicted on the basis of the molar ratio of glucose to other monosaccharides in the sugar molecule. This explains why maltose (a disaccharide with two glucose units) has a score close to glucose at 100, whereas sucrose (a disaccharide of glucose and fructose) has a glycemic index of only 61. Honey, which contains mixtures of glucose and fructose, may therefore have index values with various ranges (Doner, 1977).

![High GI vs Low GI Foods](image)

Certain findings state that pure fructose has a GI value of 12, when measured against a glucose scale. This is because fructose is absorbed much slowly when consumed alone than when consumed together with other carbohydrate (Shi et al., 1997; Uusitupa, 1994).
In a cross sectional study carried out the glycemic index of two types of Iranian honey, their floral sources and fructose to glucose ratio were determined and their postprandial blood sugar changes were compared. Ten healthy subjects of mean age 28±2.7 year and a mean body mass index of 24.3±2.6 participated in this study. Subjects on 3 different days, at 1 week interval, after 10-12 hours overnight fasting referred to the laboratory and their blood sugar was measured in the fasting state and 15, 30, 45, 60, 90 and 120 minutes after taking glucose solution, thyme honey from Bushehr plain or clover honey from Khorramabad. The incremental area under the blood glucose changes curve (IAUC) was calculated, using the trapezoid frame ignoring fasting values. Glycemic index for thyme honey and clover honey were 65.9 and 64.9 respectively with no statistically significant difference. IAUC after eating thyme (140.2±36.5 mmol.min/l) and clover (137.7±47.7 mmol.min/l) honey were not significantly different, although both were significantly lower than glucose (214.4±53.0 mmol.min/l) (p=0.001) (Masoumeh Tehrani et al., 2013).

Another study showed that the mean AUC of the Malaysian and Australian honeys, 174±19 and 158±16 mmol×min/l, respectively, did not differ significantly from each other but were significantly less than that after glucose, 259±15 mmol×min/l (p<0.001). The mean GI of Malaysian wild honey, 65±7, did not been statistically significant difference from that of Australian honey, 59±5, but both were significantly less than the GI of glucose, 100 (p<0.001) (Robert et al., 2009).

The Observation that the 5 Manuka honey samples were selected from different geographical locales around the North Island of New Zealand and tested for GI in 10 healthy volunteers in a single blinded, randomised study. Participants were fed honey containing 25 g of available carbohydrate in 200 ml water and the blood glucose responses measured
(incremental area under the curve) and compared to that of 25 g of available carbohydrate from glucose. All five honey samples were shown to have moderate GI values (54–59) although variation amongst the group was high (Chepulis et al., 2013).

The hyperglycemic effect of carbohydrate in the forms of 20 g each of glucose and sucrose and 26 g of honey were studied in eight normal volunteers and 22 type 2 diabetic patients. There was no significant change in the glycemic response in normal group when challenged with glucose, sucrose or honey. However, in the diabetic group there was some attenuation in the glycemic response and was significant (p<0.05) after two hours of treatment with glucose, sucrose or honey used. The glycemic index (GI) showed considerable variability within subject groups. The results led us to speculate that honey could be a valuable sugar substitute for type 2 diabetic individuals and have a favorable GI for diabetes (Ibrahim Khalil et al., 2006).

3.6 Impaired Glucose Tolerance

Impaired glucose tolerance (IGT) is a pre-diabetic state of hyperglycemia that is associated with insulin resistance and increased risk of cardiovascular pathology. IGT may precede type 2 diabetes mellitus by many years. IGT represent intermediate states of abnormal glucose regulation that exists between normal glucose homeostasis and diabetes. Blood glucose levels normally rise after eating a meal then gradually fall as the meal is digested. However in people with impaired glucose tolerance, these levels remain elevated. IGT is defined by an elevated 2 hour plasma glucose concentration after a 75 g glucose load on the oral glucose tolerance test (Nathan et al., 2007).
In a national study it was observed that subjects under 40 years of age had a higher prevalence of impaired glucose tolerance than diabetes (12.8% vs 4.6%, p<0.0001). Diabetes showed a positive and independent association with age, BMI, WHR, family history of diabetes, monthly income and sedentary physical activity. Age, BMI and family history of diabetes showed associations with impaired glucose tolerance. This study shows that the prevalence of diabetes is high in urban India. There is a large pool of subjects with impaired glucose tolerance at a high risk of conversion to diabetes (Ramachandran et al., 2001).

A cross-sectional study was conducted among police personnel (N=1817) in Bankura District, West Bengal, 2011 and reported that DM was found in 15%, 1.1% had IFG and 5.7% had IGT. Age >50 years, family history of diabetes, hypertension, and abdominal obesity were found to be significantly associated with DM and IGT, whereas IFG was significantly associated with the family history of diabetes and hypertension. High prevalence of diabetes and pre-diabetic condition warrants early effective intervention to keep the police force healthy and agile (Kumar et al., 2013).

A study determined the prevalence of impaired glucose tolerance and impaired fasting glucose (both combined termed as Pre Diabetes) in the population of Gujarat. The crude prevalence of IFG in Gujarati population is around 2.76 % and IGT is around 6.12 %. But the age adjusted prevalence of IFG is around 2.72% and IGT is around 4.67%. High prevalence of IGT validates that there are chances of the pandemic trend in Gujarat, as eventually IGT may get converted into Diabetes in near future. These results need urgent attention to develop a public awareness programme (Chirag Shah et al., 2013).
Review of Literature

In a study it was noted that the crude rates of diabetes and IGT were 15.7% and 8.8%, respectively in an underdeveloped urban locale of Eastern India. Similarly age-standardized rates of diabetes and IGT were 11.1% and 6.7%, respectively. Both diabetes and IGT had shown a male preponderance. Diabetes and IGT were very highly prevalent in this urban populace. Cardio metabolic risk factors like older age, central obesity, inadequate fruit intake, hypertension, hypertriglyceridemia and socio economic status were found to be significant predictors of diabetes in this study (Prasad et al., 2012).

Risk of developing type 2 diabetes is high in subjects with impaired glucose tolerance (IGT). A great deal of heterogeneity exists in the conversion rate of IGT to diabetes (Alherti, 1996). Diagnosis and intervention to prevent the progression of IGT to diabetes has been targeted as an important tool in primary prevention of type 2 diabetes (Alherti, 1996; Diabetes prevention program research group, 2000; Tuomilehto et al., 2001; Eriksson et al., 1991; Pan et al., 1997). IGT is not only a risk factor for diabetes, but also for coronary heart disease (Stengard et al., 1992).

In India, prevalence of type 2 diabetes and IGT are on the increase. In 2000 AD, a national survey of diabetes and IGT was conducted in six major cities of India which showed age adjusted prevalence of 12.1% for diabetes and 14.0% for IGT. IGT to diabetes ratio was equal to or more than one in four out of six cities, which may be an indicator of further increase in the prevalence of diabetes in future. We also observed that the prevalence rates of IGT in the < 40 and ≥ 40 year age groups, did not differ as much as or diabetes which showed nearly a five-fold higher prevalence in the older group (Ramachandran et al., 2001).
3.7 Diabetes

Diabetes has long been viewed as a disorder of carbohydrate metabolism due to its hallmark feature of hyperglycemia. Indeed; hyperglycemia is the cause of the acute symptoms associated with diabetes such as polydypsia, polyuria and polyphagia. The long-term complications (retinopathy, nephropathy and neuropathy) associated with diabetes also believed to result from chronically elevated blood glucose levels. In addition, hyperglycemia may contribute to the development of macro vascular disease, which is associated with the development of coronary artery disease the leading cause of death in individuals with diabetes (Quaseem et al., 2007; Hjelm et al., 2003).

Diabetes mellitus is a metabolic disorder resulting from a defect in insulin secretion, insulin action, or both. Insulin deficiency in turn leads to chronic hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism (Kumar et al., 2002; Beverley et al., 2003; Lindberg et al., 2004). As the disease progresses tissue or vascular damage ensues leading to severe diabetic complications such as retinopathy (Barse et al., 2004; Hove et al., 2004), neuropathy (Seki et al., 2004; Moran et al., 2004), nephropathy (Huang et al., 2002; Shukla et al., 2004), cardiovascular complications (Svensson et al., 2004; Saely et al., 2004), and ulceration (Wallace et al., 2002). Thus, diabetes covers a wide range of heterogeneous diseases. The incidence of the disease is high worldwide and varies between populations because of differences in genetic susceptibility and other modifiable risk factors.

The prevalence of diabetes is rapidly rising all over the globe at an alarming rate (Huizinga et al., 2006). Over the past 30 year, the status of diabetes has changed from being considered as a mild disorder of the elderly to one of the major causes of morbidity and
mortality affecting the youth and middle aged people. It is important to note that the rise in prevalence is seen in all six inhabited continents of the globe (Wild et al., 2004).

Nowhere is the diabetes epidemic more pronounced than in India. The World Health Organization (WHO) reports show that 32 million people had diabetes in the year 2000 (Wild et al., 2004). The International Diabetes Federation (IDF) estimates the total number of diabetic subjects to be around 40.9 million in India and this is further set to rise to 69.9 million by the year 2025 (Sicree et al., 2006).