Abstract
Diabetes both Type 1 and Type 2 is on the increase in Indian subcontinent and both nature and nurture has to blame. In Indian rural populace the initial lower prevalence is increased and comparable to urban leading to effective management protocols (phytotherapy) optimized to rural settings. The present paper deals with the effects of mangiferin obtained from mango leaves, isolated and characterised as per existing scientific protocol (isolated mangiferin and cyclodextrin complex). Evaluation was done in respect to enzyme inhibition studies and animal experimentation models. Our findings shows enzyme inhibition studies shows to statistically significance. Further, animal experimentation studies on Type1 diabetic rat model shows mangiferin thus isolated has promising hypoglycaemic potentials in and also inhibition studies shows to statistically significance. Further, animal experimentation studies on Type1 diabetic rat model shows mangiferin thus isolated has promising hypoglycaemic potentials in and also inhibition studies shows to statistically significance. Further, animal experimentation studies on Type1 diabetic rat model shows mangiferin thus isolated has promising hypoglycaemic potentials in and also inhibition studies shows to statistically significance. Further, animal experimentation studies on Type1 diabetic rat model shows mangiferin thus isolated has promising hypoglycaemic potentials in and also inhibition studies shows to statistically significance. Further, animal experimentation studies on Type1 diabetic rat model shows mangiferin thus isolated has promising hypoglycaemic potentials in and also inhibition studies shows to statistically significance. Further, animal experimentation studies on Type1 diabetic rat model shows mangiferin thus isolated has promising hypoglycaemic potentials in and also inhibition studies shows to statistically significance. Further, animal experimentation studies on Type1 diabetic rat model shows mangiferin thus isolated has promising hypoglycaemic potentials in and also inhibition studies shows to statistically significance. Further, animal experimentation studies on Type1 diabetic rat model shows mangiferin thus isolated has promising hypoglycaemic potentials in and also inhibition studies shows to statistically significance. Further, animal experimentation studies on Type1 diabetic rat model shows mangiferin thus isolated has promising hypoglycaemic potentials in and also inhibition studies shows to statistically significance. Further, animal experimentation studies on Type1 diabetic rat model shows mangiferin thus isolated has promising hypoglycaemic potentials in and also inhibition studies shows to statistically significance. Further, animal experimentation studies on Type1 diabetic rat model shows mangiferin thus isolated has promising hypoglycaemic potentials in and also inhibition studies shows to statistically significance. Further, animal experimentation studies on Type1 diabetic rat model shows mangiferin thus isolated has promising hypoglycaemic potentials in and also inhibition studies shows to statistically significance. Further, animal experimentation studies on Type1 diabetic rat model shows mangiferin thus isolated has promising hypoglycaemic potentials in and also inhibition studies shows to statistically significance. Further, animal experimentation studies on Type1 diabetic rat model shows mangiferin thus isolated has promising hypoglycaemic potentials in and also inhibition studies shows to statistically significance. Further, animal experimentation studies on Type1 diabetic rat model shows mangiferin thus isolated has promising hypoglycaemic potentials in and also inhibition studies shows to statistically significance. Further, animal experimentation studies on Type1 diabetic rat model shows mangiferin thus isolated has promising hypoglycaemic potentials in and also inhibition studies shows to statistically significance. Further, animal experimentation studies on Type1 diabetic rat model shows mangiferin thus isolated has promising hypoglycaemic potentials in and also inhibition studies shows to statistically significance. Further, animal experimentation studies on Type1 diabetic rat model shows mangiferin thus isolated has promising hypoglycaemic potentials in and also inhibition studies shows to statistically significance. Further, animal experimentation studies on Type1 diabetic rat model shows mangiferin thus isolated has promising hypoglycaemic potentials in and also inhibition studies shows to statistically significance. Further, animal experimentation studies on Type1 diabetic rat model shows mangiferin thus isolated has promising hypoglycaenic properties on Type 1 diabetes rat model

Keywords: Mangiferin, cyclodextrin, diabetes, hypoglycaemia, hypolipidaemia, phytotherapy.

1. Introduction
Worldwide, a 122% rise is projected in Type 2 diabetes, from the total of 135 to 300 million. The multi-factorial cause mainly points population ageing and growth, as well as obesity, un pattern and improper diets and sedentary lifestyles. Of the different types of diabetes [1] Type 2 is most common, though in present day prevalence of both types of diabetes are on the increase and mainly due to nature and nurture effects. These factors are closely associated with urbanization and industrialization and usually exist from childhood [2]. In the next 25 years, India will not only have the largest number of people with diabetes in the world but also the greatest increase in the disease burden [3]. In India, he pooled estimates of prevalence rates for diabetes mellitus for urban and rural areas were found to be 118.02 per thousand and 38.67 per thousand respectively. The overall prevalence rate of diabetes in urban and rural areas combined was estimated as 62.47 per thousand [4]. It has been reported that diabetes occurs at a younger age in the developing countries. In the developed world, most people with diabetes are over 65 years of age while in developing countries the majority is in the age group 45-64, a trend that will accentuate [5]. Considering the devastation and catastrophe of diabetes in socio-economic scenario in India and gaps in Heath Survey Research an alternative strategy to combat the disease particularly in rural sectors is essential. Herbal medicine having wide cultural and traditional acceptance and being considerably cheap in India needs to be widely explored. Presently ethno-pharmaceutical documents more than 600 plants having anti-diabetic effects in India but all of them are not explicitly studied and evidence based documentation with toxicological profile lacking [6, 7, 8]. The present work is focussed on mangiferin obtained from Mangifera indica, available in all areas of India and its effect on Type 1 diabetes.

Though advanced technology is being used for the treatment of diabetes, we are far away in investigating many aspects of this disease. A number of oral anti-diabetic drugs available for the treatment of diabetes have shown side effects and drug-drug interactions. Further, considering the chronic nature of the disease the cumulative cost involvement will be the additional burden. This has been the rationale for the development of new anti-diabetic drugs, which includes herbal agents also. Indian Medicinal plants and their derivatives have been an invaluable source of therapeutic agents to treat various disorders including diabetes.
The reported pharmacological activities of mangiferin include antioxidant, radio protective, antitumor, immunomodulatory, anti-allergic, anti-inflammatory, antidiabetic, lipolytic, anti-bonersorpcion, monoamine oxidase inhibiting, antiviral, antifungal antibacterial and antiparasitic properties, which may support the numerous traditional uses of the plant\[^9\]. Antioxidant activity of mangiferin does not necessarily lead to an in vivo biological response due to its poor bioavailability and also due to its low solubility in water; 0.111 mg/mL. This problem can be minimized by using cyclodextrins (CDs) that present special ability to complex with a variety of guest molecules and achieve a controlled release of certain constituents, and also increase its antioxidant activity\[^10\].

In this paper we made an attempt to explore the effects of mangiferin obtained from leaves in slow release capsule of chitosan to evaluate its antidiabetic and hypolipidaemic potentials. Our lab has already documented the effects of mangiferin obtained from stem bark of *Mangifera indica* and validated its hypoglycaemic and hypolipidaemic effects in Type 2 diabetes\[^10\]. The active ingredients from leaves of *Mangifera indica*, mangiferin will be validated for its hypoglycaemic and hypolipidaemic effects in Type 1 diabetes.

2. Methodology

2.1 Reagents
Chemicals and reagents Standard mangiferin, allophan, starch azure, porcine pancreatic amylase, alpha glucosidase from yeast Saccharomyces cerevisiae, para-nitrophenylglucopyranoside, Tris-HCl buffer and melting point capillary tubes were procured from Sigma Chemicals, USA. Dimethyl sulfoxide, acetic acid, calcium chloride, petroleum ether, acetone, ethanol, methanol, potassium bromide, potassium dihydrogen phosphate, dipotassium hydrogen phosphate and sodium carbonate were purchased from Merck, India. The thin layer chromatography plates were obtained from Merck (silica gel 60 F254 grade, Germany). DMSO-d6 was obtained from Cambridge Isotope Laboratories Inc, USA. Two types of β-cyclodextrin (β-CD) [CAS Number 7585-39-9 (for DSC studies) and CAS Number 68168-23-0 were purchased from Sigma–Aldrich.

2.2 Extraction, identification and authentication of leading bioactive molecules from leaves of *Mangifera indica*\[^11, 12\]
Conventional extraction methods present some drawbacks, among them low selectivity and/or low extraction yields, time consuming processes, use of large volumes of toxic organic solvents, and extended concentration steps that results possibly in loss or degradation of antioxidants. High pressure extraction techniques, such as supercritical fluid extraction (SFE) and pressurized liquid extraction (PLE), have been used in recent years so result interesting alternatives to overcome the above mentioned drawbacks. In lab set up we followed conventional method\[^13\].

Soxhlet extraction was used as reference method, which yielded 57 mg/g in 5 h. Under optimal conditions such as microwave irradiation time 5 min, ammonium sulphate concentration 40% w/v, power 272 W, solute to solvent ratio 1:20, slurry to β-butanol ratio 1:1, soaking time 5 min and duty cycle 50%, the mangiferin yield obtained was 54 mg/g by microwave assisted three phase partitioning extraction (MTPP)\[^12\].

*Mangifera indica* leaves (2 kg) were collected from the upper Assam region and Arunachal Pradesh in the month of December 2015. The leaves were authenticated by Prof. S. Dey, Professor Biotechnology, Indian Institute of Technology, Kharagpur. A careful inspection of the leaves was done to isolate healthy leaves, collected and stored hygienically for a brief period of 72 hours to observe any desired effects due to contaminants. *Mangifera indica* leaves after collection were dried aseptically in lab conditions; the dried materials were then ground to fine powder using electric grinder (Bajaj appliances, Mumbai). The dried powdered leaves of *Mangifera indica* thus collected (2 kg) was serially extracted with boiling petroleum ether (2 x 2 L; 6 hr each and every time) to remove fatty matter, cold acetone (4 x 2 L; 24 hreach and every time) to remove tannins and with 70% ethanolic solvent (4 x 1 L; 6 hreach and every time). The ethanolic fraction was concentrated under reduced pressure using rotary evaporator (Buchi Rotavapor R- 210). Mangiferin separated as a dry yellow colour powder (2.4 gm). Confirmative test for mangiferin thus isolated was performed. Mangiferin isolated was dissolved in aqueous ethanol showing deep yellow colour solution. Alcoholic solution of isolated mangiferin being treated with ferric chloride gave deep green colour while with ferric chloride and hydrochloric acid it showed greenish yellow precipitate\[^14\].

HPTLC analysis\[^10\] was made using silica gel 60F254 plates. Known amounts (0.3 mg) of isolated and standard mangiferin solutions were applied to the layers as band 6mm wide, 10mm from the bottom of the plate using Camag Linomat 5 automated TLC applicator with nitrogen flow. Delivery was made by syringe and was 10µl/sample. Plates developed at room temperature with ethyl acetate-methanol-water-formic acid (10:1:1:0.5) as solvent system in a Camag twin-trough glass chamber saturated for 15 min with mobile phase vapour. The plate developed was dried at 105°C for 15 min. Peak areas for the isolated were recorded and compared with standard mangiferinat 270 nm using Camag Model-3 TLC Scanner (CAMAG, Switzerland) Win CATS 4 software. Small amount of mangiferin was taken in a melting point capillary tube (sigma) and placed in the melting point apparatus (SUNBIM). The temperature was increased gradually. At certain temperature range (271 °C-274 °C) the mangiferin melted and this temperature noted as melting point of mangiferin. FTIR spectra of the isolated mangiferin were recorded and compared with standard mangiferin in an FTIR spectrometer (Nexus-870) using potassium bromide pellet. Molecular weight of isolated mangiferin was determined using ESI-MS spectrometer (Waters, UK). ESI-MS spectrometer was operated in positive ionization mode. Structural identification of isolated mangiferin was performed by 13C NMR ((DMSO-d6; 50 MHz) and 1H NMR (DMSO-d6; 200MHz)). DMSO-d6 used as a solvent. All the spectra were on a Bruker 200 NMR spectrometer using Topspin software.

2.3 Preparation of the complexes of Mangiferinand β-cycloexextrin (β–CD)
The physical mixture of mangiferin and β-cyclodextrin was prepared in an equimolar ratio (1:1), and mixed thoroughly by use of an agate mortar, until homogenization of mixturesoccurs. Co-evaporation leads to the complex (1:1) thus obtained. Mangiferin and β-cyclodextrin the equimolar ratio (1:1) were added to an aqueous solution of 5 mL ethanol/100 mL water. The solution was kept in dark and shaken in a mechanical shaker at 170 rpm at 25 °C (Tarson) for 24 h, ethanol from the reaction mixture was evaporated, the uncomplexed mangiferin was removed by filtration. After that water was evaporated under reduced pressure in a Büchi Rotavapor (Büchi, Germany) and dried in vacuum, giving the mangiferin: β-cyclodextrin complex\[^15\].
2.4 Sample preparations for evaluating the activities

The magniferin and mangiferin: β-Cyclodextrin complex were prepared with 5 mL ethanol/100 mL water. The solution of the Mangiferin: β-Cyclodextrin (1:1) complex was prepared at concentrations of 50 μmol L−1. The solutions were stirred (170 rpm) for 24 h at 25 °C. Toxicity profile shows it is nontoxic orally even to a dose of 1g/kg b.w. of mice [16, 17].

2.5 Animals

Sprague-Dawley rats, the body weight of which was 350 to 415 g were used for the investigation. The animal experiment was carried out vide 473/01/a/CPCSEA dated 5/9/2013 of IRM, Kolkata maintain the guidelines. Animals had been reared in barrier rooms and tested frequently for multiple pathogens. They had been found to be test negative for certain parasites, including mites and pinworms.

2.6 Induction of Type 1 Diabetes

Alloxan was dissolved in 0.9% NaCl solution (200mg/kg bw of rat) and was injected intraperitoneally (i.p). We test blood glucose concentration frequently (at least twice per day) for the first 48 h after alloxan administration and allow animals unlimited access to a tasty oral sugar-containing fluid for the first week after alloxan treatment. Type-1 DM is characterized by marked, unpredictable swings in glycaemia, whereas the hyperglycaemia of Type 2 DM is more stable. If blood ketone concentration is ≥ 1.5 mM, the rat is considered to have Type 1 DM. We measure venous ketone concentration in the conscious animal by puncture of the saphenous vein. Beginning 4 h after alloxan is given, we measure blood glucose concentration approximately every 8 h for the first 2 days. If the glucose value is > 200 mg/dl, we assay blood ketone concentration. If ketone values are >1.5 mM, we initiate insulin [18]. Ultimately, if DM remains consistently well controlled, experiment is started usually after 2 days fasting blood sugar level is more than 225mg/dl and remains stable.

2.7 Experimental Design for Type 1 Diabetes

Group-I served as normal control
Group-II served as diabetic control
Group III received 100 mg/kg of mangiferin: β-Cyclodextrin complex orally daily
Group IV received 200 mg/kg of mangiferin: β-Cyclodextrin complex orally daily
Group V received 40 IU/ml Insulin (Positive control)

2.8 Biochemical parameters

Biochemical parameters particularly fasting blood sugar (FBS), total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL), very low-density lipoprotein (VLDL) and high-density lipoprotein (HDL) level in blood were measured (Semi-Autoanalyzer, Microlab 300, Merck) by using reagents and diagnostic kits obtained from Merck, India.

2.9 In vitro alpha amylase inhibitory assay

The assay was carried out following the method laid down by [19] Starch azure (2 mg) was added in a tube containing 0.2ml of 0.5 M Tris-HCl buffer (pH 6.9). Another tube was containing 0.01 M calcium chloride (substrate). The tube was then boiled for 5 min and then incubated at 37º C for 5 min. Required quantities (1mg) of mangiferin: β-Cyclodextrin complex (1:1) dissolved with 1ml of 0.1% of dimethyl sulfoxide in order to obtain concentrations of 10, 20, 40, 60, 80 and 100 μg/ml. 0.2 ml of mangiferin: β-Cyclodextrin complex of a particular concentration was added in the tube containing the substrate solution. 0.1 ml of porcine pancreatic amylase in Tris-HCl buffer (2units/ml) was then added to the tube containing the mangiferin and substrate solution and the reaction was allowed at 37º C for 10 min. The reaction was stopped by addition of 0.5 ml of 50% acetic acid. The reaction mixture was centrifuged (Eppendorf-5804 R) at 3000 rpm for 5 min at 4º C. The absorbance of resulting supernatant was measured at 595nm using spectrophotometer (Perkin Elmer Lambda 25 UV-VIS). The assay was repeated thrice. The concentration of the mangiferin: β-Cyclodextrin complex required to inhibit 50% of alpha amylase activity was the IC50 value. The α-amylase inhibitory activity was calculated as follows:

\[ \text{IC}_{50} = \frac{(Ac+)-(Ac-)-(As-Ab)}{(Ac+)-(Ac-) \times 100} \]

Where, Ac+, Ac-, As, Ab are defined as the absorbance of 100% enzyme activity (only solvent with enzyme), 0% enzyme activity (only solvent without enzyme), a test sample (with enzyme) and a blank (a test sample without enzyme) respectively.

2.10 In vitro alpha glucosidase inhibitory assay

The in vitro alpha glucosidase inhibitory assay was performed with standard protocol [20] Alpha glucosidase (2U/ml) was mixed with 20 μl of mangiferin: β-Cyclodextrin complex at various concentrations (10, 20, 40, 60, 80 and 100 μg/ml) and was then incubated for 5 min at 37°C. 1mM para-nitrophenylgluco-panoside (pNPG) (20 μl) in 50mM of phosphate buffer (pH 6.8) was added to initiate the reaction. The mixture was incubated at 37°C for 20 min. The reaction was stopped by addition of 50μl of 1M sodium carbonate and the final volume was made up to 150μl. Alpha glucosidase activity was determined spectrophotometrically at 405nm on a BioradMicroplate reader by measuring the quantity of paranitrophenol released. The assay was done thrice. The concentration of the mangiferin: β-Cyclodextrin complex required to inhibit 50% of alpha glucosidase activity was the IC50 value.

2.11 Statistical analysis

All values were expressed mean ± standard deviation. All the data were analyzed by one way analysis of variance followed by multiple comparison test (Tukey’s test) at the 5% level of significance. P < 0.05 was considered statistically significant. In vitro inhibitory assay statistical difference and linear regression analysis were performed using Graphpad prism 5 statistical software.

3. Results

Mangiferin (Figure 1), a natural glucosylxanthone [14]. The HPTLC analysis showed that retention factor (Rf) of standard and isolated mangiferin compound were found to be ≈ 0.50 and ≈ 0.51 respectively (Figure 2). Mangiferin is a yellow powder with structure C19 H18 O11, melting point: 271ºC-274ºC. FTIR spectrum (Figure 3) results of isolated mangiferin compound showed that peaks at 3316 cm−1 indicated presence of secondary OH- bond, peak at 2942 cm−1 showed presence of C-H anti-symmetric stretching, peak at 2830 cm−1 and 1115 cm−1 indicated presence of C-H
symmetric stretching, C–O stretching, CH–CH bending and C–O bond. Peak at 1023 cm⁻¹ showed presence of C–C stretching in the mangiferin structure.

¹H NMR and ¹³C NMR (DMSO-d₆ solvent)-¹H NMR (DMSO-d₆): δ 13.78 (1H, 1-OH), 10.57 (2H, 6,7-OH), 9.85 (1H, 3-OH), 4.90 (2H, 3’,4’-OH), 4.58 (1H, 6’-OH), 3.73 (1H, 2’-OH), 7.39 (1H, 8-H), 6.88 (1H, 5-H), 6.39 (1H, 4-H).

¹³C NMR (DMSO-d₆): (Ring A): δ 162.26 (1-C), 108.56 (2-C), 164.31 (3-C), 93.74 (4-C), 156.70 (4a-C), 101.79 (8b-C). (Ring B): 151.25 (4b-C), 103.10 (5-C), 154.50 (6-C), 144.21 (7-C), 108.11 (8-C), 112.21 (8a-C), 179.57 (C=O). Additional signals due to glucopyranosyl carbons: δ 82.06 (5’-C), 79.48 (3’-C), 73.58 (1’-C), 71.14 (4’-C), 70.73 (2’-C), 62.00 (6’-C).

MS (m/z,% intensity): m/z 423 [M+H]⁺

3.1 Physicochemical characterization of Mangiferin:β-Cyclodextrin complex

Differential Scanning Calorimetry (DSC) and Fourier Transform Infrared spectroscopy (FTIR) DSC analysis was carried out for mangiferin, β-Cyclodextrin and magniferin:β-cyclodextrin complex with a DSC-60 calorimeter (range 25–500 °C) (Shimadzu, Kyoto, Japan). The temperature was calibrated using α-alumina powder. Samples (5.0–10.0 mg) were placed in standard aluminum pans and measurements were being performed at a heating rate of 5 °C min⁻¹ from 25 to 400 °C in a dynamic nitrogen atmosphere (flow rate = 20 mL/min) (Figure 4). The FTIR spectra of mangiferin, β-Cyclodextrin and magniferin:β-cyclodextrin complex were recorded at room temperature in a spectral region between 4000 and 500 cm⁻¹. Samples were prepared as small pellets by mixing each of them with KBr in a mortar (1:100) and then the resultant mixture is pressed. A blank KBr disc was also used as a background (Figure 5).
3.2 Alpha amylase and alpha glucosidase inhibitory effects of mangiferin: β-Cyclodextrin complex

In addition, comparing alpha amylase and alpha glucosidase inhibitory effects of mangiferin: β-Cyclodextrin complex (Figure 6), it was observed that mangiferin exhibited appreciable effect alpha amylase inhibitory effects (IC50 value 66.35 ± 1.4 µg/ml) and alpha glucosidase inhibitory effects (IC50 37.88 ± 1.5 µg/ml) when compared with acarbose (IC50 83.33 ± 1.2 µg/ml).

In Type 1 diabetic model, the body weight was slightly increased in normal control rats compared to initial body weight whereas alloxan-induced diabetic rats showed loss of body weight (192 ± 1.72g) after 30 days as compared with initially weight of diabetic rats (201.8 ± 2.69g). Body weight of diabetic rats was restored significantly (P < 0.05) by treating with insulin (40 IU/ml) in Type 1 diabetic model respectively. In Type 1 diabetic model, body weight of diabetic rats was restored by treating with mangiferin: β-Cyclodextrin complex (at a dose 100 and 200 mg/kg, orally) daily for 30 days when compared with diabetic control (Table 1).

In Type 1 diabetic model, insulin showed significant anti-diabetic and hypolipidemic effects. But the mangiferin (at a dose 100 and 200 mg/kg, orally) showed anti-diabetic and hypolipidemic effects in Type 1 diabetic model on being compared with insulin (Table 2).

4. Discussion

The present study was done to investigate the anti-diabetic and hypolipidemic effects of mangiferin, β-Cyclodextrin complex in Type 1 diabetic rats model. Mangiferin (1,3,6,7-tetrahydroxy-2-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl)xanthen-9-one) is poorly absorbable in water and absorption is erratic in oral route. By complexing with β-Cyclodextrin the effects were observed in Type 1 diabetic rats, the complex being given orally. Mangifera indica is a freely available species in India; its stem bark is documented containing mangiferin. Here an attempt is made from easy available source, i.e. leaves. When compared with the FTIR spectra, Electron-Spray Ionization (ESI) - Mass spectrum, 1H and 13C NMR spectrum of standard mangiferin, the sample (isolated mangiferin) showed significant similarity. Insulin was the drug for Type 1 diabetic model rats. It is well established that insulin activate glucose uptake in various tissues including adipocytes and muscles, nerve cells etc. In the present study indicated that daily administration of mangiferin: β-Cyclodextrin complex (at a dose of 200 mg/kg, orally) up to 30 days showed anti-diabetic and hypolipidemic effects in Type 1 diabetic rats. This is an interesting, as the continuous use of mangiferin in the Type 1 diabetic rats will not result in hypoglycemic episodes.

Our group [10] had earlier documented in Type 2 diabetic model rats, an increase in blood sugar levels in diabetic rats were prevented by use of mangiferin (at a dose 10 and 20 mg/kg, i.p.). The effects were comparable to the standard drug
glibenclamide. This effect is due to potentiating the effect of insulin and more of its release from the bound form. Diabetes is usually accompanied with dyslipidaemia particularly hyperlipidaemia. Therefore ideal treatment of diabetes selection of an agent preferably natural in origin yet cheap and acceptable which will have a favorable effect on lipid profiles. High level of TC and LDL are major coronary risk factors [20]. TG itself is independently related to coronary heart disease [21, 22]. Dyslipidaemia may play an important role in occurrence of premature and severe atherosclerosis, which affects patients with diabetes [23].

In this study, mangiferin: \(\beta\)-Cyclodextrin complex (at a dose 200 mg/kg orally) showed significant reduction in TC, TG, LDL, VLDL levels and increased level of HDL in Type 1 diabetic model rats and thus directs further researches to be used as hypoglycaemic and hypolipidaemic agent in Type 1 diabetes. In Type 1 diabetic model, body weight of diabetic rats was partially restored (p=0.046) by treating with mangiferin: \(\beta\)-Cyclodextrin complex (at a dose 20 mg/kg, orally) daily for 30 days in comparison to with insulin (40IU/ml) in Type 1 diabetic model. Several studies reported that Mangifera indica and its polyphenol compound mangiferin possess anti-diabetic activity. Oral administration of aqueous extract (1g/kg) of Mangifera indica showed hypoglycemic activity in diabetic mice [17, 24]. Stem bark extract of Mangifera indica showed potent antioxidant effects both in vitro and in vivo [25]. However the researches are mainly concentrated on Type 2 diabetic animals and the intraperitoneal mode of application of stem bark yield mangiferin [26]. Plant bioactive effect depends on many factors and of the agronomic conditions soil is most important. Here the leaves are collected from upper altitudes of upper Assam and Arunachal where particular soil may have some potentiating effects which need to be further explored. Cyclodextrin has a special ability to complex with a variety of molecules and thus has effects on their stability, bioavailability, solubility, protection to light-induced decomposition and also to suppress unpleasant odors or tastes and achieve a controlled release of certain constituents), but still increase the antioxidant activity of many compounds. The exact cause of its effects on Type 1 diabetes is unknown. It may be due to its anti inflammatory effectswith respect to Nfkb, PPAR\(\gamma\) and the immune system, effects on angiogenesis, oxidative stress through Nrf2/ARE signalling, ROS elimination and catalase activity [27].Mangiferin is protective to diabetic cardiac neuropathy and nephropathy. In diabetic mice it hinders the hypoglycaemic and atherogenic changes. The accumulating evidences suggest that both pancreatic and extra pancreatic mechanisms might be involved in its anti-diabetic or anti-hyperglycemic action [28, 29]. The reduction of triglycerides following administration with mangiferin would also facilitate the glucose oxidation and utilization and subsequently the reduction of hyperglycemia [30]. Mangiferin showed anti-diabetic activity in KK-Ay mice [31]. Components of stem bark extract of Mangifera indica such as terpenoids, cathchen, fatty acids and microelements exhibited antioxidant properties [32, 33]. Aqueous extract from the bark of Mangifera indica was used as a food supplement in Cuba showed potent in vitro and in vivo antioxidant activities [34].Mangiferin improves serum lipid profiles in overweight patients with hyperlipidaemia [35]. Mangiferin improves serum lipid profiles in overweight patients with hyperlipidaemia [35]. Mangiferin improves serum lipid profiles in overweight patients with hyperlipidaemia [35]. The plant based alpha amylase and alpha glucosidase inhibitor offers a prospective therapeutic approach for the management of post-prandial hyperglycemia [36]. In the present study, mangiferin exhibited appreciable alpha amylase inhibitory and alpha glucosidase inhibitory effects when compared with acarbose. Therefore, mangiferin could be useful in management of post-prandial hyperglycemia due to inhibition of both alpha amylase and alpha glucosidase enzymes.

5. References

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