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REVIEW ARTICLE

Can Polyherbal Medicine be used for the Treatment of Diabetes? - A Review of Historical Classics, Research Evidence and Current Prevention Programs

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Abstract: Diabetes mellitus (DM), a chronic medical condition, has attained a global pandemic status over the last few decades affecting millions of people. Despite a variety of synthetic drugs available in the market, the use of herbal medicines for managing diabetes is gaining importance because of being comparatively safer. This article reviews the result of a substantial literature search on polyherbal formulations (PHFs) developed and evaluated with potential for DM. The accumulated data in the literature allowed us to enlist 76PHFs consisting of different parts of 147 plant species belonging to 58 botanical families. The documented plant species are laden with bioactive components with anti-diabetic properties and thus draw attention. The most favoured ingredient for PHFs was leaves of *Gymnema sylvestre* and seeds of *Trigonella foenum-graecum* used in 27 and 22 formulations, respectively. Apart from herbs, shilajit (exudates from high mountain rocks) formed an important component of 9 PHFs, whereas calcined *Mytilus margaritiferus* and goat pancreas were used in Dolabi, the most commonly used tablet form of PHF in Indian markets. The healing properties of PHFs against diabetes have been examined in both pre-clinical studies and clinical trials. However, the mechanism(s) of action of PHFs are still unclear and considered the pitfalls inherent in understanding the benefits of PHFs. From the information available based on experimental systems, it could be concluded that plant-derived medicines will have a considerable role to play in the control of diabetes provided the challenges related to their bioavailability, bioefficacy, optimal dose, lack of characterization, ambiguous mechanism of action, and clinical efficiency are addressed.

Keywords: Diabetes mellitus, hyperglycemia, hypoglycaemia, herbal formulations, polyherbal formulations, polyherbal medicine.

1. INTRODUCTION

Diabetes mellitus (DM) is a pancreatic dysfunction characterized by an elevated blood sugar level. Diabetes is broadly classified into two types, namely type I diabetes (T1DM), and type II diabetes (T2DM). T1DM is also referred to as juvenile diabetes in which β-cells of Islets of Langerhans in the pancreas are destroyed and thus fail to produce insulin resulting in insulin dependency of the patient. T2DM occurs due to impaired insulin secretion by the β-cells and endogenous glucose output [1]. Notably, gestational diabetes is a form of diabetes that is characterized by an increased level of blood glucose in pregnant women who has not been diagnosed with the same prior to pregnancy. Shaw *et al.* [2] estimated that there will be a considerable increase in both T1DM and T2DM worldwide, which is expected to be 439 million adults by 2030. However, Cho *et al.* [3], in their study on the incidence of diabetes during 2017, found that about 451 million people were diabetic, which was higher than the projection made by Shaw *et al.* [2] for the year 2030. This clearly indicates the escalating rate with which people are developing diabetes, as the number, which was predicted to rise in 20 years, was crossed in just 8 years. It is a matter of serious concern. If preventive measures are not adopted at the earliest, the figure might become alarming

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though about 693 million are expected to be diabetic by 2045 [3].

2. CURRENT STATUS IN INDIA

As per the World Health Organization (WHO) report, the Indian continent has the major burden of heart-related diseases and the largest patient base for diabetes in the world. The number of diabetic patients in India, China, Russia, and Brazil is 31.7, 20.8, 4.6, and 4.6 million, respectively. This also burdens the country as productivity loss (estimated to be 0.85% of the GDP) on account of mortality in 2004 and increased to 1.2% for India as per the current scenario for nutrition-related disorders. According to the report, nearly 30% and 34% of the population in urban areas and rural areas, respectively, are in pre-diabetic stage due to the high intake of calories and less micronutrient-rich foods [4].

3. FACTORS RESPONSIBLE FOR DIABETES

Diabetes has been a major health issue for centuries. Though the basic understanding regarding the incidence of diabetes is still at a rudimentary level, it is associated with a number of factors, which, if not monitored, may lead to serious consequences [5].

3.1. Obesity and Diabetes

Obesity or gained weight, considered the primary risk factor, accounts for 60% to 90% of total T2DM [6]. The notion behind the link between T2DM and obesity is the ability of the latter to engender resistance toward insulin [7].

3.2. Physical Inactivity and Diabetes

Exercise or physical activity and diabetes are indispensable. Inactiveness leads to impaired glycemic load in addition to insulin resistance [8].

3.3. Family History and Diabetes

The occurrence of T2DM cannot be neglected in person with a family history. A person having family history of T2DM tends to become obese and physically unfit, which in turn results in insulin secretion by the damaged beta cells [9].

3.4. Ethnicity and Diabetes

The association between the occurrence of diabetes and a particular ethnic group or race is still ambiguous. However, the fact that the inhabitants residing in certain parts of the globe are more prone to diabetes than others cannot be neglected [10].

Apart from this, there are a number of factors that are associated directly or indirectly with diabetes or diabetes related complications such as hypertension (high blood pressure) [11], and diet [12]. Dietary habit certainly has a major role in combating the onset of diabetes and its complication. The coexistence of diabetes and hypertension is fatal as it escalates the incidence of vascular complications along with kidney related disorders [11].

4. SYNTHETIC DRUGS USED FOR DIABETES

At present, a number of drugs are reported to maintain hyperglycemia *i.e*. elevated blood glucose level like insulin, sulphonyl ureas, biguanides, etc. but the use of these drugs at higher doses may lead to various disorders like increased sweat, inaudible speech, tachycardia, coma, *etc*.

Due to its improved pharmacokinetics qualities compared to other commercially available medications, liraglutide, a glucagon-like peptide-1 receptor agonist, is appropriate for once-daily treatment in persons with type 2 diabetes mellitus. Age, race, ethnicity, body weight, sex, or injection site dosing regimens for liraglutide typically do not need to be changed, and the clearance mechanism suggests a low risk of drug-drug interactions. Liraglutide is a suitable therapy option for many type 2 diabetes patients due to its advantageous pharmacodynamic activities, which include enhanced glucose-dependent glycaemic control, decreased appetite and energy intake, and lowered postprandial lipid profiles [7].

Lazzaroni *et al.* [13] tried to explain and make a connection between obesity and weight loss utilising diabetic prescription medications. Their findings recommended that anti-diabetic medications can be alienated into three groups based on how well they work to reduce weight: metformin, acarbose, empagliflozin, and exenatide triggered a mild weight loss (less than 3.2% of starting weight); canagliflozin, ertugliflozin, dapagliflozin, and dulaglutide caused a moderate weight loss (between 3.2% and 5%). This study demonstrates that the most efficient new anti-diabetic medications for causing weight loss in type 2 diabetes patients are GLP1-RA and tirzepatide. It is interesting that exenatide seems to be the only GLP1-RA to cause a slight loss of weight [13].

Although synthetic oral hyperglycaemic drugs are effective, they are still accompanied by undesirable side effects like weight loss; so, in recent years, interest has gradually shifted towards polyherbal drugs.

5. CONCEPT OF POLYHERBAL FORMULATION

Since time immemorial, plants and plant-derived products have been used to prevent or treat a host of illnesses, including diabetes [14]. However, these claims were not backed by science. Herb-herb combinations are the collection of herbs formulated to cure diseases [15]. WHO estimated that 80% of the world's inhabitants still immobilize traditional and complementary medicines (CAM) for their health care. Herbal formulations combined together become more effective than the single herb, probably due to their catalyzing effect with one another. In recent years, the claims of medicinal efficiency and lack of toxicity of many plants have been scientifically ascertained [16-18]. At present, many polyherbal formulations (PHFs) are commercially available to treat diabetes [19].

5.1. Advantages of Herbal Formulations

- Plants are a viable source of medicine.
- Plants need less processing than the synthesis of drugs.
- They are cost-effective.
- They are comparably safer with fewer side effects than synthetic drugs.

5.2. Disadvantages of Herbal Formulations

- The process of curing with herbal medicine takes a longer time compared to synthetic drugs.
- Plant-based medicine is moderately processed and contains various ingredients, and so it may cause allergic reaction(s).
- The PHFs sometime may get contaminated with some toxic substances (heavy metals, toxic pesticides, *etc*.) that can be present in the soil as plants absorb those substances.

6. NEED FOR STANDARDIZATION

Standardization is essential for herbal formulations to measure the quality based on the number of their active constituents [20]. When used in large quantities, plant material may show variations in its chemical constituents based on time and environmental conditions [21]. Assuring the quality of Ayurvedic medicines was a traditional responsibility of the physician who prepared the medicine himself and maintained a fiduciary relationship with the patient [22]. Standardization and improvement of protocols for Ayurvedic formulations using modern techniques of analysis are very important [23]. The WHO has acknowledged the indispensable relationship between people belonging to developing nations and medicinal plants for their health care and thus took the necessary initiative to formulate the guidelines to maintain the quality and standards of the PHFs worldwide [24].

7. POLYHERBAL FORMULATION: CONCEPT OF AYURVEDA

Ayurveda, known popularly as "Mother of All Healing", is made up of two Sanskrit words, "*ayu*r (life) and *veda* (science or knowledge)". The exclusivity of this ancient system lies in the immeasurable multiplicity of healing processes used, such as animal juices, herbal formulations, and natural energies (sun and water) [25]. The eight branches of treatment, "*Ashtanga"* was mentioned here as well: "*Kaya Chikitsa* (Internal medicine), *Shalya Tantra* (Surgery), *Shalakya Tantra* (Ear, nose, throat and eye diseases), *Kaumarbhritya* (Pediatrics), *Agada Tantra* (Toxicology), *Bhuta Vidya* (Psychiatry), *Rasayana* (Rejuvenation therapy), and *Vajeekarana* (Aphrodisiac therapy)".

The *Ayurvedic* system has indicated herbs and their products as one of powerful healing elements, and it could be found recorded in Vedas and Samhitas. These herbs are categorized as *rasa*, *veerya*, *vipaka*, *prabhava* and *karma,* and are understood to normalize body cleansing, proper functioning and nourish the individual body.

Ayurvedic literature "*Sarangdhar Samhita*" has recorded the concept of polyherbalism in this historic medicinal system (1300 A.D). The two basic principles used for drug formulation in *Ayurveda* are either employing a single entity (drug) or a combination of two or more two drugs (PHF). The reason behind combining several medicines was to achieve additional therapeutic effectiveness.

8. POLYHERBAL FORMULATIONS FOR DIABETES

A total of 76PHFs standardized for the management of diabetes have been documented in this review. The names of the formulations, their composition (plants/plant parts), the experimental models used, and the effect(s) of PHFs in comparison to reference drugs are summarised in Table **1**. India alone houses over 62 million individuals diagnosed with diabetes [26] and thus efforts are made to search and develop plant-based therapeutic agents to overcome the epidemic. PHFs have been widely embraced in many developing and developed countries to treat various diseases [27]. Referred to as the medicinal garden of the world [28], India contributes the maximum for the development of PHFs with 56 reports out of 70 reported, followed by Pakistan (6), Iran (3), Korea (3), Bangladesh (2), Indonesia (2), China (1), Eritrea (1), Iraq (1), Israel (1) and Nigeria (1).

Table 1. List of Polyherbal formulations for antidiabetic activity with commercial name, scientific names, animal studies for management of diabetes and country of origin.

Commercial Name	Formulations with Scientific Names	Experimental Model	Effects of Polyherbal Preparation	Effects of Reference Drug	Study Design and Country	Additional Property	References
Diabecon (D-400)	*Asparagus racemosus*, *Balsamodendron mukul*, *Eugenia jambolana,Gymnema sylvestre*, *Momordica charantia*, *Ocimum sanctum*, *Pterocarpus marsupium*	Patients with diabetic retinopathy. Micro-aneurysm= 2.22 Hemorrhage= 2.034 Exudation = 2.034 Retinitis proliferans= 0.583	Diabecon (2tablets thrice daily) for 12 weeks ↓Micro-aneurysm = 0.466 ↓Hemorrhage = 0.866 ↓Exudation= 1.316 ↓Retinitis proliferans = 0.550	No data available	Clinical Trials; India	-	[64]

(Table 1) Contd…

Commercial Name	Formulations with Scientific Names	Experimental Model	Effects of Polyherbal Preparation	Effects of Reference Drug	Study Design and Country	Additional Property	References
Cogent db	*Azadirachta indica*, *Curcuma longa*, *Phyllanthus emblica*, *Rotula aquatica*, *Syzygiumcumini*, *Terminalia chebula*, *Terminalia bellirica*, *Tribulus terrestris*, *Trigonella foenum graecum*.	Alloxan (150mg/Kg BW)-induced diabetic rats FBG= 230.50mg/100ml HbA1c = 5.96g/100ml Insulin= 11.10µU/ml Haemoglobin=5.96g/100ml Urine sugar= > 1%	At 0.45 g/kg ↓FBG= 83.40mg/100ml ↓HbA1c = 0.25g/100ml ↑Insulin= 22.60µU/ml ↑Haemoglobin=12.60g/100ml ↓Urine sugar= NIL	Glibenclamide (600 µg/kg) ↓FBG= 91.20mg/100ml ↓HbA1c = 0.31g/100ml ↑Insulin= 20.80µU/ml ↑Haemoglobin=10.80g/100ml ↓Urine sugar= Trace	*In vivo;* India	Anti-hyperlipidemic	[113, 114]
Hyponidd	*Cassia auriculata*, *Curcuma longa*, *Emblica officinalis*, *Enicostemmalittorale*, *Eugenia jambolana*, *Gymnemasylvestre*, *Melia azadirachta*, *Momordicacharantia*, *Pterocarpus marsupium*, *Tinosporacordifolia*, *Swertiachirata*.	STZ (45mg/Kg BW)-induced diabetic rats Blood glucose=351.09mg/dl Plasma insulin= 8.20µU/ml HbA1c= 0.98mg/dl Glycogen= 1.74g/100g wet tissue Haemoglobin= 6.09mg/dl	At 200 mg/kg ↓Blood glucose= 98.51mg/dl ↑ Plasma insulin= 16.10µU/ml ↓HbA1c= 0.52mg/dl ↑Glycogen= 3.08g/100g wet tissue ↑Haemoglobin= 10.84mg/dl	Glibenclamide (600 µg/kg): ↓Blood glucose= 108.39 mg/dl ↓ Plasma insulin= 14.70µU/ml ↓HbA1c= 0.58mg/dl ↑Glycogen= 2.39g/100g wet tissue ↓↑Haemoglobin= 9.27mg/dl	*In vivo;* India	Anti-hyperlipidemic Prokinetic effect	[115-117]
Okchun-San	*Coixlacryma-jobi*(or *Oryzasativa*), *Glycyrrhizauralensis*, *Puerariathunbergiana*, *Rehmanniaglutinosa*, *Schisandrachinensis*, *Trichosantheskirilowii*.	*db/db* type-2 diabetic mice	Okchun-San+ Coicis semen (200mg/Kg) ↓FBG ↑Glucose tolerance Okchun-San+ Oryzae semen (200mg/Kg) ↓FBG ↑Glucose tolerance	Acarbose (5 mg/kg) ↓FBG ↑Glucose tolerance	*In vivo;* Korea	-	[118]
Diakyur	*Cassia javanica*, *Cassia auriculata*, *Salacia reticulata*, *Gymnema sylvestre*, *Mucuna pruriens*, *Syzygium jambolanum*, *Terminalia arjuna*.	Alloxan (150 mg/Kg *i.p.*)-induced diabetic rodents FBG= 246–253mg/dl	At 1600 mg/Kg ↓FBG= 64.90mg/dl (rats) and 87.3mg/dl (rabbits)	Glibenclamide (2 mg/kg rats and 5g/Kg rabbits): ↓FBG= 56.90 mg/dl (rats) and 68.50mg/dl (rabbits)	*In vivo*; India	Anti-lipidperoxidative	[30]

(Table 1) Contd…

Commercial Name	Formulations with Scientific Names	Experimental Model	Effects of Polyherbal Preparation	Effects of Reference Drug	Study Design and Country	Additional Property	References
Diabegon	*Aegle marmelos* (Leaves), *Asfetum punjabinum* , *Berberis aristata* (Tuber/root), *Citrullus colocynthis* (Root), *Curcuma longa* (Tuber/root), *Cyperus rotundus* (Root), *Emblica officinalis* (Fruit), *Eugenia jambolana* (Fruit pulp), *Gymnema sylvestre* (Leaves), *Momordica charantia* (Fruits juice), *Piper longum* (Fruit), *Piper longum* (Root), *Pterocarpus marsupium* (Leaves), *Plumbago zeylanica* (Root), *Swertia chirata* (Leaves), *Terminalia bellirica* (Fruit), *Terminalia chebula* (Fruit).	High fructose diet-fed rats FBG= 11.10 mmol/l HbA1c= 7.11% Plasma insulin= 465.2 U/ml Liver glycogen=10.98 mg/g tissue Urine sugar= 1.98g/24h	At 100mg/Kg BW ↓FBG= 7.10 mmol/l ↓HbA1c= 4.98% ↑Plasma insulin= 278.80 U/ml ↓Liver glycogen=7.11 mg/g tissue ↓Urine sugar= 0.56 g/24h	Rosiglitazone (60 µg/Kg): ↓FBG= 9.88 mmol/l ↓HbA1c= 5.11% ↑Plasma insulin= 319.90 U/ml ↓Liver glycogen=7.39 mg/g tissue ↓Urine sugar= 0.98 g/24h	*In vivo*; India		[119]
		High fructose diet-fed rats	At 200 mg/Kg BW ↓FBG ↑Plasma insulin	Glibenclamide and Rosiglitazone ↓FBG ↑Plasma insulin	*In vivo*; India		[65]
		Human subjects with type 2 diabetes	At 100 mg/Kg BW ↓FBG ↑Plasma insulin	Glibenclamide and Rosiglitazone ↓FBG ↑Plasma insulin	Clinical trials; India		[65]
		Human subjects with type 2 diabetes	At 10 mg/day ↓FBG ↓HbA1c ↓Glycosuria		Clinical trials; India		[66]
		Human subjects with type 2 diabetes age Group= 35 to >65 yrs	At 4 g twice daily for 18 months ↓FBG= 12.30-42.00% ↓Postprandial BG= 28-32%		Clinical trials; India	Anti-hyper-lipidemic	[67]
DRF/AY /5001	*Allium cepa*, *Allium sativum*, *Aloe vera*, *Cajanus cajan*, *Coccinia indica*, *Caesalpinia bonducella*, *Momordica charantia*, *Ocimum sanctum*, *Pterocarpus marsupium*, *Swertia chirata*, *Syzygium cumini*, *Tinospora cordifolia* and *Trigonella foenum-graecum*.	Alloxan-induced diabetic rats	At 600 mg/kg ↓FBG ↓HbA1c ↑Hepatic glycogen ↓Histological damage in the pancreas ↓Epinephrine-induced hyperglycemia	Glibenclamide (4 mg/Kg) ↓FBG ↓HbA1c ↑Hepatic glycogen ↓Histological damage in the pancreas ↓Epinephrine-induced hyperglycemia	*In vivo*; India		[120]

(Table 1) Contd…

Commercial Name	Formulations with Scientific Names	Experimental Model	Effects of Polyherbal Preparation	Effects of Reference Drug	Study Design and Country	Additional Property	Reference
Glucolevel	*Atriplex halimus* (Leaves), *Juglansregia* (Leaves), *Olea europaea* (Leaves), *Urticadioica* (Leaves).	Human subjects with type 2 diabetes	At 1 tablet thrice daily for 4 weeks ↓FBG ↓HbA1c	–	Clinical trials; Israel		[68]
Karnim Plus	*Momordica charantia*, *Azadirachta indica*, *Picrorhiza kurroa*, *Ocimum sanctum* and *Zingiber officinale*.	Alloxan(120mg/Kg) induced diabetic rats FBG= 370.50 mg/dl Urea=73.88 mg/dl Creatinine=1.65mg/dl	At 400 mg/kg (11 days) ↓FBG= 206.17mg/dl ↓Urea =65.95mg/dl ↓Creatinine=1.30mg/dl	Glibenclamide (4 mg/kg): ↓FBG=115.00 mg/dl ↓Urea=28.68 mg/dl ↓Creatinine =1.11 mg/dl	*In vivo*; India		[31]
		Human subjects with type 2 diabetes	At 2 capsules/ twice daily ↓FBG ↓HbA1c ↓Postprandial BG ↓Urine sugar	Metformin capsule 2 capsules/twice daily ↓FBG ↓HbA1c ↓Postprandial BG ↓Urine sugar	Clinical trials; India		[69]
Dihar	*Syzygium cumini* (Seed), *Momordica charantia* (Fruit), *Emblica officinalis* (Fruit), *Gymnema sylvestre* (Leaves), *Enicostemma littorale* (Entire plant), *Azadirachta indica* (Leaves), *Tinospora cordifolia* (Root) and *Curcuma longa* (Rhizome).	Streptozotocin (45mg/Kg)-induced diabetic rats Serum glucose= 426.60mg/dl Serum insulin= 12.67µU/ml AUCglucose=44.60 (mg/dl.min)x10^3 AUCinsulin=1.65 (µU/ml.min)x10^3	At 100 mg/Kg ↓ Serum glucose= 314.30mg/dl ↑Serum insulin=17.67µU/dl ↓AUCglucose= 21.25 (mg/dl.min)x10^3 ↑AUCinsulin= 2.96 µU/ml.min)x10^3		*In vivo*; India	Antihyperlipidemic	[110]
SR10	*Radix astragali* (Root), *Radix codonopsis* (Root), *Cortex lycii* (Root).	*db/db* type 2 diabetic mice	At 927 mg/Kg Glucose tolerance= not significant ↓FBG ↑Insulin	Metformin (200 mg/Kg) ↑Glucose tolerance Not checked for other parameters.	*In vivo*; China	Antioxidant, Protective effect	[57, 121]

(Table 1) Contd…

Commercial Name	Formulations with Scientific Names	Experimental Model	Effects of Polyherbal Preparation	Effects of Reference Drug	Study Design and Country	Additional Property	References
ESF/AY/500	*Aegle marmelos*, *Aerva lanata*, *Bambusa bambos*,, *Catharanthus roseus*, *Eruca sativa*, *Eruca vesicaria*, *Ficus benghalensis*, *Salacia reticulata*, *Syzygium cumini*.	STZ-induced diabetic rats	At 500mg/Kg ↑superoxide dismutase (SOD) ↑catalase (CAT) ↑glutathione peroxidase (GP_x) ↑ reduced glutathione (GSH) ↓ lipid peroxidation		*In vivo*; India		[122]
5EPHF	*Aegle marmelos* (Root), *Murraya koenigii* (Root), *Aloe vera* (Leaves), *Pongamia pinnata* (Stem/bark) and *Elaeodendron glaucum* (Leves).	Alloxan-induced diabetic rats	At 200 mg/kg ↓FBG ↑Insulin ↓HbA1c ↓Histological damage in the pancreas	Tolbutamide (250 mg/kg) ↓FBG ↑Insulin ↓HbA1c ↓Histological damage in the pancreas	*In vivo*; India		[123]
Polyherbal preparation	*Eugenia jambolana*, *Momordica charantia* and *Ocimum sanctum*.	Alloxan (125mg/Kg)-induced diabetic rats Blood glucose= 438.67mg/dl Urea= 66.33mg/100ml Creatinine= 1.75mg/100ml	At 400 mg/kg ↓ Blood glucose= 100.67mg/dl ↓Urea= 66.33mg/100ml ↓Creatinine= 1.75mg/100ml	Glibenclamide 0.5 mg/kg ↓ Blood glucose= 89.66mg/dl ↓Urea= 25.67mg/100ml ↓Creatinine= 0.65mg/100ml	*In vivo*; India		[33]
PM021	*Mori folium* and *Aurantii fructus*.	Type 2 diabetes Otsuka Long–Evans Tokushima Fatty (OLETF) rats Blood glucose= 125.60mg/dl Urine output= 288.30 (control as 100%)	↓ Blood glucose= 109.30mg/dl ↓Urine output= 228.60 (control as 100%)	–	*In vivo*; Korea		[124]
APKJ-004	*Eugenia jambolana* and *Cinnamomum zeylanicum*.	In 3T3-L1, C2C12, HepG2 cell lines	α-glucosidase inhibitory activity (IC50=147.20µg/ml) Insulin mimetic activity in 3T3-L1 cell lines= 42% Insulin mimetic activity in C2C12 cell lines= 87.20% Insulin mimetic activity in HepG2 cell lines=89.50%	Acarbose α-glucosidase inhibitory activity (IC50=132.20µg/ml)	*In vitro*, India		[125]

(Table 1) Contd…

Commercial Name	Formulations with Scientific Names	Experimental Model	Effects of Polyherbal Preparation	Effects of Reference Drug	Study Design and Country	Additional Property	References
		STZ (45mg/Kg BW)-induced diabetic rats Blood glucose= 268.01mg/dl Insulin= 06.75µU/ml	At 800mg/Kg ↓Blood glucose= 97.01mg/dl ↑Insulin= 23.13µU/ml	Glibenclamide (2mg/Kg) ↓Blood glucose= 89.30mg/dl ↑Insulin= 19.02µU/ml	*In vivo*; India		[29]
Ziabeen	*Aloe barbadensis*, *Azadirachta indica*, *Eugenia jambolana*, *Gymnema sylvestre*, *Swertia chirata*, *Momordica charantia*, *Holarrhena antidysenterica*and *Piper nigrum*.	Alloxan (150mg/Kg BW)-induced diabetic rabbits	At 4 g/kg ↑Glucose tolerance ↓FBG	Pioglitazone (1 mg/Kg) No significant effect on glucose tolerance ↓FBG	*In vivo;* Pakistan		[58]
DIA-2	*Allium sativum* (Blub) and *Lagerstroemia speciosa* (Leaves).	High-fat diet + STZ (35mg/Kg BW)-induced type 2 diabetic rats	At 125 mg/kg ↓FBG= 60.04% ↑Insulin= 39.26%	Rosiglitazone (8 mg/kg): ↓FBG= 57.91% ↑Insulin= 11.11%	*In vivo*; India	Ameliorates protein oxidation	[36]
HAL(14)	*Withania somnifera* (Root) *Momordica charantia* (Fruit), *Trigonellafoenum-graecum* (Seed).	STZ (50mg/Kg)-induced diabetic rats	At 500 mg/kg ↓FBG =52% ↑Hepatic glycogen= 163%	Metformin (500 mg/kg): ↓FBG= 55% ↑Hepatic glycogen= 183%	*In vivo*; India		[126]
Polyherbal Mixture	*Allium sativum*, *Cinnamomum zeylanicum*, *Citrullus colocynthis*, *Juglans regia*, *Nigella sativa*, *Olea europaea*, *Punica granatum*, *Salvia officinalis*, *Teucrium polium*, *Trigonella foenum-graecum*, *Urtica dioica*, and *Vaccinium arctostaphylos*.	STZ (55mg/Kg)-induced diabetic rats FBG=374.00mg/dl Urine output= 72.00ml/24h	At 15% w/w of diet ↓FBG =263 mg/dl ↓Urine output= 30ml/24h		*In vivo*; Iran	Antihyperlipidemic	[127]

(Table 1) Contd…

Commercial Name	Formulations with Scientific Names	Experimental Model	Effects of Polyherbal Preparation	Effects of Reference Drug	Study Design and Country	Additional Property	References
MAC-ST/001	*Azadirachta indica* (Seed), *Caesalpinia bonducella* (Seed), *Momordica charantia* (Fruit), *Syzygium cumini* (Seed), *Trigonella foenum-graecum* (Seed).	STZ (55mg/Kg BW)-induced diabetic rats Blood glucose= 399.30mg/dl BUN= 116.20mg/dl	At 400 mg/Kg ↓ Blood glucose= 112.10mg/dl ↓BUN=48.42mg/dl ↓Histological damage in the pancreas	Glibenclamide (10 mg/Kg) ↓ Blood glucose= 132.30mg/dl ↓BUN= 45.72mg/dl ↓Histological damage in the pancreas	*In vivo*;India		[128]
NIDDWIN	*Tinospora cordifolia*, *Gymnema sylvestre,Terminalia tomentosa*, *Tribulus terrestris*, *Emblica officinalis*, *Mucuna pruriens*, *Sida cordifolia*, *Withania, somnifera*, *Terminaliabellirica*, *Terminalia chebula*,*Momordica charantia* and *Asphaltum*.	Alloxan (150 mg/Kg)-induced diabetic rats	At 100 mg/Kg ↓Glucose (50.50%)	Glibenclamide (10 mg/Kg) ↓ Glucose (57.91%)	*In vivo*;India		[93]
SPHAG	*Alstoniascholaris* (Leaves), *Gymnemasylvestre* (Leaves), *Holarrhenapubescens* (Bark), *Premnacorymbosa* (Leaves), *Solanum nigrum* (Leaves).	Alloxan (150mg/Kg BW)-induced diabetic rats HbA1c= 9.73% Urea=77.00mg/dl Creatinine= 1.60mg/dl	At 500 mg/Kg ↓HbA1c= 5.71% ↓ Urea= 53.16mg/dl ↓ Creatinine- 1.10mg/dl		*In vivo*; India	Antioxidant	[129]
PHPE	*Azadirachtaindica* (Leaves), *Bougainvillea spectabilis* (Leaves), *Trigonellafoenumgraecum* (Seed).	STZ-induced diabetic rats FBG= 352.10mg/dl	At 600 mg/Kg ↓FBG= 298.00mg/dl ↑ Restoration in size and number of Islet of Langerhans.	Glibenclamide (500µg/Kg) ↓FBG= 108.10mg/dl ↑ Restoration in size and number of Islet of Langerhans.	*In vivo*; India		[42]

(Table 1) Contd…

Commercial Name	Formulations with Scientific Names	Experimental Model	Effects of Polyherbal Preparation	Effects of Reference Drug	Study Design and Country	Additional Property	References
ADC05	*Syzygium cumini* (Seed), *Trigonella foenum graecum* (Seed), *Azadirachta indica* (Leaves), *Emblica officinalis* (Fruit), *Cassia auriculata* (Leaves), *Gymnema sylvestre* (Leaves), *Andrographis paniculata* (Leaves), *Tribulus terrestris* (Fruit), *Pterocarpus marsupium* (Bark).	STZ (65mg/Kg)-induced diabetic rats FBG= 326.50mg/dl	At 200 mg/Kg ↓FBG= 183.00mg/dl α-amylase inhibitory activity (IC50=61.86µg/ml) α-glucosidase inhibitory activity (IC50=34.49µg/ml)	Glibenclamide (5 mg/Kg) ↓FBG= 164.80mg/dl α-amylase and α-glucosidase inhibitory activity not measured	*In vivo*;India		[46]
PHF	*Curcuma caesia* (Rhizome), *Evolvulus-alsinoides* (Whole plant), *Citrulluslanatus* (Seed), *Gymnemasylvestre* (Leaves), *Tinosporacordifolia* (Stem), *Withaniacoagulans* (Fruit) and *Caesalpiniabonduc* (Seed).	Alloxan (150mg/Kg)-induced diabetic rats Blood glucose= 330.80mg/dl	At 400 mg/Kg ↓Blood glucose= 100.30mg/dl)	Glibenclamide (10 mg/Kg) ↓Blood glucose= 107.2mg/dl	*In vivo*;India		[130]
Mixture extract	*Artemisia sieberi*, *Nigella sativa*and *Teucriumpolium*.	Alloxan (120mg/Kg)-induced diabetic rats Blood glucose= 280.00mg/dl	At 150 mg/Kg ↓Blood glucose= 153.63mg/dl	Glibenclamide (5 mg/Kg) ↓Blood glucose= 142.72mg/dl	*In vivo*;Iraq	Hypolipidemic	[52]
PHF	*Tinospora cordifolia,Cinnamomumzeylanicum*, *Curcuma longa*, *Trigonellafoenum-graecum*, *Azadirachtaindica,Piper nigrum*.	STZ (65mg/Kg) nicotinamide (90mg/Kg)-induced diabetic rats Blood glucose= 348.30mg/dl Total protein= 0.27g/dl	At 57.42 mg/Kg ↓Blood glucose= 119.40mg/dl ↑Total protein=0.73g/dl ↑ Restoration in size and number of Islet of Langerhans.	Metformin (150 mg/Kg) ↓Blood glucose= 112.60mg/dl ↑Total protein= 0.91g/dl ↑ Restoration in size and number of Islet of Langerhans.	*In vivo*;India		[53]

(Table 1) Contd…

Commercial Name	Formulations with Scientific Names	Experimental Model	Effects of Polyherbal Preparation	Effects of Reference Drug	Study Design and Country	Additional Property	References
Diasulin	*Cassia auriculata* (Flower), *Cocciniaindica* (Fruit), *Curcuma longa* (Rhizome), *Emblica officinalis* (Fruit), *Gymnema sylvestre* (Leaves), *Momordica charantia* (Fruit), *Scoparia dulcis* (Whole plant), *Syzygium cumini* (Seed), *Tinospora cordifolia* (Root), *Trigonella foenum-graecum* (Seed).	Alloxan (150 mg/kg) induced diabetic rats FBG= 265.00 mg/dl Plasma insulin= 3.55 µU/mL	At 200 mg/kg ↓FBG = 104.16 nmg/dl ↑Plasma insulin= 7.05 (µU/mL)	Glibenclamide (600 µg/kg) ↓FBG= 111.60 mg/dl ↑Plasma insulin= 6.32 µU/mL	*In vivo*;India	Antihyperlipidemic and Antiperoxidative	[131, 132]
		Alloxan (150 mg/kg) induced diabetic rats FBG= 265 mg/dl Plasma insulin= 3.55 µU/mL Hb= 6.44 g/dl HbA1c= 0.82 mg/gHb BGL= 311.6 mg/dl	At(0.20g/kg) ↓FBG= 104.1(mg/dl) ↑Plasma insulin= 7.05 µU/ml ↑Hb= 11.04 g/dl ↓HbA1c= 0.36 mg/gHb ↓BGL= 102.5 mg/dl	Glibenclamide (600 µg/kg) ↓FBG= 111.6 mg/dl ↑Plasma insulin= 6.32 µU/ml ↑Hb= 10.65 g/dl ↓HbA1c= 0.46 mg/gHb ↓BGL= 110.8 mg/dl			
PHF	*Aloe vera* (Leaf pulp), *Camellia sinensis* (Leaves), *Capparis decidua (*Flower), *Musa sapientum* (Flower), *Phyllanthus amarus* (Entire palant), *Punica granatum* (Flower & seed), *Tinospora cordifolia* (Stem).	STZ (60 mg/kg/day) induced diabetic rats ↓Body weight= 146 g ↑Food intake= 67.96 g/day ↑Water intake= 344.31 g ↑Blood glucose= 312.6 mg/dL ↓Liver glycogen= 18.89 µg/g	At 400 mg/kg ↓Boold glucose= 96.23 mg/dL ↑ Liver glycogen= 46.42 µg/g ↓Liver Histopathology marked decrease in the microdroplet build-up.	Glibenclamide (600 µg/kg) ↓Blood glucose= 106.00 mg/dL ↑ Liver glycogen= 43.17 µg/g	*In vivo*;India		[133]
G-400	*Salacia oblonga*, *Tinospora cordifolia*, *Emblica officinalis*, *Curcuma longa* and *Gymnema sylvestre*.	STZ (55 mg/kg, i.p.)-induced diabetic rates.	At 100 mg/kg BW ↓FBG ↑Plasma glucose	Glibenclamide (0.025 mg/kg BW) ↓FBG ↑Plasma glucose	*In vivo*; India	Hypolipidemic	[134, 135]
		STZ (55 mg/kg, i.p.)-induced diabetic rates.	At 100 mg/kg BW ↑FBG ↑Plasma insulin ↑Glucose-6-Phosphatase	Glibenclamide (0.025 mg/kg BW) ↑ Glucose-6-Phosphatase	*In vivo*; Bangladesh		

(Table 1) Contd…

Commercial Name	Formulations with Scientific Names	Experimental Model	Effects of Polyherbal Preparation	Effects of Reference Drug	Study Design and Country	Additional Property	References
PHF	*Citrullus colocynthis*, *Syzygium cumini* and *Holarrhena antidysenterica*.	STZ induced diabetic rates. ↑Blood glucose	PHF at 0.5 mg/ml α- glucosidase inhibitory (IC_{50} =235 µg/mL). At 500 mg/kg ↓Blood glucose= 258.5 mg/dL.	Glibenclamide (600 µg//kg) ↓Blood glucose= 221.5 mg/dL.	*In vivo;* Pakistan	Antioxidant and Hypolipidemic	[55]
Polyherbal formulation	*Azadirachtaindica*, *Camellia sinensis* and *Asparagus racemosus*.	STZ (55mg/kg, I.P) induced diabetic rates. ↑Blood glucose= 304.8 mg/dl ↓SOD= 1.39 ↓GHS= 6.63 ↓CAT= 6.71 ↓TBAR= 2.87	At 200 mg/kg ↓F1 Blood glucose= 139.2 mg/dl ↓F2 Blood glucose= 149.7 mg/dl ↓F3 Blood glucose= 154.9 mg/dl ↑SOD =2.33 ↑GHS= 13.7 ↑CAT= 14.5 ↑TBAR= 2.8		*In vivo;* India	Antioxidant and Hypolipidemic	[136]
Glyoherb	Gudmar Extract, Mahamejva Extract, Katuki Ext, Chirata Ext, Karela Ext, Indrajav Ext, Amla Ext, Gokshur Ex, Harde Ext, Jambubij Ext, Methi Ext, Neem patti Ext, Chanraprabha, Arogyavardhini, Harida Ext, Bang bhasma and Devdar Ext.	STZ (70 mg/kg) induced diabetic rates. Serum glucose= 319.9 mg/dl Oral glucose= 506.5 mg/dl Creatinine= 2.15 mg/dl Urea= 58.8 mg/dl SOD= 3.6 units/min/mg protein Catalase= 4.2 units/min/mg protein GHS= 40.3 mg/gm protein TBARS= 21.7 nmoles/mg protein	At(600 mg/kg, PO, 28 days) ↑Serum glucose= 80.2 mg/dl ↓Oral glucose= 222.3 mg/dl ↓ Creatinine= 1.19 mg/dl ↓Urea= 38.4 mg/dl ↑SOD= 4.8 units/min/mg protein ↑Catalase= 8.6 units/min/mg protein ↑GHS= 56.6 mg/gm protein ↓TBARS= 8.4 units/min/mg protein	Glibenclamide (5 mg/kg, PO, 28 days) ↑Serum glucose= 99.4 mg/dl ↓Oral glucose= 160.5 mg/dl ↓ Creatinine= 1.15 mg/dl ↓Urea= 38.8 mg/dl	*In vivo*;India	Antioxidant and Antihyperlipidemic	[59]
Polyherbal extract	*Adiantum capillus* (Whole plant), *Astera canthalongifolia* (Seed), *Callicarpa macrophylla* (Fruit), *Ficus benghalensis* (Bark), *Melia azedarach* (Aerial parts).	STZ(65mg/kg) induced diabetic rats Serum glucose=393.2 mg/dl HbA1c= 15.03 % Liver glycogen= 6.69 mg/gm GSH= 34.1µg/mg of protein SOD= 4.5 (unit/min/gm tissue)	At 200 mg/kg ↓Serum glucose= 124.3 mg/dl ↓HbA1c= 9.71% ↑Liver glycogen=14.9 mg/gm ↑GHS= 46.011 µg/mg of protein ↑SOD= 13.8 unit/min/gm tissue	Glibenclamide (10 mg/kg) ↓Serum glucose= 120.6 mg/dl ↓HbA1c= 6.16% ↑Liver glycogen= 16.5 mg/gm ↑GHS= 56.3 µg/mg of protein ↑SOD= 12.2 unit/min/gm tissue	*In vivo*; India	Antioxidant and Antihyperlipidemic	[35]

(Table 1) Contd…

Commercial Name	Formulations with Scientific Names	Experimental Model	Effects of Polyherbal Preparation	Effects of Reference Drug	Study Design and Country	Additional Property	References
Diashis	*Syzygium cumini* (Seed), *Gymnema sylvestre* (Leaves), *Holarrhena antidysenteric* (Seed), *Tinospora cordifolia* (Root), *Pongamia pinnata* (Seed), Asphaltum(Gum), *Psoralea corylifolia* (Seed), *Momordica charanta* (Seed).	STZ (100 mg/kg bw./rat/day)induced diabetic rats. Body weight= 138.5g HbA1c= 3.76 % Hb= 5.56 g/dl FBG= 382.5 mg/dl Hexokinase= 109.7 µg/mg of tissue Glucose-6-phosphate=6.1 unit/mg of tissue Glucose-6-phosphatase=33.9 mg of IP/g of tissue SGPT= 111.8 SGOT= 60.3	At (5 mg/0.5 mL of distilled water/100 g body weight/rat/day) ↑Body weight= 151.01g ↓HbA1c= 2.06 % ↑Hb= 11.04 g/dl ↓FBG= 98.02 mg/dl ↓ Hexokinase= 131.4 (µg/mg of tissue) ↑ Glucose-6-phosphate= 11.04 unit/mg of tissue ↓ Glucose-6-phosphatase= 24.8 mg of IP/g of tissue ↓SGPT= 89.0 IU/L ↓SGOT= 47.6 IU/L	Glibenclamide(2mg/0.5 mL distilled water/100 g body weight/ rat/day) ↑Body weight= 152.2 g ↓HbA1c= 1.98 % ↑Hb= 11.84 g/dl ↓FBG= 95.12 mg/dl ↓ Hexokinase= 129.07 µg/mg of tissue ↑ Glucose-6-phosphate=10.7 unit/mg of tissue ↓ Glucose-6-phosphatase= 23.9 mg of IP/g of tissue ↓SGPT= 87.5 IU/L ↓SGOT= 49.0 IU/L	*In vivo*;India	Antioxidative	[34, 137]
		STZ (100g/b.w./rat/day) induced diabetic rats. Body weight= 138.5 gm HbA1c= 4.76 % Serum insulin= 5.13 µIU/ml FBG= 382.5 mg/dl	Diashis (5 mg / 0.5 ml of distilled water/ 100 g body weight / rat/day) ↑Body weight= 149 gm ↓HbA1c= 3.06 % ↑Serum insulin= 12.53 µIU/ml ↓FBG= 92(mg/dl) Diashis +Normoglycaemic(5 mg / 0.5 ml of distilled water/ 100 g body weight / rat/day) ↑Body weight= 161.4 gm ↓HbA1c= 2.72 % ↑Serum insulin= 14.96 µIU/ml ↓FBG= 76.3 mg/dl	Glibenclamide(2mg mg / 0.5 ml of distilled water/ 100 g body weight / rat/day ↑Body weight= 152.8 gm ↓HbA1c= 2.93 % ↑Serum insulin= 12.92 µIU/ml ↓FBG= 77.2 mg/dl Glibenclamide + Normoglycaemic(2mg mg / 0.5 ml of distilled water/ 100 g body weight / rat/day ↑Body weight= 159.5gm ↓HbA1c= 2.77 % ↑Serum insulin= 15.47 (µIU/ml) ↓FBG= 77.3 mg/dl		Antihyperlipidemic	

(Table 1) Contd…

Commercial Name	Formulations with Scientific Names	Experimental Model	Effects of Polyherbal Preparation	Effects of Reference Drug	Study Design and Country	Additional Property	References
Madhurakshak (Mdr)	*Pterocarpus marsupium*, *Cinnamomum tamala*, *Eugenia jambolana*, *Gymnema sylvestre*, *Piper nigrum*, *Azadira chtaindica*, *Trigonella foenum-graecum*, *Momordica charantia*, *Phyllanthus emblica*, *Terminalia chebula*. *Terminalia bellirica* and ShudhShilajit.	STZ(40mg/kg i.p single dose) induced diabetic rats. Blood glucose= 15.2 Creatinine= 0.94 Urea= 35.7 AST= 126.9 ALT= 157.8 ALP= 129.9	Mdr concentrate (300mg/kg oral) ↓Blood glucose= 4.7 ↓Creatinine= 0.68 ↓Urea= 15.9 ↓AST= 77.3 ↓ALT= 98.4 ↓ALP= 101.0 Madhurakshak powder(MP 600mg/kg) ↓Blood glucose= 4.8 ↓Creatinine= 0.68 ↓urea= 15.3 ↓AST= 75.6 ↓ALT= 96.6 ↓ALP= 98.8	Diabecon (250 mg/kg) ↓Blood glucose= 3.9 ↓Creatinine= 0.62 ↓Urea= 14.5 ↓AST= 68.7 ↓ALT= 81.7 ↓ALP= 59.2	*In vivo*; India		[39]
DS-01	*Gymnema sylvestre*, *Syzygium cumini*, *Momordica charantia*, *Tinospora cordifolia*, *Cinnamomum zeylanicum*, *Plumbago zeylanica* and *Asphaltum*.	STZ (30mg/kg s.c.) induced diabetic rats FBG= 354.6 mg/dl Creatinine= 0.8mg/dl TP= 7.6g/L ALP= 131U/L Urea= 81.1mg/dl	At 500 mg/kg ↓FBG= 276.5 mg/dl ↑Creatinine= 0.8mg/dl ↑TP= 334.7 g/L ↓ALP= 7.1U/L ↓Urea= 59.1mg/dl	Glibenclamide (10mg/kg) ↓FBG= 275.7 mg/dl ↓Creatinine= 0.7mg/dl ↓TP= 7.3 g/L ↓ALP=719U/L ↓Urea=4.5mg/dl	*In vivo*; India		[47]
Polyherbal extract	*Andrographis paniculata* extract, *Gymnema sylvester* extract, *Momordica charantia* extract, and *Myristica fragrans*shodhana extract.	STZ(90mg/kg) induced Type2 diabetic rats. Blood glucose levels= 302.4 mg/dl	At 400mg/kg ↓Blood glucose levels= 122.5 mg/dl	Glibenclamide at (0.25 mg/kg) ↓Blood glucose levels= 115.4mg/dl	*In vivo*; India		[43]

(Table 1) Contd…

Commercial Name	Formulations with Scientific Names	Experimental Model	Effects of Polyherbal Preparation	Effects of Reference Drug	Study Design and Country	Additional Property	References
PH	*Aegle marmelos* (Leaves and fruit pulp), *Aloe barbadensis* (Leaves pulp) , *Azadirachta indica*(Leaves) and *Trigonella foenum-graecum* (Seed).	STZ (60 mg/kg) induced diabetic rats ↑Bloog glucose= 269 mg/dl ↑ Serum creatinine= 1.61 m/dl	PH (3.63 g/2 ml/kg) ↓Blood glucose= 120.6 mg/dl ↓Serum creatinine= 0.33 mg/dl APH-A [(5 mg of Gliclazide + 1.81 g of PH)/2 ml/kg]. ↓Blood glucose= 120.0 mg/dl ↓Serum creatinine= 0.39 mg/dl APH-B [(4 mg of Gliclazide + 2.17 g of PH)/2 ml/kg]. ↓Blood glucose= 116.4 mg/dl ↓Serum creatinine= 0.38 mg/dl APH-C [(2 mg of Gliclazide + 2.904 g PH)/2 ml/kg]. ↓Blood glucose= 110.4 mg/dl ↓Serum creatinine= 0.35 mg/dl	Gliclazide (10 mg/ml/kg) ↓Blood glucose= 138 mg/dl ↓Serum creatinine= 0.75 mg/dl	*In vivo*; India	Hypolipidemic	[138]
HF1& HF2	*Phyllathus emblica* and *Annona squamosa*.	STZ (60mg/kg) induced Type 2 diabetic rats. Plasma glucose= 145.1mg/dl HbA1c= 253.1mg/dl	HF1(20mg/kg/BW) ↓Plasma glucose= 106.9mg/dl ↓HbA1c= 94.8mg/dl HF2(20mg/kg BW) ↓Plasma glucose= 95.3mg/dl ↓HbA1c= 80.0mg/dl	Glibenclamide (0.5mg/kg) ↓Plasma glucose= 84.9mg/dl ↓HbA1c= 78.7mg/dl	*In vivo*; India	Anti-hyperlipidaemic	[44]
PHF	*Salacia oblonga*, *Salacia roburghii*, *Garcinia indica* and *Lagerstroemia parviflora*.	STZ (35gm/kg) induced high-fat diet (HFD) diabetic rats. Blood glucose= 19.35 mmol/L Insulin= 68.62 pg/L	At 400mg/kg/b.w ↓Blood glucose= 9.54 mmol/L ↑Insulin= 94.22 pg/L	Metformin (250 mg/kg b.w.) ↓Blood glucose= 8.20 mmol/L ↑Insulin= 104.52 pg/L	*In vivo*; India		[139]
PHF	*Syzygium cumini* (Leaves), *Ficus glomerata* (Bark), *Butea superb* (Flower).	Alloxan monohydrate induced diabetic rats. Blood glucose= 413mg/100ml	At 500mg/kg body wt ↓Blood glucose= 132mg/100ml	Glibenclamide 600µg/kg body wt ↓105mg/100ml	*In vivo*; India		[81]

(Table 1) Contd…

Commercial Name	Formulations with Scientific Names	Experimental Model	Effects of Polyherbal Preparation	Effects of Reference Drug	Study Design and Country	Additional Property	References
PHF	*Allium sativum* (Cloves juice), *Aloe vera* (Leaf juice), *Nigella sativa* (Seed powder), *Plantago psyllium* (Seed husk), *Silybum marianum* (Seed extract) and *Trigonella foenum-graecum* (Seed powder).	Human subjects to type 2 diabetes	25 patients Male 11, Female 14 for 40 days ↓FBG= 146 mg/dl ↓HbA1c= 7.7 % ↑Urea= 28 mg/dl ↓Creatinine= 1 %		Clinical trials; Iran	Dyslipidemia	[70]
Mixed spices	*Zingiber officinale, Allium sativum, Allium cepa, Capsicum annuum, Curcuma longa, Cuminum cyminum, Cinnamon, Syzygium aromaticum, Trigonella foenum-graecum, Piper Nigrum, Nigella sativa,* Caromseed and *Elettaria cardamomum*.	Alloxan monohydrate (150mg/kg b.w.) ↑FBG= 13.0 mmol/L ↑Body weight= 224 g Chronic effect of spice mix on two hours post-prandial glucose concentration of alloxan induced type 2 diabetic model rats. ↑2hPG=27.40 mmol/L	At 200mg/kg/b.w. ↓FBG= 7.00 mmol/L ↓Body weight= 223 gm ↓2hPG=10.90 mmol/L	Glibenclamide (0.5mg/kg/b.w.) ↓FBG= 6.30 mmol/L ↓Body weight= 221 g ↓2hPG=10.2 mmol/L	*In vivo*; Bangladesh		[48]
PH	*Momordica charantia* (Fruit), *Syzygium cumini* (Seed), *Elettaria cadamomum*(Seed), *Cicer arietinum* (Seed), *Foeniculum vulgare*(Seed), *Vachellia nilotica* (Leaves) and *Gymnemasylvestre* (Leaves).	Alloxan(150 mg/kg) induced monodhydrate rats. ↑Serum glucose= 375.20 mg/dl ↓Serum insulin= 6.26 U/L ↑HbA1c= 13.92 % ↓Leptin= 1.78 ng/ml ↓Liver glycogen= 9.24 mg/g	At 600mg/kg ↓Serum glucose= 142.60 mg/dl ↑Serum insulin= 16.87 U/L ↓HbA1c= 6.62 % ↑Leptin= 2.78 ng/ml ↑Liver glycogen= 33.72 mg/g ↑enhanced the performance of pancreatic β cells by upregulating the expression of insulin signaling cascade.	Glibenclamide ↓Serum insulin= 128.40 mg/dl ↑Serum insulin= 17.54 U/L ↓HbA1c= 6.05 % ↑Leptin= 3.08 ng/ml ↑Liver glycogen= 39.24 mg/g	*In vivo*; Pakistan	Insulin signaling cascade	[140]

(Table 1) Contd…

Commercial Name	Formulations with Scientific Names	Experimental Model	Effects of Polyherbal Preparation	Effects of Reference Drug	Study Design and Country	Additional Property	References
Gluconorm-5	*Camellia sinensis* (Leaves), *Punica granatum* (outer rind), *Macrotyloma uniflorum* (Seed), *Foeniculum vulgare miller* (Seed), *Trigonella foenum-graecum*b (Seed).	STZ (60mg/kg) induced diabetic rats. ↑Blood glucose level= 460.4 mg/dl	At 600mg/kg ↓Blood glucose level= 74.3 mg/dl	Glibenclamide (1mg/kg) ↓Blood glucose level= 101.1 mg/dl	*In vivo*;India	Antihyperlipidemic and hepato-protective activity	[141]
Sugar remedy	*Momordica charantia*, *Gymnema sylvestre*, *Withania somifera*, *Syzygium cumini*, *Asphaltum*, *Trigonella foenum-graecum*, *Phyllanthus emblica*, *Terminalia bellirica*, *Terminalia chebula*, *Cinnamomum zeylanicum*, *Pterocarpus marsupium*.	STZ (60mg/kg) induced type 2 diabetic rats. ↑Serum glucose= 350.26 mg/dl ↑Serum creatinine= 2.55 mg/dl ↑Uric acid= 9.26 mg/dl	At 740mg/kg ↓Serum glucose= 129.72 mg/dl ↓Serum creatinine= 1.01 mg/dl ↓Uric acid= 4.33 mg/dl	Metformin (500 mg/kg/day,orally) ↓Serum glucose= 128.20 mg/dl ↓ Serum creatinine= 1.69 mg/dl ↓Uric acid= 6.09 mg/dl	*In vivo*;India	Hyperlipidemia and antioxidant	[94]
PHF Polyherbal Formulation	*Gymnemasylvestre* (Leaves), *Trigonella foenum-graecum* (Seed) and *Phyllanthus emblica* (Fruit).	STZ (120mg/kg) induced diabetic rats. ↑Blood glucose= 136.2 mg/dl ↑FBG= 302.5 mg/dl	HF1 at 20mg/kg/b.w. ↓Blood glucose= 92.1 mg/dl ↓FBG= 90.4 mg/dl HF2 at 20mg/kg/b.w. ↓Blood glucose= 79.3 mg/dl ↓FBG= 80.3 mg/dl HF3 at 20mg/dl/b.w. ↓Blood glucose= 83.6 mg/dl ↓FBG= 85.9 mg/dl HF4 at 20mg/dl/b.w. ↓Blood glucose= 85.7 mg/dl ↓FBG= 86.1 mg/dl	Glibenclamide (0.5 mg/kg) ↓Blood glucose= 75.3 mg/dl ↓FBG= 76.4 mg/dl	*In vivo*;India	Antihyperlipidemic	[54]

(Table 1) Contd…

Commercial Name	Formulations with Scientific Names	Experimental Model	Effects of Polyherbal Preparation	Effects of Reference Drug	Study Design and Country	Additional Property	References
OJ	*Aegle marmelos*, *Trigonellafoe-num-graecum*, *Carumcarvi*, *Emblica officinalis*, *Terminalia chebula*, *Terminalia bellirica*, *Swertica chirata*, *Tinospora cordifolia*, *Eugenia jambolana*, *Picrorhiza kurroa*, *Gymnema sylvestre*, *Salacia chinensis*, *Curcuma longa* and *Melia azadirachta*.	STZ (60mg/kg) induced diabetic rats. ↓Body weight= 227 g ↑Urine volume= 10.50 ml/5h ↑Serum glucose= 348 mg/dl	At 0.28ml/kg twice daily for 21 days ↓Body weight= 285 g ↓Urine volume= 2.37 ml/5h ↓Serum glucose= 143 mg/dl ↓ Histological damage in liver and pancreatic tissue	Metformin (100mg/kg) ↑Body weight= 355 g ↓Urine volume= 5.47 ml/5h ↓Serume glucose= 170 mg/dl	*In vivo*; India	Antihyper-lipidemic	[142]
PHF	*Lawsonia inermis* and *Azadira chtaindica*.	Alloxan (120mg/kg) monohydrate induced diabetic rats for 10 days ↑Blood glucose= 268.2 mg/dl	F1 ↓Blood glucose= 200.8 mg/dl F2 ↓Blood glucose= 215.7 mg/dl F3 ↓Blood glucose= 222.3 mg/dl F4 Blood glucose= 246.1 mg/dl F5 Blood glucose= 252.7 mg/dl	Glibenclamide (0.5 mg/kg p.o. 10% w/v, 1ml/200 g rat) ↓Blood glucose= 182.6(mg/dl)	*In vivo*; India		[37]
		STZ (60mg/kg) induced diabetic rats for 21 day ↓Body weight= 127.1 g ↑Blood glucose level=325.5 mg/dl	F1 ↑Body weight= 156.6 g ↓Blood glucose= 129.1mg/dl F2 ↑Body weight= 160.1g ↓Blood glucose= 115.3 mg/dl F3 ↑Body weight= 158.1g ↓Blood glucose= 101.6 mg/dl F4 ↑Body weight= 157.3 g ↓Blood glucose= 90 mg/dl F5 ↑Body weight= 155.3 g ↓Blood glucose= 103.2 mg/dl	Glimiperide drug(1 mg/kg) ↑Body weight= 159.5 g ↓Blood glucose= 82 mg/dl			

(Table 1) Contd…

Commercial Name	Formulations with Scientific Names	Experimental Model	Effects of Polyherbal Preparation	Effects of Reference Drug	Study Design and Country	Additional Property	References
Diabac	*Gymnema sylvestre*, *Eugenia jambolana*, *Aegle marmelos*, *Ficus benghalensis*, *Asphaltum*.	STZ (60mg/kg i.p) induced type 2 diabetes. ↑FBG= 319.2 mg/dl ↓Hb= 8.16 g/dl ↑HbA1c= 11.75 % ↓Serum insulin= 0.27 mu/L ↓Liver glycogen= 7.86 mg/g ↑Serum creatinine=1.85 mg/dl ↑Urea= 59.93 mg/dl ↑Uric acid= 8.26 mg/dl	At (1000 mg/kg, p.o.) ↓FBG= 119.2 mg/dl ↑Hb= 14.10 g/dl ↓HbA1c= 7.18 % ↑Serum insulin= 0.40 mU/L ↑Liver glycogen= 47.21 mg/g ↓Serum creatinine= 0.87 mg/dl ↓Urea= 35.86 mg/dl ↓Uric acid= 4.12 mg/dl	Glibenclamide (5 mg/kg, p.o.) ↓FBG=132.7 mg/dl ↑Hb= 12.48 g/dl ↓HbA1c= 6.78 % ↑Serum insulin= 0.76 mU/L ↑Liver glycogen= 48.33 mg/g ↓Serum creatinine= 0.87 mg/dl ↓Urea= 36.64 mg/dl ↓Uric acid= 3.30 mg/dl	*In vivo*; India	Antihyperlipidemic	[95]
Aloe camperi , Meriandradi-anthera and PH	*Aloe camperi* (Leaves), *Meriandradi anthera* (Leaves), *Lepidium sativum* (Seed), *Brassica nigra* (Seed) and *Nigella sativa* (Seed).	Alloxan monohydrate (150 mg/kg, i.p.) ↑Blood glucose level= 239.2 mg/dl	At 200kg/kg AC (Aloe camperi) ↓Blood glucose level= 144.3 mg/dl MD (Meriandra dianthera) ↓Blood glucose level= 144.3 mg/dl PH (Polyherbal drug) ↓Blood glucose level= 160.4 mg/dl At 400mg/kg AC (Aloe camperi) ↓Blood glucose level= 135.1 mg/dl MD (Meriandra dianthera) ↓Blood glucose level= 135.1 mg/dl PH (Polyherbal drug) ↓Blood glucose level= 154.2 mg/dl	Metformin (5 mg/kg) ↓Blood glucose level=124.2 mg/dl	*In vivo*; Eritrea		[41]
PH	*Swertia chirata*, *Artemisia absinthium*, *Caesalpinia bonduc*, *Bunium persicum*, *Gymnema sylvestre*, *Citrullus colocynthis*, *Sphaeranthus indicus* and *Cuminum cyminum*.	Alloxan monohydrate (150mg/kg) induced diabetic rats. ↑Serum glucose= 518 mg/dl ↓Serum insulin= 6.58 mg/dl ↑HbA1c= 13.92 % ↓Glucokinase= 111.2 µmolG6PO4/min/mg proteins	At 600 mg/kg ↓Serum glucose= 143.1 mg/dl ↑Serum insulin= 15.78 mg/dl ↓HbA1c= 6.84 % ↑Glucokinase= 176.2 µmolG6PO4/min/mg proteins	Glibenclamide (10 mg/kg) ↓Serum glucose= 138.20 mg/dl ↑Serum insulin= 17.65 mg/dl ↓HbA1c= 6.14 % ↓Glucokinase= 181.6 µmolG6PO4/min/mg proteins	*In vivo*; Pakistan	Antihyperlipidemic	[49]

(Table 1) Contd…

Commercial Name	Formulations with Scientific Names	Experimental Model	Effects of Polyherbal Preparation	Effects of Reference Drug	Study Design and Country	Additional Property	References
ADD1 and ADD2	DIA ARECA and ASANADI KAHSAYA CHOORNA	STZ(40mg/kg) induced diabetic rats. ↑Blood glucose level= 448.8 mg/dl	At (3.1ml/200g) ADD1 ↓Blood glucose level= 296.7 mg/dl ADD2 ↓Blood glucose level= 312.3 mg/dl At (6.2ml/200g) ADD1 ↓Blood glucose level= 244.6 mg/dl ADD2 ↓Blood glucose level= 154 mg/dl	Metformin (500mg/kg) ↓Blood glucose level= 134 mg/dl	*In vivo*; India		[56]
PHF	Wheat germ (Oil), *Coriander sativum* (Juice) and *Aloe vera* (Juice).	Alloxan monohydrate (250mg) induced diabetic mice. ↑FBG= 261.4 mg/dl	At (1.0ml/kg) PH-1 ↓FBG= 202.2 mg/dl PH-2 ↓FBG= 117.6 mg/dl PH-3 ↓FBG= 137 mg/dl At (2.0ml/kg) PH-1 ↓FBG= 180.4 mg/dl PH-2 ↓FBG= 137.2 mg/dl PH-3 ↓FBG= 132.6 mg/dl	Glibenclamide (600 µg/kg) ↓FBG= 132.6 mg/dl	*In vivo*; India		[50]
Saptaran gyadi Ghanavati	*Salacia chinensis* (Root), *Momordicacharantia*(Seed), *Trigonella foenum-graecum* (Seed), *Tinospora cordifolia* (Stem), *Terminalia chebula*, *Terminalia bellirica* and *Emblica officinalis* (Fruit pericrap).	Swiss albino mice (400 mg/kg) ↑Blood glucose= 106.00 mg/dl	At 400mg/kg ↓Blood glucose level= 70.7 mg/dl	Glibenclamide(0.65mg/kg) ↓Blood glucose level= 67.8 mg/dl	*In vivo*; India		[40]

(Table 1) Contd…

Commercial Name	Formulations with Scientific Names	Experimental Model	Effects of Polyherbal Preparation	Effects of Reference Drug	Study Design and Country	Additional Property	References
PHF Polyherbal formulation	*Eugenia jambolana* (Seed), *Tinospora cordifolia* (Root), *Gymnema sylvestre* (Leaves), *Cressa cretica* (Leaves), *Casearia esculenta* (Root), *Curcuma longa* (Rhizome), *Swertia chirata* (Leaves), *Centratherum anthelminticu* (Seed), *Picrorrhiza kurroa* (Rhizome), *Trigonella foenum-graec*um (Seed), *Terminalia chebula* (Fruit), *Holarrhena antidysenterica* (Bark), *Pterocarpus marsupium* (Leaves), *Glycyrrhiza glabra* (Rhizome), Mineral pitch, *Tribulus terrestris* (Seed), *Withania somnifera* (Leaves), *Nardostachys jatamansi* (Rhizome) and *Bacopa monniera* (Leaves).	STZ induced diabetic nephropathy rats. ↓Urine volume= 4.0 ml/rat/day ↓Urinary urea= 0.01 mg/dl ↑Serum creatinine= 2.40 mg/dl ↓Urine creatinine= 5.8 mg/dl ↑ Protein urine= 24.70 mg/day ↑ UAER= 16.8 µg/day ↑ AGES(AU)= 455	At 500mg/kg ↑Urine volume= 13.2 ml/rat/day ↑Urinary urea= 3.67 mg/dl ↓Serum creatinine= 0.94 mg/dl ↑Urine creatinine= 23.8 mg/dl ↓Protein urine= 0.08 mg/day ↓UAER= 2.9 µg/day ↓AGES(AU)= 227		*In-vivo*; India		[143]
NPF Novel Polyherbal Formulation	*Holarrhena antidysenterica* (Seed), *Centratherum anthelminticum* (Seed) and *Trigonella foenum-graecum* (Seed).	Type 2 diabetic patients.	Patient was advised to take one teaspoon of the powder with cold water twice daily in the morning and evening. ↓Blood glucose level		Clinical trials; Bangladesh		[71]

(Table 1) Contd…

Commercial Name	Formulations with Scientific Names	Experimental Model	Effects of Polyherbal Preparation	Effects of Reference Drug	Study Design and Country	Additional Property	References
Madhum ehantak churna (MMC)	*Mangifera indica*, *Momordica charantia*, *Syzygium cimini*, *Azadirachta indica*, *Allium cepa*, *Vachellia nilotica*, *Sida cordifolia*, *Trigonella foenum-graecum*, *Gymnema sylvestre*, *Curcuma longa* and *Terminalia chebula*.	STZ induced type 2 diabetic rats. ↑Blood glucose= 330 mg/dl	Low-dose MMC ↓Blood glucose= 118 mg/dl High-dose MMC ↓Blood glucose= 128 mg/dl	Glibenclamide(10mg/kg/day) ↓Blood glucose= 120 mg/dl	*In-vivo*; India		[19]
Talapotaka churna	*Cassia auriculata*, *Emblica officinalis*, *Curcuma longa* and *Berberis aristata*.	Type 2 diabetic patients	4g Talapotaka churna TID before meal with buttermilk. ↑FBG= 119.5 mg/dl ↓Postprandial blood sugar= 158.0 mg/dl ≈HbA1c= 7.55 % 4g Talapotaka churna TID before meal with warm water ↓FBG= 119.1 mg/dl ↑ Postprandial blood sugar= 185.8 mg/dl ≈HbA1c= 7.85 % 4g Talapotaka churna TID before meal with & ongoing allopathic treatment ↓FBG= 132.5 mg/dl ↑ Postprandial blood sugar= 216.0 mg/dl ↑HbA1c= 8.03 % ↓minimize diabetic symptoms.	1gm Glimipride BD before meal with water ↓FBG= 114.8 mg/dl ↑ Postprandial blood sugar=178.6 mg/dl ≈ HbA1c= 7.61 %	Clinical trials; India		[72]

(Table 1) Contd…

Commercial Name	Formulations with Scientific Names	Experimental Model	Effects of Polyherbal Preparation	Effects of Reference Drug	Study Design and Country	Additional Property	References
PHADT	*Gymnema sylvestre* (Leaves) *Momordica charantia* (Seed), *Phyllanthus amarus* (Fruit), *Ocimum sanctum* (Leaves), *Trigonella foenum-graecum* (Seed), *Allium sativum* (Bulb).	STZ (55 mg/kg b.w. p.o) induced diabetic rats. Body weight= 139.3 g Feed intake= 24.5 g BSL= 368.7 mg/dl BGL= 398 mg/dl	At (400 mg/kg) ↑Body weight= 190.3 g ↓Feed intake= 21.3 g ↓BSL= 260.2 mg/dl ↓BGL= 312 mg/dl ↓ Significant regeneration of pancreatic β cells	Glibenclamide(10mg/kg b.w.p.o) ↑Body weight= 214.7 g ↓Feed intake= 20.5 g ↓BSL= 255.0 mg/dl ↓BGL= 296 mg/dl ↓ Significant regeneration of pancreatic β cells	*In vivo*; India	Antihyperlipidemic	[45]
Herbal combination	*Andrographis paniculata*, *Lagerstroemia paniculata, Lagerstroemia speciosa*.	Alloxan monohydrate (150mg/kg BW) induced diabetic mice. BGL= 465.8 mg/dl	Combination of *A. paniculata*and *L. speciosa*(ratio 2:1) 0.4ml/20g body wt. ↓BGL= 339.6 mg/dl Combination of *A. paniculata* and *L. speciosa* (ratio 1:1) 0.4ml/20g body wt ↑BGL= 464.6 mg/dl Combination of *A. paniculata* and *L. speciosa* (ratio 1:2) 0.4ml/20g body wt ↓BGL= 411.8 mg/dl	Glibenclamide (0.013 mg/20g BW) ↓BGL= 154.6 mg/dl	*In vivo*; Indonesia		[38]
Combination	*Azadirachta indica* and *Gynura procumbens*.	Alloxan monohydrate(150mg/kg BW) induced diabetic rats.	Combination1(*A. indica* 150 mg/kgBW+ *G.procumbens* 37.5 mg/kgBB) Combination 2(*A. indica* 100 mg/kgBW + *G.procumbens* 75 mg/kgBW) Combination 3(*A. indica* 50 mg/kgBW + *G.procumbens* 112.5 mg/kgBW) ↑Postprandial= 64.74 % ↑Preprandial= 74.91 % ↑Insulin ↓Evaluated glucose concentration Histological studies indicated that this combination improved the morphology of the islets of Langerhans and β cells	Glibenclamide(0.45 mg/kgBW)	*In vivo*; Indonesia		[144]

(Table 1) Contd…

Commercial Name	Formulations with Scientific Names	Experimental Model	Effects of Polyherbal Preparation	Effects of Reference Drug	Study Design and Country	Additional Property	References
Dolabi	*Gymnema sylvestre*, *Bambusa bambos*, *Rumex vesicarius*, *Acacia Arabica*, Calcined Mytilusmargaritiferus, Aphalt and Goat pancreas.	STZ (110mg/kg) induced diabetic rats.	At (35.2 mg•kg^{-1}•day^{-1}) ↓FPG ↓Guctosamine ↓Blood glucose	Pioglitazone(2.7 mg•kg^{-1}•day^{-1}), ↓FPG ↓Guctosamine ↓Blood glucose	*In vivo*; Pakistan		[98]
PH	*Ocimum gratissimum* (Leaves) and *Gongronema latifolium* (Leaves).	Alloxan(100mg/kg/b.w) monohydrate induced diabetic rats ↑FGL= 248.0 mg/dl	At 400 mg/kg ↓FBG= 107.2 mg/dl		*In vivo*; Nigeria	Reproductive function	[145]
PHP	*Curcuma long*, *Lavandula stoechas*, *Aegle marmelos* and *Glycyrrhiza glabra*.	Alloxan(150mg/kg b.w.) induced diabetic mice ↑FBGL	At 150mg/kg b/w. ↓FBGL	Pioglitazone (1mg/kg b.w.) ↓FBGL	*In vivo*; Pakistan		[146]
SMK001	*Coptis chinensis* and *Trichosanthes kirilowii*.	STZ (60mg/kg) induced diabrtic rats. Body weight=169.6 BGL= 410.2 UGL= 10026.4 Pancreas weight= 0.70 No. of islets= 2.20 No. of insulin producing cell= 3.60 No. of glucagon producing cell= 78.60	At 500mg/kg ↑Body weight= 215.4 ↓BGL= 280.4 ↓UGL= 5042.2 ↑Pancres weight= 0.88 ↑ No. of islets= 6.60 ↑ No. of insulin producing cell= 6.60 ↓ No. of glucagon producing cell= 43.80	Glibenclamide(5mg/kg) ↑Body weight= 177.6 ↓BGL= 345.8 ↓UGL= 7329.4 ↑Pancreas weight= 0.077 ↑No. of islets= 4.60 ↑ No. of insulin producing cell= 15.40 ↓ No. of glucagon producing cell= 51.40	*In vivo*; Korea		[147]
Tetraherbs	*Cinnamomun zeylanicum*, *Trigonella foenum-graecum*, *Allium stipitatum*, *Syzygium aromaticum*.	STZ (55mg/kg) induced diabetic rats. Body weight= 151.3 g FBG= 497.6 mg/dL AUC= 63,597.5 mg/dL No. of islets(N/10mm2)= 5.07 Area of islets(mm2)= 0.0090 Diameter of islet (um)= 0.0143 No. of islet(N/100um2)= 4.33	At 300mg/kg ↑Body weight= 160.1 g ↓FBG= 144.7 mg/dL ↓AUC= 28,650.0(mg/dL) ↑ No. of islets(N/10mm2)= 19.73 ↑ Area of islets(mm2)= 0.0197 ↑ Diameter of islet (um)= 164.8 ↑ No. of islet(N/100um2)= 13.05	Metformin(500mg/kg) ↑Body weight= 161.8 g ↓FBG= 111.6 mg/dL ↓AUC= 28,697.5 mg/dL ↑ No. of islets(N/10mm2)= 18.77 ↑ Area of islets(mm2)= 0.0143 ↑ Diameter of islet (um)= 142.3 ↑ No. of islet(N/100um2)= 6.49	*In vivo*; Iran	Hypolipidemic	[51]

(Table 1) Contd…

Commercial Name	Formulations with Scientific Names	Experimental Model	Effects of Polyherbal Preparation	Effects of Reference Drug	Study Design and Country	Additional Property	References
PHF	*Gymnema sylvestre, Emblica officinalis and Salacia reticulata*	STZ (45mg/kg) induced diabetic rats ↑Blood glucose= 215.50mg/dl	At 200 mg/kg ↓Blood glucose=96.50mg/dl At 400 mg/kg ↓Blood glucose=99.50mg/dl	Glibenclamide (0.5 mg/kg, p.o) ↓Blood glucose=106.00mg/dl	*In vivo*, *In vitro*; India	Anti-hyperglycemic and antioxidant activities	[148]
PHF	*Allium cepa* (bulb), *Allium sativum* (bulb), *Trigonella foenum-graecum* (seed), and *Curcuma longa* (rhizome)	STZ (60mg/kg) induced diabetic rats ↑Fasting blood glucose= 317.45mg/dl	At 100 mg/kg ↑ Fasting blood glucose= 105.89mg/dl AT 200 mg/kg ↑Fasting blood glucose= 104.95mg/dl At 400 mg/kg ↑Fasting blood glucose= 99.47mg/dl	Glibenclamide (10 mg/kg): ↓99.19mg/dl	*In vivo*; India	Hyperglycaemia	[149]
FD1	*Alstonia scholaris,* Leaves, *Pterocarpus marsupium* Heartwood, *Embelia ribes* Heartwood.	STZ (60mg/kg) induced diabetic rats ↑Blood glucose level=412.2mg/dl	At 200 mg/kg ↓Blood glucose level=70.05mg/dl	Glipizide (0.25mg/kg) ↓Blood glucose level=75.66mg/dl	*In vivo*; India		[150]
PHF		STZ (120mg/kg) induced diabetic rats ↑Blood glucose level=353.6mg/dl	F1 at 200 mg/kg ↓Blood glucose level=109.2mg/dl F1 at 400 mg/kg ↓Blood glucose level=88.9mg/dl F2 at 200 mg/kg ↓Blood glucose level=116.5mg/dl F2 at 400 mg/kg ↓Blood glucose level=84.9mg/dl F3 at 200 mg/kg ↓Blood glucose level=113.6mg/dl F3 at 200 mg/kg ↓Blood glucose level=86.5mg/dl F4 at 200 mg/kg ↓Blood glucose level=103.8mg/dl F4 at 400 mg/kg ↓Blood glucose level=86.4mg/dl	Glibenclamide (0.50mg/kg) ↓Blood glucose level=82.9mg/dl	*In vivo*; India	Hyperglycemia	[151]

(Table 1) Contd…

Commercial Name	Formulations with Scientific Names	Experimental Model	Effects of Polyherbal Preparation	Effects of Reference Drug	Study Design and Country	Additional Property	References
Saf¯uf-i-Dhay¯ab¯ıtus	*Gudmar Booti (Gymnema sylvestre R. Br.), Gilo (Tinospora cordifolia (Willd.) Miers.), Zanjabeel (Zingiber officinale Rosc.), Satt-i-Salajeet (Asphaltum), Kushta-i-Faulad (Calx of Iron) and Maghz-i-Khasta Jamun (Syzygium cumini (L.)*	STZ (55 mg/kg b.w.) ↓Body weight= 127.2g ↑Food intake= 43.00g ↑Fasting blood sugar= 244.33mg/dl	Saf¯uf-i-Dhay¯ab¯ıtus at 500 mg/ kg b. w. a ↑Body weight= 184g ↓Food intake= 31.60g ↓Fasting blood sugar=153.4mg/dl Saf¯uf-i-Dhay¯ab¯ıtus at 500 mg/ kg b. w. along with glibenclamide at 0.6 mg / kg b. w. p. o. ↑Body weight= 169.3g ↓Food intake= 32.17g ↓Fasting blood sugar=134md/dl	Glibenclamide at 0.6 mg/ kg. b. w. ↑Body weight= 181.7g ↓Food intake= 37.33g ↓Fasting blood sugar=202.5mg/dlN	*In vivo*; India	hypoglycaemic, hepatoprotective, nephroprotective and hypocholesterolemi	[152]
Polyherbal combination	*Taraxacum officinale* and *Momordica charantia*	STZ induced diabetic rats (120mg/kg b.w.) Blood glucose level ↓Blood glucose level=13.70mmol/l	62.5 mg/kg b.w ↑Blood glucose level=18.24mmol/l 250 mg/kg b.w ↑Blood glucose Blevel=16.66mmol/l 1000 mg/kg b.w ↑Blood glucose level=13.79mmol/l	Glibenclamide (1mg/kg b.w.) ↑Blood glucose level=21.89mmol/l	*In vivo*; India		[153]
		STZ induced diabetic rats (120mg/kg b.w.) Blood glucose level ↑Blood glucose Level= 26.89mmol/l	62.5 mg/kg b.w ↓Blood glucose level=26.09mmol/l 250 mg/kg b.w ↓Blood glucose level=14.51mmol/l 1000 mg/kg b.w ↓Blood glucose level=25.59mmol/l	Glibenclamide (1mg/kg b.w.) ↓Blood glucose level=18.91 mmol/l Metformin 50 mg/kg ↓Blood glucose level=18.06mmol/l Sitagliptin 10 mg/kg ↓Blood glucose level=20.41mmol/l			

Abbreviations: STZ: Streptozotocin, FBG: fasting blood glucose, BGL: Blood glucose level, SBL: Serum glucose level, UGL- Urine glucose level, HbA1c: Glycosylated haemoglobin, UAER: Urinary albumin excretion rate, AGES: Advanced glycation end products, AU: Arbitrary unit; PPAR: peroxisome proliferator-activated receptor, SOD: Superoxide dismutase, GSH: Reduced glutathione, TBAR: Serum thiobarbituric, AUC: Area under curve.

8.1. *In vitro* Analyses

Among the 76 PHFs, only APKJ-004, composed of *Eugenia jambolana* and *Cinnamomum zeylanicum,* was subjected to *in-vitro* assay on 3T3-L1, C2C12 and HepG2 cell lines to ascertain their α-glycosidase inhibitory activity compared to acarbose as standard [29].

8.2. Preclinical Trials

Seventy-one PHFs were tested for their therapeutic efficiency on the biochemical parameters of alloxan- or streptozotocin-induced diabetic rodents (Table **1**). The anti-diabetic activity of Diakyur [30], Karnim Plus [31], PHF [32], Polyherbal preparation [33], Diashis [34], APKJ-004 [29], Polyherbal extract [35], DIA-2 [36], PHF [37], Herbal combinations [38], Madhurakshak (Mdr) [39], *Saptarangyadi Ghanavati* [40]*, Aloe camperi*, *Meriandra dianthera* and polyherbal drug [41], PHPE [42], Polyherbal extract [43], HF1& HF2 [44], PHADT [45], ADC05 [46], DS-01 [47], Mixed spices [48], PH [49], PHF [50], Tetraherbs [51], Mixture extract [52], PHF [53], PHF [54], PHF [55], ADD1 and ADD2 [56], PHF, PHF, Safuf-i-Dhayabitus, Polyherbal formulation were less when compared to the reference drug. All other PHFs were found to be more effective than the stand-

ard drugs like acarbose, glibenclamide, glimepiride, pioglitazone, rosiglitazone, tolbutamide and metformin used in the studies.

In 2009, Chan and co-workers [57] investigated the effect of SR10, a PHF comprising roots of *Radix astragali*, *Radix codonopsis*, and *Cortex lycii,* on blood glucose level (BGL) in diabetic mice. They inferred that both the low (464 mg/kg/day) and high (927 mg/kg/day) doses failed to bring back the glucose level to normal when compared to the standard drug metformin.

Akhtar and his team [58] studied the effect of Ziabeen, a herbal formulation composed of different parts of eight herbs, on BGL by the oral glucose tolerance test (OGTT) in diabetic rabbits. Their study indicated that administration of Ziabeen (4 g/kg) down-regulated the BGL after 30 min in contrast to the reference drug pioglitazone, where the BGL was up-regulated significantly ($P<0.05$) until 5 h. The efficacy of PHF Madhumehantak churna (MMC) was studied by Bhattacharya and Reddy [19] on diabetic rats. Both the low (216 mg/day) and high (648 mg/day) doses of MMC were able to bring back the BGL to near normal in a manner comparable to standard glibenclamide (10 mg/kg/day). However, the low dose of MMC was more effective at 14 and 28 days when compared to the high dose.

Thakkar and Patel [59] formulated Glyoherb, which consisted of 14 plant extracts as enlisted in Table **1**. In addition to this, they also included commercially available formulations, which are available in the market as Arogyavardhini vati, bang bhasma and chanraprabha vati. The Arogyavardhini vati is composed of *Picrorhiza kurroa*, *Terminalia chebula*, *Terminalia bellerica*, *Emblica officinalis*, *Commiphora wightii*, *Ricinus communis*, *Azadirachta indica*, and Asphaltum (Shilajit), and metals including purified mercury, purified sulphur, iron, mica and copper, and have been claimed to be effective in the treatment of various ailments [60]. Bang bhasma is a herbo-metallic ayurvedic substance prepared from tin. Chandraprabha is a proven formulation having glucose-lowering and anti-hyperlipidemic activities and is a blend of 37 herbo-mineral ingredients [61].

Mawleih and co-workers, in 2020 [56] evaluated the antidiabetic potentiality of two commercially available antidiabetic food supplements Dia Areca (areca nut, beetle vine, lime, lemon, jamboo, and edible grasses) [62] and Asanadi Kashaya Choorna composed of different parts of 23 plants [63]. The relevance of evaluation of anti-diabetic activity of already available commercial drugs for treating diabetes by Mawleih *et al.* [56] is, however, unclear. Instead of carrying out routine experimental work against diabetes, the researchers could have made an attempt to study the mechanism of action of these ayurvedic food supplements.

Recently in 2022 Safuf-i-Dhayabitus composed of Gymnema sylvestre, Tinosopra cordifolia, Zingiber officinalis, Syzygium cumini and other than plants Salajeet (Asphaltum) and metals Kushta-i-Faulad (Calx of iron) in combination with standard drug glibenclamide possesses significant antidiabetic, hepatoprotective and nephroprotective properties.

8.3. Clinical Trials

The efficacy of PHFs on T2DM patients through clinical trials was conducted on 7 formulations namely Diabecon (D-400) [64], Diabegon [65-67], Glucolevel [68], Karnim Plus [69], PHF [70], novel PHF [71], and Talapotaka churna [72].

Kant *et al.* [64] studied the effect of Diabecon (D-400) on various parameters, including micro-aneurysm, hemorrhage, exudation, and retinitis proliferans in patients with diabetic retinopathy. They inferred that 2 tablets of Diabecon (D-400) thrice daily for 12 weeks helped to ameliorate the retinal changes that occurred due to diabetes. However, the clinical efficiency of Diabecon (D-400) was not compared with a reference drug.

The PHF, Diabegon was subjected to clinical trials on patients with T2DM by three groups of researchers [65-67]. Diabegon (100 mg/kg body weight) demonstrated dose-dependent depletion in blood glucose and augmented insulin secretion, possibly by stimulating pancreatic β-cells and/or elevated insulin susceptibility by extra-pancreatic action. The results were comparable to standard glibenclamide and rosiglitazone [65]. Mahajan and his team [66] experimented with the effect of decoction obtained from Diabegon (10 g) on patients with T2DM. Oral administration of decoction on an empty stomach for 6 months revealed that the PHF could restore the level of blood glucose and glycosylated hemoglobin (HbA1c) to normal. In addition, it improved glycosuria and proteinuria. The clinical management of T2DM subjects with metabolic syndrome was conducted by supplementing with 4 g Diabegon twice daily for 18 months [67]. After one and a half years of therapy, Yadav *et al.* [67] reported a decrease in both fasting blood glucose (FBG) and postprandial blood glucose (PPBG) by 12.30-42.00% and 28-32%, respectively. Both the studies by Mahajan *et al.* [66] and Yadav *et al.* [67] were not backed by reference drugs to judge the efficacy of Diabegon. The hypoglycemic activity of Diabegon might be attributed to the synergistic effect of various bioactive components present in different plant and plant parts used as ingredients in the formulation.

The anti-hyperglycemic activity of Glucolevel, a blend of leaves of *Juglansregia*, *Olea europaea*, *Urticadioica*, and *Atriplexhalimus,* was studied on human subjects by Said *et al.* [68]. The patients were supplemented with one tablet of Glucolevel thrice daily for 4 weeks and monitored FBG and HbA1c levels. The levels of both FBG and HbA1c were concurrent with the normal range after 4 weeks of treatment with Glucolevel. However, this study was not supported by comparable results with a reference compound.

The hypoglycaemic activity of Karnim Plus capsule was evaluated on human volunteers in comparison to metformin capsule at a dose of 2 capsules twice daily before a meal for 24 weeks [69]. Karnim Plus capsule was found to be less potent in managing the levels of FBG and PPBG up to two weeks of administration when compared to metformin capsule; however, after four weeks of therapy, they were concurrent with each other. In addition, they reported Karnim Plus was more effective in regulating HbA1c in contrast to conventional metformin.

Zarvandi *et al.* [70] standardized a PHF with *Allium sativum* (cloves juice), *Aloe vera* (leaf juice), *Nigella sativa*

(seed powder), *Plantago psyllium* (seed husk), *Silybum marianum* (seed extract), and *Trigonella foenum-graecum* (seed powder) as nutra-ingredients and assessed the safety and efficacy on patients with the advanced stage of T2DM. Despite being medicated with statins (lipid-lowering medication) and oral hypoglycemic drugs, the patients had hyperlipidemia and hyperglycemia. Thirty such volunteers were supplemented with one sachet of PHF twice daily for a period of 40 days in addition to the normal medication they received before experimentation. Clinical assessment after 40 days revealed that PHF had a significant effect on FBG, HbA1c and serum lipid levels, which were restored back to near normal. However, PHF had no significant effect on serum biochemical and hematological parameters. Administration of PHF caused mild nausea in two subjects, while two others had diarrhea.

Rashid *et al.* [71] reported that oral administration of novel PHF (one teaspoon twice daily with cold water) in diabetic patients was effective in reducing FBG. Their claim was, however, not supported by any parameters or statistical data.

Talapotaka churna, a PHF composed of tetra herbs (*Cassia auriculata*, *Emblica officinalis*, *Curcuma longa* and *Berberisaristata*), was tested in patients with T2DM [72]. Three mode trials were conducted to ascertain the efficiency of PHF along with standard glimepiride (1 mg twice a day). Six patients received churna with buttermilk as a vehicle, other six patients were given churna with warm water, while 12 patients were fed with churna in addition to their normal allopathic medicine. All the doses were fixed at 4 g thrice daily before meals. The effect of glimepiride was tested in another six patients. The patients were advised to avoid carbohydrate and fat-rich food. All the trials were successful in bringing back the FBG to the clinically acceptable range in a significant way. The reduced level of PPBG was highly significant in patients who were supplemented with churna along with buttermilk, while others were not significant. The Talapotaka churna also did not show a significant reduction in HbA1c.

The above analysis indicated that PHFs composed of different plant parts seem to act differently but synergistically to regulate glucose level and thus are effective remedies in controlling T2DM in an effective way without any adverse effects.

9. PLANTS USED IN POLYHERBAL FORMULATIONS FOR DIABETES

Since the bioactive components of individual plants are insufficient to attain the desired therapeutic effect, the concept of polyherbalism has evolved [73]. Over 1200 plants have been used traditionally for the treatment of diabetes worldwide since ancient times. The nutra-ingredients of 70 PHFs included in this review resulted in the documentation of 147 species of plants belonging to 58 families (Table **2**). Based on plant diversity, Fabaceae is the most dominating family with 19 species. Of the 76 PHFs enlisted, the leaves of *Gymnema sylvestre* (Apocynaceae) were the most favoured and is one of the ingredients for 29 formulations, followed by the seeds of *Trigonella foenum-graecum* (Fabaceae) and *Momordica charantia* (Cucurbitaceae) for 27 and 24 formulations, respectively. Likewise, numerous bioactive compounds have been isolated, purified and identified from various plants used to treat diabetes for centuries. The bioactive compounds having insulin-mimetic properties obtained from 147 plants under study have been summarized in Table **2**.

For instance, gymnemic acid, being one of the active constituents of *Gymnema sylvestre*, aids in the treatment of diabetes by a number of mechanisms. Gymnemic acid inhibits the absorption of sugar molecules by the intestine by blocking the receptor sites for sugar and thus leading to reduced blood sugar levels [74]. It also up-regulates the activity of insulin-dependent enzymes and down-regulates the activity of insulin-independent enzymes [75]. Similarly, diosgenin, a well-known steroid sapogenin present in the seed of *Trigonella foenum-graecum* (commonly known as fenugreek), displayed potential as a therapeutic adjunct in the management of diabetes [76]. Diosgenin ameliorates oxidative stress and inhibits lipid peroxidation [77]. It has been reported that diosgenin rejuvenates the distorted pancreas morphology and improves insulin concentration [78]. Besides, diosgenin also triggers the expression of PPARγ [79]. Another important phytoconstituent of fenugreek is 4-hydroxyisoleucine, which improves insulin secretion and thus possesses hypoglycaemic activity [80].

Curcumin, a major component of *Curcuma longa,* exhibits anti-diabetic activities by protecting pancreatic β-cells by diminishing inflammatory response (decreasing TNF-α, IL-1β and IFN-γ levels) and impeding endoplasmic reticulum (ER)/ mitochondrial related apoptosis. Curcumin is also a potential inducer of heme-oxygenase-1 (HO-1), nuclear factor erythroid 2-related factor 2 (Nrf-2), and glucose transporter (GLUT-2), and thus helps in reducing oxidative stress [81].

The flower of *Butea superba* forms an ingredient of PHF standardized by Karigar and Shariff [32], along with *Syzygium cumini* (leaves), *Ficus glomerata* (bark), which is effective in lowering the BGL in diabetic rodents. Although a number of bioactive components from *B. superba,* like daidzein [82-84], Genistein [85-87], biochanin A [88, 89], have been reported to have anti-diabetic activity, the plant has not been explored for the same till date.

Widyawaruyanti *et al.* [38] developed an herbal combination to manage diabetes with three plants, *Andrographis paniculata*, *Lagerstroemia speciosa*, and *Lagerstroemia paniculata*. The aerial parts of *A. paniculata* and *L. speciosa* have been well established as anti-hyperglycemic, but there is no such report for *L. paniculata* (Table **2**).

Triticum aestivum (wheat germ oil) has been used by Srivatsava and Rai [50] along with the juice of *Coriander sativum* and *Aloe vera* as a remedy against diabetes, but to date, there is no evidence of wheat germ oil having anti-diabetic activity.

Apart from this, there are a number of plants that form an ingredient of various PHFs having insulin-mimetic properties on their own. Despite the fact that many bioactive compounds have been reported from those plants, compounds

Table 2. Plants species forming the ingredients of the poly herbal formations having compounds with anti-diabetic potentiality.

Family	Species	Parts Used	Compounds with Anti-diabetic Potentiality
Acanthaceae	*Andrographis paniculata*	Aerial part [154-157]	Andrographolide [158, 155,159]
	Asteracantha longifolia	Leaf [160]	Betulin [161]; Lupeol [162]; Stigmasterol [163]
Amaranthaceae	*Aerva lanata*	Leaf [164, 165]; Aerial part [166]; Root [167]	β-carboline [168]
	Atriplex halimus	Leaf [169]	NR
Amaryllidaceae	*Allium cepa*	Bulb [170-172]	Allicin [173]
	Allium sativum	Bulb [174-176]	Alliin [177,178]; Allicin [173]
	Allium stipitatum syn. *A. hirtifolium*	Bulb [179]	9-hexadecenoic acid or palmitoleate [180]
Anacardiaceae	*Mangifera indica*	Endopserm [181]; Leaf [182, 183]	Mangiferin [184, 185]; Linalool [186]
Annonaceae	*Annona squamosa*	Leaf [187]	Quercetin-3-O-glucoside [188]
Apiaceae	*Bunium persicum*	Seed [189]	Caryophyllene [190]; γ-terpinene [191]
	Carum carvi	Seed [192]	Carvone [193], [194]; D-limonene [195]
	Coriandrum sativum	Seed [196, 197]	Linalool [186]
	Cuminum cyminum	Seed [198-200]	Cuminaldehyde [201]; Cuminol [201]; p-cymene [202]
	Foeniculum vulgare	Essential oil [203]; Seed [204, 205]	trans-anethole [206]; Fanchone [207]
	Trachyspermum ammi	Seed [208]	Thymol [209]; p-cymene [202]; Pinene [210]; Carvone [193, 194]; D-limonene [195]
Apocynaceae	*Alstonia scholaris*	Leaf [211-214]	NR
	Catharanthus roseus	Leaf [215-219]	Vindogentianine [220]; Vindolidine [221]
	Gongronema latifolium	Leaf [222, 223]	Lupanine [224, 225]
	Gymnema sylvestre	Leaf [226, 227]	Gymnemic acid [228]
	Holarrhena antidysenterica	Seed [229-232]	NR
	Holarrhena pubescens	Bark [233]	NR
Asparagaceae	*Asparagus racemosus*	Root [234]; Leaf [235]	Sarsasapogenin [236]
Asphodelaceae	*Aloe barbadensis*	Gel [237]; Plant [238]	Aloin/ Barbaloin[239, 240]
	Aloe camperi	Leaf [241]	Aloin/ Barbaloin [239, 240]; Emodin [242, 243]
	Aloe vera	Leaf gel [244-249]	Aloin/ Barbaloin [239, 240]; Aloesin [250]; Emodin [242, 243]
Asteraceae	*Artemisia absinthium*	Plant [251]	Thujone [252]
	Artemisia sieberi	Essential oil [253]	1,8-cineole or Eucalyptol [254]
	Centratherumant helminticum	Seed [255, 256, 257]	Gallic acid [258]; Protocatechuic acid [259]; Caffeic acid [260]; Ellagic acid [261]; Ferulic acid [262]; Quercetin [263]; Kaempferol [264]
	Gynura procumbens	Leaf [265, 266]	Kaempferol 3-O-glucoside or Astragalin [267]
	Mori folium	Leaf [268]	Kaempferol 3-O-glucoside or Astragalin [267]
	Silybum marianum	Plant [269]	Silymarin [270]; Mariamides A [271]; Mariamides B [271]

(Table 2) Contd…

Family	Species	Parts Used	Compounds with Anti-diabetic Potentiality
	Sphaeranthus indicus	Root [282, 272-274]	Quercetin [263]
Berberidaceae	*Berberis aristata*	Root [275, 276]; Leaf [277]	Berberine [278]
Boraginaceae	*Rotula aquatica*	Root [279]; Leaf [280]	NR
Brassicaceae	*Brassica nigra*	Seed [281]	Sinigrin [282]; Glucoraphanin [283, 284]
	Eruca sativa	Leaf [285]	trans-Vaccenic acid [286]; Quercetin [263]
	Eruca vesicaria	Essential oil [287]	Erucin [287]
	Lepidium sativum	Seed [288-290]	Lepidine [291]
Burseraceae	*Commiphora wightii*	Resin [292]	Diasesartemin[293]; *epi*-muklin [293]; (Z)-guggulsterone [293]
Campanulaceae	*Codonopsis pilosula (Radix codonopsis)*	Residue [294]	NR
Capparaceae	*Capparis decidua*	Aerial parts [295]	Phthalic Acid [296]
Caprifoliaceae	*Nardostachys jatamansi*	Root [297, 298]	β-sitosterol [299]
Celastraceae	*Elaeodendron glaucum*	Stem bark [300]	β-sitosterol [299]; Lupeol [162]; Friedelin [301]
	Salacia chinensis	Root [302]	Mangiferin [303]; Salacinol [304]
	Salacia oblonga	Root [305, 306]	Mangiferin [303]; Salacinol [304]; Kotalanol [307]
	Salacia reticulata	Leaf [308]; Root [309]; Stem [309]	Mangiferin [303]; Salacinol [304]; Kotalanol [307]
	Salacia roxburghii	NR	Mangiferin [303]
Clusiaceaec	*Garcinia indica*	Fruit [310, 311]	Garcinol [312, 313]; Gambogic acid [314]
Combretaceae	*Terminalia arjuna*	Bark [315-317]; Leaf [318]	Arjunetin [319]; Arjungenin [319]; Ellagic acid [319]; Arjunic acid [319]
	Terminalia bellirica	Fruit [320]	Ellagic acid [261]; β-sitosterol [299]
	Terminalia chebula	Fruit [321]; Seed [322]	Chebulagic acid [323]; Punicalagin [324, 325]
	Terminalia tomentosa	Leaf [326]; Bark [327]	Arjunolic acid [328]; β-sitosterol [299]
Convolvulaceae	*Cressacretica*	Whole plant [329, 330]	Umbelliferone [331]
	Evolvulus alsinoides	Whole plant [332, 333]	Piperine [334]; Squalene [335]
Cucurbitaceae	*Citrullus colocynthis*	Fruit [336-340]; Seed [341]; Pulp [342]; Root [343, 344]	*Beta-pyrazol-1-yl-alanine* [345]
	Citrullus lanatus	Seed [346-350]; Leaf [351]; Juice [352]	Oleic acid [353]; β-sitosterol [299]; Lupeol [162]
	Coccinia indica	Leaf [354, 355]	β-sitosterol [299]; Betulin [161]
	Momordica charantia	Fruit [356, 357]; Seed [358]	Momordicin [359]; Charantin [360, 361]; Vicine [359]
	Trichosanthes kirilowii	Root [362]	Allantoin [363]
Cyperaceae	*Cyperus rotundus*	Rhizome [364, 365]	Cassigarol [366]; Scirpusin A [366]; Scirpusin B [366]
Ericaceae	*Vaccinium arctostaphylos*	Fruit [367-369]; Leaf [368]	Dalphinidin [370]; Quercetin [371]
Fabaceae	*Acacia arabica*	Bark [372, 373]	Daidzein [82-84]

(Table 2) Contd…

Family	Species	Parts Used	Compounds with Anti-diabetic Potentiality
	Butea superba	NR	Daidzein [82-84]; Genistein [86, 87]; Biochanin A [88, 89]
	Caesalpinia bonduc	Seed [374, 375]	NR
	Caesalpinia bonducella	Seed [376-378]	NR
	Cajanus cajan	Leaf [379, 380, 381]	Biochanin A [88, 89]; Betulinic acid [382]
	Cassia auriculata	Flower [376-378]; Leaf [386]	kaempferol-3-O -rutinoside [387]; Luteolin [388]
	Cassia javanica	Leaf [389]	Emodin [242, 390]
	Cicer arietinum	Seed and Sprout [391]	Formononetin [392, 393]; Biochanin A [88, 89]
	Glycyrrhiza glabra	Root [394]	Glycyrrhizin [395]; Glabridin [396]; Isoliquiriti-genin [397]; Liquiritigenin [397]
	Glycyrrhiza uralensis	Root [398]	Glycyrrhizin [395]; Glycyrrhetinic acid [399]
	Macrotyloma uniflorum	Seed [400, 401]	p-coumaric acid [402, 403]; p-hydroxy benzoic acid [404]
	Mucuna pruriens	Seed [405, 406]; Leaf [407]	Fagopyritol B1, Fagopyritol B2 [408]
	Pongamia pinnata	Flowers[409]; Leaf [410]; Bark [411]; Seed [412]	Cycloart-23-ene-3β, 25-diol [413]; Pongamol [414]; Karanjin [414]
	Psoralea corylifolia	Seed [415]	Bavachin [416]; Corylifol [417]; 4′-O-methylbavachalcone [417]; Psoralidin [417]; Neo-bavaisoflavone [417]
	Pterocarpus marsupium	Wood [418-420]; Bark [419]; Leaf [421]	Pterostilbene [422, 423]; (−)-epicatechin [424]
	Pueraria thunbergiana	Plant [425]	Tectorigenin [426]; Kaikasaponin III [426]
	Astragalus membranaceus	Root [427]	Formononetin [392, 393]; Astragalinm [427]; Astragalosides I [427]; Astragalosides II [427]; Astragalosides IV [427]; Isoastragaloside I [427]
	Trigonella foenum-graecum	Leaf [428]; Seed [429, 430]	Diosgenin [431, 432]; 4-Hydroxyisoleucine [76]; Trigonelline [433]; Tannic acid [434]
	Vachelliani lotica syn. *Acacia nilotica*	Pod [435]; Leaf [436]; Bark [437]	(−)-epicatechin [433]; Ellagic acid [261]; Proto-catechuic acid [259]; Umbelliferone [331]
Gentianaceae	*Enicostemma littorale*	Whole plant [438-442]	Gentianine [443]; Swertiamarin [444, 445]
	Swertia chirata	Root [446]; Whole plant [447]	Swerchirin [448]; Swertiamarin [444]
Juglandaceae	*Juglans regia*	Leaf [449-451]; Fruit peel [452]	(3S,5R,6R,7E,9S)-3,5,6,9- Tetrahydroxymega-stigman-7-ene [451]
Lamiaceae	*Callicarpa macrophylla*	Fruit [453]	β- amyrin [454]
	Lavandula stoechas	Essential oil [207]	α-pinene [210];Camphene [455]; Linalool [186];Limonene [186]
	Meriandra dianthera	Leaf [456]	1,8-cineole [261]; Linalool [186]
	Ocimum gratissimum	Leaf [457-460]	Chicoric acid [459]; Eugenol [461]
	Ocimum sanctum	Leaf [462, 463]	Eugenol [461]
	Premna corymbosa	Root [464]	NR
	Salvia officinalis	Leaf [465-467]	Thujone [252]

(Table 2) Contd…

Family	Species	PARTS USED	Compounds with anti-diabetic potentiality
	Teucrium polium	Aerial part [468, 469]	Rutin [469]; Apigenin [469]
Lauraceae	*Cinnamomum tamala*	Leaf [470, 471]	Myricetin [472]; Kaempferol [473]; Quercetin [263]; Kaempferol-3-O-Glucoside [267]; Quercetin-3-O-Rutinoside or rutin [469]
	Cinnamomum sp.	Bark [430, 474, 475]	Cinnamaldehyde [476, 477]
Lythraceae	*Lagerstroemia paniculata*	NR	NR
	Lagerstroemia parviflora	Aerial part [478]	NR
	Lagerstroemia speciosa	Leaf [479, 480]	Corosolic acid [481, 479]; Arjunolic acid [328]
	Lawsonia inermis	Whole plant [482, 483]	Betulin [484]; Betulinic acid [485, 484]; Lupeol [162]
	Punica granatum	Flower [486, 487]; Seed [488]; Peel [489-491]; Leaf [491]	Punicalagin[492]; Punicalin [492]; Ellagic acid [261]; Tricetin [493]
Magnoliaceae	*Schisandra chinensis*	Stem [494]; Fruit [495]	Gomisin J [495]; Gomisin N [495]; Schisandrin A [493]; Schisandrin C [493]; SCP-BII [496]
Malvaceae	*Sida cordifolia*	Aerial parts [497, 498, 499];Whole plant [500]	Pterostilbene [423]; hypaphorine [501]
Meliaceae	*Azadirachta indica*	Leaf [502, 503]; Seed oil [502]; Root bark [504]	Nimbidiol [505]; Gedunin [506]; Azadiradione [506]
	Melia azadirachta	Leaf [507]	NR
	Melia azedarach	Leaf [508, 509]; Twig [510]; Fruit [508]	Azedarachic acid [508]; Kaempferol [473]; Quercetin [263]; Kaempferol-3-O-Glucoside [267]; Quercetin-3-O-Rutinoside or rutin [469]
Menispermaceae	*Tinospora cordifolia*	Root [511]; Stem [512, 513]; Leaf [514]	Saponarin [515]; Palmatine [516]; Magnoflorine [517, 514, 518]; Jatrorrhizine [519]
Moraceae	*Ficus benghalensis*	NR	NR
	Ficus glomerata	Leaf [520]; Stem [521]; Root [522]; Bark [522]	Lupeol [162]; genistein [87]
Musaceae	*Musa sapientum*	Flower [523, 524]; Root [525]; Stem [526]; Leaf [527]	Naringenin [528]
Myristicaceae	*Myristica fragrans*	Seed [529-531]	Eugenol [461]; Pinene [210]
Myrtaceae	*Eugenia jambolana* syn. *Syzygium cumini*or *Syzygium jambolanum*	Seed [532, 533]; Fruit pulp [534]	Ursolic acid [535]; Rubuphenol [536]; Valoneic acid dilactone [536]
	Psidium guajava	Leaf [537, 538]; Fruit [539]; Fruit peel [540]	Strictinin [541]; Isotrictinin [541]; Pedunculagin [541]
	Syzygium aromaticum	Flower bud [542, 543]	Oleanolic acid [544, 545]; Maslinic acid [545]; Kaempferol [473]; Ellagic acid [261]
Nyctaginaceae	*Bougainvillea spectabilis*	Root bark [546]; Stem bark [547]; Leaf [548]	Pinitol [549]
Oleaceae	*Olea europaea*	Leaf [550-552]	Oleuropein [553]; Ligstroside [551]; Tyrosol [551]; Hydroxytyrosol [551]
Orobanchaceae	*Rehmannia glutinosa*	Root [554, 555]	Catalpol [556, 557]
Phyllanthaceae	*Emblica officinalis*	Bark [558]; Leaf [559]; Fruit [560]	Gallic acid [258]; Gallotanin [561]; Ellagic acid [261]; Corilagin [561]

(Table 2) Contd…

Family	Species	Parts used	Compounds with anti-diabetic potentiality
	Phyllanthus amarus	Leaf [562, 563]; Stem [562]; Seed [563]; Whole plant [564]	Phyllanthin [565]; Gallic acid [258]; Ellagic acid [261]
Pinaceae	*Cedrus deodara*	Stem bark [566]; Heart wood [567]; Essential oil [568]	α-pinene [210]
Piperaceae	*Piper longum*	Root [569]; Oil [570]	Piperine [570]
	Piper nigrum	Seed [571]; Leaf [572]	Piperine [570]
Plantaginaceae	*Bacopa monnieri*	Aerial part [573]; Whole plant [574]	Bacosine [575]; Stigmasterol [163]
	Picrorhiza kurroa	Rhizome [576, 577]	NR
	Plantago psyllium	Husk fiber [578]	Psyllium [579, 580]
	Scoparia dulcis	Whole plant [581, 582]	Scoparic acid D [583]; Coixol [584]; Glutinol [584]
Plumbaginaceae	*Plumbago zeylanica*	Root [585]	Plumbagin [586]
Poaceae	*Bambusa bambos* syn. *Bambusa arundinacea*	Leaf [587]	Stigmast-5, 22-dien-3β-ol [588]; Stigmast-5-en-3β-ol-β-D-glucopyranoside [588]
	Coixlacryma-jobi	Bran oil [589]; Seed [590]	Oleic acid [353, 591]
	Triticum aestivum(germ oil)	NR	NR
Polygonaceae	*Rumex vesicarius*	Whole plant [592]	Naringin [593]
Pteridaceae	*Adiantum capillus*	Whole plant [594, 595]	Quercetin [263]; Quercetin-3-O-Rutinoside or rutin [469]; Catechin [596]; Syringicacidm [597]
Ranunculaceae	*Coptis chinensis*	Plant [598]; Inflorescence [599, 600]	Berberine [598, 278]
	Nigella sativa	Seed [601-603]; Oil [603]	Thymoquinone [604]
Rutaceae	*Aegle marmelos*	Leaf [605-607]; Seed [608]; Fruit [609, 607]; Bark [610]	Aegeline 2 [611]
	Murraya koenigii	Leaf [612, 613]; Fruit [614]; Root [615]	Mahanimbine [616]
	Aurantii fructus	[617]	Naringin [593]; Hesperidin [593]; Synephrine [618]; Neohesperidin [619]
Salicaceae	*Casearia esculenta*	Root [620]	3-hydroxymethyl xylitol [621]
Solanaceae	*Capsicum annuum*	Pepper [622, 623]	Capsaicin [624]
	Cortex lycii	Root [625, 626]	Daucosterol [627]
	Solanum nigrum	Fruit [628, 629]; Leaf [630, 631]	Quercetin 3- glucosldeor Isoquercetin [632]
	Withania coagulans	Fruit [633-637]; Flower [638]	Coagulanolide [639]
	Withania somnifera	Root [640]; Leaf [640]	Withaferin A [641]
Theaceae	*Camellia sinensis*	Leaf [642, 643]	Epigallocatechin gallate[644]; Arabinogalactan [645]
Urticaceae	*Urtica dioica*	Aerial part [646]; Leaf [647, 648]	Chlorogenic acid [649]
Zingiberaceae	*Curcuma caesia*	Rhizome [650]	α-santalol [651]
	Curcuma longa	Rhizome [652, 653]	Curcumin [654, 655]; demethoxycurcumin [656]; Bisdemethoxycurcumin [657]; ar-turmerone [656]

(Table 2) Contd…

Family	Species	Parts used	Compounds with anti-diabetic potentiality
	Elettaria cardamomum	Seed [658]; Fruit [659]	1,8-cineole or Eucalyptol [257]; Limonene [286]; α-pinene [210]
	Zingiber officinale	Rhizome [660-665]	6-gingerol [666, 667]; Zingerone [668, 669]
Zygophyllaceae	*Tribulus terrestris*	Aerial part [670, 671]	Rutin [469]

Note: Park *et al.*, 2007: Article in Korean language.

effective against diabetes are not known till date. For instance, *Alstonia scholaris* (SPHAG), *Atriplex halimus* (Glucolevel), *Caesalpinia bonduc* (PHF and PH), *Caesalpinia bonducella* (MAC-ST/001 and DRF/AY/5001), *Holarrhena antidysenterica* (Ziabeen, PHF, Diashis, NPF), *Holarrhena pubescens* (SPHAG), *Lagerstroemia parviflora* (PHF), and *Picrorhiza kurroa* (Karnim plus, OJ).

10. ADDITIONAL INGREDIENTS OF PHFS OTHER THAN THE PLANTS

10.1. Shilajit

Shilajit, a herbo-mineral drug, is emitted from steep mountainous regions of the world [90, 91]. Shilajit finds its place in both Ayurvedic and Siddha systems of Indian medicine [92]. Shilajit forms one of the crucial elements in several formulations under study like NIDDWIN [93], Madhurakshak [39], Sugar remedy [94], Diashis [34], Diabec [95], Safuf-i-Dhayabitus. Basnet [96] studied the antidiabetic property of shilajit and inferred that it was effective in treating diabetes in non-obese diabetic rodents.

10.2. *Mytilus margaritiferus*

Mytilus margaritiferus (family *Mytilidae*) is popularly known as Mukta Shukti in Ayurveda. It is used as a laxative, sedative and nutritive besides being a stimulant, tonic and aphrodisiac [97]. Rahman *et al.* [98] have incorporated calcined *Mytilus margaritiferus* in their herbal formulation for diabetes, Dolabi. However, there is no documentation of Mukta Shukti having hypoglycemic activity.

10.3. Goat Pancreas

Rahman *et al.* [98] used goat pancreas (14.58 mg) as one of the ingredients of Dolabi for the management of diabetes along with *Gymnema sylvestre*, *Bambusa bambos*, *Rumex vesicarius*, *Acacia arabica*, alphatand calcined *Mytilus margaritiferus*.

10.4. Kushta-i-Faulad (Calyx of Iron)

Kushta-i-Faulad (calyx of iron) is a herbo-mineral preparations used in traditional systems of medicine (Unani and Ayurvedic). It helps in blood formation and thus used in the management of anaemia. Kushat-i-Faulad (calayx of iron), as one of the ingredients of Safuf-i-Dhayabitus in the formulation of diabetes. However, there is no report of having hypoglycaemic activity.

11. LIMITATIONS OF HERBAL DRUGS

No doubt that the concept of using botanical preparations and bioactive components obtained from them has escorted in a new revolution in pharmaceuticals because of their promising biological effects. Though considered as safe with minimal side effects, the use of herbal drugs must be with caution as the risk associated with it cannot be neglected because safety is our first priority. The approval of nutraceuticals based on preclinical and anecdotal clinical trials with improper experimental designs, without control groups, perplexed assessment indicators, and lack of long-term effectiveness and follow-up may probably lead to severe consequences, which is evident from lack of high quality, peer-reviewed publications supporting the efficacy of herbal remedies based on clinical trials [99]. Apart from this, the other problem that emerges is the bioavailability, bioaccessibility, and bioefficiency of bioactive components, which are mainly responsible for the therapeutic actions of herbal preparations. It is the bioavailability that ensures the bioefficiency of herbal drugs. Bioavailability is affected by the size, molecular structure, metabolizing enzymes, and bioaccessibility of the molecule. It involves a complex mechanism, including liberation, absorption, distribution, metabolism and elimination phases (LADME) [100]. For instance, curcumin is one of the most extensively explored compounds that have the potential to regulate diabetes but exhibits very poor bioavailability. A number of studies have been conducted to enhance the bioavailability of curcumin, which in turn, will improve its pharmacokinetic profile and cellular uptake. These include the use of adjuvants such as piperine [101], microencapsulation [102, 103], formulation of nanoparticles [104-106], liposomes [107], and phospholipid complexes [108, 109] of curcumin.

12. COMMERCIAL FORMULATION

There are a few PHFs such as Dihar and Diabet, marketed in the Indian market for diabetes by Rajsha Pharmaceuticals and Herbal Galenicals, respectively [110, 111]. Dihar is majorly used for hyperlipidemia and contains *S. cumini, M. charantia, E. officinalis, G. sylvestre, E. littorale, A. indiica, T. cordifolia, and C. longa*. The major components of Diabetes are *C. longa, C. fenestratum, S. potatorum, T. indica, T. terrestris and Phyllanthus reticulates* [112].

CONCLUSION

Human beings have been depending on medicinal plants to combat various ailments since the beginning of life. Despite the presence of effective modern drugs, in recent years, developed and developing countries are attracted to herbal drug with a trust that they are safe and have lesser side effects than synthetic drugs [27]. The scientific intervention gained momentum in the last two decades to back up the traditional claims. This intervention has led to the isolation, purification and identification of the bioactive compounds and elucidation of their mechanism(s) of action in the man-

agement of diabetes. Basically, the food components, the bioactive compounds have a positive impact on health [114]. Despite the fact that the characterization and structural elucidation of the active ingredients have been successfully achieved with the advancement of science and technology, the quantity in which they are present in the natural source restricts to attain the desired therapeutic effects. Thus, the concept of compound formulae or PHFs has evolved with the belief that unlike a single chemical entity targeting a single site, multiple components acting on multiple sites will be more effective in preventing or treating ailments. It is the synergistic effect of various individual components which makes the PHFs more effective than the individual components in combating diabetes.

There is also a need for strict regulatory control for manufacturers to keep the quality of formulations, so it helps in making the final formulation safe for consumers and their health. To do this, preventive and corrective measures need to be taken to trim down the hazardous contaminants of the formulations.

Though plant-based therapies are considered safe with limited side effects, many challenges still need to be addressed regarding their bioavailability, bioefficacy, optimal dose, lack of characterization, public's inadequate knowledge, toxicity studies, ambiguous mechanism of action, and clinical efficiency. At the same, the attempt to develop meticulously evaluated herbal leads should not be given up as they present a ubiquitous and secular history of use.

LIST OF ABBREVIATIONS

ER = Endoplasmic Reticulum

HO-1 = Heme-Oxygenase-1

FBG = Fasting Blood Glucose

PPBG = Postprandial Blood Glucose

CONSENT FOR PUBLICATION

Not applicable.

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CONFLICT OF INTEREST

The authors have no conflicts of interest, financial or otherwise.

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Abstract

In recent years, mankind has relied largely on herbal medicines to treat a variety of ailments. The aim of the current study is to investigate the pharmacognostic and physicochemical characterisation of some medicinal plants such as *Bambusa balcooa* (leaf) (BBL), *Phyllanthus emblica* (fruit) (PEF), *Hodgsonia heteroclita* (fruit pulp) (HHP), and *Punica granatum* (fruit peel) (PGP) used by the local *Bodo* tribe for the treatment of diabetes, which can be combined together to develop a novel polyherbal formulation. The preliminary phytochemical screening, microscopic evaluation, organoleptic and flow properties and qualitative heavy metal estimation was carried out using standard protocols. The preliminary phytochemical screening revealed the existence of carbohydrates, phenolics, alkaloids in all. However, amino acids were present in *P. granatum* and *P. emblica*, whereas triterpenoids were inferred in *P. officinalis*. Microscopical analysis of crude showed the presence of stone cells (BBL, HHP and PGP), xylem (PEF, HHP and PGP), trichome (PGP), fibres (all) and epidermis (PEF). The macroscopical study of crushed powder was overall acceptable to sense organs. The physical evaluation of flow properties was found to be good for *P. emblica* fruit when compared to others which was fair to passable. The heavy metal test showed the absence of bismuth, cadmium and lead in all species. Accordingly, the results obtained from the study is endowed with essential information for the authentication and quality assessment of these herbal drugs.

Keywords

Bambusa balcooa, herbal formulation*, Hodgsonia heteroclita,* Pharmacognostic*, Phyllanthus emblica, Punica granatum*

Introduction

Plants being the main source of nutrients to mankind, plays a substantial role in the health care system and prevention of many diseases (1). Since ancient times, plants and their products have been used to prevent or treat many illnesses, including diabetes (2). Herbal formulations combined become more effective than the single herb, probably due to their catalysing effect with one another. In recent years, the claims of medicinal efficiency and lack of toxicity of many plants have been scientifically ascertained. (3). Standardisation is essential for herbal formulations to measure the quality and control of herbal ingredients during the manufacturing process (4). World Health Organization (WHO) has acknowledged the indispensable relationship between the people belonging to developing nations and medicinal plants for their health care and thus took the necessary initiative to

formulate the guidelines to maintain the quality and standards of the polyherbal formulations (PHFs) worldwide (5). Ayurveda, popularly known as "Mother of All Healing", is made up of two Sanskrit words, "*ayur* (life) and *veda* (science or knowledge)" (6). The exclusivity of this ancient system lies in the immeasurable diversity of healing processes used, such as animal juices, herbal formulations and natural energies (sun and water) (6). At present, there is a need for the development of a safer drug for the treatment of several ailments. Thus, there is a growing interest in the plants and traditional systems of medicine in the pharmaceutical industry for drug discovery and development (7). Hence, 4 different plant species and parts such as *Bambusa balcooa* (leaf), *Phyllanthus emblica* (fruit), *Hodgsonia heteroclita* (fruit pulp) and *Punica granatum* (fruit peel) were selected based on traditional claims by the Bodo tribe of Assam for the treatment of diabetes.

Bambusa balcooa Roxb. (Poaceae) is locally called Owa burkha by Bodos (8, 9). It possesses various phytoconstituents like flavonoids, saponins, resins, fixed oils, phytosterols, phenolics and tannins, which could be used in curing diseases and drug formulations (10). *B. balcooa* has also been reported to possess antidiabetic activity because of the presence of three compounds rutin, gallic acid and β sitosterol as reported (3).

Hodgsonia heteroclita Hook. f. & Thomson, commonly known as the Chinese lard plant, belongs to the family Cucurbitaceae and is locally known as Hagrani jwgwnar among the Bodo (11-13). Different parts of the plant, like the seed, fruit pulp are known for medicinal properties. *H. heteroclita* being bitter in taste, is used in the traditional system of medicine for curing diabetes by the Bodo tribe (11). *H. heteroclita* has also been reported to possess anti-diabetic properties (12, 13). The presence of caffeic acid could be responsible for anti-diabetic as reported (13).

Phyllanthus emblica L. (Phyllanthaceae), universally recognised as Indian gooseberry or amla, is the most important plant used in the traditional system of medicine in India, including folklore, Ayurveda and Unani (14). Different parts of the plant have been reported to treat various diseases like the common cold (14), fever (14), anti-inflammatory (14), hair tonic (14), anti-diabetic (14), anti-cancerous (15), hypolipidemic (16), antibacterial (16), anti-oxidant (16), hepatoprotective (16), gastroprotective (16), chemopreventive (16), and antimutagenic activity (16), anti-viral (17). The anti-diabetic activity of amla is probably due to the presence ellagic acid, estradiol, sesamine, kaempferol, zeatin, quercetin, and leucodelphinidin (18).

Punica granatum L., popularly designated as pomegranate, belongs to the family Punicaceae. Traditionally in the Indian sub-continent, it is known as 'Anar' or 'Dadima' (19, 20). *P. granatum* is an extensively used medicinal fruit of the indigenous system of medicine (21). *P. granatum* has a plethora of medicinal uses like anti-microbial, hepatoprotective, cardioprotective, anti-hyperglycemic, anti-inflammatory, anti-hypertensive, anti-anaemic, antioxidant, immunomodulatory properties, anti-cancer (22, 23). The presence of valoneic acid dilactone (VAD) isolated from fruit rinds of *Punica granatum* might be associated with the anti-diabetic activity of *P. granatum* (24).

Materials and Methods

Plant material selection, collection and preparation of extract

Matured fruits of *Phyllanthus emblica* and *Punica granatum* were collected from the local market, *Hodgsonia heteroclita* from the forest of Kokrajhar district and leaf of *Bambusa balcooa* was collected from the Bambusetum, Bodoland University, Kokrajhar, BTR, Assam, India (Table 1). The voucher specimens were deposited at Botanical Survey of India, Central National Herbarium, Howrah and was identified and authenticated vide letter no. CNH/Tech.II/2021/43 date 26-11-2021.

Table 1. List of plants with information on parts used, vernacular names and GPS coordinates of the collection site

Botanical Name	Part Used	Vernacular names		GPS coordinates	
		Bodo Name	Assamese Name	Latitude	Longitude
Bambusa balcooa Roxb.	Leaf	Owa burkha	Bhaluka bah	26.4694332 °N	90.292971 °E
Phyllanthus emblica L.	Fruit	Amlai	Amalaki	26.4720043 °N	90.2979632 °E
Hodgsonia heteroclita Hook.f. & Thomson	Fruit pulp	Hagrani jwgwnar	Not Known	26.4011 °N	90.2729 °E
Punica granatum L.	Peel	Dalim	Dalim	26.5288799 °N	90.2495364 °E

The individual plant parts such *Bambusa balcooa* (leaf), *Phyllanthus emblica* (fruit), *Hodgsonia heteroclita* (fruit pulp) and *Punica granatum* (fruit peel) used by the local *Bodo* tribe for the treatment of diabetes were dried at room temperature and powdered using mechanical grinder. The powder was sieved using sieve of 600 µm mesh size and stored in airtight glass bottles for analysis. The powder was subjected to Soxhlation using double distilled water (1:10 *w/v* ratio of the sample and solvent). The extraction was carried out for 6 hrs at the boiling temperature and evaporated under pressure at 50 °C and stored at 4 °C for further experimental analysis.

Preliminary Phytochemical Screening

The prepared extracts were subjected to the preliminary phytochemical test to detect the presence or absence of phytochemical constituents like alkaloids, carbohydrates, phenolics, amino acids and triterpenoids as per standard protocols of Trease and Evans (25) with modification (1, 26).

Organoleptic evaluation

Organoleptic evaluation of food products is important in ascertaining the censoring acceptability or rejection of foodstuffs available in the market (27). The texture, aroma, flavour/ taste and colour of crushed powder were recorded using various sense organs.

Microscopic study

Individual powdered samples were mounted on a clear glass slide using water and covered with a coverslip. The slides were visualised under the binocular microscope (Labomed Vision 2000) and the photographs were taken using a Samsung Galaxy phone.

Determination of physical characteristics of powder

Angle of repose

The angle of repose determines the flow rate of the powder. The angle of repose was done using the funnel method. The powder (15 g) was allowed to flow through the funnel till the heap of the powder touched the tip of the funnel placed above the graph paper placed on the horizontal surface. The diameter of the powder cone was recorded, and the angle of repose was calculated using the following formula (28)

$$\text{Angle of repose} = \tan^{-1} h / r$$

where, h= height of pile r= radius of the pile

Bulk density

The powder was sieved through the muslin cloth, and apparent bulk density was measured by pouring 15 g of powder into a 100 ml measuring cylinder without compacting, and initial reading was noted. The bulk density was calculated by using the following formula (28)

$$Db = M / Vb$$

where, M= the mass of powder, Vb = the bulk Volume of the powder, Db = bulk density

Tapped density

After measuring the bulk density, the cylinder containing the powder was tapped manually for 500 times until further change in volume was noted. The tapped density was calculated using the following formula (28):

$$\rho tap = M / Vf$$

where, ρtap = Tapped density, M = Weight of the powder, Vf = Tapped volume.

Carr's index

It indicates the powder flow properties of the powder. It is expressed in percentage and is calculated according to the following formula (28).

$$\text{Carr's index (\% compressibility)} = 100 \times (1 - D_b / D_t)$$

where D_b = Bulk density, D_t = Tapped density

Hausner ratio

Hausner ratio is an indirect method of quantifying powder. It was calculated by the following formula (28)

$$\text{Hausner ratio} = D_t / Db$$

where D_b = Bulk density and D_t = Tapped density.

Qualitative estimation of heavy metals

Procedure outlined (29) was followed to qualitatively determine the occurrence of heavy metals like cadmium, lead and bismuth in different plant parts. It is determined to ascertain the safe use of plants.

Results and Discussion

Preliminary phytochemical screening

The current experiment was conducted to estimate the pharmacognostic and physicochemical characterisation of potential plants for anti-diabetic herbal formulations. The therapeutic potential of the plants is attributed to the occurrence of secondary metabolites like alkaloids, carbohydrates, phenolics, amino acids, etc. Among all the extracts, *E. officinalis* revealed the presence of alkaloids, carbohydrates, phenolics, amino acids and triterpenoids. Similar observations were previously reported (30-32). However, It was (30) reported that *E. officinalis* was devoid of triterpenoids during preliminary screening (Table 2). Among the different tests conducted, *P. granatum* fruit peel showed the absence of triterpenoids which was in conjunction with the earlier study (33). It was also reported the absence of alkaloids and amino acids (33). However, they documented the presence of carbohydrates. Recent studies conducted also reported the presence of carbohydrates, alkaloids, amino acids and phenolics in pomegranate peel (34, 35). Aqueous extract of *B. balcooa* leaf and *H. heteroclita* fruit pulp showed the presence of carbohydrates, phenolics and alkaloids, whereas amino acids and triterpenoids were absent in both samples. As per one report (10), Alkaloids were absent in *B. balcooa,* which is contradictory to our results. Likewise, reports are on the presence of alkaloids, carbohydrates and phenolics in *H. heteroclita* (36, 37). Thus, the presence of these secondary metabolites in the different plants may be the factor behind the anti-diabetic activity. The phytochemical analysis is tabulated in Table 2.

Organoleptic parameters

Organoleptic properties constitute an important role in industrial production, carrying or augmenting the consistency of the formulation, ameliorating patient compliance and ascertaining overall product performance (38). The organoleptic evaluation of plants relating to their texture, aroma, flavour/ taste and colour were recorded and summarised in Table 3.

Powder microscopy

Microscopy plays a vital role in the identification of impure drugs, and it is considered an unavoidable step before undertaking any test (39). The structural and cellular features of crude powder help in the primary identification and authentication of the plant to be used as pharmaceutical materials (REF in link). Stone cells are observed in all the samples except in *E. officinalis,* and its primary function is to provide strength or support soft tissues. Epidermis was seen in *H. heteroclita*. The epidermis helps in the exchange of gases into the cell and protects against the loss of water in plants. Trichome was observed in *H. heteroclita* and *P. granatum*. Trichomes are the epidermal outgrowth and help in water absorption and minerals. Xylem tissue was observed in *E. officinalis*, *H. heteroclita* and *P. granatum.* Xylem helps in the conduction of water minerals nutrient upward from root to leaves. Fibre was observed in all the samples. Fibres are part of the supporting tissues and provide mechanical support and

Table 2. Preliminary phytochemical screening of various plant parts under study

Constituent	Chemical Test	Procedure	*Bambusa balcooa* (Leaf)	*Phyllanthus emblica* (Fruit)	*Hodgsonia hetroclita* (Fruit pulp)	*Punica granatum* (Fruit peel)
Alkaloids	Mayer's reagent test	Extract+ Dil. HCl + 3mL Mayer's reagent	+	+	+	+
	Dragendroff's test	Extract + Dil. HCl + 3mL Dragendroff's reagent	White ppt	Yellow ppt	White ppt	Bright Yellow ppt
Carbohydrate's	Fehling's test	1mL Fehling A+ 1mL B Fehling mixed and boiled for a minute	Brick red	Brick red	Brown red	Brick red
	Benedict's test	2 mL extract + Few drops of Benedict's reagent + Boiled for 2 min	Green	Red	Yellow	Brick red
	Molisch's test	Extract + Few drops of Molisch's reagent + Conc. H_2SO_4	Violet ring	Violet ring	Light	Violet ring
Phenolics	$FeCl_3$	Extract + $FeCl_3$	Brown	Greyish	Light brown	Deep black
	Lead acetate test	Extract + Lead acetate	White ppt	White ppt	White ppt	Deep black
Amino acids	Millon's test	Extract + Few drops of Millon's reagent	ND	Red colour	ND	Red colour
Triterpenods	Salkowski test	Extract + Few drops of chloroform + few drops of conc. H_2SO_4	ND	Red colour	ND	ND

ND= Not Detected; Brick red (Fehling's test)= presence of reducing sugars; Green (Benedict's test)= traceable, yellow= small, red=moderate; Red and Brick red (Millon's test) = presence of tyrosine; white ppt (Lead acetate) = phenolics, Yellow= flavonoids; Red (Salkowski)= steroids; ppt= precipitate

Table 3. Organoleptic parameters of various plant parts under study

Parameters	*Bambusa balcooa* (Leaf)	*Phyllanthus emblica* (Fruit)	*Hodgsonia hetroclita* (Fruit pulp)	*Punica granatum* (Fruit peel)
Texture	Dry, fibrous	Granular, powder	Granular, spongy	Granular
Aroma	Grassy	Fruity	Wheaties	Rancid
Flavour/ taste	Slightly sweet	Sour and sweet	Bitter	Betel nut, sweet, bitter
Colour	Fern green	Tawny brown	Beige	Sandstone orange

firm strength to the plant (40, 41). Xylem and fibre were also observed previously in *P. emblica* (30, 42, 43). Observations are on stone cells, xylem vessel, collenchyma cells of epicarp, prism type crystal of calcium oxalate and compound starch grain in *P. granatum,* whereas stone cell, xylem, trichome and fibre were observed in this study (20). However, no such study was reported for *B. balcooa* leaf and *H. heteroclita* fruit pulp. The results of powder microscopy of various plant parts are depicted in Fig. 1.

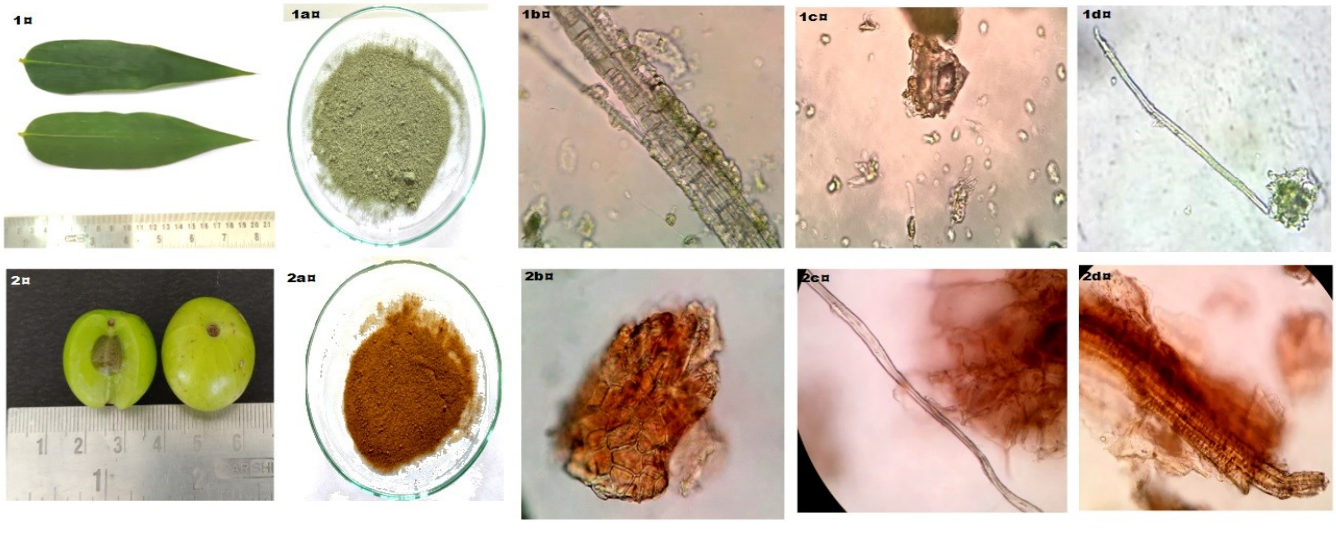

Fig. 1a. Photomicrographs of microscopic evaluation (400x) **1**. *Bambusa balcooa* leaf, **1a**. *B. balcooa* leaf powder, **1b.** Fibre bundle, **1c**. Stone cell, **1d**. Fibre, **2**. *Emblica officinalis* fruit, **2a**. *E. officinalis* fruit powder, **2b**. Epidermis, **2c.** Fibre, **2d**. Xylem.

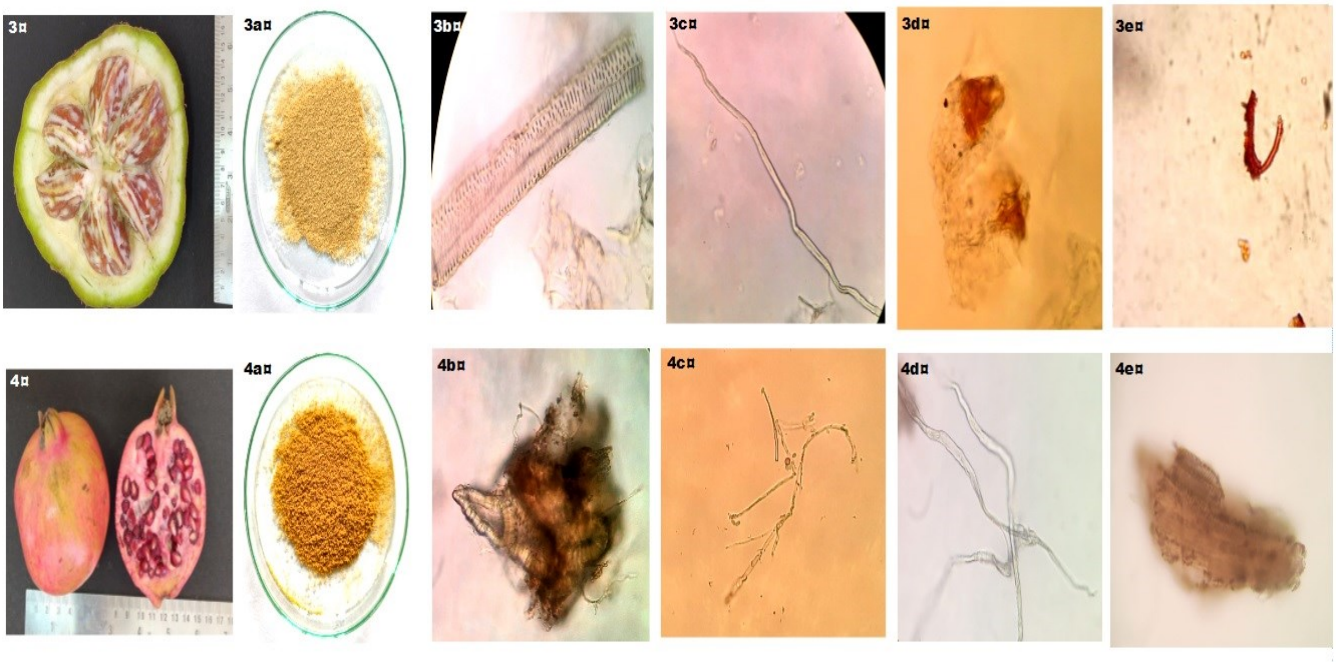

Fig. 1b. Photomicrographs of microscopic evaluation (400x) **3**. *Hodgsonia heteroclita* fruit, **3a**. *H. heteroclita* fruit pulp powder. **3b**. Xylem, **3c.** Fibre, **3d**. Stone cells, **3e**. Dwarf trichome, **4**. *Punica granatum* fruit, **4a**. *P. granatum* peel powder, **4b**. Stone cell, **4c**. Trichome, **4d**. Fibre, **4e**. Xylem.

Flow ability

Evaluation of physical parameters like the angle of repose, bulk density, tapped density, Carr's index and Hausner ratio is important in the pharmaceutical industry to determine the flow properties of drug. The angle of repose of *E. officinalis* powder was 33.99±0.49, which indicates the passable flow of powder, Carr's index was found to be 15.97±0.015 representing good compressibility and Hausner ratio was found to be 1.19±0.010, indicative of fair flow properties. These parameters were comparatively higher than reported (44). The angle of repose for *P. granatum*, *B. balcooa* and *H. heterclita* were in passbale range. The Hausner ratio was fair for *P. granatum* and *H. heterclita* but passbale for *B. balcooa*. The Carr's index for *P. granatum*, *B. balcooa* and *H. heterclita* were in the fair to passbale range. Since no work has been reported earlier, the flow ability of *P. granatum* peel, *B. balcooa* leaf and *H. heterclita* fruit pulp were evaluated for the first. The result of the physical evaluation of powder indicated that the parameters were satisfactory, as recorded in Table 4.

Heavy metal test

The incidence of heavy metals in plants reveals their purity and adulteration (29). In the current study, the heavy metals, namely cadmium, bismuth and lead, were found to be absent in all samples as summarised in Table 5, which indicates no contamination of heavy metals and thus can be safely incorporated as an ingredient of various herbal formulations. Of the 4 plant parts, the detection of heavy metals was reported only for *P. emblica* fruit (45, 46), whereas the other plants were accessed for the first time.

Conclusion

Standardisation is essential for herbal drugs to measure the quality based on the number of their active constituents. Today a newer and advanced method is available to standardise herbal drugs. According to WHO, the pharmacognostic and physicochemical characterisation may be the initial step in establishing the identity and purity of herbal plants and should be conducted before performing any tests (39). The presence of various pharmacological and phytochemical constituents in *Bambusa balcooa*, *Phyllanthus emblica*, *Hodgsonia heteroclita*, *Punica granatum* reveals that they have therapeutic potentials. The oragnoleptic and micromorphological features might help in authentication of the plant species, whereas the flow poperties is essential for various purposes such as blending, filling of capsules and tablet manufacturing. Therefore, the current study might provide helpful information with respect to its identification, validation, standardisation and the nature of adulteration. However, further research study is required for the isolation, structural elucidation and screening of active principal compounds to point out the real activity of herbal.

Table 4. Flow characteristics of the powder of various plant parts under study

Batch	Angle of repose	Bulk density (g/mL)	Tapped density (g/mL)	Hausner ratio	Carr's index
Bambusa balcooa	38.08±0.25	0.31±0.010	0.39±0.005	1.26+0.005	20.83±0.100
Phyllanthus emblica	33.99±0.49	0.60±0.015	0.72±0.010	1.19±0.010	15.97±0.015
Hodgsonia heteroclita	36.62±0.25	0.26±0.005	0.32±0.005	1.25±0.005	19.88±0.010
Punica granatum	37.72±0.36	0.35±0.010	0.42±0.005	1.22±0.005	18.23±0.050

Angle of repose = 30-40 (Passable) (28), Carr's index= 12-16 (Good), 18-31 (Fair to passable) (28), Hausner ratio = 1.19-1.25 (Fair), 1.26-1.34 (Passable) (47).

Table 5. Determination of heavy metals in various plant parts

Sample solution		Heavy metals					
		Cadmium (Cd)	Cadmium (Cd)	Bismuth (Bi)	Bismuth (Bi)	Lead (Pb)	Lead (Pb)
	Procedure	Sample solution + NH_4OH	Sample solution + Potassium Ferrocyanide	Sample solution + NH_4OH	Sample solution + H_2S	Sample solution + Dil HCl (37%)	Sample solution + KI
Bambusa balcooa	Observation	No white ppt.	No white ppt.	No white ppt.	No dark brown ppt.	No white ppt.	No yellow ppt.
	Inference	Absent	Absent	Absent	Absent	Absent	Absent
Phyllanthus emblica	Observation	No white ppt.	No white ppt.	No white ppt.	No dark brown ppt.	No white ppt.	No yellow ppt.
	Inference	Absent	Absent	Absent	Absent	Absent	Absent
Hodgsonia heteroclita	Observation	No white ppt.	No white ppt.	No white ppt.	No dark brown ppt.	No white ppt.	No yellow ppt.
	Inference	Absent	Absent	Absent	Absent	Absent	Absent
Punica granatum	Observation	No white ppt.	No white ppt.	No white ppt.	No dark brown ppt.	No white ppt.	No yellow ppt.
	Inference	Absent	Absent	Absent	Absent	Absent	Absent

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Authors contributions

AKG conceptualized and designed the study. SB, BM, MK carried out the research work and acquired the data. All the authors analyzed the data and wrote the first draft of the manuscript. Finally all the authors edited the manuscript and approved the final version for submission.

Compliance with ethical standards

Conflict of interest: Authors do not have any conflict of interests to declare.

Ethical issues: None

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§§§

Certificate of Participation

REVA UNIVERSITY
Bengaluru, India

School of Applied Sciences, Department of Biotechnology
REVA University in collaboration with
Faculty of Medicine and Health Sciences
Universiti Malaysia Sabah

UMS
UNIVERSITI MALAYSIA SABAH

This is to certify that **Sudem Brahma,** has presented a paper entitled

Pharmacognostic and physiochemical characterization of potential plants for anti-diabetic herbal formulations

(Authors: **Sudem Brahma, Banjai Mochahary, Mrinal Kalita, Jangila Basumatary, Sushil Kumar Middha, Talambedu Usha, Arvind Kumar Goyal***)

during the 1st International Conference on **"Global Trends in Health and Life Sciences"** held from 27th -29th September 2021.

Dr. M. Dhanamjaya
Vice-Chancellor
REVA University

Prof. Dr. Mohammad Saffree Jeffree
Dean,
Faculty of Medicine and Health Sciences,
Universiti Malaysia Sabah

Prof. Shilpa. BR
Convener-ICGTHL-2021
REVA University

Dr. Pasupuleti Visweswara Rao
Convener, ICGTHL-2021
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Centre for Bodo Studies, Bodoland University

National Seminar on
'Ethnobotany and Resource Management of the Bodos'
(December 10, 2021)

CERTIFICATE

As Paper Presenter

This is to certify that Sudem Brahma of Bodoland University, Assam, has presented a paper entitled *In vitro* studies on quality assessment of novel polyherbal formulation for diabetes (Author(s): Sudem Brahma and Arvind Kumar Goyal) in the National Seminar organized by the Centre for Bodo Studies, Bodoland University held on 10th December, 2021.

Dr. Prahlad Basumatary
Director
Centre for Bodo Studies
Bodoland University

Prof. Laishram Ladusingh
Vice Chancellor
Bodoland University

CENTRE FOR BODO STUDIES CBS/BUIERMB2021/1019

CENTRE FOR BODO STUDIES, BODOLAND UNIVERSITY * ETHNOBOTANY AND RESOURCE MANAGEMENT OF BODOS * HELD ON 10TH DECEMBER, 2021 NATIONAL SEMINAR 2021

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To whom it may concern

This is to certify that **Ms Sudem Brahma**, Department of Biotechnology, Bodoland University has received one month training on '***Animal handling***' from 11th July, 2022 to 25th July, 2022 and also carried out the *in vivo* experiments of her Ph.D. thesis entitled "***Intigation to Formulate and standardize and Evaluate an Anti-Diabetic Herbal Formulation***" in the Animal House facility of Maharani Lakshmi Ammanni College for Women (Autonomous), Bengaluru, Karnataka, India.

I may mention that the *Animal House* Facility of Maharani Lakshmi Ammanni College for Women (Autonomous), Bengaluru, Karnataka, India has been registered for CPCSEA under the Department of Animal Husbandry and Dairying (DAHD), Ministry of Fisheries, Animal Husbandry and Dairying (MoFAH&D) bearing registration number **1368/ac/10/CPCSEA**.

I wish her success in life.

Dr. Sushil Kumar Middha

Research Coordinator

Malleshwaram, Science Post, Bangalore - 560 012.
Tel. : 080-2334 9311 email : mlacw@mlacw.org, www.mlacw.edu.in

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1972-2022

To whom it may concern

This is to certify that **Ms Sudem Brahma**, Department of Biotechnology, Bodoland University has carried out the Histopathological analysis of her Ph.D. thesis entitled "***Intigation to Formulate and standardize and Evaluate an Anti-Diabetic Herbal Formulation***" in the Life Science Research Centre of Maharani Lakshmi Ammanni College for Women (Autonomous), Bengaluru, Karnataka, India from 6thJune, 2023 to 12th June, 2023.

I wish her success in life.

Dr. Sushil Kumar Middha

Research Coordinator

Malleshwaram, Science Post, Bangalore - 560 012.
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Appendix-A

Thesis related publication and presentation 2024

◊ Brahma S, AK Goyal, P Dhamodhar, MR Kumari, S Jayashree, T Usha, SK Middha (2024). Can polyherbal medicine be used for treatment of diabetes? - A review of historical classics, research evidence and current prevention programs. Current Diabetes Reviews. 20(2): e140323214600. DOI: 10.2174/1573399819666230314093721. (Bentham Science Publishers, JCR IF:3.3).

◊ Brahma S, B Mochahary, M Kalita, AK Goyal (2022). Pharmacognostic and physicochemical characterization of potential plants for anti-diabetic herbal formulations. Plant Science Today. 9 (sp2): 1-7. DOI:10.14719/pst.1704. (Horizon e-publishing group, JCR IF:0.9)

Thesis related presentations in seminar/conference 2024

◊ Presented (Oral) a paper on ***"Pharmacognostic and physiochemical characterization of potential plants for anti-diabetic herbal formulations"*** in the International Conference and Workshop on " Global Trends in Health and Life Sciences" jointly organized by Reva university, Bengaluru, INDIA and Universiti Malayasia Sabha , MALAYSIA from 27th to 29th September, 2021.

◊ Presented (Oral) a paper on ***" In vitro studies on quality assessment of novel polyherbal formulations for diabetes"*** in National Seminar on "Ethnobotany and Resource Management of the Bodos" organized by centre for Bodo Studied, Bodoland University, 10th December, 2021.Presented (Oral) a paper on ***" Physicochemical and antioxidant properties of Amaini muli, a polyherbal formulation for hepatoprotection"*** in National Seminar on "Science & Technology for sustainable Development (STSD-2022" jointly organized by Science College, Kokrajhar & Vijnana Bharati, NESM held on 9th- 10th September, 2022 at Science College, Kokrajhar.

◊ Presented (Oral) a paper on ***" Identification of Bioactive Components and Antioxidant Activity of HOPE– a Novel Polyherbal Formulation for Diabetes"*** in National Seminar on "Science & Technology for sustainable Development (STSD-2022" jointly organized by Science College, Kokrajhar & Vijnana Bharati, NESM held on 9th- 10th September, 2022 at Science College, Kokrajhar.

Appendix-B

Chemicals and buffers used

Sl. No.	Chemical name	Make	Product Code
1.	1% Triton-x-100	HiMedia	TC286
2.	1X PBS	HiMedia	ML116
3.	alpha keto-glutarate	Sigma-Aldrich	75890
4.	Benedict's reagent	Merck	DH7DF67777
5.	Carbonate buffer	Sigma-Aldrich	C3041
6.	Epinephrine	Amneal Pharmaceuticals of New York LLC	0115-1694-30
7.	Gallic acid monohydrate	HiMedia	PCT1546
8.	Fehling's A and B	Merck	DK7DF1222, DK7DF1166
9.	Glibenclamide	SimSon Pharma Limited	10238-21-8
10.	Glutathione	HIMEDIA	PCT0309
11.	Glutathione reductase	Sigma-Aldrich	G3664
12.	Ketamine	Usp_{TM}	1356009
13.	L-Alanine	HIMEDIA	TC249M
14.	Magnesium ribbon	LOBA Chemicals	0445900025
15.	Mayer's reagents	LOBA Chemicals	0453700125
16.	Metal Magnesium	LOBA Chemicals	0445900025
17.	Millons reagent	LOBA Chemicals	4690D00125
18.	NADH	MERCK	606-68-8
19.	NADPH	MERCK	2646-71-1
20.	Ninhydrin solution	HiMedia	GRM248
21.	Phosphate buffer	HiMedia	M461-500G
22.	Potassium ferricyanide (K_3 Fe $(CN)_6$)	HiMedia	GRM627
23.	Reduced glutathione (GSH)	HiMedia	TC134
24.	Silybon-140 mg	Micro Lab Limited, India	
25.	Standard rat pellet		
26.	t-butyl hydro-peroxide	HiMedia	RM2022
27.	Trimethylchlorosilane (Me3SiCl)	EREZTECH	75-77-4
28.	Tris buffer	HiMedia	GRM1218
29.	Xylazine	Usp_{TM}	7361-61-7

Continues from previous page

Sl. No.	Chemical name	Make	Product Code
30.	Caffeine reagent	HiMedia	GRM1056-250G
31.	2,2-diphenyl-1-picryl hydrazyl (DPPH)	HiMedia	RM5169-1G
32.	ABTS	HiMedia	RM9270-500G
33.	Bovine serum albumin	HiMedia	GRM3151-100G
34.	Butylated hydroxytoluene (BHT)	HiMedia	GRM797-500G
35.	Dragendorff's reagent	LOBA Chemicals	03603 00125
36.	Eosin blue	LOBA Chemicals	03640 00025
37.	Ferric chloride (FeCl3)	LOBA Chemicals	03818 00500
38.	Gallic acid	LOBA Chemicals	03910 00100
39.	Molisch's reagent	LOBA Chemicals	4694D 00100
40.	Potassium hydroxide (KOH)	LOBA Chemicals	05380 00500
41.	Absolute alcohol	Merck	1.00983.0511
42.	Carbon tetrachloride (CCl_4)	Merck	1.02222.2500
43.	Copper (II) sulphate pentahydrate	Merck	1.93616.0521
44.	Ethylenediamine tetra acetic acid (EDTA)	Merck	1.93321.0121
45.	Folin- Ciocalteu phenol reagent	Merck	1.09001.0100
46.	Formalin	Merck	1.94989.5021
47.	Glacial acetic acid	Merck	1.93402.2521
48.	Hematoxylin	Merck	1.04302.0025
49.	HCL	Merck	1.00317.2500
50.	Metallic Zinc	Merck	1.93800.0521
51.	N,O-Bis (trimethylsilyl) trifluoro-acetamide (BSTFA)	Merck	1.10255.0025
52.	Nitric Acid	Merck	1.00456.2510
53.	Phloroglucinol	Merck	1.07069.0025
54.	Picric acid	Merck	1.00623.0500
55.	Potassium di-hydrogen phosphate (KH_2PO_4)	Merck	1.93605.0521
56.	Potassium hydroxide pellets	Merck	1.93503.0521
57.	Pyridine	Merck	1.09728.1000
58.	Quercetin	Merck	1.00336.4835
59.	Sodium dihydrogen phosphate	Merck	1.06346.1000
60.	Sodium dodecyl sulphate (SDS)	Merck	1.13760.0100

Continues from previous page

Sl. No.	Chemical name	Make	Product Code
61.	Sodium nitrite (NaNO2)	Merck	1.06537.0500
62.	Sulfanilic acid	Merck	1.00686.0250
63.	Thiobarbituric acid (TBA)	Merck	1.08180.0025
64.	Trichloroacetic acid (TCA)	Merck	1.94971.0521
65.	Zinc Dust	Merck	1.93800.0521
66.	Acetic acid	Merck	1.93002.0521
67.	Aluminium chloride ($AlCl_3$)	Merck	8.01081.0251
68.	Ammonia	Merck	01078 00500
69.	Ammonium hydroxide (NH_4OH)	Merck	1336-21-6
70.	Ascorbic acid	Merck	01550 00100
71.	Benzene	Merck	1.07033.0521
72.	Chloroform	Merck	1.07024.0521
73.	Conc. H2SO4	Merck	1.93001.0521
74.	di-Potassium hydrogen phosphate (K2HPO4)	Merck	1.05104.1000
75.	DMSO	Merck	1.16743.0521
76.	DPX	Merck	1.00579.0500
77.	Ethanol	Merck	1.00983.1011
78.	Ethyl acetate	Merck	1.07048.0521
79.	Hydrogen peroxide (H_2O_2)	Merck	1.93007.0521
80.	Lead acetate	Merck	1.93679.0521
81.	Methanol	Merck	8.22283.1000
82.	Paraffin wax	Merck	61759305001730
83.	Sodium carbonate (Na_2CO_3)	Merck	1.93211.0521
84.	Sodium chloride (NaCl)	Merck	1.93206.0521
85.	Sodium hydroxide (NaOH)	Merck	1.93502.0521
86.	Xylene	Merck	1.94600.0521
87.	Aammonium molybdate	Rankem	A0521

Appendix-C

List of instrument used

Sl. No.	Instruments	Make	Model No.
1.	Automatic tissue processor	Leica, Germany	TP1020
2.	Balance	Shimadzu, Japan	ATY224 Analytical Balance
3.	Binocular Microscope	Labomed, India	Lx500
4.	Biospectrometer	*ELICO*, India	Version 1.0.8 double beam; *ELICO* BL222
5.	Centrifuge	Plastocraft, India	RV/FM, super spin,
6.	Deep freeze	White whale, India	WF-3046KSS and FORMA 700 Series
7.	ELISA	Thermo Scientific, USA	Multiskan GO
8.	Hot air oven	Thermostatic India, India	Thermostatic RSTI-101
9.	GCMS	Spectra Lab Scientific Inc., India	Perkin Elmer Autosystem XLGC Autosampler
10.	Incubator	REMI, India	CIS-24 *PLUS*
11.	Lyophiliser	Telstar, India	Telstar Lyoquest Freeze Dryer
12.	Magnetic stirrer	REMI, India	5MLH
13.	Micropipette	Tarsons, India	1-10µl, 10-100µl , 100-1000µl
14.	Mixer grinder	Bajaj, India	Rex 500
15.	pH meter	*ELICO*, India	LI617
16.	Rotary evaporator	Superfit, India	ROTA VAP Model: PBU-6D
17.	Rotary microtome	Leica, Germany	RM2125 RTS
18.	Soxhlet apparatus	BOROSIL, India	IIC122
19.	UV-VIS Spectrophotometer	Systronics India Ltd, India	A119158
20.	Ultra deep freezer -80°C	Blue Star, India	CRESCENT
21.	Water bath incubator shaker	REMI, India	KWBS-2