# Chapter 2
# REVIEW OF LITERATURE

Exploring through internet sources, Google scholar, PubMed, science direct and others using keywords like 'polyherbal formulation' AND/OR 'antidiabetic activity' AND/OR 'hyperglycaemia' AND/OR 'hypoglycaemia' resulted in the documentation of a number of formulations.

## 2.1 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 2.1**. India alone houses over 62 million individuals diagnosed with diabetes (Puri et al., 2020) 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 (Ekor, 2014). Referred to as the medicinal garden of the world (Dukare et al., 2017), India contributes maximum for the development of PHFs with 56 reports out of 70 reported, followed by Pakistan (Anderson et al., 2003), Iran (Cho et al., 2018), Korea (Cho et al., 2018), Bangladesh (Shaw et al., 2010), Indonesia (Shaw et al., 2010), China, Eritrea, Iraq, Israel and Nigeria (Kamtekar and Keer 2014).

## 2.2 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 (Jamil et al., 2012).

## 2.3 Preclinical trials

Seventy-one PHFs were tested for their therapeutic efficiency on the biochemical

**Table 2.1: 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 |
|---|---|---|---|---|---|---|---|
| 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<br>FBG= 230.50mg/100ml<br>HbA1c = 5.96g/100ml<br>Insulin= 11.10µU/ml<br>Haemoglobin=5.96g/100ml<br>Urine sugar= > 1% | At 0.45 g/kg<br>↓FBG= 83.40mg/100ml<br>↓HbA1c = 0.25g/100ml<br>↑Insulin= 22.60µU/ml<br>↑Haemoglobin=12.60g/100ml<br>↓Urine sugar= NIL | Glibenclamide (600 µg/kg)<br>↓FBG= 91.20mg/100ml<br>↓HbA1c = 0.31g/100ml<br>↑Insulin= 20.80µU/ml<br>↑Haemoglobin=10.80g/100ml<br>↓Urine sugar= Trace | *In vivo;* India | Anti-hyperlipidemic | Pari and Saravanan 2002; Saravanan and Psri 2003 |
| Diabecon (D-400) | *Asparagus racemosus*, *Balsamodendron mukul*, *Eugenia jambolana,Gymnema sylvestre*, *Momordica charantia*, *Ocimum sanctum*, *Pterocarpus marsupium* | Patients with diabetic retinopathy.<br>Micro-aneurysm= 2.22<br>Hemorrhage= 2.034<br>Exudation=2.034<br>Retinitis proliferans=0.583 | Diabecon (2tablets thrice daily) for 12 weeks<br>↓Micro-aneurysm=0.466<br>↓Hemorrhage=0.866<br>↓Exudation=1.316<br>↓Retinitis proliferans= 0.550 | No data available | Clinical Trials; India | '-' | Kant et al., 2007 |

| Commercial Name | Formulations with scientific names | Experimental model | Effects of polyherbal preparation | Effects of reference drug | Study design and Country | Additional property | References |
|---|---|---|---|---|---|---|---|
| Hyponidd | *Cassia auriculata*, *Curcuma longa*, *Emblica officinalis*, *Enicostemma littorale*, *Eugenia jambolana*, *Gymnema sylvestre*, *Melia azadirachta*, *Momordicacharantia*, *Pterocarpus marsupium*, *Tinospora cordifolia*, *Swertia chirata* | STZ (45mg/Kg BW)-induced diabetic rats<br>Blood glucose =351.09mg/dl<br>Plasma insulin = 8.20µU/ml<br>HbA1c = 0.98mg/dl<br>Glycogen = 1.74g/100g wet tissue<br>Haemoglobin = 6.09mg/dl | At 200 mg/kg<br>↓Blood glucose= 98.51mg/dl<br>↑ Plasma insulin= 16.10µU/ml<br>↓HbA1c= 0.52mg/dl<br>↑Glycogen= 3.08g/100g wet tissue<br>↑Haemoglobin= 10.84mg/dl | Glibenclamide (600 µg/kg):<br>↓Blood glucose= 108.39 mg/dl<br>↓ Plasma insulin= 14.70µU/ml<br>↓HbA1c= 0.58mg/dl<br>↑Glycogen= 2.39g/100g wet tissue<br>↓↑Haemoglobin= 9.27mg/dl | *In vivo;* India | Anti-hyperlipidemic<br>Prokinetic effect | Babu and Prince 2004; Babu and Ignacimuthu 2007 |
| Diakyur | *Cassia javanica*, *Cassia auriculata*, *Salacia reticulata*, *Gymnema sylvestre*, *Mucuna pruriens*, *Syzygium jambolanum*, *Terminalia arjuna*. | Alloxan (150mg/Kg *i.p.*)-induced diabetic rodents<br>FBG= 246–253mg/dl | At 1600mg/Kg<br>↓FBG= 64.90mg/dl (rats) and 87.3mg/dl (rabbits) | Glibenclamide (2 mg/kg rats and 5g/Kg rabbits):<br>↓FBG= 56.90mg/dl (rats) and 68.50mg/dl (rabbits) | *In vivo*; India | Anti-lipidperoxidative | Joshi et al., 2007 |

| Commercial Name | Formulations with scientific names | Experimental model | Effects of polyherbal preparation | Effects of reference drug | Study design and Country | Additional property | References |
|---|---|---|---|---|---|---|---|
| Okchun-San | *Coixlacryma-jobi* (or *Oryzasativa*), *Glycyrrhizauralensis*, *Puerariathunbergiana*, *Rehmanniaglutinosa*, *Schisandrachinensis*, *Trichosanthes kirilowii*. | *db/db* type-2 diabetic mice | Okchun-San+ Coicis semen (200mg/Kg)<br>↓FBG<br>↑Glucose tolerance<br>Okchun-San+ Oryzae semen (200mg/Kg)<br>↓FBG; ↑Glucose tolerance | Acarbose (5 mg/kg)<br>↓FBG<br>↑Glucose tolerance | *In vivo;* Korea | '-' | Chang et al., 2006 |
| 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<br>↓FBG<br>↓HbA1c<br>↑Hepatic glycogen<br>↓Histological damage in the pancreas<br>↓Epinephrine-induced hyperglycemia | Glibenclamide (4 mg/Kg)<br>↓FBG<br>↓HbA1c<br>↑Hepatic glycogen<br>↓Histological damage in the pancreas<br>↓Epinephrine-induced hyperglycemia | *In vivo*;India | '-' | (Mandlik et al., 2008 |

| 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<br>FBG= 11.10 mmol/l<br>HbA1c= 7.11%<br>Plasma insulin= 465.2 U/ml<br>Liver glycogen=10.98 mg/g tissue<br>Urine sugar= 1.98g/24h | At 100mg/Kg BW<br>↓FBG= 7.10 mmol/l<br>↓HbA1c= 4.98%<br>↑Plasma insulin= 278.80 U/ml<br>↓Liver glycogen=7.11mg/g tissue<br>↓Urine sugar= 0.56g/24h | Rosiglitazone (60 µg/Kg):<br>↓FBG= 9.88 mmol/l<br>↓HbA1c= 5.11%<br>↑Plasma insulin= 319.90U/ml<br>↓Liver glycogen=7.39mg/g tissue<br>↓Urine sugar= 0.98g/24h | *In vivo*;India | '-' | Yadav et al., 2007 |
| | | High fructose diet-fed rats | At 200mg/Kg BW<br>↓FBG<br>↑Plasma insulin | Glibenclamide and Rosiglitazone<br>↓FBG<br>↑Plasma insulin | *In vivo*; India | '-' | Pachauri et al., 2009 |
| | | Human subjects with type 2 diabetes | At 100mg/Kg BW<br>↓FBG<br>↑Plasma insulin | Glibenclamide and Rosiglitazone<br>↓FBG<br>↑Plasma insulin | Clinical trials; India | '-' | Panchauri et al., 2007 |
| | | Human subjects with type 2 diabetes | At 10mg/day<br>↓FBG<br>↓HbA1c<br>↓Glycosuria | - | Clinical trials; India | '-' | Mahajan et al., 2013 |
| | | Human subjects with type 2 diabetes age Group= 35 to >65 yrs | At 4g twice daily for 18 months<br>↓FBG= 12.30-42.00%<br>↓Postprandial BG= 28-32% | - | Clinical trials; India | Anti-hyperlipidemic | Yadav et al., 2014 |

| Commercial Name | Formulations with scientific names | Experimental model | Effects of polyherbal preparation | Effects of reference drug | Study design and Country | Additional property | References |
|---|---|---|---|---|---|---|---|
| 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<br>↓FBG<br>↓HbA1c | No data available | Clinical trials; Israel | '-' | Said et al., 2008 |
| Karnim Plus | *Momordica charantia*, *Azadirachta indica*, *Picrorhiza kurroa*, *Ocimum sanctum* and *Zingiber officinale*. | Alloxan(120mg/Kg) induced diabetic rats<br>FBG= 370.50 mg/dl<br>Urea=73.88 mg/dl | At 400 mg/kg (11 days)<br>↓FBG= 206.17mg/dl<br>↓Urea =65.95mg/dl<br>↓Creatinine=1.30mg/dl | Glibenclamide (4 mg/kg):<br>↓FBG=115.00 mg/dl<br>↓Urea=28.68 mg/dl<br>↓Creatinine =1.11 mg/dl | *In vivo*;India | '-' | Bangar et al., 2009 |
| Karnim Plus | *Momordica charantia*, *Azadirachta indica*, *Picrorhiza kurroa*, *Ocimum sanctum* and *Zingiber officinale*. | Human subjects with type 2 diabetes | At 2 capsules/ twice daily<br>↓FBG<br>↓HbA1c<br>↓Postprandial BG<br>↓Urine sugar | Metformin capsule 2 capsules/twice daily<br>↓FBG<br>↓HbA1c<br>↓Postprandial BG | Clinical trials; India | '-' | Shrirang et al., 2017 |

| Commercial Name | Formulations with scientific names | Experimental model | Effects of polyherbal preparation | Effects of reference drug | Study design and Country | Additional property | References |
|---|---|---|---|---|---|---|---|
| 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<br>Serum glucose= 426.60mg/dl<br>Serum insulin= 12.67µU/ml<br>AUCglucose=44.60 (mg/dl.min)x$10^3$<br>AUCinsulin=1.65 (µU/ml.min)x$10^3$ | At 100 mg/Kg<br>↓ Serum glucose= 314.30mg/dl<br>↑Serum insulin=17.67µU/dl<br>↓AUCglucose= 21.25 (mg/dl.min)x$10^3$<br>↑AUCinsulin= 2.96 µU/ml.min)x$10^3$ | No data available | *In vivo*;India | Anti-hyperlipidemic | Rein et al., 2013 |
| SR10 | *Radix astragali* (Root), *Radix codonopsis* (Root), *Cortex lycii* (Root). | *db/db* type 2 diabetic mice | At 927 mg/Kg<br>Glucose tolerance= not significant<br>↓FBG<br>↑Insulin | Metformin (200 mg/Kg)<br>↑Glucose tolerance<br>Not checked for other parameters. | *In vivo*; China | Antioxidant, Protective effect | Chan et al., 2008; Chan et al., 2009 |

| 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<br>↑superoxide dismutase (SOD)<br>↑catalase (CAT)<br>↑glutathione peroxidase ($GP_x$)<br>↑ reduced glutathione (GSH)<br>↓ lipid peroxidation | No data available | *In vivo*;India | '-' | Sajeeth et al., 2010 |
| 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<br>↓FBG<br>↑Insulin<br>↓HbA1c<br>↓Histological damage in the Pancreas | Tolbutamide (250 mg/kg)<br>↓FBG<br>↑Insulin<br>↓HbA1c<br>↓Histological damage in the pancreas | *In vivo*;India | '-' | Lanjhiyana et al., 2011 |

| Commercial Name | Formulations with scientific names | Experimental model | Effects of polyherbal preparation | Effects of reference drug | Study design and Country | Additional property | References |
|---|---|---|---|---|---|---|---|
| Polyherbal preparation | *Eugenia jambolana*, *Momordica charantia* and *Ocimum sanctum*. | Alloxan (125mg/Kg)-induced diabetic rats<br>Blood glucose= 438.67mg/dl<br>Urea= 66.33mg/100ml<br>Creatinine= 1.75mg/100ml | At 400 mg/kg<br>↓ Blood glucose= 100.67mg/dl<br>↓Urea= 66.33mg/100ml<br>↓Creatinine= 1.75mg/100ml | Glibenclamide 0.5 mg/kg<br>↓ Blood glucose= 89.66mg/dl<br>↓Urea= 25.67mg/100ml<br>↓Creatinine= 0.65mg/100ml | *In vivo*;India | '-' | Kumar et al., 2010 |
| PM021 | *Mori folium* and *Aurantii fructus*. | Type 2 diabetes Otsuka Long–Evans Tokushima Fatty (OLETF) rats<br>Blood glucose= 125.60mg/dl<br>Urine output= 288.30 (control as 100%) | ↓ Blood glucose= 109.30mg/dl<br>↓Urine output= 228.60 (control as 100%) | No data available | *In vivo*;Korea | '-' | Kim et al., 2011 |
| 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<br>↓FBG= 60.04%<br>↑Insulin= 39.26% | Rosiglitazone (8 mg/kg):<br>↓FBG= 57.91%<br>↑Insulin= 11.11% | *In vivo*;India | Ameliorates protein oxidation | Kesavanarayanan et al., 2013 |

| Commercial Name | Formulations with scientific names | Experimental model | Effects of polyherbal preparation | Effects of reference drug | Study design and Country | Additional property | References |
|---|---|---|---|---|---|---|---|
| APKJ-004 | *Eugenia jambolana* and *Cinnamomum zeylanicum*. | In 3T3-L1, C2C12, HepG2 cell lines | α-glucosidase inhibitory activity (IC50=147.20µg/ml)<br>Insulin mimetic activity in 3T3-L1 cell lines= 42%<br>Insulin mimetic activity in C2C12 cell lines= 87.20%<br>Insulin mimetic activity in HepG2 cell lines=89.50% | Acarbose<br>α-glucosidase inhibitory activity (IC50=132.20µg/ml) | *In vitro*,India | '-' | Roa and Jamil 2011 |
| APKJ-004 | *Eugenia jambolana* and *Cinnamomum zeylanicum*. | STZ (45mg/Kg BW)-induced diabetic rats<br>Blood glucose= 268.01mg/dl<br>Insulin= 06.75µU/ml | At 800mg/Kg<br>↓Blood glucose= 97.01mg/dl<br>↑Insulin= 23.13µU/ml | Glibenclamide (2mg/Kg)<br>↓Blood glucose= 89.30mg/dl<br>↑Insulin= 19.02µU/ml | *In vivo*; India | '-' | Jamil and Amarachinta 2012 |
| HAL(14) | *Withania somnifera* (Root) *Momordica charantia* (Fruit), *Trigonellafoenum-graecum* (Seed). | STZ (50mg/Kg)-induced diabetic rats | At 500 mg/kg<br>↓FBG =52%<br>↑Hepatic glycogen= 163% | Metformin (500 mg/kg):<br>↓FBG= 55%<br>↑Hepatic glycogen= 183% | *In vivo*;India | '-' | Gauttam and Kalia 2013 |

| Commercial Name | Formulations with scientific names | Experimental model | Effects of polyherbal preparation | Effects of reference drug | Study design and Country | Additional property | References |
|---|---|---|---|---|---|---|---|
| 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<br>↑Glucose tolerance<br>↓FBG | Pioglitazone (1 mg/Kg)<br>No significant effect on glucose tolerance<br>↓FBG | *In vivo;* Pakistan | '-' | Akhtar etal., 2012 |
| HAL(14) | *Withania somnifera* (Root) *Momordica charantia* (Fruit), *Trigonellafoenum-graecum* (Seed). | STZ (50mg/Kg)-induced diabetic rats | At 500 mg/kg<br>↓FBG =52%<br>↑Hepatic glycogen= 163% | Metformin (500 mg/kg):<br>↓FBG= 55%<br>↑Hepatic glycogen= 183% | *In vivo*;India | '-' | Gauttam and Kalia 2013 |

| Commercial Name | Formulations with scientific names | Experimental model | Effects of polyherbal preparation | Effects of reference drug | Study design and Country | Additional property | References |
|---|---|---|---|---|---|---|---|
| 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<br>FBG=374.00mg/dl<br>Urine output= 72.00ml/24h | At 15% w/w of diet<br>↓FBG =263 mg/dl<br>↓Urine output= 30ml/24h | No data available | *In vivo*;Iran | Anti-hyperlipidemic | Ghorbani et al., 2013 |
| 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<br>Blood glucose= 399.30mg/dl<br>BUN= 116.20mg/dl | At 400 mg/Kg<br>↓ Blood glucose= 112.10mg/dl<br>↓BUN=48.42mg/dl<br>↓Histological damage in the pancreas | Glibenclamide (10 mg/Kg)<br>↓ Blood glucose= 132.30mg/dl<br>↓BUN= 45.72mg/dl<br>↓Histological damage in the pancreas | *In vivo*;India | '-' | Yadav et al., 2013 |

| Commercial Name | Formulations with scientific names | Experimental model | Effects of polyherbal preparation | Effects of reference drug | Study design and Country | Additional property | References |
|---|---|---|---|---|---|---|---|
| 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<br>↓Glucose (50.50%) | Glibenclamide (10 mg/Kg)<br>↓ Glucose (57.91%) | *In vivo*;India | '-' | Sruthi et al., 2014 |
| SPHAG | *Alstoniascholaris* (Leaves), *Gymnemasylvestre* (Leaves), *Holarrhenapubescens* (Bark), *Premnacorymbosa* (Leaves), *Solanum nigrum* (Leaves). | Alloxan (150mg/Kg BW) -induced diabetic rats<br>HbA1c= 9.73%<br>Urea=77.00mg/dl<br>Creatinine= 1.60mg/dl | At 500 mg/Kg<br>↓HbA1c= 5.71%<br>↓ Urea= 53.16mg/dl<br>↓ Creatinine- 1.10mg/dl | No data available | *In vivo*;India | Antioxidant | Thamizh et al., 2015 |

| Commercial Name | Formulations with scientific names | Experimental model | Effects of polyherbal preparation | Effects of reference drug | Study design and Country | Additional property | References |
|---|---|---|---|---|---|---|---|
| PHPE | *Azadirachtaindica* (Leaves), *Bougainvillea spectabilis* (Leaves), *Trigonellafoenumgraecum* (Seed). | STZ-induced diabetic rats<br>FBG= 352.10mg/dl | At 600 mg/Kg<br>↓FBG= 298.00mg/dl<br>↑ Restoration in size and number of Islet of Langerhans. | Glibenclamide (500µg/Kg)<br>↓FBG= 108.10mg/dl<br>↑ Restoration in size and number of Islet of Langerhans. | *In vivo*;India | '-' | Gupta et al., 2016 |
| 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<br>FBG= 326.50mg/dl | At 200 mg/Kg<br>↓FBG= 183.00mg/dl<br>α-amylase inhibitory activity (IC50=61.86µg/ml)<br>α-glucosidase inhibitory activity (IC50=34.49µg/ml) | Glibenclamide (5 mg/Kg)<br>↓FBG= 164.80mg/dl<br>α-amylase and α-glucosidase inhibitory activity not measured | *In vivo*;India | '-' | Sur and Hazar 2017 |

| Commercial Name | Formulations with scientific names | Experimental model | Effects of polyherbal preparation | Effects of reference drug | Study design and Country | Additional property | References |
|---|---|---|---|---|---|---|---|
| PHF | *Curcuma caesia* (Rhizome), *Evolvulus-alsinoides* (Whole plant), *Citrullus-lanatus* (Seed), *Gymnemasylvestre* (Leaves), *Tinospora-cordifolia* (Stem), *Withania-coagulans* (Fruit) and *Caesalpinia-bonduc* (Seed). | Alloxan (150mg/Kg)-induced diabetic rats<br>Blood glucose= 330.80mg/dl | At 400 mg/Kg<br>↓Blood glucose= 100.30mg/dl) | Glibenclamide (10 mg/Kg)<br>↓Blood glucose= 107.2mg/dl | *In vivo*;India | '-' | Mahajan et al., 2018 |
| PHF | *Tinospora cordifolia,Cinnamomumzeylanicum*, *Curcuma longa*, *Trigonellafoenum-graecum*, *Azadirachtaindica, Piper nigrum*. | STZ (65mg/Kg) nicotinamide (90mg/Kg)-induced diabetic rats<br>Blood glucose= 348.30mg/dl<br>Total protein= 0.27g/dl | At 57.42 mg/Kg<br>↓Blood glucose= 119.40mg/dl<br>↑Total protein=0.73g/dl<br>↑ Restoration in size and number of Islet of Langerhans. | Metformin (150 mg/Kg)<br>↓Blood glucose= 112.60mg/dl<br>↑Total protein= 0.91g/dl<br>↑ Restoration in size and number of Islet of Langerhans. | *In vivo*;India | '-' | Mali et al., 2019 |

| Commercial Name | Formulations with scientific names | Experimental model | Effects of polyherbal preparation | Effects of reference drug | Study design and Country | Additional property | References |
|---|---|---|---|---|---|---|---|
| Mixture extract | *Artemisia sieberi*, *Nigella sativa*and *Teucriumpolium*. | Alloxan (120mg/Kg)-induced diabetic rats<br>Blood glucose= 280.00mg/dl | At 150 mg/Kg<br>↓Blood glucose= 153.63mg/dl | Glibenclamide (5 mg/Kg)<br>↓Blood glucose= 142.72mg/dl | *In vivo*;Iraq | Hypolipidemic | Muhsin et al., 2019 |
| Diasulin | *Cassia auriculata* (Flower), *Coccinia indica* (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<br>FBG= 265.00 mg/dl<br>Plasma insulin= 3.55 µU/mL | At 200 mg/kg<br>↓FBG = 104.16 nmg/dl<br>↑Plasma insulin= 7.05 (µU/mL) | Glibenclamide (600 µg/kg)<br>↓FBG= 111.60 mg/dl<br>↑Plasma insulin= 6.32 µU/mL | | | |
| | | Alloxan (150 mg/kg) induced diabetic rats<br>FBG= 265 mg/dl<br>Plasma insulin= 3.55 µU/mL<br>Hb= 6.44 g/dl<br>HbA1c= 0.82 mg/gHb<br>BGL= 311.6 mg/dl | At(0.20g/kg)<br>↓FBG= 104.1(mg/dl)<br>↑Plasma insulin= 7.05 µU/ml<br>↑Hb= 11.04 g/dl<br>↓HbA1c= 0.36 mg/gHb<br>↓BGL= 102.5 mg/dl | Glibenclamide (600 µg/kg)<br>↓FBG= 111.6 mg/dl<br>↑Plasma insulin= 6.32 µU/ml<br>↑Hb= 10.65 g/dl<br>↓HbA1c= 0.46 mg/gHb<br>↓BGL= 110.8 mg/dl | *In vivo*;India | Antihyperlipidemic and Antiperoxidative | Pari and Saravanan 2004; Saravanan and Pari 2005 |

| Commercial Name | Formulations with scientific names | Experimental model | Effects of polyherbal preparation | Effects of reference drug | Study design and Country | Additional property | References |
|---|---|---|---|---|---|---|---|
| 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<br>↓Body weight= 146 g<br>↑Food intake= 67.96 g/ day<br>↑Water intake= 344.31 g<br>↑Blood glucose= 312.6 mg/dL<br>↓Liver glycogen= 18.89 µg/g | At 400 mg/kg<br>↓Boold glucose= 96.23 mg/ dL<br>↑ Liver glycogen= 46.42 µg/ g<br>↓Liver Histopathology<br>marked decrease in the microdroplet build-up. | Glibenclamide (600 µg/kg)<br>↓Blood glucose= 106.00 mg/dL<br>↑ Liver glycogen= 43.17 µg/g | *In vivo*;India | '-' | Majhi et al., 2018 |
| 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<br>↓FBG<br>↑Plasma glucose | Glibenclamide (0.025 mg/ kg BW)<br>↓FBG<br>↑Plasma glucose | *In vivo*; India | Hypolipidemic | Kurian et al., 2014 |

| Commercial Name | Formulations with scientific names | Experimental model | Effects of polyherbal preparation | Effects of reference drug | Study design and Country | Additional property | References |
|---|---|---|---|---|---|---|---|
| G-400 | *Salacia oblonga*, *Tinospora cordifolia*, *Emblica officinalis*, *Curcuma longa* and *Gymnema* | STZ (55 mg/kg, i.p.)-induced diabetic rates. | At 100 mg/kg BW<br>↑FBG<br>↑Plasma insulin<br>↑Glucose-6-Phosphatase | Glibenclamide (0.025 mg/kg BW)<br>↑ Glucose-6-Phosphatase | *In vivo*; Bangladesh | '-' | Kurian 2016 |
| Polyherbal formulation | *Azadirachtaindica*, *Camellia sinensis* and *Asparagus racemosus*. | STZ (55mg/kg, I.P) induced diabetic rates.<br>↑Blood glucose= 304.8 mg/dl<br>↓SOD= 1.39<br>↓GHS= 6.63<br>↓CAT= 6.71<br>↓TBAR= 2.87 | At 200 mg/kg<br>↓F1 Blood glucose= 139.2 mg/dl<br>↓F2 Blood glucose= 149.7 mg/dl<br>↓F3 Blood glucose= 154.9 mg/dl<br>↑SOD =2.33<br>↑GHS= 13.7<br>↑CAT= 14.5 | No data available | *In vivo;* India | Antioxidant and Hypolipidemic | Mishra et al., 2014 |

| 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.<br>↑Blood glucose | PHF at 0.5 mg/ml<br>α- glucosidase inhibitory ($IC_{50}$ =235 µg/mL).<br>At 500 mg/kg<br>↓Blood glucose= 258.5 mg/dL. | Glibenclamide (600 µg//kg)<br>↓Blood glucose= 221.5 mg/dL. | *In vivo;*<br>Pakistan | Antioxidant and Hypolipidemic | Ghauri et al., 2020 |
| 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.<br>Serum glucose= 319.9 mg/dl<br>Oral glucose= 506.5 mg/dl<br>Creatinine= 2.15 mg/dl<br>Urea= 58.8 mg/dl<br>SOD= 3.6 units/min/mg protein<br>Catalase= 4.2 units/min/mg protein<br>GHS= 40.3<br>mg/gm protein<br>TBARS= 21.7 nmoles/mg protein | At( 600 mg/kg, PO, 28 days)<br>↑Serum glucose= 80.2 mg/dl<br>↓Oral glucose= 222.3 mg/dl<br>↓ Creatinine= 1.19 mg/dl<br>↓Urea= 38.4 mg/dl<br>↑SOD= 4.8 units/min/mg protein<br>↑Catalase= 8.6 units/min/mg protein<br>↑GHS= 56.6 mg/gm protein<br>↓TBARS= 8.4 units/min/mg protein | Glibenclamide (5 mg/kg, PO, 28 days)<br>↑Serum glucose= 99.4 mg/dl<br>↓Oral glucose= 160.5 mg/dl<br>↓ Creatinine= 1.15 mg/dl<br>↓Urea= 38.8 mg/dl | *In vivo*; India | Antioxidant and Antihyperlipidemic | Thakkar and Patel 2010 |

| Commercial Name | Formulations with scientific names | Experimental model | Effects of polyherbal preparation | Effects of reference drug | Study design and Country | Additional property | References |
|---|---|---|---|---|---|---|---|
| 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<br>Serum glucose=393.2 mg/dl<br>HbA1c= 15.03 %<br>Liver glycogen= 6.69 mg/gm<br>GSH= 34.1µg/mg of protein<br>SOD= 4.5 (unit/min/gm tissue) | At 200 mg/kg<br>↓Serum glucose= 124.3 mg/dl<br>↓HbA1c= 9.71%<br>↑Liver glycogen=14.9 mg/gm<br>↑GHS= 46.011 µg/mg of protein<br>↑SOD= 13.8 unit/min/gm tissue | Glibenclamide (10 mg/kg)<br>↓Serum glucose= 120.6 mg/dl<br>↓HbA1c= 6.16%<br>↑Liver glycogen= 16.5 mg/gm<br>↑GHS= 56.3 µg/mg of protein<br>↑SOD= 12.2 unit/min/gm tissue | *In vivo*; India | Antioxidant and Antihyperlipidemic | Ramesh et al., 2012 |
| PHF | *Salacia oblonga*, *Salacia roburghii*, *Garcinia indica* and *Lagerstroemia parviflora*. | STZ (35gm/kg) induced high-fat diet (HFD) diabetic rats.<br>Blood glucose= 19.35 mmol/L<br>Insulin= 68.62 pg/L | At 400mg/kg/b.w<br>↓Blood glucose= 9.54 mmol/L<br>↑Insulin= 94.22 pg/L | Metformin (250 mg/kg b.w.)<br>↓Blood glucose= 8.20 mmol/L<br>↑Insulin= 104.52 pg/L | *In vivo*; India | '-' | Subhasree et al., 2015 |

| 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.<br>Body weight= 138.5g<br>HbA1c= 3.76 %<br>Hb= 5.56 g/dl<br>FBG= 382.5 mg/dl<br>Hexokinase= 109.7 µg/mg of tissue<br>Glucose-6-phosphate=6.1 unit/mg of tissue<br>Glucose-6-phosphatase=33.9 mg of IP/g of tissue<br>SGPT= 111.8<br>SGOT= 60.3 | At (5 mg/0.5 mL of distilled water/100 g body weight/rat/day)<br>↑Body weight= 151.01g<br>↓HbA1c= 2.06 %<br>↑Hb= 11.04 g/dl<br>↓FBG= 98.02 mg/dl<br>↓ Hexokinase= 131.4 (µg/mg of tissue)<br>↑ Glucose-6-phosphate= 11.04 unit/mg of tissue<br>↓ Glucose-6-phosphatase= 24.8 mg of IP/g of tissue<br>↓SGPT= 89.0 IU/L<br>↓SGOT= 47.6 IU/L | Glibenclamide(2mg/0.5 mL distilled water/100 g body weight/ rat/day)<br>↑Body weight= 152.2 g<br>↓HbA1c= 1.98 %<br>↑Hb= 11.84 g/dl<br>↓FBG= 95.12 mg/dl<br>↓ Hexokinase= 129.07 µg/mg of tissue<br>↑Glucose-6-phosphate=10.7 unit/mg of tissue<br>↓ Glucose-6-phosphatase= 23.9 mg of IP/g of tissue<br>↓SGPT= 87.5 IU/L<br>↓SGOT= 49.0 IU/L | *In vivo*;<br>India | Antioxidant and Antihyperlipidemic | Ramesh et al., 2012 |

| 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 (100g/b.w./rat/day) induced diabetic rats.<br>Body weight= 138.5 gm<br>HbA1c= 4.76 %<br>Serum insulin= 5.13 µIU/ml<br>FBG= 382.5 mg/dl | Diashis (5 mg / 0.5 ml of distilled water/ 100 g body weight / rat/day)<br>↑Body weight= 149 gm<br>↓HbA1c= 3.06 %<br>↑Serum insulin= 12.53 µIU/ml<br>↓FBG= 92(mg/dl)<br>Diashis +Normoglycaemic(5 mg / 0.5 ml of distilled water/ 100 g body weight / rat/day)<br>↑Body weight= 161.4 gm<br>↓HbA1c= 2.72 %<br>↑Serum insulin= 14.96 µIU/ml | Glibenclamide(2mg mg / 0.5 ml of distilled water/ 100 g body weight / rat/day<br>↑Body weight= 152.8 gm<br>↓HbA1c= 2.93 %<br>↑Serum insulin= 12.92 µIU/ml<br>↓FBG= 77.2 mg/dl<br>Glibenclamide + Normoglycaemic(2mg mg / 0.5 ml of distilled water/ 100 g body weight / rat/day<br>↑Body weight= 159.5gm<br>↓HbA1c= 2.77 %<br>↑Serum insulin= 15.47 (µIU/ml)<br>↓FBG= 77.3 mg/dl | *In vivo*;<br>India | Antihyperlipidemic | Ramesh et al., 2012 |

| 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.<br>Blood glucose= 15.2<br>Creatinine= 0.94<br>Urea= 35.7<br>AST= 126.9<br>ALT= 157.8<br>ALP= 129.9 | Mdr concentrate (300mg/kg oral)<br>↓Blood glucose= 4.7<br>↓Creatinine= 0.68<br>↓Urea= 15.9<br>↓AST= 77.3<br>↓ALT= 98.4<br>↓ALP= 101.0<br>Madhurakshak powder(MP 600mg/kg)<br>↓Blood glucose= 4.8<br>↓Creatinine= 0.68<br>↓urea= 15.3<br>↓AST= 75.6<br>↓ALT= 96.6<br>↓ALP= 98.8 | Diabecon (250 mg/kg)<br>↓Blood glucose= 3.9<br>↓Creatinine= 0.62<br>↓Urea= 14.5<br>↓AST= 68.7<br>↓ALT= 81.7<br>↓ALP= 59.2 | *In vivo*; India | '-' | Madan et al., 2014 |

| Commercial Name | Formulations with scientific names | Experimental model | Effects of polyherbal preparation | Effects of reference drug | Study design and Country | Additional property | References |
|---|---|---|---|---|---|---|---|
| DS-01 | *Gymnema sylvestre*, *Syzygium cumini*, *Momordica charantia*, *Tinospora cordifolia*, *Cinnamomum zeylanicum*, *Plumbago zeylanica* and *Asphaltum*. | STZ (30mg/kg s.c.) induced diabetic rats<br>FBG= 354.6 mg/dl<br>Creatinine= 0.8mg/dl<br>TP= 7.6g/L<br>ALP= 131U/L<br>Urea= 81.1mg/dl | At 500 mg/kg<br>↓FBG= 276.5 mg/dl<br>↑Creatinine= 0.8mg/dl<br>↑TP= 334.7 g/L<br>↓ALP= 7.1U/L<br>↓Urea= 59.1mg/dl | Glibenclamide (10mg/kg)<br>↓FBG= 275.7 mg/dl<br>↓Creatinine= 0.7mg/dl<br>↓TP= 7.3 g/L<br>↓ALP=719U/L<br>↓Urea=4.5mg/dl | *In vivo*; India | '-' | Jagtap et al., 2018 |
| Polyherbal extract | *Andrographis paniculata* extract, *Gymnema sylvester* extract, *Momordica charantia* extract, and *Myristica fragrans*shodhana extract. | STZ(90mg/kg) induced Type2 diabetic rats.<br>Blood glucose levels= 302.4 mg/dl | At 400mg/kg<br>↓Blood glucose levels= 122.5 mg/dl | Glibenclamide at (0.25 mg/kg )<br>↓Blood glucose levels= 115.4mg/dl | *In vivo*; India | '-' | Tripathi et al., 2016 |

| 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<br>↑Bloog glucose= 269 mg/dl<br>↑ Serum creatinine= 1.61 m/dl | PH (3.63 g/2 ml/kg)<br>↓Blood glucose= 120.6 mg/dl<br>↓Serum creatinine= 0.33 mg/dl<br>APH-A [(5 mg of Gliclazide + 1.81 g of PH)/2 ml/kg].<br>↓Blood glucose= 120.0 mg/dl<br>↓Serum creatinine= 0.39 mg/dl<br>APH-B [(4 mg of Gliclazide + 2.17 g of PH)/2 ml/kg].<br>↓Blood glucose= 116.4 mg/dl<br>↓Serum creatinine= 0.38 mg/dl<br>APH-C [(2 mg of Gliclazide + 2.904 g PH)/2 ml/kg].<br>↓Blood glucose= 110.4 mg/dl<br>↓Serum creatinine= 0.35 mg | Gliclazide (10 mg/ml/kg)<br>↓Blood glucose= 138 mg/dl<br>↓Serum creatinine= 0.75 mg/dl | *In vivo*; India | Hypolipidemic | Kumar et al., 2015 |

| Commercial Name | Formulations with scientific names | Experimental model | Effects of polyherbal preparation | Effects of reference drug | Study design and Country | Additional property | References |
|---|---|---|---|---|---|---|---|
| HF1& HF2 | *Phyllathus emblica* and *Annona squamosa*. | STZ (60mg/kg) induced Type 2 diabetic rats.<br>Plasma glucose= 145.1mg/dl<br>HbA1c= 253.1mg/dl | HF1(20mg/kg/BW)<br>↓Plasma glucose= 106.9mg/dl<br>↓HbA1c= 94.8mg/dl<br>HF2(20mg/kg BW)<br>↓Plasma glucose= 95.3mg/dl<br>↓HbA1c= 80.0mg/dl | Glibenclamide (0.5mg/kg)<br>↓Plasma glucose= 84.9mg/dl<br>↓HbA1c= 78.7mg/dl | *In vivo*; India | Anti-hyperlipidaemic | Chaudhuri and Sharma 2016 |
| 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<br>↓FBG= 146 mg/dl<br>↓HbA1c= 7.7 %<br>↑Urea= 28 mg/dl<br>↓Creatinine= 1 % | No data available | Clinical trials; Iran | Dyslipidemia | Zarvandi et al., 2017 |

| Commercial Name | Formulations with scientific names | Experimental model | Effects of polyherbal preparation | Effects of reference drug | Study design and Country | Additional property | References |
|---|---|---|---|---|---|---|---|
| PHF | *Syzygium cumini* (Leaves), *Ficus glomerata* (Bark), *Butea superb* (Flower). | Alloxan monohydrate induced diabetic rats.<br>Blood glucose= 413mg/100ml | At 500mg/kg body wt<br>↓Blood glucose= 132mg/100ml | Glibenclamide 600µg/kg body wt<br>↓105mg/100ml | *In vivo*; India | '-' | Rashid and Sil 2015 |
| 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* | Alloxan monohydrate (150mg/kg b.w.)<br>↑FBG= 13.0 mmol/L<br>↑Body weight= 224 g<br>Chronic effect of spice mix on two hours post-prandial glucose concentration of alloxan induced type 2 diabetic model rats.<br>↑2hPG=27.40 mmol/L | At 200mg/kg/b.w.<br>↓FBG= 7.00 mmol/L<br>↓Body weight= 223 gm<br>↓2hPG=10.90 mmol/L | Glibenclamide (0.5mg/kg/ b.w.)<br>↓FBG= 6.30 mmol/L<br>↓Body weight= 221 g<br>↓2hPG=10.2 mmol/L | *In vivo*; Bangladesh | '-' | Islam et al., 2018 |

| Commercial Name | Formulations with scientific names | Experimental model | Effects of polyherbal preparation | Effects of reference drug | Study design and Country | Additional property | References |
|---|---|---|---|---|---|---|---|
| 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.<br>↑Serum glucose= 375.20 mg/dl<br>↓Serum insulin= 6.26 U/L<br>↑HbA1c= 13.92 %<br>↓Leptin= 1.78 ng/ml<br>↓Liver glycogen= 9.24 mg/g | At 600mg/kg<br>↓Serum glucose= 142.60 mg/dl<br>↑Serum insulin= 16.87 U/L<br>↓HbA1c= 6.62 %<br>↑Leptin= 2.78 ng/ml<br>↑Liver glycogen= 33.72 mg/g<br>↑enhanced the performance of pancreatic β cells by up-regulating the expression of insulin signaling cascade. | Glibenclamide<br>↓Serum insulin= 128.40 mg/dl<br>↑Serum insulin= 17.54 U/L<br>↓HbA1c= 6.05 %<br>↑Leptin= 3.08 ng/ml<br>↑Liver glycogen= 39.24 mg/g | *In vivo*; Pakistan | Insulin signaling cascade | Majeed et al., 2018 |
| 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.<br>↑Blood glucose level= 460.4 mg/dl | At 600mg/kg<br>↓Blood glucose level= 74.3 mg/dl | Glibenclamide (1mg/kg)<br>↓Blood glucose level= 101.1 mg/dl | *In vivo*; India | Antihyperlipidemic and hepato-protective activity | Gengiah et al., 2014 |

| Commercial Name | Formulations with scientific names | Experimental model | Effects of polyherbal preparation | Effects of reference drug | Study design and Country | Additional property | References |
|---|---|---|---|---|---|---|---|
| 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.<br>↑Serum glucose= 350.26 mg/dl<br>↑Serum creatinine= 2.55 mg/dl<br>↑Uric acid= 9.26 mg/dl | At 740mg/kg<br>↓Serum glucose= 129.72 mg/dl<br>↓Serum creatinine= 1.01 mg/dl<br>↓Uric acid= 4.33 mg/dl | Metformin (500 mg/kg/day,orally)<br>↓Serum glucose= 128.2 0 mg/dl<br>↓ Serum creatinine= 1.69 mg/dl<br>↓Uric acid= 6.09 mg/dl | *In vivo*; India | Hyperlipidemia and antioxidant | Singhal et al., 2014 |
| NPF<br>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.<br>↓Blood glucose level | No data available | Clinical trials; Bangladesh | '-' | Rashid et al., 2018 |

| Commercial Name | Formulations with scientific names | Experimental model | Effects of polyherbal preparation | Effects of reference drug | Study design and Country | Additional property | References |
|---|---|---|---|---|---|---|---|
| PHF<br>Polyherbal Formulation | *Gymnemasylvestre* (Leaves), *Trigonella foenum-graecum* (Seed) and *Phyllanthus emblica* (Fruit). | STZ (120mg/kg) induced diabetic rats.<br>↑Blood glucose= 136. 2 mg/dl<br>↑FBG= 302.5 mg/dl | HF1 at 20mg/kg/b.w.<br>↓Blood glucose= 92.1 mg/dl<br>↓FBG= 90.4 mg/dl<br>HF2 at 20mg/kg/b.w.<br>↓Blood glucose= 79.3 mg/dl<br>↓FBG= 80.3 mg/dl<br>HF3 at 20mg/dl/b.w.<br>↓Blood glucose= 83.6 mg/dl<br>↓FBG= 85.9 mg/dl<br>HF4 at 20mg/dl/b.w.<br>↓Blood glucose= 85.7 mg/dl<br>↓FBG= 86.1 mg/dl | Glibenclamide (0.5 mg/kg)<br>↓Blood glucose= 75.3 mg/dl<br>↓FBG= 76.4 mg/dl | *In vivo*; India | Antihyperlipidemic | Shah et al., 2019 |
| PH | *Ocimum gratissimum* (Leaves) and *Gongronema latifolium* (Leaves). | Alloxan(100mg/kg/b.w) monohydrate induced diabetic rats<br>↑FGL= 248.0 mg/dl | At 400 mg/kg<br>↓FBG= 107.2 mg/dl | No data available | *In vivo*; Nigeria | Reproductive function | Onuka et al., 2014 |

| 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*, *Trigonellafoenum-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.<br>↓Body weight= 227 g<br>↑Urine volume= 10.50 ml/5h<br>↑Serum glucose= 348 mg/dl | At 0.28ml/kg twice daily for 21 days<br>↓Body weight= 285 g<br>↓Urine volume= 2.37 ml/5h<br>↓Serum glucose= 143 mg/dl<br>↓ Histological damage in liver and pancreatic tissue | Metformin (100mg/kg)<br>↑Body weight= 355 g<br>↓Urine volume= 5.47 ml/5h<br>↓Serume glucose= 170 mg/dl | *In vivo*; India | Antihyperlipidemic | Choudhari et al., 2017 |

| Commercial Name | Formulations with scientific names | Experimental model | Effects of polyherbal preparation | Effects of reference drug | Study design and Country | Additional property | References |
|---|---|---|---|---|---|---|---|
| PHF | *Lawsonia inermis* and *Azadira chtaindica*. | Alloxan (120mg/kg) monohydrate induced diabetic rats for 10 days<br>↑Blood glucose= 268.2 mg/dl | F1: ↓Blood glucose= 200.8 mg/dl<br>F2: ↓Blood glucose= 215.7 mg/dl<br>F3:↓Blood glucose= 222.3 mg/dl<br>F4: Blood glucose= 246.1 mg/dl<br>F5: Blood glucose= 252.7 mg/dl | Glibenclamide (0.5 mg/kg p.o. 10% w/v, 1ml/200 g rat)<br>↓Blood glucose= 182.6(mg/dl) | *In vivo*; India | '-' | Rajwar and Khatri 2013 |
| PHF | *Lawsonia inermis* and *Azadira chtaindica*. | STZ (60mg/kg) induced diabetic rats for 21 day<br>↓Body weight= 127.1 g<br>↑Blood glucose level=325.5 mg/dl | F1: ↑Body weight= 156.6 g<br>↓Blood glucose= 129.1mg/dl<br>F2: ↑Body weight= 160.1g<br>↓Blood glucose= 115.3 mg/dl<br>F3: ↑Body weight= 158.1g<br>↓Blood glucose= 101.6 mg/dl<br>F4: ↑Body weight= 157.3 g<br>↓Blood glucose= 90 mg/dl<br>F5: ↑Body weight= 155.3 g<br>↓Blood glucose= 103.2 mg/dl | Glimiperide drug(1 mg/kg)<br>↑Body weight= 159.5 g<br>↓Blood glucose= 82 mg/dl | *In vivo*; India | '-' | Rajwar and Khatri 2013 |

| 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.<br>↑FBG= 319.2 mg/dl<br>↓Hb= 8.16 g/dl<br>↑HbA1c= 11.75 %<br>↓Serum insulin= 0.27 mu/L<br>↓Liver glycogen= 7.86 mg/g<br>↑Serum creatinine=1.85 mg/dl<br>↑Urea= 59.93 mg/dl<br>↑Uric acid= 8.26 mg/dl | At (1000 mg/kg, p.o.)<br>↓FBG= 119.2 mg/dl<br>↑Hb= 14.10 g/dl<br>↓HbA1c= 7.18 %<br>↑Serum insulin= 0.40 mU/L<br>↑Liver glycogen= 47.21 mg/g<br>↓Serum creatinine= 0.87 mg/dl<br>↓Urea= 35.86 mg/dl<br>↓Uric acid= 4.12 mg/dl | Glibenclamide (5 mg/kg, p.o.)<br>↓FBG=132.7 mg/dl<br>↑Hb= 12.48 g/dl<br>↓HbA1c= 6.78 %<br>↑Serum insulin= 0.76 mU/L<br>↑Liver glycogen= 48.33 mg/g<br>↓Serum creatinine= 0.87 mg/dl<br>↓Urea= 36.64 mg/dl<br>↓Uric acid= 3.30 mg/dl | *In vivo*; India | Antihyperlipidemic | Agrawal et al., 2015 |
| PHP | *Curcuma long*, *Lavandula stoechas*, *Aegle marmelos* and *Glycyrrhiza glabra*. | Alloxan(150mg/kg b.w.) induced diabetic mice<br>↑FBGL | At 150mg/kg b/w.<br>↓FBGL | Pioglitazone (1mg/kg b.w.)<br>↓FBGL | *In vivo*; Pakistan | '-' | Mustafa et al., 2019 |

| Commercial Name | Formulations with scientific names | Experimental model | Effects of polyherbal preparation | Effects of reference drug | Study design and Country | Additional property | References |
|---|---|---|---|---|---|---|---|
| Aloe camperi , Meriandradiant hera 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.)<br>↑Blood glucose level= 239.2 mg/dl | At 200kg/kg<br>AC (Aloe camperi)<br>↓Blood glucose level= 144.3 mg/dl<br>MD (Meriandra dianthera)<br>↓Blood glucose level= 144.3 mg/dl<br>PH (Polyherbal drug)<br>↓Blood glucose level= 160.4 mg/dl<br>At 400mg/kg<br>AC (Aloe camperi)<br>↓Blood glucose level= 135.1 mg/dl<br>MD (Meriandra dianthera)<br>↓Blood glucose level= 135.1 mg/dl<br>PH (Polyherbal drug)<br>↓Blood glucose level= 154.2 mg/dl | Metformin (5 mg/kg)<br>↓Blood glucose level=124.2 mg/dl | *In vivo*;<br>Eritrea | '-' | Demoz et al., 2015 |

| Commercial Name | Formulations with scientific names | Experimental model | Effects of polyherbal preparation | Effects of reference drug | Study design and Country | Additional property | References |
|---|---|---|---|---|---|---|---|
| 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.<br>↑Serum glucose= 518 mg/dl<br>↓Serum insulin= 6.58 mg/dl<br>↑HbA1c= 13.92 %<br>↓Glucokinase= 111.2 µmolG6PO4/min/mg proteins | At 600 mg/kg<br>↓Serum glucose= 143.1 mg/dl<br>↑Serum insulin= 15.78 mg/dl<br>↓HbA1c= 6.84 %<br>↑Glucokinase= 176.2 µmolG6PO4/min/mg proteins | Glibenclamide (10 mg/kg)<br>↓Serum glucose= 138.20 mg/dl<br>↑Serum insulin= 17.65 mg/dl<br>↓HbA1c= 6.14 %<br>↓Glucokinase= 181.6 µmolG6PO4/min/mg proteins | *In vivo*; Pakistan | Antihyperlipidemic | Iftikhar et al., 2018 |
| 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$^{-1}$)<br>↓FPG<br>↓Guctosamine<br>↓Blood glucose | Pioglitazone(2.7 mg•kg$^{-1}$•day$^{-1}$),<br>↓FPG<br>↓Guctosamine<br>↓Blood glucose | *In vivo*; Pakistan | '-' | Rahman etal., 2016 |

| 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.<br>↑Blood glucose level= 448.8 mg/dl | At (3.1ml/200g)<br>ADD1<br>↓Blood glucose level= 296.7 mg/dl<br>ADD2<br>↓Blood glucose level= 312.3 mg/dl<br>At (6.2ml/200g)<br>ADD1<br>↓Blood glucose level= 244.6 mg/dl<br>ADD2<br>↓Blood glucose level= 154 mg/dl | Metformin (500mg/kg)<br>↓Blood glucose level= 134 mg/dl | *In vivo*; India | '-' | Mawlieh et al., 2020 |
| PHF | *Gymnema sylvestre, Emblica officinalis and Salacia reticulata* | STZ (45mg/kg) induced diabetic rats<br>↑Blood glucose= 215.50mg/dl | At 200 mg/kg<br>↓Blood glucose=96.50mg/dl<br>At 400 mg/kg<br>↓Blood glucose=99.50mg/dl | Glibenclamide (0.5 mg/kg, p.o)<br>↓Blood glucose=106.00mg/dl | *In vivo*, *In Vitro*; India | Anti-hyperglycemic and antioxidant activities | Barti et al., 2021 |

| Commercial Name | Formulations with scientific names | Experimental model | Effects of polyherbal preparation | Effects of reference drug | Study design and Country | Additional property | References |
|---|---|---|---|---|---|---|---|
| PHF | Wheat germ (Oil), *Coriander sativum* (Juice) and *Aloe vera* (Juice). | Alloxan monohydrate (250mg) induced diabetic mice.<br>↑FBG= 261.4 mg/dl | At (1.0ml/kg)<br>PH-1<br>↓FBG= 202.2 mg/dl<br>PH-2<br>↓FBG= 117.6 mg/dl<br>PH-3<br>↓FBG= 137 mg/dl<br>At (2.0ml/kg)<br>PH-1<br>↓FBG= 180.4 mg/dl<br>PH-2<br>↓FBG= 137.2 mg/dl<br>PH-3<br>↓FBG= 132.6 mg/dl | Glibenclamide (600 µg/kg)<br>↓FBG= 132.6 mg/dl | *In vivo*;India | '--' | Srivastava and Rai 2018 |

| Commercial Name | Formulations with scientific names | Experimental model | Effects of polyherbal preparation | Effects of reference drug | Study design and Country | Additional property | References |
|---|---|---|---|---|---|---|---|
| *Saptarangyadi Ghanavati* | *Salacia chinensis* (Root), *Momordicacharantia*(Seed), *Trigonella foenum-graecum* (Seed), *Tinosporacordifolia* (Stem), *Terminalia chebula*, *Terminalia bellirica* and *Emblica officinalis* (Fruit pericrap). | Swiss albino mice (400 mg/kg)<br>↑Blood glucose= 106.00 mg/dl | At 400mg/kg<br>↓Blood glucose level= 70.7 mg/dl | Glibenclamide(0.65mg/kg)<br>↓Blood glucose level= 67.8 mg/dl | *In vivo*;India | '-' | Singh et al., 2014 |
| Madhumehantak 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.<br>↑Blood glucose= 330 mg/dl | Low-dose MMC<br>↓Blood glucose= 118 mg/dl<br>High-dose MMC<br>↓Blood glucose= 128 mg/dl | Glibenclamide(10mg/kg/day)<br>↓Blood glucose= 120 mg/dl | *In-vivo*;<br>India | '-' | Bhattacharya and Reddy 2018 |

| Commercial Name | Formulations with scientific names | Experimental model | Effects of polyherbal preparation | Effects of reference drug | Study design and Country | Additional property | References |
|---|---|---|---|---|---|---|---|
| PHF<br>Polyherbal formulation | *Eugenia jambolana (Seed), Tinospora cordifolia (Root),*<br>*Gymnema sylvestre (Leaves), Cressa cretica (Leaves),*<br>*Casearia esculenta (Root), Curcuma longa (Rhizome),*<br>*Swertia chirata* (Leaves),<br>*Centratherum anthelminticu (Seed),*<br>*Picrorrhiza kurroa (Rhizome), Trigonella foenum-graec*um (Seed), *Terminalia chebula* (Fruit),<br>*Holarrhena antidysenterica (*Bark), *Pterocarpus marsupium* (Leaves),<br>*Glycyrrhiza glabra* (Rhizome), Mineral pitch, *Tribulus terrestris* (Seed), *Withania somnifera* (Leaves),<br>*Nardostachys jatamansi (Rhizome)* | STZ induced diabetic nephropathy rats.<br>↓Urine volume= 4.0 ml/rat/day<br>↓Urinary urea= 0.01 mg/dl<br>↑Serum creatinine= 2.40 mg/dl<br>↓Urine creatinine= 5.8 mg/dl<br>↑ Protein urine= 24.70 mg/day<br>↑ UAER= 16.8 µg/day<br>↑ AGES(AU)= 455 | At 500mg/kg<br>↑Urine volume= 13.2 ml/rat/day<br>↑Urinary urea= 3.67 mg/dl<br>↓Serum creatinine= 0.94 mg/dl<br>↑Urine creatinine= 23.8 mg/dl<br>↓Protein urine= 0.08 mg/day<br>↓UAER= 2.9 µg/day<br>↓AGES(AU)= 227 | | *In-vivo*;<br>India | '-' | Reddy et al., 2019 |

| Commercial Name | Formulations with scientific names | Experimental model | Effects of polyherbal preparation | Effects of reference drug | Study design and Country | Additional property | References |
|---|---|---|---|---|---|---|---|
| Talapotaka churna | *Cassia auriculata*, *Emblica officinalis*, *Curcuma longa* and *Berberis aristata*. | Type 2 diabetic patients | 4g Talapotaka churna TID before meal with buttermilk.<br>↑FBG= 119.5 mg/dl<br>↓Postprandial blood sugar= 158.0 mg/dl<br>≈HbA1c= 7.55 %<br>4g Talapotaka churna TID before meal with warm water<br>↓FBG= 119.1 mg/dl<br>↑ Postprandial blood sugar= 185.8 mg/dl<br>≈HbA1c= 7.85 %<br>4g Talapotaka churna TID before meal with & ongoing allopathic treatment<br>↓FBG= 132.5 mg/dl<br>↑ Postprandial blood sugar= 216.0 mg/dl<br>↑HbA1c= 8.03 %<br>↓minimize diabetic symptoms. | 1gm Glimipride BD before meal with water<br>↓FBG= 114.8 mg/dl<br>↑ Postprandial blood sugar=178.6 mg/dl<br>≈ HbA1c= 7.61 % | Clinical trials; India | '-' | Nille et al., 2017 |

| 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.<br>Body weight= 139.3 g<br>Feed intake= 24.5 g<br>BSL= 368.7 mg/dl<br>BGL= 398 mg/dl | At (400 mg/kg)<br>↑Body weight= 190.3 g<br>↓Feed intake= 21.3 g<br>↓BSL= 260.2 mg/dl<br>↓BGL= 312 mg/dl<br>↓ Significant regeneration of pancreatic β cells | Glibenclamide(10mg/kg b.w.p.o)<br>↑Body weight= 214.7 g<br>↓Feed intake= 20.5 g<br>↓BSL= 255.0 mg/dl<br>↓BGL= 296 mg/dl<br>↓ Significant regeneration of pancreatic β cells | *In vivo*; India | Antihyperlipidemic | Suman et al., 2016 |
| Herbal combination | *Andrographis paniculata*, *Lagerstroemia paniculata, Lagerstroemia speciosa*. | Alloxan monohydrate (150mg/kg BW) induced diabetic mice.<br>BGL= 465.8 mg/dl | Combination of *A. paniculata*and *L. speciosa*(ratio 2:1) 0.4ml/20g body wt.<br>↓BGL= 339.6 mg/dl<br>Combination of *A. paniculata* and *L. speciosa* (ratio 1:1) 0.4ml/20g body wt<br>↑BGL= 464.6 mg/dl<br>Combination of *A. paniculata* and *L. speciosa* (ratio 1:2) 0.4ml/20g body wt<br>↓BGL= 411.8 mg/dl | Glibenclamide (0.013 mg/20g BW)<br>↓BGL= 154.6 mg/dl | *In vivo*; Indonesia | '-' | Widyawaruyanti et al., 2013 |

| Commercial Name | Formulations with scientific names | Experimental model | Effects of polyherbal preparation | Effects of reference drug | Study design and Country | Additional property | References |
|---|---|---|---|---|---|---|---|
| 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)<br>Combination 2(*A. indica* 100 mg/kgBW + *G.procumbens* 75 mg/kgBW)<br>Combination 3(*A. indica* 50 mg/kgBW + *G.procumbens* 112.5 mg/kgBW)<br>↑Postprandial= 64.74 %<br>↑Preprandial= 74.91 %<br>↑Insulin<br>↓Evaluated glucose concentration<br>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 | '-' | Sunarwidhi et al., 2014 |

| Commercial Name | Formulations with scientific names | Experimental model | Effects of polyherbal preparation | Effects of reference drug | Study design and Country | Additional property | References |
|---|---|---|---|---|---|---|---|
| SMK001 | *Coptis chinensis* and *Trichosanthes kirilowii*. | STZ (60mg/kg) induced diabrtic rats.<br>Body weight=169.6<br>BGL= 410.2<br>UGL= 10026.4<br>Pancreas weight= 0.70<br>No. of islets= 2.20<br>No. of insulin<br>producing cell= 3.60<br>No. of glucagon producing cell= 78.60 | At 500mg/kg<br>↑Body weight= 215.4<br>↓BGL= 280.4<br>↓UGL= 5042.2<br>↑Pancres weight= 0.88<br>↑ No. of islets= 6.60<br>↑ No. of insulin<br>producing cell= 6.60<br>↓ No. of glucagon producing cell= 43.80 | Glibenclamide(5mg/kg)<br>↑Body weight= 177.6<br>↓BGL= 345.8<br>↓UGL= 7329.4<br>↑Pancreas weight= 0.077<br>↑No. of islets= 4.60<br>↑ No. of insulin<br>producing cell= 15.40<br>↓ No. of glucagon producing cell= 51.40 | *In vivo*; Korea | '-' | Jong et al., 2006 |
| FD1 | *Alstonia scholaris,* Leaves, *Pterocarpus marsupium* Heartwood, *Embelia ribes* Heartwood. | STZ (60mg/kg) induced diabetic rats<br>↑Blood glucose level=412.2mg/dl | At 200 mg/kg<br>↓Blood glucose level=70.05mg/dl | Glipizide (0.25mg/kg)<br>↓Blood glucose level=75.66mg/dl | *In vivo*; India | '-' | Mandoria et al., 2021 |

| Commercial Name | Formulations with scientific names | Experimental model | Effects of polyherbal preparation | Effects of reference drug | Study design and Country | Additional property | References |
|---|---|---|---|---|---|---|---|
| Tetraherbs | *Cinnamomun zeylanicum*, *Trigonella foenum-graecum*, *Allium stipitatum*, *Syzygium aromaticum*. | STZ (55mg/kg) induced diabetic rats.<br>Body weight= 151.3 g<br>FBG= 497.6 mg/dL<br>AUC= 63,597.5 mg/dL<br>No. of islets(N/10mm2)= 5.07<br>Area of islets(mm2)= 0.0090<br>Diameter of islet (um)= 0.0143<br>No. of islet(N/100um2)= 4.33 | At 300mg/kg<br>↑Body weight= 160.1 g<br>↓FBG= 144.7 mg/dL<br>↓AUC= 28,650.0(mg/dL)<br>↑ No. of islets(N/10mm2)= 19.73<br>↑ Area of islets(mm2)= 0.0197<br>↑ Diameter of islet (um)= 164.8<br>↑ No. of islet(N/100um2)= 13.05 | Metformin(500mg/kg)<br>↑Body weight= 161.8 g<br>↓FBG= 111.6 mg/dL<br>↓AUC= 28,697.5 mg/dL<br>↑ No. of islets(N/10mm2)= 18.77<br>↑ Area of islets(mm2)= 0.0143<br>↑ Diameter of islet (um)= 142.3<br>↑ No. of islet(N/100um2)= 6.49 | *In vivo*; Iran | Hypolipidemic | Kiani et al., 2018 |
| PHF | *Allium cepa* (bulb), *Allium sativum* (bulb), *Trigonella foenum-graecum* (seed), and *Curcuma longa* (rhizome) | STZ (60mg/kg) induced diabetic rats<br>↑Fasting blood glucose= 317.45mg/dl | At 100 mg/kg<br>↑ Fasting blood glucose= 105.89mg/dl<br>AT 200 mg/kg<br>↑Fasting blood glucose= 104.95mg/dl<br>At 400 mg/kg<br>↑Fasting blood glucose= 99.47mg/dl | Glibenclamide (10 mg/kg):<br>↓99.19mg/dl | *In vivo*; India | Hyperglycaemia | Nair et al., 2019 |

| Commercial Name | Formulations with scientific names | Experimental model | Effects of polyherbal preparation | Effects of reference drug | Study design and Country | Additional property | References |
|---|---|---|---|---|---|---|---|
| PHF | | STZ (120mg/kg) induced diabetic rats<br>↑Blood glucose level=353.6mg/dl | F1 at 200 mg/kg<br>↓Blood glucose level=109.2mg/dl<br>F1 at 400 mg/kg<br>↓Blood glucose level=88.9mg/dl<br>F2 at 200 mg/kg<br>↓Blood glucose level=116.5mg/dl<br>F2 at 400 mg/kg<br>↓Blood glucose level=84.9mg/dl<br>F3 at 200 mg/kg<br>↓Blood glucose level=113.6mg/dl<br>F3 at 200 mg/kg<br>↓Blood glucose level=86.5mg/dl<br>F4 at 200 mg/kg<br>↓Blood glucose level=103.8mg/dl<br>F4 at 400 mg/kg<br>↓Blood glucose level=86.4mg/dl | Glibenclamide (0.50mg/kg)<br>↓Blood glucose level=82.9mg/dl | *In vivo*; India | Hyperglycemia | Roy et al., 2021 |

| 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.)<br>↓Body weight= 127.2g<br>↑Food intake= 43.00g<br>↑Fasting blood sugar= 244.33mg/dl | Saf¯uf-i-Dhay¯ab¯ıtus at 500 mg/ kg b. w. a<br>↑Body weight= 184g<br>↓Food intake= 31.60g<br>↓Fasting blood sugar=153.4mg/dl<br>Saf¯uf-i-Dhay¯ab¯ıtus at 500 mg/ kg b. w. along with glibenclamide at 0.6 mg / kg b. w. p. o.<br>↑Body weight= 169.3g<br>↓Food intake= 32.17g<br>↓Fasting blood sugar=134md/dl | Glibenclamide at 0.6 mg/ kg. b. w.<br>↑Body weight= 181.7g<br>↓Food intake= 37.33g<br>↓Fasting blood sugar=202.5mg/dlN | *In vivo*; India | hypoglycaemic, hepatoprotective, nephroprotective and hypocholesterolemi | Nasir et al., 2022 |

| Commercial Name | Formulations with scientific names | Experimental model | Effects of polyherbal preparation | Effects of reference drug | Study design and Country | Additional property | References |
|---|---|---|---|---|---|---|---|
| Polyherbal combination | *Taraxacum officinale* and *Momordica charantia* | STZ induced diabetic rats (120mg/kg b.w.)<br>Blood glucose level<br>↓Blood glucose level=13.70mmol/l | 62.5 mg/kg b.w<br>↑Blood glucose level=18.24mmol/l<br>250 mg/kg b.w<br>↑Blood glucose Blevel=16.66mmol/l<br>1000 mg/kg b.w<br>↑Blood glucose level=13.79mmol/l | Glibenclamide (1mg/kg b.w.)<br>↑Blood glucose level=21.89mmol/l | *In vivo*; India | '-' | (Perumal et al., 2022) |
| Polyherbal combination | *Taraxacum officinale* and *Momordica charantia* | STZ induced diabetic rats (120mg/kg b.w.)<br>Blood glucose level<br>↑Blood glucose<br>Level= 26.89mmol/l | 62.5 mg/kg b.w<br>↓Blood glucose level=26.09mmol/l<br>250 mg/kg b.w<br>↓Blood glucose level=14.51mmol/l<br>1000 mg/kg b.w<br>↓Blood glucose level=25.59mmol/l | Glibenclamide (1mg/kg b.w.)<br>↓Blood glucose level=18.91 mmol/l<br>Metformin 50 mg/kg<br>↓Blood glucose level=18.06mmol/l<br>Sitagliptin 10 mg/kg<br>↓Blood glucose level=20.41mmol/l | *In vivo*; India | '-' | Perumal et al., 2022 |

parameters of alloxan- or streptozotocin-induced diabetic rodents (table 1). The anti-diabetic activity of Diakyur (Joshi et al., 2007), Karnim Plus (Bangar et al., 2009), PHF (Karigar and Shariff 2009), Polyherbal preparation (Kumar et al., 2010), Diashis (Bera et al., 2010), APKJ-004 (Jamil and Amarachinta 2012), Polyherbal extract (Ramesh et al., 2012), DIA-2 (Kesavanarayanan et al., 2013), PHF (Rajwar and Khatri 2013), Herbal combinations (Widyawaruyanti et al., 2013), Madhurakshak (Mdr) [Mandan et al., 2014], Saptarangyadi Ghanavati (Singh et al., 2014), Aloe camperi, Meriandra dianthera and polyherbal drug (Demoz et al., 2015), PHPE (Gupta et al., 2016), Polyherbal extract (Tripathi et al., 2016), HF1& HF2 (Chaudhuri and Sharma 2016), PHADT (Suman et al., 2016), (ADC05 Sur and Hazar 2017), DS-01 (Jagtap et al., 2018), Mixed spices (Islam et al., 2018), PH (Iftikhar etal., 2010), PHF (Srivastava and Rai 2018), Tetraherbs (Kiani et al., 2018), Mixture extract (Muhsin et al., 2019), PHF (Mali et al., 2019), PHF (Shah et al., 2019), PHF (Ghauri et al., 2020], ADD1 and ADD2 (Mawlieh et al., 2020), PHF [Nair et al., 2021), PHF (Roy et al., 2021), Safuf-i-Dhayabitus (Nasir et al., 2022), Polyherbal formulation (Perumal et al., 2022) were less when compared to the reference drug. All other PHFs were found to be more effective than the standard drugs like acarbose, glibenclamide, glimepiride, pioglitazone, rosiglitazone, tolbutamide and metformin used in the studies.

In 2009, Chan and co-workers (Chan et al., 2009) investigated the effect of SR10, a PHF comprising of 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.

An experiment by Akhtar and colleagues (Akhta et al., 2012) looked at how Ziabeen, a mix of eight different herbs, affected blood glucose levels (BGL) as measured 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 (Bhattacharya and Reddy 2018) on diabetic rats. Both the low (216 mg/day) and high (648 mg/day) dose 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 et al., 2012, 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, also known as Shilajit, along with metals such as pure mercury, purified sulphur, iron, mica, and copper, have been purported to possess therapeutic properties for treating different illnesses (Kumar et al., 2013). Bang bhasma is a herbo-metallic ayurvedic preparation prepared from tin. Chandraprabha is a proven formulation having glucose-lowering and anti-hyperlipidemic activities and is a blend of 37 herbo-mineral ingredients (Wanjari et al., 2016).

Mawleih and co-workers et al., 2020, evaluated the anti-diabetic potentiality of two commercially available anti-diabetic food supplements Dia Areca (areca nut, beetle vine, lime, lemon, jamboo, and edible grasses) (https://www.shopclues.com/dia-areca-food-supplementary-for-manage-diabetes-65-days-course-500ml-x-4) and Asanadi Kashaya Choorna composed of different parts of 23 plants (https:// www.ayurmedinfo.com/2012/07/14/asanadi kashayam-benefits-dosage-ingredients-side-effects/).The relevance of evaluation of anti-diabetic activity of already available commercial drugs for treating diabetes by Mawleih et al. (Mawleih et al., 2020) is, however, unclear. Instead of carrying out the 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 standarded drug glibenclamide possesses significant antidiabetic, hepatoprotective and nephroprotective (Nasir et al., 2022).

### 2.4 Clinical trials

The efficacy of PHFs on T2DM patients through clinical trials was conducted on 7 formulations namely Diabecon (D-400) (Kant et al., 2000), Diabegon (Pachauri et al., 2009; Mahajan etal., 2013; Yadav et al., 2014), Glucolevel (Said et al., 2008), Karnim Plus (Shrirang et al., 2017), PHF (Zarvandi et al., 20170, novel PHF (Rashid etal., 2018), and Talapotaka churna (Nille et al., 2017).

Kant et al. (Kant et al., 2000) 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 the patients with T2DM by three groups of researchers (Pachauri et al., 2009; Mahajan etal., 2013; Yadav et al., 2014). 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 (Pachauri et al., 2009). Mahajan and his team (Mahajan etal., 2013) experimented 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 (Yadav et al., 2014). After one and a half year of therapy, Yadav et al. (Yadav et al., 2014). 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. (Mahajan etal., 2013) and Yadav et al. ((Yadav et al., 2014) 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. (Said et al., 2008). The patients were supplemented with one tablet of Glucolevel thrice daily for 4 weeks and monitored for the 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 meal for 24 weeks (Shrirang et al., 2017). 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 to each other. In addition, they reported Karnim Plus was more effective in regulating HbA1c in contrast to conventional metformin.

Zarvandi et al., 2017, 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., 2018, 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 *Berberis aristata*) was tested in patients with T2DM (Nille et al., 2017) 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.

### 2.5 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 (Parasuraman et al., 2014). 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 2.2**.

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 (Kanetkar et al., 2007). It also up-regulates the activity of insulin-dependent enzymes and down-regulates the activity of insulin-independent enzymes (Khan et al., 2019). 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 (Fuller and Stephens 2015). Diosgenin ameliorates oxidative stress and inhibits lipid peroxidation (Chen et al., 2015). It has been reported that diosgenin rejuvenates the distorted pancreas morphology and improves insulin concentration (Saravanan et al., 2014). Besides, diosgenin also triggers the expression of PPARγ (Sangeetha et al., 2013). Another important phytoconstituent of fenugreek is 4-hydroxyisoleucine, which improves insulin secretion and thus possesses hypoglycaemic activity (Sauvaire et al., 1998).

Curcumin, a major component of Curcuma longa, exhibits anti-diabetic activities by protecting pancreatic β-cells by diminishing inflammatory response (decreasing

**Table 2.2: 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 (Zhang and Tan, 2000a; 2000b; Nugroho et al., 2012; Augustine et al., 2014; Akhtar et al. 2016) | Andrographolide (Yu et al., 2003; Nugroho et al., 2012; (Widjajakusuma et al., 2019) |
| | *Asteracantha longifolia* | Leaf (Muthulingam, 2010) | Betulin (Tang et al., 2011); Lupeol (Gupta et al., 2012), Stigmasterol (Ghosh et al., 2014) |
| Amaranthaceae | *Aerva lanata* | Leaf (Deshmukh et al., 2008; Akanji et al., 2018), Aerial part (Appia Krishnan et al., 2009), Root (Agrawal et al., 2013) | β-carboline (Cooper et al., 2003) |
| | *Atriplex halimus* | Leaf (Chikhi et al., 2014) | Atriplexoside A and atriplexoside B |
| Amaryllidaceae | *Allium cepa* | Bulb (Campos et al., 2003; Akash et al., 2014; Airaodion et al, 2020) | Allicin (Dhanarasu, 2015) |
| | *Allium sativum* | Bulb (Eidi et al., 2006; Poonam et al., 2013; Waheed et al., 2014) | Alliin (Nasim et al., 2011; Zhai et al., 2018), Allicin (Dhanarasu, 2015) |
| | *Allium stipitatum syn. A. hirtifolium* | Bulb (Khaleghi et al., 2016) | 9-hexadecenoic acid or palmitoleate (Araujo Nunes and Rafacho 2017) |
| Anacardiaceae | *Mangifera indica* | Endopserm (Saprudin et al., 2020), Leaf (Kemasari et al., 2011; Villas Boas et al., 2020) | Mangiferin (Muruganandan et al., 2005; Sekar et al., 2019), Linalool (More et al., 2014) |
| Annonaceae | *Annona squamosa* | Leaf (Gupta et al., 2005; Kaleem et al., 2006) | Quercetin-3-O-glucoside (Panda and Kar, 2007) |

| Family | Species | Parts used | Compounds with anti-diabetic potentiality |
|---|---|---|---|
| Apiaceae | *Bunium persicum* | Seed (Giancarlo et al., 2006) | Caryo-phyllene (Kumawat and Kaur, 2020,γ-terpinene (Habtemariam, 2018) |
| | *Carum carvi* | Seed (Eddouks et al., 2004; Eidi et al., 201 | Carvone (Muruganathan et al., 2013; Muruganathan and Srinivasan, 2016) [202] D-limonene (Bacanlı et al., 2017) |
| | *Coriandrum sativum* | Seed (Eidi et al., 2009), Leaf and Stem (Sreelatha and Inbavalli, 2012) | Linalool (More et al., 2014) |
| | *Cuminum cyminum* | Seed (Andallu and Ramya, 2007; Jag-tap and Patil 2010; Srivastava et al., 2011) | Cuminaldehyde (Patil et al., 2013), Cuminol (Patil et al., 2013), p-cymene (Joglekar et al., 2014) |
| | *Foeniculum vulgare* | Essential oil (El-Soud et al., 2011), Seed (Anitha et al., 2014 ; Dongare et al., 2010; Mhaidat et al., 2015) | trans-anethole (Sheikh et al., 2015), Fanchone (Sebai et al., 2013) |
| | *Trachyspermum ammi* | Seed (Kaskoos, 2019) | Thymol (Saravanan and Pari, 2015), p-cymene (Joglekar et al., 2014) , Pinene (Özbek and Yılmaz 2017), Carvone (Muruganathan et al., 2013; Muruganathan and Srinivasan, 2016), D-limonene (Bacanlı et al., 2017) |

| Family | Species | Parts used | Compounds with anti-diabetic potentiality |
|---|---|---|---|
| | *Alstonia scholaris* | Leaf (Jong-Anurakkun et al., 2007; Arulmozhi et al., 2010; Anusha et al., 2016; Wanjari et al., 2019) | Alschomine |
| | *Catharanthus roseus* | Leaf (Singh et al., 2001; Islam et al., 2009; Rasineni et al., 2010; Jayanthi et al., 2010;Al-Shaqha et al., 2015), Twig (Singh et al., 2001) | Vindogentianine (tiong et al., 2015), Vindolidine (Aba and Asuzu, 2018, Vindolinine (Aba and Asuzu, 2018) |
| Apocynaceae | *Gongronema latifolium* | Leaf (Ugochukwu and Babady, 2003; Akah et al., 2011) | Lupanine (Bobkiewicz-Kozłowska et al., 2007; Wiedemann et al., 2015) |
| | *Gymnema sylvestre* | Leaf (Leach, 2007; Mall et al., 2009) | Gymnemic acid (Sugihara et al., 2000) |
| | *Holarrhena antidysenterica* | Seed (Ali et al., 2009; Mana et al., 2010; Pathak et al., 2015; Sheikh et al., 2016) | NR |
| | *Holarrhena pubescens* | Bark (Bhusal et al., 2014) | NR |
| Asparagaceae | *Asparagus racemosus* | Root (Somani et al., 2012), Leaf (Vadivelan et al., 2011; , Vadivelan et al., 2019) | Sarsasapogenin (Liu et al., 2018) |
| Asphodelaceae | *Aloe barbadensis* | Gel (Akinmoladun and Akinloye, 2007), Plant (Moniruzzaman et al., 2012) | Aloin/ Barbaloin (Ghamari et al., 2013; Younus and Anwar, 2018) |
| | | Leaf (Demoz et al., 2015) | Aloin/ Barbaloin (Ghamari et al., 2013; Younus and Anwar, 2018), Emodin (Xue et al., 2010), Wu et al., 2014) |
| | | Leaf gel (Rajasekaran et al.,2004, Noor et al., 2008; Kim et al., 2009; Yagi et al., 2009; Huseini et al., 2012; Sultana et al., 2020) | Aloin/ Barbaloin (Ghamari et al., 2013; Younus and Anwar, 2018), Aloesin (Yimam et al., 2015), Emodin (Xue et al., 2010); Wu et al., 2014) |

| Family | Species | Parts used | Compounds with anti-diabetic potentiality |
|---|---|---|---|
| | *Artemisia absinthium* | Plant (Daradka et al., 2014) | Thujone (Baddar et al., 2011) |
| | *Artemisia sieberi* | Essential oil (Irshaid et al., 2010) | 1,8-cineole or Eucalyptol (Kim et al., 2018) |
| | *Centratherum anthelminticum* | Seed (Ani and Naidu, 2008; Arya et al., 2012; Swarnkar et al., 2017) | Gallic acid (Punithavathi et al., 2011), Protocatechuic acid (Harini and Pugalendi, 2010), Caffeic acid (Jung et al., 2006), Ellagic acid (Malini et al., 2011), Ferulic acid (Ramar et al., 2012), Quercetin (Abdelmoaty et al., 2010) , Kaempferol (Zhang et al., 2015) |
| Asteraceae | *Gynura procumbens* | Leaf (Hasan et al., 2010; Algariri et al., 2013) | Kaempferol 3-O-glucoside or Astragalin (Riaz et al., 2018) |
| | *Mori folium* | Leaf (Kwon et al., 2015) | Kaempferol 3-O-glucoside or Astragalin (Riaz et al., 2018) |
| | *Silybum marianum* | Plant (Kazazis et al., 2014) | Silymarin (Sheela et al., 2013), Mariamides A (Qin et al., 2017), Mariamides B (Qin et al., 2017 |
| | *Sphaeranthus indicus* | Root (Prabhu et al., 2008; Ramchandran et al., 2011; Swetha and Raju, 2014) | Quercetin (Abdelmoaty et al., 2010) |
| Berberidaceae | *Berberis aristata* | Root (Semwal et al., 2011; Bhutkar et al., 2017), Leaf (Upwar et al., 2011) | Berberine (Cicero and Tartagni, 2012) |
| Boraginaceae | *Rotula aquatica* | Root (Shyam et al., 2013), Leaf (Priya et al., 2014) | |

| Family | Species | Parts used | Compounds with anti-diabetic potentiality |
|---|---|---|---|
| Brassicaceae | *Brassica nigra* | Seed (Anand et al., 2007) | Sinigrin (Abbas et al., 2017), Glucoraphanin (Xu et al., 2018; Nagata et al., 2017) |
| | *Eruca sativa* | Leaf (Hetta et al., 2017) | trans-Vaccenic acid (Wang et al., 2016), Quercetin (Abdelmoaty et al., 2010) |
| | *Eruca vesicaria* | Essential oil (Hichri et al., 2019) | Erucin (Hichri et al., 2019) |
| | *Lepidium sativum* | Seed (Eddouks et al., 2005; Chauhan et al., 2012; Attia et al., 2019) | Lepidine (Boyadzhieva, 1981) |
| Burseraceae | *Commiphora wightii* | Resin (Bhardwaj et al., 2014) | Diasesartemin (El-Mekkawy et al., 2013), *epi*-muklin (El-Mekkawy et al., 2013), (Z)-guggulsterone (El-Mekkawy et al., 2013) |
| Campanulaceae | *Codonopis pilosula (Radix codonopsis)* | Residue (Liu et al., 2018) | NR |
| Capparaceae | *Capparis decidua* | Aerial parts (Zia-Ul-Haq et al., 2011) | Phthalic Acid (Sivajothi and Shruthi, 2013) |
| Caprifoliaceae | *Nardostachys jata-mansi* | Root (Mahesh et al., 2007; Aleem et al., 2014) | β-sitosterol (Gupta et al., 2011) |
| Celastraceae | *Elaeodendron glaucum* | Stem bark (Lanjhiyana et al., 2011) | β-sitosterol (Gupta et al., 2011), Lupeol (Gupta et al., 2012), Friedelin (Susanti et al., 2013) |
| | *Salacia chinensis* | Root (Sikarwar and Patil, 2012) | Mangiferin (Sellamuthu et al., 2013, Salacinol (Morikawa et al., 2015) |
| | *Salacia oblonga* | Root (Krishnakumar et al., 1999; 2000; Huang et al., 2006) | Mangiferin (Sellamuthu et al., 2013), Salacinol (Morikawa et al., 2015), Kotalanol (Xie et al., 2011) |
| | *Salacia reticulata* | Leaf (Yoshino et al., 2009), Root (Ruvin Kumar et al., 2005), Stem (Ruvin Kumar et al., 2005) | Mangiferin (Sellamuthu et al., 2013), Salacinol (Morikawa et al., 2015), Kotalanol (Xie et al., 2011) |
| | *Salacia roxburghii* | | Mangiferin (Sellamuthu et al., 2013)[313] |

| Family | Species | Parts used | Compounds with anti-diabetic potentiality |
|---|---|---|---|
| Clusiaceaec | *Garcinia indica* | Fruit (Khatib and Patil, 2011; Swathi et al., 2015) | Garcinol (Madhuri and Naik, 2017; Mail et al., 2017), Gambogic acid (Cui et al., 2018) |
| Combretaceae | *Terminalia arjuna* | Bark (Ragavan and Krishnakumari, 2006; Morshed et al., 2011; Kumar et al., 2013, Leaf (Biswas et al., 2011) [328] | Arjunetin (Mohanty et al., 2019), Arjungenin (Mohanty et al., 2019), Ellagic acid (Mohanty et al., 2019), Arjunic acid (Mohanty et al., 2019) |
| | *Terminalia bellirica* | Fruit (Gupta et al., 2020) | Ellagic acid (Malini et al., 2011), β-sitosterol (Gupta et al., 2011) |
| | *Terminalia chebula* | Fruit (Kumar et al., 2006), Seed (Rao and Nammi, 2006) | Chebulagic acid (Huang et al., 2012), Punicalagin (Zhong et al., 2015; Nadia et al., 2019) |
| | *Terminalia tomento-sa* | Leaf (Alladi et al., 2012), Bark (Sharma et al., 2013) | Arjunolic acid (Manna et al., 2009), β-sitosterol (Gupta et al., 2011) |
| Convolvu-laceae | *Cressa cretica* | Whole plant (Chaudhary et al., 2010; Verma et al., 2014) | Umbelliferone (Rames and Pugalendi, 2005; 2006) |
| | *Evolvulus alsinoides* | Whole plant (Gomathi et al., 2013; Duraisamy et al., 2013) | Piperine (Atal et al., 2012), Squalene (Simonen et al., 2008) |

| Family | Species | Parts used | Compounds with anti-diabetic potentiality |
|---|---|---|---|
| Cucurbitaceae | *Citrullus colocynthis* | Fruit (Abdel-Hassan et al., 2000; Huseini et al., 2009; Ostovar et al., 2020; Ahangarpour et al., 2020; Karimabad et al., 2020), Seed (Al-Ghaithi et al., 2014), Pulp (Dallak, 2011), Pulp and seed (Ghauri et al., 2020), Root (Agarwal et al., 2012; Kalva et al., 2018) | Beta-pyrazol-1-yl-alanine (Heydari et al., 2019)[355] |
| | *Citrullus lanatus* | Seed (Varghese et al., 2013; Omigie and Agoreyo, 2014; Sani, 2015; Oseni et al., 2015; Deshmukh and Jain, 2015; Ogbeifun et al., 2020), Leaf (Aruna et al., 2014), Juice (Ajiboye et al., 2020) | Oleic acid (Ryan et al., 2000), β-sitosterol (Gupta et al., 2011), Lupeol (Gupta et al., 2012) |
| | *Coccinia indica* | Leaf (Venkateswaran and Pari, 2002; Jose and Usha, 2010) | β-sitosterol (Gupta et al., 2011), Betulin (Tang et al., 2011) |
| | *Momordica charantia* | Fruit (Vangoori and Mishra, 2013; Efird et al., 2014), Seed (Ahmad et al., 2012) | Momordicin (Singh et al., 2011), Charantin (Wang et al., 2014; Desai and Tatke, 2015), Vicine (Singh et al., 2011) |
| | *Trichosanthes kirilowii* | Root (Lo et al., 2017) | Allantoin (Go et al., 2015) |
| Cyperaceae | *Cyperus rotundus* | Rhizome (Raut and Gaikwad, 2006; Singh et al., 2015) | Cassigarol E (Tran et al., 2014), Scirpusin A (Tran et al., 2014), Scirpusin B (Tran et al., 2014) |
| Ericaceae | *Vaccinium arctostaphylos* | Fruit (Feshani et al., 2011; Kianbakht and Hajiaghaee, 2013; Kianbakht et al., 2013), Leaf (Kianbakht and Hajiaghaee, 2013) | Dalphinidn (Gharib et al., 2013, Quercetin (Nickavar and Amin, 2011) |

| Family | Species | Parts used | Compounds with anti-diabetic potentiality |
|---|---|---|---|
| Fabaceae | *Acacia arabica* | Bark (Yasir et al., 2010; Hegazy et al., 2013) | Daidzein (Choi et al., 2008; Cheong et al., 2014; Das et al., 2018) |
| | *Butea superba* | NR | Daidzein (Choi et al., 2008; Cheong et al., 2014; Das et al., 2018), Genistein (Fu et al., 2010; Behloul and Wu, 2013), Biochanin A (Harini et al., 2012; Oza and Kulkarni, 2018) |
| | *Caesalpinia bonduc* | Seed (Kishalay et al., 2010; Jana et al., 2012) | NR |
| | *Caesalpinia bonducella* | Seed (Chakrabarti et al., 2003; Kannur et al., 2006; Widhiantara et al., 2018) | NR |
| | *Cajanus cajan* | Leaf (Jaiswal et al., 2008; Ezike et al., 2010; Dolui and Sengupta, 2012) | Biochanin A (Harini et al., 2012; Oza and Kulkarni, 2018), Betulinic acid (Ajala -Lawal et al., 2020) |
| | *Cassia auriculata* | Flower (Pari and Latha, 2002; Latha and Pari, 2003; Nagarajaperumal et al., 2018) [394], Leaf (Gupta et al., 2009) | kaempferol-3-O -rutinoside (Habtemariam, 2011, Luteolin (Zhang et al., 2016) |
| | *Cassia javanica* | Leaf (Kumavat et al., 2012) | Emodin (Xue et al., 2010; Wang et al., 2012) |
| | *Cicer arietinum* | Seed and Sprout (Prathapan et al., 2011) | Formononetin (Qiu et al., 2017; Oza and Kulkarni, 2018), Biochanin A (Harini et al., 2012; Oza and Kulkarni, 2018) |
| | *Glycyrrhiza glabra* | Root (Kartikeson and Lakshmi, 2017 | Glycyrrhizin (Sen et al., 2011, Glabridin (El-Ghffar, 2016), Isoliquiritigenin (Gaur et al., 2014), Liquiritigenin (Gaur et al., 2014) |
| | *Glycyrrhiza uralensis* | Root (Mae et al., 2003) | Glycyrrhizin (Sen et al., 2011), Glycyrrhetinic acid (Ko et al., 2007) |

| Family | Species | Parts used | Compounds with anti-diabetic potentiality |
|---|---|---|---|
| | *Macrotyloma uniflorum* | Seed (Gupta et al., 2011;Mohan and Elyas, 2018) | p-coumaric acid (Amalan et al., 2016; Abdel-Moneim et al., 2018), p-hydroxy benzoic acid (Peungvicha et al., 1998) |
| | *Mucuna pruriens* | Seed (Bhaskar et al., 2008; Majekodunmi et al., 2011 ), Leaf (Murugan and Reddy, 2009) | Fagopyritol B1, Fagopyritol B2 (Wu et al., 2018) |
| | *Pongamia pinnata* | Flowers (Punitha and Manoharan, 2006), Leaf (Sikarwar and Patil, 2010), Bark (Badole and Bodhankar, 2009a), Seed (Vadivel and Biesalski, 2011) | Cycloart-23-ene-3β, 25-diol (Badole and Bodhankar, 2009b; 2010), Pongamol (Tamrakar et al., 2008), Karanjin (Tamrakar et al., 2008) |
| | *Psoralea corylifolia* | Seed (Kamboj et al., 2011; Dhar et al., 2013; Seo et al., 2014) | Bavachin (Lee et al., 2016), Corylifol A (Oh et al., 2010), 4′-O-methylbavachalcone (Oh et al., 2010), Psoralidin (Oh et al., 2010), Neobavaisoflavone (Oh et al., 2010) |
| Fabaceae | *Pterocarpus marsupium* | Wood (Mukhtar et al., 2005; Maruthupandian and Mohan, 2011; Pradhan et al., 2019), Bark (Maruthupandian and Mohan, 2011), Leaf (Kalaivani et al., 2011) | Pterostilbene (Pari and Satheesh, 2006; Kosuru and Singh, 2017), (−)-epicatechin (Sheehan et al., 1983) |
| | *Pueraria thunbergiana* | Plant (Park et al., 2015) | Tectorigenin (Lee et al., 2000), Kaikasaponin III (Lee et al., 2000) |
| | *Astragalus membranaceus* | Root (Sang et al., 2010) | Formononetin (Qiu et al., 2017; Oza and Kulkarni, 2018), Astragalin (Riaz et al., 2018), Astragalosides I (Agyemang et al,, 2013 , Astragalosides II (Agyemang et al,, 2013), Astragalosides IV (Agyemang et al,, 2013), Isoastragaloside I (Agyemang et al,, 2013) |
| | *Trigonella foenum-graecum* | Seed (Raju et al., 2001; Xue et al., 2007; Sharma et al., 2020) | Diosgenin (Pari et al., 2012; Naidu et al., 2015), 4-Hydroxyisoleucine (Fuller and Stephens, 2015), Trigonelline (Zhou et al., 2012; 2013), Tannic acid (Babby et al., 2014) |

| Family | Species | Parts used | Compounds with anti-diabetic potentiality |
|---|---|---|---|
| Gentianaceae | *Enicostemma littorale* | Whole plant (Maroo et al., 2002; Vishwakarma et al. 2010; Sonawane et al., 2010;Ahamad et al., 2020), Leaf (Sri, 2020) | Gentianine (Vaidya et al., 2013), Swertiamarin (Vaidya et al., 2009; Dhanavathy, 2015) |
| | *Swertia chirata* | Root (Rajesh et al., 2017), Whole plant (Hossian et al., 2007) | Swerchirin (Bajpai et al., 1991), Swertiamarin (Vaidya et al., 2013) |
| Juglandaceae | *Juglans regia* | Leaf (Asgary et al., 2008; Hosseini et al., 2014; Forino et al., 2016), Fruit peel (Javidanpour et al., 2012) | (3S,5R,6R,7E,9S)-3,5,6,9-Tetrahydroxymegastigman-7-ene (Forino et al., 2016) |
| Lamiaceae | *Callicarpa macrophylla* | Fruit (Jawaid et al., 2016) | β- amyrin (Santos et al., 2012) |
| | *Lavandula stoechas* | Essential oil (Sebai et al., 2013) | α-pinene (Özbek and Yılmaz 2017), Camphene (Mishra et al., 2018), Linalool (More et al., 2014), Limonene (More et al.,2014) |
| | *Meriandra dianthera* | Leaf (Sium et al., 2017) | 1,8-cineole (Kim et al., 2018), Linalool (More et al., 2014) |
| | *Ocimum gratissimum* | Leaf (Egesie et al., 2006; Ayinla et al., 2011; Casanova et al., 2014; Okoduwa et al., 2017) | Chicoric acid (Casanova et al., 2014), Eugenol (Srinivasan et al., 2014) |
| | *Ocimum sanctum* | Leaf (Khan et al., 2010; Lokhande and Yadav, 2018) | Eugenol (Srinivasan et al., 2014) |
| | *Premna corymbosa* | Root (Shilpa et al., 2012; Muhammed Rashid, 2018) | |
| | *Salvia officinalis* | Leaf (Eidi et al., 2005; Eidi and Eidi, 2009; Hasanein et al., 2016) | Thujone (Baddar et al., 2011) |
| | *Teucrium polium* | Aerial part (Esmaeili and Yazdanparast, 2004; Esmaeili et al., 2009) | Rutin (Esmaeili et al., 2009), Apigenin (Esmaeili et al., 2009) |

| Family | Species | Parts used | Compounds with anti-diabetic potentiality |
|---|---|---|---|
| Lauraceae | *Cinnamomum tamala* | Leaf (Chakraborty and Das, 2010; Bisht and Sisodia, 2011) | Myricetin (Li and Ding, 2012), Kaempferol (Zhang et al., 2015), Quercetin (Abdelmoaty et al., 2010), Kaempferol-3-O-Glucoside (Riaz et al., 2018), Quercetin-3-O-Rutinoside or rutin (Esmaeili et al., 2009) |
| | *Cinnamomum* sp. | Bark (Rajadurai et al., 2013; Ranasinghe et al., 2017; Sharma et al., 2020) | Cinnamaldehyde (Zhu et al., 2017; Abdelmageed et al., 2019) |
| Lythraceae | *Lagerstroemia paniculata* | NR | NR |
| | *Lagerstroemia parviflora* | Aerial part (Pullaiah and Naidu, 2003) | NR |
| | *Lagerstroemia speciosa* | Leaf (Miura et al., 2012; Guo et al., 2020) | Corosolic acid (Judy et al., 2003; Miura et al., 2012; Arjunolic acid; Manna et al., 2009) |
| | *Lawsonia inermis* | Whole plant (Choubey et al., 2010), Leaf Chikaraddy et al., 2012) | Betulin (Ko et al., 2016), Betulinic acid (Genet et al., 2010; Ko et al., 2016, Lupeol (Gupta et al., 2012) |
| | *Punica granatum* | Flower (Li et al., 2005; Bagri et al., 2009), Seed (Das et al., 2001), Peel (Middha et al., 2012; Gautam and Sharma, 2012; Salwe et al., 2015), Leaf (Salwe et al., 2015) | Punicalagin (Bellesia et al., 2015), Punicalin (Bellesia et al., 2015), Ellagic acid (Malini et al., 2011), Tricetin (Wu and Tian, 2019) |
| Magnoliaceae | *Schisandra chinensis* | Stem (Fang et al., 2014), Fruit (Zhang et al., 2010) | Gomisin J (Zhang et al., 2010; Gomisin N (Zhang et al., 2010), Schisandrin A (Zhang et al., 2010), Schisandrin C (Zhang et al., 2010), SCP-BII (Gao et al., 2009) |

| Family | Species | Parts used | Compounds with anti-diabetic potentiality |
|---|---|---|---|
| Malvaceae | *Sida cordifolia* | Aerial parts (Kaur et al., 2011; Ahmad et al., 2014), Root (Prabhakar et al., 2009), Whole plant (Narasimha Rao et al., 2020) | Pterostilbene (Kosuru and Singh, 2017), hypaphorine (Luan et al., 2017) |
| Meliaceae | *Azadirachta indica* | Leaf (Khosla et al., 2000; Ezeigwe et al., 2020), Seed oil (Khosla et al., 2000), Root bark (Patil et al., 2013) | Nimbidiol (Mukherjee and Sengupta, 2013), Gedunin (Ponnusamy et al., 2015), Azadiradi-one (Ponnusamy et al., 2015) |
| | *Melia azadirachta* | Leaf (Vijayanand, S., & Wesely, 2011) | NR |
| | *Melia azedarach* | Leaf (Khan et al., 2014; Seifu et al., 2017), Twig (Khan et al., 2018), Fruit (Khan et al., 2014) | Azedarachic acid (Khan et al., 2014), Kaempferol (Zhang et al., 2015), Quercetin (Abdelmoaty et al., 2010), Kaempferol-3-O -Glucoside (Riaz et al., 2018), Quercetin-3-O-Rutinoside or rutin (Esmaeili et al., 2009) |
| Menisperma-ceae | *Tinospora cordifolia* | Root (Sanely et al., 2000), Stem (Rajalakshmi et al., 2009 Puranik et al., 2010), Leaf (Cherku, 2019) | Saponarin (Sengupta et al., 2009), Palmatine (Sangeetha et al., 2013), Magnoflorine (Patel and Mishra, 2012; Cherku, 2019; Xu et al., 2020), Jatror-rhizine (Yan et al., 2005) |
| Moraceae | *Ficus benghalensis* | NR | NR |
| | *Ficus glomerata* | Leaf (Sharma et al., 2010), Stem (Ahmed and Urooj, 2008), Root (Samyal et al., 2014, Bark (Samyal et al., 2014) | Lupeol (Gupta et al., 2012), genistein (Behloul and Wu, 2013) |

| Family | Species | Parts used | Compounds with anti-diabetic potentiality |
|---|---|---|---|
| Musaceae | *Musa sapientum* | Flower (Pari and Umamaheswari, 2000; Dhanabal et al., 2005), Root (Adewoye et al., 2009), Stem (Dikshit et al., 2012), Leaf (Adewoye and Ige, 2013) | Naringenin (Annadurai et al., 2012) |
| Myristicaceae | *Myristica fragrans* | Seed (Somani and Singhai, 2008; Lestari et al., 2012; Pashapoor et al., 2020) | Eugenol (Srinivasan et al., 2014), Pinene (Özbek and Yılmaz 2017) |
| Myrtaceae | *Eugenia jambolana* syn. *Syzygium cumini* or *Syzygium jambolanum* | Seed (Ravi et al., 2005; Sharma et al., 2008, Fruit pulp (Sharma et al., 2006) | Ursolic acid (Jang et al., 2009), Rubuphenol (Sawant et al., 2015), Valoneic acid dilactone (Sawant et al., 2015) |
| | *Psidium guajava* | Leaf (Oh et al., 2005; Manikandan et al., 2013), Fruit (Huang et al., 2011, Fruit peel (Rai et al., 2009) | Strictinin (Alagesan et al., 2012), Isotrictinin (Alagesan et al., 2012), Pedunculagin (Alagesan et al., 2012) |
| | *Syzygium aromaticum* | Flower bud (Kuroda et al., 2012; Chaudhry et al., 2013) | Oleanolic acid (Nguban et al., 2011; Khathi et al., 2013), Maslinic acid (Khathi et al., 2013), Kaempferol (Zhang et al., 2015), Ellagic acid (Malini et al., 2011 |
| Nyctaginaceae | *Bougainvillea spectabilis* | Root bark (Jawla et al., 2011), Stem bark (Jawla et al., 2012), Leaf (Chauhan et al., 2016) | Pinitol (Narayanan et al., 1987) |
| Oleaceae | *Olea europaea* | Leaf (Eidi et al., 2009; Zhang et al., 2014; Al-Attar and Alsalmi, 2019) | Oleuropein (Sato et al., 2007), Ligstroside (Zhang et al., 2014), Tyrosol (Zhang et al., 2014), Hydroxytyrosol (Zhang et al., 2014) |
| Orobanchaceae | *Rehmannia glutinosa* | Root (Zhang et al., 2004; Qin et al., 2018) | Catalpol (Shieh et al., 2011; Zhu et al., 2016) |

| Family | Species | Parts used | Compounds with anti-diabetic potentiality |
|---|---|---|---|
| Phyllanthaceae | *Emblica officinalis* | Bark (Sharan et al., 2013), Leaf (Nain et al., 2012), Fruit (Akhtar et al., 2011) | Gallic acid (Punithavathi et al., 2011), Gallotanin (D'souza et al., 2014), Ellagic acid (Malini et al., 2011), Corilagin (D'souza et al., 2014) |
| | *Phyllanthus amarus* | Leaf (Raphael et al., 2002; Adeneye, 2012), Stem (Raphael et al., 2002), Seed (Adeneye, 2012), Whole plant (Tamil et al., 2010) | Phyllanthin (Jagtap et al., 2016), Gallic acid (Punithavathi et al., 2011, Ellagic acid (Malini et al., 2011) |
| Pinaceae | *Cedrus deodara* | Stem bark (Singh et al. 2013), Heart wood (Jain et al., 2014), Essential oil (Xu et al., 2017) | α-pinene (Özbek and Yılmaz 2017) |
| Piperaceae | *Piper longum* | Root (Nabi et al., 2013), Oil (Kumar et al., 2013) | Piperine (Kumar et al., 2013) |
| | *Piper nigrum* | Seed (Kaleem et al., 2005), Leaf (Onyesife et al., 2014) | Piperine (Kumar et al., 2013) |
| | *Bacopa monnieri* | Aerial part (Ghosh et al., 2008, Whole plant (Taznin et al., 2015) | Bacosine (Ghosh et al., 2011), Stigmasterol (Ghosh et al., 2014) |
| | *Picrorhiza kurroa* | Rhizome (Husain et al., 2014; Kumar et al., 2017) | |
| Plantaginaceae | *Plantago psyllium* | Husk fiber (Amed et al., 2010) | Psyllium (Feinglos et al., 2013; Noureddin et al., 2018) |
| | *Scoparia dulcis* | Whole plant (Latha and Pari, 2004; Zulfiker et al., 2010) | Scoparic acid D (Latha et al., 2009, Coixol (Sharma et al., 2015), Glutinol (Sharma et al., 2015) |

| Family | Species | Parts used | Compounds with anti-diabetic potentiality |
|---|---|---|---|
| Plumbaginaceae | *Plumbago zeylanica* | Root (Kumar et al., 2007) | Plumbagin (Sunil et al., 2012) |
| Poaceae | *Bambusa bambos* syn. *Bambusa arundinacea* | Leaf (Nazreen et al., 2011; Menaria, 2017) | Stigmast-5, 22-dien-3β-ol (Soni et al., 2013), Stigmast-5-en-3β-ol-β-D-glucopyranoside (Soni et al., 2013) |
| | *Coix lacryma-jobi* | Bran oil (Tseng et al., 2019, Seed (Chen et al., 2019) | Oleic acid (Ryan et al., 2000; Palomer et al., 2018) |
| | *Triticum aestivum* (germ oil) | NR | NR |
| Polygonaceae | *Rumex vesicarius* | Whole plant (Reddy et al., 2016) | Naringin (Ahmed et al., 2012) |
| Pteridaceae | *Adiantum capillus* | Whole plant (Ranjan et al., 2014; Kasabri et al., 2017) | Quercetin (Abdelmoaty et al., 2010), Quercetin-3-O-Rutinoside or rutin (Esmaeili et al., 2009), Catechin (Samarghandian et al., 2017), Syringicacid (Muthukumaran et al., 2013) |
| Ranunculaceae | *Coptis chinensis* | Plant (Chen and Xie, 1986), Inflorescence (Yuan et al., 2006; Ma et al., 2016) | Berberine (Chen and Xie, 1986; Cicero and Tartagni, 2012) |
| | *Nigella sativa* | Seed (Kaleem et al., 2006; Bamosa et al., 2010; Heshmati and Namazi, 2015), Oil (Hesmati et al., 2015) | Thymoquinone (Abdelmeguid et al., 2010) |

| Family | Species | Parts used | Compounds with anti-diabetic potentiality |
|---|---|---|---|
| Rutaceae | *Aegle marmelos* | Leaf (Sharma et al., 1996; Narendhirakannan et al., 2010; Mudi et al., 2017), Seed (Kesari et al., 2006), Fruit (Kamalakkannan and Prince, 2003; Mudi et al., 2017), Bark (Gandhi et al., 2012) | Aegeline 2 (Narender et al., 2007) |
| | *Murraya koenigii* | Leaf (Yadav et al., 2002; Arulselvan and Subramanian, 2007), Fruit (Tembhurne and Sakarkar, 2009), Root (Lanjhiyana et al., 2011) | Mahanimbine (Mitra and Mahadevappa, 2010) |
| | *Aurantii fructus* | Park et al., 2007 | Naringin (Ahmed et al., 2012), Hesperidin (Ahmed et al., 2012) Synephrine (Taslimi et al., 2017), Neohesperidin (Sinha et al., 2019) |
| Salicaceae | *Casearia esculenta* | Root (Prakasam et al., 2003) | 3-hydroxymethyl xylitol (Chandramohan et al., 2008) |
| Solanaceae | *Capsicum annuum* | Pepper (Kwon et al., 2007; Tundis et al., 2011) | Capsaicin (Yuan et al., 2016) |
| | *Cortex lycii* | Root (Gao et al., 2007; Wang and Ye, 2016) | Daucosterol (Asghari et al., 2015) |
| | *Solanum nigrum* | Fruit (Sohrabipour et al., 2013; Umamageswari et al., 2017), Leaf (Maharana et al., 2011;Kasali et al., 2016) | Quercetin 3- glucoslde or Isoquercetin (Jayachandran, 2018) |
| | *Withania coagulans* | Fruit (Hemalatha et al., 2004; Jaiswal et al., 2009; Upadhyay and Gupta, 2011; Datta et al., 2013; Meeran et al., 2020), Flower (Bharti et al., 2012) | Coagulanolide (Maurya et al., 2008; Singh et al., 2012) |
| | *Withania somnifera* | Root (Udayakumar et al., 2009), Leaf (Udayakumar et al., 2009) | Withaferin A (Gorelick et al., 2015) |

| Family | Species | Parts used | Compounds with anti-diabetic potentiality |
|---|---|---|---|
| Theaceae | *Camellia sinensis* | Leaf (Al-Attar and 2010; Islam et al., 2011, Yang et al., 2018) | Epigallocatechin gallate (Roghani and Baluchnejadmojarad, 2010), Arabinogalactan (Wang et al., 2015) |
| Urticaceae | *Urtica dioica* | Aerial part (Bnouham et al., 2003), Leaf (Golalipour and Khori, 2007; Kianbakht et al., 2013) | Chlorogenic acid (Ong et al.,2013) |
| Zingiberaceae | *Curcuma caesia* | Rhizome (Majumder et al., 2017) | α-santalol (Misra and Dey, 2013) |
| | *Curcuma longa* | Rhizome (Mohan kumar and Mc Farlane 2011; Ghorbani et al., 2014) | Curcumin (Babu and Srinivasan, 1997; Chuengsamarn et al., 2012), demethoxycurcumin (Kuroda et al., 2005), Bisdemethoxycurcumin (Ponnusamy et al., 2012), arturmerone (Kuroda et al., 2005) |
| | *Elettaria cardamomum* | Seed (Bhat et al., 2015), Fruit (Ahmed et al., 2017) | 1,8-cineole or Eucalyptol (Kim et al., 2018), Limonene (More et al.,2014), α-pinene (Özbek and Yılmaz 2017) |
| | *Zingiber officinale* | Rhizome (Al-Amin et al., 2006; Li et al., 2012; Mahluji et al., 2013; Shidfar et al., 2015; Kazeem et al., 2015; Jafarnejad et al., 2017) | 6-gingerol (Singh et al., 2009; Samad et al., 2017), Zingerone (Ahmad et al., 2018; Anwer et al., 2019) |
| Zygophyllaceae | *Tribulus terrestris* | Aerial part (El-Tantawy and Hassanin, 2007; Samani et al., 2016) | Rutin (Esmaeili et al., 2009) |

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 (Rashid and Sil 2015).

The flower of Butea superba forms an ingredient of PHF standardized by Karigar and Shariff (Karigar and Shariff 2009) 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 (Choi et al., 2008; Cheong et al., 2014; Das et al., 2018), Genistein (Fu et al., 2010; Fu et al., 2012; Behloul and Wu 2013), biochanin A (Harini et al., 2012; Oza and Kulkarni 2018) [have been reported to have anti-diabetic activity, the plant has not been explored for the same till date.

Widyawaruyanti et al. (Widyawaruyanti et al., 2013) 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 (Srivastava and Rai 2018) along with the juice of *Coriander sativum* and *Aloe vera* as a remedy against diabetes, but till 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 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).

## 2.6 Additional ingredients of PHFs other than the plants

### *2.6.1 Shilajit*

Shilajit, a herbo-mineral drug, is emitted from steep mountainous regions of the world (Agarwal et al., 2007; Wilson et al., 2011). Shilajit finds its place in both

Ayurvedic and Siddha systems of Indian medicine (Cagno et al., 2015). Shilajit forms one of the crucial elements in several formulations under study like NIDDWIN (Sruthi et al., 2014), Madhurakshak (Madan et al., 2014), Sugar remedy (Singhal et al., 2014), Diashis (Bera et al., 2010), Diabec (Agrawal et al., 2015), Safuf-i-Dhayabitus (Nasir et al., 2022). Basnet (Basnet 2001) studied the anti-diabetic property of shilajit and inferred that it was effective in treating diabetes in non-obese diabetic rodents.

### *2.6.2 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 (Nadkarni and Nadkarni 1996). Rahman et al. (Rahman et al., 2016) have incorporated calcined *Mytilus margaritiferus* in their herbal formulation for diabetes, Dolabi. However, there is no documentation of Mukta Shukti having hypoglycemic activity.

### *2.6.3 Goat pancreas*

Rahman et al. (Rahman et al., 2016) 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*.

### *2.6.4 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 ingeredients of Safuf-i-Dhayabitus in formulation of diabetes. However, there is no report of having hypoglycaemic activity (Nasir et al., 2022).

## 2.7 Future prospects

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, the developed and developing countries are attracted towards the herbal drug with a trust that they are safe and have lesser side effects than the synthetic drugs. 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 mechanisms of action in the management of diabetes. Basically, the food components, the bioactive

compounds have a positive impact on health (Saravanan and Pari 2003). 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.