HERBAL FORMULATIONS FOR MANAGEMENT OF DIABETES MELLITUS

Abstract

Diabetes mellitus, characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both, presents a significant global health challenge. Despite the availability of conventional medications, many individuals seek alternative therapies due to concerns about side effects and the desire for more natural approaches. Herbal formulations have emerged as promising candidates due to their perceived safety and potential efficacy. Various herbal formulations such as Gymnema sylvestre, bitter melon, fenugreek, cinnamon, and ginseng etc, have shown promising results in improving glycemic control, insulin sensitivity, and reducing complications associated with diabetes. This chapter aims to provide an overview of the current evidence on herbal formulations used for the management of diabetes mellitus, discussing their diverse constituents, pharmacological actions, and therapeutic applications, as well as explores the activities of herbal formulations, exerting their effects, including antioxidant, anti-inflammatory, anti-microbial, and immunomodulatory properties. Herbal formulations show promise as adjunctive therapies for diabetes mellitus. Integrating evidence-based herbal therapies into comprehensive diabetes care may offer personalized and effective approaches to improve glycemic control and reduce the burden of diabetes-related complications. Furthermore, future research efforts should focus on elucidating the underlying mechanisms of action, optimizing formulation strategies, and conducting well-designed clinical trials to establish the efficacy and safety profiles of herbal formulations in different disease settings.

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Overall, herbal formulations represent a rich source of bioactive compounds with potential applications in promoting health and combating various ailments, highlighting their importance in integrative and personalized approaches to healthcare.

Keywords: Hyperglycemia, Diabetes Mellitus, Diabetes Management, Medical Nutrition Therapy, Herbal Formulations, Activities.

I. HERBAL PRODUCTS

Herbal products comprise of herbal formulations made from one or more herbs.

1. **Herbal Medications:** Ayurvedic herbal medications are defined as extracts from combination of herbs, single herbs, ayurvedic proprietary medicines or a compound of herbs in any form (tablets, capsules, powder, crude extract or decoction).[1] The various part of herbs like roots, leaves, stems, barks are utilised for the preparation of the herbal medications.

   Herbal formulations are the basis for finished herbal products and may include milled or pulvarised herbal materials, or extracts, tinctures and fatty oils of herbal materials.[2] Herbal preparations are produced by extraction, fractionation, purification or concentration or by other physical or biological processes.[3]

   Herbal materials include, in addition to herbs, fresh juices, gums, fixed oils, essential oils, resins and dry powders of herbs.[4]

2. **Herbs:** Herbs include crude plant material such as leaves, flowers, fruit, seed, stems, wood, bark, roots, rhizomes or other plant parts, which may be entire, fragmented or powdered.[5]

II. DIABETES MELLITUS

Diabetes is a chronic, metabolic disease indicated by elevated levels of blood glucose (or blood sugar), which leads over time to serious damage to the heart, blood vessels, eyes, kidneys and nerves.

Diabetes is an illness where the insulin processing functions aberrantly due to pancreas not being able to secrete the hormone in adequate amounts. This in turn leads to uncontrollable levels of glucose or sugars in blood circulation and affects energy metabolism and kidney function in the affected individual.[6]

- **Types of diabetes**

  - **Type 1 diabetes mellitus (T1D)** is an autoimmune disease that leads to the destruction of insulin- producing pancreatic beta cells. [7]

  - **Type 2 Diabetes Mellitus (T2DM)** is one of the most common metabolic illness worldwide and its development is primarily caused by a combination of two main factors: faulty insulin release by pancreatic β-cells and the incapability of insulin-sensitive tissues to respond to insulin [8]

III. GESTATIONAL DIABETES

Gestational diabetes (GD) is a type of diabetes that develops in gestation when blood sugar magnitude gets too high. Gestational diabetes usually appears during the middle of pregnancy, between 24 and 28 weeks. Developing Gestational diabetes doesn't mean you

already had diabetes before you got pregnant. This condition in fact appears because of the high blood sugar elevation during pregnancy.

IV. PREDIABETES

A condition in which blood sugar level has spiked, but is not sufficiently high enough to be type 2 diabetes. Without intervention, it's likely to lead to type 2 diabetes.

Diabetes mellitus can be managed by maintaining a healthy diet, avoiding junk food, following good sleep patterns, regular exercises etc.

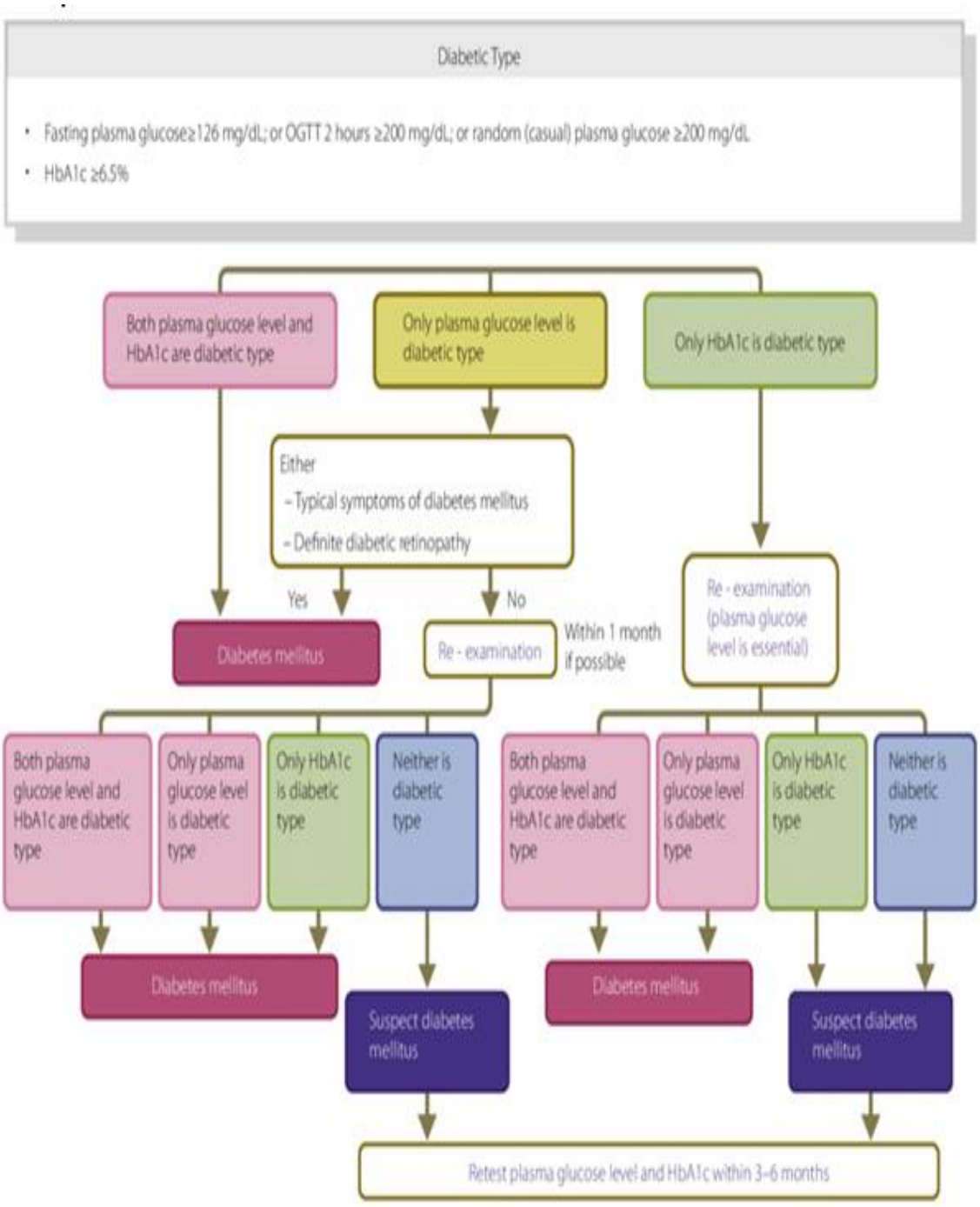
Nowadays, diabetes mellitus can be managed by including nutraceutical substances in the diet.

Some of these nutraceutical substances are sugar apple, curry leaves, amla, banana stem, bitter gourd etc.

How is diabetes diagnosed?[14]

- The detection of diabetes mellitus should be as extensive as possible. It is verified by the presence of chronic hyperactive glycemia, and by the presence of other factors, such as associated symptoms, clinical laboratory findings, a family history of diabetes, and body weight history of the patient. [9-13]
- For the diagnosis of diabetes, either of the following approaches shall be followed:

  - Two assessments of the diabetic type in each patient (one blood glucose test is obligatory).
  - One assessment of the diabetic type (with obligatory blood glucose testing) along with the presence of chronic hyperactive glycemic symptoms*. (*typical symptoms of chronic hyper- glycemia (e.g., dry mouth, polyposis, polyuria, body weight loss, or diabetic retinopathy).
  - Substantiation of a prior diagnosis of ‘diabetes’.



Flow chart outlining the steps in the clinical diagnosis of diabetes mellitus. OGTT, Oral glucose tolerance test.[14]

How is hyper-glycemia assessed?

- The cases are to be classified into the normal type, borderline type, or diabetic type, according to the combination of fasting and 2-h post-75 g oral glucose tolerance test (OGTT) glucose values.
- The cases where fasting glucose values are 100–109 mg/dL (5.6–6.1 mmol/L) are classified into the 'high - normal' category as part of the normal type[15].

- The OGTT is to be proactively considered in high-risk individuals (i.e., those who are suspected to have diabetes or the borderline type, those whose fasting glucose values are indicated to be 'high-normal', those with HbA1c values of ≥5.6%, cases with obesity or dyslipidemia, and those with strong family history of diabetes[13]).
- At present, HbA1c values are calculated by point-of-care testing (POCT) and devices are not to be used for the diagnosis[13].

V. GOALS AND STRATEGIES FOR DIABETES MANAGEMENT

What are the objectives of diabetes management?

- The objectives of diabetes management are to ameliorate metabolic dysfunctions rising from hyper- glycemia, to arrest the evolution or advancement of diabetic problems and conditions associated with diabetes, and to enable affected persons to maintain their quality of life (QOL) and life probability similar to those of healthy individuals.

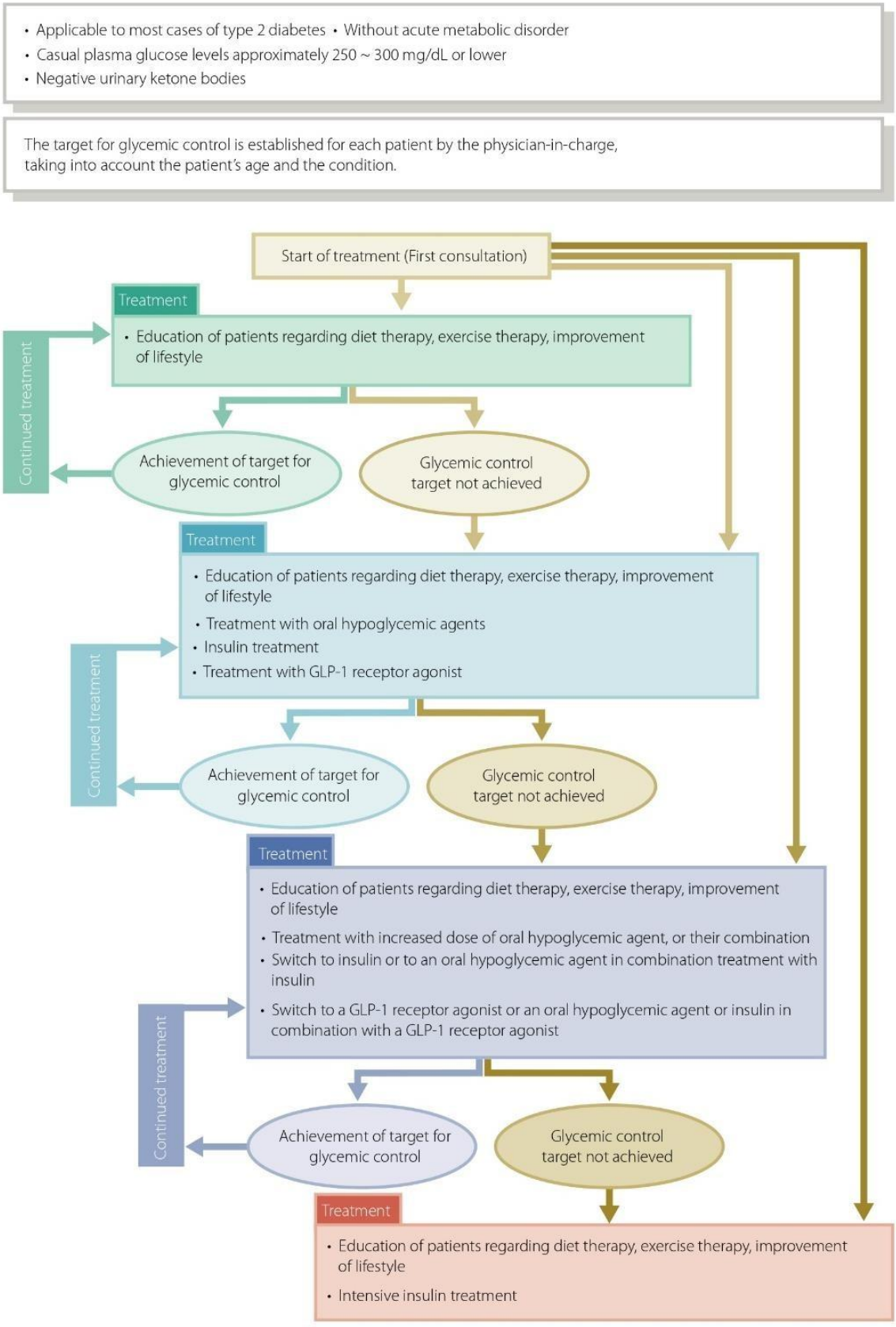
- How is a basic treatment strategy developed for each diabetic patient?

  - The treatment strategy for diabetes may vary depending on the type, complaint condition, age, metabolic abnormality, and status of diabetic complications.
  - Insulin remedy is to be given not only to cases who are insulin-dependent but also to pregnant cases, cases witnessing surgery that involves whole- body operation, and cases with severe infection, indeed if they aren't insulin-dependent. In addition, insulin remedy is to be given to those in whom glycemic pretensions aren't attainable with oral hypo- glycemic agents (OHAs) or glucagon- such as peptide 1 (GLP- 1) receptor agonists.
  - OHA and/ or GLP- 1 agonist remedy is to be given to noninsulin-dependent cases in whom favourable glycemic control isn't attainable with acceptable medical nutrition therapy (MNT) and physical exertion/ exercise continued for 2 – 3 months. OHA and/ or GLP- 1 agonist remedy or insulin remedy may be given to these cases from the onset depending on the inflexibility of the metabolic complaint involved.
  - Continued remedy is essential for cases with diabetes to help the onset or progression of complications. Team care- grounded diabetes education for these cases forms the foundation of their diabetes treatment.

VI. MEDICAL NUTRITION THERAPY (MNT)

What is the part of MNT and the optimal nutritive balance in MNT for patients with diabetes?

- Carbohydrates, proteins and fats should account for 50–60%, ≤20%, and 20–30%, respectively, of the total energy intake in MNT for patients with diabetes.
- The ratios of macronutrients may vary depending on physical activities and the severity of diabetic complications, as well as on the food preferences of each patient with diabetes.[14]



Treatment of patients in a non-insulin-dependent state. This provides a guide to the management of patients without acute metabolic disorder14

Sl no	Scientific name	Common name	Family	Parts utilized	Activity	Ref
1	*Annona squamosa* Linn	Custard apple	Annonaceae	Leaves, fruit	Leaf extracts show antidiabetic, cytotoxic, antimalarial, and immunosuppressive activities.	16
2	*Murraya koenigii* Linn	Curry leaves	Rutaceae	Leaves	Boost insulin activity	17
3	*Momordica charantia* Linn	Bitter gourd	Cucurbitaceae	Fruit, vegetable	Mimics insulin and aids in glucose utilization	19
4	*Phyllanthus emblica* Linn	Amla	Phyllanthaceae	Fruits, leaves	stimulates pancreatic insulin secretion, and restores and regenerates β-cells	20
5	*Musa sapientum* Linn.	Banana	Musaceae	Plant stem, fruit, flower	induced blood sugar reduction may be due to possible inhibition of free radicals and subsequent inhibition of tissue damage induced by alloxan	18
6	*Punica granatum* Linn.	Pomegranate	Lythraceae	Fruit, leaves	action on β-cells of pancreas thatstimulates insulin release and decreases glucose unacceptance.	21
7	*Beta vulgaris* Linn.	Beetroot	Amaranthaceae	Tap root	It is a good source of fibre which helps to increase satiety and slow down the absorption of carbohydrates preventing sudden spikes in blood sugar levels	22
8	*Withania somnifera* Linn.	Ashwagandha	Solanaceae	Root	Reduce blood sugar to normal levels by boostinginsulin Synthesis and sensitivity	23
9	*Acacia Arabica* Linn.	Babul	Fabaceae	Bark, pulp	slow down any glucose absorption and support a keto diet by keeping insulin spikes at bay	24
10	*Alliumcepa* Linn.	Onion	Amaryllidaceae	Bulb	improve insulin sensitivity and regulate blood glucose level	25
11	*Allium sativum* Linn.	Garlic	Amaryllidaceae	Bulb	Lower blood glucose level, stimulate insulin activity	26
12	*Aloe vera* (L.) Burm.f.	Aloe vera	Asphodelaceae	leaves	lowers blood glucose levels in diabetic patients. improves the responsiveness of the body tissues towards insulin	27

13	*Syzygium cumini* Linn	Jamun	Myrtaceae	Leaves, fruits, seeds	slow down the rate of sugar released into the blood and increase the insulin levels in the body	28
14	*Butea monosperma* (Lam.) Taub.	Palasa	Fabaceae	Flowers, leaves	It might reduce blood sugar levels by improving glucose Tolerance and regulation of excessive blood sugar levels	29
15	*Bombax diffusa*	semul	Malvaceae	Flowers	Lower the hyperlipidemic problems associated with diabetes mellitus., enhance the insulin release	30
16	*Areca catechu* Linn	supari	Arecaceae	Nut	Reduce the blood sugar level	26
17	*Artemisia pallens* Wall. ex DC.	Davana	Asteraceae	Leaves and flowers	significant blood glucose lowering effect	26
18	*Trigonella foenum graceum* Linn	Fenugreek	Fabaceae	Seeds and leaves	activating of insulin synthesis and promote its release from the pancreatic β-cells	31
19	*Gymnema sylvestre* R. Br.	Gurmar	Apocynaceae	Leaves	delaying the glucose absorption in the blood.	32
20	*Chamaecostus cuspidatus* (Nees & Mart.) C.Specht & D.W.Stev.	Insulin plant	Costaceae	Whole plant	Reduce the blood sugar level	33
21	*Abroma agustum* Linn	Abroma agusta	Steruliaceae	Root	Hypoglycemic and antilipidemic effect	34
22	*Acer saccharum* Marshall	Sugar Maple	Sapindaceae	Juice	Hhypoglycemic and antioxidant effect	35
23	*Coccinia Indica* (L.) Voigt	Ivy gourd	Cucurbitaceae	Leaves	Antioxidant, antihyperglycemic and antilipidemic	36
24	*Acalypha wilkesiana* Müll.Arg.	Copperleaf	Euphorpiaceae	Leaves	Hypoglycemic and antioxidant	37
25	*Acorus calamus* Linn.	Sweet flag	Acoraceae	Leaves/bark	α-Glucosidase inhibition and hypolipidemic	
26	*Aegle marmelos* (L.) Corrêa	Bael	Rutaceae	Leaves/bark/root	Antidiabetic, Antioxidant and anti cataract activity	39
27	*Afzelia Africana* Sm.	African mahogany	Fabaceae	Stem bark	Antidiabetic and hematological effect	40

28	*Eriobotrya japonica* (Thunb.) Lindl.	Japanese Loquat	Rosaceae	Leaves	Antihyperglycemic	41
29	*Prosopis glandulosa* Torr.	Honey mesquite	Fabaceae	Leaves	Increase insulin secretion	42
30	*Amaranthus spinosus Linn.*	Spine amaranth	Amaranthaceae	Leaves	*α*-Amylase inhibition, antioxidant and anticholesrolemic	43
31	*Anogeissus acuminate* (Van Heurck & Müll.Arg.) Gere & Boatwr *(terminalia phillyreifolia)*	Button tree	Combretaceae	Whole plant	Antioxidant	44
32	*Artemisia Linn.*	Artemisia sphaerocephala krasch	Compositae	Gum/seed powder	Antidiabetic	45
33	*Artemisia dracunculus* Linn.	Tarragon	Asteraceae	Aerial part	Antidiabetic	46
34	*Artemisia herba-alba* Asso.	White wormwood	Asteraceae	Whole plant	Antihyperglycemic and antihyperlipidemic	47
35	*Lonicera japonica* Thunb.	Japanese honeysuckle	Caprifoliaceae	Whole plant	*α*-Glucosidase inhibition	48
36	*Ascophyllum nodosum* Linn.	Rockweed	Algae	Young tips	*α*-Glucosidase inhibition and *α*-amylase	49
37	*Aspidosperma macrocarpon* Mart.	Guatambu	Apocynaceae	Steam/Bark Root wood	*α*-Amylase inhibition	50
38	*Atractylodes macrocephala* Koidz.	Bai Zhu	Asteraceae	Whole plant	*α*-Glucosidase inhibition	48
39	*Azadirachta indica* A.Juss.	Neem	Meliaceae	Leaves, flower and seed	Antidiabetic and antihypertension	51, 52
40	*Barringtonia racemose Linn.*	Common Putat	Lecythidaceae	Seed	*α*-Glucosidase and *α*-amylase inhibition	53
41	*Bauhinia forficate*	Brazilian orchid tree	Leguminosae	Leaves	Antidiabetic	26
42	*Belamcanda chinensis* Linn.	Blackberry lily	Irdaceae	Leaves	Hypoglycemic	54
43	*Benincasa hispida* (Thunb.)	Wax gourd	Cucurbitaceae	Fruit	Antidiabetic, ameliorate the derangement in lipid metabolism in diabetics.	55

44	*Nervilia plicata*	Pleated	Orchiaceae	Stem	Antidiabetic	56
45	*Berberis vulgaris* Linn.	Barberry	Berberidaceae	Leaves	Hypoglycemic	57
46	*Psoralea corlifolia* Linn.	Purple Fleabane	Fabaceae	Leaves	Antioxidant	39
47	*Rauwolfia serpentinum* Linn.	Indian snakeroot	Apocyanaceae	Leaves	Hypoglycemic	58
48	*Silybum marianum* Linn.	milk thistle	Asteraceae	Whole plant	Antihyperglycemic	59
49	*Argyreia cuneate* Ker Gawl.	purple morning glory	Convolvulaceae	Whole plant	Antihyperglycemic	60
50	*Desmodium gangeticum* Linn.	salparni	Fabaceae	Whole plant	Antidiabetic	61

These are commonly available from the plants, in the market etc which can be used directly, or can be processed at home, and can be used in form of decoction, powder, etc

1. *Annona squamosa* Linn.[16] :

- **Synonym:** Sweetsop, Custard Apple
- **Biological source:** It comprises of dried leaves of *Annona squamosa* Linn. belonging to family Annonaceae
- **Phytochemical constituents:** anonaine, annonacin, squamocin, asimicin, phytochemical assessments have emphasised that numerous active compounds, such as acetogenins and flavonoids.
- **Description:** *Annona squamosa* Linn. is a small tree, which is well branched belonging to the family Annonaceae that bears edible fruits called sugar-apples or *sweetsops*. It tolerates a tropical flat climate and it is the most widely cultivated of its species. *Annona squamosa* Linn. is a small, semi- deciduous, branched shrub or small tree 3 to 8 metres (10 to 26 feet) tall.
- **Formulation:** decoction

  - Decoction preparation

- Chop the leaves into small pieces
- boil the leaves in water for about 5-10 min
- consume the freshly prepared decoction

2. *Murraya koenigii* Linn.[17]:

- **Synonym:** karivepaaku, karibevu kadi patta
- **Biological source:** It comprises of dried leaves of *Murraya koenigii* Linn belonging to family Rutaceae
- **Phytochemical constituents:** alkaloids, glycosides, steroids, tannins and terpenoids monoterpenes. linalool, elemol, geranyl acetate, myrcene, α-terpinene (E)-β-ocimene.
- **Description:** It's a small tree, growing 4–6 metres (13–20 ft) in height, with the trunk up to 40 cm (16 in) in width. The leaves are pinnate, aromatic, with 11–21 leaflets, each leaflet 2–4 cm ($^{3}\!/_{4}$–$1+^{1}\!/_{2}$ in) long and 1–2 cm ($^{1}\!/_{2}$–$^{3}\!/_{4}$ in) broad

- **Consumption**

  - The leaves can be directly be consumed orally
  - The leaves can be included in diet in the dishes
  - The leaves can be dried, crushed into powder and can be consumed with water.

3. *Momordica charantia* Linn.[19]:

- **Synonym:** bitter apple, bitter gourd, karela,
- **Biological source:** It comprises of the fruits and leaves of *Momordica charantia* Linn. belonging to family Cucurbitaceae
- **Phytochemical constituents:** polysaccharides, saponins, and phenolics cucurbitane-type triterpenoids, cucurbitane-type triterpene glycosides, phenolic acids, flavonoids, essential oils, fatty acids, amino acids, sterols, saponins and protein
- **Description:** The tree is medium in size, reaching 1–8 m (3 ft 3 in – 26 ft 3 in) in height. The branches are finely pubescent (not glabrous), 10–20 cm (3.9–7.9 in) long, usually deciduous. The leaves are simple, subsessile and are present close along branchlets, light green in colour, exhibit pinnate leaves. The flowers are greenish-yellow. The fruit is nearly spherical, light greenish-yellow, fairly smooth and hard on appearance.
- **Juice preparation**

  - Take a fresh bitter gourd, chop into pieces
  - Combine the bitter gourd and half cup of water in a mixer
  - Prepare a blend
  - Strain by adding little water
  - And consume immediately

4. *Phyllanthus emblica* Linn.[20]:

- **Synonym:** Indian gooseberry, āmalakī, emblic myrobalan
- **Biological source:** It comprises of the fruits and leaves of *Phyllanthus emblica* Linn. belonging to the family phyllanthaceae.
- **Phytochemical constituents:** ellagic acid, emblicanine A, emblacani B, Gallic acid, phyllantine, quercetin and phyllantidine
- **Description:** the tree is medium in size, reaching 1–8 m (3 ft 3 in – 26 ft 3 in) in height. The branches are finely pubescent (not glabrous), 10–20 cm (3.9–7.9 in) long, usually deciduous. The leaves are simple, subsessile and set nearly along the branches, resembling pinnate leaves, and are light green in appearance. The flowers are greenish-yellow. The fruit is nearly globular, light greenish-yellow, quite smooth and hard on appearance, with six vertical stripes or furrows
- **Consumption**

  - Eat the fruit fresh:
  - This is the greatest and the efficient method for the **Consumption of amla Amla juice:**
  - first remove the seed
  - crush the pulp
  - extract the juice by blending and straining with water Amla **Powder:**
  - Take fresh amla fruits
  - Cut into pieces
  - Sun-dry the amla pulp
  - grind it into a fine powder.

5. *Musa sapientum* Linn.[18]:

- **Synonym:** Common banana
- **Biological source:** It comprises of the fruit, stem of *Musa sapientum* Linn. belonging to family Musaceae
- **Phytochemical constituents:** phenolics, carotenoids, biogenic amines and phytosterols
- **Description:** The banana plant is among the largest blossomy flowering plant. All aerial parts of the plant grow from a structure usually called a "corm". Plants normally have a good height and are fairly sturdy with a treelike appearance, but what appears to be the trunk is actually a "false stem" or pseudo-stem. Bananas grow in a wide variety of soils, as long as the soil is at least 60 centimetres (2.0 ft) deep, has good water supply and isn't compacted. Banana plants are one of the rapidly growing of all plants, with diurnal surface growth rates recorded of 1.4 square metres (15 sq ft) to 1.6 square metres (17 sq ft).
- **Consumption**

  - Blend chopped banana stem with water
  - Untill it becomes a smooth paste.
  - Add some plant-based buttermilk and salt.
  - Mix well and drink it immediately.

6. *Punica granatum* Linn.[21]:

- **Synonym:** Malum granatum, Punica granatum, anar
- **Biological source:** It comprises of fruits and leaves of *Punica granatum* Linn belonging to family Lythraceae
- **Phytochemical constituents:** Punicalagin, Ellagic acid, Cyanidin. Liteolin, organic acids, phenolic acids, sterols, terpenoids, fatty acids, triglycerides, alkaloids and some other compounds.
- **Description:** *Punica granatum* Linn. is a shrub growing 5 to 10 m (16 to 33 ft) in height, and has multiple spiny branches and is long-lived, with some species in France have survived for 200 years. *Punica granatum* Linn. leaves are opposite or subopposite, glossy, narrow oblong, entire, 3–7 cm (1+¼–2+¾ in) long and 2 cm (¾ in) broad. The flowers are bright red and 3 cm (1+¼ in) in diameter, with three to seven petals. Some fruitless species of *Punica granatum* Linn. are grown only for obtaining the flowers.
- **Consumption**
- **Pomegranate tea**

  - Add 3 mugs of pomegranate seeds to a blender.
  - Store the juice in a vessel after straining.
  - Combine three-fourth mug of piping hot water with one-quarter mug of pomegranate juice.

7. *Beta vulgaris* Linn.[22]:

- **Synonym:** Beetroot, common beet, or garden beet
- **Biological source:** It comprises of taproot portion of a *Beta vulgaris* Linn. belonging to family Amaranthaceae
- **Phytochemical constituents:** betalains (e.g., betacyanins and betaxanthins), flavonoids, polyphenols, Saponins and inorganic Nitrate (NO_3)
- **Description:** Beets, *Beta vulgaris* Linn. are blossoming root vegetables in the family Chenopodiaceae grown for their consumable root. The plant leaves are seen growing on stems and is usually upright with a long main root. The leaves are arranged alternately on the stem, ovoid shaped and grow 20–40 cm (7.9– 15.7 in) in length. The roots are usually red in colour. The plant produces stalkless green flowers that can grow 1–2 m (3.3–6.6 ft) in height. Beets are usually grown as yearly plants, harvested after one growing season. Beets may also be referred to as

beetroot, garden beet or spinach beet and originated from the Mediterranean.

- **Juice preparation**

  - Take a fresh beetroot, chop into pieces
  - Combine the beetroot and half cup of water in a mixer
  - Prepare a blend
  - Strain by adding little water
  - And consume immediately

8. *Withania somnifera* Linn[23]:

- **Synonym:** Ashwagandha or winter cherry,
- **Biological source:** Ashwagandha is derived from the root of the *Withania somnifera* Linn plants belonging to family Solanaceae
- **Phytochemical constituents:** steroidal lactones, alkaloids, saponin, flavonoids, tannin, starch, phenolic content, carbohydrate, withanolides, sitoindosides, anaferine, anahygrine, β-sitosterol, chlorogenic acid, cysteine, cuscohygrine, pseudotropine, withanine, scopoletin
- **Description:** This species is a 35–75 cm (14–30 in) tall growing shrub. The branches expand spirally from the central stem. Leaves appear to be dull green, elliptic, usually up to 10–12 cm (3.9–4.7 in) long. The flowers are small in size, green coloured and bell-shaped. The fruit becomes orange-red on ripening.
- **Usage**

  - Take one glass of milk and upto its half volume water in a pan and bring it to boil.
  - Introduce Ashwagandha root powder, upto 1/2 teaspoon and boil for additional 5 minutes.
  - To the admixture add around (2 teaspoons) crushed walnut and almonds
  - Drink this admixture to maintain blood sugar level.

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