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A Retrospective Review on Indian Traditional Herbs and its Biocompounds in Diabetes

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Abstract : In the last few years there has been an exponential growth in the field of herbal medicine and its products are gaining popularity both in developing and developed countries because of their natural origin and less side effects. The World Health Organization (WHO) has listed 21,000 plants, which are used for medicinal purposes around the world. Among these 2500 species are in India, out of which 150 species are used commercially on a fairly large scale. India is the largest producer of medicinal herbs and is called as botanical garden of the world.

Diabetes is a chronic metabolic disorder including causative factors like obesity, life style, environment and genetics. Diabetes mellitus is estimated to increase from 4.0 percent in the year 1995 to 5.4 percent by the year 2025. By 2030, India's diabetes numbers are expected to cross the 100 million mark. This led to sudden increase in the number of herbal drug industries utilising traditional herbs for the preparation of herbal formulations in the treatment of Diabetes mellitus. Presently about 25% of pharmaceutical prescriptions in the United States contain atleast one plant-derived ingredient. In the 20th century, roughly 121 pharmaceutical products were formulated based on the traditional knowledge obtained from various pharmacopeias. Based on the above facts in our mind, we focussed our aim on the scientific approach of the Indian traditional plants and bioactive compounds in the treatment of Diabetes mellitus. From the presented scientific data of the Indian indigenous drugs for Diabetes mellitus, the leaves have been used predominantly in the treatment of diabetes. The families of plants with the most potent hypoglycemic effects include Liliaceae, Leguminosae, Lamiaceae etc. The most commonly used species are Momordica charantia, Trigonella foenum graecum, Ficus benghalensis and Gymnema sylvestre. The present review also revealed the antidiabetic potential of terpenoids, alkaloids and flavonoids through the insulinomimetic activity. The flavonoids majorly exhibit the antidiabetic activity by preventing beta cell apoptosis and promotes beta cell proliferation and insulin secretion. The herbal drugs Gymnema slyvestre, Syzgium cumini, Phyllanthus amarus, Aloe vera, Momordica charantia, Trigonella foenum graecum, Emblica officinalis, Azadirachta indica are more frequently found in herbal formulations for Diabetes. The present review work concluded that about forty traditional herbs and twenty phytocompounds are still used either alone or in combination for the silent killing disease – Diabetes.

Key Words : Herbal medicine, Diabetes, Hypoglycemic, Antidiabetic activity, Traditional herbs, Phytoconstituents

Introduction

In the last few years there has been an exponential growth in the field of herbal medicine and these drugs are gaining popularity both in developing and developed countries because of their natural origin and less side effects[1]. Many traditional medicines in use are derived from medicinal plants, minerals and organic matter[2].

The World Health Organization (WHO) has listed 21,000 plants which are used for medicinal purposes around the world. Among these 2500 species are in India, out of which 150 species are used commercially on a fairly large scale. India is the largest producer of medicinal herbs and is called as the botanical garden of the world[3].

Diabetes is a chronic metabolic disorder including causative factors like obesity, life style, environment and genetics.

Diabetes Mellitus Occurance in the World

Diabetes mellitus is estimated to increase from 4.0 percent in the year 1995 to 5.4 percent by the year 2025. The number of people with diabetes mellitus in the world will increase from 135 million in 1995 to 300 million in the year 2025. According to statistics, there will be a 42 percent increase, from 51 million to 72 million, in the developed countries and 70% increase, from 84 to 228 million, in the developing countries[4,5].

Statistics of Diabetes Mellitus in India

India is presently a home to 62 million diabetics. By 2030, India's diabetes numbers are expected to cross the 100 million mark.

The national urban survey conducted across the metropolitan cities of India reported similar trend : 11.7 percent in Kolkata (Eastern India), 6.1 percent in Kashmir valley (Northern India) , 11.6 percent in New delhi (Northern India) & 9.3 percent in West India (Mumbai) when compared with 13.5 percent in Chennai (South India), 16.6 percent in Hyderabad (South India) and 12.4 percent in Bangalore (South India).

Importance of Herbal Plants in the Treatment Of Diseases

The various indigenous systems of medicine such as Siddha, Ayurveda, Unani and Allopathy use several plant species to treat different diseases. This led to sudden increase in the number of herbal drug industries utilising traditional herbs for the preparation of herbal formulations in the treatment of Diabetes mellitus.

Presently about 25% of pharmaceutical prescriptions in the United States contain atleast one plant-derived ingredient. In the 20th century, roughly 121 pharmaceutical products were formulated based on the traditional knowledge obtained from various pharmacopoeias[6].

Many clinical studies have confirmed the therapeutic importance of medicinal plants in the treatment of diabetes mellitus. The effect of the medicinal plants may delay the diabetic complications and rectify the metabolic abnormalities. However during the past few decades new bioactive compounds are being isolated from the hypoglycemic plants. They showed hypoglycemic activity with more efficacy and are used in effective treatment of diabetes mellitus[7].

Based on the above facts in our mind, we focussed our aim on the scientific approach of the Indian traditional plants and bioactive compounds in the treatment of Diabetes mellitus.

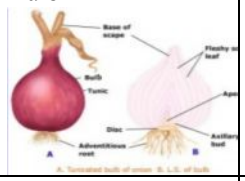
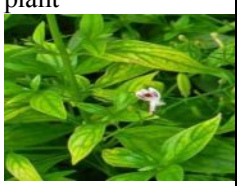
Aim and Objective

- To collect the review data of Indian indigenous plants included in official monograph used for treating Diabetes mellitus.
- To make a detailed survey on phytoconstituents of herbs of traditional system of medicine.
- To present the collected scientific data of the Indian indigenous drugs for Diabetes mellitus.

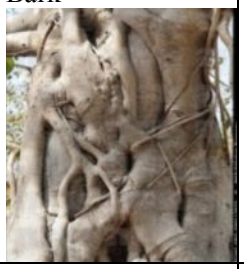
Literature Review

A number of scientific proof are available for the Indian indigenous medicinal plants used for the management of diabetes. A few are listed here

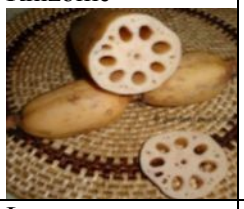
Table: 1. List of Scientifically Evaluted Indian Traditional Herbs in Diabetes

S.No	Botanical Name & Family	Common Name	Organ Used	Extract	Animal Used
1.	***Achyranthus aspera.,*** Amaranthaceae[8]	Chirchiri	Entire Plant 	Aqueous extract	Alloxan induced diabetic rabbits - 7 days[9]
2.	**Allium cepa.,** Liliaceae[8]	Common onion, Bulb Onion, Onion, Pyrax	Bulb 	Aqueous extract	Alloxan induced diabetic rats -7 days[10]
3.	***Allium sativum***., Liliaceae[1]	Garlic, Lashuna, Vellaipundu	Dried & Ground bulb 	Ethanolic extract	Normal & Sreptozotocin (STZ) induced diabetic rats - 60days[11]
4.	***Aloe vera, Aloe barbadensis.,*** Liliaceae[8]	Barbados aloe	Entire plant, Leaves  	Juice extract, Dried pulp extract/exudates	Alloxan induced diabetic rabbits - 6 weeks[10]
5.	***Andrographis paniculata.,*** Acanthaceae[8]	Kalmegh	Entire plant 	Ethanolic extract of the aerial parts	STZ induced diabetic rats - 14days[12]
6.	***Azadirachta indica.,*** Meliaceae[8]	Neem, Neem tree, Indian Lilac	Leaves, Seed, Bark, Root, Fruit, Gum	Ethanolic leaf extract	STZ & Alloxan induced diabetic rats - 21days[13]

					
7.	***Bixa orellana.,*** Bixaceae[8]	Annotta	Entire plant 	Ethyl acetate & n-butanol extracts	Alloxan induced diabetic Wistar rats - 7days[14]
8.	***Boerhaavia diffusa.,*** Nyctaginaceae[8]	Punarnava	Leaves & Entire plant 	Aqueous solution of the leaf extract	Alloxan induced diabetic rats - 28days[15]
9.	**Caesalpinia bonducella.,** Leguminose[8]	Gray Nicker, Karanju	Seed Kernels 	Aqueous & Ethanolic seed extract	Alloxan induced diabetic rats - 7days[16]
10.	***Capparis deciduas.,*** Capparidaceae[8]	Karer	Powder  	Alcoholic extract of the bark, flower & fruit	STZ induced diabetic rats - 30days[17]
11.	***Carum carvi.,*** Umbelliferae[8]	Shia jira	Fruits 	Oil extract of the seeds	Alloxan induced male albino rats of the winster strain - 70days[18]
12.	***Catharanthus roseus.,*** Apocynaceae[8]	Sadabahar	Leaves, twigs & flower 	Aqueous extract of flowers, leaves, roots & stems	Alloxan induced diabetic mice -15days[19]
13.	***Cinnamomum zeylanicum.,*** Lauraceae[8]	Dalchini	Bark & Leaves	Ethanolic extract of the leaves	Alloxan induced male albino wistar rats - 7days

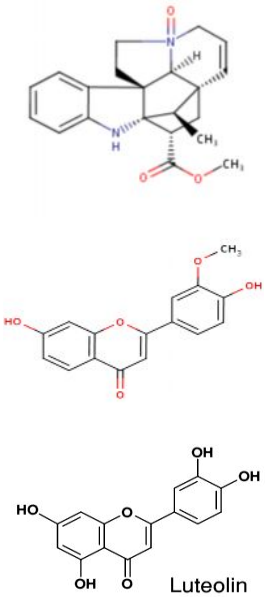
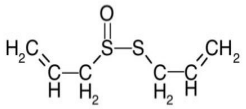
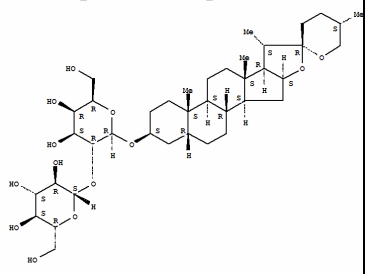
					
14.	***Cinnamomum tamala.,*** Lauraceae[20]	Indian Bay Leaf, Malabar Leaf, Indian Bark, Indian Cassia, Malabathrum	Leaves & Dried Leaves 	Ethanolic extract of the leaves	STZ induced diabetic male Wistar rats - 40days
15.	***Coriandrum sativum.,*** Umbelliferae[8]	Dhania	Seeds 	Alcoholic extract of the seeds	STZ induced diabetic rats[21]
16.	***Coscinium fenestratum.,*** Menispermaceae[8]	Jharhaldi	Stem 	Aqueous & alcoholic stem extract	STZ - nicotinamide induced diabetic rats - 12days[22]
17.	***Eclipta alba.,*** Compositae[8]	Bhringraj	Leaves 	Leaf suspension	Alloxan induced diabetic rats - 60days[23]
18.	***Embellica officinalis.,*** Euphorbiaceae[8]	Amla	Fruits 	Methanolic seed extract	STZ induced male albino Wistar rats - 45days[24]
19.	***Ficus benghalensis.,*** Moraceae[8]	Indian Banyan Bengal tree, Bargad	Bark 	Aqueous leaf extract & Ethanolic extract of different aerial parts & fruits	STZ induced diabetic rats - 30days[25]
20.	***Ficus religiosa.,*** Moraceae[8]	Peepal	Entire plant 	Ethanolic extract of the fruits	Alloxan induced albino Wistar rats - 30days[26]

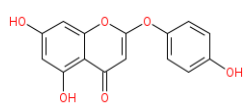
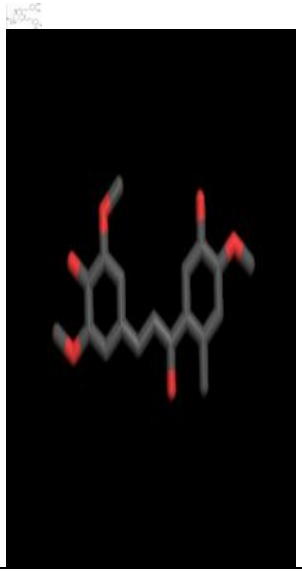
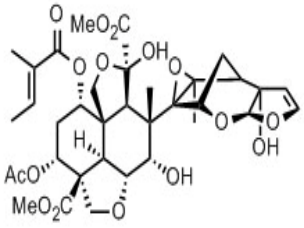
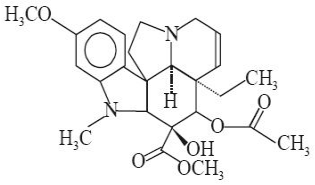
21.	***Gymnema sylvestre.,*** Asclepiadaceae[8]	Gymnema, Cow plant, Australian Cow plant, Gurmari, Gurmarbooti, Periploca of the woods, Meshasvinga, Bedki cha pala	Leaves, Roots 	Aqueous extract of the leaves	STZ induced diabetic rats - 30days[27]
22.	***Hibiscus rosasinensis.,*** Malvaceace[8]	Gudhal, China rose, Hawaiian hibiscus, Shoeblack plant	Entire plant 	Hydroalcoholic extract	Wistar rats of either sex - 4 weeks[28]
23.	***Hordeum vulgare.,*** Graminaceace[8]	Barely, Jow, Yava, Sithashuka	Seeds 	Hydroalcoholic extract	Normal & STZ induced diabetic male Wistar rats - 11 days[29]
24.	***Juniperus communis.,*** pinaceace[8]	Hauber, Horse savin,Gorst, Dwarf juniper	Fruits 	Methanolic extract	Streptozotocin nicotinamide induced diabetic rats - 20 days[30]
25.	***Mangifera indica.,*** Anacardiaceace[8]	Mango, Manaka, Aam, Ambiram	Leaves 	Aqueous extract[23]	Normal & Alloxan induced diabetic rats - 21 days[31]
26.	***Momordica charantica.,*** Cucurbitaceace[1]	Bitter melon, Karela, Goya, Bitter squash	Fruits 	Ethanolic extract	Normal & STZ induced diabetic rats
27.	***Mucuna pruriens.,*** Leguminosae[8]	Kiwach,Pillia dugu, Velvet bean, punaippidukkan	Seeds 	Ethanolic and Methanolic extract	Alloxan monohydrate induced wistar rats[32]
28.	***Murraya koenigii.,*** Rutaceace[8]	Curry leaf, karipata, Sweet nim, South india soapnut	Leaves	Diet containing curry leaves	Normal rats -7 days. Mild diabetic (alloxan induced) & Moderate diabetic (STZ induced) - 5 weeks[33]

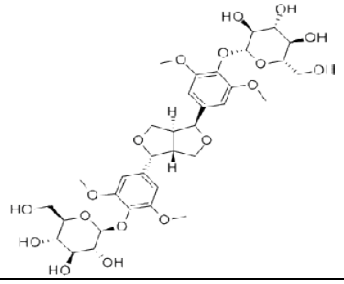
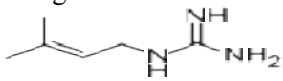
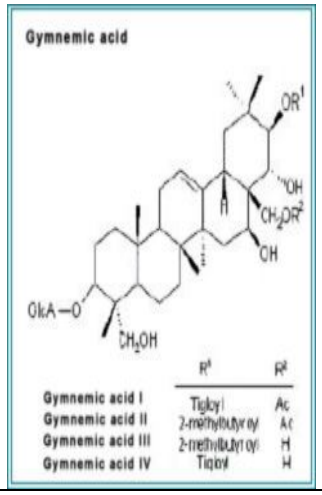
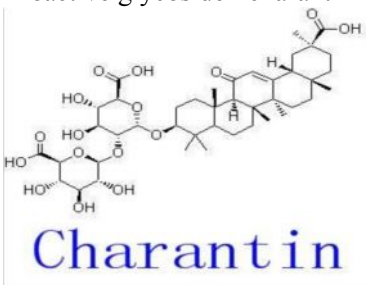
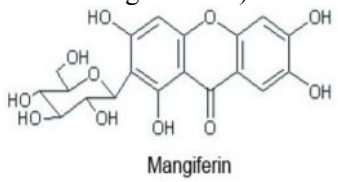
					
29.	***Nelumbo nucifera.,*** Nymphaeaceae[8]	Lotus, Kamal, Tamarai, Padam	Rhizome 	Methanol extract[24]	Streptozotocin induced diabetic rats - 12 hrs[34]
30.	***Ocimum sanctum.,*** Labiatae[1]	Tulsi, Holy basil, Trittavu	Leaves 	Aqueous extract	Normal & Alloxan induced diabetic rats - 30 days
31.	***Phyllanthus amarus.,*** Euphorbiaceae[1]	Bhuiawala, Bahupatra	Whole plant 	Methanolic extract	Alloxanized diabetic rats
32.	***Picrorhiza kurroa.,*** Scrophulariaceae[8]	Katuka, kutki, Kadugurohini ,Hellebore	Entire plant 	Alcoholic extract[27]	Alloxan induced diabetic rats - 10 days[35]
33.	***Pterocarpus marsupium.,*** Fabaceae[1]	Vijayasar kino, Malabar kino tree, Indian kino tree	Wood 	Aqueous extract	Dog
34.	***Tamarindus indica.,*** Caesalpimiaceae[8]	Imli, Indian date, Puli, Huli	Seeds 	Aqueous extract	STZ induced diabetic male rats -14 days[36]
35.	***Teramnus labialis.,*** Fabaceae[8]	Mashoni, Rabbit vine, Horse vine	Aerial parts 	Aqueous alcoholic extract	C57BL/Ks-db/db mice[37]
36.	***Tinospora cordifolia.,*** Menispermaceae[1]	Guduchi, Giloe	Roots	Aqueous extract	Alloxan induced diabetic rats

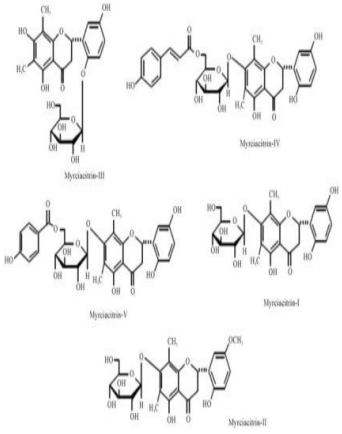
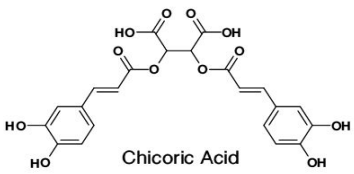
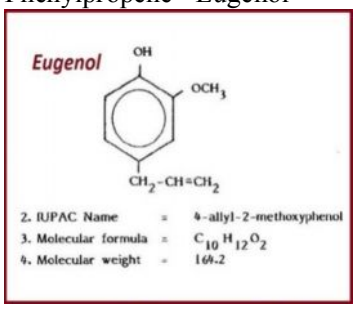
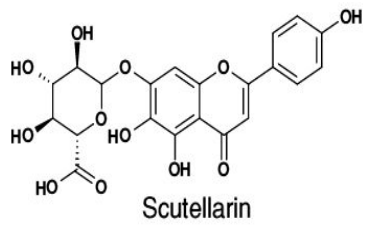
					
37.	***Tribulus terrestris.,*** Zygophyllaceae[8]	Gokhru,Burra gokhru, puncture vein	Saponin 	Alcoholic extract	STZ induced diabetic rats[38]
38.	***Trigonella foenum graceum.,*** Leguminosae[1]	Fenugreek,Methi, menthulu	Seeds 	Alcoholic extract	Normal & diabetic rats
39.	***Withania somnifera.,*** Solanaceae[1]	Indian ginseng, Poison gooseberry, Winter cherry	Roots 	Aqueous extract	Streptozotocin induced diabetic rats - 75 days[39]
40.	***Zingiber officinalae.,*** Zingiberaceae[8]	Adark, Ginger,Canton ginger	Rhizome 	Fresh &dried rhizome	STZ induced diabetic rats - 6 weeks[40]

Table: 2. List of Biocompounds of Indian Traditional Herbs in Diabetes

S.No	Source of phytoconstituents	Extract	Phytoconstituents & Structure	Method of screening
1.	***Albizzia Lebbeck.,*** Fabaceae[41]	Methanolic extract of stem bark	3 Flavonoids 5-deoxyflavone(geraldone), Luteolin, Isookanin (Inhibitior of α-glucosidase, α-amylase & DPPH 	In vitro study
2.	***Allium sativum.,*** Alliaceae[42]	Ethanolic extract, juice & oil.	Sulfur compound- Allicin. 	In vitro study (Beta cells isolated from normal rats).
3.	***Aloe vera.,*** Liliaceae[42]	Ethanolic extract.	Bitter principle - Pseudoprototinosaponin AII. 	In vitro study (gel application on STZ induced diabetic rats - 9 days , No change). In vivo study (STZ induced diabetic rats - 9 days)[34]
4.	***Artemissia dracunculus.,*** Asteraceae[44,45,46,47]	Ethanolic extract of the whole plant	4,5-di-o-Caffeoyl quinic acid, 6- demethoxy Capillarisin, & 2'4'-dihydroxy-4-methoxy dihydrochalcone	In vivo study (Diabetic mice)

			 	
5.	***Azadirachta indica*** **.,** Meliaceae[48]	Chloroform leaf extract	Tetranotriterpenoid-Azadirachtin  Azadirachtin	In vivo study (Murine diabetic model, mouse - 21 days)
6.	***Catharanthus roseus.,*** Apocynaceae[49]	Leaf extract	Alkaloids - Vindoline I, Vindolidine II, Vindolicine  III Vindoline	In vitro study

7.	***Eleutherine Americana.,*** Iridaceae[51]	Methanolic extract of the bulb	Eleutherinoside A 	In vitro study (α-glucosidase inhibitory activity)
8.	***Gallega officinalis.,*** Fabaceae[52,63,64]	Aqueous Extract of leaves & seeds	Guanide Compound - Galegine 	In vivo study (Diabetic rats)
9.	***Gymnema sylvestre.,*** Asclepiadaceae[42]	Aqueous leaf extract	Gymnemic acid molecule- Dihydroxy gymnemic triacetate 	In vitro study (mouse cells & isolated human islets). In vivo study (diabetic rats)
10.	***Momordica charantia.,*** Cucurbitaceae[53]	Fruit extract	Bioactive glycoside - charantin 	In vivo study (normal & diabetic rats)
11.	***Mangifera indica.,*** Anacardiaceae[48]	Pulp & peel methanolic extract	Polyphenol- Magniferin (1,3,6,7 tetrahydro –xanthone c2-beta-D-glucoside)  Mangiferin	In vivo study (diabetic rats – 30 days)

12.	***Mirabilis jalapa.,*** Nyctaginaceae[54]	Ethanolic root extract	Alkaloid - Trigonelline 	In vivo study (STZ induced diabetic rats).
13.	***Myrica multiflora.,*** Myrtaceae[55]	Dried leaves	Bioflavonoid- Myrciacitrins I, II, III,IV & V 	In vivo study (significant rat aldose reductase inhibitory activity)
14.	***Ocimum gratissimum.,*** Lamiaceae[55]	Leaf extract	Phenolic substance – Choric acid 	In vivo study (diabetic mice - Normal & STZ induced)
15.	***Ocimum sanctum.,*** Labiatae[57]	Leaf extract	Phenylpropene - Eugenol 	In vivo study (STZ induced diabetic rats)
16.	***Origanum majorana.,*** Lamiaceae[55]	Methanolic leaf extract	Bioflavonoid- Scutellarein (6 hydroxyapigenin) 	In vivo study (rat intestinal alpha - glucosidase inhibitory activity)

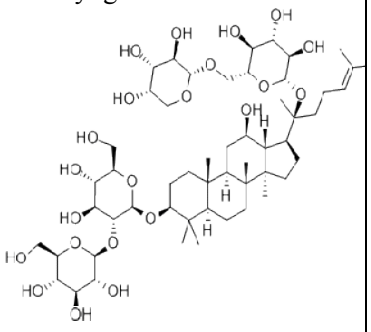
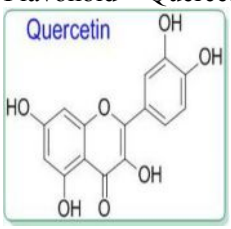
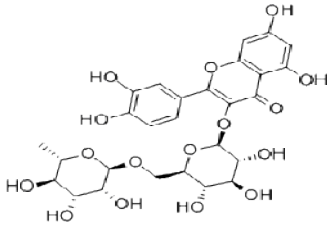
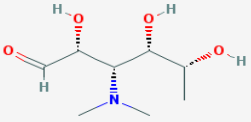
17.	***Panax ginseng.,*** Araliaceae[58]	Root extract	Malonyl ginsenosides 	In vivo study (diabetic rats - STZ induced)
18.	***Rhododendron tomentosum.,*** Ericaceae[59]	Ethanolic Fruit Extract	Flavonoid - Quercetin 	In vivo study (Caco-2 cells Diabetic rats)
19.	***Ruta graveolens.,*** Cucurbitaceae[62]	Aqueous Leaf Extract	Flavonoid – Rutin 	In vivo study (Diabetic rats)
20.	***Syzygium cumini.,*** Myrtaceae[60,61]	Ethanolic Extract of seeds, leaves & flower	Mycaminose 	In vivo study (Diabetic rats)

Table: 3. List of Formulations of The Selected Traditional Herbs and its Biocompounds

S.No	Drug	Company	Ingredients
1.	Diabecon[1]	Himalaya	*Gymnema sylvestre, Syzgium cumini, Boerhavia diffusa, Phyllanthus amarus, Aloe vera, Momordica charantia.*
2.	Diasulin[1]		*Emblica officinalis, Gymnema sylvestre, Trigonella foenum graecum, Momordica charantia.*
3.	Pancreatic tonic 180cp[1]	Ayurvedic herbal supplement	*Gymnema sylvestre, Momordica charantia, Syzygium cumini, Trigonella foenum graecum, Azadirachta indica, Cinnamomum tamala.*
4.	Bitter guard Powder[1]	Garry & Sun Natural Remedies	Bitter guard *(Momordica charantia)*
5.	Gurmar Powder[1]	Garry & Sun Natural Remedies	Gurmar *(Gymnema sylvestre)*
6.	Syndrex[1]	Plethico Laboratories	Germinated Fenugreek Seed Extract

Discussion

Diabetes is a disorder of carbohydrate, fat & protein metabolism caused due to insufficient production of insulin or due to its inhibitory action. Natural products such as plant extracts and Phytochemicals are attracting more and more attention for their potentials in the treatment of diabetes. A number of Plant extracts and natural biomolecules that have been tested for their antidiabetic properties using both *in -vivo* and *in -vitro* approaches were reviewed here. Among the various organs, the leaves have been used predominantly in the treatment of diabetes. The families of plants with the most potent hypoglycemic effects include ***Liliaceae, Leguminosae, Lamiaceae etc***. The most commonly studied species are ***Mamordica charantia, Trigonella foenum graecum, Ficus benghalensis and Gymnema sylvestre.*** In the Oral glucose tolerance test, Streptozotocin & Alloxan induced diabetic mouse or rat models were most commonly used for the screening of antidiabetic drugs.

In this review, biocompounds like terpenoids, alkaloids,phenolic compounds such as flavanoid p have shown antidiabetic potential through the insulin mimetic activity. Among the reviewed compounds, ***flavonoids*** majorly exhibit the Antidiabetic activity. It acts by preventing β-cell apoptosis and promotes β-cell proliferation and insulin secretion.The Indian traditional herbal drugs ***Gymnema sylvestre, Syzgium cumini, Phyllanthus amarus, Aloe vera, Momordica charantia, Trigonella foenum graecum, Emblica officinalis, Azadirachta indica*** are more frequently used in the formulations for diabetes.

Conclusion

Our review showed the elaborative preclinical evidence for the efficacy of the traditional herbs, either as hypoglycemic agents or as useful agents in the management of diabetic complications. This can serve to promote a more rational use of these plants as herbal medicines or the biocompounds as a new drug for diabetes based on the expected therapeutic outcome.

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