INDIGENOUS PLANT DRUGS FOR DIABETES MELLITUS

*Satyavati **GV**, Tandon Neeraj and Sharma Madhu*

Diabetes mellitus is one of the oldest diseases known to mankind and yet with the tremendous scientific advances witnessed in this century, medical science cannot claim that it knows all that needs to be known about this disease, including its management. This is the main reason for the persistent interest all over the world to explore alternative remedies from the so-called "alternative systems" of medicine.

The disease was well known to the ancient Indian medical experts. All the renowned classic texts of Ayurveda like Charaka Samhita (1000 B.C.), Sushruta Samhita (600 B.C.) and subsequent works refer to this disease under the term *Madhumeha* or *Ikshumeha* (literally meaning sugar in the urine). Apart from detailed description of its etiopathogenesis (according to Ayurvedic concepts), the two types of diabetic patients (obese and lean) and a definite familial prediction to the disease are referred to in Ayurveda, besides the importance given to dietary regulations, physical exercises and baths, in addition to the use of a number of plant drugs in the management of the disease[1].

Scientific interest in 'alternative' or 'traditional system' in this area as also literature surveys and updates on diabetes mellitus have concentrated, mainly on the screening of plant drugs (from all possible sources) for their blood-sugar lowering effect. Very few plants have been studied further, in depth, for investigating their site & mechanism of action and for possible development as anti-diabetic drugs.

Indian Council of Medical Research, New Delhi

A number of reviews have been published in the last three decades on plants screened for hypoglycemic activity in India [2-18] and elsewhere[14-16]. Very recently, two exhaustive reviews have been published based on global literature survey on 150 plants[15] and 343 plants[16] from different parts of the world.

Pharmacological Studies

Tables IA and IB list the major Indian medicinal plants reported to have shown hypoglycemic activity in experimental animals along with the plant part used/active principles isolated if any, and the model used (i.e. normal animals in Table IA and on diabetic animal models in Table IB). Similarly, major plants with hypoglycaemic activity on which clinical trials have been carried out are listed in Table II. Among these plants, some like *Allium cepa* (Onion, *piyaj), Allium sativum* (garlic, *lasun), Syzygium cumini* (Syn. *Eugenia jambolana;* (black plum; *jamun), Momordica charantia* (bitter gourd; *karela) Gymema sylvestre (Gurmar), Pterocarpus marsupium (Vijay-) sar)* etc. have attracted more attention of the scientists as well as laymen, in recent years. Only a few of these will be discussed here, in" some detail.

In most animal studies, water extracts or alcoholic extracts of the plants have been screened. In a few studies, the active principles of plants have been investigated for hypoglycemic activity.

In a systematic screening programme of plants available in India over several decades,

the Central Drug Research Institute (CDRI), Lucknow (India), reported positive bypoglycaemic activity in only 11 plants[175], none of which was considered encouraging enough for being taken up for further studies.

Among the major chemical constituents of plants credited with hypoglycaemic action (Table III) are glycosides, alkaloids, glycans, triterpenes, mucilages, polysaccharides, oils, vitamins, saponins, glycoproteins, peptides, amino acids & proteins.

Reports on as many as 20 plant mucilages showing hypoglycaemic activity have been reviewed recently[15]. Among these, mucilages isolated from Malavaceous plants which show hypoglycemic activity have been found to have highly interesting chemical structure relating to a trisaccharide structural unit which offer interesting leads on structure-activity relationship[174].

Pharmacological screening for hypoglycemic activity has been done using various animal models like normal, fasting rats & rabbits; alloxan-treated rabbits; hyperglyceraia induced in rats by adrenaline, corticoropin, somatotropin as also by streptozotocin and by pancreatectomy (Tables IA and IB).

On plants like *Momordica charantia* and *Pterocarpus mar sup um,* some contradictory results have been reported by different groups of Indian workers. *M. charantia has* revealed hypoglycemic activity in most studies. Thus, the fruit of this plant showed hypoglycaemic effect in normal & alloxan-induced diabetic rabbits[72], while *M. charantia* seeds proved hypoglycemic in streptozotocin-induced diabetes in rabbits[137], in normal rabbits[77], in normal & alloxan diabetic dogs[75], in hyperglycemia induced by anterior pituitary extract in rats[44].

In other studies on rabbits, *M. charantia* juice showed only a mild hypoglycemic effect in normal & alloxan diabetic animals, while proving to be toxic at 10 ml/kg dose[74]. It showed no effect on normal rabbits either on acute or chronic administration[176].

Clear cut data on the actual chemical constituents of bitter gourd which can be held responsible for its hypoglycemic activity are lacking, in spite of a number of reports on charantin (the non-nitrogenous neutral principle) and the polypeptide-p[80] or plant (P)-insulin [81'162] isolated from this plant.

Another plant well reputed in Ayurvedic medicine as an anti-diabetic drug and which has also shown considerable promise in initial pharmacological studies is *Pterocarpus marsupium.* After sporadic studies on various extracts of the plant (between 1959 and 1971) by different group of authors,[46,67,89,91,177] a series of investigations on rats done at Banaras Hindu University, Varanasi, claimed a novel anti-diabetic mechanism of action of the flavonoid isolated from *P. marsupium viz. (—)* epicatechin- The flavonid (isolated from the plant), as also its synthetic counterpart, were claimed to regenerate the j8-cells of the islets of pancreas in alloxon diabetic rats[44,138-141]. These startling results attributed to (—) epicatechin were, however, not confirmed by other workers from different parts of the world[178-180]. This serves as a familiar example of a few over-enthusiastic scientists jumping to premature conclusions on the identity of 'active principles' as well as a novel mode of action of plant drugs without confirmatory evidence. Despite such setbacks, as the

crude, extract of the plant has shown a hypoglycemic effect consistently and the plant continues to be used in clinical practice by Ayurvedic physicians (especially in North India) for the management of diabetes, further studies, are called for on this plant.

Gymnema sylvestre is yet another plant reputed specially in South India for its use as an antidiabetic drug. Adrenaline-induced hyperglycemia in rats was countered by injection of the leaf extract[129]. Orally, the leaves significantly reduced the hyperglycemia induced in rats by anterior pituitary extract[128]. In alloxan diabetic rabbits, the leaf extract of the plant reduced the blood sugar level and also reversed the hepatic changes produced by hyperglycemia[132]. The alcohol-water extract of *G. sylvestre* restored the elevated protein-bound polysaccharide components & glycosaminoglycans in serum & tissues of alloxan diabetic rats, and it was suggested that the plant apparently restores the synthesis of sulfated glyosaminolycans and thereby could be of possible assistance in preventing vascular complications of diabetes[65].

The seeds of *Syzygium cumini* are used by the Ayurvedic physicians (and also in Indian folklore) in the treatment of diabetes mellitus. The hypoglycaemic activity of the seeds has been studied by several workers in animal models[43,58,145]. In alloxan diabetic rats, S. *cumini* seed extract led to a decrease in the levels of blood glucose, urea and serum triglyceride levels[144].

The botanical identity of certain plants used by Ayurvedic clinicians is known to be controvertial. One such example is of the drug *'Saptarangi'* famed in Ayurveda as an antidiabetic agent. This plant was screened for hypoglycaemic activity under the Composite Drug Research Scheme (CDRS) of the Indian Council of Medical Research during 1965-69. In the initial part of the study, the drug *'Saptarangi'* was botanically identified as *Caeseria esculenta.* However, the commercially available *Saptarangi* was subsequently correctly identified[181] as *Salacia prenoides* (yellow variety) and *Salacia macrosperma* (brown variety). *S. prenoides* (aqueous extract) evinced hypoglycemic activity comparable to tolbutamide in glucose tolerance tests in male rabbits[182]. This experience illustrates and emphasizes the vital need for authentic botanical identification of the plants *before* embarking on chemical and biological studies.

Clinical Studies

As with pharmacological studies, most of the clinical trials on antidiabetic plants were also undertaken in a sporadic manner and not with any systematic approach. Among the many plants subjected to clinical trials (Table II) major ones are *Allium cepa*[30,147-151], *Clerodendron phlomides*[152-153], *Cinnamomum tamala*[154-155], *Enicostemma littorale*[157], *Ficus bengalensis*[158], *Gymnema sylvestre*[159-161], *Momordica* charantia[81,162-165], *Pterocarpus marsupium*[166-170] and *Syzygium cumini*[166-171]. Almost all these studies are open clinical trials on small number of diabetic patients. So far, gum guar (from Indian cluster beans or *Cyamopsis tetragonolobus)* is the only plant product that has reached the stage of being marketed after extensive animal studies and large scale clinical trials in the advanced parts of the world. The proven hypoglycemic (and hypocholestrolemic) activities of gum guar, are due to its dietary fibre content, causing a decrease in insulin demand and a progressive decrease in the HbAc levels[15].

Table I

A List of Indian Plants with Hypoglycemic Activity Screened on Normal Animal Models

S No	Name of the Plant	Part used (Active Principle)	Model used	Reference No.
1	2	3	4	5
1.	*Acacia arabica*	Seeds	Rats	17, 18
2.	*A. benthami*	Seeds	Rats	17
3.	*A. catechu*	Wood (flavonoid)	Rats	19
4.	*A. modesta*	Seeds	Rats	17
5.	*Adhatoda vasica*	Leaves	Rats	20
6.	*Adiantum cappilus-veneris*	Whole plant	Rabbits	21
7.	*Albizzia stipulata*	Seeds	Albino rats	22
8.	*Allium cepa*	Bulbs (oil)	Mice	23
			Fasting rabbits	21, 24,25,26
		Bulbs		27, 21, 29, 30
9.	*A.sativum*	Bulbs	Rabbits	28, 31
10.	*Azadirachta indica*	Seed oil	Rabbits	32
		(Nimbidin)	Rabbits	33
		Leaves	Dogs, rats	34, 35, 36
11.	*Caeseria esculanta*	Roots	Rats	37, 38, 39, 40 41,42
12.	*Cassia auriculata*	Seeds	Rabbits	43
13.	*C. fistula*	Seeds	Rats	22
14.	*Coccinia indica*	Fruits	Rats	44,45
		Leaves, whole plant	Guinea pigs	46,47
15.	*Cryptostegia grandiflora*	Aerial parts	Rabbits	48,49
16.	*Cyamopsis *eiragonolobus*	Fruits, seeds	Normal and glucose fed fasting rabbits	50
17.	*Dolichos biflorus*	Seeds	Rats	51
18.	*Enicostemma littorale*	Whole plant	Rats	35,36
19.	*Ensete superbum*	Seeds	Rats	52
20.	*Euphorbia prostrata*	Whole plant	Rabbits	53

1	2	3	4	5
21.	*Ficus bengalensis*	Root bark	Rabbits	54
		(Phytosterolin)	Fasting rabbits	55
		Bark	Rabbits, mice	56,57
		Bark	Male rats	58
		(Flavonoids)	Rabbits	59
		(Glycosides)	Fasting rabbits & dogs	60
		(Glycosidal fraction)	Rats	61
		Milky stap	Rats	62,63
22.	*F. glomerata*	Bark	Rabbits	21
		Bark	Rats	64
		Bark	Rabbits	25,55
		(Sitosteryl glucosides)		
23.	*Fumaria parviflora*	Whole plant	Normal rabbits	53
24.	*Glycine max*	Seeds	Rats	51
25.	*Gymnema sylvestre*	Leaves	Rats	65
		(Glycosamino glycan and protein bound polysaccharides)		
		Leaves	Rats	35, 66, 67
		Whole plant	Rabbits	21
26.	*Hamiltonia suaveloens*	Roots	Rats, dogs and monkeys	68
27.	7m//a *racemosa*	Roots	Rabbits	69
28.	*Launaea nudicaulis*	(glycoside)	Rats	70
29.	*Leucaena leucocephala*	Seed	Rats	71
30.	*Momordica charantia*	Fruits	Rabbits	72
		Fruits	Rabbits & dogs	73,74
		Fruits	Dogs	75
		Seeds	Rats	76
		Fruits	Rabbits	77
		Leaves		78
		Fruits	Rats	79
		Fruits	Rabbits	80
		(Charantin)		

1	2	3	4	5
		Fruits & Seed (Polypeptide) (Plant insulin)	Gerbils & langur monkeys	81
31.	*Mucuna pruriens*	Seed	Rats	51
32.	*Murraya koenigii*	Leaves	Dogs	82
33.	*Musa paradisiaca*	Flower	Rabbits	21, 83, 84
34.	*Npmphaea nouchali*	Root	Rabbits	21
35.	*Phyllanthus fraternus*	Leaves	Rabbits	85
		(Flavonoid)	Rats	86
36.	*Pinus roxberghii*	Bark & root	Rabbits	21
37.	*Pongamia pinnata*	Bark	Rabbits	4
38.	*Prunus persica*	Leaves	Dogs and rabbits	87
39.	*Pterocarpus marsupium*	Heart-wood	Rabbits	88, 89, 90, 91
		Wood (Pterostilbine)	Dogs	92
		Heart-wood	Rabbits	89
		Wood	Rats	93
		(Flavonoid)		94
		Wood	Albino rats	67
40.	*Rauwolfia serpentina*	(Total alkaloid) (Ajmaline)	Cats	95
41.	*Solatia macrosperma*	Leaves & roots	Rabbits	96
42.	*S. prenoides*	Root bark	Rabbits	182
43.	*Securigera securidaca*	Seeds	Cats & Rabbits	97
44.	*Syzygium cumini*	Seeds	Albino rats	58
		Fruits & seeds	Rabbits	21
		Seeds	Rats	93
45.	*Tephrosea purpurea*	Seeds	Rabbits	98
46.	*Tinospora cordifolia*	Stem	Rats	99
		Stem	Rats	100
		Stem	Rats & rabbits	101
47.	*Tricosanthes diocia*	Seeds	Albino rats	102
48.	*Trigonella foenum-graecum*	Seed (alkaloids)	Rabbits	103

Table IB

List of Indian Plants with Hypoglycemic Activity Screened on Various Animal Models with Induced Diabetes

S. No.	Name of the Plant	Part Used (Active Principles)	Animal Model	Reference No.
1	2	3	4	5
1.	*Acacia melanoxylon*	Seeds	Normal and alloxan diabetic albino rats	104
2.	*Allium cepa*	Bulbs (Allyl propyl disulphide)	Alloxan diabetic rabbits	105
		Bulbs (Allicin or diallyl disulphide oxide)		106
		Ether soluble & stem volatile fractions		30
		Juice	Alloxan diabetic rabbits	107
		Tops	Alloxan and adrenaline diabetic rats	108
3.	*A. Sativum*	Bulbs	Alloxan diabetic rabbits	109, 110
4.	*Aloe vera*	Leaves	Normal & alloxan diabetic rabbits	111
5.	*Azadirachta indica*	Seed oil	Normal & hyperglycaemic rabbits	112
6.	*Bambusa Dendrocalamus*	Leaves (Propylene glycol soluble compound)	Alloxan diabetic rabbits	113, 114
7.	*Bauhinia retusa*	Seeds	Normal & alloxan diabetic albino rats	104
8.	*Bougainvillea Spectabilis*	Leaves	Normal & alloxan diabetic mice	115
			Diabetic rats	116
		(Pinitol)	Alloxan induced mice	117
9.	*Cassia auriculata*	Seeds	Alloxan rabbits and dogs	43
10.	*Clerodendron Phlomoides*	Whole plant	Adrenaline induced rabbits	118

1	2	3	4	5
11	*Coccinia indica*	Roots	Alloxan diabetic rabbits	119
			Alloxan rats	3!, 120
		Leaves	Alloxan diabetic rats	46
12.	*Cuminum nigrum*	Seeds	Normal & alloxan diabetic rabbits	121
13.	*Cyamopsis tetragonolobus*	Fruit, seeds	Alloxan diabetic rabbits	50
14.	*Dolichos lablab*	Green pods	Alloxan diabetic rats	108
15.	*Ficus bengelensis*	Bark (Bengalinoside)	Normal and alloxan rabbits	122
		Bark	Alloxan rabbits	123, 124, 125
16.	*F. glomerata*	Bark	Normal & alloxan rabbits	126
17.	*Grewia asiatica*	Stem bark	Diabetic cats and rabbits	127
18.	*Gymnema sylvestre*	Leaves	Hyperglycamic rats	36, 45, 128, 129, 130
			Normal & diabetic rabbits	131
			Alloxan diabetic rabbits	132, 133
			Alloxan diabetic rats	134, 135
19.	*Hamiltonia suaveolens*	Roots	Alloxan diabetic rats	68
20.	*Inula racemoma*	Roots	Glucose induced hyper-glycaemia in rabbits	69
21.	*Launaea nudicaulis*	Roots	Alloxan diabetic rabbits (Glycoside)	70
22.	*Momordica charantia*	Fruits	Diabetic rabbits	72
			Alloxan diabetic dogs, rabbits	73, 74
		Fruits (Bigger variety without seed)	Alloxan diabetic rabbits	136
		Fruits	Alloxan diabetic dogs	75
			Against anterior pituitary extract in glucose fed rats	44

1	2	3	4	5
		Seed	Adrenaline induced diabetic rats	76
		Seeds	Streptozotocin induced diabetes mellitus in rabbits	137
23.	*Murraya koenigii*	Leaves	Alloxan diabetic dogs	82
24.	*Pongamia pinnata*	Bark	Alloxan diabetic rabbits	4
25.	*Pterocarpus marsupium*	Aqueous infusion	Pituitary diabetes in rats	44
		Bark	Alloxan diabetic rats	91
26.	*Pterocapus marsupium*	Bark (flavoaoid (—)—Epicatechin)	Alloxan induced necrosis of beta cell population of pancreas in rats	138, 139, 140
		(—)—Epicatechin	Alloxan diabetic rats	88,91, 141, 142
27.	*Rivea cuneata*	Heartwood & leaves	Diabetic rats	143
28.	*Syzygium cumini*	Seed kernel	Alloxan diabetic rats	144 145
		Seeds	Alloxan diabetic rats & rabbits	31
		Seeds, fruits	Diabetic rabbits and dogs	43
29.	*Tephrosia purpurea*	Extract	Alloxan induced diabetes in rabbits	98
30.	*Tinospora cordifolia*	Stem	Alloxanised rat and rabbit; adrenaline induced diabetic rabbits.	100, 146

Table II List of Indian Medicinal, Plants Subjected to Clinical Trials

Sl. No.	Name of the Plant	Nature of clinical Trial	Results	Reference No.
1	2	3	4	5
1.	*Allium cepa*	20 diabetic patients	Reduction of blood	147
	(i) Juice (100 g) orally	and 20 normal healthy controls	sugar in diabetics No alteration in blood sugar in controls.	
	(ii) Juice expressed residue of onion (50 g)	3 chronic diabetic patients	Reduced the blood sugar	30
	(iii) Allylpropyl disulphide (0.125 g/50 kg body wt)	6 Normal volunteers	Significant fall in blood sugar levels	148
	(iv) Juice (100g) orally	5 healthy volunteers (Fasting and adrenaline induced hyperglycaemia)	Decrease in blood glucose	149
	(v) Aqueous extract (25-50g)	20 healthy volunteers (Fasting and adrenaline induced hyperglycaemia)	No effect on fasting blood sugar but reduced the rise in blood sugar on glucose loading	150
	(vi) Raw onion (100 g) daily for for 3 months	20 diabetic patients.	Lowered Blood sugar	151
2.	*Clerodendron phlomoides*			
	(i) Alcoholic extract of the plant	33 diabetic patients + 10 Normal volunteers	Reduction in fasting blood sugar.	152
	(ii) Decoction of the plant (4 ml)	13 Diabetic patients	Reduction in blood sugar	153
3.	*Cinnamomum tamala*			
	(i) Leaves powder 2 teaspoon four times a day for a month	32 diabetic patients	Fall in fasting blood sugar level but not in post prandial level	154

1	2	3	4	5
	(ii) Leaves powder 3 teaspoons four times a day for 1 5 days.	5 diabetic patients	Reduction on blood glucose	155
4.	*Coccinia indica*			
	Powder (3 gm twice daily) and juice (30 ml twice daily)	41 diabetic patients	Reduction in blood sugar.	156
5.	*Enicostemma littorale*			
	Fresh juice (1-5 ounces) 3 times a day.	17 Diabetic patients	Fall in fasting blood sugar and not in postprandial blood sugar.	157
6.	*Ficus bengalensis*			
	Aqueous extract of the bark (100 ml of 10 per cent extract)	12 normal volunteers 6 diabetic patients 6 control patients	No effect in normal human, mild activity in diabetic patients	158 :
7.	*Gymnema Sylvestre Leaves*			
	Leaves and stem	Diabetic patients	Lowering of blood sugar	159
	Aqueous decoction leaves	20 diabetic patients 10 normal and 6 diabetic patients.	Lowering of blood sugar Reduction in blood sugar.	160 161
8.	*Momordica charantia*			
	(i) P-insulin	9 patients on primary diabets mellitus	Reduction in blood sugar	162
	(ii) P-insulin	19 patients of maturity onset diabetes	Reduction in blood sugar.	81
	(iii) Fruit powder (100 g daily for 2 weeks)	Normal control 25 patients of diabetes mellitus	No significant effect in either cases (But gave a false negative test for sugar in urine)	163
	(iv) Fresh juice of fruits	Diabetic patients	Lowering of blood sugar.	164, 165
9.	*Pterocarpus marsupium*			
	1. Heartwood extract	14 diabetic patients	Reduction in blood Sugar.	166

1	2	3	4	5
	2. Decoction	22 diabetic patients	Improvement in glucose tolerance in 12 patients	167
	3. Heart wood extract (250 mg) capsule	35 diabetic patients	Reduction in the sugar level in blood and urine	168
	4. Heartwood powder 5g t.d.s	20 patients of maturity onset diabetes and 1Q control patients.	Significant lowering of blood sugar.	169
	5. Beeja wood water (200 ml bid) for	10 patients of diabetes mellitus	Encouraging activity	170
10.	*Syzygium cumini*			
	Seed powder	7 diabetic patients	Reduction in blood sugar	166
	Seed powder (4-24g tds)	28 Diabetics	In 20 cases significant fall in fasting and postprandial blood sugar.	171

The search for anti-diabetic agents from the plant kingdom will continue, however, in spite of the poor returns obtained so far regarding their ultimate therapeutic efficacy mainly because of considerations such as :

(i) Interesting leads obtained on the novel chemical structure of a few active principles isolated from plants (as for example, the novel structure-activity relationship demonstrated in mucilages derived from the Malvaceae family of plant[174].

(ii) Possibility of deriving new knowledge on the mechanism of action of anti-diabetic agents which, in turn, may help in a better understanding of the etiopathogenesis and the course of clinical diabetes mellitus. An example is the hypoglycins isolated from *Blighia sapida* which act as anti-metabolites, blocking the pathway of fatty acid oxidation leading to depletion of liver glycogen and induction of hypoglycemio[15]. The mechanism also accounts for the toxicity of the plant.

(iii) Possibility of preventing/minimising complications of diabetes mellitus such as the neurological and vascular complications by the judicious use of selected plant-based drugs, based on in depth study of their mechanism of action.

Toxicity and side-effects of all plant-based drugs is a much debated issue. In clinical practice, Ayurvedic/Unani physicians rarely

Table III

Major Chemical Constituents of Plants Showing Hypoglycaemic Activity

S. No.	Chemical Principle	Plant	Reference No.
1.	Aminoacids (Hypoglycin A) (Hypoglycin B)	*Blighia sapida*	15
2.	Alcohol (Pinitol)	*Bougainvillea spectabilis*	117
3.	Alkaloids (Catharanthine) (Leurosine) (Lochnerine) Vindoline etc	*Catharanthus roseus*	15, 16
4.	Flavonoid [(—)—epicatechin]	*Pterocarpus marsupium*	138, 139, 140
5.	Glycosides (Bengalenoside)	*Ficus bengalensis* *Launaea nudicaulis*	122
6.	Glycans		
	(Anemarans A,B,C,D)	*Anemarrhena asphodeloides*	15, 16
	(Atractans A,B,C)	*Atractylodes japonica*	15, 16
	(Dioscoran A,B,C,D,E,F)	*Dioscorea japonica*	172
	Ephedrans (A,B,C,D,E)	*Ephedra distachya*	15, 16
7.	Glycoproteins (Moran A)	*Moms alba*	173
8.	Gum guar	*Cyamopsis tetragonolobus*	50
9.	Mucilage	*Planiago asiatica* *Althaea officinalis* *Abelmoschus esculentus* *Dioscorea batatas*	174
10.	Neutral substances (Nimbidin)	*Azadirachta indica*	33
11.	Oil	*Allipum cepa*	23
12.	Peptides (P-insulin)	*Momordica charantia*	81
13.	Proteins	*Acacia melanoxylon*	17
14.	Polysaccharides	*Gymnema sylvestris*	65
15.	Sulphides (Allicin) (Allylpropyldisulphide)	*Allium cepa*	105, 106
16.	Triterpenoids (Tormantic acid)	*Poterium ancisroides*	15

Table IV

List of Medicinal Plants Showing Hypoglycemic Activity (Outside India)

1	2	3	4	5
1.	*Aconitum carmichaeli*	Roots Glycans A, B, C & D	Normal and alloxan diabetic mice	184
2.	*Aloe arborescens var natalensis*	Leaves (Arboran A and arboran B)	Normal and alloxan induced diabetic mice	185
		(polysaccharide fractions)	Normal mice	186
3.	*Anacardium occidentals*	Bark (Aqueous decoction)	Adrenalectomized rats	187
4.	*Anemarrhena asphodeloidex*	Rhizomes (Anemarans A,B,C,D)	Normal and alloxan diabetic mice	188
5.	*Atractylodes japonica*	Rhizomes (Atractans A, B & C)	Normal and alloxan induced diabetic mice	189
6.	*Blighia sapida*	Unripe fruits and seeds (Hypoglycin A and B)		190
7.	*Bridelia ferruginea*	Leaves	Normal rats	191
8.	*Cannabis indica*	Wholeplant (extract)	Insulin induced rabbits	192
9.	*Coix lachryma-jobi*	Whole plant Aqueous extract Glycans A, B, C)	Normal and alloxan diabetic mice	193
10.	*Dioscorea japonica*	(Dioscoran A, B, C, D, E, F)	Normal and alloxan induced hyperglycemic mice	172
11.	*D. dumentorum*	Tubers	Fasting normal mice & rabbits Fasting alloxan diabetic rabbits	194
12.	*Eleutherococcus Senlicosus*	Roots (Eleutherans A, B, C, D, E, F, G)	Normal and alloxan induced	195

1	2	3	4	5
13.	*Ephedra distachya*	(Ephedrans (A, B, C, D, E)	Normal and alloxan induced mice	196
14.	*Eucalyptus globulus*	(Calytoside)	Alloxan diabetic rabbits	197
15.	*Galega officinalis*	Leaves	Alloxan diabetic rabbits	198
16.	*Hammada salicornica*	Wholeplant	Alloxan diabetic mice	199
17.	*Humulus lupulus*	Strobiles (Humulone and lupulone)	Streptocin induced diabetes in rats	200
18.	*Ipomoea nil*	Extracts	Rats	201
19.	*Lagerstroemic speciosa*	Leaves and ripe fruit	—	202
20.	*Lepidium ruderale*	Aerial part (lepidine)	Alloxan diabetic rats	203
21.	*Lithospermum erythrorhizon*	Lithosperman A, B&C	Normal as well as alloxan diabetic mice	204
22.	*Lupinus albus*	Seed (A fraction of seeds extract)	Rabbits	205
23.	*Lythrum salicaria*	Stem Flower	Epinephrine induced hyperglycemia in rats. Alloxan induced diabetic mice	206, 207
24.	*Momordica charantia*	Crude crystalline substance	Normal and alloxan induced diabetits rabbits	208
25.	*Momordica cochinchinemis*	Fruit (Glycosides)		209
26.	*Momordica*	Foetidin	Fasting rats	210
27.	*Morus alba*	Leaves	In diabetic animals	211
	"	Root bark (Moran A)	Normal mice and alloxan induced hyperglycemia in mice	173
28.	*Olea europaea*	Leaves	Rabbits	212
29.	*Opuntia streptacantha*	Sap	Rabbits, rats, dogs	213
30.	*Oryza saliva*	Roots (Glycans)	Normal and alloxan produced diabetic mice	214

1	2	3	4	5
31.	*Panax ginseng*	Roots	Mice	215
		(Panaxans A, B, C, D & E)	Normal and alloxan induced hyperglycemic mice and dogs	216
	"	Root (Panaxans)	Normal and alloxan induced hyperglycemic mice	217, 218
	"	DPG-3-2	Diabetic animals	219
	"	Ginseng fraction	Alloxan diabetic mice	220
32.	*Panax quinquefolium*	Roots (Glycan)	Normal mice	221
33.	*Psidium guajava*	Juice	Normal and alloxan treated diabetic mice	222
34.	*Quercus infectoria*	Galls	Rabbits	223
35.	*Rubusfruticosus*	Leaves	Normoglycrmic and alloxan-diabetic rabbits.	224
36.	*Saccharum officinarum*	Glycans	Normal and alloxan hyperglycemic mice	225
37.	*Sarcopoterium spinosum*	Root bark	Rabbits	226
38.	*Syzygium cumini*	Seeds	Mice	227
		Seed	Diabetic rats	228,229
		Seed Kernel	—	230
39.	*Tecoma stans*	Infusion	Normal dogs	231
		Leaves (Tecomine, tecostamine)	—	232
40.	*Trifolium akxandrinum*	Seeds	Normal and alloxan diabetic rabbits	233
41.	*Trigonella foenutn graecum*	Seeds	Rabbits	234
	"	"	Diabetic dogs	235
	"	Seed extract (Trigonelline-HCL)	Alloxan diabetic rats	236
42.	*Urtica dioica*	Extract	Rabbits	237
43.	*Vaccinium myrtillus*	Green leaves & stems (neomyrtillin)	Rabbits and mice	238
44.	*Xanthium strumarium*	Seeds	Rats	239

use single drugs, but employ compound formulations which, while enhancing the overall therapeutic efficacy also aim to reduce the side effects/toxicity of the main ingredients of the formulations. In controlled clinical trials, however, researchers prefer to use single plants, for obvious reasons, and therefore, the possible toxicity/side effects have to be looked for. Many hypoglycemic plant drugs, used at high doses or for a prolonged period are known to cause undesirable side effects Thus, for example, even *M. charantia* extract, has been reported to cause, on chronic administration, mass atrophy of the testes in dogs[183].

In addition to the Indian plants lifted (in Tables IA, IB and II), a large number of plants in other parts of the globe have been reported to reveal hypoglycemic activity in various models[16,16]. These include, among others, well known plants like *Aloe arborescens, Catharanthus roseus* (syn. *Vinca rosea), Morus alba, Mucuna pruriens, Murraya Koenigii, Ocimum sanctum, Oryza sativa, Panax ginseng* (ginseng), *Phyllanthus fraternus, Psidium guajaya* (guava) etc., Table IV lists the major plants in which hypoglycemic activity has been reported in other parts of the world.

In view of lack of authentic data on the clinical efficacy of reputed plant drugs, after a careful literature survey and discussions with Ayurvedic physicians, the Indian Council of Medical Research has selected two single plants *(Pterocarpus marsupium* and *Syzygium cumini* and a compound preparation (comprised *Emblica officinalis + Curcuma longa)* for double blind clinical trials in patients of diabetes mellitus. These studies are still in progress.

In conclusion, a large number of plants screened in India and elsewhere for their hypoglycemic/antidiabeiic effect, have yielded certain interesting leads, but (with the possible exception of gum guar) no plant-based drug has so far reached such an advanced stage of investigation or development as to replace or reduce the need for the currently available oral antidiabetics. The research for alternate remedies (from the plant kingdom) for diabetes mellitus will continue all over the world as the disease poses many challenges not only to the physician but also to the researcher. In future studies on plant/plant based products, it would be worthwhile to explore the other possible beneficial effects of plant-based drugs on not only blood levels but other aspects of diabetes mellitus including its complications. Such an approach is particularly called for in case of plants selected from ancient systems of medicine like Ayurveda which advocate a 'holistic' outlook on health and disease with emphasis on modified life style including dietary regulation, alterations in physical and mental status, combined with a judicious use of selected plant-based drugs.

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