RECENT RESEARCH IN INDIGENOUS ANTI-DIABETIC MEDICINAL PLANTS — AN OVER-ALL ASSESSMENT*

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Since the discovery of insulin 47 years ago diabetes mellitus has continued to attract, baffle, and reveal itself in tiny facets of its many-faced make-up ; but long ere the days of insulin, in the dim past of Ayurvedic glory. Susruta first recognised the condition when he discovered the honey sweet urine of such sufferers. The syndrome was further described as inherited or acquired, the former-lean weak, nervous and resistant to treatment ; the acquired or alimentary diabetic—fleshy with a voracious appetite, and addicted to sedentary habits, should be treated, they said, by exercise and fasting. Such a classification bears comparison with our modern juvenile and obese types of the disease.

A large number of plant and mineral compounds have been mentioned in the ancient treatises of Ayurvedic and Tibbi medicine as valuable in diabetes mellitus therapy ; besides these, remedies prevalent in folk medicine have been reported by the careful enquiries and observations of the older physicians of modern medicine. Hence, the present origin of such anti-diabetic agents is from these two sources.

The spectacular effects of insulin, gave a filip in our country to the investigation of these older remedies in the hope of finding an insulin like plant substitute, and physicians of the 1930's and the Chopra School of investigators tested some of these remedies; however, results were not encouraging and clinical trials were rather haphazard.

A greater stimulus to this work came with the introduction of the sulphonylureas, and the diguanides about 15 years ago, and the vast amount of work which followed to elucidate their mechanism of action. This work also gave a deeper insight into the possible biochemical modi operandi of the diabetic syndrome and although it still eludes complete understanding, many factors besides just absolute insulin deficiency are now known as possible causes of this condition. Hence this newer knowledge on insulin antagonists, bound insulin, insulin degradation and other aspects of carbohydrate metabolism has now widened the spectrum of the possible mechanisms of drug action in diabetes mellitus.

About this time also medical research in our country received more encouragement than ever before. As a result, a number of workers turned again to work on the indigenons anti-diabetic remedies both plant and mineral.

In Table I are listed the plants subjected to laboratory investigation over the last 15-16 years. I do not claim this list to be exhaustive ; nevertheless it reveals that at least 35 plants have been studied.

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TABLE I

Indigenous anti-diabetic medicinal plants studied recently.

	Plant	*References*		*Plant*	*References*
1.	Actinodaphne lanceolata.	1	19.	Ficus glomerata.	1, 29, 50.
2.	Adhatoda vasica.	46	20.	Ficus religiosa.	3, 13, 14, 50, 6
3.	Allium cepa.	11, 13, 21, 50.	21.	Glycine—Soja.	53
4.	Allium sativum.	14, 21, 50.	22.	Gymnema sylvestre.	24, 30, 33, 34, 4
5.	Azardirachta indica.	1			50, 64.
6.	Asparagus racemosus.	1	23.	Linaria ramosissima.	1, 19.
7.	Bambusa dendrocalamus.	8	24.	Macuna pruriens.	53
8.	Bassia longifolia.	1	25.	Mangifera indica.	1
9.	Benincasa cerifera.	1	26.	Mamordica charantia.	15, 44, 45, 59, 6
10.	Butea monosperma.	1	27.	Phaseolus mungo.	49
11.	Caeseria esculenta.	1, 4, 7, 22, 25.	28.	Pongamia glabra.	1
12.	Cassia auriculata.	1	29.	Pterocarpus marsupium.	1, 26, 38, 50, 5
13.	Coccinia indica.	10, 17, 21, 26, 50.			58, 64.
14.	Cryptostegia grandiflora.	60	30.	Rivea cuneata.	50, 54, 55, 56.
15.	Dolichos biflorus.	53	31.	Salacia microsperma.	5
16.	Dolichos lab-lab.	49, 61.	32.	Scoparia dulcis.	21, 50, 52.
17.	Eugenia jambolana.	1, 11, 51, 57, 62, 65.	33.	Syzygium cumini.	21, 50.
18.	Ficus bengalensis.	2, 12, 13, 18, 27, 28, 43, 50, 63.	34.	Tinospora cardifolia.	29, 35, 36, 37.
			35.	Vinca rosea.	1, 21, 40, 41, 50.

Extracts of agents which have shown a definite hypoglycaemic action in experimenta animals (normal or diabetic) in acute or chronic studies are listed in Table II.

In Table III however, are listed drugs which have been extensively studied—by this I mean studied by 4 or more (the first 6 shown in the Table) or 3 workers (the latter 6 on the list). have given the references as far as available to me. It seems significant that nearly all the chie workers of the above references, have since this work was reported, turned to other fields o study ; hardly any of them are currently engaged in this work.

In Table IV are listed agents which have been subjected to a broad spectrum screenin procedure for hypoglycaemia (intensive study). It will be noted that 7 of the 10 agents mentione in this table are also included in Table III. Thus, these 7 agents have been subjected to both extensive and intensive studies. The battery of tests includes more than one species, norma and diabetic animals of these species and experimental diabetes of more than one type. Such studies if carried out in one laboratory where several agents are being screened similarly, ar more valuable than when such work comes from different laboratories reporting one type o study each—e.g. if one worker reports activity in normal and alloxan diabetic (AD) rabbits, an another no action in normal and AD rats, the identity of the material used, or the preparatio

TABLE II

Agents producting hypoglycaemia in normal and diabetic animals

Plant	Animals		References
	Normal	Diabetic	
1. Allium sativum.	Rabbits		6, 14.
2. Allium cepa.	Rabbits	AD Rabbits	6, 9, 21.
		Pancrex dogs	6
3. Bambusa dendrocalamus.	Rabbits	AD Rabbits	8
4. Cassia auriculata.	Rabbits	AD Rabbits	1
		AD Dogs	1
5. Caeseria esculenta.	Rats	—	7, 25.
	Rabbits	—	1, 25.
6. Coccinia indica.	—	IHD Rats	26
	Rabbits	AD Rabbits	10, 17, 21, 64.
7. Cryptostegia grandiflora.	Rabbits	—	60
8. Eugenia jambolana.	Rabbits	AD Rabbits	11, 62.
9. Ficus bengalensis.	Rabbits	AD Rabbits	2, 12, 27.
10. Ficus glomerata.	Rabbits	—	1
	Rats	AD Rats	29
		IHD Rats	
11. Ficus religiosa.	Rabbits	AD Rabbits	13, 14.
12. Gymnema sylvestre.	Rabbits	AD Rabbits	64
	Dogs	—	24
	—	IHD Rats	33, 34.
13. Momordica charantia.	Rabbits	AD Rabbits	15, 59.
	—	IHD Rats	26
14 Linaria ramosissima.	Rabbits	AD Rabbits	1
	Dogs	—	1
15 Pterocarpus marsupium	Rabbits	AD Rabbits	64
	Dogs	—	6, 38.
	—	IHD Rats	26
16 Tinospora cardifolia.	Rabbits	—	35, 36.
	Rats	—	29, 35, 36, 37.
17. Pongamia glabra.	Rabbits	AD Rabbits	1
18. Glycine—Soja.	Rats	—	53
19. Macuna pruriens.	Rats	—	53
20. Dolichos biflorus.	Rats	—	53
21. Adhatoda vasica.	Rabbits	—	46
22. Rivea cuneata.	—	AD Rats.	55, 56.
23. Syzygium cumini.	—	AD Rabbits.	6, 21.
24. Vinca rosea.	Dogs	AD Rabbits	1, 21.

AD : Alloxan diabetes. Pancrex : Pancreatectomised IHD : Idio-hypophyseal diabetes.

of the active extract etc., used in the two cases becomes questionable. It seems desirable that such an intensive screening programme should be established in one or two laboratories.

TABLE III

Anti-diabetic medicinal plants studied extensively

Plant	*References*
1. Coccinia indica.	10, 17, 21, 26, 50, 64.
2. Eugenia jambolana.	1, 11, 51, 57, 62, 65.
3. Gymnema sylvestre.	24, 30, 33, 34, 47, 50, 64.
4. Momordica charantia.	15, 44, 45, 59, 66.
5. Pterocarpus marsupium.	1, 26, 38, 50, 57, 58, 64.
6. Caeseria esculenta.	1, 4, 7, 22, 25.
7. Allium cepa.	11, 21, 50.
8. Allium sativum.	14, 21, 50.
9. Ficus bengalensis.	2, 12, 13, 18, 27, 28, 43, 50, 63.
10. Ficus glomerata.	1, 29, 50.
11. Ficus religiosa.	3, 13, 14, 50, 67.
12. Vinca rosea.	1, 21, 40, 41, 50.

TABLE IV

Medicinal plants studied intensively for anti-diabetic action.

Plant	*Normal Animals*	*Diabetic Animals*	*References*
1. Cassia auriculata.	Rabbits	AD Rabbits	
		AD Dogs	
2. Caeseria esculenta.	Rats	—	25
	Rabbits		1, 7.
3. Coccinia indica.	Rabbits	AD Rabbits	10, 17
		IHD Rats	26
4. Eugenia jambolana.	Rabbits	AD Rabbits	1, 11.
		AD Dogs	1
5. Ficus glomerata.	Rats	IHD Rats	29
		AD Rats	
	Rabbits	—	1
6. Gymnema sylvestre.	Rats	IHD Rats	33, 34.
	Rabbits	AD Rabbits	64
	Dogs	—	24
7. Linaria ramosissima.	Rabbits	AD Rabbits	1
	Dogs	—	1
8. Momordica charantia.	Rabbits	AD Rabbits	15, 59.
		IHD Rats	26
9. Pterocarpus marsupium.	Rabbits	AD Rabbits	64
		IHD Rats	26
	Dogs	—	6, 38.
10. Tinospora cardifolia.	Rabbits	—	35, 36.
	Rats	—	29, 36, 37.

AD : Alloxan diabetes. IHD : Idio-hypophyseal diabetes.

The active principles so far isolated from the agents where extracts have shown significant hypoglycaemic action, are given in Table V; 11 active principles have been reported to give a significant action in at least one type of animal study. However, beyond this report, apparently no further studies are available because the substance was impure in some cases or the potency less than the extract (19), and/or non-availability of facilities for further refined chemical work.

TABLE V

Active principles from plants with hypoglycaemic effect

Plant	*Active principles*	*References*
1. Allium cepa.	allyl propyl disulphide.	50
2. Allium sativum.	allyl propyl disulphide.	20, 50.
	allistain I & II (glycoside).	
3. Adhatoda vasica.	non-nitrogenous principle C_{24} H_{40} O_4	46
4. Ficus bengalensis.	glycoside	
	flavonoids A, B, C.	
	B. leucoanthocyanin (glycoside)	12, 18.
	A, C—leucoanthocyanidin (less active)	
5. Ficus religiosa.	phytosteroline	
	(B-sitosteryl)	14, 67.
	(D-glycoside)	
6. Gymnema sylvestre.	Gymnemic acid.	26, 50, 64.
7. Linaria ramosissima.	amino glycoside.	19
8. Momordica charantia.	charantin (sterol glycoside phytosteroline)	45.
9. Pterocarpus marsupium.	Pterostilbene	
	3, 4, dimethoxystilbene.	6
10. Scoparia dulcis.	amellin.	52
11. Tinospora cardifolia.	glycosides.	29, 36.

There are hardly any studies where the hypoglycaemic action has been explored further to establish the mechanism of action. One laboratory has attempted such studies on the effect of the drug, and has reported an inhibition of adrenaline induced hyperglycaemia, with *Caeseria esculenta*, and *Tinospora cardifolia* ; and inhibition of ascorbic acid depletion of the adrenal glands with *Gymnema sylvestre* (Table VI).

An attempt has also been made by the same workers to study the glucose uptake by the rat diaphragm in the presence of insulin (Table VI). As in these experiments the action of the agent *per se* on glucose metabolism of the diaphragm was not studied, it cannot be definitely said that it has potentiated insulin action. Earlier it had been shown that *Ficus bengalensis* (Table VI) had no effect on the glucose uptake nor on the insulin effect in rat diaphragm studies ; the diaphragms of rats fed the drug were also studied and no difference in glucose uptake from control diaphragms was noted. Further, it was concluded using two agents, *Rivea cuneata* which had shown a hypoglycaemic action (56) and *Pterocarpus marsupium* which was not hypoglycaemic (50) that extracts were unsuitable for such *in vitro* studies (42).

TABLE VI

Plants studied for their mechanism of anti-diabetic action

Plant	*Adrenaline effect*	*Rat diaphragm studies*		*Reference*
		Potentiation of insulin effect.		
1. Caeseria esculenta extract.	inhibits hyperglycaemia	1. added *in vitro*	+	
		2. fed to donor rat	+	25, 37.
2. Ficus glomerata extract.	—	added *in vitro*	+	29
3. Gymnema sylvestre extract.	inhibits adrenal ascorbic acid depletion.	—		30, 33.
4. Tinospora cardifolia				
i. extract	inhibits	added *in vitro*	+	
ii. active principle	hyperglycaemia	added *in vitro*	+	35, 36, 3
5. Ficus bengalensis	—	*glucose uptake*		
i. extract		added *in vitro*	—	
ii. glycosidal fraction.	—	added *in vitro*	—	43
6. Pterocarpus marsupium extract.	—	added *in vitro*	—	42
7. Rivea cuneata extract.		added *in vitro*	—	42

Many of the plants mentioned so far contain tannins—e.g. *Caeseria esculenta*, *Bassi longifolia*, *Cassia auriculata*, the Ficus series and so on. The possibility, therefore, of inter ference with gastrointestinal absorption of glucose has been examined. *Ficus bengalensis* ha been reported to inhibit the absorption of glucose in mice (16). *Momordica charantia*, *Pterocarpu marsupium* and *Coccinia indica* have been similarly reported (26) in rats and *Gymnema sylvestr* (64) also in rabbits.

The blood sugar lowering action may result from a toxic effect on the liver. *Ficu bengalensis* was examined for such an action in mice ; it was concluded that while it wa potentially hepatotoxic, the dose required was very high (39). *Cyrptostegia grandiflora* reporte as causing persistent severe hypoglycaemia in humans, showed hypoglycaemia and hepatotoxicity in experimental studies (60).

There are conflicting reports on some of the agents shown as active in the previou Tables e.g. *Pterocarpus marsupium* has been reported as inactive (1,50) and active by othe groups of workers (26,64). Similarly *Caeseria esculenta* was found statistically inactive (1) hypoglycaemic (25) and (various fractions) hyperglycaemic and hypoglycaemic (22). Som agents have given negative results (1,50).

To summarise the present status of research into this area of indigenous medicinal plant reported useful in diabetes mellitus :—number of plants studied—35 ; significant hypoglycaemi reported for 23 ; extensive studies carried out on 12 ; intensive studies carried out on 10; activ principles reported hypoglycaemic—11. Although it has been mentioned earlier that thi