Proceedings of the Nutrition Society (1997), **56**, 507–517

Nature's own pharmacy: the diabetes perspective

BY ALISON M. GRAY* AND PETER R. FLATT

School of Biomedical Sciences, University of Ulster at Coleraine, Coleraine BT52 1SA

Since time immemorial man has looked to plants and their products as a source of innovative medicines. It is estimated that 66–80 % of medicines used in developing countries are based on plants (Farnsworth, 1983) and 80 % of the world's population relies on traditional medicines (Weragoda, 1980; Farnsworth, 1983). Within developed countries about 25 % of medicines contain active principles derived from plants, and the majority of drugs in current use were developed following studies of traditional plant treatments (Day & Bailey, 1988*a*). The present review considers the historical background and potential of plant remedies in the treatment of diabetes mellitus.

TRADITIONAL PLANT TREATMENTS FOR DIABETES

Before the discovery of insulin in the early 1920s by Banting, Best, McCleod and Collip, and the later development of oral hypoglycaemic agents, the major form of treatment of diabetes mellitus involved dietary manipulation and the use of plant therapies. The recommended use of plants dates back to the Eber's papyrus of about 1550 BC. More than 400 plants worldwide have been documented for the treatment of diabetes and the majority await proper scientific and medical evaluation (Day & Bailey, 1988*b*; Swanston-Flatt *et al.* 1991). Most of these traditional medicines are prepared from herbs, spices and plants which do not form part of the normal diet (Day & Bailey, 1988*a*; Bailey & Day, 1989). Some examples of these traditional plant treatments for diabetes are given in Table 1. However, several common components of the diet are traditionally recommended for regular consumption, and some are additionally taken as infusions, decoctions or alcoholic extracts. The World Health Organization has recommended accordingly that traditional plant treatments for diabetes warrant further evaluation (World Health Organization, 1980).

THE DIABETOLOGIST'S PHARMACY NEEDS

Approaches to the control of blood glucose and prevention of hyperglycaemia are central to the treatment of diabetes mellitus (Fig. 1). At present, none of these therapies either alone or in combination can reinstate normal blood glucose homeostasis, and many limitations exist in the use of anti-diabetic drugs. In insulin-dependent diabetes mellitus (IDDM) a more physiological means of insulin delivery is required. Despite attempts to develop new hypoglycaemic agents for non-insulin-dependent diabetes mellitus (NIDDM), only the α-glucosidase (*EC* 3.2.1.20) inhibitor acarbose (Bay g5241; Bayer) has been added to the clinician's current choices of diet, sulphonylureas, metformin or insulin (Rachman & Turner, 1995). New therapies are needed which reinstate a normal metabolic environment and prevent long-term complications. The development of new anti-diabetic drugs, which

*Present address: Department of Physiology and Pharmacology, University of Strathclyde, Glasgow G1 1XQ.

Table 1. *Examples of traditional plant treatments for diabetes mellitus*

Botanical name	Common name	Part of plant used	Reference
	Fruits		
Citrus limonium	Lemon	Fruit	Law (1970)
Humulus lupulus	Hop	Leaf	Peters (1957)
Juniperus communis	Juniper	Berry	Palaiseul (1983)
Optunia ficus-indica	Barbary fig	Leaf	Lewis (1949)
Momordica charanita	Cerasee (wild)	Aerial parts	Ajgaonkar (1979)
Momordica charanita	Karela (cultivated)	Fruit	Bailey *et al.* (1985)
Psidium guajava	Guava	Fruit	Perry (1980)
Pyrus communis	Pear	Leaf	Perry (1980)
Pyrus malus	Apple	Fruit	Grieve (1976)
Rubus fructicosus	Blackberry	Leaf	Farnsworth & Segelman (1971)
Rubus idoeus	Raspberry	Fruit	Messegue (1981)
Sambucus nigra	Elder	Flower	Lust (1986)
Syzgium jambos	Java plum	Fruit and seed	Mukerje (1953)
Tilia europa	Lime	Fruit	Palaiseul (1983)
Vaccinium mytillus	Bilberry	Leaf	Grieve (1976)
	Vegetables		
Allium cepa	Onion	Bulb	Bever & Zahnd (1979)
Allium sativum	Garlic	Bulb	Lewis (1949)
Brassica oleracea	Cabbage	Leaf	Farnsworth & Segelman (1971)
Brassica rapa	Turnip	Root	Farnsworth & Segelman (1971)
Letuca sativa	Lettuce	Leaf	Lewis (1949)
Medicago sativa	Lucerne	Leaf	Lust (1986)
Phaseolus vulgaris	Haricot bean	Pod	Lewis (1949)
Pisum sativum	Pea	Seed	Lewis (1949)
Solanum tuberosum	Potato	Tuber	Palaiseul (1983)
	Herbs and spices		
Agrimony eupatoria	Agrimony	Leaf	Lewis (1949)
Arctium lappa	Burdock	Leaf	Lewis (1949)
Artemisia dracunculus	Tarragon	Leaf	Duke (1985)
Capsicum fructescens	Chile pepper	Seed	Farnsworth & Segelman (1971)
Coriandrum sativum	Coriander	Seed	Farnsworth & Segelman (1971)
Eucalyptus globulus	Eucalyptus	Leaf	Lewis (1949)
Galega officinalis	Goat's rue	Leaf	Bunney (1984)
Glycyrrhiza glabra	Liquorice	Root	Grieve (1976)
Panax ginseng	Ginseng	Root	Lewis (1949)
Salvia officinale	Sage	Leaf	Atkinson (1979)
Taraxacum officinale	Dandelion	Root and leaf	Peters (1957)
Thymus vulgaris	Thyme	Leaf	Duke (1985)
Trigonella foenum-graecum	Fenugreek	Seed	Ajgaonkar (1979)
Urtica diocia	Nettle	Aerial parts	Lewis (1949)
Viscum album	Mistletoe	Leaf and stem	Peters (1957)
Zingiber officinale	Ginger	Root	Farnsworth & Segelman (1971)
	Mushrooms and Fungi		
Agaricus bisporus	Edible button mushroom	Fruiting body	Ahmad *et al.* (1984)
Agaricus campestris	Edible field mushroom	Fruiting body	Ewart *et al.* (1975)
Amanita phalloides	Fool's mushroom	Fruiting body	Lewis (1949)
Amanita verna	Destroying angel	Fruiting body	Potron (1956)
Amanita virosa	Death cap	Fruiting body	Potron (1956)
Coprinus comatus	Ink cap	Fruiting body	Kronberger (1964)
	Yeast		
Saccharomyces cerevisiae	Brewer's yeast	Cell extract	Collip (1923)

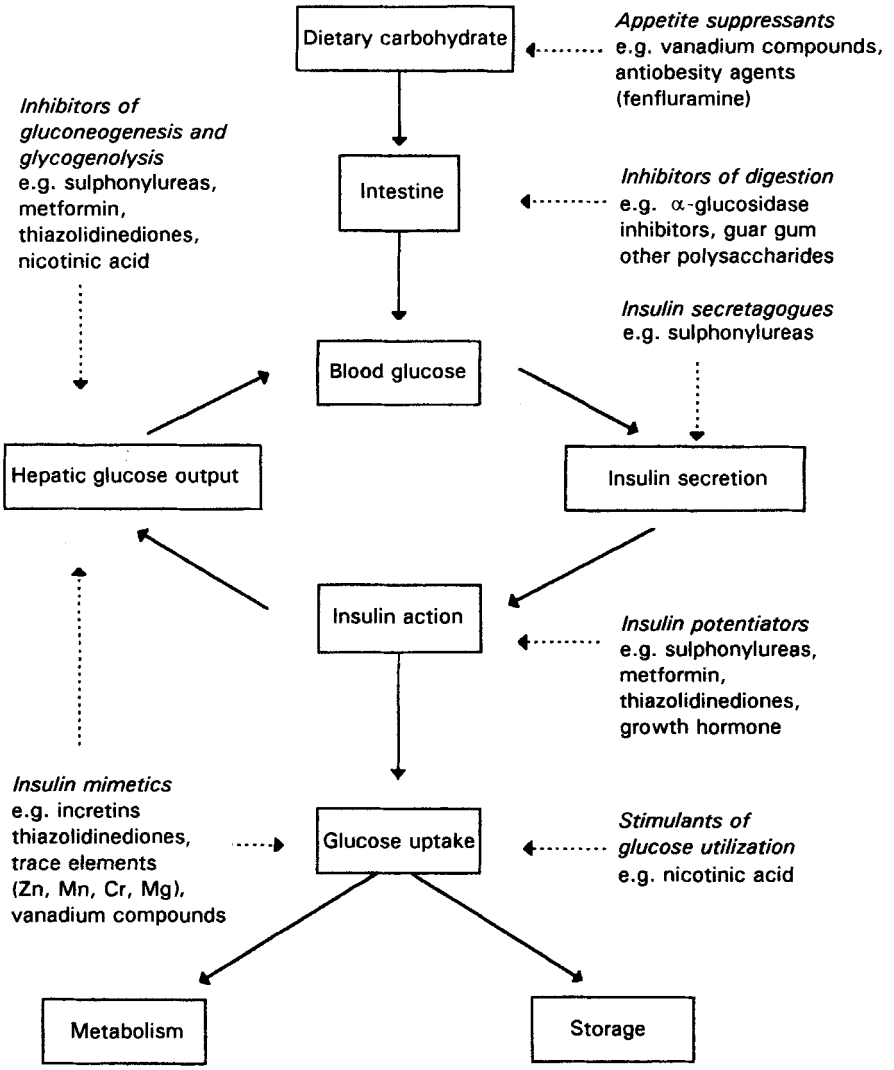

Fig. 1. Approaches to the control of hyperglycaemia. α-Glucosidase, *EC* 3.2.1.20. (Adapted from Bailey & Flatt, 1995).

address the underlying metabolic lesions in NIDDM, ideally requires new pharmacological treatments which stimulate both the secretion and the action of insulin (Bailey & Flatt, 1995).

HYPOGLYCAEMIC AGENTS FROM PLANTS

With few exceptions, traditional plant treatments for diabetes have not claimed to be alternatives to insulin therapy in IDDM. Isolated reports have described plant-derived materials that exert an insulin-like effect in IDDM (Chandola & Tripathl, 1981; Khanna *et al.* 1981). However, these reports have not been independently evaluated, and there is no evidence that they could provide a long-term botanical substitute for insulin. A small

Table 2. *Purported hypoglycaemic chemicals from plant sources*
(Compiled from Bever & Zahnd, 1979; Duke, 1985; Ling-Hua & Pei-Gen, 1993)

Aconitan A-D (glycans)	Ganoderan A & B (glycans)	Nicotinamide
Allican (diallyl disulphide oxide)	Ginsenin	Obaculactone
Allylpropyl disulphide (APDS)	Ginsenoside Rb_2	Oxypeudedanin
Amellin	Guanidine	Panacem
Ammeran A-D (glycans)	Gymnemic acid	Panaquellin
Antimellin	Hypoglycin A (α-amino-2-cyclo-propylpropionic acid)	Panax acid
Atractan A-C (glycans)		Panaxan A-E (peptidoglycans)
B-sitosterol-D-glucoside	Hypoglycin B (γ-glutamyl-hypoglycin A)	Phallacin
Bassic acid	Inulin	Phallacidin
Bengalenoside	Kampferol	Phalloidin
Berberine	Khellin	Phaseolan
Catharathine	Lepidin	2-Propenyl-disulphide
Charantin (momordicin)	Leurosine	Puerarin
Clauseanacoumarine	Lithosperman A-C (glycans)	Quercitin
Coixol	Lochnerine	Rutin
Coumarin	Lupanine	Saccharan A-F (glycans)
Diallyl trisulphide	Matrine	Scopoletin
Dioscoran A-F (glycans)	Momordicin (charantin)	Tecomine
Diphenylamine	Myricetin	Tecostamine
Emeriamine (R-3-acetylamine-4-trimethylaminobutyric acid)	Mytillin	Tecostamine-B-sitosterol
Eritadenine	N-methylnicotinic acid	Tetrahydroalstonine
Ephedran A-E (glycans)	Neomyrtillin (7-methyl-delphinidin)	Trigonelliine
Epicatechin	Nicotinic acid	Urticin
Foetidin		Vegulin
Forskolin		Vindoline
Galegine		Vindolinine

number of review articles exist which document hypoglycaemic agents derived from plant treatments for diabetes (e.g. Bever & Zahnd, 1979; Duke, 1985; Day, 1990; Ling-Hua & Pei-Gen, 1993). Several anti-diabetic plants have shown sufficient hypoglycaemic activity to warrant at least partial characterization of the active principle (Table 2). Many traditional plant treatments owe their folklore reputation, at least in part, to the presence of polysaccharides, which achieve beneficial effects through reduction of gastointestinal processing and postprandial hyperglycaemia. Plants which have yielded anti-diabetic polysaccharides are shown in Table 3. However, for the majority of traditional plant treatments the active principles present together with their mode of action have yet to be characterized (Ajgaonkar, 1979; Day & Bailey, 1988*a*). Hypoglycaemic compounds from plants that help directly combat insulin resistance and/or promote endogenous insulin release are realistic possibilities.

CELLULAR MECHANISMS OF ACTION

A few comprehensive studies of traditional anti-diabetic plants have been carried out (Swanston-Flatt *et al.* 1989*a*,*b*, 1990*a*). The anti-hyperglycaemic actions of thirty-seven European plants traditionally used as adjuncts to the treatment of diabetes were investigated using streptozotocin-treated mice and *db/db* mice (Swanston-Flatt *et al.* 1990*b*). A number of plants tested were found to have variable beneficial effects (Swanston-Flatt *et al.* 1990*b*). The mechanism of action of aqueous extracts of a number of

Table 3. *Plants purported to obtain hypoglycaemic activity from polysaccharides*
(Adapted from Bailey & Day, 1989)

Botanical name	Common name	Part of plant used	Proposed activity	Activity shown	Reference
Aconitum carmichaeli	Monkshood	Root	Aconitan A-D	Diabetic mice	Konno *et al.* (1985*c*)
Amorphophallus konjac	Lily	Tuber	Konjac mannan	NIDDM, IDDM patients	Doi *et al.* (1979)
Anemarrhena asphodeloides	Chinese zhi mu	Rhizome	Ammeran A-D	Diabetic mice	Takahashi *et al.* (1985*a*)
Atractylodes japonica	Byaku jutsu	Rhizome	Atractan A-C	Diabetic mice	Konno *et al.* (1985*d*)
Cyamopsis tetragonolobua	Guar	Seed and pod	Galactomannan	NIDDM, IDDM patients	Pillai *et al.* (1980)
Dioscorea japonica	Mexican yam	Rhizophor	Dioscoran A-F	Diabetic mice	Hikino *et al.* (1986*a*)
Eleutherococcus senticosus	Siberian ginseng	Root	Eleutherans A-G	Diabetic mice	Hikino *et al.* (1986*c*)
Ephedra distachya	Joint fir	Aerial	Ephedran A-E	Diabetic mice	Konno *et al.* (1985*b*)
Ganoderma lucidum	Bracket fungus	Fruit body	Ganoderan A, B	Diabetic mice	Hikino *et al.* (1985)
Lithospermum erythrorhizon	Red gromwell	Root	Lithosperman A-C	Diabetic mice	Konno *et al.* (1985*a*)
Oryza sativa	Rice	Root	Oryzaran A-D	Diabetic mice	Hikino *et al.* (1986*b*)
Panax ginseng	Ginseng	Root	Panaxans	Diabetic mice	Day (1986)
Panax quinquefolium	American ginseng	Root	Quinquefolan A-C	Diabetic mice	Oshima *et al.* (1987)
Saccharum officinarum	Sugar cane	Stalk	Saccharan A-F	Diabetic mice	Takahashi *et al.* (1985*b*)

NIDDM, non-insulin-dependent diabetes mellitus; IDDM, insulin-dependent diabetes mellitus.

Table 4. *Mechanism of action of traditional plant treatments for diabetes*

Common name	Botanical name	Part used	Extra-pancreatic effect	Pancreatic effect
Agrimony	*Agrimony eupatoria*	Leaf	✓	✓
Coriander	*Coriandrum sativum*	Seed	✓	✓
Elder	*Sambucus nigra*	Flower	–	✓
Eucalyptus	*Eucalyptus globulus*	Leaf	✓	✓
Juniper	*Juniperus communis*	Dried berry	–	?
Lucerne	*Medicago sativa*	Leaf	✓	✓
Mistletoe	*Viscum album*	Leaf and stem	–	✓
Mushroom	*Agaricus campestris*	Fruiting body	✓	✓

✓, beneficial (enhancing) effect; –, not investigated; ?, effect queried.

these plants has recently been investigated. At the cellular level, plants could elicit beneficial anti-hyperglycaemic effects via extra-pancreatic and/or pancreatic actions. Aqueous plant extracts, prepared by methods similar to those used in previous animal studies, were investigated for possible extra-pancreatic and/or pancreatic effects. Glucose uptake and metabolism by abdominal muscle isolated from weanling mice was used to evaluate the extra-pancreatic potential of plant extracts. Insulin-secreting BRIN-BD11 cells (McClenaghan *et al.* 1996) were used to investigate the possible pancreatic actions of plant extracts. Aqueous extracts of agrimony (*Agrimony eupatoria*), lucerne (*Medicago sativa*), coriander (*Coriandrum sativum*) and edible mushroom (*Agaricus campestris*) enhanced insulin secretion and mimicked the effect of insulin on glucose metabolism *in vitro* (Gray *et al.* 1994; Gray & Flatt, 1994, 1996, 1997). Such dual pancreatic and extra-pancreatic actions would prove to be an important advance on existing therapies used to treat and control diabetes, such as oral hypoglycaemic drugs (which act either by enhancing insulin secretion or by improving the action of insulin). Findings for these and additional plant extracts are outlined in Table 4.

INHERENT DIFFICULTIES WITH STUDIES

Discrepancies do arise between findings reported in the literature. Juniper (*Juniperus communis*) berries have in the past been documented as a traditional remedy for diabetes (Palaiseul, 1983) and serve as an illustration of the inherent difficulties encountered when examining data to hand. Juniper reduced loss of body weight, decreased polydipsia and countered the early hyperglycaemia of streptozotocin-treated mice (Swanston-Flatt *et al.* 1990*a*). A significant dose-dependent hypoglycaemic effect has been reported in normoglycaemic rats, and weight gain in chronic treatment of streptozotocin-diabetic rats administered a decoction of juniper berries (DeMedina *et al.* 1994). However, more recent studies in streptozotocin-treated mice failed to show an anti-hyperglycaemic effect and, if anything, polydipsia and glycaemia worsened with juniper treatment (Fig. 2). A confounding factor in all these studies is the difficulty in making direct comparisons between them. Sensitivity to streptozotocin varies with species, strain, sex, age and nutritional state (Bailey & Flatt, 1991). In general terms, animals in the studies of DeMedina *et al.* (1994) received approximately a 10-fold greater amount of juniper when compared with results of our studies (Fig. 2) or those of Swanston-Flatt *et al.* (1990*a*). Juniper berries vary in their content of volatile oil (2–34 g/kg) depending on the geographical location, altitude, degree of ripeness and other factors (Duke, 1985). Anti-

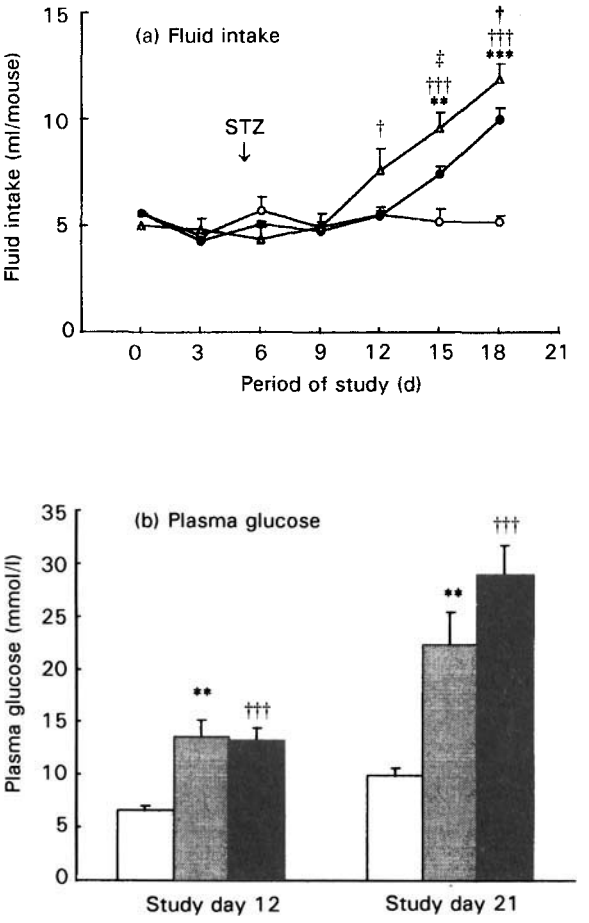

Fig. 2. Effect of juniper (*Juniperus communis*) on streptozotocin (STZ)-treated mice on (a) fluid intake and (b) non-fasting plasma glucose concentrations. Juniper was administered for 21 d (62·5 g/kg feed, 1 g/400 ml in place of drinking water) *ad libitum*. STZ was administered to non-fasting animals on study day 5 (200 mg/kg intraperitoneally). Treatment groups were: normal mice receiving normal diet (–○–, □), STZ mice receiving normal diet (–●–, ▨), STZ mice receiving juniper (–△–, ■). Values are means with their standard errors represented by vertical bars for groups of five to eight adult male mice. Mean values for STZ mice were significantly different from those for normal mice at the same time point. $^{**}P < 0{\cdot}01$, $^{***}P < 0{\cdot}001$; mean values for STZ mice receiving juniper were significantly different from those for normal mice at the same time point: $\dagger P < 0{\cdot}05$, $\dagger\dagger\dagger P < 0{\cdot}001$; mean values for STZ mice receiving juniper were significantly different from those for STZ mice at the same time point: $\ddagger P < 0{\cdot}05$.

diabetic components in this plant may be variable from one batch to the next and may explain previous favourable findings for this plant. Recent studies examined the possible pancreatic action of juniper (Table 4). The insulin-releasing potential of an aqueous extract of juniper was evaluated using insulin-secreting BRIN-BD11 cells (Fig. 3). The increase at 10 mg/ml appears to be an artefact of this experimental situation, since at this concentration the extract is toxic to the cells. DeMedina *et al.* (1994) reported an increase in glucose uptake by rat diaphragm at doses equivalent to 0·1 mg/ml, but this has yet to be independently evaluated.

https://doi.org/10.1079/PNS19970051 Published online by Cambridge University Press

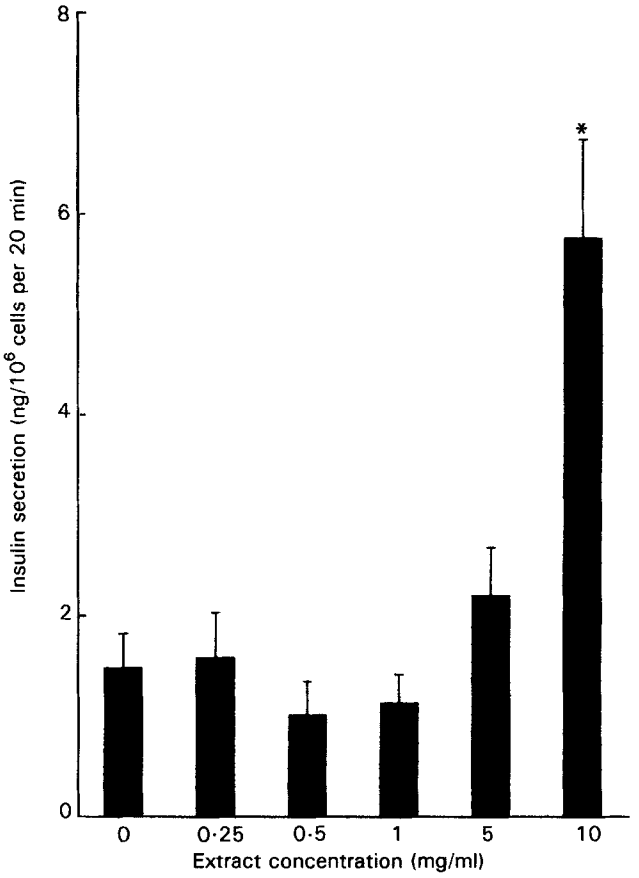

Fig. 3. Effect of aqueous extract of juniper (*Juniperus communis*) berries on insulin secretion by BRIN-BD11 cells. Extract was produced by 15 min hot infusion (ground plant material placed in boiling water, covered, removed from heat and allowed to stand for 15 min before being filtered). Values are means with their standard errors represented by vertical bars for four to six independent observations. Mean values were significantly different from those for control incubations performed without extract: $*P < 0{\cdot}001$.

FROM PLANT TO PHARMACY

Besides providing active raw materials, plants can offer molecules that serve as templates for the development of new drugs. Goat's rue (*Galega officinalis*), used in Europe as a treatment for diabetes since medieval times, yields a hypoglycaemic principle rich in guanidine (Bailey, 1985). Further derivatives of this principle have given rise to biguanides and the present anti-diabetic agent, metformin (Sterne, 1969). A balanced approach to traditional plant treatments for diabetes is required which allows for proper scientific and medical evaluation together with cautious optimism in the face of sometimes conflicting scientific evidence.

CONCLUDING THOUGHTS

The rapidly increasing prevalence of diabetes mellitus in many parts of the world, coupled with increasing life expectancy and related demographic changes, will continue to

https://doi.org/10.1079/PNS19970051 Published online by Cambridge University Press

challenge the resourcefulness of scientists and clinicans in refining existing therapies and developing new approaches to counter diabetes mellitus (Bailey & Flatt, 1995). Given the large number of plants and plant extracts reputed to possess anti-diabetic properties (Day, 1990), few have received equitable scientific and medical scrutiny, and only a small number of purportedly-active compounds have been wholly or partially characterized. The scope for the discovery and development of new anti-diabetic therapies from nature's pharmacy is vast and merits corresponding consideration.

A.M.G. was supported by the Department of Health and Social Services, Northern Ireland.

REFERENCES

Ahmad, N., Khan, M. M., Rastogi, A. K. & Kidwai, J. R. (1984). Effect of age on *Agaricus bisporus* PHA-B stimulated insulin release and $^{45}Ca^{2+}$ uptake *in vitro* by islets of Langerhans. *Acta Diabetologia Latina* **21**, 349–355.

Ajgaonkar, S. S. (1979). Herbal drugs in the treatment of diabetes. *International Diabetes Federation Bulletin* **24**, 10–17.

Atkinson, M. (1979). *Herbs for Your Health*. New York: Dalesman Books.

Bailey, C. J. (1985). The anti-hyperglycaemic action of metformin. In *Diabetes and Metformin. A Research and Clinical Update*, pp. 17–26 [H. M. J. Krans, editor]. London: Royal Society of Medicine.

Bailey, C. J. & Day, C. (1989). Traditional plant medicines as treatments for diabetes. *Diabetes Care* **12**, 553–564.

Bailey, C. J., Day, C. & Leatherdale, B. A. (1985). Cerasee, a traditional treatment for diabetes. Studies in normal and streptozotocin diabetic mice. *Diabetes Research* **2**, 81–84.

Bailey, C. J. & Flatt, P. R. (1991). Animal models of non-insulin-dependent diabetes mellitus. In *Textbook of Diabetes*, pp. 228–239 [J. C. Pickup and G. Williams, editors]. London: Blackwell Scientific Publications.

Bailey, C. J. & Flatt, P. R. (1995). Development of antidiabetic drugs. In *Drugs, Diet and Disease*, vol. 2, *Mechanistic Approaches to Diabetes*, pp. 279–326 [C. Iaonnides and P. R. Flatt, editors]. London: Ellis Horwood.

Bever, B. O. & Zahnd, G. R. (1979). Plants with oral hypoglycaemic action. *Quarterly Journal of Crude Drug Research* **17**, 139–196.

Bunney, C. (1984). *The Illustrated Book of Herbs. Their Medicinal and Culinary Uses*. London: Octopus.

Chandola, H. M. & Tripathl, S. N. (1981). Hypoglycaemic response to *C. tamala* in diabetes. *Abstracts of Second World Congress on Diabetes in the Tropics and Developing Countries*, Bombay, Abstr 80.

Collip, J. B. (1923). Glucokinin. A new hormone present in plant tissue. *Journal of Biological Chemistry* **56**, 513–543.

Day, C. (1986). Guar gum. *Industrial Biotechnology* **6**, 137–138.

Day, C. (1990). Hypoglycaemic compounds from plants. In *New Antidiabetic Drugs*, pp. 267–278 [C. J. Bailey and P. R. Flatt, editors]. London: Smith-Gordon.

Day, C. & Bailey, C. J. (1988*a*). A diabetologist's herbal. *Royal Society of Medicine, Current Medical Literature —Diabetes* **5**, 31–35.

Day, C. & Bailey, C. J. (1988*b*). Hypoglycaemic agents from traditional plant treatments for diabetes. *International Industrial Biotechnology* **8**, 5–8.

DeMedina, F. S., Gamez, M. J., Jimenez, I., Osuna, J. I. & Zarzuelo, A. (1994). Hypoglycaemic activity of juniper 'berries'. *Planta Medica* **60**, 197–200.

Doi, K., Matsuura, M., Kawara, A. & Baba, S. (1979). Treatment of diabetes with glucomannan (konjac mannan). *Lancet* **i**, 987–988.

Duke, J. A. (1985). *Handbook of Medicinal Herbs*. Boca Raton, FL: CRC Press.

Farnsworth, N. R. (1983). The role of medicinal plants in drug development. In *Natural Products and Drug Development*, pp. 17–30 [P. Krogsgaard-Larsen, S. Brogger-Christensen and S. Kofod, editors]. Copenhagen: Munksgaard.

Farnsworth, N. R. & Segelman, A. B. (1971). Hypoglycaemic plants. *Tile and Till* **57**, 52–55.

Ewart, R. B. L., Kornfeld, S. T. & Kipnis, D. M. (1975). Effect of lectins on hormone release from isolated rat islets of Langerhans. *Diabetes* **24**, 705–714.

Gray, A. M., Day, C. & Flatt, P. R. (1994). Investigation of the antihyperglycaemic and insulin-releasing effects of *Medicago sativa*. *Diabetic Medicine* **11**, S20.

Gray, A. M. & Flatt, P. R. (1994). Evaluation of the antidiabetic effects of an edible mushroom (*Agaricus campestris*). *Proceedings of the Nutrition Society* **53**, 125A.

Gray, A. M. & Flatt, P. R. (1996). Investigation of the efficacy and mode of action of the traditional anti-diabetic plant, *Agrimony eupatoria*. *Diabetic Medicine* **13**, S30.
Gray, A. M. & Flatt, P. R. (1997). Evaluation of the antidiabetic effects of coriander (*Coriandrum sativum*). *Proceedings of the Nutrition Society* **56**, 45A.
Grieve, M. (1976). *A Modern Herbal*. Harmondsworth: Penguin.
Hikino, H., Konno, C., Miriu, Y. & Hayashi, T. (1985). Isolation and hypoglycaemic activity of ganoderans A and B, glycans of *Ganoderma lucidum* fruit bodies. *Planta Medica* **51**, 339–340.
Hikino, H., Konno, C., Takahashi, M., Murakami, M., Kato, Y., Karikure, M. & Hayashi, T. (1986*a*). Isolation and hypoglycaemic activity of discoran A, B, C, D, E and F: glycans of *Discorea japonica* rhizophors. *Planta Medica* **52**, 168–171.
Hikino, H., Murakami, M., Oshima, Y. & Konno, C. (1986*b*). Isolation and hypoglycaemic activity of oryzarans A, B, C and D, glycans of *Oryza sativa* roots. *Planta Medica* **52**, 490–492.
Hikino, H., Takahashi, M., Otake, K. & Konno, C. (1986*c*). Antidiabetic drugs 20: isolation and hypoglycaemic activity of eleutheran-A, eleutheran-B, eleutheran-C, eleutheran-D, eleutheran-E, eleutheran-F and eleutheran-G: glycans of *Eleurthero*coccus *senticosus* roots. *Journal of Natural Products* **49**, 293–295.
Khanna, P., Jain, S. C., Panagiriya, A. & Dixit, V. P. (1981). Hypoglycaemic activity of polypeptide-p from a plant source. *Journal of Natural Products* **44**, 648–655.
Konno, C., Mizuno, T. & Hikino, H. (1985*a*). Isolation and hypoglycaemic activity of lithospermans A, B and C, glycans of *Lithospermum erythrorhizon* roots. *Planta Medica* **51**, 157–158.
Konno, C., Mizuno, T. & Hikino, H. (1985*b*). Isolation and hypoglycaemic activity of ephedrans A, B, C, D and E, glycans of *Ephedra distachya* herbs. *Planta Medica* **51**, 162–163.
Konno, C., Morayana, M., Sugiyama, K., Arai, M., Murakami, M., Takahashi, M. & Hikino, H. (1985*c*). Isolation and hypoglycaemic activity of aconitans A, B, C and D, glycans of *Aconitum carmichaeli* roots. *Planta Medica* **51**, 160–161.
Konno, C., Suzuki, Y., Oishi, K., Munakata, E. & Hikino, H. (1985*d*). Isolation and hypoglycaemic activity of atractans A, B and C, glycans of *Atractylodes japonica* rhizomes. *Planta Medica* **51**, 102–103.
Kronberger, K. (1964). Pilze und Diabetes (Fungi and diabetes). *Bericht Naturwiss Gesellsch Bayreuth* **11**, 231–235.
Law, D. (1970). *Herbs for Cooking and for Healing*. London: Foulsnam.
Lewis, J. J. (1949). Diabetes and the insulin administration problem. *Physiological Reviews* **29**, 75–90.
Ling-Hua, Z. & Pei-Gen, X. (1993). Recent advances in studies of antihyperlipidaemic and antihyperglycaemic compounds from Chinese traditional and herbal medicines. *Phytotherapy Research* **7**, 217–226.
Lust, J. (1986). *The Herb Book*. Reading: Bantam Books, Cox and Wyman.
McClenaghan, N. H., Barnett, C. R., Ah-Sing, E., Abdel-Wahab, Y. H. A., O'Harte, F. P. M., Yoon, T-W, Swanston-Flatt, S. K. & Flatt P. R. (1996). Characterization of a novel glucose-responsive insulin-secreting cell line, BRIN-BD11, produced by electrofusion. *Diabetes* **45**, 1132–1140.
Messegue, M. (1981). *Health Secrets of Plants and Herbs*. London: Pan Books.
Mukerje, B. (1953). *Indian Pharmaceutical Codex*, vol. 1, p. 127. New Delhi, India: Indian Pharmaceutical Society.
Oshima, Y., Sato, K. & Hikino, H. (1987). Isolation and hypoglycaemic activity of quinquefolans A, B and C, glycans of *Panax quinquefolium* roots. *Journal of Natural Products* **50**, 188–190.
Palaiseul, J. (1983). *Grandmother's Secrets. Her Green Guide to Health from Plants*. Reading: Penguin Books, Cox and Wyman.
Perry, L. M. (1980). *Medicinal Plants of East and Southeast Asia. Attributed Properties and Uses*. Cambridge, MA: The MIT Press.
Peters, G. (1957). Ubersichten Insulin-Ersatzmittel pflanzlichen Ursprungs (Review of insulin substitutes from vegetable sources). *Deutsch Medizin Wochenschrift* **82**, 320–322.
Pillai, N. R., Seshadri, C. & Santhakumari, G. (1980). Hypoglycaemic effect of *Cyamopsis tetragonoloba* taub (gowar). *Indian Journal of Medical Research* **72**, 128–131.
Potron, M. (1956). Champignons et diabete (Mushrooms and diabetes). *Concours Medical* **36**, 3795–3796.
Rachman, J. & Turner, R. C. (1995). Drugs on the horizon for treatment of type 2 diabetes. *Diabetic Medicine* **12**, 467–478.
Sterne, J. (1969). Pharmacology and mode of action of the hypoglycaemic guanidine derivatives. In *Pharmacology and Mode of Action of the Hypoglycaemic Guanidine Derivatives*, pp. 193–245 [G. D. Campbell, editor]. New York: Academic Press.
Swanston-Flatt, S. K., Day, C., Bailey, C. J. & Flatt, P. R. (1989*a*). Evaluation of traditional plant treatments for diabetes: studies in streptozotocin diabetic mice. *Acta Diabetologia Latina* **26**, 51–55.
Swanston-Flatt, S. K., Day, C., Bailey, C. J. & Flatt, P. R. (1990*a*). Traditional plant treatments for diabetes. Studies in normal and streptozotocin diabetic mice. *Diabetologia* **33**, 462–464.
Swanston-Flatt, S. K., Day, C., Flatt, P. R. & Bailey, C. J. (1990*b*). Evaluation of the antihyperglycaemic properties of traditional plant treatments for diabetes in streptozotocin-diabetic and db/db mice. In *Frontiers in Diabetes Research. Lessons from Animal Diabetes*, vol. 3, pp. 286–293 [E. Shafrir, editor]. London: Smith-Gordon.

Swanston-Flatt, S. K., Day, C., Flatt, P. R., Gould, B. J. & Bailey, C. J. (1989*b*). Glycaemic effects of traditional European plant treatments for diabetes. Studies in normal and streptozotocin diabetic mice. *Diabetes Research* **10**, 69–73.

Swanston-Flatt, S. K., Flatt, P. R., Day, C. & Bailey, C. J. (1991). Traditional dietary adjuncts for the treatment of diabetes mellitus. *Proceedings of the Nutrition Society* **50**, 641–651.

Takahashi, M., Konno, C. & Hikino, H. (1985*a*). Isolation and hypoglycaemic activity of anemarans A, B, C and D, glycans from *Anemarrhena asphodeloides* rhizomes. *Planta Medica* **51**, 100-102.

Takahashi, M., Konno, C. & Hikino, H. (1985*b*). Isolation and hypoglycaemic activity of saccharans A, B, C, D, E and F, glycans of *Saccharum officinarium* stalks. *Planta Medica* **51**, 258–260.

Weragoda, P. B. (1980). Some questions about the future of traditional medicine in developing countries. *Journal of Ethnopharmacology* **2**, 193–194.

World Health Organization (1980). *World Health Organization Expert Committee on Diabetes Mellitus. Second Report. Technical Report Series* no. 646. Geneva: WHO.