Invited commentary

Traditional plant treatments for diabetes mellitus: pharmaceutical foods

Recent decades have seen a resurgent interest in traditional plant treatments for diabetes. This has pervaded nutrition, the pharmaceutical industry and academic research, fuelled by a growing public interest and awareness of so-called complementary and natural types of medicine. Before the advent of insulin therapy in 1922, starvation diets and traditional plant treatments were the cornerstone of antidiabetic therapies. Traditional herbal preparations continue to form the predominant therapeutic approach in many deprived regions of the globe, but in occidental societies insulin was soon recognized as the miracle life-saver and traditional plant treatments were forgotten (Day & Bailey, 1988).

Plants are not a known source of insulin, and aside from some unsubstantiated anecdotal claims there is no known herbal insulin substitute. So how can we explain the renewed and increasing interest in traditional antidiabetic plants? There are probably several contributing factors, including changes in the epidemiology of diabetes and attitudes to its control. As illustrated by the paper of Gray & Flatt (1998*a*), there is gathering scientific validation for the use of certain traditional antidiabetic plants, and this has encouraged botanical exploration in the quest for new antidiabetic drugs. Additionally there is the wider appeal of ‘natural’ dietary adjuncts as functional foods through which patients can gain added benefits to the management of their disease (Swanston-Flatt *et al*. 1991).

The occurrence of both type 1 (juvenile-onset) insulin-dependent diabetes and type 2 (maturity-onset) non-insulin-dependent diabetes is increasing in most communities. Type 2 diabetes now probably accounts for more than 90% of all cases of diabetes, and the latter half of this century has witnessed an epidemic in type 2 diabetes extending far beyond that which can be attributed to improved detection and screening programmes. Genes for survival during nutritional deprivation have become an encumbrance in times of nutritional plenty and increased longevity. Estimates for the world-wide prevalence of diabetes have increased from around 60 million in 1980 to about 118 million in 1995, and are set to increase to 220 million by the year 2010 (Amos *et al*. 1997).

Although insulin is a life-saver it is not a cure-all. The majority of type 2 patients are sufficiently insulin-resistant that even supra-normal insulin concentrations, which often occur during early stages of the disease, are insufficient to control the hyperglycaemia. For these patients more insulin is not necessarily the ideal treatment strategy. Both type 1 and type 2 diabetes carry an appalling burden of chronic macrovascular, retinal, renal and neuropathic complications. These complications are associated with the extent and duration of hyperglycaemia, and improved glycaemic control defers their onset and slows their progression. Unfortunately, neither insulin injections nor oral antidiabetic drugs (sulphonylureas, metformin and acarbose) reinstate a normal pattern of glycaemic control, whether used alone or in combination, and whether administered as a standard or intensive regimen (UKPDS Group, 1995). The yawning gap for additional agents to combat hyperglycaemia and its accompanying complications presents an opening to revisit traditional antidiabetic plants (Gray & Flatt, 1997*a*).

Diet is, of course, the foundation of diabetic control, and the dietary recommendations for diabetic patients are entirely consistent with a normal healthy balanced diet. Energy from carbohydrate, taken almost entirely from complex sources high in natural fibre and starch, should exceed 50% of the total daily energy intake. Fat should contribute less than 30% of the energy, with saturates counting less than 10%, while protein accounts for the remaining energy, typically more than 10%. Salt, refined sugars and foods rich in cholesterol should be minimized, while ensuring adequate vitamins and minerals.

Traditional antidiabetic plant treatments provide an object lesson in the functionality of foods (Swanston-Flatt *et al*. 1991). Enriching the diet with natural fibre, complex carbohydrate, vegetable protein, antioxidants and minerals is encouraged. Added value occurs by achieving this with plants that have antidiabetic properties in their own right.

Many traditional antidiabetic plants probably act at least in part through their fibre, vitamin or mineral content. Mineral deficiencies are common in diabetes and can exacerbate insulin resistance. Several of these minerals are co-factors for signalling intermediaries of insulin action and key enzymes of glucose metabolism. Mineral supplements can benefit patients with mineral deficiencies, as demonstrated with magnesium and zinc. Plants rich in minerals have also been shown to benefit glycaemic control in diabetic patients, for example manganese in lucerne, chromium in brewer’s yeast, and a cocktail of minerals in *Atriplex halimus* (saltbush) (Day, 1990).

Several plants have provided entirely new hypoglycaemic compounds such as castanospermine in *Castanospermum australe* and neomyrtillin in bilberry (Day, 1990). Unfortunately, many of these compounds are alkaloids, flavonoids and glycosides which do not lend themselves readily to pharmaceutical development (Day, 1995). It is also likely that traditional antidiabetic plants are sources of agents which can benefit the co-morbid conditions of dyslipidaemia, hypertension or atherosclerosis, for example the lipid-lowering properties of garlic. Complications of diabetes may also be targeted by antidiabetic plants, for example evening primrose oil, a source of γ-linolenic acid, has been shown to benefit nerve conduction disorders in diabetes.

An ethnobotanical approach to the search for new antidiabetic drugs (Oubre *et al*. 1997) is gaining credibility and urgency – test now while rain forests last. Yet so vast is nature's warehouse and so complicated are the isolation and testing procedures that progress has been slow, requiring whole-organism screening and rigorous control procedures. Although more than 1000 plants have been claimed to offer special benefits in the treatment of diabetes, few have received detailed scientific investigation, leaving scope for extensive further work.

Academic programmes of research which vindicate claims of antidiabetic activity and identify modes of action are exposing potential antidiabetic compounds and possible novel targets for intervention (Swanston-Flatt *et al*. 1989, 1990; Gray & Flatt, 1997*b*, 1998*a*). As the work of Peter Flatt's group has recently highlighted, several traditional antidiabetic plant materials which are components of a normal diet do indeed exert antidiabetic activity by improving various parameters of glucose metabolism: agrimony, mushrooms and karela are good examples (Day *et al*. 1989, Swanston-Flatt *et al*. 1989, 1990; Gray & Flatt, 1998*a*, 1988*b*).

While looking to exploit traditional antidiabetic plant products we must be mindful that natural is not necessarily safe (Bailey & Day, 1989). Certain foods should not be taken in excess or to the exclusion of a normal balanced diet. Indeed some plants exert their efficacious effects via toxic routes, for example unripe ackee apple (*Blighia sapida*) inhibits gluconeogenesis, and excessive quantities can be fatal. Nevertheless traditional antidiabetic plants provide us with the opportunity to pick the brains of generations of experience, and we should not overlook the possibility that some potentially valuable treatments are already on the plate in front of us.

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