หอสมุดกลาง จุฬาลงกรณมหาวิทยาลัย



# Chapter I

## INTRODUCTION

Diabetes mellitus is a disease of derangement of glucose metabolism which is usually due to an insufficient output of endogenous insulin, as a result of which the blood sugar level is abnormally high and sugar appears in the urine. The most common symptoms of the disease are polyuria, polydipsia, tiredness and loss of weight. The disturbance in carbohydrate metabolism is associated with the fact that the liver and skeletal muscles cannot store glycogen and the tissues are unable to utilise glucose. Protein metabolism in the liver is also deranged and an excessive amount of protein is transformed into carbohydrate. In addition the amount of fat metabolised by the diabetic patient is excessive, and since normal fat catabolism can only proceed at limited rate, ketone bodies are present in the blood and the urine in much large amounts than normally. These substances are excreted in the urine as β-hydroxybutyric acid, acetoacetic acid, and as acetone; the latter also appears in the breath. Accumulation of these acids in the blood produces acidosis; furthermore acetoacetic acid has a toxic effect which leads to coma, circulatory collapse and death of the patient (Wilson and Schild, 1968).

It is believed that the usual cause of diabetes is the hereditary degeneration of the beta cells of the islets of Langerhans in the pancreas. It is well known that two types of diabetes can be differentiate: juvenile and maturity onset diabetes. Juvenile diabetes is caused by a true lack of insulin

and can be treated only by regular injections of inculin. In contrast, maturity onset diabetes occurs only in adults. This type of diabetes is not caused by a simple lack of endogenous insulin supply; in fact, plasma insulin levels in these patients are normal or even higher than normal. It might be assumed that there are so many factors involved in this maturity onset diabetes. Maturity onset diabetes is influenced beneficially by dietary control, by a number of synthetic hypoglycomic drugs, and by certain natural medicinal herbs. Jain and Sharma (1967) investigated the hypoglycemic activity of about 56 species of Indian indegenous plants. Only nine species were found to possess the hypoglycemic activity in normal rabbits; the observed decrease in the blood sugar levels, in milligrams per cent, between the 2nd and the 5th hour after the administration of the drug, is shown in Table 1. Some of the crude drugs used in South East Asia against diabetes were studied by Mueller-Oerlinghausen and his coworkers in 1971 on the hypoglycemic activity in certain healthy animals; the results of these studies are shown in Table 2.

Among the various Thai medicinal plants which have been popularly claimed by traditional old-styled Thai doctors and diabetic patients to be effective against diabetes are Solanum sanitwongsei and Solanum trilobatum.

Solanum sanitwongsei Craib. (Mawaeng-kreua) is a thorny, half woody, climbing hearb, 0.5 to 1 meter in height, of the

Table 2 Crude drugs used in South East Asia against diabetes*

| Name of Plant | Thai Common Name | Part of Plant | Experimental Condition | Dose g/kg | Effect |
|---|---|---|---|---|---|
| Anacardium occidentale | Ma-muang-himma-phan | leaves | 50% alcoholic extract rabbits, n = 4 | 2.5 - 10 | not different from controls |
| Coccinia indica | Tum-lung | root | alcoholic extract rabbits, n = 11 | 2.5 | slight rise of blood sugar within 4 hrs, + 18% |
| Cymbopogon citratus Stapf. | Ta-khrai | root | water extract rabbits, n = 4 | 2.5 | not different from controls |
| Eugenia jambolana | Luk-wa | seeds | 50% alcoholic extract rabbits, n = 6 | 2.5 - 5.0 | rise of blood sugar, 2 hrs after administration |
| | | | 95% alcoholic extract rabbits, n = 8 | 0.5 - 5.0 | not different from controls |
| | | | rats, n = 4 | 3.0 | slight decrease of blood sugar, 10% |
| Ficus religiosa | Pho | root | water extract | 2.5 | not different form controls |
| Psidium guajava Linn. | Fa-rung | leaves | water extract rabbits, n = 2 | 2.5 | not different from controls |
| | | | mice, n = 6 | 1.0 | not different from controls |
| | | | | 5.0 | rise of blood sugar, + 16% |
| | | | 50% alcoholic extract rabbits, n =2 | 5.0 | not different from controls |
| | | | mice, n = 6 | 1.0 - 5.0 | not different from controls |
| Solanum sanitwongsei | Ma-waeng-khrua | fruits | 50% alcoholic extract (cold) from fresh extract rabbits, n = 8 | 5.0 | slight decrease of blood sugar, 10% further investigation required |
| Solanum tovum | Ma-Khua-phuang | fruits | 50% alcoholic extract rabbits, n = 8 | 5.0 | not different from controls |
| Vinca rosea | Phang-phuai-fa-rang | whole plant | 50% alcoholic extract rabbits, n = 4 | 2.5 - 5.0 | strong rise of blood sugar, 51% all animal died within 6 days after administration |
| Zea mays Linn. | Khao-pot | hairy part of the corn ear (corn silk) | 50% alcoholic extract rabbits, n = 4 | 2.5 | not different from controls |

*From Mueller-Oerlinghausen et al. (1971)

Table 1

Hypoglycemic effect of different plant species on normal rabbits*

| Effective plants | Part of the plants | Hypoglycemic produced** |
|---|---|---|
| Allium cepa | bulbs | 20-30 mg |
| Adiantum capillus-vereris | entire plant | 10-15 mg |
| Ficus glomerata | bark | 13-21 mg |
| Gymnema sylvestre | entire plant | 10-18 mg |
| Momordica charantia | small variety, unripe fruits | 10-18 mg |
| Musa sapientum | flowers | 15-24 mg |
| Nymphaea lotus | roots | 14-15 mg |
| Pinus roxburghii | bark and roots | 10-15 mg |
| Syzigium cumini | fruits and seeds | 12-23 mg |

*From Jain and Sharma (1967)

**Blood sugar level decreased from normal

genus Solanum, Solanaceae. The leaves are oblong-ovate, 5 to 9 centimeters long, 3.5 to 8 centimeters wide, blunt at the tip, heart-shaped, square-shaped or pointed at the base, lobed in the margins and thorny underneath midrib. The flowers are violet, on 8 to 15 millimeter stalks, and borne on racemes. The calyx is oblong-triangular, being about 4 millimeters long. The corolla lobes are oblong-lanceolate,about 8 millimeters long, and 5 millimeters wide. The fruit or berry is smooth, smoewhat rounded, about 1 centimeter in diameter, and has a bitter taste. The young berry is white with green stripes and the ripe one is red. The seeds are compressed, pale, copiously punctulate, and 2 millimeters in diameter (Quisumbing, 1951). (Fig. 1).

The ripe berries of S. sanitwongsei have long been recognized in local medicine and largely used as an adjuvant for their bitter taste and their juice has been used as the vehicle mostly for mixing with other well ground drugs to make a pasty mass, popularly known as "Ya Kwad" which is usually administered to small children as an antitussive. It has been also claimed that S. sanitwongsei berries possess the hypoglycemic action and the isolation of active principles has been from time to time attempted by some investigators.

Smith (1927) reported that S. sanitwongsei berries taken orally had marked effect on the sugar content of urine in diabetes. He continued that the discovery of the virtue of this plant was made by the late Dr. Yai S. Sanitwongse. He

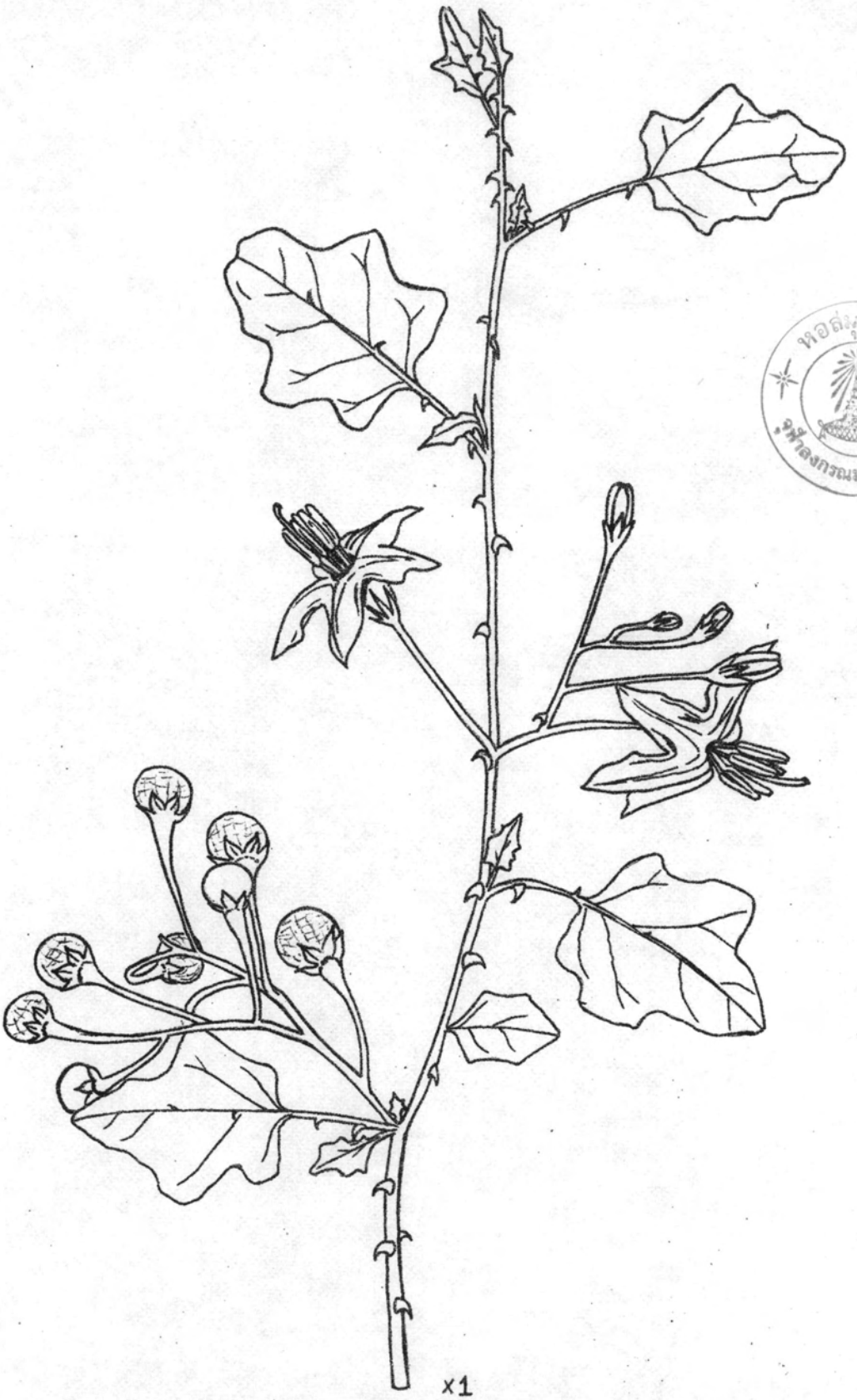


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Fig.1 Solanum sanitwongsei Craib. (Mawaeng-kreua)

claimed that the daily ingestion of these berries in a very small quantity at each meal, could keep the blood sugar of a diabetic in abeyance and led to the improvement in the general condition of the patients without any restriction in the diet, in spite of the fact that the Thai diet is comprised of a large portion of carbohydrates. The presence of sugar in urine was stopped and would remain undetectable for about twenty hours after the berries were taken. Smith also reported that the beneficial results were noted immediately, and after six months of taking at each meal ten of the fresh berries (about 1.5-2.0 grams in weight) and without the use of any other antidiabetics or any systematic regulation of diet, the physical condition was greatly improved; the sugar was being kept entirely in abeyance and he found that it was not necessary to increase the number of the berries.

In 1928, S. sanitwongsei berries evoked much interest, but the ground of its reputation as a cure for diabetes might be designated as unproved. Owing to its popular reputation a crop of fruit was collected from known and cultivated species, and was sent abroad for chemical and clinical investigation by the British Drug Houses Ltd. Unfortunately, the results so far obtained were entirely negative. The berries contained no alkaloids, glycosides nor any guanidine derivatives, and large doses of an extract administered to the rabbits produced no change in blood sugar (Report, 1928-1930).

Long and Bischoff (1929) reported that after an extract of 6.5 ml, representing 25 g of S. sanitwongsei berries, was given to a rabbit subcutaneously, blood sugar and urea nitrogen of the animal were markedly increased, indicating that the berries extract contained certain active principle sharing the hyperglycemic property of adrenaline, and that it could hardly be regarded as a substitute for insulin.

Karunyavanich and Suvagondh (1949) found that Mawaeng-kreua (S. sanitwongsei) berries contained at least two types of active constituents, alkaloidal and glycosidal. Both showed antagonistic effects on the blood sugar levels. The alkaloidal fraction possesses hyperglycemic property. This may be correlated to results of the experiment shown by Long and Bischoff. The glycosidal fraction possesses hypoglycemic property when given either subcutaneously or orally, and can maintain the blood sugar at lower levels for hours.

In 1954, Sumondit and Youngnoi gave a crude aqueous extract of S. sanitwongsei berries to rabbits to study its hypoglycemic action, but the result obtained was not satisfactory.

Wongmanee (1966) found that the extract of the Mawaeng-kreua berries contained three basic organic compounds which are likely to be alkaloids, having $R_f$ values of 0.07, 0.24 and 0.53, galactose and an unknown free carbohydrate.

Solanum trilobatum Linn. (Mawaeng-ton) is a scandent undershrub, 6 to 12 feet in height, nearly glabrous, prickles

short, stout, compressed and recurved. The leaves are irregularly sinuate-lobed, base broad often emarginate, 7 to 8 centimeters long, 3.5-4 centimeters wide, hairy underneath, and petiole 1.5 to 4 centimeters long. Peduncles are short, mostly extra-axillary, pedicels umbelled, 1.5 to 4 centimeters long, with short, strong and recurved prickles. Calyx-lobes are ovate-oblong, 0.5 centimeter long minutely stellately pubescent or glabrate, rarely prickly, hardly enlarged in fruit. The corolla lobes are triangular-lanceolate, about 2.5 to 4 centimeters across, violet. The fruit or berry is smooth, rounded, 0.7 to 1 centimeter in diameter. The young berry is light green with dark green stripes, and the ripe one is orange with the bitter taste. This herb is native of South East Asia and found in gardens or sometimes on waste ground in the Malay Peninsula. (Fig. 2).

It is much used by the Tamils as a medicine under the name "thuthuvelai", the bitter root and young shoots being given as an electuary, a decoction, or a powder for consumption. The Tamils seemed to have introduced its use into Malaya, where Chinese herbalists sometimes stocked it (Burkill, 1935). Berries and flowers were given in cough, and its decoction was used in chronic bronchitis (Chopra et al., 1956). Its berries were said to contain an alkaloid, saponin and an alkaloidal glycoside (Lekavanichtharmbhitak, 1946). In Thailand, some diabetic patients and old-styled Thai doctors claimed that daily use of the berries of S. sanitwongsei or of S. trilobatum in a very

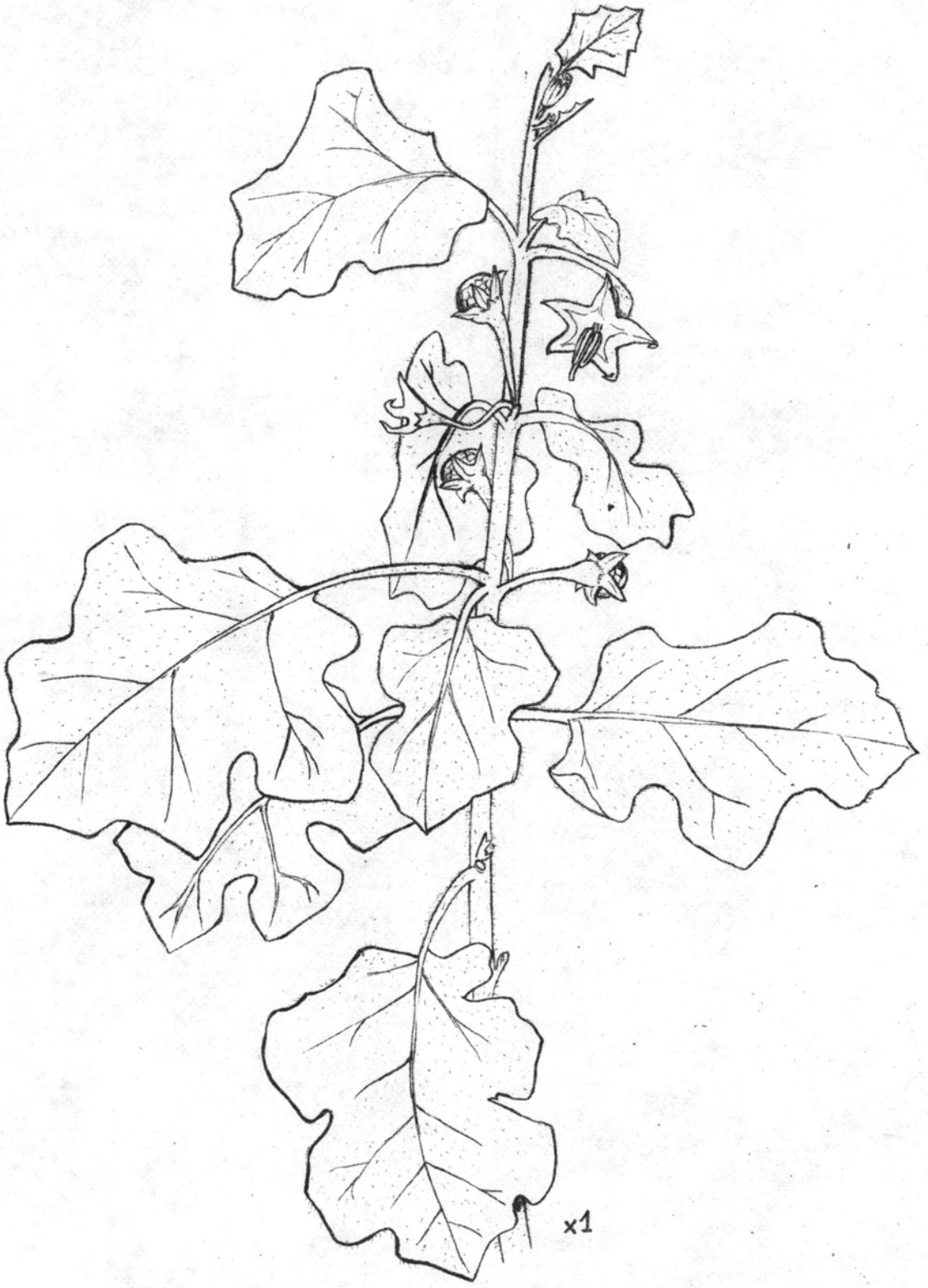


Fig.2 Solanum trilobatum Linn. (Mąwaeng-ton)

small quantity at each meal, or in the form of a decoction, showed a beneficial effect in diabetes.

In order to test this hypothesis, the present work has undertaken to investigate the hypoglycemic activity of S. santiwongsei and of S. trilobatum in the intact healthy rabbits.