CHAPTER III

LITERATURE REVIEW

Ancient people used Aloe vera for various diseases. In Mesopotemia, clay tablets dated 1750 B.C.E. recorded the use of Aloe vera for treatment of diseases. Books from ancient Egypt and from ancient Greek also mentioned the therapeutic use of Aloe vera. Aloe was used mostly as a cathartic medicine, but people also use Aloe vera for other kinds of diseases. Reported applications of Aloe vera include seborrheic dermatitis, thermal burns and sunburn, cystic acne, peptic ulcers, laceration, colds, tuberculosis, gonorrhea, ashtma, dysentery, and headaches. However, most applications do not have scientific and clinical evidences to support their uses. Recent studies on Aloe vera focus mainly on its anti-inflammatory effect and the application of Aloe vera in inflammatory skin and joint conditions. A few studies explored the use of Aloe vera in treating diabetes mellitus.

The first report that demonstrated the hypoglycemic activity of aloe plant(Aloe arborescens) appeared in 1958(Kuraev et al, 1958). Injection of aloe extract to partially-pancreatectomized rats stimulated the regeneration of the remaining pancreas(Kalinichave, 1975). The constituents that have hypoglycemic effects are polysaccharides(Hikino et al, 1986 and anthraquinones(Ghannam, 1985). The polysaccharide constituent lowered blood glucose levels in mice and in human(Ghannam, 1985, Hikino et al, 1986). The anthraquinone constituent showed hypoglycemic activity in non-insulin-dependent diabetes patients and diabetic mice(Ghannam, 1985, Ajabnoor, 1990).

Both polysaccharides and anthraquinones may mediate their hypoglycemic activity through stimulating the pancreatic b-cells to synthesize and/or release more insulin(Ajabnoor, 1990). However, the mechanism of action of Aloe vera in lowering blood glucose is controversial.

Aloe gel which contained active polysaccharides showed no toxic effects in animal models(Watanasrisin, 1988, Jirakulchaiwong, 1991). Lyophilized aloe gel given orally in doses of 1, 4, 16 and 64 mg/kg body weight two times a day did not change serum glutamic oxaloacetic transaminase ((SGOT), serum glutamic pyruvic transaminase (SGPT), blood urea nitrogen (BUN) or creatinine (Cr) levels in albino rats (Watanasrisin, 1988). In another study fresh and preserved aloe gel also showed no toxic effects in an oral dose of 5 gm/kg for 45 days. These studies demonstrated lack of serious systemic adverse effects of Aloe vera in animals.

In a study in hyperlipidemic Presbytis monkeys Aloe vera extracts lowered blood lipid levels significantly during the 48-hour study period(Dixit, 1983). However, we need to examine the hypolipidemic effect in human subjects after a longer period of administration of Aloe vera.

Agarwal(1985) reported the largest study on the effect of Aloe vera on blood glucose and blood lipid levels in 5,000 patients. Fresh flesh gelatin of Aloe vera lowered blood glucose from diabetic ranges to normal levels in 94.4% of the patients who had high blood glucose and lowered serum cholesterol levels from hypercholesterolemic to normal in 93.0% of the patients. The serum triglyceride levels also lowered from hypertriglyceridemic to normal in 93.0% of the patients. However, the study was not well-designed and details of the study were not available. The study had no control

group. Patients were not randomized and outcome measurements were ill-defined. Questions remained on the way the investigator conducted such a huge study and on both the internal and external validities of the study. However, this study offered a positive evidence on hypoglycemic effect of Aloe vera.

Ghannam(1985) conducted a clinical and experimental study on the hypoglycemic effect of Aloe vera in alloxan-induced diabetic mice and in non-insulin dependent diabetes mellitus patients. Aloe vera had hypoglycemic effects both in normal mice and in alloxan-induced diabetic mice. Aloe vera still had hypoglycemic effect in alloxan-induced diabetic mice after glibenclamide lost its hypoglycemic effect in diabetic mice. Since alloxan-induced mice develop diabetes mellitus because alloxan damages beta cell of the islets of Langerhans in the pancreas, Aloe vera might not exert its hypoglycemic effect through the synthesis and release of insulin by the beta cell.

Ajabnoor (1990) reported the effect of Aloe on blood glucose levels in normal and alloxan diabetic mice. The oral dosage of Aloe was half that used by Ghannam et al(1985). The investigator did not observe a statistically significant hypoglycemic effect of Aloe given orally in diabetic mice. But Aloe given intraperitoneally showed good hypoglycemic effect. The investigator suggested that the hypoglycemic effect of Aloe may be mediated through stimulating synthesis and/or release of insulin from the beta cells of Langerhans. This suggestion did not have firm scientific support and was in contradiction with the result by Ghannam's study. The exact mechanism of action of Aloe in lowering blood glucose levels remains controversial.

Roman-Ramos et al(1991) compared the hypoglycemic effect in rabbits of 12 medicinal plants used in Mexico for controlling

diabetes mellitus. The rabbits did not have diabetes mellitus. The study compared the area under glucose tolerance test curves derived from subjecting rabbits to water as a negative control, tolbutamide as a positive control, and a preparation of 12 medicinal plants. Only Aloe did not decrease the area under glucose tolerance curve compared with water. The suggestion from this study that Aloe did not have hypoglycemic effect may not be valid for two reasons. First, the area under glucose tolerance curve is not a standard way to demonstrate a hypoglycemic effect of any substance. Instead the glucose tolerance test gives the area under glucose tolerance curve as a measure of hyperglycemic effect of diet or substance. The area under glucose tolerance curve is not equal to or does not represent hypoglycemic effect. Second, rabbits in the study did not have diabetes mellitus. Their blood glucose responses to tolbutamide and medicinal plants may not be the same as in diabetic rabbits. The results from normal rabbits should be interpreted cautiously.

In summary, a few studies showed that Aloe vera has hypoglycemic effect in diabetic animals and in human diabetics. One study suggested that Aloe might not have hypoglycemic effect.

This study intends to add information about the efficacy of Aloe vera in lowering blood glucose levels in human subject suffering from diabetes mellitus. The design is a randomized, double-blinded, placebo-controlled clinical trial which is the "gold standard" for evaluating the efficacy of an intervention.