CHAPTER 1

DIABETES : LITERATURE REVIEW

1.1 INTRODUCTION

Diabetes mellitus is recognized as being a syndrome, a collection of disorders that have hyperglycaemia and glucose intolerance as their hallmark, due either to insulin deficiency or to the impaired effectiveness of insulin's action, or to a combination of these. In order to understand diabetes it is necessary to understand the normal physiological process occurring during and after a meal. Food passes through the digestive system, where nutrients, including proteins, fat and carbohydrates are absorbed into the bloodstream. The presence of sugar, a carbohydrate, signals to the endocrine pancreas to secrete the hormone insulin. Insulin causes the uptake and storage of sugar by almost all tissue types in the body, especially the liver, musculature and fat tissues (Roussel, 1998).

Unfortunately, there is no cure for diabetes yet but by controlling blood sugar levels through a healthy diet, exercise and medication the risk of long-term diabetes complications can be decreased. Long-term complications that can be experienced are:

- eyes – cataracts and retinopathy (gradual damaging of the eye) that may lead to blindness
- kidneys – kidney disease and kidney failure
- nerves – neuropathy (gradual damaging of nerves)
- feet – ulcers, infections, gangrene, etc.
- cardiovascular system – hardening of arteries, heart disease and stroke (Heart foundation, 2003).

The progressive nature of the disease necessitates constant reassessment of glycaemic control in people with diabetes and appropriate adjustment of therapeutic regimens. When glycaemic control is no longer maintained with a single agent, the addition of a second or third drug is usually more effective than switching to another single agent.

Medicinal plants which have showed anti-diabetic activity during earlier investigations include *Panax* species, *Phyllanthus* species, *Acacia arabica, Aloe vera, Aloe barbadensis, Artemisia pallens, Momordica charantia, Alium cepa, Trigonella foenum-graecum* etc (Soumyanath, 2006). Very few South-African plants have been scientifically analyzed for their anti-diabetic characteristics. The most recent work was done by Van Huyssteen (2007) and Van de Venter *et al*. (2008).

1.2. CLASSIFICATION OF DIABETES MELLITUS

A major requirement for orderly epidemiologic and clinical research on and for the management of diabetes mellitus is an appropriate classification. Furthermore the process of understanding the etiology of a disease and studying its natural history involves the ability to identify and differentiate between its various forms and place them into a rational etiopathologic framework (Harris and Zimmet, 1997).

The contemporary classification of diabetes and other categories of glucose intolerance, based on research on this heterogeneous syndrome, was developed in 1979 by the National Diabetes Data Group. Two major forms of diabetes are recognized in Western countries; insulin dependent diabetes mellitus (IDDM, type I diabetes) and non-insulin dependant diabetes (NIDDM, type II diabetes). The evidence of this heterogeneity is overwhelming and includes the following:

a) there are many distinct disorders, most of which are individually rare, in which glucose intolerance is a feature;
b) there are large differences in the prevalence of the major forms of diabetes among various racial or ethnic groups world-wide;
c) glucose tolerance presents variable clinical features, for example, the differences between thin ketosis-prone, insulin dependant diabetes and obese, non-ketotic insulin resistant diabetes;
d) genetic, immunologic and clinical studies show that in Western countries, the forms of diabetes with their onset primarily in youth or in adulthood are distinct entities;

e) the type of non-insulin requiring diabetes in young people, which is inherited in an autosomal dominant fashion is clearly different from the classic acute diabetes of juveniles; and

f) in tropical countries, several clinical presentations occur, including fibrocalcific pancreatitis and malnutrition-related diabetes.

This and other collective evidence have been used to divide diabetes mellitus into four distinct types namely;

- insulin dependant diabetes,
- non-insulin dependant diabetes,
- malnutrition-related diabetes,
- other types of diabetes.

The classification highlights the marked heterogeneity of the diabetic syndrome. Such heterogeneity has important implications not only for clinical management of diabetes but also for biomedical research (Harris and Zimmet, 1997). In this study the focus was mainly on type II diabetes while type I diabetes was discussed briefly to point out the differences between the two types of diabetes.

1.2.1 Insulin dependant diabetes mellitus (IDDM)

The subclass of diabetes, type I diabetes, is generally characterized by the abrupt onset of severe symptoms, dependence on exogenous insulin to sustain life and proneness to ketosis even in the basal state, all of which is caused by absolute insulin deficiency. IDDM is the most prevalent type of diabetes among children and young adults in developing countries, and was formally termed juvenile diabetes (Harris and Zimmet, 1997). It is a catabolic disorder in which circulating insulin is virtually absent, plasma glucagon is elevated, and the pancreatic B cells fail to respond to all insulinogenic stimuli (Nolte and Karam, 2001).

Type I diabetes is thought to result from an infectious or toxic environmental contingency in people whose immune systems are genetically predisposed to develop a vigorous autoimmune response against pancreatic B cell antigens. Extrinsic factors that might affect

B cell functioning include damage caused by viruses such as the mumps virus and coxsackie virus B4, by chemical agents, or by destructive cytotoxins and antibodies released from sensitized immunocytes. An underlying genetic defect relating to pancreatic B cell replication or function may predispose a person to the development of B cell failure after viral infections. In addition, specific HLA genes may increase susceptibility to a diabetogenic virus or may be linked to certain immune response genes that predispose patients to a destructive autoimmune response against their own islet cells (auto-aggression). Observations that pancreatic B cell damage appears to be lessened when immunosuppressive drugs such as cyclosporine or azathioprine are given at the initial manifestation of type I diabetes support the importance of auto-aggression by the immune system as a major factor in the pathogenesis of this type of diabetes (Nolte and Karam, 2001).

1.2.2 Non-insulin dependant diabetes mellitus (NIDDM)

Type II diabetes greatly out numbers all other forms of diabetes. Patients with NIDDM are not dependant on exogenous insulin for prevention of ketonuria and are not prone to ketosis. However, they may require insulin for the correction of fasting hyperglycaemia if this cannot be achieved with the use of diet or oral agents, and they may develop ketosis under special circumstances such as severe stress precipitated by infections or trauma (Harris and Zimmet, 1997).

The pathogenesis in type II diabetes is that the pancreas produces insulin but the body does not utilize the insulin correctly. This is primarily due to peripheral tissue insulin resistance where insulin-receptors or other intermediates in the insulin signaling pathways within body cells are insensitive to insulin and consequently glucose does not readily enter the tissue leading to hyperglycaemia or elevated blood glucose concentrations (Albright, 1997). Obesity, which generally results in impaired insulin action, is a common risk factor for this type of diabetes, and most patients with type II diabetes are obese (Nolte and Karan, 2001) and will ultimately require multiple anti-diabetic agents to maintain adequate glycaemic control (Gerich, 2001).

1.3 DIABETES MELLITUS IN AFRICA

Most countries in Africa are undergoing a demographic transition, and African urban societies are increasingly coming within the sphere of the influence of Western market economies. The lifestyle of city dwellers tends to be material-behavioural, with the adoption of cosmopolitan behaviour and consumption of resources and food, especially fast foods. This has led to an increase in the consumption of fat, sugar and salt. Rural African societies, however, have seen an increase in nutritional deficiencies, which appear to be related to drought, poverty, war and socio-economic deprivation rather than to culture or religion. In these rural areas, the focus has been on maintaining food availability rather than equitable distribution. Lifestyle changes and a very rapid increase in the urban population of Africa has led to inadequate production of local cereals and staples like sorghum, millet, maize, yam and plantain. This phenomenon has led to many countries having a low daily *per capita* dietary energy supply, and has led to a difference in food patterns between the urban and rural dwellers and the occurrence of diabetes mellitus. These lifestyle changes have evolved against a background of increasing prevalence of diabetes mellitus and diabetic complications in Africa (Yajnik, 1990; King and Rewers, 1993).

In South Africa a number of studies have been conducted and it is estimated that there are at least 6.5 million known diabetics and possibly up to an equal number who are currently undiagnosed (Healt 24, 2006). The prevalence of diabetes in South Africa is high, and is estimated to be 14% in the Coloured community, 13% in the Indian community, 6% in the African community and 6% in the European community (Society of Endocrinology, Metabolism and Diabetes in South Africa, 2003).

There is certainly, a demand for more nutrition education of the more cosmopolitan diabetic population by the limited number of poorly equipped staff who need to formulate new approaches that are more relevant to the needs of their patients (Mbanya and Gwangwa'a, 1997).

1.4 RATIONALE

The first description of diabetes is credited to Arataeus of Cappadocia in Asia Minor in the first century AD. The first attempts for treating diabetes, when no more was known about it than the polyuria, were made by Dr. John Rollo, Surgeon General to the Royal Artillery, 1796 through dietary restrictions. The discovery of insulin in 1921 by Dr Frederick Banting was a major breakthrough in the history of medicine and the treatment of diabetes (Pyke, 1997).

Diabetes mellitus (DM) is the most common endocrine disorder, and affects more than 100 million people worldwide (6% of the population) and in the next 10 years it may affect five times more people than it does now (World Health Organization and American Diabetes Association). The World Health Organization has pointed out that the prevention of diabetes and its complications is not only a major challenge for the future, but essential if health for all is to be an attainable target, and strongly emphasize the optimal, rational use of traditional and natural indigenous medicines (World Health Organization 1985, 1994).

Though the development of modern medicine resulted in the advent of modern pharmaceuticals including insulin, biguanides, sulfonylureas and thiazolidinediones there is still a need to look for new drugs as no drug (except strict glycaemic management with insulin) has been shown to control diabetic complications effectively. In relation to plants also, barring a few studies, most of the studies have not assessed the impact of these plants on the course of diabetic complications. It is necessary to evaluate plant species traditionally used against diabetes mellitus to discover new compounds that can be used effectively against this disease as well as lessen diabetic complications.

1.5. PATHOPHYSIOLOGY OF DIABETES MELLITUS

1.5.1 Physiological mechanisms and management

1.5.1.1 The Endocrine pancreas

The human pancreas is basically composed of two types of secretory cells that are both involved in nutrient handling: 98% of the cells- the exocrine type – secrete a food-processing enzyme-bicarbonate mixture into the duodenum, while the remaining 2% - the endocrine type- have a metabolic function and secrete a mixture of nutrient-generated hormones into the portal vein. This small endocrine part is of vital importance in maintaining glucose homeostasis through the action of the 51-amino acid peptide insulin. Four endocrine cell types can be distinguished: A cells (alpha), B cells (beta), D cells (delta) and PP cells (pancreatic polypeptide) (Klöppel and In't Veld, 1997). These endocrine cells are distributed throughout the pancreas in areas known as islets.

1.5.1.2 Diabetes-related islet changes

The islet changes, from a morphological point of view, associated with various types of diabetes can be divided into those with and without severe beta-cell loss. Severe beta-cell loss is found in type I diabetes and some uncommon forms of diabetes such as virus-related diabetes and congenital diabetes. Islets without severe loss of beta-cells are encountered in type II diabetes and in the secondary forms of diabetes (Klöppel and In't Veld, 1997).

1.5.2 Insulin

The beta-cells of the pancreatic islets synthesize insulin from a single chain precursor of 110 amino acids termed preproinsulin. After translocation through the membrane of the rough endoplasmic reticulum, the 24-amino-acid N-terminal signal peptide of preproinsulin is rapidly cleaved off to form proinsulin. Here the molecule folds and the disulfide bonds are formed. On the conversion of human proinsulin to insulin in the Golgi-complex, four basic amino acids and the remaining connector or C peptide are removed by proteolysis. This gives rise to the two-peptide chains (A and B) of the insulin molecule, which contains one intra-subunit and two inter-subunit disulfide bonds. The A chain usually is composed of 21 amino acids and the B chain 30. The two chains of insulin form a highly ordered structure with several α helical regions in both the A and B chains (Figure 1.1).

Two ions of Zn^{2+} are coordinated in a proinsulin hexamer and this form of insulin presumably is stored in the granules of the pancreatic ß cells. It is believed that Zn^{2+} has a

functional role in the formation of crystals and that crystallization facilitates the conversion of proinsulin to insulin, as well as the storage of the hormone (Davis and Granner, 1996).

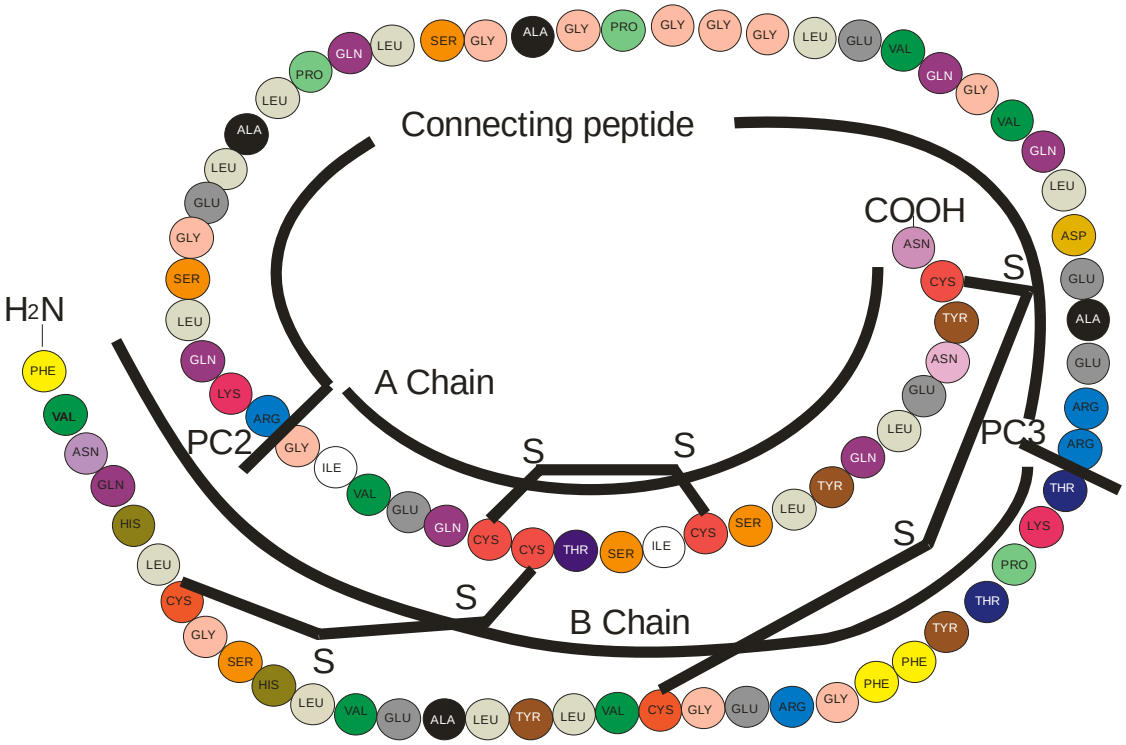

Figure 1.1. Structure of human proinsulin. Insulin is shown as the shaded peptide chains, A and B (Davis and Granner, 1996).

1.5.2.1 Insulin secretion

Insulin is released from pancreatic ß-cells at a low basal rate and at a much higher rate in response to a variety of stimuli, especially glucose. Hyperglycaemia results in increased intracellular ATP (adenosine triphosphate) levels, which close the ATP-dependent potassium channels. Decreased outward potassium current through this channel results in depolarization of the ß-cell and the opening of voltage-gated calcium channels. The resulting increased intracellular calcium triggers the secretion of the hormone (Figure 1.2).

1.5.2.2 Insulin degradation

The liver and kidney are the two main organs that remove insulin from circulation, presumably by hydrolysis of the disulfide connection between the A and B chains through the action of glutathione insulin transhydrogenase (insulinase). After this reductive cleavage further degradation by proteolysis occurs. The liver normally clears the blood of

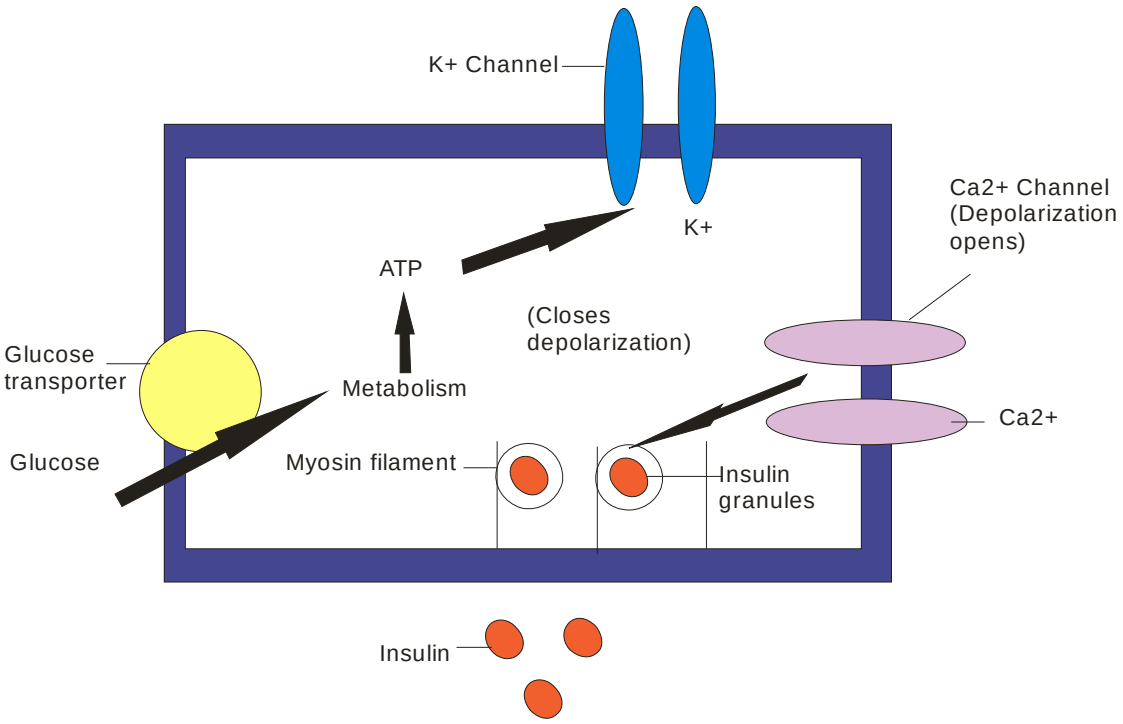

Figure 1.2. Model of the control of insulin release from the pancreatic ß-cells by glucose (Nolte and Karam, 2001).

approximately 60% of the insulin released from the pancreas by virtue of its location as the terminal site of the portal vein blood flow, with the kidneys removing 35 – 40% of the endogenous hormone. However, in insulin-treated diabetics receiving subcutaneous insulin injections, this ratio is reversed, with 60% of exogenous insulin being cleared by the kidney and the liver removing no more than 30-40%. The half-life of circulating insulin is 3-5 minutes (Nolte and Karam, 2001).

1.5.2.3 The insulin receptor

Once insulin has entered the circulation, it is bound by specialized receptors that are found on the membranes of most cells. However, the biological responses promoted by these insulin–receptor complexes have only been identified in a few target tissues, e.g. liver, muscle and adipose tissue. The receptors bind insulin with high specificity and affinity in the picomolar range. The full insulin receptor consists of two heterodimers, each containing an alpha subunit, which is entirely extra cellular and constitutes the recognition site, and a beta subunit that spans the membrane (Figure 1.3). The ß- subunit contains a tyrosine kinase. When insulin binds to the alpha subunit on the outer surface of the cell, tyrosine kinase activity is stimulated in the beta portion. Although the αß dimeric form is capable of binding insulin, it does so with a much lower affinity than the tetrameric ααßß form. Self–phosphorylation of the ß portion of the receptor causes both increased aggregation of αß heterodimers and stabilization of the activated state of the receptor tyrosine kinase.

In clinical situations associated with elevated levels of circulating insulin, such as obesity or insulinoma, the concentration of insulin receptors is reduced. This down regulation of insulin receptors seems to provide an intrinsic mechanism whereby the target cells limit their response to excessive hormone concentrations (Nolte and Karam, 2001).

1.5.2.4 Effects of insulin on its targets

Insulin promotes the storage of fat as well as glucose within specialized target cells and influences cell growth and the metabolic functions of a wide variety of tissues.

1.5.2.5 Action of insulin on glucose transporters (GLUT)

Insulin has an important effect on several transport molecules that facilitate glucose movement across cell membranes. These transporters may play a role in the etiology as well as the manifestation of diabetes. GLUT 4, quantitatively the most important in terms of lowering blood glucose, is inserted into the membranes of muscle and adipose cells from intracellular storage vesicles by insulin. Defects in GLUT 2 mediated transport of glucose into pancreatic ß-cells may contribute to the reduced insulin secretion that characterizes type II diabetes.

1.5.2.6 Action of insulin on the liver

The first major organ reached by endogenous insulin via the portal circulation is the liver, where its function is to increase storage of glucose as glycogen and to reset the liver to the fed state by reversing a number of catabolic mechanisms, such as glycogenolysis,

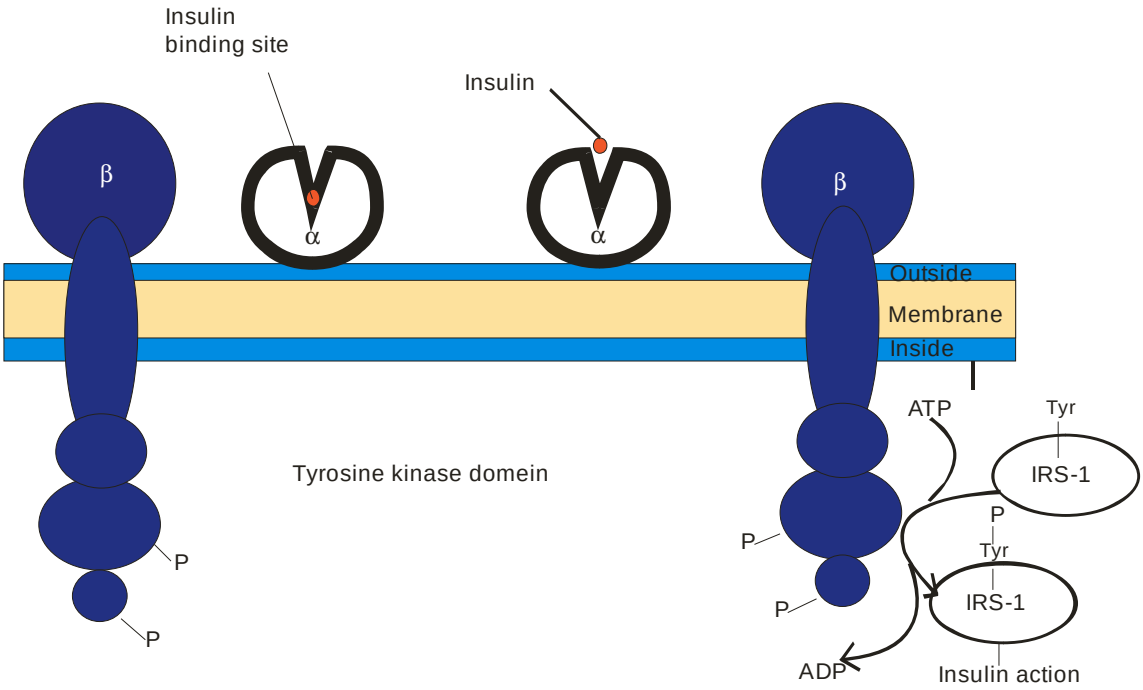

Figure 1.3. Schematic diagram of the probable structure of the insulin receptor tetramer in the activated state (Nolte and Karam, 2001).

ketogenesis, and gluconeogenesis, which are associated with the post-absorptive state. These effects are brought about directly through insulin-induced phosphorylations, which activate pyruvate kinase, phosphofructokinase and glucokinase, while reprieving gluconeogenic enzymes, including pyruvate carboxylase, phosphoenolpyruvate carboxykinase, fructose bisphosphatase, and glucose 6-phosphatase. Insulin also exerts indirect effects to decrease hepatic gluconeogenesis and ketogenesis by reducing the fatty acid flux to the liver through its antilipolytic action on adipocytes. In addition, insulin decreases urea production, protein catabolism, cAMP (cyclic adenosine monophosphate) in the liver, promotes triglyceride synthesis and, increases potassium and phosphate uptake by the liver.

1.5.2.7 Effect of insulin on muscle

Insulin promotes protein synthesis by increasing the amino acid transport and by stimulating ribosomal activity. It also promotes glycogen synthesis to replace the glycogen stores expended by muscle activity. This is accomplished by increasing the glucose transport into the muscle cells, inducing glycogen synthase, and inhibiting glycogen phosphorylase.

1.5.2.8 Effect of insulin on adipose tissue

Insulin acts on reducing circulating free fatty acids and promoting triglyceride storage in adipocytes by three mechanisms:

1) induction of lipoprotein lipase, which actively hydrolyzes triglycerides from circulating lipoproteins;
2) glucose transport into cells to generate glycerophosphate as a metabolic product, which permits esterification of fatty acids supplied by lipoprotein hydrolysis; and
3) reduction of intracellular lipolysis of stored triglyceride by a direct inhibition of intracellular lipase (Nolte and Karam, 2001).

1.6 COMPLICATIONS OF INSULIN THERAPY

Oral hypoglycaemic agents/insulin is the mainstay of the treatment of diabetes and is effective in controlling hyperglycaemia. However, it has prominent side effects and fails to significantly alter the course of diabetic complications (Rang and Dale, 1991). The main complications of insulin therapy are 1) Hypoglycaemia which may result from a delay in taking a meal, unusual physical exertion or a dose of insulin that is too large for immediate needs. Autonomic warning signals of hypoglycaemia and the manifestation of insulin excess are mainly those of impaired functions of the central nervous system such as mental confusion, bizarre behaviour and ultimately coma. More rapid development of hypoglycaemia from the effects of regular insulin use causes signs of autonomic hyperactivity, both sympathetic (tachycardia, palpitations, sweating, tremulousness) and parasympathetic (nausea, hunger) that may progress to convulsions and coma if untreated. 2) Immunopathology of insulin therapy includes i) insulin allergy, ii) immune insulin

resistance (development of anti-insulin antibodies) and iii) lipodystrophy at injection sites (Nolte and Karam, 2001).

1.7 ORAL ANTIDIABETIC AGENTS

Four categories of oral antidiabetic agents are available namely; insulin secretagogues, biguanides, thiazolidinediones, and alpha-glucosidase inhibitors (Nolte and Karam, 2001).

1.7.1 Insulin secretagogues: sulfonylureas

The major action of sulfonylureas is to increase insulin release from the pancreas. Sulfonylureas binds to a 140kDa high-affinity sulfonylurea receptor that is associated with a beta cell inward rectifier-type ATP-sensitive potassium channel. The binding of a sulfonylurea inhibits the efflux of potassium ions through the channel and results in depolarization. Depolarization, in turn, opens a voltage-gated calcium channel that results in a calcium influx and the release of insulin. Insulin synthesis is not stimulated and may even be reduced by sulfonylureas. Some evidence indicates that after prolonged sulfonylurea therapy, serum insulin levels no longer increase but may even decrease. It was also established that chronic administration of sulfonylureas to type 2 diabetic patients reduced serum glucagon levels but increased the binding of insulin to the tissue receptors (Nolte and Karam, 2001). Seven sulfonylurea drugs are available in the USA and are conventionally divided into first and second generation agents, which differ primarily in their potency. The first-generation includes tolbutamide, tolazamide, acetohexamide and chlorpropamide and the second generation includes glyburide, glipizide and glimepiride.

1.7.2 Insulin secretagogues: meglitinides

Meglitinides are a new class of insulin secretagogues. Repaglinide, the first member of the group, was approved for clinical use by the FDA in 1998. These drugs modulate Beta cell insulin release by regulating potassium efflux through the potassium channels. Meglitinides and sulfonylureas overlap in their molecular binding sites since meglitinides have two binding sites in common with sulfonylureas and one unique binding site. They have however, no direct effect on insulin exocytosis as does sulfonylureas (Nolte and Karam, 2001).

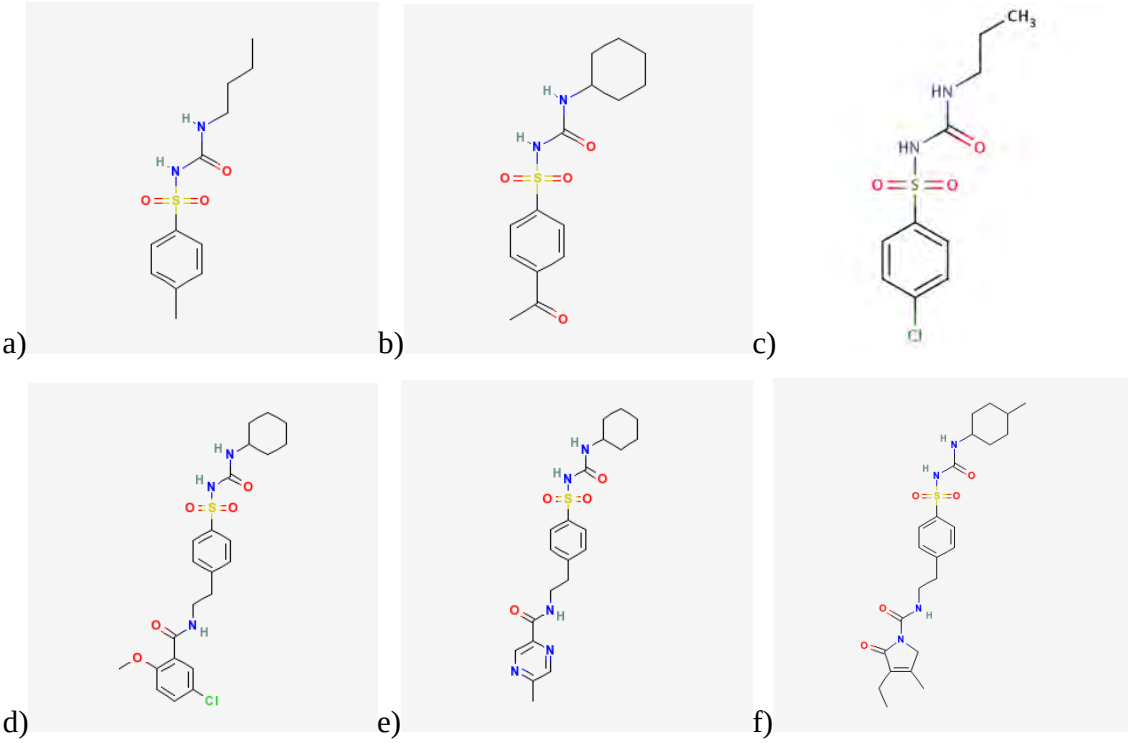

Figure 1.4 Chemical structure of the first generation sulfonylurea (a) tolbutamide, (b) tolazamide (c) chloroproamide and the second generation sulfonylurea (d) glyburide (e) glipzide and (f) glimepiride (PubChem Public Chemical Database, 2009).

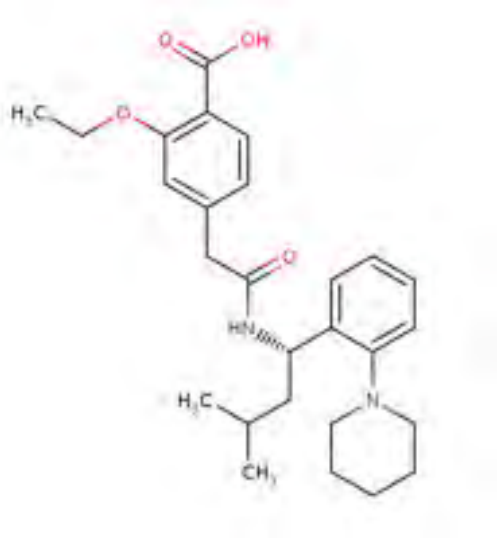

Fig 1.5 Chemical structure of the meglitinide repaglinide (PubChem Public Chemical Database, 2009).

1.7.3 Biguanides

Three types of biguanides are being used in the treatment of diabetes namely phenformin, buformin and metformin. The use of the first two mentioned was discontinued in the United States of America due to its association with lactic acidosis (Nolte and Karam, 2001).

Metformin originates from the French lilac, *Galega officinalis* L., a perennial herb known for centuries to reduce the symptoms of diabetes. The active compound is galegine, a guanidine derivative. Metformin's clinical trails were successfully completed in 1995 and its use approved in the United States of America. The full extent of the mechanism of the action of biguanides is unknown, but its blood glucose-lowering action does not depend on the presence of functioning pancreatic beta cells. Proposed mechanisms of action includes direct stimulation of glycolysis in the tissue, and the increase of glucose removal from the blood; reduced hepatic gluconeogenesis; slowing of glucose absorption from the gastrointestinal tract; with increase glucose to lactate conversion by enterocytes and the reduction of plasmaglucagon levels (Nolte and Karam, 2001).

Biguanides have been most often prescribed for patients with refractory obesity whose hyperglycemia is due to insulin resistance. As metformin is an insulin-sparing agent and does not increase weight or provoke hypoglycemiait it has the advantage over insulin and sulfonylureas in treating hyperglycemia. The most frequent toxic affects of metformin are gastrointestinal and there is a risk of lactic acidosis.

1.7.4 Thiazolidinediones

Thiazolidinediones is a recently introduced class of oral antidiabetic drug that enhances target tissue insulin sensitivity. Two types are commercially available namely rosiglitazone and pioglitazone. The exact mechanism of their action is not known, but their major action is to diminish insulin resistance in muscle and adipose tissue.

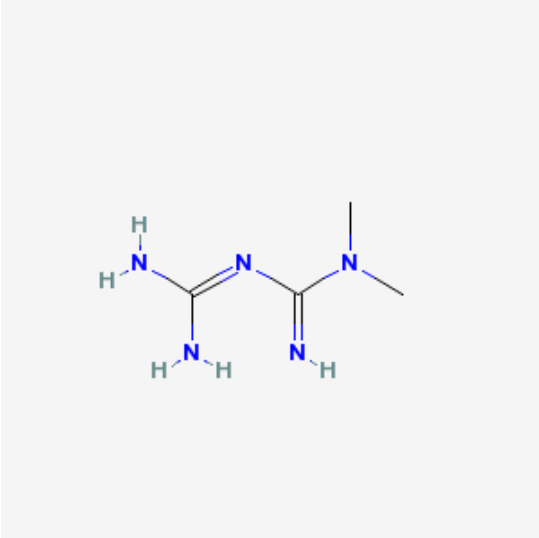

Fig 1.6 Chemical structure of the biguanide metformin (PubChem Public Chemical Database, 2009).

Figure 1.7 *Galega officinalis* Van Wyk and Wink (2004).

Troglitazone was the first thiazolidinedione to be approved but was withdrawn due to its association with a low but significant rate of idiosyncratic liver damage. Two other thiazolidinediones namely rosiglitazone and pioglitazone demonstrated efficacy similar to that of troglitazone but with no evidence of hepatictoxoxicity (Nolte and Karam, 2001).

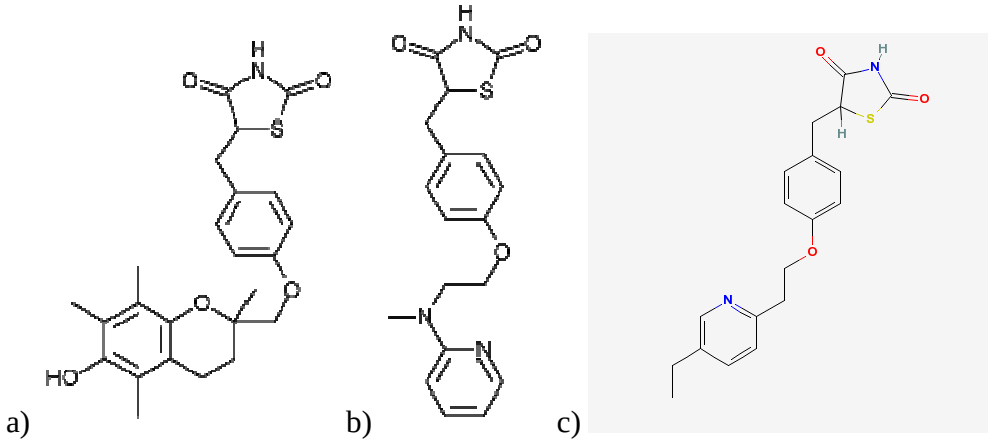

Fig 1.8 Chemical structure of the thiazolidinediones, a) troglitazone, b) rosiglitazone and c) pioglitazone (PubChem Public Chemical Database, 2009)

1.7.5 Alpha-glucosidase inhibitors

Acarbose and miglitol are the two agents available in this class. Alpha-glucosidase inhibitors act by inhibiting the enzymes, pancreatic alpha-amylase and alpha-glucosidase, found in the brush border cells that line the small intestine. They cleave the more complex carbohydrates such as starches, oligosaccharides and disaccharides into monosaccharide molecules before being absorbed in the duodenum and upper jejunum (Luna and Feinglos, 2001; Nolte and Karam, 2001). Acarbose and miglitol are competitive inhibitors of alpha-glucosidase and modulate the postprandial digestion and absorption of starch and disaccharides. Miglitol differs structurally from acarbose and is six time more potent in inhibiting sucrase. The binding affinity of the two compounds differ, acarbose and miglitol both target alpha-glucosidases: sucrase, maltase, glycoamylase, dextranase. Isomaltase and Beta-glucosidase are targeted only by miglitol and alpha-amylase only by acarbose. The clinical consequence of enzyme inhibition is to minimize upper intestinal digestion and absorption of ingested starch and disaccharides in the distal small intestine, lowering postmeal glycemic excursions and creating an insulin-sparing effect (Nolte and Karam, 2001). Prominent adverse effects include flatulence, diarrhoea, and abdominal pain which results from the appearance of undigested carbohydrate in the colon that is then fermented into short-chain fatty acids, releasing gas (Nolte and Karam, 2001).

1.8 HERBAL PRODUCTS CURRENTLY AVAILABLE IN SOUTH AFRICA FOR THE TREATMENT OF DIABETES.

Few herbal products are available on the South African market for the maintanence of blood glucose levels. The most commonly used includes Probetix, Manna, Diabecinn and Cinnachrome. Probetix (Nappi code: 711050-001) is a herbal supplement developed from the leaf extract of the indigenous shrub *Sutherlandia frutescens* (L.) R. Br.. Research done on this plant extract found that it reversed insulin resistance and decreased intestinal glucose uptake (Chadwick *et al.,* 2007). Scientifically identified biological active chemicals isolated from the seeds of *Sutherlandia frutescens* include L-canavanine, a non-protein α-mino acid and pinitol, the latter associated with hypoglycaemic effects (Van Wyk *et al.*, 2005).

Manna DFM43 (Nappi code705846-001) is a high fibre, low fat nutritional food supplement developed from the pods of the invasive tree *Prosopis glandulosa* Torr. var. *torreyana* (L.D. Benson) M.C. Johnst. Research indicated that it retards the absorption of glucose in the blood and reduces the Glycaemic Index (GI) value of foods. The active ingredient is galactomannan, a polysaccharide combination of galactose and mannose (Dune Foods, 2005).

Diabecinn (Nappi code 704686-001) is a food supplement that may reduce blood sugar levels, triglycerides, LDL cholesterol and total cholesterol in patients with type 2 diabetes. Diabecinn is a waterbased cinnamon bark extract (ZN112) that has shown in animals to increase the *in vitro* glucose uptake and glycogen synthesis and to increase the phosphorylation of the insulin receptor. This increases insulin sensitivity, which improves blood glucose levels. Khan *et al*. 2003 stated that the dietary components beneficial in the prevention and treatment of type 2 diabetes and cardiovascular diseases have not been clearly defined, but it is postulated that spices may play a role. Spices such as cinnamon, cloves, bay leaves and turmeric display insulin-enhancing activity *in vitro.*

Cinnachrome (Napppi code 708102-001) contains the active ingredient cinnulin PF produced from cinnamon bark as well as the active substance methyl-hydroxy-chalcone polymer. It is alledged that Cinnachrome may assist in regulating blood sugar levels (Holford, 2009).

A number of South African plant species are being used traditionally for the treatment of diabetes, however, not many scientific studies have been conducted on these plant species. This necessitates researchers to investigate the potential of South African plant species for hypoglycaemic activity.

1.9 HYPOTHESIS AND OBJECTIVES OF THIS STUDY

The hypothesis of this thesis was that the different plant species used by traditional healers and herbalists for the treatment of diabetes would show hypoglycaemic activity.

The primary objectives of this study were to validate four plant species for their hypoglycaemic activity by

a) evaluating their inhibiting effects on the carbohydrate-hydrolising enzymes, alpha-glucosidase and alpha-amylase,

b) screening these plant extracts against C2C12 myocytes, 3T3-L1 preadipocytes and Chang liver cells by measuring glucose uptake,

c) the cytotoxicity of these plant extracts on cell lines

d) the four plant species extracts according to a scoring system to establish which extracts are the best with regard to their hypoglycaemic potential.

e) bioassay-guided fractionation of the active extract in order to identify the bioactive principles

f) the isolated compounds for hypoglycaemic activity

1.10 SCOPE OF THIS THESIS

The scope of this thesis is a literature review on diabetes in Chapter 1. Chapter 2 deals with the importance of medicinal plants in general, and South Africa in particular. It also includes a literature review on plant species used in the treatment of diabetes. In chapter 3 the hypoglycaemic activity of the four selected plant species traditionally used in South Africa for the treatment of diabetes is discussed. Chapter 4 deals with the isolation of the bioactive compounds from *E. undulata* rootbark as well as the evaluation of these isolated compounds for hypoglycaemic activity. Chapter 5 comprises a general discussion and conclusion.

1.11 CONCLUSION

As the knowledge of the heterogeneity of diabetes mellitus increases, there is a need to look for more efficacious agents with fewer side effects. Complications are the major cause of morbidity and mortality in diabetes mellitus (Grover, Yadav and Vats, 2002). These complications include the specific diabetic problems of retinopathy, nephropathy and neuropathy which are often termed diabetic micro-angiopathic or microvascular disease and the non-specific macrovascular problems of occlusive atherosclerotic disease affecting the heart, brain and legs (Paul, 2002).

South Africa is a country with a rich diverse flora with a long history of use of indigenous plants by herbalists and traditional healers for the treatment of various diseases such as diabetes. According to Mulholand and Drewes (2004) 80% of the South African population is still making use of traditional medicines, coupled with a sympathetic attitude towards traditional healers. It is therefore, necessary that research should be done on the various plant species being used by traditional healers for treatment not only of diabetes but for other diseases as well, and to verify their activity and toxicity to possibly discover new effective drugs.

1.12 REFERENCES

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An extensive literature review was conducted on the use of plants for the treatment of diabetes by South African herbalists and traditional healers. A brief description is given of each plant in Chapter 2. Appendix 1. contains photos of the plants described in Chapter 2.

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CHAPTER 2

Plant Species Used in the Treatment of Diabetes by South African Traditional Healers: An Inventory

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2.1 Abstract

The indigenous people of southern Africa have a long history of traditional plant usage for medicinal purposes, with about 4,000 taxa being so employed. Traditional medicines continue to play a significant role in the treatment of life-threatening diseases such as malaria, tuberculosis, diabetes and AIDS in the developing world, although no adequate scientific evidence has been documented in support of their healing properties. The primary goal of this paper was to summarize information on some of the plants species used by traditional healers for the treatment of diabetes in South Africa. The information obtained is from published literature as well as personal communication with various traditional healers and herbalists from different areas. In total, the information of 32 plant species, representing 20 families, traditionally used by healers in the treatment of diabetes, is discussed, of which 14 are currently being investigated for their hypoglycemic activity by various scientists at the University of Pretoria.

Keywords: Diabetes, herbalists, plants, South Africa, traditional healers.

2.2 Introduction

Most African countries are undergoing a demographic transition and are increasingly coming under Western influences, leading to the adoption of a cosmopolitan lifestyle and a Western food culture**,** thus giving rise to an increase in the consumption of fat, sugar and salt. Rural African societies have maintained their traditional diet. However, an increase in nutritional deficiencies has occurred which appears to be related to drought, poverty, war and socioeconomic deprivation rather than to culture or religion. These lifestyle changes and a rapid increase in the urban population of Africa have led to an increase in nutritional deficiencies and, subsequently, a rise in the occurrence of diabetes mellitus (Mbanya and Gwangwa, 1997).

Diabetes mellitus is a common endocrine disorder, and affects more than 100 million people worldwide (World Health Organization, 1994). It is recognized as being a syndrome, a collection of disorders that have hyperglycaemia and glucose intolerance as a

hallmark, due either to insulin deficiency or to impaired effectiveness of insulin's action, or a combination of both.

Ethnopharmacological studies can contribute greatly to modern medicine, and can lead to the discovery of many novel and useful drugs, although the modern and the traditional uses may be entirely different (Holmstedt and Bruhn, 1995). The identification of biologically active compounds needs to be interpreted in the light of the traditional use and preparation of the plant (Holmstedt and Bruhn, 1995). It should comprise a chemical and pharmacological evaluation of the traditional drug preparation in order to establish dose-effect relationships for the quantitative use of the remedy.

The use of plants as medicine goes back to early man. Certainly, the great civilizations of the ancient Chinese, Indians, and Egyptians provided written evidence of man's ingenuity in utilizing plants for the treatment of a wide variety of diseases.

It was not until the 19th century that man began to isolate the active compounds of medicinal plants, and one particular landmark was the discovery of quinine from *Cinchona* bark by the French scientists Caventou and Pelletier. Such discoveries led to an interest in plants from the New World and expeditions scoured the almost impenetrable jungles in the quest for new medicines (Phillipson, 2001).

Prior to World War II, a series of natural products isolated from higher plants became clinical agents and a number are still in use today, such as morphine, codeine, digoxin, atropine and hyoscine. The antibiotic era dawned during and after World War II, with the discovery of the antibacterial effects of a whole series of natural products isolated from species of *Penicillium*, *Cephalosporium,* and *Streptomyces*. In the post-war years there were relatively few discoveries of new drugs from higher plants. Despite the discoveries of reserpine and vincristine, the impact of phytochemistry on new drug development waned and inevitably the innovative pharmaceutical industry turned to synthetic chemicals (Phillipson, 2001). During recent years, the attention of the pharmaceutical industry has switched once more to the natural world and this is illustrated by the development of three clinical drugs: taxol, etoposide, and artemisinin (Phillipson, 1999).

2.3 Ethnobotany in South Africa

The indigenous people of southern Africa have a long history of traditional plant usage for medicinal purposes, with about 4,000 taxa being so employed. The trade in medicinal plants is an important part of the regional economy with over 700 plant species being reported as traded (Mander, 1998). In South Africa, it is estimated that there are 27 million consumers of traditional medicine (Mulholland and Drewes, 2004).

The value of trade in ethnomedicinal plants in KwaZulu-Natal alone was estimated to be worth R60 million in 1998. Most households spend between 4% and 8% of their annual income on traditional medicinal services. In addition, in KwaZulu-Natal, between 20,000 and 30,000 people derive an income from trading indigenous plants (Mulholland and Drewes, 2004).

The use of plants in traditional medicine finds its natural expression and further development in primary health care. Current estimates suggest that, in many developing countries, a large proportion of the population relies heavily on traditional practitioners and medicinal plants to meet primary health care needs. Although modern medicine may be available in these countries, herbal medicine has often maintained popularity for historical and cultural reasons. Traditional medicines also continue to play a significant role in the treatment of life-threatening diseases such as malaria, tuberculosis and AIDS in the developing world, although no adequate scientific evidence has been documented in support of their healing properties.

The primary goal of this paper was to summarize information on some of the plants used by traditional healers and herbalists for the treatment of diabetes in South Africa. The information obtained is from published literature as well as personal communication with various traditional healers from different areas. The traditional healers and herbalists interviewed were recommended by healthcare professionals and local community workers active in the respective areas. Plant material used in this study was authenticated by Ms. M. Nel and Prof. A.E. van Wyk at the H.G.W.J. Schweickert Herbarium, University of Pretoria, where voucher specimens are being kept. In total, the information of 32 plant species representing 20 families traditionally used by healers in the treatment of diabetes is

discussed. The information on the first ten plants mentioned was provided by various traditional healers and herbalists. The medicinal use of the other 22 plants was obtained from literature.

2.4 Plant material

2.4.1 *Elaeodendron transvaalense*

Elaeodendron transvaalense (Burtt Davy) R.H. Archer (Celastraceae); common names: Transvaal saffronwood (English); Transvaalsafraan (Afrikaans); ingwavuma (Zulu); mukuvhazwivhi (Venda). Plant parts used: bark.

2.4.1.1 Description

This is a shrub or small multi-stemmed tree, usually around 5 m tall but may reach 10 m or more. The bark is smooth and has a characteristic pale, grey colour. Tufts of leaves are crowded on the ends of rigid shoots. The leaves are oblong in shape with a firm texture and conspicuous venation on the upper and lower surfaces. The leaf margin is sometimes toothed. Small and inconspicuous greenish flowers are produced in summer, followed by oblong, yellow to dark orange, edible berry-like fruits (Coates Palgrave, 1984). The species is widely distributed in the northeastern parts of South Africa. It occurs along the coastal parts of KwaZulu-Natal and in Mpumalanga, Gauteng, and Limpopo.

2.4.1.2 Medicinal uses

An infusion of the bark is taken as a stomach cleanser and used as an enema for stomach aches, fever and to treat intestinal cramps and diarrhoea. The leaves are chewed and the juices swallowed for a sore throat (Van Wyk *et al*., 2005). A teaspoon of powdered bark is boiled in water and no more than two cups are taken per day (Pujol, 1990). The powdered bark may also be licked from the palm of the hand, and washed down with a small amount of water. The bark is known to be toxic so the dosage should be carefully controlled. The species is used for the treatment of diabetes by local herbalists and

traditional healers in the Venda region, Limpopo (Dr. Emmanuel Tshikalange, Department of Plant Science, University of Pretoria, Pretoria,0002, South Africa, personal communication).

2.4.1.3 Phytochemistry/bioactivity

The beneficial effects of the bark have been ascribed to its high tannin content (Frost, 1941). A phenolic compound, elaeocyanidin, has been isolated from both *E. transvaalense* and *E. croceum* (Thunb.) DC. (Drewes and Mashimbye, 1993). The latter species also contains gallotannins and ouratea proanthocyanidin A, and it is likely that these or similar compounds will be present in *E. transvaalense*, together with the reported triterpenoids (Drewes and Mashimbye, 1993). Tannins are sometimes used for their astringent and antidiarrhoeal properties (Bruneton, 1995). The bioactivity for stomach ailments by *E. transvaalense* and *E. croceum* bark can at least be explained by the presence of these phenolic compounds and tannins (Van Wyk *et al*., 2005).

2.4.2 *Euclea undulata*

Euclea undulata Thunb. (Ebenaceae) common names: guarrie (Khoi); common guarri (E); gewone ghwarrie (A); umgwali (Xhosa); mokoerekoere (Tswana); gwanxe, inkunzane; umshekizane; umbophanyamazane (Z); inhlangula (Swati); chizuzu (Shona); mokwere kwere (Sotho). Plant parts used: roots.

2.4.2.1 Description

This is a dense, erect, twiggy, evergreen dioecious shrub or small tree. The leaves are alternate or arranged in pseudo-whorls and crowded at the ends of the branches. The leaves are small, obovate to narrow elliptic, leathery, yellowish green to dark green or blue-green above and paler green below, sometimes rustic-brown due to glands dotted over the surface. The flowers are small and whitish in auxiliary raceme-like sprays up to 2 cm long. The fruit is spherical, thinly fleshed, reddish brown becoming black when mature (Coates Palgrave, 1984). The species is widespread occuring on rocky slopes in all the provinces except the Free State; *Euclea undulata* var. *undulata* occurs from Worcester in the Western

Cape to Komga in the Eastern Cape while *E. undulata* var. *myrtina* (small leaved guarrie) is found in Namibia, Limpopo and into KwaZulu-Natal, Mpumalanga and Swaziland.

2.4.2.2 Medicinal uses

The plant is an old-fashioned Cape remedy for heart diseases and the powdered bark is a Southern Sotho headache remedy. An infusion of the root bark is said to be a purgative. It is also reported that the root is used in South Africa as a remedy for toothache and other pains (Watt and Breyer-Brandwijk, 1962). Leaf preparations are taken orally in the Western Cape to treat diarrhoea and disorders of the stomach, and as a gargle to relieve tonsillitis. Elsewhere in the country root infusions are used as an enematic or as an ingredient of *inembe* (medication taken regularly during pregnancy to ensure a trouble-free confinement). Root preparations are used to induce emesis or purgation (South African National Biodiversity Institute, 2005). Herbalists and traditional healers in the Venda region of Limpopo make use of *E. undulata* to treat diabetes (Dr. Emmanuel Tshikalange, Department of Plant Science, University of Pretoria, Pretoria, 0002, South Africa, personal communication).

2.4.2.3 Phytochemistry/bioactivity

Earlier studies on the phytochemistry of *Euclea* species have identified triterpenoids and aliphatics in the branches and leaves (Costa *et al*., 1978) and naphthoquinones in the root, stem and fruit (Van der Vyver and Gerritsma, 1973, 1974). In another study, the naphthoquinones 7-methyl-juglone and diospyrin were isolated from the roots and isodiospyrin from the fruits of *E. undulata* var. *myrtina.* Stems appeared to be devoid of napthoquinones. The leaves were not included in the latter survey. Chemical tests indicated the presence (in leaves and stems) of tannins, saponins and reducing sugars, but not of alkaloids or anthraquinones or cardiac glycosides. The bark is reported to contain 3.26% tannin (South African National Biodiversity Institute, 2005).

In vitro antimicrobial activity against *Staphylococcus aureus* was demonstrated by aqueous extracts prepared from dried leaf material, at a concentration of 40 mg/ml. This result, together with the demonstrated presence of tannins in the leaves of this species, supports its use as an anti-diarrhoeal and for the relief of tonsillitis. No activity against *Pseudomonas*

aeruginosa, *Candida albicans* or *Mycobacterium smegmatis* was found in the preliminary tests (South African National Biodiversity Institute, 2005).

As both anti-diarrhoeal and purgative actions are reported for this species, dosage and method of preparation require standardisation. Its use as an anti-diarrhoeal by pregnant women and children is not recommended.

2.4.3 *Euclea natalensis*

Euclea natalensis A.DC. **(**Ebenaceae); common names: Natal guarri (E); Natalghwarrie (A); mutanqule (V). Plant parts used: bark and root (Van Wyk and Van Wyk, 1997).

2.4.3.1 Description

This is a shrub or small to medium-sized tree with a somewhat spreading crown. The leaves are elliptic to obovate-oblong, tough and leathery, glossy dark green above and densely covered with pale rusty woolly hairs below. The flowers borne in dense, branched, auxiliary heads, are small greenish white to cream in colour and sweetly scented. The fruit is a spherical red berry becoming black when mature (Van Wyk and Van Wyk, 1997). It occurs from coastal dune bush to about 1 000 m above sea level in a variety of habitats from dry arid areas to open woodland and riverine fringes. It is also common among rocks and on koppies (Coates Palgrave, 1984).

2.4.3.2 Medicinal uses

An infusion of *Euclea natalensis* is used by the Zulu people as a purgative and for abdominal complaints, but is liable to produce emesis. The plant is thought to be poisonous but is an ingredient in a Zulu scrofula remedy (Watt and Breyer-Brandwijk, 1962). Among the Shangaan the charred and powdered root is applied to skin lesions in leprosy and taken internally for ancylostomiasis. The Tshonga apply the powdered root for the relief of toothache and headaches (Watt and Breyer-Brandwijk, 1962). Van Wyk and Van Wyk (1997) also reported its medicinal usage. The twigs are used as toothbrushes. In the Venda region roots of *E. natalensis* are used to treat diabetes by herbalists and traditional healers

(Dr. Emmanuel Tshikalange, Department of Plant Science, University of Pretoria, Pretoria, Pretoria, 0002, South Africa, personal communication).

2.4.3.3 Phytochemistry/bioactivity

According to the literature, the following compounds were isolated from *E. natalensis:* natalenone (Ferreira *et al*., 1977); diospyrin, 7-methyl-juglone, euclein (Van der Vyver, 1974; Lall and Meyer, 1999, 2001); isodiospyrin, mamegaquinones, BN-quinones, 8,8-dihydroxy-4.40 dimethoxy-6.6-dimethyl-2.2-binaphtyl-1.1-quinone (Tannock, 1973) and 4,8-dihydroxy-6-methyl-1-tetralone (Khan, 1985). According to Lall and Meyer (2001), the naphthoquinones present in ***Euclea. natalensis*** was found to have inhibitory activity against *Mycobacterium tuberculosis.*

2.4.4 *Lannea edulis*

Lannea edulis (Sond.) Engl. (Anacardiaceae); common names: wild grape (E); wildedruif (A); pheho (Ts); muporotso (V); mutshutsuhgwa (V). Plant parts used: bark of the woody underground rootstock.

2.4.4.1 Description

This is a small shrublet of up to 1 m in height, with short, leafy branches developing from an underground rootstock. The compound leaves are densely hairy, particularly on the lower side. Small yellowish flowers are borne in erect clusters, followed by numerous small red to purplish-black fleshy berries (Van Wyk and Malan, 1988). It is widely distributed in the grassland areas of the summer rainfall region of South Africa (Van Wyk *et al.,* 2005).

2.4.4.2 Medicinal uses

Decoctions or infusions of the root bark are used to treat diarrhoea. Leaf poultices or leaf infusions are sometimes applied externally to treat sore eyes, boils, and abscesses (Van Wyk *et al*., 2005). Herbalists and traditional healers in Venda use *L. edulis* to treat

diabetes (Dr. Emmanuel Tshikalange, Department of Plant Science, University of Pretoria, Pretoria, 0002, South Africa, personal communication).

2.4.4.3 Phytochemistry/Bioactivity

Little is known about the chemistry or bioactivity of *L. edulis,* however, the bark has been found to be rich in phenolic compounds and tannins (Van Wyk *et al*., 2005).

2.4.5 *Spirostachys africanus*

Spirostachys africanus Sond. (Euphorbiaceae); common names: tamboti (E); tambotie (A); muonze (V). Plant parts used: bark.

2.4.5.1 Description

This is a medium-sized deciduous tree with a rounded crown. The leaves are ovate to elliptic with two minute blackish glands at the junction with the petiole (van Wyk and Van Wyk, 1997). It contains a milky latex and the sexes are separated on the same plant. The flowers are very small and are produced in the axils of distinctive reddish bracts in slender catkin-like spikes (Coates Palgrave, 1984). The bark is dark grey to blackish and cracked in a grid-like pattern. It is found in the Bushveld, usually at low altitudes, on heavy soils along rivers and streams.

2.4.5.2 Medicinal use

Inhalation of the smoke causes headaches and nausea, and food directly exposed to the smoke is said to be poisonous. The latex is toxic and may cause skin irritation (Van Wyk and Van Wyk 1997). Although no evidence has been found in the literature on the plant's use by the Venda traditional healers for diabetes it has been personally communicated that a decoction made from the stem bark is used to treat diabetic patients (Dr. Emmanuel Tshikalange, Department of Plant Science, University of Pretoria, Pretoria, 0002, South Africa)

2.4.5.3 Phytochemistry/bioactivity

The latex from the wood of tamboti contains diterpenes, such as stachenone, stacenol and other structurally related acid metabolites and diosphenols (Van Wyk *et al*., 2002)

2.4.6 *Schkuhria pinnata*

Schkuhria pinnata (Lam.) Cabrera (Asteraceae) ; common names: dwarf marigold (E); kleinkakiebos (A); canchalagua, escobilla, vassourinha, (Spanish); gakuinini (Kikuyu). Plant parts used: whole plant.

2.4.6.1 Description

Schkuhria pinnata is a small, herbaceous plant, which was introduced into South Africa from the mountainous regions of South America (Taylor, 2006). It is a common highly branched annual herb up to 60 cm tall with deep and finely divided leaves. Flowerheads are borne in branched, flat-topped inflorescences. The disc and ray florets are yellow. This common weed was first recorded in South Africa in 1898, when British soldiers introduced it with imported fodder for their horses (Bromilow, 1995). It occurs in cultivated lands, gardens, along roadsides, in overgrazed grasslands and wastelands (Grabandt, 1985). In South America it grows in remote places, in valleys and on slopes at 2,000 to 3,000 m above sea level (Taylor, 2006).

2.4.6.2 Medicinal uses

Andean healers (South America) recommended its use as a way to improve and support healthy looking skin. Topically it is being used as a skin tonic, for blackheads, pimples, eye wash, wound wash, insect bites and swellings (Taylor, 2006). Traditionally, a mild bitter tonic is prepared which is used as a blood cleanser and kidney tonic. *S. pinnata* is also used for leprosy, swelling, respiratory problems, bronchitis, fever, throat problems, as an aphrodisiac, for menstrual problems, stomach problems, headaches and as a strong anti-spasmodic. Furthermore, it is said to be excellent for hypertension and nervousness, for diarrhoea, venereal disease, as a diuretic, and for the treatment of diabetes. It is used to promote and support normal metabolism and blood cleansing, which can also lead to overall

improvement of the skin, as it is regarded as tonic for both the liver and kidneys (Taylor, 2006).

It is considered to be anti-diarrhoeal and anti-emetic. Antiseptic leaf decoctions are used for wounds and fever. Mixed with maternal milk, it is used as an anti-emetic for infants. Leaf decoctions are also used in antipyretic baths and in poultices for migraine and as a tea for pain and swelling. Brazilians add powdered root to bathwater when "cleaning their blood". They apply strained leaf juice for eye ailments and to infected wounds (erysipelas). A tea can be made by steeping one or more teaspoons of dried plant material per cup. *S. pinnata* is used by traditional healers and herbalists in the Ga-Rankuwa area, Gauteng to treat diabetes (Sr. Lia Matibe, Medical University of South Africa,Pretoria, 0002, South Africa, personal communication).

The common names escobilla, chanchalagu and vassourina are used for the description of concoctions of two different plant species from two separate families, *S. pinnata* and *Scoparia dulcis* L. In the literature it is not clear exactly which concoction from which plant is used for which specific ailment and if both are used for all the above mentioned ailments (Taylor, 2006).

According to Watt and Breyer-Brandwijk (1962), the powdered leaf of *S. pinnata* is swallowed with water as a remedy for malaria, influenza and for colds. The Kikuyu name implies “one with quinine”, probably due to the bitter taste. It plays a significant role in the treatment of malaria in central Kenya.

2.4.7 *Pteronia divaricata*

Pteronia divaricata (P.J.Bergius) Less. (Asteraceae); common names: geel gombos, geelknopbos, spalkpenbos (A). Plant parts used: whole plant.

2.4.7.1 Description

This is a twiggy, dense shrublet up to 1 m tall. The leaves are round, elliptic and velvety. Six or seven large yellow disc flower heads are clustered at the ends of the branchlets,

flowering from September to November. It occurs on sandy and rocky soils from Namibia to Hopetown in the Northern Cape (Manning and Goldblatt, 2000).

2.4.7.2 Medicinal uses

In the literature, no evidence was obtained of the medicinal uses of *Pteronia divaricata*, although some *Pteronia* species have been reported to be toxic to livestock, e.g., *P. pallens* L.f. (Van Wyk *et al*., 2000) and others do have medicinal value such as *P. camphorata* (L.) L., *P. onobromoides* DC., and *P. stricta* Aiton (Watt and Breyer-Brandwijk, 1962). *P. divaricata* is being used to treat diabetes in the Clanwilliam area, Western Cape (Mr Peter Maltz, Traditional Health Practitioner, 96 Arum Road, Kommetjie, Westren Cape, South Africa, personal communication).

2.4.8 *Ziziphus mucronata*

Ziziphus mucronata Willd. **(**Rhamnaceae); common names: buffalo-thorn (E); blinkblaarwag-'n-bietjie (A); mokgalo (North Sotho; Ts); umphafa (Xh, Z); umlahlankosi (Z). Plant parts used: leaves.

2.4.8.1 Description

This is a small shrub to medium-sized tree. The leaves are ovate to broadly ovate, glossy dark green above and the lower surface slightly hairy. The leaf base is markedly asymmetric and the margin finely toothed over the upper two-thirds. The stipules are spinescent, one hooked, the other straight, or the plant is unarmed. Flowers are in axillary clusters and are small, yellowish green. The fruit is a sub-globose drupe, shiny reddish to yellow brown (Van Wyk and Van Wyk, 1997). These trees occur in a wide variety of habitats throughout South Africa.

2.4.8.2 Medicinal uses

According to Coates Palgrave (1984) it is used as a remedy for pain, as a poultice for the treatment of boils and other skin infections as well as for the treatment of tubercular gland swellings. It is also used by sufferers of dysentery and lumbago. The Zulu use it for the

relief of chest pains and coughs (Coates Palgrave, 1984; Van Wyk and Van Wyk, 1997). Warm infusions of the root, bark or leaves are taken orally as tea or decoctions are used topically to treat sores, boils and swelling (Van Wyk *et al*., 2005). According to Mushtaq (2007), 4–5 fresh leaves of *Ziziphus jujube* Miller are plucked, washed and chewed daily by diabetics in the Attock district of Pakistan to lower blood glucose levels. According to Ms. G. Masuku, a local herbalist in the Pilanesberg area, North West (Ms Grace Masuku, Herbalist P.O. Box 377, Saulsport, 0318, North West, South Africa, personal communication), a tea is prepared from the leaves of *Ziziphus mucronata* combined with powdered material from *Viscum* species for the treatment of diabetes.

2.4.8.3 Phytochemistry/bioactivity

Several alkaloids such as mucronine D, commonly referred to as peptide alkaloids are known from *Ziziphus* species (Van Wyk *et al*., 2005). The alkaloid frangufoline, is a strong sedative and is structurally closely related to some of the alkaloids extracted from *Z. mucronata* (Van Wyk *et al*., 2005).

2.4.9 *Aloe ferox*

Aloe ferox Mill. (Asphodelaceae);. common names: bitter aloe (E); bitteraalwyn, Kaapse aalwyn (A); umhlaba (Xh,Z,S). Plant parts used: leaves.

2.4.9.1 Description

Aloe ferox is a robust single-stemmed plant between 2 and 5 m tall. The leaves are broad and fleshy, usually a dull to greyish green with brown spines on the edges as well as on the upper and lower surfaces. The inflorescence is a raceme with bright orange-red flowers (Van Wyk and Smith, 1996). It is a widely distributed *Aloe* species occurring from the Western to the Eastern Cape as well as in southern KwaZulu-Natal and the extreme southeastern parts of the Free State. It occurs in a wide range of habitats varying from mountain slopes, rocky ridges and flat open plains (Van Wyk and Smith, 1996).

2.4.9.2 Medicinal uses

This plant is an important commercial laxative but is also used for arthritis, eczema, conjunctivitis (Watt and Breyer-Brandwijk, 1962; Bruce, 1975), hypertention and stress (Pujol, 1990). According to Van Wyk *et al*. (2005) a small crystal of the crude drug, about twice the size of a match head, is taken orally as a laxative and half the dose for arthritis. The fresh bitter sap is instilled directly for conjunctivitis and sinusitis. *A. ferox* is also used to treat diabetes according to Margaret Roberts, a well-known South African herbalist (Ms. Margarte Roberts, P.O. Box 41, DeWildt, 0251, North West, South Africa, personal communication).

2.4.9.3 Phytochemistry/bioactivity

The main purgative ingredient is anthrone C-glucoside alion (= barbalion). The wound healing properties of aloe gel are ascribed to glycoproteins. Anthraquinone derivatives act as stimulant laxatives (Bruneton, 1995).

2.4.10 *Warburgia salutaris*

Warburgia salutaris (G.Bertol.) Chiov. (Canellaceae);. common names: pepperbark tree (E); peperbasboom (A); isibhaha, amazwecehllabayo (Z); mulanga, manaka (V); shibaha (Ts). Plant parts used: stem bark.

2.4.10.1 Description

This is a slender tree between 5 and 10 m tall. The bark is rough and a rich brown colour with yellow corky lenticels (Venter and Venter, 1996; Coates Palgrave, 2002). The leaves are simple and alternately arranged, elliptic to lanceolate, a dark glossy green above and a pale dull green below. The bisexual flowers can be green or white and are solitary or in flower-heads or cymes. The ten stamens are joined together to form a tube in the centre of the flower, enveloping the ovary and most of the style. The fruit is a spherical berry that turns black when mature (Coates Palgrave, 1984). It occurs in evergreen forests and wooded ravines in the northeastern areas of southern Africa (Coats Palgrave, 1984).

2.4.10.2 Medicinal uses

Warburgia is one of the most important medicinal plant species in southern Africa. The inner bark is reddish, bitter and peppery and has a variety of applications. It is used to treat common colds, to open sinuses, for chest complaints as well as against malaria (Coates Palgrave, 1984). According to Van Wyk and Gericke (2000) it is also used as a natural antibiotic, for venereal diseases, abdominal pain, constipation, in the treatment of cancer, for rheumatism, and stomach ulcers. Powdered bark decoctions and infusions are taken orally against malaria. It is also applied externally to cuts as well as on the temples for headaches (Van Wyk and Gericke, 2000). It is ground and snuffed to open sinuses, chewed or smoked and inhaled for chest complaints (Coates Palgrave, 1984). It is also used to treat diabetes (Ms. Margaret Roberts, P.O. Box 41, De Wildt 0251, North West, South Africa, personal communication)

2.4.10.3 Phytochemistry/bioactivity

The bark contains numerous drimane sesquiterpenoides, such as warburganal and polygodial, as well as tannins and mannitol (Watt and Beyer-Brandwijk, 1962: Van Wyk and Gericke, 2000). Warburganal and polygodial both showed profound anti-candidal activity (Van Wyk and Gericke, 2000). Polygodial is potentially useful in clinical medicine as an adjustment to treatment with antibiotics and antifungals which have poor membrane permeability (Iwu, 1993). Mannitol is used against dyspepsia and as a diuretic (Bruneton, 1995). According to Hutchings *et al.* (1996) drimenin has insect antifeedant properties and also showed anti-bacterial and anti-ulcer activity (Van Wyk *et al.*, 2005). Potential antifungal activity was exhibited by an isolated sesquiterpenoid dialdehyde (Hutchings *et al.*, 1996). Muzigadial, another sesquiterpenoid, is according to Rabe and Van Staden (1997, 2000) responsible for the antibacterial activity.

2.4.11 Momordica balsamina

Momordica balsamina L. (Cucurbitaceae**);** common names: balsam pear (E); laloentjie (A); mohodu (S); nkaka (Tshonga). Plant parts used: fruit.

2.4.11.1 Description

Balsam pear is a perennial creeping herb with slender stems, lobed leaves and tendrils for attachment. The solitary trumpet yellow flowers are followed by pointed fruits that turn orange to red when mature. The edible seeds have bright red arils that are also considered to be edible. Leaves and young fruit are cooked and used as vegetables (Van Wyk and Gericke, 2000). Commonly found in tree savannas in sandy soils (Van Rooyen, 2001).

2.4.11.2 Medicinal uses

Momordica balsamina is said to be effective in treating diabetes (van Wyk and Gericke, 2000: Van Rooyen, 2001). Although it is used as an anti-diabetic, careful tests do not support its use. It showed moderate hypoglycaemic action when tested in rabbits, however, there has been no definite assurance of insulin-like properties (*Momordica balsamina*, 2006). *M. balsamina* emits a strong unpleasant smell when bruised (Watt and Breyer-Brandwijk, 1962) A liniment, made by infusing the fruit (minus the seed) in olive oil or almond oil, is used as an application to chapped hands, burns and haemorrhoids and the mashed fruit is used as a poultice. An extract is administered for the relief of dropsy. The plant is much used in West Africa as a medicine in both man and horse, particularly as a bitter stomachic, as a wash for fever and for yaws, and as a purgative (Watt and Breyer-Brandwijk, 1962). The fruit pulp, mixed with oil, is used as an antiphlogistic dressing. The root is used as an ingredient in an aphrodisiac or with the seeds and fruit as an abortifacient and in the treatment of urethral discharge. Among the Pedi, the fruit is believed to be deadly poisonous and this view is supported by the report that a few drachms of it, given to a dog, is fatal, death being due to violent vomiting and purging (Watt and Breyer-Brandwijk, 1962). The Shangaan prepare tea from the leaves as a blood purifier and for liver deficiencies. In dry seasons, postnatal mothers eat the leaves to stimulate milk production (*Momordica balsamina*, 2006). One small cup of fresh *M. charantia* L. fruit juice daily is used to lower blood glucose levels in the Attock district in Pakistan. It is also taken in the form of a tea for various other ailments (Mushtaq *et al*., 2007).

2.4.11.3 Phytochemistry/bioactivity

M. balsamina contains a bitter principle, momordocin and two resin acids. The

plant also contains a highly aromatic volatile oil, a fixed oil, carotene, a resin and two alkaloids, one of which is a saponin. Momordocin is an amaroid obtained as a crystalline powder. A leaf extract has shown positive antibacterial activity. An infusion of the plant has shown mild, but inconsistent, anti-malarial effects hence the use of this plant by the Portuguese for "paludismo" or sometimes referred to as "yellow fever tree sickness" (Mushtaq *et al*., 2007).

2.4.12. Kedrostis nana

Kedrostis nana (Lam.) Cogn (Cucurbitaceae); common names: ystervarkpatat (A).
Plant parts used: underground tuber.

2.4.12.1 Description

This is a tuberous climber with annual stems that attach to their support by tendrils. The leaves are alternate, lobed and shining dark green (Manning and Goldblatt, 2000). It has a strong odour of carbon bisulphide (Watt and Breyer-Brandwijk, 1962). The greenish-yellow flowers are unisexual and borne on separate plants during February and March. The male flowers are in short clusters whereas the female flowers are solitary. The flowers are followed by fleshy, yellow-orange fruits (Manning and Goldblatt, 2000). *Kedrostis nana* is frequently found among bushes at low altitudes, especially near the sea from the Western Cape to KwaZulu-Natal (Manning and Goldblatt, 2000).

2.4.12.2 Medicinal uses

The tuber is used as a cleansing emetic, and as a laxative. An infusion mixed with honey is taken for haemorrhoides. Infusions are used for diabetes and cancer, and in low doses for diarrhoea. A decoction of baked tuber, combined with *Dicerothamnus rhinocerotis* (L.f.) Koekemoer is taken as a contraceptive (Rood, 1994) and may have an abortifacient action, since *K. gijef* (J.F.Gmel.) C.Jeffrey has been reported to cause abortion in goats (Hutchings *et al*., 1996). *K. nana* has been found experimentally to produce a severe type of irritant poisoning in sheep and rabbits. The runners and roots are poisonous to sheep and rabbits, producing nausea, vomiting and diarrhoea, and death after large doses from respiratory paralysis.

The early colonists of the Cape used the roots of *K. nana* var. *latiloba* as an emetic and an infusion in wine or brandy as a purgative (Watt and Breyer-Brandwijk, 1962).

2.4.13 Artemisia afra

Artemisia afra Jacq. ex. Willd. (Asteraceae); common names: umhlonyane (Xh, Z); lengana (S,Ts); als, wildeals (A); African wormwood (E). Plant parts used: leaves.

2.4.13.1 Description

This is a highly aromatic, erect, perennial shrub of up to 2 m in height. The leaves are finely-divided and have a silver-greyish green colour due to the presence of fine hairs. The flowers are inconspicuous, yellow and borne at the ends of branches in globose capitula (Hilliard, 1977). It occurs widespread in all provinces of South Africa, with the exception of the Northern Cape, also in Lesotho, Swaziland, and northwards into tropical Africa, usually in montane habitats along forest margins and streamsides (Hilliard, 1977).

2.4.13.2 Medicinal uses

Artemisia afra is one of the most widely used traditional medicines in South Africa. It is mainly used for the treatment of coughs, croup, whooping cough, influenza, fever, diabetes, gastro-intestinal disorders and intestinal worms. It is also used as an inhalation for the relief of headaches and nasal congestion, or as a lotion to treat haemorrhoides (Van Wyk *et al.*, 2005). In traditional practice a fresh leaf is inserted into the nostril to relieve nasal congestion or placed in boiling water as a steam bath for menstrual pain or after child birth. Warmed leaves may be applied externally as a poultice to relieve inflammation and aqueous infusions are administered per rectum or applied as a lotion to treat haemorrhoids (South African National Biodiversity Institute, 2006a). *A. afra* is used mainly as an aqueous decoction or an infusion applied externally or is taken orally. The extremely bitter taste can be masked by the addition of sugar or honey. An infusion may be made with two tablespoons full (7 g) of dried ground herb to which 1 l of boiling water is added. If fresh leaves are being used four tablespoons of freshly chopped leaves are infused in 1 L of

boiling water. Fresh leaves may be added to boiling water and the vapours inhaled (South African National Biodiversity Institute, 2006a).

2.4.13.3 Phytochemistry/bioactivity

Microchemical tests indicated the presence of tannins and saponins but not of alkaloids or cardiac, cyanogenic or anthraquinone glycosides. Studies done by Silbernagel *et al*. (1990) identified the triterpenes σ- and β-amyrin and friedelin as well as the alkanes ceryl cerotinate and *n*-nonacosane in the leaves of the South African collections of *A. afra*. The investigation of leaf exudate flavonoids revealed the presence of two luteolin methyl ethers (Wollenweber *et al*., 1989). Jakupovic *et al.* (1988) analyzed the sesquiterpene lactones of *Artemisia* and 10 guaianolides and 5 glaucolides were detected. Analyses of the essential oils obtained from the leaves have demonstrated considerable variation in oil composition. The major components of the oil appear to be α- and β-thujone, 1,8-cineole, camphor and α-pinene (Graven *et al.*, 1992). Also present are terpenoids of the eudesmadien- and germacratien types as well as coumarins and acetylenes (Van Wyk *et al*., 2005)

Antihistaminic and narcotic analgesic effects have been reported following preliminary tests (Hutchings *et al*., 1996; Van Wyk *et al*., 2005). The volatile oil, which contains mainly 1,8-cineole, α-thujone, β-thujone, camphor and boreol, has antimicrobial and anti-oxidative properties (Graven *et al*., 1992). Anti-malaria assays done on dried aerial parts of Tanzanian plants showed weak activity against *Plasmodium falciparum*. Fresh ethanol leaf extracts showed no activity against Leuk-L1210 and Sarcoma–WM256(IM) lines (Charlson, 1980). According to Watt and Breyer-Brandwijk (1962), *A. afra* is being used to keep urine free from sugar in the case of diabetes mellitus.

2.4.14 Catharanthus roseus

Catharanthus roseus (L.) G.Don (Apocynaceae); common names: Madagascar periwinkle (E); kanniedood (A); isisushlungu (Z). Plant parts used: aerial parts.

2.4.14.1 Description

This is a semi-woody evergreen perennial herb up to 900 mm in height. The leaves are opposite and a glossy dark green, with a prominent white midrib. The five petaled flowers are up to 40 mm in diameter and vary from pink to white. The flowers are tubular, with a slender corolla tube. Periwinkles are commonly grown in South African gardens, but originate from Madagascar and have become naturalized in tropical and sub-tropical regions of the world (Van Wyk *et al*., 2005).

2.4.14.2 Medicinal uses

The plant is traditionally used in South Africa for the treatment of diabetes and rheumatism (Watt and Breyer-Brandwijk, 1962). Alkaloid extracts of the aerial parts are used to treat various forms of cancer such as breast and uterine cancer and Hodgkin's and non-Hodgkin's lymphoma (Bruneton, 1995). An infusion of the leaf is used to treat diabetes, but even diluted mixtures can be extremely toxic. The two main alkaloids of the plant are used in combined chemotherapy and small doses are injected weekly or monthly (Van Wyk *et al.*, 2005). According to Mushtaq *et al*. (2007), extracts obtained from fresh leaves are being used for diabetes in Pakistan. A small teaspoon full is taken in the morning.

2.4.14.3 Phytochemistry/bioactivity

Various alkaloids such as catharanthine, leurosine and vindoline are responsible for the hypoglycemic effect. The two binary indole alkaloids vincristine and vinblastine are used in cancer chemotherapy (Van Wyk *et al*., 2005). The binary alkaloids prevent cell division in the metaphase by binding to the protein tubulin and blocking its ability to polymerise into microtubules (Bruneton, 1995; Van Wyk *et al*., 2005).

2.4.15 Cnicus benedictus

Cnicus benedictus L. (Asteraceae); common names: karmedik (A); holy thistle (E).
Plant parts used: leaves.

2.4.15.1 Description

This is an annual herb up to 70 cm tall with a rosette of basal leaves. The lance-shaped leaves are indented with spiny edges. Yellow flowers are borne in a terminal flower head surrounded by a circle of spiny bracts (Van Wyk *et al.*, 2005). *Cnicus benedictus* is native to Europe and Asia, but was introduced to South Africa more than 150 years ago and is currently a widely distributed weed in the Cape as well as on the Highveld (Henderson and Anderson, 1966; Smith, 1966).

2.4.15.2 Medicinal uses

The plant is used as a cholagogue, stomachic and tonic (Bruneton, 1995). The recorded uses in South Africa include brandy tinctures for internal cancers, for diabetes and arthritis (Watt and Beyer-Brandwijk, 1962, Smith, 1966 and Rood, 1994). This medicine is used as an aromatic bitter to stimulate the secretion of gastric juices which increase the appetite (Van Wyk *et al*., 2005). The use of *Cnicus benedictus* for bacterial infections, indigestion and flatulence as well as for viral infections has been investigated but the scientific evidence to substantiate its healing properties is still lacking. It is also used as a contraceptive, as an appetite stimulant, an astringent, for bleeding, as a blood purifier, for boils, colds as well as in the treatment of cancer, heart and liver ailments and malaria (Basch *et al*., 2006). Boiling water is poured over 1.5 to 3g of the ground dried herb, steeped for 10 to 15 min to prepare a tea and then taken three times daily (Basch *et al*, 2006). A cup of the unsweetened infusion is taken half an hour before meals (Van Wyk *et al*., 2005).

2.4.15.3 Phytochemistry / bioactivity

A bitter sesquiterpenoid lactone, cnicin, is probably the main active ingredient (Bruneton, 1995). Lignan lactones, such as trachelogenin, contribute to the bitterness of the plant. The plant also contains volatile oil with the terpenoids *p*-cymene, fenchone, and citral and the aromatic substances cinnamaldehyde and benzoic acid all of which can contribute towards the pharmacological activity of the plant (Van Wyk *et al.*, 2005).

2.16 Psidium guajava

Psidium guajava L. (Myrtaceae); common names: guava (E); koejawel (A); ugwawa (Z). Plant parts used: leaves.

2.16.1 Description

This is an evergreen shrub or small tree, 2 to 5 m tall (Henderson, 2001). The bark peels off in flakes, revealing the characteristic smooth trunk. The large bronze, turning to light green, ovate to oblong-elliptic leaves are borne opposite each other. The veins are conspicuously impressed above and raised below. Small white flowers with numerous stamens are produced in groups of 1-3 during October to December, followed by rounded or pear-shaped many-seeded berries. Guavas are an important commercial crop due to their delicious taste and high vitamin C content. The guava occurs naturally in tropical America up to Peru, but has become naturalized in many parts of the world. It is found as a weed in the warm subtropical areas of KwaZulu-Natal, Mpumalanga and Limpopo in South Africa (Van Wyk *et al*., 2005) and is currently classified as a category 2 invasive weed in South Africa.

2.4.16.2 Medicinal uses

Guava leaves are commonly used in South Africa as a remedy for diarrhoea (Watt and Breyer-Brandwijk, 1962; Hutchings *et al*., 1996). The leaves are also used for several other ailments including diabetes, fever, coughs, ulcers, boils and wounds (Watt and Breyer-Brandwijk, 1962; Hutchings *et al*., 1996). The main ethnotherapeutic use in Africa is said to be for malaria (Iwu, 1993). Crushed leaves are boiled in water and the infusion is either taken orally as a tea or as an enema (Hutchings *et al*., 1996). A common use in Pakistan is to make a hot water extract from dried guava leaves to reduce blood glucose levels in diabetes (Mushtaq *et al.*, 2007).

2.4.16.3 Phytochemistry/bioactivity

Numerous tannins and phenolic compounds have been identified from *Psidium guajava* of which the glycoside of ellagic acid, amritoside, is of particular importance. Other

biologically interesting compounds are guiajaverin and arabinopyroside of quercetin. The leaves contain essential oils and triterpenoids (Anonymous, 1996). Ellagic acid, is a known intestinal astringent and haemostatic (Anonymous, 1996). Bruneton (1995) explains the therapeutic value of the plant against diarrhoea and dysentry. The tannins are of value because of their vasoconstricting effects and their ability to form a protective layer on the skin and mucous membranes (Bruneton, 1995). These effects, together with proven antibacterial and antifungal activity, result in the effective treatment of both internal and external infections (Bruneton, 1995). Quercetin contributes to the efficacy of the medicine, because it is a known antioxidant with anticarcinogenic, anti-HIV and antibiotic effects (Anonymous, 1996).

2.4.17 Terminalia sericea

Terminalia sericea Burch. ex. DC. **(**Combretaceae); common names: silver cluster-leaf (E); vaalboom (A); mogonono (T); moxonono (NS); mususu (Sh, V); amangwe (Z); mangwe (Ndebele). Plant parts used: stem bark.

2.4.17.1 Description

It is a small to medium-sized deciduous tree up to 8 m tall, with a single erect trunk and wide spreading canopy (Coates Palgrave, 1984; Van Wyk and Van Wyk, 1997; 2000). The bark is thick, fibrous, dark grey and deeply longitudinally fissured. The leaves are clustered towards the ends of the branches, narrowly obovate-elliptic and densely covered with silky, silvery hairs (Van Wyk *et al.*, 2000). Small pale cream flowers are borne in axillary spikes and have an unpleasant smell. The fruit is surrounded by two broad papery wings, and are pink to purplish red when mature (Van Wyk *et al.*, 2000). These trees are normally found in the Bushveld, on deep sandy soils, often in dense stands (Van Wyk *et al.*, 2000).

2.4.17.2 Medicinal uses

Root decoctions are used as a traditional Tswana remedy for stomach disorders and diarrhoea (Watt and Beyer-Brandwijk, 1962; Coates Palgrave, 1984; Hutchings *et al.*, 1996). Decoctions of the roots, that have a very bitter taste, are taken to cure diarrhoea, to

relieve colic but are also used as an eye wash. Hot root infusions are used for the treatment of pneumonia (Coates Palgrave, 1984) whereas the bark is taken for diabetes (Watt and Beyers-Brandwijk, 1962). Decoctions and infusions are taken orally or applied externally. Ground bark eaten with maize meal is taken for diabetes (Van Wyk *et al*., 2005).

2.4.17.3 Phytochemistry/bioactivity

Several pentacyclic triterpenoids have been isolated from *Terminalia* species (Buckingham, 1996), of which sericic acid and an ester thereof, known as sericoside, are the main compounds in the roots (Bombardelli *et al*., 1974). The medicinal activity of the Combretaceae family is mainly ascribed to stilbenoids, triterpenoids, and saponins (Rogers, 1996). Triterpenoids and saponins are well known for their antimicrobial and anti-inflammatory activity. The antidiarrhoeal effects may be due to tannins (Bruneton, 1995).

2.4.18 Sutherlandia frutescens

Sutherlandia frutescens (L.) R.Br. (Fabaceae); common names: kankerbos, gansies (A); cancer bush (E). Plant parts used: aerial parts.

2.4.18.1 Description

This is an attractive small shrub up to 1.2 m high. The compound leaves are greyish green, slightly to densely covered with hair giving it a silvery appearance. The characteristic red pea family flowers are followed by bubble-like, duck shaped pods giving rise to the Afrikaans common name “gansies”. *Sutherlandia frutescens* is a small genus consisting of five members, mainly restricted to southern Africa with representatives in South Africa, Botswana and Namibia where they are widely distributed in the dry areas of the Western and Northern Cape, often in disturbed places.

2.4.18.2 Medicinal uses

S. frutescens is used internally for the treatment of cancer, gastric ailments, gynaecological problems, rheumatism, oedema and fevers and also as a bitter tonic or blood purifier. According to tradition and folklore the plant’s uses include remedies for colds, influenza, chicken-pox, diabetes, varicose veins, piles, inflammation, liver problems, backache and

rheumatism. Externally it is used to treat eye infections and wounds and as a douche for the prolapse of the uterus.

Approximately 10 g (± 3 tablespoons full) of dried ground herb is infused in 1 L of boiling water, strained and when cold taken in half a teacupful dose (90 ml) three-times daily. Children 6-12 years are given 45 ml (South African National Biodiversity Institute, 2006b).

2.4.18.3 Phytochemistry/bioactivity

The plant is rich in amino acids and pinitol, but has small quantities of saponins and no alkaloids, according to current biosystematic and chemosystematic studies done (Van Wyk *et al.,* 2005). The non-protein α-amino acid canavanine has been detected in the seeds of the species (Bell *et al.,* 1978). Studies using 50% ethanol extracts of the fresh flowers of *Sutherlandia frutescens* found no antitumour activity against CA-Lewis lung, Leuk-L 1210 or Sarcoma 180 solid tumours in mice. Similar extracts, assayed for cytotoxicity against CA-9KB cell lines, at a concentration of 2 µg/ml, proved to be inactive (Charlson, 1980). *S. frutscens* seeds contain canavanine that has according to Southon (1994) antitumourigenic properties and it is possible that this, or some other amino acid, is responsible for the reported benefits in treating cancer (Van Wyk *et al*., 2005). No *in vitro* antimicrobial activity against *Pseudomonas aeruginosa*, *Candida albicans* or *Mycobacterium smegmatis* was observed. Some activity was recorded against *Staphylococcus aureus* (South African National Biodiversity Institute, 2006b). The presence of pinitol, however, explains the traditional anti-diabetic use (Van Wyk *et al.,* 2005).

2.4.19 Bridelia micrantha

Bridelia micrantha (Hochst.) Baill. (Euphorbiaceae); common names: coastal goldenleaf; mitzeerie/mzerie, wild coffee (E); bruinstinkhout (A); mitserie (A); incinci, isihlalamangewibi, isihlalamangwibi, umhlahle, umshonge, umhlalamagwababa, umhlalamgwababa, umhlalimakwaba, umhlalamkhwaba (Z). Plant parts used: stem bark.

2.4.19.1 Description

This is a medium to large deciduous tree with a spreading crown characterised by scattered bright red leaves, while the rest of the leaves are glossy dark green above but paler green below. The venation of the leaves is prominent in a herringbone pattern. The very small flowers are bore in axillary clusters and are yellowish green. Flowers are followed by small edible black berries (Van Wyk and Van Wyk, 1997). The bark is brown to grey, slightly flaking and rough in mature specimens (Coates Palgrave, 2002). It occurs in coastal, riverine, and swamp forest, usually in moist places (Van Wyk and Van Wyk, 1997).

2.4.19.2 Medicinal uses

In southern Africa the stembark is used as an expectorant, as a laxative, and in the therapy of diabetes (Iwu, 1993). Powdered bark is applied topically to burns, which reputedly enhances the rate of healing (Venter and Venter, 1996). The Venda also use it to treat wounds, burns, toothache and venereal diseases (Mabogo, 1990). According to Hutchings *et al.* (1996) the Zulu people take an infusion as an emetic.

2.4.19.3 Phytochemistry/bioactivity

The following compounds were isolated from *Bridelia micrantha* (Pegel and Rogers, 1968 cited in Hutchings *et al.*, 1996): epifreidelinol, taraxol, gallic acid and ellagic acid. Gallic acid and ellagic acid seem to have antifungal and antiviral properties. Gallic and ellagic acid are antioxidants and were found to show cytotoxicity against cancer cells (Phytochemicals, 2007ab). Gallic acid is used as a remote astringent in cases of internal haemorrhage as well as in the treatment of albuminuria and diabetes.

2.4.20 Sclerocarya birrea

Sclerocarya birrea (A.Rich.) Hochst. (Anacardiaceae); common names: marula, cider tree (E); maroela (A); umganu (Z); morula (NS). Plant parts used: roots, bark, and leaves.

2.4.20.1 Description

This is a medium to large deciduous tree with an erect trunk and rounded, spreading crown. The leaves consists of 3 to 7 pairs of leaflets with a terminal one, dark green above and a paler bluish green below (Van Wyk and Van Wyk, 1997). The flowers are borne in small,

oblong clusters. Male and female flowers occur separately, usually, but not always on separate trees, before the new leaves. The flowers are small, with red sepals and yellow petals. The rough bark is flaky, with a mottled appearance due to contrasting grey and pale brown patches (Van Wyk *et al.*, 2005). A watery latex is present (Van Wyk *et al.*, 2000). An almost spherical fleshy fruit is borne in late summer to mid-winter, ripening to yellow after falling to the ground. The stone is hard with two to three openings plugged by lids. The tree is widely distributed throughout South Africa in bushveld and woodland (Van Wyk *et al.*, 2005).

2.4.20.2 Medicinal uses

Sclerocarya birrea is being used for diarrhoea, dysentery and unspecified stomach problems. It is also being used to combat fever and in the treatment of malaria (Watt and Breyer-Brandwijk, 1962; Hutchings, 1989; Hutchings *et al.*, 1996). Pujol (1990) reported that it is used as a general tonic, for indigestion and for the treatment of diabetes Decoctions or leaf infusions are taken for diabetes (Iwu, 1993).

2.4.20.3 Phytochemistry/bioactivity

According to Galvez *et al.* (1993) the bark contains procyanidins whereas Watt and Breyer-Brandwijk (1962) and Iwu (1993) reported that it contain gallotannins, flavonoids and catechins. No detailed information has been documented. The antidiarrhoeal effects have been experimentally linked to the procyanidins (Galvez *et al.*, 1993). Claims have also been made that it possesses hypoglycaemic effects (Iwu, 1993).

2.4.21 Brachylaena discolor

Brachylaena discolor DC. (Asteraceae); common names: coast silver oak (E); kusvaalbos(A); muakawura, mupasa (Sh); iphahla, umpahla (Z). Plant parts used: leaves.

2.4.21.1 Description

An evergreen shrub or small tree usually 4 to 10 m in height. The bark is rough, dark grey to brownish-grey. The leathery leaves are lanceolate to obovate, dark green above and pale whitish below and covered with dense hairs. The leaf margin is entire or obscurely and

irregularly toothed. The sexes are on different plants. The flowerheads are grouped in terminal panicles with creamy-white individual flowers. The fruit is a small achene, tipped with a tuft of bristly hairs (Coates Palgrave, 1984; Van Wyk and Van Wyk., 1997). It occurs in coastal woodland and bush as well as littoral scrub and on the margins of evergreen forests (Coates Palgrave, 1984).

2.4.21.2 Medicinal uses

According to Watt and Breyer-Brandwijk (1962) this species is being used for diabetes, renal conditions and as a tonic. Leaf infusions are used by the Zulu in the treatment of diabetes (Venter and Venter, 1996) and for intestinal parasites and for round worms (Watt and Breyer-Brandwijk, 1962).

2.4.21.3 Phytochemistry/bioactivity

Onopordopicrin has been isolated from aerial parts of *Brachylaena discolor* (Hutchings *et al*., 1996). Cytotoxic, antibacterial, and antifungal activities have been reported for onopordopicrin (Lonergan *et al*., 1992).

2.4.22 Brachylaena elliptica

Brachylaena elliptica (Thunb.) DC. (Asteraceae); common names: bitterleaf (E); bitterblaar (A); isiduti (X); iphahle, uhlunguhlungu (Z). Plant parts used: leaves.

2.4.22.1 Description

This is a shrub or small tree up to 4 m tall with a light grey to brown bark that becomes rough with age. The leaves are lanceolate, elliptic to ovate, dark green above and white felted below. The leaf margin is irregularly toothed and often with 2 lobes near the base giving the leaf a 3-lobed effect. The creamy white flowers are born in terminal and axillary flowerheads. The fruit is a small achene, tipped with a tuft of bristly hair (Coates Palgrave, 1984; Van Wyk and Van Wyk, 1997). *Brachylaena elliptica* occurs in bushveld on rocky outcrops and along coastal margins (Van Wyk and Van Wyk, 1997).

2.4.22.2 Medicinal uses

The leaves, which are extremely bitter tasting, are used medicinally (Van Wyk and Van Wyk, 1997) and valued by the Xhosa and Zulu as a treatment for diabetes. An infusion serves as a gargle and mouthwash (Coates Palgrave, 1984).

2.4.22.3 Phytochemistry/bioactivity

Watt and Breyer-Brandwijk (1962) stated that a *B. elliptica* infusion is bitter, contains one or more glucosides, probably no resin, and tested negative for alkaloids. It was also found that the leaf contains mucilage, tannin and a bitter ingredient which may be an alkaloid (Watt and Breyer-Brandwijk, 1962). Research has shown that infusions have no effect upon carbohydrate metabolism and little or no improvement in glycosuria or blood sugar percentages (Watt and Breyer-Brandwijk, 1962; Hutchings *et al.*, 1996). The benefit derived from its local use as a gargle arises from the demulcent and astringent effects of the mucilage and the tannins, respectively (Watt and Breyer-Brandwijk, 1962).

2.4.23 Brachylaena ilicifolia

Brachylaena ilicifolia (Lam.) E. Phillips & Schweick. (Asteraceae); common names: small bitter leaf (E); fynbitterblaar (A). Plant parts used: leaves.

2.4.23.1 Description

This is a shrub or small tree between 3 and 4 m in height with a grey to brown bark. The leaves are often on short lateral branches, small, narrowly oblong, lanceolate to ovate, green above and covered with whitish-green hairs below. The leaf apex is rounded with a sharp spine-like tip, the margin entire or with small teeth. The flowerheads are thistle-like and the individual flowers are cream to yellow and grouped into a capitilum. The flowers give rise to a small achene with whitish bristly hairs (Coates Palgrave, 1984). *Brachylaena ilicifolia* occurs in bush, scrub forest and on rocky hillsides (Coates Palgrave, 1984).

2.4.23.2 Medicinal uses

The leaves, which are intensely bitter, are used by Africans to treat diabetes (Coates Palgrave, 1984). It may be used in the same way as *B. elliptica* (Watt and Breyer-Brandwijk, 1962).

2.4.23.3 Phytochemistry/bioactivity

In the literature no information could be found on the phytochemistry or bioactivity of *B. ilicifolia.*

2.4.24 Bulbine latifolia

Bulbine latifolia (L.f.) Spreng. var. ***latifolia*** (Asphodelaceae); common names: broad-leaved Bulbine (E); ibhucu (Z); rooiwortel, geelkopieva (A); incelwane (Xh). Plant parts used: fresh leaves and roots.

2.4.24.1 Description

This is a perennial with tuberous roots. The leaves are thick fleshy, bright green to yellow and arranged in a rosette. The inflorescence is borne on a long stem in a cluster consisting of yellow flowers. It occurs widespread in hot dry areas in the eastern and northern parts of South Africa (Pooley, 1998).

2.4.24.2 Medicinal uses

The sap of *Bulbine* species is widely used for the treatment of wounds, burns, rashes, itches, ringworm, cracked lips (Watt and Breyer-Brandwijk, 1962; Rood, 1994; Pujol, 1990) and Herpes (Van Wyk *et al.,* 2005). Root infusions of *Bulbine latifolia* are taken orally to quell vomiting and diarrhoea (Pujol, 1990), convulsions, venereal diseases, diabetes, urinary complaints, rheumatism and blood disorders (Van Wyk *et al.,* 2005; Pooley, 1998). Leaf sap is applied directly to the skin or in the form of a warm poultice. An infusion of the roots or sometimes a brandy tincture is taken two or three-times daily (for internal use) (Watt and Breyer-Brandwijk, 1962).

2.4.24.3 Phytochemistry/ bioactivity

The stems and roots of *Bulbine* species contain anthaquinones such as chrysophanol and kinpholone (Van Staden and Drewes, 1994; Van Wyk *et al*., 1995), but these compounds are probably of minor importance in the healing of wounds. Chrysophanol has been shown to have antibacterial properties (Bruce, 1975). The healing effect is likely to be due to glycoproteins such as, aloctin A and B, in the leaf gel (Suzuki, 1981).

2.4.25 Carpobrotus edulis

Carpobrotus edulis (L.) L. Bolus (Mesembryanthemaceae); common names: suurvy, perdevy, vyerank (A); gaukum (K); t'kobovy (Nama); sour fig (E). Plant parts used: leaf juice and leaf pulp.

2.4.25.1 Description

A creeping succulent perennial with light green leaves often tinted red. The long leaves are slightly bent, tapered to the apex to give a more or less triangular shape. The large yellow flowers change to pink as they mature (Le Roux, 2005). The fragrant fruit contains a jellylike, sweet-sour pulp with a multitude of small, brown seeds (Van Wyk *et al*., 2005). Originally found in sandy, dry riverbeds along the coastlines of Namaqualand and south and eastwards along the coastline of the Western and Eastern Cape (Le Roux, 2005).

2.4.25.2 Medicinal uses

Juice from the leaves is gargled to treat throat and mouth infections (Rood, 1994). It is also taken orally for dysentery, digestive ailments, tuberculosis and as a diuretic (Watt and Breyer-Brandwijk, 1962). It is highly astringent and is applied externally to treat eczema, wounds and burns (Watt and Breyer- Brandwijk, 1962; Rood, 1994). It is also said to be effective against toothache, earache and oral and vaginal thrush. The fresh juice is taken orally or gargled whereas the leaf pulp is applied to the skin to treat wounds and infections (Watt and Breyer- Brandwijk, 1962; Rood, 1994). *C. edulis* has traditionally been used in South Africa for the treatment of diabetes mellitus (Van Huyssteen, 2003).

2.4.25.3 Phytochemistry/bioactivity

The beneficial medicinal effects are probably due to the presence of tannins. Tannins have the ability to form complexes with proteins, such as digestive enzymes and fungal or viral toxins. In addition to their antiseptic activity, tannins have a vasoconstricting effect and reduce fluid loss from wounds and burns, thereby enhancing tissue regeneration (Bruneton, 1995). The juice is said to be mildly antiseptic and highly astringent. The leaves also contain malic and citric acid (Watt and Breyer-Brandwijk, 1962).

2.4.26 Chironia baccifera

Chironia baccifera L. (Gentianaceae); common names: aambeibossie, bitterbossie, agdaegeneesbossie, perdebossie (A); Christmas berry, Wild Gentian (E). Plant parts used: whole plant.

2.4.26.1 Description

This is a much branched shrublet between 0.5 and 1m tall. The stems are rigid, angled or narrowly winged. The narrow, thin or slightly fleshy leaves are semiclasped at the base with a hooked tip. Solitary pink flowers with conspicuous yellow anthers are borne terminally from August to February (Pooley, 1998). The flowers are followed by bright red berries when ripe (Van Wyk *et al.*, 2005). This shrublet is found from the Cape Peninsula northwards to the Kamiesberg and eastwards into the Eastern Cape and KwaZulu-Natal. It usually grows in dry, sandy soils in the shade of other plants as well as in full sun (Van Wyk *et al.*, 2005; Dyer *et al*. 1963).

2.4.26.2 Medicinal uses

Chironia baccifera is traditionally used by the Khoi as a purgative and for the treatment of boils (Watt and Breyer-Brandwijk, 1962). It is also used in traditional medicine as a purgative and for the treatment of haemorrhoids (Watt and Breyer-Brandwijk, 1962; Smith, 1966; Rood, 1994; Pooley, 1998). A decoction of the whole plant is taken as a blood purifier to treat acne, sores and boils (Van Wyk *et al.*, 2005). Infusions may be used as a remedy for diarrhoea or for leprosy (Watt and Breyer-Brandwijk, 1962). According to Van

Wyk and Gericke (2000), the plant is used as a bitter tonic and infusions and tinctures from the leaves and stems are used to treat diabetes. Decoctions, tinctures or infusions are taken, but the plant is potentially toxic therefore use should be controlled. Plant material is fried in butter and then applied externally to sores (Watt and Breyer-Brandwijk, 1962). Infusions are also applied to haemorrhoids (Van Wyk *et al.*, 2005).

2.4.26.3 Phytochemistry/bioactivity

The roots of *C. baccifera* contain various secoiridoids, of which gentiopicrosid is the main component, together with small quantities of swertiamarine, chironoiside and others (Wolfender *et al.*, 1993). The bitter iridoids are known to stimulate appetite, but the compounds responsible for the healing properties appear to be unknown (Van Wyk *et al.*, 2005).

2.4.27 Cissampelos capensis

Cissampelos capensis L.f. (Menispermaceae); common names: dawidjiewortel (A). Plant parts used: rhizomes and roots.

2.4.27.1 Description

A perennial climber with twining stems and rounded, bright green leaves (Botha, 1980). The plant supports itself by twining around the stems of other plants. The flowers, borne in clusters are small, hairy and greenish and are followed by orange berries (Van Wyk *et al.*, 2005). It is widely distributed in the western parts of South Africa (Van Wyk *et al.*, 2005).

2.4.27.2 Medicinal uses

A well-know medicinal plant in the Western Cape which is traditionally used as a blood purifier for boils and syphilis, and also taken for bladder ailments, diarrhoea, colic and cholera (Watt and Breyer-Brandwijk, 1962). The Xhosa apply a paste of the leaves to wounds and sores (Watt and Breyer-Brandwijk, 1962). It is traditionally taken as a brandy tincture, as an infusion or decoction with *Pentzia incana* (Thunb.) Kuntze and *P. globosa* Less. and externally applied as a poultice (Watt and Breyer-Brandwijk, 1962). Fresh or dry

rhizomes are chewed or taken directly as an infusion or tincture for diabetes (Van Wyk and Gericke, 2000).

2.4.27.3 Phytochemistry/bioactivity

A large number of biologically active alkaloids of the bisbenzyltetrahydroisoquinoline type have been isolated from several *Cissampelos* species, of which cissampareine is a typical example (Van Wyk *et al.*, 2005). According to Watt and Breyer-Brandwijk (1962) *Cissampelos* species contains the alkaloid cissampeline. Sedative, antispasmodic and antitumour properties have been ascribed to Menispermaceae alkaloids (Anonymous, 1996; Bruneton, 1995).

2.4.28 Harpagophytum procumbens

Harpagophytum procumbens (Burch.) DC. ex. Meisn. (Pedaliaceae); common names: devil's claw, grapple plant (E); duiwelsklou (A); ghamaghoe (K). Plant parts used: secondary roots.

2.4.28.1 Description

A perennial plant with creeping, annual stems protruding from a fleshy corn. The leaves are blue-green on top and silver-grey underneath. The tubular flowers are a deep purple to pink with a yellow centre. The characteristic fruit has numerous "tentacles" with sharp, hooked thorns as well as two straight thorns on the upper surface (Van Rooyen, 2001). It occurs in sandy soils in the northwestern parts of southern Africa as well as the dune veld of the Kgalagadi Transfrontier Park (Van Rooyen, 2001).

2.4.28.2 Medicinal uses

H. procumbens is an important medicinal plant, the corms and roots are used for ailments of the gallbladder and kidneys, for diabetes, arteriosclerosis, osteoarthritis, rheumatism, ulcers, high blood pressure and fever (Van Wyk and Gericke, 2000; Van Rooyen, 2001). Dried root infusions are taken as a cure for digestive disorders and as a tonic (Van Wyk *et al.*, 2005). The fresh tuber is made into an ointment and applied to sores,

ulcers, boils and other skin lesions (Watt and Breyer-Brandwijk, 1962). An infusion of 1.5 g of powdered material in a cup of boiling water and strained, can be taken daily. Standardised extracts are available in the form of capsules, tablets, tinctures and ointments (Van Wyk *et al*., 2005).

2.4.28.3 Phytochemistry/bioactivity

According to Van Wyk *et al*. (2005) the roots are rich in sugars but also contain phytosterols, triterpenoids and flavonoids. The active ingredients in the roots are considered to be a cinnamic acid ester, harpagoside, harpagide (possibly a degradation product of harpagoside) and procumbide (Czygan and Krüger, 1977; Pourrat *et al.*, 1986; Anonymous, 1996). According to Bruneton (1995), animal studies indicated slight analgesic and anti-arthritic effects. In Germany it is used in supportive therapy for degenerative disorders of the locomotor system, for lack of appetite and dyspeptic problems (Van Wyk *et al*., 2005). A recent clinical study indicated effectiveness in the treatment of acute low backache (Chrubasik *et al*., 1996).

2.4.29 Hoodia currorii

Hoodia currorii (Hook.) Decne. (Asclepiadaceae); common names: Ghaap; !khobab (K). Plant parts used: fleshy stem.

2.4.29.1 Description

These are leafless succulent plants with thick fleshy erect stems with rows of small thorns. The disc-like, flesh-coloured flowers smell strongly of decaying meat, attracting flies and blowflies for pollination (Van Wyk and Gericke, 2000). It occurs in the dry north-western parts of southern Africa.

2.4.29.2 Medicinal uses

Hoodia currorii is eaten as a food, used as an appetite-suppressant, and is used to treat indigestion, hypertention, diabetes and stomachache (Van Wyk and Gericke, 2000).

According to Von Koenen (2001) the plant is known as a diabetes remedy to the Damara people of Namibia.

2.4.29.3 Phytochemistry/ bioactivity

Hoodia species contains a pregnane glycosides P57 that suppress hunger (Van Wyk and Wink, 2004).

2.4.30 Nymphaea nouchali

Nymphaea nouchali Burm.f. var. ***caerulea*** (Savigny) Verdc. (Nymphaeaceae); common names: egyptian blue lily; sacred blue lily; blue water lily (E); blouwaterlelie, kaaimanblom (A); iZubu (Z). Plant parts used: seeds.

2.4.30.1 Description

This is a perennial hydrophyte with tuberous rhizomes anchored in pond mud by spreading roots. It does not have a true stem but the leaves are born on long leaf stalks that arise directly from the rhizome. The leaves are large, flat, and oval with smooth margins and a deep sinus where the petiole is attached. The showy, blue, bisexual flowers appear above the water at the tip of a sturdy stalk from September until April. Colour variations may occur varying from white to mauve. Numerous blue-tipped bright yellow stamens occupy the centre of the flower. In Africa this species occurs from tropical to southern Africa where it is common. In South Africa it is found in waterbodies in the Highveld, Lowveld as well as in KwaZulu-Natal (Viljoen and Notten, 2002).

2.4.30.2 Medicinal uses

The seeds of *Nymphaea nouchali* are used as a remedy for diabetes. An infusion of the root and stem is emollient and diuretic and is used in treating blenorrhagia and infections of the urinary passages. A decoction of the flower is said to be a narcotic as well as an aphrodisiac. The flowers have been used as a remedy for dysuria and for coughs (Watt and Breyer-Brandwijk, 1962).

2.4.30.3 Phytochemistry/bioactivity

N. nouchali contains the alkaloids nuciferine and apomorphine. Recent studies have also shown it to have euphoric properties (Perry *et al.*, 2002).

2.4.31 Trigonella foenumgraecum

Trigonella foenumgraecum L. (Fabaceae); common names: fenugreek; fenugrec (France); fieno Greco (Italian); alholva, feno-greco (Sp); helba (Arabic); methi (Indian). Plant parts used: seeds.

2.4.31.1 Description

A highly aromatic, erect, annual herb with trifoliate oblong-lanceolate leaflets. Yellowish flowers are borne in the leaf axil. The fruit is a long, narrow, sickle-like pod containing the brownish oblong seeds that are divided by a furrow into two unequal lobes (Suttie, 2007). Fenugreek is originally from the Mediterranean regions, northeastern Africa and western Asia (Van Wyk and Wink, 2004), but currently cultivated in India and neighbouring countries as well as in France, Turkey, and China. Fenugreek grows on a wide range of well-drained soils (Suttie, 2007).

2.4.31.2 Medicinal uses

Fenugreek is an important medicinal plant and is used for the treatment of abdominal colic, bronchitis, coughs, sprains, diabetes, asthma, emphysema, gastrointestinal troubles, constipation, fever, sterility, a treatment after child birth, and also as a digestive, an abortive, a purgative, a galactagogue, an emmenagogue, a stomachic, reconstituent, sedative for palpitations, icterus, an anthelmintic and an aphrodisiac (Suttie, 2007). A herbal mixture consisting of 5 g of *Tylophora hirsuta* Wight. leaves, 25 g of *T. foenumgraecum* seeds and 50 g of the aerial parts of *Fumaria indica* in water is being used for diabetes (Mushtaq *et al.*, 2007).

2.4.31.3 Phytochemistry/bioactivity

The seeds are rich in mucilage, mainly glactomannans, lipids, proteins, and protease inhibitors (Van Wyk and Wink, 2004). Steroidal saponin and the aglycone diosgenin and its epimer yamogenin are found in the seed oil of fenugreek whereas the alkaloid trigonelline

was extracted from the seeds. Small amounts of an alkaloid, trigonelline, and a steroidal peptide, foenugraecin, may contribute to the medicinal properties. Fenugreek also contains the furostanol glycosides trigofoenosides A/G (Van Wyk and Wink, 2004; Suttie, 2007). The saponins could be responsible for the observed antidiabetic, lipid and cholesterol lowering activities (Van Wyk and Wink, 2004).

2.4.32 Vernonia oligocephala

Vernonia oligocephala (DC.) Sch.Bip. ex Walp. (Asteraceae); common names: groenamara, bitterbossie (A); mofolotsane (SS); sefafatse (Ts); ihlambihloshane (Z). Plant parts used: aerial parts.

2.4.32.1 Description

It is an erect, perennial, herbaceous plant up to 1 m tall. The stems develop from a woody rootstock. The elliptic leaves are pale green above and silver below due to the presence of a velvet hair cover. The dark pink flowerheads are grouped together on the branch tips (Van Wyk and Malan, 1988). *V. oligocephala* is widespread throughout the grassland regions of South Africa (Van Wyk and Malan, 1988; Van Wyk *et al.*, 2005).

2.4.32.2 Medicinal uses

Infusions are taken as stomach bitters to treat abdominal pains and colic. It is also used for the treatment of rheumatism, dysentery and diabetes (Watt and Breyer-Brandwijk, 1962; Pujol, 1990; Hutchings *et al.*, 1996). Infusions are made of the leaves (Van Wyk *et al.*, 2005).

2.4.32.3 Phytochemistry/bioactivity

Various sesquiterpenoid lactones have been isolated from *Vernonia* species (Anonymous, 1996), including germacranolides and glaucolides for example glaucolide A (Bohlman *et al.*, 1984).

2.5 Conclusions

The trade in traditional medicines forms part of a multi-million rand economy in southern Africa (Cunningham, 1997), stimulated by high population growth, rapid urbanization, unemployment, and a high cultural value of traditional medicines (Dold and Cocks, 2002). The trade is now greater than at any time in the past and is certainly the most complex resource managing issue facing conservation agencies, health care professionals and resource users in South Africa (Dold and Cocks, 2002).

The popularity of herbal medicines has led to increasing concerns over their safety, quality and efficacy. In many countries the herbal medicine market is poorly regulated and products are neither registered nor controlled. There is a lack of detailed documentation on the use of medicinal plants in South Africa. The need to document traditional knowledge is a priority because the rapid pace of urbanization and aculturation in this country could easily lead to the permanent loss of this knowledge (Van Wyk *et al.*, 2005).

A study was conducted to look at mortality from traditional medicine of patients admitted at Ga-Rankua Hospital, South Africa. The results of this study have reinforced the concerns of the Medicines Control Council about the safety of some traditional medicines. Some medicinal plants species used by traditional healers in South Africa have shown a significant degree of toxicity, which obviously outweighs their benefits (South African Traditional Medicine Research Unit, 2005).

In the quest for discovering new hypoglycaemic substances it is necessary to scientifically validate the claimed medicinal properties of traditional medicines. This inventory will assist researchers in the selection of plant species to evaluate for their hypoglycaemic activities. This study also gives an indication of the toxicity of some of the plant extracts where this information was available. The method of preparation and administration of medicines used by traditional healers is the starting point to design experimental protocols aimed at finding scientific evidence of efficacy and toxicity. The ability to produce safe, standardized medicinal plant products for further clinical evaluation is a major stumbling block in most countries wishing to enhance the quality of their traditional medicines (South African Traditional Medicine Research Unit, 2005).

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