CHAPTER ONE

INTRODUCTION

1.1 Problem statement

Diabetes Mellitus (DM) Type II is a complex metabolic disorder triggered by lifestyle factors superimposed on a genetic predisposition. DM Type II is responsible for approximately 90% of all diabetes, and accounts for most of the public health and cost burden attributable to diabetes. Although DM Type II is mainly a condition found in adults, recent studies highlight its increasing prevalence in adolescents and children. The rapid rise of childhood obesity and its causal link to diabetes has led Olshansky *et al*. to forecast that DM Type II has the potential to result in a decline in the overall life expectancy of the population within the first half of this century (Colagiuri *et al.*, 2006).

DM Type II is reaching epidemic proportions worldwide. According to the Independent Diabetes Federation (IDF), DM Type II currently affects 200 million people. This figure is expected to reach 300 million by 2020. The IDF has shown that diabetes is one of the leading causes of death worldwide through its effects on cardiovascular disease: 70 to 80 percent of people with diabetes die of cardiovascular disease (Nevin, 2005). In addition to increasing the cost of cardiovascular mortality, renal failure, amputations and blindness, there are substantial concerns over the cost of treating patients with diabetes and its complications (Chammas and Shotliff, 2002).

Head of Endocrinology and Metabolism at Johannesburg Hospital, Professor Derek Raal, stated at a diabetic conference that four million South Africans currently live with diabetes and many of them are undiagnosed. Raal also states that DM Type II was considered a disease of the middle age, but one third of new cases of diabetes in children aged 10-19 years are now Type II (Nevin, 2005).

Arsenicum album, *Phosphoricum acidum, Uranium nitricum, Lactic acid* and *Insulinum* are remedies beneficial in the treatment of DM Type II (Dewey, 2001) (Nash, 2003) (Varma and Vaid, 2002).

1.2 Aim of study

- The objective of this study was to determine the efficacy of a homoeopathic complex formulation consisting of *Arsenicum album 6CH*, *Phosphoricum acidum 6CH, Uranium nitricum 6CH, Lactic acid 6CH* and *Insulinum 7CH* in the treatment of DM Type II over a two-month period.

- The above information would be utilised in improving the current treatment of DM Type II. The information would introduce a complementary homoeopathic approach to the mainstream management of DM Type II.

1.3 Hypothesis

It is anticipated that the complex formulation of the following homoeopathic remedies *Arsenicum album 6CH*, *Phosphoricum acidum 6CH, Uranium nitricum 6CH, Lactic acid 6CH* and *Insulinum 7CH* will reduce the blood-glucose levels and HbA_{1C} levels in people with DM Type II.

1.4 Null Hypothesis

It is anticipated that the homoeopathic complex formulation of *Arsenicum album 6CH, Phosphoricum acidum 6CH, Uranium nitricum 6CH, Lactic acid 6CH* and *Insulinum 7CH* will not be beneficial in reducing the blood-glucose levels and HbA_{1C} levels in people with DM Type II.

1.5 Importance of the problem

Diabetes is now cited as a global epidemic and is intertwined with the obesity epidemic. The International Diabetes Federation estimate that there were 189 million people with diabetes in 2003 and predicts an increase to 324 million in 2025. The World Health Organization (WHO) estimates an increase from 171 million in 2000 to 366 million in 2030. Approximately 70% of this growth is predicted to occur in the developing world and will increasingly affect people aged younger than 65 years who are still in the productive stages of their life cycle. The increase in the younger aged group being diagnosed with DM Type II poses an economic threat over and above the more direct disease cost to the public (Colagiuri *et al.*, 2006).

Due to the increase in the prevalence of DM Type II and due to the fact that this epidemic is reaching the younger aged groups, this disease is of substantial concern. The cost in treating and managing DM Type II (Chammas and Shotliff, 2002) as well as patient education has risen. An alternative, cost-effective approach in lowering blood-glucose levels of DM Type II is required.

Homoeopathy presents an alternative to the 'high costs' and the considerable drug-related risks of modern medicine. In cases that are susceptible to medical management alone, homoeopathy offers an approach to health care that produces the least possible disturbance within the organism. This is due to the miniscule doses administered in homoeopathy and the well-established effects of the drugs that are used. Homoeopathy increases resistance to disease (Weiner, 1989).

Arsenicum album, *Phosphoricum acidum, Uranium nitricum, Lactic acid* and *Insulinum* are remedies considered to be beneficial in the treatment of DM Type II. Conventionally DM Type II is homoeopathically treated using a single remedy (i.e. similimum prescribing). Dr. Ramakrishnan conducted a homoeopathic study consisting of 500 diabetes mellitus cases. These cases were followed for approximately five years. Participants were treated constitutionally i.e. the study used single remedy prescription. The application of a constitutional remedy varies considerably with each patient's constitution. The results of this trial concluded that in 410 cases the blood glucose levels were normalised. In 160 cases participants did not require further treatment. However Dr, Ramakrishnan does state that in addition to the constitutional remedy, "other remedies can be used for quick blood sugar control" (Hardy, 2000).

This study is a compilation of homoeopathic remedies used for lowering blood-glucose levels. The trial may allow for an effective and a more rapid approach to the homoeopathic treatment of DM Type II should the medication prove to be successful. This would aid in providing a cost-effective approach in lowering blood-glucose levels, thus allowing a complementary and effective approach to the homoeopathic treatment of DM Type II. Other research into the homoeopathic treatment of DM Type II may be initiated following this study.

CHAPTER TWO

LITERATURE REVIEW

2.1 Introduction

Diabetes Mellitus is one of the most common chronic medical disorders and is expected to present one of the twenty-first century's biggest medical challenges. The number of people with diabetes is escalating worldwide and DM Type II in particular is increasing at an alarming rate (Clark, 2004). Lifestyle changes characterised by increased energy intake and decreased physical activity together promotes obesity. These are strong risk factors for diabetes (Bantle *et al.,* 2006). Amongst the chronic illnesses diabetes is unique in the degree to which patient behaviour influences the application and outcomes of therapy (Clark, 2004).

2.1.1 Definition

Diabetes Mellitus is a condition characterised by collection of disorders that have hyperglycaemia and glucose intolerance as their hallmark. Diabetes Mellitus may be due to insulin deficiency, impaired effectiveness of insulin's action, or a combination of the two (Alberti *et al*., 1997). Lack of insulin whether relative or absolute leads to a derangement in carbohydrate, fat, protein, electrolytes and water metabolism (Sahni, 2003) (Pavri, 2001). Chronically deranged metabolism is associated with permanent and irreversible functional and structural changes in body cells. These changes are responsible for the 'complications' of diabetes, which mainly affects the cardiovascular system, eyes, kidneys and nervous system (Pavri, 2001).

The clinical diagnoses of diabetes mellitus is made in terms of plasma glucose levels:

- A fasting glucose level of more than 7.8 mmol/L
- A plasma glucose level of more than 11.1 mmol/L more than two hours after food is last taken (Rippey, 1999).

2.1.2 Incidence of Diabetes Mellitus

The global incidence of all types of diabetes is steadily increasing. Approximately 2% of people have diabetes, although a third of these are undiagnosed. DM Type II accounts for about 85% of all diabetes, and the prevalence has risen by 50% in the past 20 years (Warren, 2002). According to World Health Organisation at least one in 10 deaths in adults aged 35-64 is caused by diabetes in most developing countries (Miller, 2004).

Diabetes is prevalent in the population greater and equal to 65 years of age. The greatest increases in prevalence are expected among the elderly: from 252% among 65-74years of age to 537% among men greater and equal to 75 years of age (McBean *et al*., 2004).

Approximately four million people in South Africa have diabetes, according to the Chronic Disease of Lifestyle Unit of the Medical Research council. An estimated 3-5% of white South Africans have been diagnosed with DM Type II, whilst an average of 8% of black South Africans and 14% of Indians have the disease (Miller, 2004).

2.1.3 Anatomy of the Pancreas

The pancreas lies within the abdomino-pelvic cavity in the J-shaped loop between the stomach and the small intestine (Martini, 1998) (Refer to Figure 2.1). It is a slender, soft, grayish-pink digestive gland. The adult pancreas is 12-15 cm long and weighs about 80g (Moore, 1992).

The pancreas is divided into a head, body, and tail. The broad head of the pancreas lies within the loop formed by the duodenum as it leaves the pylorus. The slender body extends transversely toward the spleen, and the tail is short and bluntly rounded (Martini, 1998).

The pancreas acts as an endocrine and exocrine gland. It produces an external secretion that enters the duodenum via the pancreatic duct and an internal secretion that enters the blood. The external secretion is pancreatic juice and the internal secretion is made up of glucagon and insulin (Moore, 1992).

The exocrine pancreas makes up roughly 99% of the pancreatic volume and consists of clusters of gland cells, called *pancreatic acini,* and their attached glands. As an exocrine gland the pancreas secretes pancreatic juice through the pancreatic duct into the duodenum (Fox, 2006). The endocrine pancreas consists of small groups of cells scattered amongst the exocrine cells. The endocrine clusters are known as pancreatic islets or the *islets of Langerhans* (Martini, 1998).

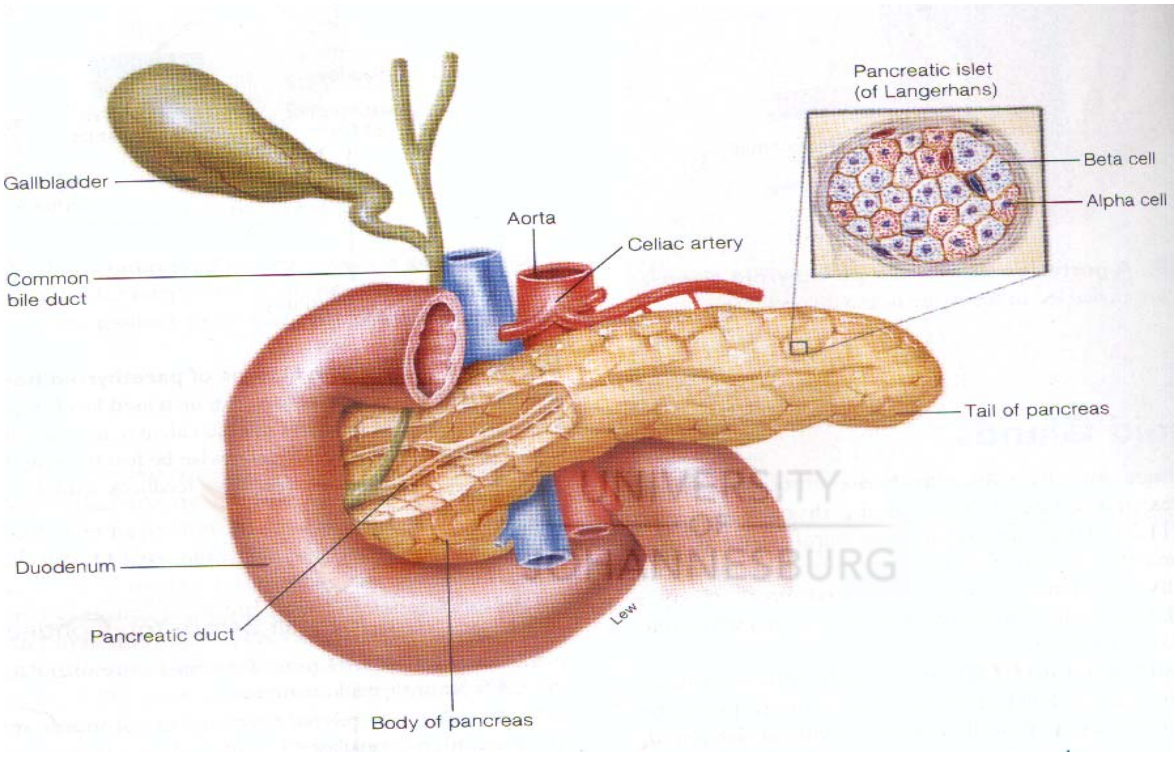

Figure 2.1 Anatomy of the Pancreas (Fox, 2006)

An extensive capillary network that carries its hormones into the circulation surrounds the pancreatic islets. Each islet contains four different cell types:

- Alpha cells produce the hormone glucagon. Glucagon raises blood glucose levels by increasing the rates of glycogen breakdown and glucose release by the liver (Cahill, 1999).
- Beta cells produce the hormone insulin. Insulin lowers blood glucose by increasing the rate of glucose uptake and utilization by most body cells and increasing glycogen synthesis in skeletal muscles and the liver (Martini, 1998).

- Delta cells produce a peptide hormone identical to somatostatin, a hypothalamic regulatory hormone. Somatostatin that is produced in the pancreas suppresses glucagon and insulin release by other islet cells and slows the rates of food absorption and enzyme secretion along the digestive tract (Martini, 1998).
- F cells produce the hormone pancreatic polypeptide, which inhibits gallbladder contractions and regulates the production of some pancreatic enzymes. It may help control the rate of nutrient absorption by the digestive tract (Martini, 1998).

Insulin and glucagon are the hormones responsible for the regulation of blood-glucose concentrations. These hormones interact to control blood-glucose levels. When blood-glucose levels rise, beta cells secrete insulin, which then stimulates the transport of glucose across cell membranes. When blood-glucose levels decline, alpha cells secrete glucagon, which stimulates glucose release by the liver (Martini, 1998) (Refer to Figure 2.2).

2.1.4 Action of insulin

Insulin is a peptide hormone, manufactured by the beta cells of the islets of Langerhans in the pancreas. It is secreted and stored in membrane bound vesicles in the cells and released on demand, usually in response to an increase in plasma glucose levels. Glucose also stimulates insulin synthesis by the cells (Rippey, 1999). Insulin secretion is also stimulated by elevated levels of some amino acids including arginine and leucine (Martini, 1998).

Insulin exerts its effects on cellular metabolism in a series of steps that begins when insulin binds to receptor proteins on the cell membrane. Insulin receptors are present in most cell membranes, such cells are called insulin-dependant. However, cells in the brain, kidneys, lining of the digestive tract and red blood cells lack insulin receptors. These cells are called insulin- independent, because they can utilize and absorb glucose without insulin stimulation (Martini, 1998).

The most important action of insulin is to facilitate the entry of glucose into cells, especially voluntary muscle cells, fibroblasts and fat cells. Insulin also increases glycogen formation and promotes the synthesis of proteins from amino acids. In fat cells insulin is necessary for the conversion of glucose to triglycerides. This process thus inhibits the breakdown of neutral fat (Rippey, 1999).

Insulin and insulin-like growth factors can bring about DNA synthesis in cells, and stimulate growth and differentiation. Glucose is maintained at a plasma glucose level of 3.0-5.0mmol/l by the action of insulin, which lowers the level, and the activity of the liver. The liver can store glucose as glycogen or produce glucose from glycogen or non-carbohydrate sources such as amino acids from protein and fat (Rippey, 1999).

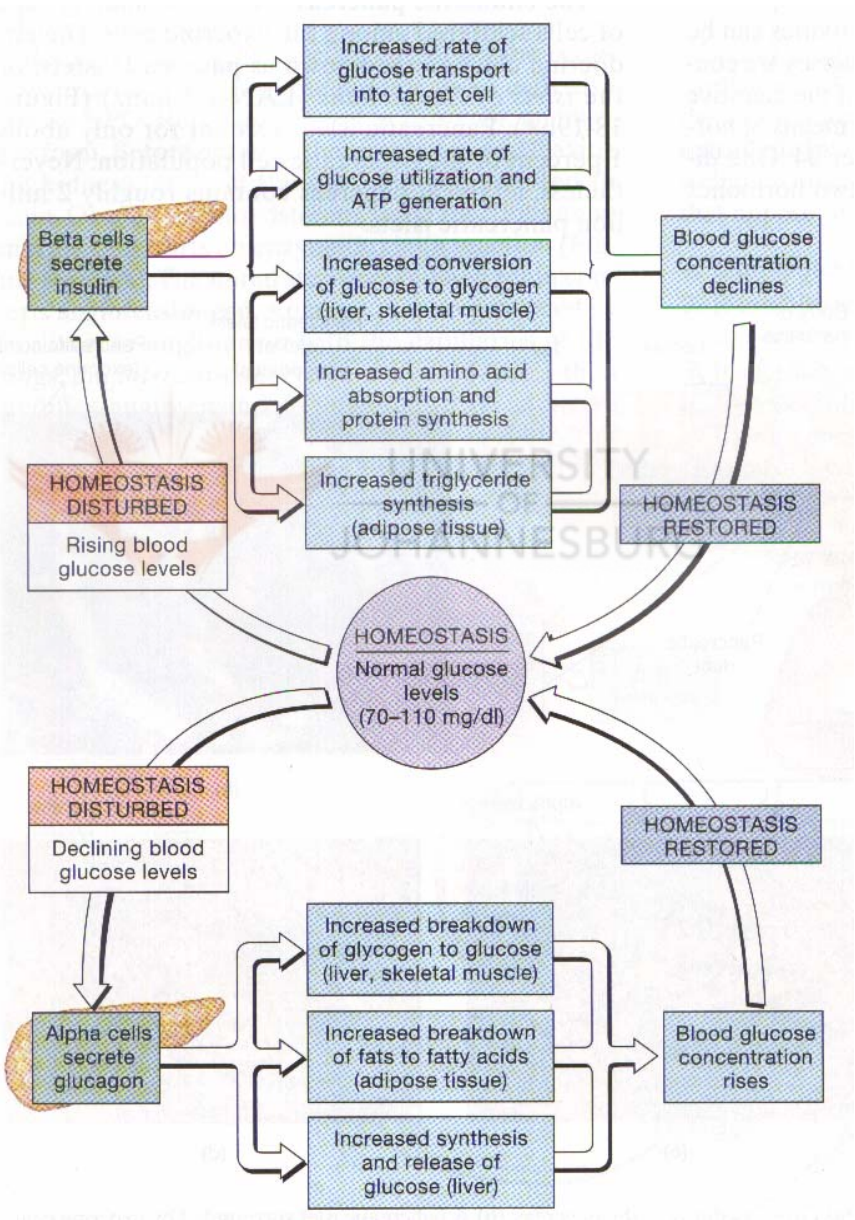

Figure 2.2 The Regulation of Blood Glucose Concentrations (Martini, 1998)

2.2 Classification

The categories of diabetes include:

- DM Type I
- DM Type II
- Gestational diabetes mellitus (GDM)
- Secondary diabetes
- Various others (Cahill, 1999).

2.2.1 DM Type I

DM Type I commonly develops in childhood and early adolescence and is predominantly the type of diabetes mellitus diagnosed before the age of 30, however according to the American Diabetes Association, DM Type I can occur at any age even in 8th and 9th decades of life (American Diabetes Association[a], 2005). It is clinically characterised by hyperglycaemia. This form of diabetes, which accounts for only 5-10% of those with diabetes, was previously encompassed by the terms insulin-dependent diabetes or juvenile-onset diabetes (American Diabetes Association[a], 2005). DM Type I is primarily a failure of insulin production resulting from an autoimmune destruction of the pancreatic islet cells (Kligler and Lynch, 2003). The pancreas produces little or no insulin (Beers and Berkow, 1999). DM Type I indicates the processes of beta-cell destruction that may ultimately lead to diabetes mellitus in which "insulin is required for survival" to prevent the development of ketoacidosis, coma and death (WHO, 1999).

In this form of diabetes, the rate of beta-cell destruction is quite variable, being rapid in some individuals (mainly infants and children) and slow in others (mainly adults). Some patients, particularly children and adolescents, may present with ketoacidosis as the first manifestation of the disease. Others have modest lasting hyperglycaemia that can rapidly change to severe hyperglycaemia and/or ketoacidosis in the presence of infection or other stress. Still others, particularly adults, may retain residual beta-cell function sufficient to prevent ketoacidosis for many years; such individuals eventually become dependent on insulin for survival and are at risk of ketoacidosis (American Diabetes Association[a], 2005). Individuals with DM Type I are at a risk of

other autoimmune disorders such as Grave's disease and pernicious anaemia (Kligler and Lynch, 2003).

2.2.2 DM Type II

DM Type II accounts for 90-95% of those with diabetes. This form of diabetes was previously referred to as non-insulin-dependent or adult-onset diabetes (American Diabetes Association[a], 2005). DM Type II is characterised by two metabolic defects: insulin resistance and impaired insulin secretion (Gregory, 2003). DM Type II results from progressive beta-cell failure superimposed on long-standing insulin resistance. The insulin resistance is associated with many metabolic abnormalities, including central obesity, hypertension, dyslipidemia (elevated plasma triglycerides, low high-density lipoprotein [HDL] cholesterol levels and postprandial hyperlipidaemia), hyperinsulinaemia and elevated plasminogen activator inhibitor-1 levels. These factors collectively increase the risk of developing macrovascular disease (Reasner and Defronzo, 2001).

In DM Type II the aetiology is unknown but a strong genetic component is present. A reduction in the number of insulin receptors, which is often associated with obesity, is another aetiology (Neal, 2002). Early in the disease patients respond well to change of lifestyle i.e. diet and exercise and oral antidiabetic agents, but many ultimately need insulin treatment (Gregory, 2003).

The incidence of DM Type II is rising concurrent with the epidemic of obesity. A recent steady demographic shift in DM Type II to younger populations is noted (Kligler and Lynch, 2003).

2.2.3 Gestational Diabetes Mellitus (GDM)

Gestational Diabetes Mellitus is defined as any degree of glucose intolerance with onset or first recognition during pregnancy. The definition applies regardless of whether insulin or only diet modification is used for treatment or whether the condition persists after pregnancy (American Diabetes Association[a], 2005).

Symptoms are usually mild, though untreated GDM can cause a number of complications (Cahill, 1999). Gestational Diabetes Mellitus can lead to foetal macrosomia, shoulder dystocia and metabolic problems in the newborn. Clinical recognition is important because treatment and

antepartum foetal surveillance can reduce perinatal morbidity and mortality. Women fall into a high-risk group because of a strong family history, prior GDM, unexplained prior intrauterine death, or abnormal fasting glucose prior to pregnancy. Current practice is to screen all women for GDM between 24 and 28 weeks of gestation but those in the high-risk group should be screened earlier (Kligler and Lynch, 2003).

2.2.4 Secondary Diabetes

Diabetes may arise as a secondary condition as well (Cahill, 1999). Several forms of diabetes are associated with defects in Beta cell function. These forms of diabetes are frequently characterised by onset of hyperglycaemia at an early age. They are referred to as maturity onset diabetes of the young (MODY) and are characterised by impaired insulin secretion with minimal or no defects in insulin action (American Diabetes Association[a], 2005).

Genetic defects in insulin action can also result in diabetes. There are unusual causes of diabetes that result from genetically determined abnormalities of insulin action. The metabolic abnormalities associated with mutations of the insulin receptor may range from hyperinsulinaemia and modest hyperglycaemia to severe diabetes (American Diabetes Association[a], 2005).

Diabetes may also develop as a result of other diseases of the pancreas or any process that diffusely injures the pancreas (Clark, 2004). Acquired processes include pancreatitis, trauma, infection, pancreatectomy and pancreatic carcinoma (American Diabetes Association[a], 2005).

Hormonal diseases such as Cushing's syndrome or acromegaly may result in diabetes as a side effect of the main illness (Clark, 2004). This generally occurs in individuals with pre-existing defects in insulin secretion, and hyperglycaemia typically resolves when the hormone excess is resolved. Diabetes may also be induced through drugs or chemicals (American Diabetes Association[a], 2005).

This research focused on DM Type II.

2.3. Pathophysiology of DM Type II

Hyperglycaemia in DM Type II is the result of two major abnormalities:

- Insulin resistance i.e. decreased insulin effectiveness in stimulating glucose uptake (Beers and Berkow, 1999) in skeletal muscle and the liver, and
- A progressive decline in insulin production by the pancreas (Reasner and Defronzo, 2001).

Insulin resistance results from as yet unknown genetic defects combined with environmental factors. These environmental factors are predominantly obesity and physical inactivity (Reasner and Defronzo, 2001).

In insulin resistance the amount of insulin produced by the pancreas may be normal, decreased or even increased. However the insulin is unable to bind with receptor sites. When insulin cannot bind with a receptor, glucose outside the cell cannot enter the cell membrane and be utilised for energy. Insulin's inability to bind to receptor sites may be attributed to a defect at the receptor site, a decreased number of receptor sites or a defect at the post-receptor site located inside the cell (Cahill, 1999).

The following illustrations demonstrate the role of receptor sites in a normal cell and in insulin-resistant cell:

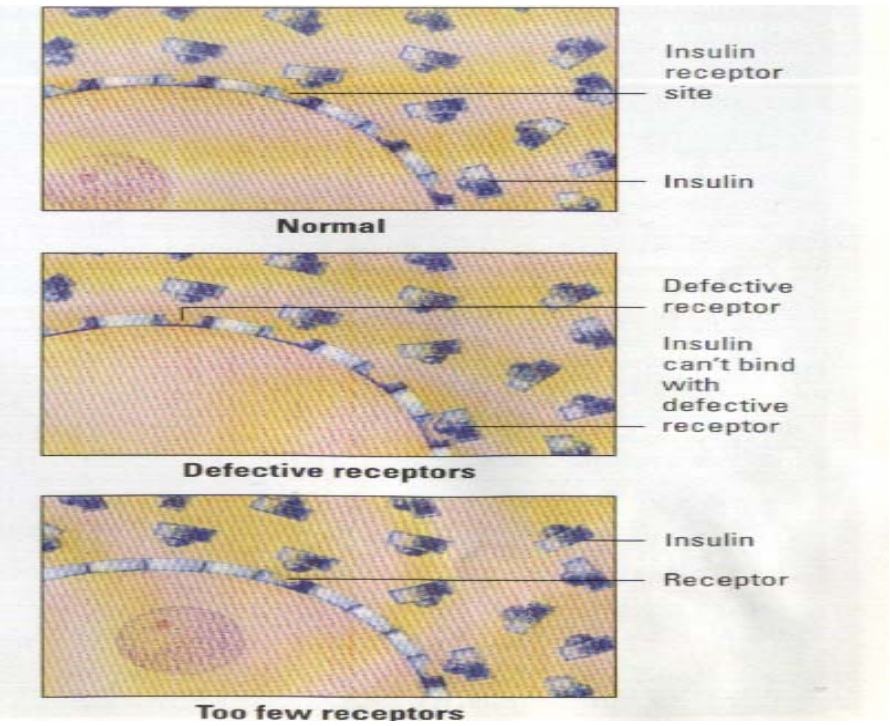

Figure 2.3 Insulin Resistance (Cahill, 1999)

Current research suggests that only a small number of cases of DM Type II are caused by a single-gene defect. These cases include maturity-onset diabetes mellitus of the youth (mutated MODY gene), syndrome of insulin resistance (insulin receptor defect), and maternally inherited diabetes mellitus and deafness (mitochondrial gene defect) (Quinn, 2002). MODY occurs in young, non-obese individuals with an autosomal dominant inheritance. Many families with MODY have a mutation in the glucokinase gene. Impairments in insulin secretion and in hepatic glucose regulation have been demonstrated in these patients (Beers and Berkow, 1999).

The genetic component of the more common form of DM Type II is complex and involves the interactions of several genes and environmental factors. Recent genome scan studies have been conducted to identify major susceptibility loci that are linked with DM Type II. This will probably help identify the polygenetic nature of this disease (Quinn, 2002).

Early in the natural history of DM Type II, the insulin-resistant normoglucose tolerant person compensates by secreting an excessive amount of insulin. Hyperglycaemia (i.e. impaired glucose tolerance and eventual overt diabetes) results when the pancreas can no longer secrete sufficient amounts of insulin to offset the insulin resistance in the peripheral muscle and hepatic tissues (Reasner and Defronzo, 2001).

2.3.1 Sequence in the development of DM Type II

Insulin resistance and a reduction in insulin secretion are present at diagnosis of DM Type II, thus it is difficult to determine which of these metabolic abnormalities is the primary defect. Regardless of the primary defect, however, the development of DM Type II follows a typically evolving course, which can be divided into three distinct stages:

First Stage: Within this stage there are genetic factors influencing both insulin sensitivity and insulin secretion. In addition, there are usually environmental factors associated with the development of insulin resistance, such as obesity and physical inactivity. There is an initial period of hyperinsulinaemia in which the pancreatic beta-cell is able to overcome insulin resistance and maintain normal glucose tolerance. At this stage, although there is an underlying defect in insulin secretion, the pancreatic beta-cell is able to produce a high level of insulin and normal glucose homeostasis is maintained by a compensatory hyperinsulinaemia (Quinn, 2002).

Second Stage: Insulin resistance increase and this compensatory hyperinsulinaemia become insufficient to maintain normal glucose homeostasis. Insulin resistance in visceral fats leads to increased fatty acid production, exacerbating insulin resistance in liver and muscle. Impairments in insulin mediated glucose uptake, particularly at the muscle, become evident. Insulin-mediated glucose transport into skeletal muscle, the major target for glucose disposal, becomes impaired. Fasting plasma glucose levels remain normal but postprandial plasma glucose levels rise (Quinn, 2002).

The reason fasting plasma glucose remains normal is that even though the liver is resistant to the action of insulin; the hyperinsulinaemia in persons with impaired glucose tolerance is sufficient to prevent hepatic glucose output. This prevents the plasma glucose concentration from rising above normal. With time however the hepatic insulin resistance worsens, and hepatic glucose production increase leading to a small increase in the fasting plasma concentration. Such persons are characterised as having impaired fasting plasma-glucose concentration of 6.1-6.9 mmol/L. Eventually the secretion of insulin begins to decline, leading to marked excess in production of glucose by the liver throughout the sleeping hours, and this results in overt fasting hyperglycaemia (fasting-plasma glucose of 7mmol/L or more) (Reasner and Defronzo, 2001).

Third Stage: There is a further increase in insulin resistance. The restraining effects of insulin on hepatic glucose production become impaired and plasma glucose levels increase. In addition, there are toxic effects of worsening hyperglycaemia on the pancreatic beta-cell and insulin secretion subsequently declines. With increasing insulin resistance, fatty acids are no longer restrained. The increase in free fatty acids (FFA) causes a further increase in insulin resistance. Fasting and postprandial hyperglycaemia result from increased insulin resistance, unrestrained hepatic glucose production, and glucose toxicity (Quinn, 2002).

2.4 Symptoms of DM Type II

DM Type II may present with symptomatic hyperglycaemia (i.e. increased blood-glucose levels) (Beers and Berkow, 1999).

Typical symptoms of diabetes are thirst, polyuria, and weight loss. Other presentations include tiredness, pruritus vulvae, blurred vision, ulceration, balanitis, recurring or hard to heal infections, and tingling or numbness of the hands and feet (Warren, 2002).

2.5 Diagnosis of Diabetes

Diagnostic tests are used to confirm a diagnosis of diabetes if there are symptoms or other indicators of the disease (Clark, 2004).

Screening for DM Type II is essential since it is the leading cause of blindness, end-stage renal disease and lower extremity amputations. The risk for microvascular complications (e.g. retinopathy, nephropathy) can be reduced by intensive glucose control, hence early detection and the rationale to screen for diabetes becomes important (Khan and Hershey, 2001).

People are tested for diabetes either as part of the surveillance of high-risk groups such as pregnant women and those with a genetic family history or because they present with typical diabetic symptoms such as thirst, polyuria and weight loss (Warren, 2002).

To establish a diagnosis of DM Type II, patients must undergo a screening test. If the result is abnormal, a confirmatory test should be performed to establish the diagnosis conclusively (Khan and Hershey, 2001).

Several methods can be used to screen for DM Type II.

2.5.1 Questionnaire

Various questionnaires have been developed to aid in screening for DM Type II. Their differences demonstrate the lack of agreement about the importance of individual risk factors, and some questionnaires may not be applicable to all patient populations. Questionnaires are helpful as non-invasive tools to rule out diabetes with a good certainty. However, they are poor positive predictive values (Khan and Hershey, 2001).

2.5.2 Fasting Plasma Glucose

The American Diabetes Association (ADA) recommends fasting plasma glucose (FPG) as the screening test of choice. For the purpose of screening, fasting is defined as no calorie intake for eight hours before the test (Khan and Hershey, 2001).

A glucose level of 6-7 mmol/L implies impaired fasting glucose. If the patient has no diabetic symptoms, diagnosis should not be based on a single glucose value (Longmore *et al*., 2001).

2.5.3 Random Plasma Glucose

Random plasma glucose (RPG) refers to measuring plasma glucose without regard to the last food intake (Khan and Hershey, 2001). A blood glucose level greater than 11 mmol/L is indicative of diabetes mellitus (Haslett *et al*., 1999). The American Diabetes Association however considers an RPG value of 8.9mmol/L and above as abnormal (Khan and Hershey, 2001).

The RPG is less standardised and has a lower sensitivity and specificity than FPG. However, it is clearly easier and convenient to obtain because blood can be drawn during the same office visit (Khan and Hershey, 2001).

2.5.4 Oral Glucose Tolerance test

When random blood glucose values are elevated but are not diagnostic of diabetes, glucose tolerance is usually assessed (Haslett *et al*., 1999). The oral glucose tolerance test (OGTT) requires ingestion of a glucose load of 75g anhydrous glucose dissolved in water. A plasma glucose value of 11.1 mmol/L or more 2 hours after ingestion of the glucose load is abnormal. The ADA recommends fasting plasma glucose measurement over OGTT because FPG is easier and faster to perform, more convenient and acceptable to patients and less expensive. However this opinion is not universally shared, some authorities still recommend the use of OGTT (Khan and Hershey, 2001).

2.5.5 Plasma HbA_{1C} Levels

Glycosylated haemoglobin (=HbA_{1c}) is formed when erythrocytes permeated with glucose slowly bind to haemoglobin. The amount of A_{1C} formed is directly related to the patients' glucose levels (Griffin, 2003). Its presence reflects the level of blood glucose concentration and its exposure to haemoglobin (Khan and Hershey, 2001). Testing for A_{1C} provides a glycaemic history for the past 120 days, the life-span of an erythrocyte (Griffin, 2003). HbA_{1c} is formed at rates that increase with increasing plasma levels (Beers and Berkow, 1999). If the HbA_{1c} level is greater than 7% diabetes mellitus is likely and the risk of microvascular complications may occur. Complications increase in frequency with increasing HbA_{1c} levels (Longmore *et al.*, 2001).

During glycosylation the greatest influence on HbA_{1C} formation is recent hyperglycaemia. It has been suggested that with stable glucose control, a patient forms 50% of the HbA_{1C} in a month before the screening, 25% between 1 and 2 months before, and the remaining 25% between 2 and 4 months before screening. Hence, the rate of glycosylation is not linear. Further it has been found that among non-diabetic patients with the same level of glucose control, there was up to 2% variation in HbA_{1C} values. The variation may be due to differences in rates of glycosylation or erythrocyte life span (Khan and Hershey, 2001). Factors other than glycaemia are known to affect the HbA_{1C} level as well. Haemolytic anaemias (leading to shortened lifespan of erythrocytes), cirrhosis, and high intake of vitamins C and E have been shown to lower the value of HbA_{1C}. Haemolytic variants (e.g., haemoglobin F) can affect certain assays and produce falsely high results (Khan and Hershey, 2001).

2.5.6 Urinalysis

Testing the urine for glucose using glucose specific dipsticks is the usual procedure for detecting diabetes but does not exclude it (Haslett *et al*., 1999). Insulin-treated patients who do not have access to facilities for self-measurement of blood glucose should test urine samples passed after rising, before main meals and before going to bed. Non-insulin-dependant patients do not need to monitor their urine so frequently (WHO, 1999).

Urinalysis should not be used as a screening tool for diabetes, mainly because of physiologic reasons. For most patients, the renal threshold for excretion of glucose is 180mg/dL. Hence, glucose may remain undetectable in urine until levels exceed 180mg/dL in plasma (Khan and Hershey, 2001).

Urine tests, though no longer recommended for blood glucose control, still play an important role in diabetes care. If the body burns fat for fuel in the absence of insulin, ketones are produced, and these substances are detectable in the urine. When the kidney's filtering process becomes impaired, microscopic amounts of protein (microalbuminuria) spill into the urine, which is an early sign of kidney disease. Urine tests are essential since they can detect the presence of harmful ketones; new tests can even measure indicators of kidney health (American Diabetes Association[b], 2005).

2.5.7 Finger- Stick Glucose

The American Diabetes Association allows capillary blood testing by glucometer for screening in the community. A positive screen by finger-test glucose should be confirmed on two or more occasions using venous plasma samples. Many glucometers measure glucose values in whole blood and not in plasma. Plasma glucose values are 10% to 15% higher than corresponding whole blood glucose values. The cut-off for a positive screen fasting whole blood glucose is a level of 6.1 mmol/L or above and for a random whole blood glucose value, the cut-off is 7.8 mmol/L or above (Khan and Hershey, 2001).

2.5.8 Future Diagnostic Methods

Scientists are now working to develop more convenient and less painful ways for people with diabetes to monitor their blood glucose levels. Potential non-invasive methods include:

- Shining a beam of light onto the skin or through body tissues
- Measuring the energy rays (infrared radiation emitted by the body)
- Applying radio waves to the fingertips
- Using ultrasound and
- Checking the viscosity (thickness) of fluids in tissues underneath the skin (SerVaas, 2004).

Cygnus, Inc.'s GlucoWatch G2 Biographer is approved to detect glucose level trends in people with diabetes. The prescription device, which looks like a wristwatch, pulls fluid from the skin using a low electric current and then measures the glucose in the fluid. However it must be used with conventional glucose monitoring of blood samples (SerVaas, 2004).

The University of Central Florida in the USA is developing a test that uses teardrops to measure blood-glucose levels. This could signal the end of finger-prick testing for diabetics. A prototype created by scientists needs one teardrop to analyse blood glucose levels. A solution in the device would change to pink if levels are normal. The device would turn dark red if blood glucose levels are high. The teardrop test is in early stages of development and is unlikely to be available for several years (Hagan, 2006).

2.6 Complications of Diabetes

Diabetes can lead to severe increases in blood glucose and ketoacid levels, causing significant complications. Early complications of diabetes include diabetic ketoacidosis, hyperosmolar hyperglycaemic nonketotic syndrome, and hypoglycaemia. Late complications affect every system of the body, with signs and symptoms varying depending on the system affected (Cahill, 1999)

2.6.1 Early complications

2.6.1.1 Diabetic Ketoacidosis

Diabetic ketoacidosis (DKA) is a common, life-threatening complication of diabetes. The diagnosis of DKA relies on signs and symptoms and laboratory findings. The laboratory findings are a blood glucose of >250 mg/dL, an anion gap of ≥15 mmol/L, and carbon dioxide of ≤18 mmol/L when other causes of acidosis are excluded (Naunheim *et al.,* 2006).

Diabetic Ketoacidosis occurs when glucose levels are extremely high (Cahill, 1999). Diabetic Ketoacidosis has a reported average mortality of approximately five percent in western countries. Mortality is generally higher at the extremes of age (Krentz, 2004).

Ketoacidosis develops when there is absolute or, more commonly, a relative insulin deficiency. This usually occurs together with an increase in catabolic hormone concentrations (Krentz, 2004).
The signs and symptoms of DKA include:

- Abdominal tenderness
- Anorexia
- Crusty mucous membranes
- Decreased bowel sounds
- Deep and fast respirations (Kussmaul's respirations)
- Extreme weakness
- Fever (suggesting infection)
- Fruity, acetone-like breath odour
- Low blood pressure
- Nausea or vomiting
- Neurological symptoms, including dullness, confusion, lethargy, and diminished reflexes (early) and coma (later)
- Extreme thirst
- Warm, flushed, dry, and loose skin
- Weak, rapid pulse
- Weight loss (Cahill, 1999)

2.6.1.2 Hyperosmolar hyperglycaemic nonketotic syndrome

Hyperosmolar hyperglycaemic non-ketotic syndrome (HHNS) is another acute complication of hyperglycaemic crisis and usually occurs in patients with DM Type II (Cahill, 1999). Hyperosmolar nonketotic hyperglycaemia is a serious consequence of concomitant illnesses and advancing age to over 50% (Hardman, 2001).

This syndrome is characterized by:

- Severe hyperglycaemia
- Dehydration with pre-renal uraemia and without ketoacidosis
- Hyperosmolarity (Hardman, 2001)

Precipitating factors include conditions or medications leading to severe dehydration and impaired insulin secretion and/or insulin resistance. The most common are infection, sepsis, stroke, renal failure, heat stroke, hypothermia, pancreatitis, severe thermal burns and endocrine diseases (Krentz, 2004). Signs and symptoms of HHNS are similar to DKA with three notable exceptions (Cahill, 1999):

- Focal neurological signs including hemiplegia usually occur
- Respirations are rapid but not deep
- Breath odour is normal (Cahill, 1999)

2.6.1.3 Hypoglycaemia

Hypoglycaemia or insulin shock may occur in non-diabetic people, however people with diabetes are much more at risk (Cahill, 1999). Hypoglycaemia occurs following ingestion of drugs such as aspirin or alcohol and in those who develop an insulinoma. The commonest cause is insulin treatment in people with insulin-treated diabetes. Most episodes are due to the limitations of current subcutaneous insulin delivery (Krentz, 2004).

The human brain primarily uses glucose as its source of energy. Under normal conditions, the brain is unable to synthesise or store glucose and is vulnerable to glucose deprivation (Zammit and Frier, 2005).

Severe hypoglycaemia leads to impaired cognition, confusion and coma. Very low levels (<1 mmol/L) that are prolonged for hours can cause death or permanent cerebral damage (Krentz, 2004).

With increasing duration of DM Type I or DM Type II, both the hormonal and symptomatic responses to hypoglycaemia often become impaired. This change may be observed due to intensive insulin therapy. This makes it more difficult for patients to identify the onset of hypoglycaemia, and although not a major problem if mild, poses a considerable risk to those severely affected (Krentz, 2004).

Hypoglycaemia used to be considered a minor problem of the treatment modalities used for DM Type II. According to Zammit and Frier (2005) the burden of covert hypoglycaemia associated with oral antidiabetic agents may be underestimated.

Hypoglycaemia with oral antidiabetic agents is predominantly associated with the insulin secretagogues. Hypoglycaemia is not a common side effect of treatment with biguanides (metformin), thiazolidinediones, or α-glucosidase inhibitors. However hypoglycaemia has been in association with metformin when food intake is limited. The frequency of hypoglycaemia is lower in people treated with sulphonylureas than in those treated with insulin but is probably underestimated (Zammit and Frier, 2005).

2.6.2 Late Complications

Diabetic patients may experience numerous systemic complications late in the disease. The most common late complications of diabetes include:

- Cardiovascular and peripheral vascular disease
- Nephropathy
- Neuropathy and
- Retinopathy (Cahill, 1999).

There are a number of purported mechanisms suggested in the genesis of diabetes mellitus-related complications. These mechanisms revolve around metabolic derangements initiated by hyperglycaemia and insulin resistance. In addition, there are likely unidentified mechanisms involved in the development of complications (Quinn, 2002).

2.6.2.1 Cardiovascular and peripheral vascular disease

Partial or complete occlusion of blood vessels is the basic pathology here. Large blood vessels are occluded by atheromatous plaques and smaller vessels (arterioles) by endateritis. This leads to myocardial infarction, intermittent claudication, diminution or loss of peripheral pulsations and predisposes to gangrene. Many diabetics may suffer from what is termed 'silent' myocardial infarctions i.e. the element of pain is greatly diminished or may even be absent (Pavri, 2001).

The relationship of DM Type II to cardiovascular disease (CVD) is complex, with the increased CVD risk associated with several abnormalities, resulting from the interplay between insulin resistance and hyperglycaemia and ultimately resulting in structural and functional changes in vascular tissue (Quinn, 2002). CVD manifesting as coronary artery disease, is the leading cause of morbidity and mortality among patients with DM Type II and many of the primary risk factors for coronary artery disease coexist among these patients (Bhaskarabhatla and Birrer, 2004).

The incidence and prevalence of angina, myocardial infarction, sudden unexpected death, and congestive cardiac failure are increased in the diabetic patient. Awareness of the increased frequency of these clinical manifestations of ischaemic heart disease in a diabetic is important and provides the basis for the identification, evaluation, and treatment of diabetic patients with or without symptoms of ischaemic heart disease (Davidson, 1991).

The increased incidence of heart failure in individuals with diabetes mellitus does not appear to be related to coronary heart disease alone, as the size of ischaemic areas following myocardial infarction in diabetic and non-diabetic subjects appear to be similar. The increased susceptibility of patients with DM Type II to develop heart failure following a myocardial infarction has been attributed to 'diabetic cardiomyopathy'. Diabetic cardiomyopathy is associated with a variety of morphological, functional and metabolic changes in the heart (Quinn, 2002).

The prevention of CVD in DM Type II requires optimal management of not only glucose, but also lipids and hypertension. Therapies that attempt to normalise hyperglycaemia and insulin resistance (weight loss, diet, medications) may, therefore, have positive effects at multiple levels (Quinn, 2002).

2.6.2.2 Visual Disturbances

In general, people with DM Type II are at increased risk for three types of visual problems: glaucoma, cataracts, and diabetic retinopathy. Most diabetes-related visual problems can be delayed or prevented with early detection and proper control of blood-glucose levels (Peterson, 2003).

2.6.2.2.1 Glaucoma

Glaucoma is an increase of fluid pressure in the eye. The elevated pressure leads to damage of the optic nerve and loss of vision and possibly blindness. There are two forms of glaucoma more common in patients with diabetes: open angle glaucoma and neurovascular glaucoma (Fong and Ross, 1998).

The most common symptoms of glaucoma are loss of peripheral vision, headaches, haloes around light, nausea and vomiting (Marandino, 2000).

2.6.2.2.2 Cataracts

A cataract is an opacity of the lens whether it is a small local opacity or complete loss of transparency (Murrill *et al.*, 1994). The cloudiness prevents light from passing through and reaching the retina. "What clouds the eye lens is the damage from oxidation, a biochemical process set in motion when a highly reactive form of oxygen changes within our cells" says James Duke, Ph.D., author of The Green Pharmacy. Studies have shown that the condition develops earlier among diabetics, smokers and those who take diuretics, steroids or tranquillisers (Marandino, 2000).

Cataracts may occur secondary to hereditary factors, trauma, inflammation, metabolic or nutritional defects, radiation or the effects of aging (Murrill *et al.*, 1994).

Diabetes is a common cause of cataracts. It causes swelling of the lens and changes in refractive error, as well as changes in the clarity of the lens. The lens is comprised primarily of water and protein. The protein is arranged in an ordered way to allow light to pass through. With diabetes and

age, some of the protein may clump together, forming a cloudy area in the lens. The cloudy areas distort and block vision and may lead to double vision (Fong and Ross, 1998).

Cataracts are the cause of blindness worldwide; however, in most cases, vision loss from cataracts is reversible (Ronk, 2000).

2.6.2.2.3 Diabetic Retinopathy

Diabetic retinopathy develops when increased blood glucose levels lead to damages in the blood vessels of the retina (Fong and Ross, 1998). Diabetic retinopathy remains the leading cause of vision impairment and blindness among working-age adults, yet the fundamental cause remains uncertain (Antonetti *et al.*, 2006)

The abnormalities comprising diabetic retinopathy are:

- Venous engorgement of retinal vessels
- Capillary microaneurysms
- 'Waxy' exudates
- Retinal proliferans (new vessel formation)
- Retinal detachment
- Vitreous fibrosis
- Haemorrhage- small blots (intraretinal), preretinal (subhyaloid) or into the vitreous (Pavri, 2001).

Patients with microaneurysms, retinal haemorrhages and exudates have simple or background retinopathy. Those with preretinal haemorrhage, new vessel formation or fibrous proliferation have malignant or proliferative retinopathy (Pavri, 2001).

The impaired vision associated with diabetic retinopathy is due to macular oedema, macular ischaemia, and epiretinal membranes that distort or elevate the macula, or vitreous haemorrhages that obscure the ocular media (Antonetti *et al.*, 2006).

The risk of developing diabetic retinopathy increases with the duration of the diabetes (Shaw, 1996). Improved medical care over the past 3 decades has reduced the risk of vision-threatening retinopathy therefore; retinopathy can be prevented (Antonetti *et al.*, 2006).

2.6.2.3 Nephropathy (Renal Disease)

Fifteen percent of diagnosed diabetics have proteinuria. In patients suffering from long standing renal disease associated with Diabetes Mellitus, it is likely that 75% will develop renal failure. Microalbuminuria, which is too slight to show on a dipstick, is a marker for a high risk of progression of diabetes to frank nephropathy. Perfect control of blood pressure prevents renal failure (Warren, 2002).

Diabetes predisposes to pyelonephritis, which may be associated with papillary necrosis. Diabetes also results in two kinds of glomerulosclerosis; one is the diffuse proliferative type and consists of a general thickening of the basement membrane. The other is a nodular variety in which hyaline rounded masses called Kimmelsteil-Wilson bodies are seen. Renal vascular changes secondary to atherosclerosis and hypertension may also be seen (Pavri, 2001).

According to a study from Canada, "The incidence of end-stage renal disease (ESRD) owing to diabetes has continued to increase despite the extensive use of angiotensin-converting enzyme (ACE) inhibitors to prevent diabetic nephropathy. The data from the clinical trial concluded that ACE inhibitors might actually increase the risk of ESRD, which may possibly contribute to the continued increasing incidence of ESRD owing to diabetes (Oqawa and Suissa, 2006).

2.6.2.4 Neuropathy

Diabetes may affect both the central and peripheral nerves (Shaw, 1996). Neuropathy is a relatively early and common complication affecting approximately 30% of diabetic patients. In a few patients neuropathies can cause severe disability but it is usually symptomless in the majority of sufferers (Haslett *et al.*, 1999).

Diabetic polyneuropathy results in significant disability and morbidity including severe pain, loss of ambulation, and an increased risk of non-healing ulcers and amputation (Poncelet, 2003).

Diabetic neuropathy occurs more often in older patients. Poor control of diabetes predisposes to an early onset and increased incidence of diabetic neuropathy (Pavri, 2001).

The main categories of neuropathy associated with diabetes are:

- Peripheral neuropathy

  It may be either distal, symmetrical, mixed sensory-motor polyneuropathy; which causes symmetrical, distal paresthesia, glove and stocking sensory loss, distal weakness and loss of ankle jerks; or sensory neuropathy. The sensory neuropathy is distal and symmetrical. It presents with numbness and paresthesia extending proximally. There is loss of position and vibration sense. Due to sensory loss trophic ulcers and Charcot's joints may be seen (Pavri, 2001).

- Motor neuropathy

  This is asymmetrical and proximal neuropathy. It is also known as Diabetic amyotrophy and presents with asymmetrical wasting of the quadriceps with diminished or absent knee jerks (Pavri, 2001).

- Mononeuritis multiplex

  Several spinal nerves are affected either concurrently or serially. The signs are 'patchy' and asymmetrical (Pavri, 2001).

- Autonomic neuropathy

  Autonomic neuropathy affects the nervous supply of internal organs. Symptoms for this form of neuropathy are much more subtle and are harder to attribute strictly to the disease. Digestive and genito-urinary function may be affected, causing nausea, stomach fullness, changes in bowel function, incontinence or an inability to urinate effectively, and loss of sexual function (Braunstein, 2001).

The most common manifestation of diabetic neuropathy is the impairment of sensation to a small injury (Peterson, 2003). Appropriate diagnosis of diabetic polyneuropathy, exclusion of other treatable causes, and treatment are important to prevent secondary complications and improve quality of life (Poncelet, 2003)

2.7 Exercise and Diabetes

Exercise is defined as regular or repeated use of a faculty or bodily organ; bodily exertion for the sake of developing and maintaining physical fitness (The New Webster's Pocket Dictionary, 1997).

Hippocrates, a Greek physician who was born in 460 BC and who became known as the founder of medicine, said, "If we could give every individual the right amount of nourishment and exercise, not too little and not too much, we would have found the safest way to health" (Goodpaster, 2005).

Exercise is a recommended component of diabetes management. In DM Type I and Type II, exercise can increase insulin sensitivity, lower blood glucose, and have positive psychological effects (White *et al.*, 1999). Adequate glycaemic control and selection of appropriate physical activity are essential to avoid associated complications (Bhaskarabhatla and Birrer, 2004).

Most experts agree that the exercise regimen recommended for those with diabetes should be aimed at both increasing cardio-respiratory fitness and muscle strength. Walking, jogging, swimming, aerobics and circuit-type resistance training have all been successful strategies (Kligler and Lynch, 2003). Patients on diabetes medications should monitor blood glucose levels and adjust their diet to minimise fluctuations in blood glucose during exercise (Bhaskarabhatla and Birrer, 2004).

Investigators have found an inverse relationship between physical activity, insulin resistance and the subsequent development of DM Type II. Recent clinical evidence strongly supports the role of physical activity in the prevention of DM Type II. Two randomised trials each found that lifestyle interventions reduced the risk of progression from impaired glucose tolerance to DM Type II by 58%. These lifestyle interventions included 150 min/week of physical activity and diet-induced weight loss of 5-7%. A cluster-randomised trial found that diet alone; exercise alone, and combined diet and exercise were equally effective in reducing the progression from impaired glucose tolerance to diabetes (Sigal *et al.*, 2006).

Exercise increases insulin-mediated glucose disposal rates and improves endothelial nitric oxide release and insulin-mediated vasodilation and substantially lowers elevated blood pressure, an important risk factor in patients with DM Type II (Bhaskarabhatla and Birrer, 2004).

Exercise for 30 minutes or more at a moderate level of intensity on most, preferably all, days of the week can improve insulin sensitivity and glycaemic control and decrease the need for oral medications or insulin (Bhaskarabhatla and Birrer, 2004) (Kligler and Lynch, 2003). Investigators feel that other types of moderate physical activity-household work, work-related physical activity, and gardening; are probably as effective as structured exercise and can reasonably be included (Kligler and Lynch, 2003).

Nurses' Health Study investigators have found that television watching is a major risk factor for obesity and diabetes in adults, independent of exercise levels: each 2-hour/day increment in TV watching was associated with a 23% increase in obesity and a 14% increase in risk of diabetes. Inquiring and counselling specifically regarding hours of television watched per day may be an important part of the integrative approach to preventing diabetes (Kligler and Lynch, 2003).

Although exercise has many advantages, prolonged and vigorous exercise can potentiate risks. Hypoglycaemia and hyperglycaemia are the most significant potential risks associated with diabetes during exercise. Hyperglycaemia during exercise can result from insufficient insulin intake or overeating (Braunstein, 1999). Hyperglycaemia is a risk for patients with poor metabolic control. Without adequate insulin, muscle cells cannot utilise glucose during exercise, glucagon-induced production of glucose from the liver is unopposed, and fatty acids are mobilized to supply fuel. This results in increasing hyperglycaemia, ketosis, and acidosis (White *et al.*, 1999).

Hypoglycaemia is of greater concern for patients who have DM Type I than for those who have DM Type II. Strategies for avoiding exercise-induced hypoglycaemia include adjusting insulin or oral agents dose and/or food intake before exercise, ingesting carbohydrate snacks during sustained activity, and monitoring glucose levels scrupulously (White *et al.*, 1999).

To ensure that any exercise programme is optimally safe, effective, and enjoyable, it is important that individuals at risk of DM Type II, or already affected, undergo health screening before beginning any exercise programme (Bhaskarabhatla and Birrer, 2004). Attention to diabetes management factors such as blood glucose monitoring, diet, insulin, and medication would reduce the risks associated with exercise (White *et al.*, 1999).

2.8 Diabetic Diet

All patients with diabetes should be advised on their diet, regardless of what other therapy they may be using. Access to and advice from a dietician is essential for optimal management. The diet should be tailored to the individual's needs and tastes. The aim of the diabetic diet is to ensure that glucose from food is released into the blood in a gradual manner. Even highly sophisticated regimens of insulin injection cannot hope to match the efficiency of a normally functioning pancreas (Warren, 2002).

Medical nutrition therapy is important in preventing diabetes, managing existing diabetes, and preventing, or at least slowing, the rate of development of diabetes complications. The debate as to the potential role of low-glycaemic index and glycaemic load diets in prevention of DM Type II continues. Some studies have demonstrated an association between glycaemic load and risk for diabetes; other studies have been unable to confirm this relationship. There is not sufficient, consistent information to conclude that low-glycaemic load diets reduce risk for diabetes. However, low-glycaemic index foods that are rich in fibre and other important nutrients are to be encouraged (Bantle *et al.,* 2006).

The controversy over whether total calories, fat calories, or glycaemic index are most important in control of diabetes notwithstanding, the basics of a healthy diet for patients with this condition are now fairly clear. The fat profile of the diet should be high in monounsaturated fats, with moderate polyunsaturated and low saturated fatty acid and trans fatty acid content. The diet should be high in fibre (goal of 50g) per day and provide adequate protein. A macronutrient content of the diet of approximately 40% carbohydrates, 30% protein and 30% fat is commonly used, and calories can be adjusted accordingly. Refined grains are eliminated and whole grains are emphasised (Kligler and Lynch, 2003). Studies have provided evidence for reduced risk of diabetes with increased intake of whole grains and dietary fibre. Whole grain containing foods have been associated with improved insulin sensitivity, independent of body weight. Dietary fibre has been associated with improved insulin sensitivity and improved ability to secrete insulin adequately to overcome insulin resistance (Bantle *et al.*, 2006). Starchy vegetables are restricted but non-starchy vegetables are unrestricted. Fruits with high glycaemic index are limited and low to moderate glycaemic index fruits are encouraged in moderate amounts to minimise glycaemic load. Legumes are emphasized due to their low glycaemic index. Lean proteins, fatty fish, and nuts are encouraged. Weight control is a high

priority, as even weight loss of 5% of body weight can make an enormous difference in glycaemic control (Kligler and Lynch, 2003).

A study was conducted by Boden *et al.* to determine the effects of a strict low-carbohydrate diet on body weight, body water, energy intake and expenditure, glycaemic control, insulin sensitivity, and lipid levels in obese patients with DM Type II. Results of the study showed that a low-carbohydrate diet followed for two weeks resulted in spontaneous reduction in energy intake to a level appropriate to their height; weight loss that was completely accounted for by reduced caloric intake; much improved 24-hour blood glucose profiles; insulin sensitivity, and HbA_{1C}; and decreased plasma triglycerides and cholesterol levels (Boden *et al.*, 2005).

2.9 Management of Diabetes

2.9.1 Allopathic treatment

Loss of weight (diet and exercise) reduces insulin resistance and controls about one third of Type II diabetics. Another one third of Type II diabetics are controlled by diet and exercise together with oral antidiabetic drugs. Type II diabetics not controlled by diet, exercise and oral antidiabetic drugs require insulin injections. These tend to be the thinner patients (Neal, 2002).

Current approaches to managing DM Type II recognise the disease's progressive nature. They are directed initially toward reducing hepatic glucose production and increasing muscle glucose uptake. Over time, the decline in insulin production with disease progression causes most patients to eventually need multiple agents, including insulin, to reach target glucose levels. The most effective first step toward attaining overall glycaemic control is to lower fasting plasma glucose. Current ADA treatment goals, as well as clinical practice recommendations, advise achieving normal or near-normal levels of preprandial and bedtime glucose and HbA_{1C} (Funnell and Kruger, 2004).

The choices of treatment for a patient with DM Type II is based on patient history, present level of glucose control, patient preference, and the mechanism of action and side effect profile of available agents. Most newly diagnosed patients begin treatment with a referral to a dietician for medical nutrition therapy, attending diabetes self-management classes, receiving education in blood glucose

monitoring and being advised to increase their physical activity or exercise (Funnell and Kruger, 2004).

2.9.1.1 Oral antidiabetic drugs

Oral agents for DM Type II reduce or normalise FPG and HbA_{1C} by various methods of action (Funnell and Kruger, 2004).

When diet and exercise are no longer adequate, clinicians often initiate pharmacological monotherapy. However secondary failure rates for monotherapy are fairly high, especially in patients with long-standing disease. Combination therapy using agents that have different mechanisms of action can often re-establish control (Funnell and Kruger, 2004).

The oral antidiabetic drugs consist of Sulphonylureas, Biguanides, Prandial glucose regulators, Thiazolidinediones and the Alpha-Glucosidase inhibitors.

Prior to 1994 selecting an oral agent for the treatment of DM Type II was as simple as choosing which sulphonylurea to use. Since then a variety of newer agents with unique mechanisms of action and even some combination agents have been released for use of monotherapy or any number of combination regimens (Sheehan, 2003).

There are three ways in which oral agents work toward improving glycaemic control:

- Increasing insulin secretion (insulin secretagogues)
- Increasing insulin action (insulin sensitizers)
- Decreasing insulin need (inhibitors of glucose absorption) (Sheehan, 2003).

2.9.1.1.1 Increasing insulin secretion (secretagogues)

- **Sulphonylureas**

There are a large number or sulphonylureas on the market, such as Amaryl, Glycomin, and Diamicron (Popplewell, 2003). Sulphonylureas are indicated in patients in whom diet fails to control the hyperglycaemia (Neal, 2002). They are first-choice treatment for diabetics who are of normal weight. Sulphonylureas work mainly by boosting the insulin output of the failing pancreas. All sulphonylureas may cause rashes and weight gain (Warren, 2002). Most of the sulphonylureas are metabolised by the liver to form inactive metabolites that are excreted by the kidney. However, two sulphonylureas, namely glibenclamide and glimepiride are metabolised to form active metabolites. People with renal impairment and older people in particular are therefore at risk of developing hypoglycaemia with these two medications compared with other sulphonylurea agents (Popplewell, 2003).

- **Non-sulphonylurea secretagogues**

Prandial glucose regulators, nateglinide and repaglinide can be taken just before the main meal. Repaglinide and nateglinide were used for the treatment of DM Type II since 1998 and 2001, respectively (Sheehan, 2003). They stimulate the release of insulin from the pancreas (Warren, 2002). They reduce the risk of interprandial hypoglycaemia. They act in a similar way to sulphonylureas, however they are more rapidly absorbed and more quickly eliminated (90% by the biliary route) than the sulphonylureas (Popplewell, 2003). These drugs differ from the sulphonylureas in two ways: dosing at each meal and potentially less risk of hypoglycaemia, especially if a meal is missed. As these agents are metabolised and excreted by hepatic mechanisms exclusively, these agents can be safely used in more advanced renal insufficiency (Sheehan, 2003). Caution should be used in elderly groups who have a significantly higher mean diurnal variation and lower clearance than younger individuals (Popplewell, 2003).

2.9.1.1.2 Increasing insulin action (insulin sensitizers)

- **Biguanides**

Biguanides such as metformin and glucophage increases glucose uptake by an unknown mechanism (Neal, 2002). It also reduces glucose absorption from the gut, and increases insulin sensitivity. It is the only diabetic treatment that reduces circulating insulin, and does not cause weight gain nor does it cause hypoglycaemic episodes. It is the first choice treatment for overweight diabetics (Warren, 2002). Biguanides do not undergo metabolism and are excreted unchanged in the urine. Metformin when used alone does not cause hypoglycaemia (Popplewell, 2003). Adverse effects include nausea, vomiting, diarrhoea and occasionally, fatal lactic acidosis (Neal, 2002). At high doses metformin may promote diarrhoea. Metformin is particularly indicated in those people with diabetes who have elevated blood glucose levels in the morning before breakfast. Here metformin will inhibit the production of glucose by the liver during the night. Metformin is absolutely contraindicated in individuals with renal impairment, and it should not be used in patients over 80 years (Popplewell, 2003).

- **Thiazolidinediones**

The glitazones are recommended for use in combination with either a sulphonylurea or metformin when a combination of these two is unsuccessful (Warren, 2002). They are not approved for use in most triple therapy regimens (Sheehan, 2003). They enhance insulin sensitivity in the liver adipose tissue and muscles without effecting insulin secretion. They are antihyperglycaemic agents and do not cause hypoglycaemia when used in monotherapy (Popplewell, 2003). They have no demonstrated advantages over older therapies and their long-term safety is unknown (Neal, 2002). However, the weight gain and oedema seen with the Thiazolidinediones can be limiting in some patients (Sheehan. 2003). The major concern about the thiazolidinedione group is hepatotoxicity, and troglitazone was taken off the market after 150 cases of severe hepatotoxicity were reported. Their once-daily dosing schedule and lack of hypoglycaemia when used in monotherapy may be very useful in elderly patients with DM Type II. However, costs and limited safety data need to be explored before future recommendations can be made (Popplewell, 2003).

2.9.1.1.3 Decreasing insulin need (inhibitors of glucose absorption)

- **Alpha-glucosidase inhibitors**

The two agents in this class currently available, acarbose and miglitol, were released in 1996. These drugs only affect post-prandial glucose levels and do so by competitively inhibiting the binding of oligosaccharides to the alpha-glucosidase enzyme in the brush border of the small intestine. This enzyme cleaves oligosaccharides to monosaccharides, which can then be absorbed. Thus, when taken with the first bite of food, these agents delay the absorption of carbohydrate (Sheehan, 2003).

Flatulence and loose stools are a natural consequence of treatment with alpha glucosidase inhibitors. When they are used in monotherapy, hypoglycaemia does not occur. However when combined with sulphonylurea treatment, hypoglycaemia may occur (Popplewell, 2003).

2.10 Homoeopathy

"The physician's high and only mission is to restore the sick to health, to cure, as it is termed" (Hahnemann, 2003). The above aphorism simply states that a homoeopaths highest and only calling is to restore health to the sick.

2.10.1 Definition of Homoeopathy

Homoeopathy is defined as "a therapeutic method which clinically applies the Law of Similars and which uses medicinal substances in weak or infinitesimal doses" (Jouanny, 1991). Homoeopathy comes from two Greek words, "homoios" meaning same or similar and "pathos" meaning suffering (Eizayaga, 1991).

Within the total context of medicine, homoeopathy may be defined as a form of regulatory therapy. The aim is to influence auto- regulation with the aid of a homoeopathic substance, which relates to the way the individual patient reacts (Koehler, 1989) (See 2.10.4).

Homoeopathy is not herbal medicine nor is it a dietary regimen. It is a philosophy of health and a formal system of drug therapeutics (Weiner, 1989). The philosophy of homoeopathy is to treat the patient and not simply the disease (Lange, 2002).

2.10.2 History of Homoeopathy

The founder of homoeopathy was a German physician Christian Frederick Samuel Hahnemann (Koehler, 1989). Dr. Hahnemann brought Homoeopathy to light in the year 1810, with the publication of first edition of the Organon. Then he wrote the volumes of Materia Medica Pura during 1811 to 1821. These are records of symptoms of medicines proved on healthy human beings (Kanodia, 1999).

Dr. Hahnemann challenged the attempts of physiologists to isolate disease processes as the sole cause of disease. He concluded that medicine could not be based on "the shifting sands of medical theories", but must have a rational basis. He asserted that manipulating physiology with medication was insufficient since this did not address the integrity and complexity of the organism as a whole. Homoeopathy prioritises the mental and emotional symptoms of the sick as well as the symptoms that characterise the uniqueness of individual symptoms. Priority is given to these symptoms in understanding the disease process (Lange, 2002).

2.10.3 Provings of Remedies

Dr. Hahnemann says in the Organon, Aphorism 21:
"therefore, we have only to rely on the morbid phenomena which the medicines produce in the healthy body as the sole possible revelation of their in-dwelling curative power, in order to learn what disease-producing power, and at the same time what disease-curing power, each individual medicine possesses" (Hahnemann, 2003).

Hahnemann reasoned that in order to know what healing properties are contained in a given substance, one must observe what the substance will do in a healthy person. Homoeopathy uses a systematic administration of substances, derived from animal, vegetable and mineral kingdoms, to healthy persons in order to observe their effects (Weiner, 1989). In homoeopathy such testing of drugs on healthy subjects is defined as *Provings* (Lange, 2002).

According to Dr. Jeremy Sherr provings are the pillars upon which homoeopathic practice stands. Without accurate provings all prescribing indications are bound to be vague guesses at best, and pure fiction at worst (Sherr, 1994).

2.10.4 Law of Similars

Homoeopathy is a science that is based on the Law of Similars, which states "let likes be cured by likes". This means that a medicine capable of producing symptoms when taken by a healthy human being is capable of curing an illness that displays similar symptoms (Sankaran, 1994).

The law of similars is the formulation of a physiological state, which had been observed twenty-five centuries ago by Hippocrates, the founder of medicine. Hippocrates stated: " The strangury which is not, cures the strangury which is". Dr. Hahnemann studied the above statement and concluded that remedies are capable of curing symptoms analogous to those, which they themselves produce (Jouanny, 1991). The remedy therefore presents with a symptom picture during the proving of it and this picture is matched with that of the patients' symptoms to find the appropriate remedy (Nash, 2003).

2.10.5 Potentisation of Drugs

The process of preparation of remedies as per direction of Dr. Hahnemann is known as potentisation. Potentisation is a physical process by which the *latent curative properties* of remedies are brought into activity (Banerjee, 2004).

There are three essential processes involved in the preparation of remedies, i.e. serial dilution, succussion and trituration (Banerjee, 2004). Dilution is the process of mixing two liquids together (Banerjea, 1995), and is a means to reduce the toxicity of the original crude drug. Serial dilution means that each dilution is prepared from the dilution that immediately preceded it (Banerjee, 2004). Succussion and trituration are methods by which mechanical energy is delivered to preparations in order to imprint the pharmacological message of the original drug upon the molecules of the diluents. Succussion is rhythmical shaking of the diluted substance, by either using hand or machine. For soluble substances, mother tinctures (alcohol-water extraction) of the plant material are used, and alcohol and water are applied. Insoluble substances are prepared through the

process termed trituration. Trituration is prolonged circular grinding of insoluble substances with pure lactose in a mortar and pestle. Once a trituration has obtained $1/10^6$, this can be dispensed into an alcohol-water diluent. Thereafter it is treated as a soluble substance. Thus the term potency refers to any dilution that has either been succussed or triturated (Banerjee, 2004).

Three scales are used for the preparations of the homoeopathic potencies of liquid drug substances. The scales used are denoted as "C" for centesimal scale and "X" for decimal scale and "M" for millesimal (Banerjee, 2004). Dr. Hahnemann introduced the centesimal scale. This scale is based on the principle that the first potency should contain a one-hundredth part of the original drug and each succeeding potency should contain a one-hundredth part of the one preceding it. Dr. Constantine Hering introduced the decimal scale. This scale is based on the principle that the first potency should contain a one tenth part of the original drug and each succeeding potency should contain a one tenth part of the one preceding it (Banerjea, 1995). The fifty millesimal scale was introduced in the 6th edition of the Organon of Medicine. In this scale the first potency should contain 1/50 000th part of the original drug and the second potency should contain 1/50 000th part of the first potency and so on (Banerjee, 2004).

2.10.6 Methods of Prescribing

Homoeopaths generally adhere to one of three "schools" of prescribing:

- Unicist: often called 'classical', it is giving a single remedy at a time, as outlined in Dr. Hahnemann's organon. Often the remedy is given as a single dose. The classical approach to homoeopathy follows the teachings of Dr's Hahnemann, Kent and others who were instrumental in the development of Homoeopathy. The principles of homoeopathy (e.g. the Law of Similars and the Law of Cure) are followed very rigidly with little variation, if any (Winston, 1999).

  Dr. Hahnemann states in the Organon, Aphorism 2:
  "The highest ideal of cure is rapid, gentle and permanent restoration of the health, or removal and annihilation of the disease in its whole extent, in the shortest, most reliable, and most harmless way, on easily comprehensible principles" (Hahnemann, 2003).

Thus the concept of "single dose, single remedy" is applied in accordance with Aphorism 2 of the Organon. This simply states that the administered remedy must be given the minimum number of doses and the lowest potency possible that is required to restore the patient to health and that will not harm the patient in any way, i.e. it is completely therapeutic in nature (Winston, 1999).

- Pluralist: Often referred to as the 'French School', this approach often gives more than one remedy at a time with the idea that there is more than a single disease to treat (Winston, 1999).

- Complexist: several remedies are combined into a single dose and given, often daily (Winston, 1999). In combination therapy several remedies are combined and prescribed for a specific disease. The theoretical advantage is that by combining for example, five of the most commonly prescribed remedies for e.g. an earache the practitioner is able to bypass the necessity to individualise each case and give every earache patient the same prescription. The assumption is either that whichever remedy in the combination is most similar to the earache of the person being treated will act and the other, non-indicated remedy will do nothing, or that a group of remedies known to bear similarity to the typical symptoms of earache, will, collectively, bring about a curative response (Watson, 1999) Combination remedies are not individualised (Shelton, 2004).

2.11 Homoeopathic remedies used in this research

The following remedies were used in the complex for this research:

2.11.1 Arsenicum album

The chemical symbol for *Arsenicum album* is $As_2 O_3$. In a hydrated state *Arsenicum album* forms arsenious acid. When freshly prepared it consists of large, vitreous, amorphous masses, which gradually become opaque, crystalline and porcelain-like. It is slowly soluble and is obtained by roasting certain arsenic ores (Patil, 2000).

Arsenicum album is a profoundly acting remedy that targets every organ and tissue. Its characteristic symptoms and correspondence to many severe types of diseases make its homoeopathic employment constant. *Arsenicum album's* general symptoms consist of debility, exhaustion, restlessness with nightly aggravation and burning pains (Vermeulen, 2000).

Arsenicum album is often used in newly diagnosed cases of diabetes mellitus where there is prostration that is out of proportion to the physical condition. The patient requiring this remedy would be restless and would have a desire for heat. The symptom picture would include a thirst for small quantities of water and there would be frequency of micturition (Moiloa, 2002).

2.11.2 Uranium nitricum

Uranium nitricum is a salt prepared from the Pitch Bland (Choudhuri, 2003). Pure nitrate of Uranium is triturated for its homoeopathic use (Allen, 1994).

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Uranium nitricum is a remedy for glycosuria and increased urination. The general symptoms of this remedy are excessive thirst, nausea, vomiting, an increased appetite, profuse urination, great languor, debility, vertigo, complete loss of sexual power, dryness of the mouth and tenacious salivation (Choudhuri, 2003) (Phatak, 2002). Its characteristic action is marked on the kidneys (Choudhuri, 2003). It is a remedy used in diabetes mellitus and diabetes insipidus (Phatak, 2002).

Dr Laning stated that no remedy gives such universally good results in diabetes, as does *Uranium nitricum*. He recommends prescription of *Uranium nitricum* in a 3x trituration. *Uranium nitricum* lessens the glucose levels and quantity of the urine. *Uranium nitricum* is the remedy when diabetes is due to assimilative derangements and symptoms such as defective digestion, languor, debility and much glucose in the urine, enormous appetite and thirst, yet the patient continues to emaciate (Dewey, 2001). Many cases of diabetes have been relieved and cured by *Uranium nitricum* (Choudhuri, 2003).

2.11.3 Phosphoricum acidum

The 1st centesimal dilution of this remedy is prepared when one part of pure glacial phosphoric acid is dissolved in ninety parts of distilled water and ten parts of alcohol is added (Allen, 1994).

The main tissue affinity of *Phosphoricum acidum* is with the nervous system as it induces both mental depression and muscular weakness of the progressive type (Gibson, 1994). *Phosphoricum acidum* produces general weakness, with a quiet apathetic state (i.e. profound nervous prostration without excitement), (Allen, 1994). This remedy is indicated whenever the system has been exposed to the ravages of acute disease, sexual excesses, grief and loss of vital fluids (Murphy, 1995).

Dr. Allen states that with *Phosphoricum acidum* the collateral symptoms of diabetes mellitus are pronounced, and its curative power with regards to this disease is undoubted (Allen, 1994). *Phosphoricum acidum* is prescribed for diabetes of nervous origin, i.e. there is grief and anxiety, which precipitates the condition (Moiloa, 2002). *Phosphoricum acidum* has a strong action over the kidneys as is seen from its tendency to cause polyuria (Choudhuri, 2003). The patient would pass milky urine and would be lethargic due to loss of vital bodily fluids (Phatak, 2002).

Phosphoricum acidum suits cases due to grief, worriment and anxiety and those patients who are indifferent and apathetic and poor in mental and physical force. *Phosphoricum acidum* is curative of diabetes mellitus in the early stages. *Phosphoric acidum* is indicated when patients pass large quantities of pale colourless urine or when there is much phosphatic deposit in the urine. The patient requiring *Phosphoricum acidum* would be experiencing loss of appetite; unquenchable thirst and perhaps the patient will be troubled with boils (Dewey, 2001).

2.11.4 Lactic acid

Lactic acid is a corrosive acid that was first discovered in sour milk, the result of spontaneous fermentation of sugar of milk under the influence of casein. It is also found in many vegetable products, which have turned sour (Choudhuri, 2003).

Lactic acid is one of the leading remedies for diabetes mellitus. It is especially indicated if in addition to the thirst, voracious hunger and profuse urine loaded with glucose there are rheumatic pains in the joints (Nash, 2003). Additional indications for the use of *Lactic acid* are acrid and profuse sweat, rheumatic inflammation of elbows, knees and small joints, thick white coating of the tongue and offensive sweating of feet (Choudhuri, 2003).

The symptoms that a patient would have when requiring this remedy are: urinates copiously and freely, urine light yellow and saccharine, thirst, nausea, debility, voracious appetite and costive bowels. A dry skin and tongue as well as gastralgia may accompany the above symptoms (Dewey, 2001).

2.11.5 Insulinum

Insulinum is an aqueous solution of an active principle from the pancreas, which affects glucose metabolism (Murphy, 1995).

Insulinum is used in the treatment of diabetes, restoring the lost ability to oxidise carbohydrates and storing glycogen in the liver. *Insulinum* is used in gouty transitory glycosuria when skin manifestations such as erythemas with itching eczema, are persistent. *Insulinum* is well indicated when skin irritation, boils or varicose ulceration with polyuria are prevalent (Varma and Vaid, 2002).

Dr. Boericke says that Insulinum maintains the blood glucose at a normal level and the urine remains free of glucose (Dewey, 2001).

CHAPTER THREE

METHODOLOGY

3.1 Study Population

The study population consists of Diabetes Mellitus Type II patients in Lenasia.

3.2 Study Sample

The study was conducted on thirty participants with Diabetes Mellitus Type II, over a period of two months. Certain criteria had to be fulfilled in order to participate in the trial:

The inclusion criteria were:

- Participants had to be between the ages of 30-60 years,
- Have been previously diagnosed with Diabetes Mellitus Type II between five-ten years prior to the trial
- Participants currently using oral-antidiabetic drugs namely; Diamicron, Glucophage, Amaryl or Glycomin

The exclusion criteria were:

- Participants using any other form of alternative diabetic treatment
- Insulin-dependant diabetic patients
- Diabetic patients with neuropathies or any other pathological changes

The selected participants represented a sample of the population suffering from Diabetes Mellitus Type II in Lenasia.

3.3 Methodology

3.3.1 Study Design

This study was a placebo-controlled double blind evaluation. The study comprised of two groups, namely an experimental group and a control group. The experimental group was given a complex formulation comprising of *Arsenicum album* 6CH, *Phosphoricum acidum* 6CH, *Uranium nitricum* 6CH, *Lactic acid* 6CH and *Insulinum* 7CH. The control group was given a placebo.

3.3.2 Stage one

The trial began with the recruitment of thirty participants, during the period September 2004 to May 2005. The researcher gave a presentation to possible participants, concerning the research study and what it entails. The presentation was held at the Jocod centre, which is based in Lenasia and was addressed to a group of diabetic patients. Advertising in relevant areas and within the local newspaper namely the Lenasia Times (Appendix E) was also conducted. On interviewing prospective candidates, a screening process was carried out to ascertain prerequisites in the trial (Appendix B). Participants were recruited once the criteria were fulfilled.

3.3.3 Stage two

Participants had to sign a Consent form (Appendix A) prior to the involvement in the trial, after having been briefed on the nature and extent of the trial and their participation. Participants were furthermore requested to complete a Participant Form (See Appendix B) in order to obtain a concise case taking and history of their condition in relation to DM Type II. The Participant Form also included an evaluation of the participants' vital signs.

3.3.4 Stage three

Participants were required to have their HbA_{1C} blood levels tested prior to administration of the remedy or the placebo. The blood test was taken at Pathsure Laboratories, which is based in Lenasia.

Pathsure laboratories generously sponsored the testing procedures. Randox Laboratories, South Africa, sponsored the actual testing equipment required for the HbA_{1C}.

3.3.5 Stage four

The medications used for this trial, were a homoeopathic complex formulation, consisting of the remedies *Arsenicum album, Phosphoricum acidum, Uranium nitricum, Lactic acid and Insulinum*. These remedies were selected by the researcher on account of their effects in the treatment of DM Type II. The remedies were prepared to the sixth centesimal dilution with the exception of *Insulinum*. *Insulinum* was prepared to the seventh centesimal dilution. The complex remedy was administered to the experimental group. Placebos were dispensed to the control group. The medication was prepared and labelled accordingly by Natura Laboratories.

Each participant received two 50ml amber glass bottles consisting of either the remedy or the placebo. The researcher instructed participants, to administer 10 drops of the medication thrice daily, for the duration of the two-month trial. Medication had to be taken two hours after meals.

This study was a double-blind study. Natura Laboratories double-blinded the trial. The researcher was unaware as to which participants were in the experimental group and which participants were placed in the control group. The information concerning the allocation of participants into prospective groups was disclosed to the researcher on completion of the trial.

3.3.6 Stage five

Participants received a Result Sheet (Appendix C) in which to record their blood glucose readings. Participants were, initially, required to test their blood glucose levels thrice daily for two months. However due to the high cost of the glucose testing strips as well as problems with patient compliance, participants were asked to test their glucose levels twice a day, i.e. one fasting blood glucose test and one non-fasting blood-glucose test.

Due to the reluctance of participants to test their blood-glucose levels because of the cost of glucose testing strips, the research was delayed. The researcher had to find sponsorship for glucose strips and did so at Roche Laboratories.

A monthly consultation with each participant ensued and a Follow-up Sheet (Appendix D) was completed. The purpose of the consultation was to monitor participants' blood glucose levels as well as their general health. Participants' vital signs, inspection of their skin and sensory system as well as opthalmoscopy were assessed during these consultations.

The participants were instructed to contact the researcher at any time during the trial should they have any queries and if there was a marked deterioration in their blood glucose levels.

3.3.7 Stage six

At the end of the two month trial participants had to have another HbA_{1c} blood test. The results of the HbA_{1C} were analysed and delivered to the researcher, by Pathsure Laboratories.

The Consent Form (Appendix A), the Participant Form (Appendix B), the Result Sheet (Appendix C) and the Follow-up Sheet (Appendix D) were all completed and collected at the end of the two month trial. All these appendices and the HbA_{1C} blood test results served as a means for data collection and provided information regarding the action of the medication, for purposes of analysis.

3.4 Data Analysis

The data collected from the trial was analysed using different methods of statistical analysis. Information from the Participant Form (Appendix B) was analysed using the Independent Sample t-test.

Comparisons between the experimental and control groups were done to determine if the groups were equivalent at onset. Independent Sample t-tests were used to determine the comparability between the Control and Experimental groups. Due to the small sample size as well as the non-normality of data the Non-parametric Mann Whitney test was conducted to determine the differences between the Control and Experimental groups.

Further analyses explored differences over time within each group using the Paired-Sample t-test.

3.4.1 Analysis of association between various factors in the questionnaire

The associations between fasting and non-fasting blood-glucose levels and the homoeopathic complex remedy were analysed.

CHAPTER FOUR

RESULTS

4.1 Introduction

The aim of this research study was to determine the efficacy of a homoeopathic complex formulation consisting of *Arsenicum album 6CH*, *Phosphoricum acidum 6CH, Uranium nitricum 6CH, Lactic acid 6CH* and *Insulinum 7CH* in the treatment of DM Type II.

The sample group consisted of thirty participants between the ages of 30-60 years. Participants had to have been diagnosed with DM Type II within ten years prior to the study, and had to meet the inclusion and exclusion criteria before being selected.

This two-month trial was a double-blind study in which participants were divided into two groups namely the experimental and the control group. The control group received a placebo whilst the experimental group received the remedy. All participants were advised to administer ten drops of the medication supplied, three times daily. It was recommended that participants have a two-hour interval after meals, before taking their medication.

Participants were requested to have their HbA_{1C} levels tested. This test had to be done twice for purposes of this trial. The first test had to be prior to administration of the remedy and the second test was taken once the two-month trial period had passed. In addition to the HbA_{1C} blood test, participants had to test their blood-glucose levels, twice daily, using a blood-glucose finger-prick test. A fasting glucose test was done in the morning before meals and a non-fasting glucose test was taken after a meal.

The researcher had follow-up consultations with participants on a monthly basis.

Results statistically analysed were obtained from the Participant Form (Appendix B), the Result Sheet (Appendix C), the Laboratory Results for the HbA_{1C} blood tests, and the Follow-up Sheets

(Appendix D). The participant form gathered frequency data, which were analysed using the Independent Sample t-test.

Comparisons between the experimental and control groups were done to determine if the groups were equivalent at onset. Independent Sample t-tests and the Non-parametric Mann Whitney test were used to determine the comparability between the Control and Experimental groups. Further analyses explored differences over time within each group using the Paired-Sample t-test.

4.2 Analysis according to Demographics

Refer to Appendix F for further statistical analysis.

4.2.1 Age

Participants between the ages of 30 and 60 years were recruited. Age was determined according to frequency as indicated in Figure 4.1. The mean age of all 30 participants was determined to be between 40-49 years.

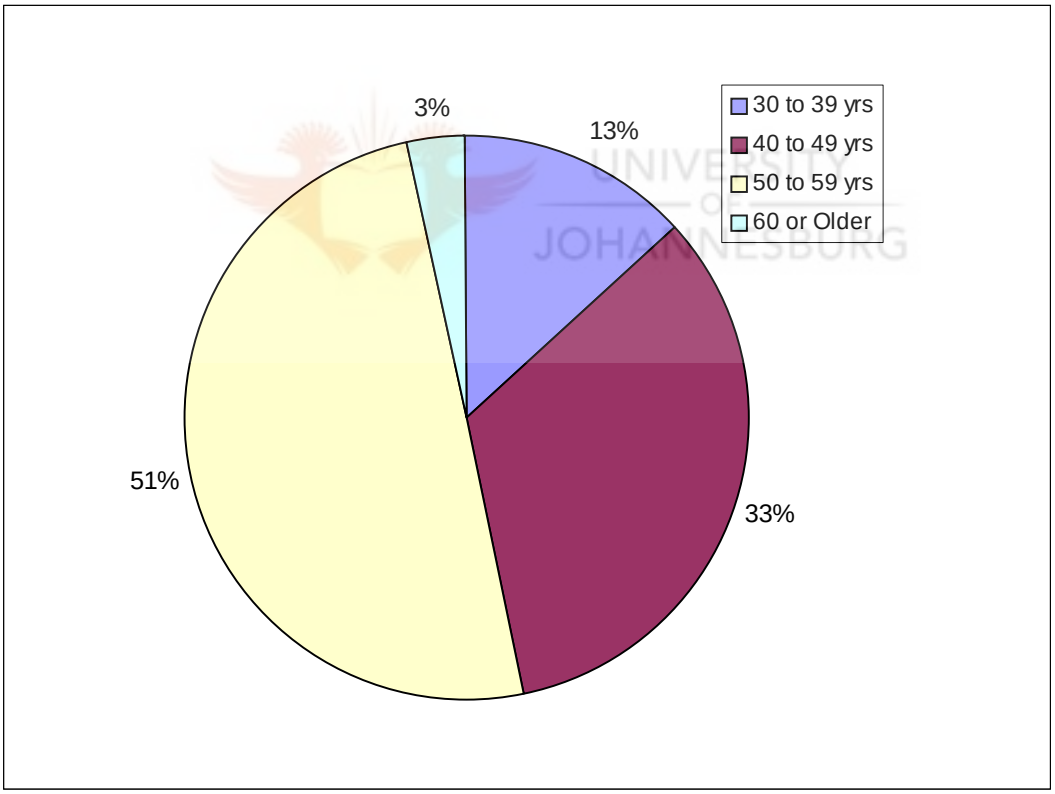

Figure 4.1 Graph depicting the age of participants

4.2.2 Gender

Both male and female participants were recruited. It was determined that 21 of the participants were male and 9 were female. This is depicted in Figure 4.2.

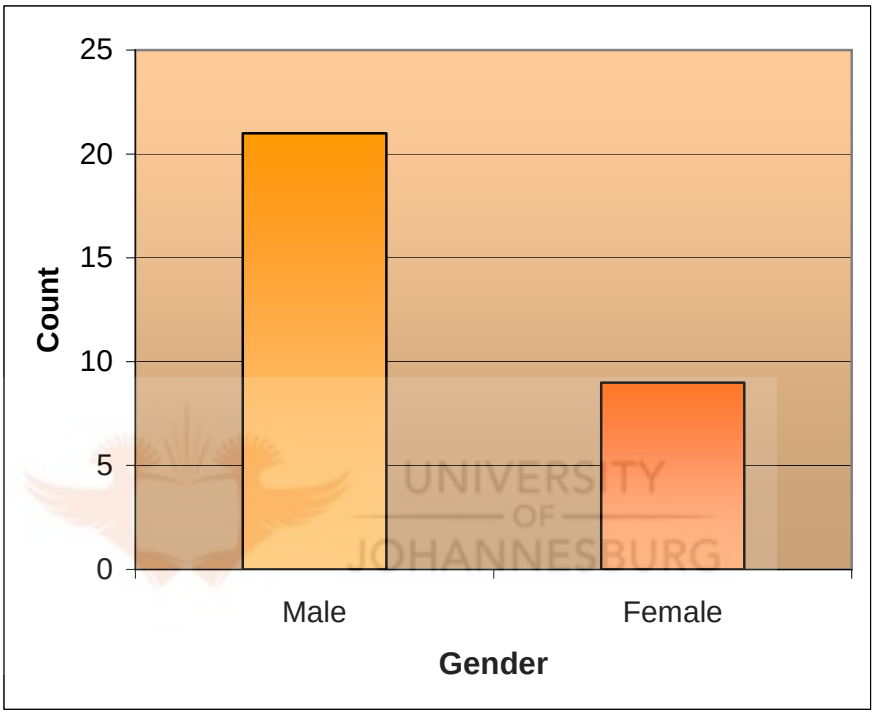

Figure 4.2 Graph depicting gender of participants

4.2.3 Time of diagnosis

Participants diagnosed with DM Type II between five to ten years prior to the study were recruited. Three participants were diagnosed one year ago and three participants were diagnosed two years ago. Six participants were diagnosed three years ago and six participants were diagnosed fours years ago. Four participants were diagnosed five years previously, five participants were diagnosed six years ago and three participants were diagnosed seven years prior to selection for the research. This is depicted below in Figure 4.3.

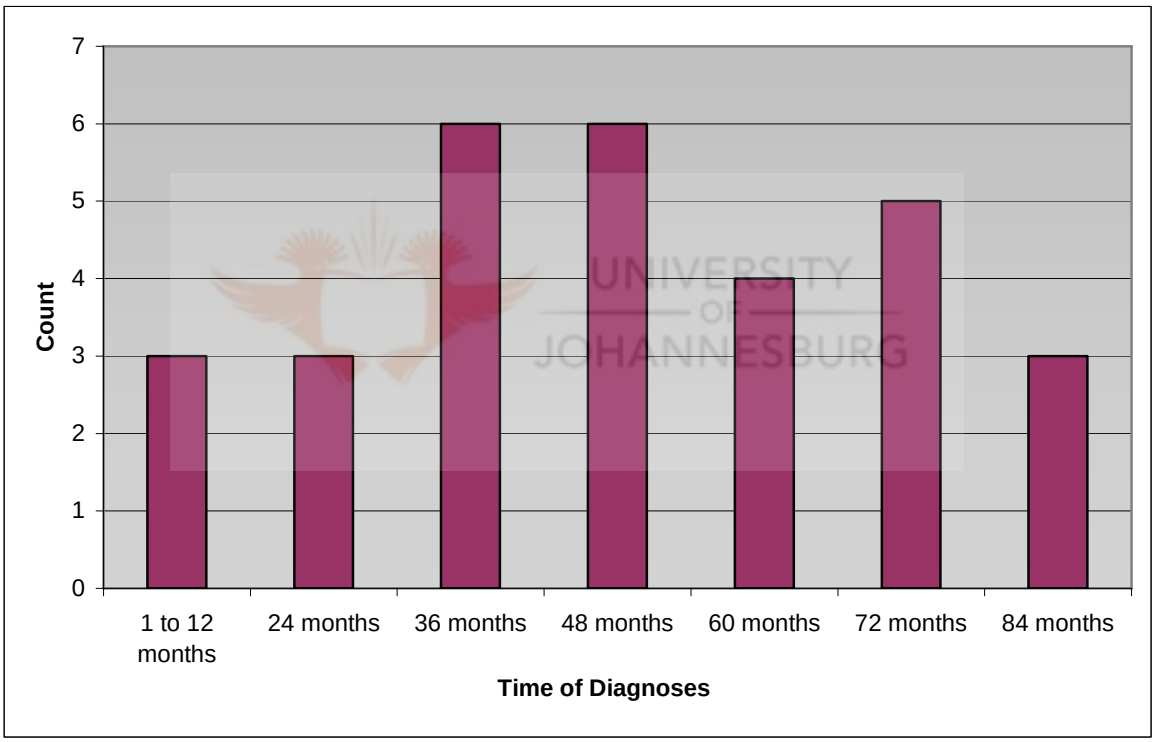

Figure 4.3 Graph depicting period of diagnosis

4.3 Data obtained from Participant Form

The findings of the Participant Form (Appendix B) representing participant details are depicted below in Table 4.1.

Table 4.1 Participant details

Case	*Group*	*Type of medication*	*Other medication*	*Other illness*	*Increased Thirst*	*Increased appetite*	*Increased Urination*	*Urination Evening*	*Fungal Infections*	*Numbness & Tingling*
1	Experimental	A,B	Yes	No	No	No	No	Yes	No	Yes
2	Control	B,C	Yes	Yes	No	No	No	No	No	Yes
3	Control	A,B	No	No	No	No	No	No	Yes	No
4	Experimental	A,B	No	No	No	No	No	Yes	Yes	No
5	Experimental	A,B	Yes	No	No	No	Yes	No	No	No
6	Control	D	No	No	Yes	No	Yes	Yes	No	Yes
7	Control	A,B	Yes	Yes	No	No	No	Yes	No	No
8	Control	A	No	No	Yes	Yes	Yes	Yes	Yes	Yes
9	Experimental	B	No	No	No	Yes	Yes	Yes	No	Yes
10	Experimental	A,B	No	Yes	No	No	No	Yes	No	Yes
11	Experimental	B,C	Yes	Yes	No	No	No	No	Yes	No
12	Control	A,B	No	No	Yes	Yes	Yes	Yes	Yes	Yes
13	Control	A,B	Yes	No	No	Yes	No	No	No	Yes
14	Experimental	A,B	Yes	Yes	No	No	No	Yes	Yes	Yes
15	Control	A,B	No	No	Yes	Yes	Yes	Yes	Yes	No
16	Experimental	A,B	No	Yes	Yes	No	No	No	No	No
17	Experimental	A,B	No	No	Yes	No	No	No	Yes	Yes
18	Control	A,B	No	No	No	No	No	No	No	Yes
19	Control	A,B	Yes	No	No	No	Yes	No	No	No
20	Experimental	A	No	Yes	Yes	No	No	Yes	No	No
21	Control	A	No	No	No	No	No	No	No	No
22	Experimental	A,B	No	No	No	No	No	No	No	No
23	Experimental	A	Yes	Yes	No	Yes	No	No	Yes	No
24	Control	B	Yes	Yes	Yes	No	Yes	Yes	Yes	No
25	Experimental	B,C	Yes	Yes	No	No	Yes	Yes	No	Yes
26	Control	B,D	No	No	Yes	No	No	Yes	Yes	Yes
27	Control	A,B	No	No	Yes	No	No	No	No	Yes
28	Control	B	No	Yes	Yes	No	Yes	Yes	No	No
29	Experimental	A,B	No	No	No	No	No	No	Yes	Yes
30	Experimental	A,B	No	Yes	Yes	No	Yes	Yes	Yes	No

Key to Table 4.1

A	Diamicron
B	Glucophage
C	Amaryl
D	Glycomin

Data obtained from Appendix B was used to determine the percentage of participants experiencing an increase in thirst, increase in appetite, increased urination, increased urination during the evening, occurrence of fungal infections and numbness and tingling in limbs. The type of conventional medication that participants themselves were taking was also considered. Participants were selected on the basis of the oral anti-diabetic agents they were using. Only specific oral anti-diabetic agents were eligible for purposes of this trial (Refer to the Key to Table 4.1).

The frequency analysis of the above variables suggests the following: 60 % didn't experience an increase in thirst while 40% complained of increased thirst. 80% didn't experience an increase in appetite and 20% did experience an increase in appetite. Only 36.7% of participants suffered from increased urination while 63.3% did not experience an increase in urination. However 53.3% of participants complained of increased urination during the evening and 46.7% did not experience increased urination during the evening. 43.3% of participants reported the incidence of fungal infections and 56.7% did not experience fungal infections. 50% of participants complained of numbness and tingling in limbs and 50% of participants did not experience this symptom. All this data was taken prior to recruitment, however on completion of the trial, the severity of the above symptoms was not reassessed. The researcher failed to include a reassessment of these symptoms during follow-up consultations.

4.4 Data obtained from the Laboratory

Participants were required to take two HbA_{1C} blood tests, the first test before the study and the second test at the end of the two-month trial period.

A Paired-Sample t-test was conducted to evaluate the impact of the homoeopathic remedy on HbA_{1C} levels.

4.4.1 HbA_{1C} levels of the Control group

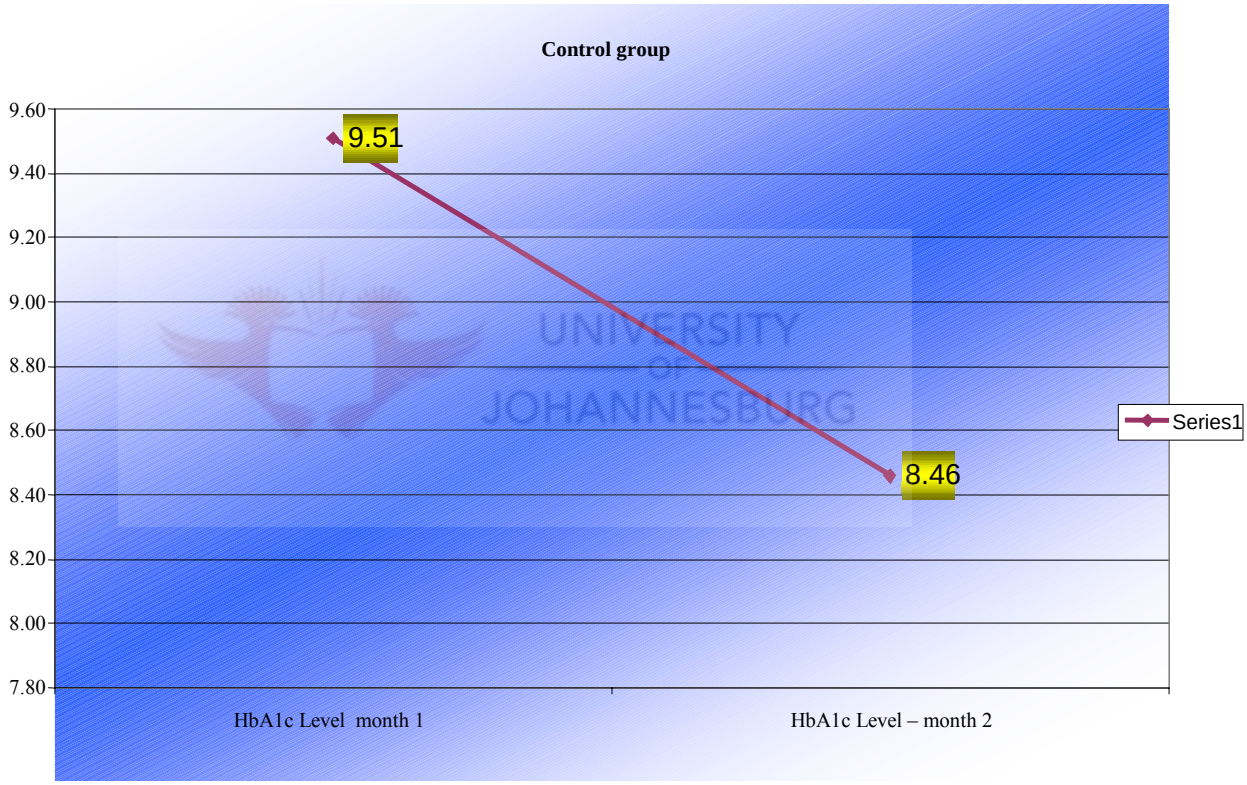

Figure 4.4 Graph depicting HbA_{1c} levels of the control group

A paired sample t-test was conducted to evaluate the homoeopathic remedies influence on participants' HbA_{1C} levels. For the control groups HbA_{1C} levels the results were statistically non-significant from Month 1 (M=9.51, SD=3.42) to Month 2 [M=8.46, SD=2.23, t (13)=1.12, p=0.282]. For further statistical analysis refer to Appendix G.

4.4.2 HbA_{1C} levels of the Experimental group

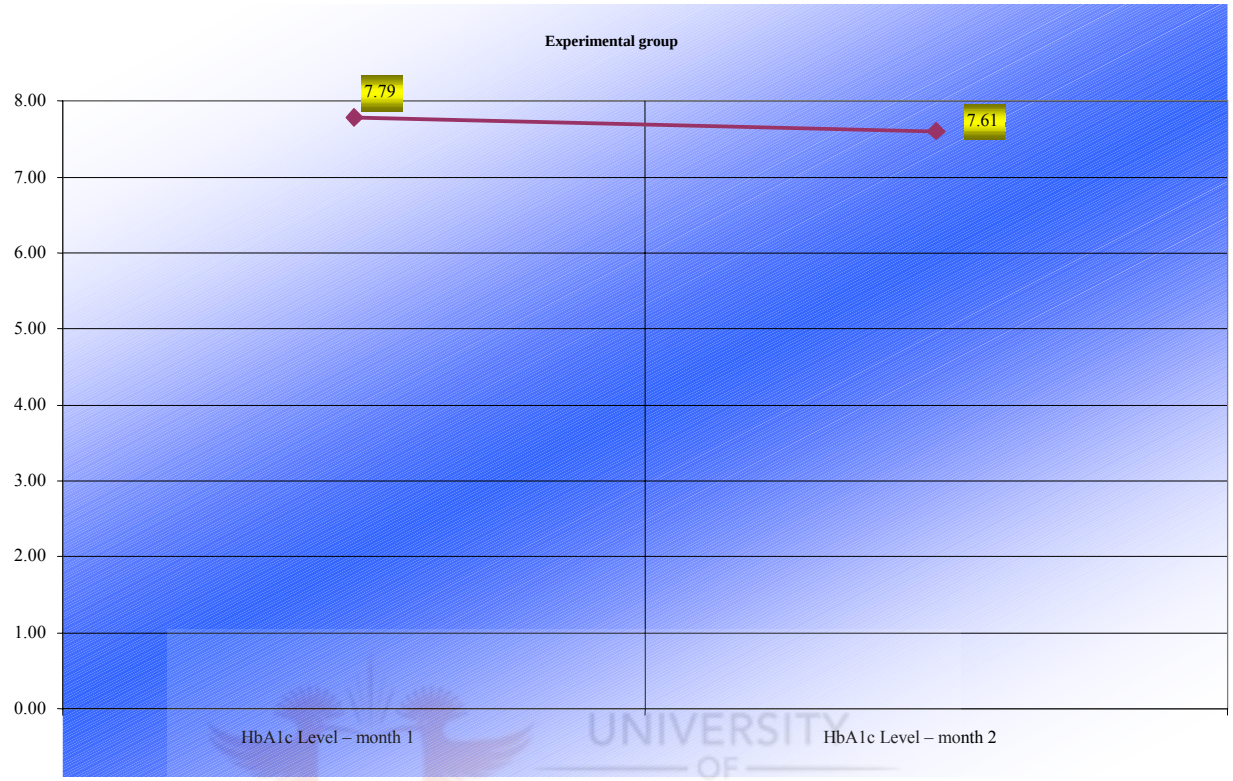

Figure 4.5 Graph depicting HbA_{1C} levels of the experimental group

There were statistically non-significant findings in the HbA_{1C} levels of the experimental group from Month 1 (M=7.79, SD=1.52) to Month 2 [M=7.60, SD=1.16, t (12)=0.49, p=0.631]. Refer to Appendix H for statistical elaboration.

4.5 Data obtained from Result Sheets

A Result Sheet was given to each participant (See Appendix C). Participants were required to take a blood glucose reading twice daily. The first test was a fasting glucose test while the second was a non-fasting glucose test. All results were recorded on the sheet given.

The fasting and non-fasting blood glucose results were statistically analysed using the Paired-Sample t-test.

4.5.1 Fasting glucose levels of the Control group

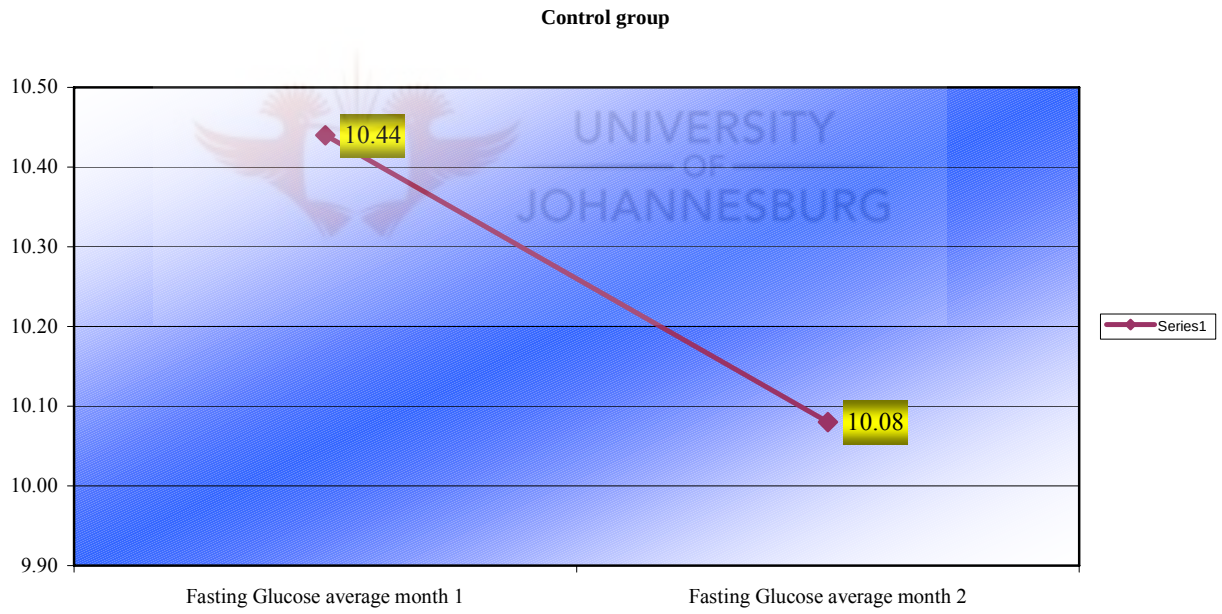

Figure 4.6 Graph depicting fasting glucose levels of the control group

The results for the control group from Month 1 (M=10.44, SD=3.60) to Month 2 [M=10.08, SD=3.56, t(14)=1.59, p=0.134], were statistically non-significant. Refer to Appendix G for further statistical analysis.

4.5.2 Fasting glucose levels of the Experimental group

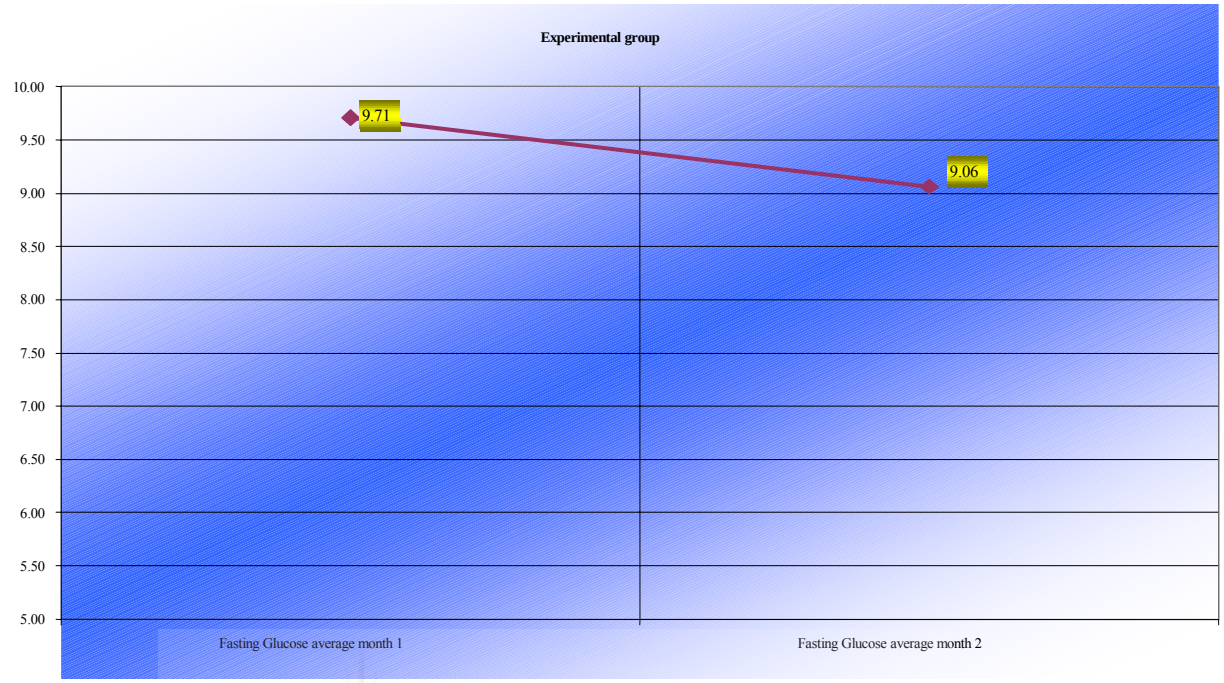

Figure 4.7 Graph depicting fasting glucose levels of the experimental group

The results of the fasting glucose levels of the experimental group were statistically analysed using the Paired- Sample t-test. There was a statistically significant decrease in fasting glucose levels of the experimental group from Month 1 (M=9.71, SD=2.23) to Month 2 [M=9.06, SD=1.96, t(13)=2.236, p=0.043]. The statistic p=0.043 indicated a significant effect. Refer to Appendix H for further statistical data.

4.5.3 Non-fasting glucose levels of the Control group

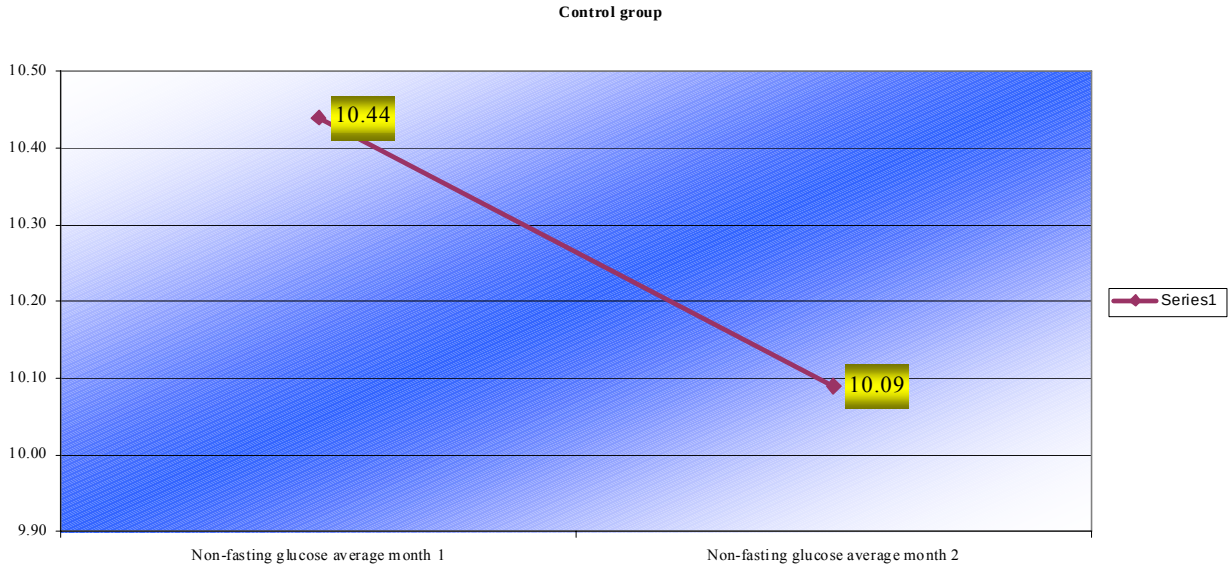

Figure 4.8 Graph depicting non-fasting glucose levels of the control group

In Figure 4.8 the non-fasting glucose levels of participants in the control group is portrayed. The results were statistically non-significant from Month 1 (M=10.44, SD=3.63) to Month 2 [M=10.09, SD=3.60, t(14)=1.51, p=0.153]. Refer to Appendix G for statistical elaboration.

4.5.4 Non-fasting glucose levels of the Experimental group

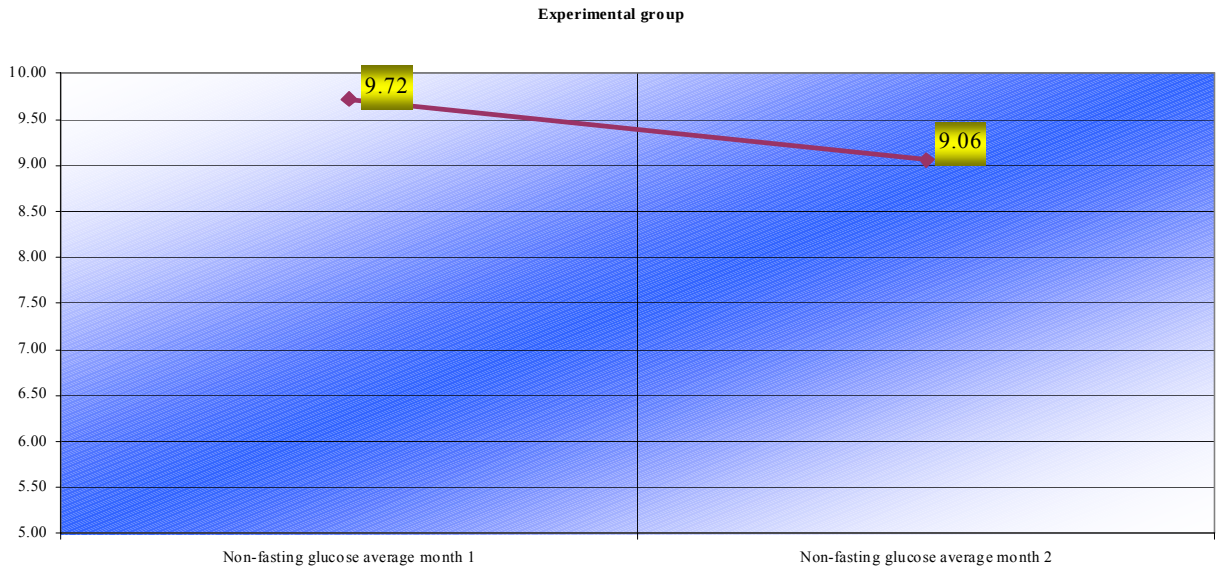

Figure 4.9 Graph portraying non-fasting glucose levels of the experimental group

The homoeopathic remedies influence on the non-fasting glucose level was analysed. There was a statistically significant decrease from Month 1 (M=9.72, SD=2.25) to Month 2 [M=9.06, SD=1.97, t(13)=2.17, p=0.049]. Refer to Appendix H for further statistical data.

4.6 Data obtained from Follow-up Sheets

Follow-up sessions with every participant were conducted on a monthly basis (See Appendix C). Participants' vital signs, i.e. pulse, blood pressure, respiratory rate, and temperature were assessed during each consultation. Figures 4.10- 4.15 depicts the statistical findings. Independent-Sample T-Tests were conducted to compare the changes in pulse rates, blood pressure readings, respiratory rates, temperature and weight fluctuations over the two-month period. Refer to Appendix I for statistical elaboration.

4.6.1 Pulse Rate

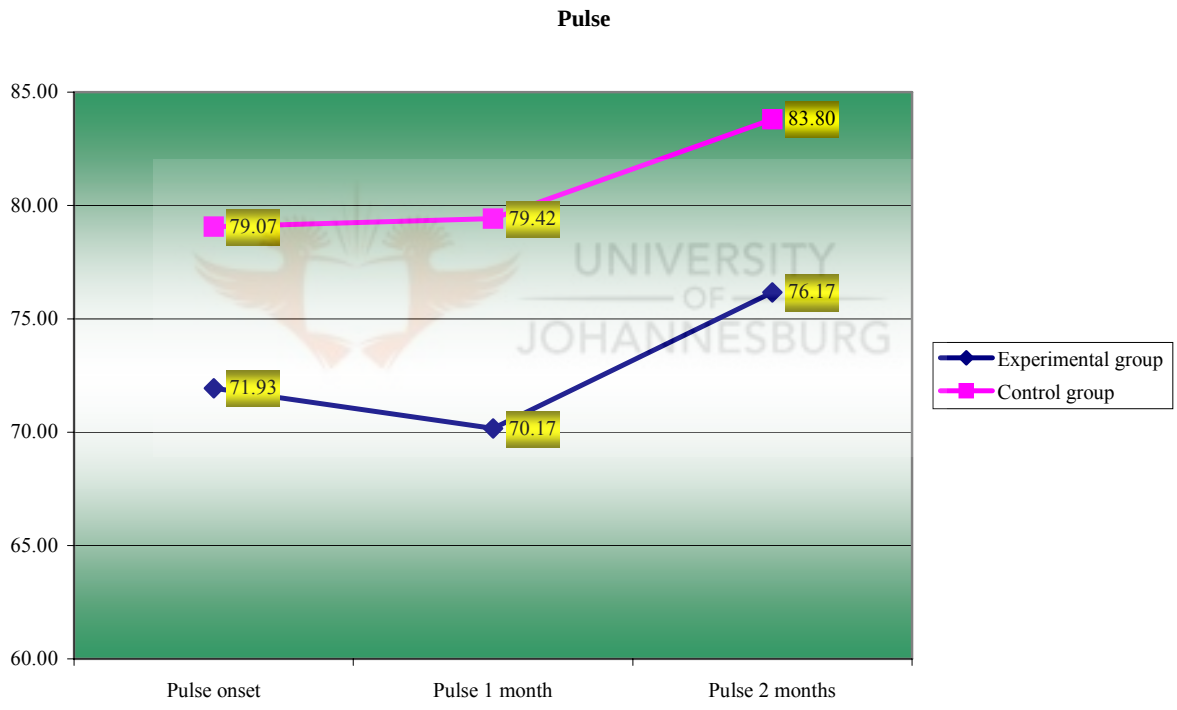

Figure 4.10 Graph demonstrating pulse rates at the end of each month

The control groups average pulse rate at the time of onset was 79,07 beats/min. At month one it was 79,42 beats/min and the final result at month two was 83,80 beats/min. The pulse rates in the experimental group started at 71,93 beats/min then decreased to 70,17 beats/min at month 1, but escalated to 76,17 beats/min at the end of the trial.

No significant findings were discovered when comparing pulse rates. This is true for both the experimental and control groups.

4.6.2 Blood Pressure Systolic

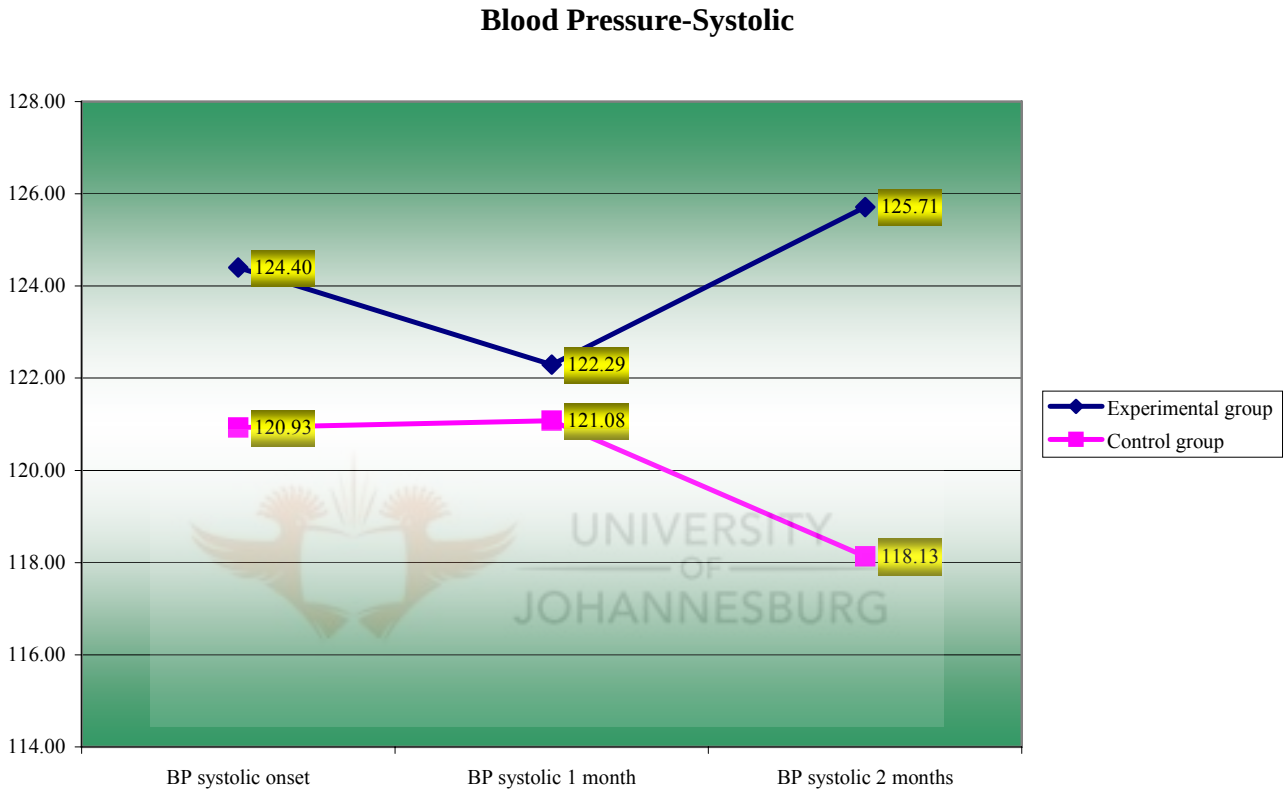

Figure 4.11 Graph showing the systolic blood pressure at the end of each month

Within the experimental group the systolic blood pressure was 124,40 mmol/l. This result of 124,40 mmol/l was during the first consultation. During the second consultation the blood pressure decreased to 122,29 mmol/l but increased to 125,71mmol/l at the end of month 2.

The control groups systolic blood pressure at onset, was 120,93 mmol/l. The systolic blood pressure remained almost constant at the end of month 1 with a reading of 121,08 mmol/l. At the end of month 2 it had decreased to 118,13 mmol/l.

However, statistically there were no significant findings.

4.6.3 Blood Pressure Diastolic

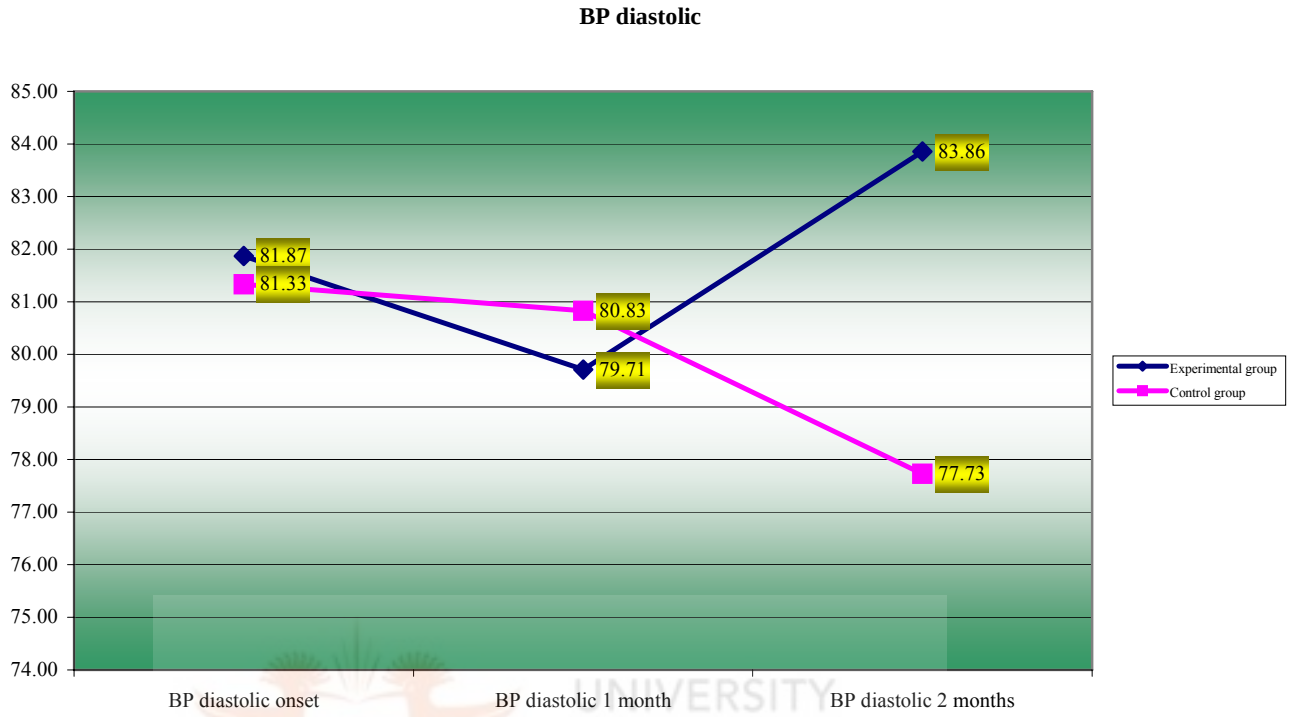

Figure 4.12 Graph depicting diastolic blood pressure during the two-month trial

The diastolic blood pressure reading of the experimental group began at 81,87 mmol/l and decreased to 79,71 mmol/l at the end of month 1. This groups diastolic blood pressure escalated to 83,86 mmol/l at the end of month 2.

The control groups diastolic blood pressure was 81,33 mmol/l at onset and remained almost constant as readings at the end of month 1 was 80,83 mmol/l. Diastolic blood pressure readings of the control group at the end of month 2 dropped to 77,73 mmol/l.

Statistically results were non-significant.

4.6.4 Respiratory Rate

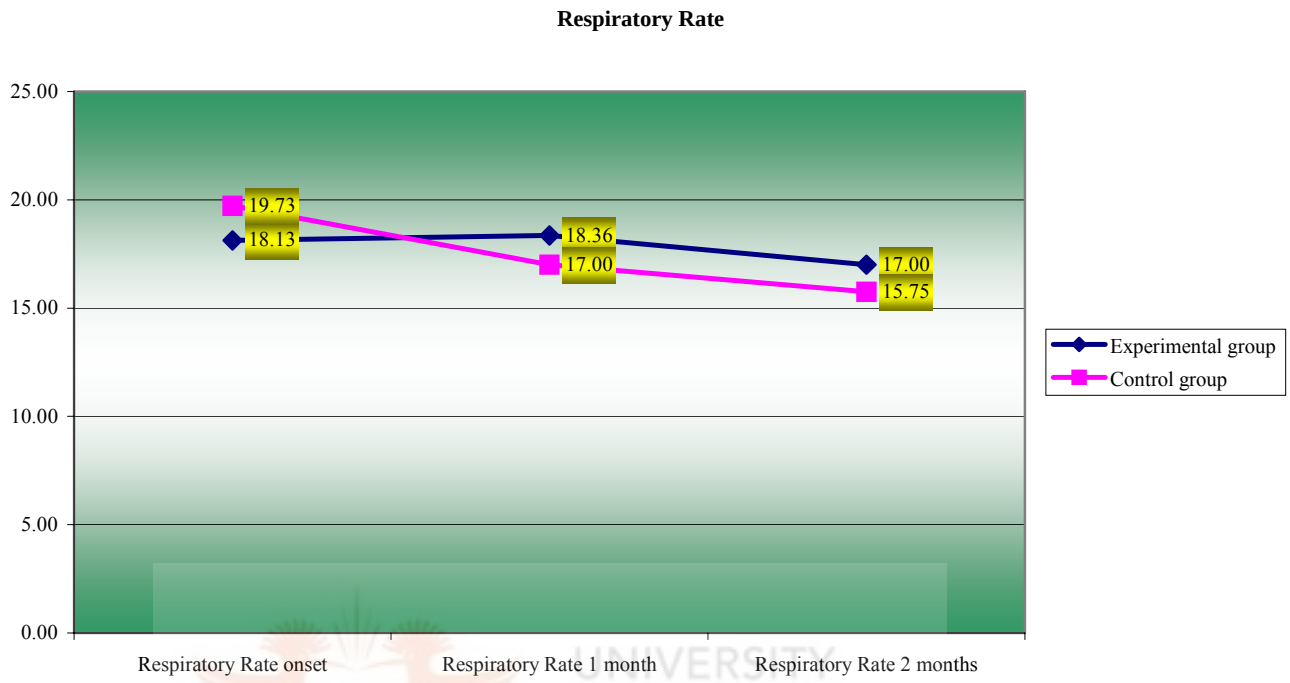

Figure 4.13 Graph portraying respiratory rates at the end of each month

The respiratory rate of the control group was 19,73 breaths/min at onset and decreased to 17,00 breaths/min at the end of month 1. By month 2 the control groups respiratory rate reached a low of 15,75 breaths/min.

During the first consultation the experimental groups average respiratory rate was 18,13 breaths/min. At the end of month 1 the respiratory rate was 18,36 breaths/min and decreased slightly to 17,00 breaths/min at the end of month 2.

However statistically these findings were non-significant.

4.6.5 Temperature

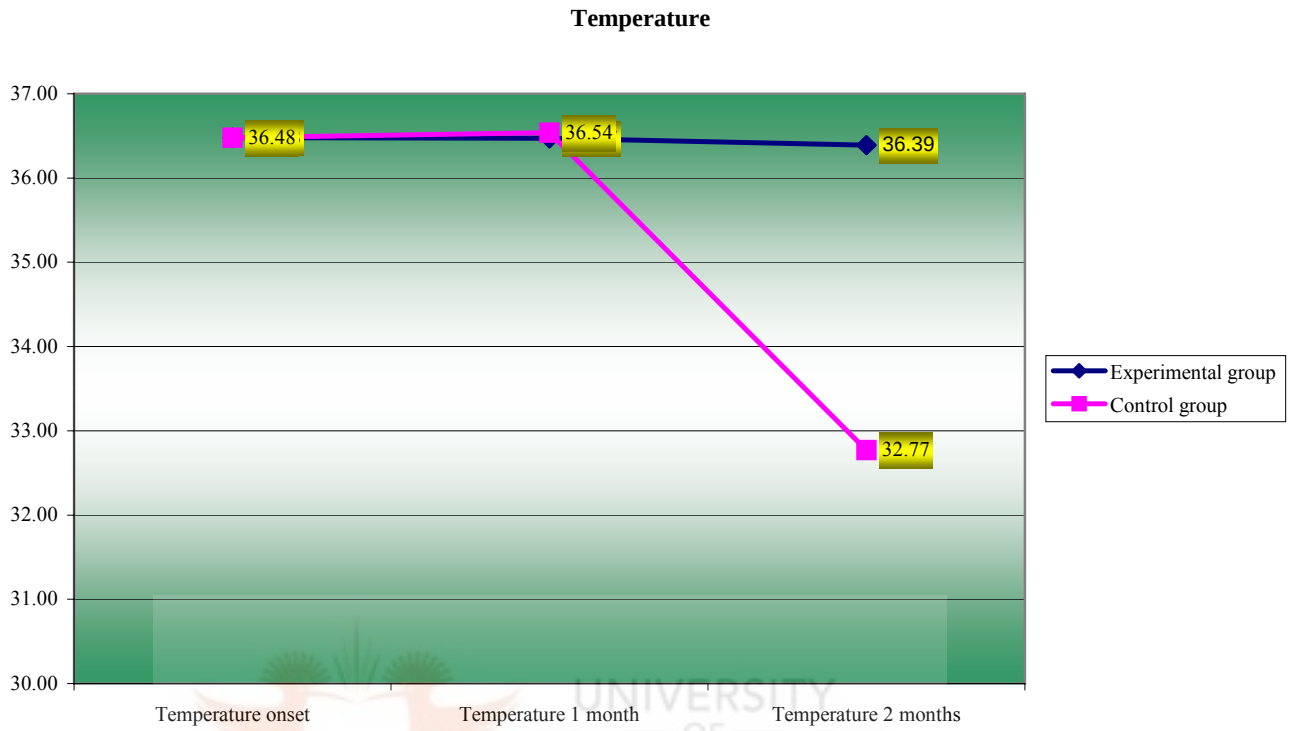

Figure 4.14 Graph demonstrating temperature readings for two months

The temperature readings of both the experimental and control groups began at 36,48 ^{o}C. At the end of month 1 both groups' readings were 36,54 ^{o}C. However reading at month 2 showed that the control groups' temperature decreased to 32,77 ^{o}C and the experimental groups readings remained almost constant with the final reading of 36,39 ^{o}C.

This data was excluded because the data gathering was flawed.

4.6.6 Weight

Figure 4.15 Graph depicting weight fluctuations during the two-month trial

At the beginning of the trial the average weight of the control group was 76,00 kg. The control groups weight increased to 77,43 kg at month 1 but after completion of the two-month trial the control groups weight decreased to 75,21kg

In comparison the experimental groups average weight was 83,24 kg at commencement of the trial. This groups weight decreased slightly to 81,23 kg at the end of month 1 but increased to 81,92 kg at the end of month 2. The differences between month 1 and month 2 were on a minor scale.

The results, however, were statistically non-significant.

CHAPTER FIVE

DISCUSSION

5.1 Introduction

The study conducted was to determine the efficacy of a complex homoeopathic remedy on Diabetes Mellitus Type II. The complex remedy consisted of *Arsenicum album 6CH*, *Phosphoricum acidum 6CH, Uranium nitricum 6CH, Lactic acid 6CH* and *Insulinum 7CH.*

This research project was a double-blind study consisting of thirty participants. Participants recruited had to be between the ages of 30-60 years and had to have developed DM Type II within ten years prior to the study. Any complication of DM Type II was used as an exclusion criterion. The duration of the trial was two months.

Participants' were divided into two groups namely the experimental and the control group. The experimental group received the remedy while a placebo was administered to the control group. All participants' had to take ten drops of the remedy three times daily. Medication had to be taken two hours after meals

.

HbA_{1C} blood tests were conducted at a laboratory, on all participants. The first test was taken before commencement of the trial while the second test was done on completion of the research.

Every participant was required to test his or her glucose levels, twice daily, using a blood-glucose finger-prick test. The first test had to be in the morning before meals i.e. fasting glucose test. The second test was after a meal i.e. the non-fasting glucose test. These results were recorded on a daily basis.

5.2 Demographic Results

Thirty participants were recruited for the trial and divided randomly into two groups, viz. an Experimental group and a Control group. Twenty-one of the participants recruited were male and nine were female. With regard to age, the mean age of the participants was determined to be between 40-49 years, (Refer to Figure 4.2 for further details).

Only participants who were diagnosed with DM Type II within a ten-year period prior to the study were recruited. The time of diagnoses indicated that three participants were diagnosed one year ago and three participants were diagnosed two years ago. Six participants were diagnosed three years ago and six participants were diagnosed fours years ago. Four participants were diagnosed five years previously, five participants were diagnosed six years ago and three participants were diagnosed seven years prior to selection for the research. This is shown in Figure 4.3. Thus the majority of participants recruited were diagnosed within three to four years prior to the study.

5.3 Data obtained from Participant Form

Information extracted from the Participant Form (Appendix B) indicated that 60 % of participants didn't experience an increase in thirst while 40% complained of increased thirst. 80% didn't experience an increase in appetite and 20% did experience an increase in appetite. Only 36.7% of participants suffered from increased urination while 63.3% did not experience an increase in urination. However 53.3% of participants complained of increased urination during the evening and 46.7% did not experience increased urination during the evening. 43.3% of participants reported the incidence of fungal infections and 56.7% did not experience fungal infections. 50% of participants complained of numbness and tingling in limbs and 50% of participants did not experience this symptom. All this data was taken prior to participant recruitment, to test the severity of the participants' DM Type II.

The conventional oral anti-diabetic agents participants were using and their effect on the trial could not be statistically analysed.

The researcher failed to record an increase or decrease of the above symptoms during follow-up sessions, and realisation of the error occurred after all the data was captured. Thus rectification of the error was difficult

5.4 Results obtained from Laboratory Tests

Each participant had to have two HbA_{1C} blood tests. The first test was taken before commencement of the trial and the second at the end of the two-month trial.

The data portrayed a statistical non-significant result in both the experimental and control groups. The P-value of control group was p=0.282 and the experimental group was p=0.631. Both groups P-values are >0.05 indicating no statistical significant difference (Refer to Figures 4.4-4.5).

An HbA_{1C} blood test is usually and ideally taken every three months for a more accurate reading (Griffin, 2003) (D'Arrigo, 2006). However due to this trial being a two month trial the HbA_{1C} blood test result could be slightly inaccurate. A longer trial duration should prove beneficial.

5.5 Data obtained from Result Sheets

Participants were required to record all blood-glucose finger prick tests on the result sheet supplied by the researcher (See Appendix C). This test was done
twice daily, i.e. the fasting glucose and the non-fasting glucose tests.

With regards to the fasting glucose test of the control group it was discovered that with a p-value of 0.134 (Refer to Figure 4.6), the results were statistically non-significant.

The results of the experimental groups fasting glucose showed a p-value of 0.043 (Refer to Figure 4.7). This indicates a significant decrease in fasting glucose levels of the experimental group between month 1 and month 2. This statistical analysis indicates that the complex remedy contributed to decreasing fasting glucose levels of participants with DM Type II.

The non-fasting glucose readings of the control group brought forward a p-value of 0.153 (Refer to Figure 4.8). This indicates a statistical non-significant finding. The experimental groups non-fasting glucose results showed a p-value of 0.049 (Refer to Figure 4.9) signifying a statistical significance. This data demonstrates a significant decrease in non-fasting blood-glucose results showing that the complex homoeopathic remedy had a positive effect on blood glucose levels.

A homoeopathic research study of DM Type II was previously conducted. However this trial focused on similimum prescribing. The results of this trial proved beneficial in the treatment of DM Type II (Hardy, 2000).

The results of this trial show that complex homoeopathic prescribing helps in decreasing blood-glucose levels in DM Type II patients.

5.6 Data obtained from Follow-up Sheets

At the end of each month a follow-up consult (Appendix D) with each participant was undertaken. During these consultations participants' vital signs, i.e. pulse, blood pressure, respiratory rate and temperature were monitored. Participants' weight, inspection of skin, examination of the sensory system and opthalmoscopy were also tested.

Opthalmoscopy, inspection of skin and the examination of the sensory system could not be used statistically, because a grading system was not used to record a deterioration or an improvement of the systems tested.

The results of the vital signs and weight measurements were used to compare differences between the control and the experimental group (Refer to Figures 4.10 - 4.15). The results were statistically non-significant.

5.6.1 Pulse Readings

The pulse rates for both the experimental and control groups were within the normal range. Both the control and experimental groups pulse rates decreased at month 1, and then increased by month 2. However the pulse readings did not deviate from the normal range. According to Haslett *et al.*, 1999

this is acceptable as normal variations in pulse volume reflect physiological changes in stroke volume and arterial resistance. These variations may be influenced by many factors such as age, fitness level, arousal and pregnancy.

Although the experimental groups pulse readings were lower than the control groups it was within the normal range thus statistically non-significant.

Pulse readings were taken as a pre-requisite of the vital signs. However pulse readings did not vary much in this study. Therefore pulse readings are not an important statistic for purposes of this research.

5.6.2 Blood Pressure Readings

5.6.2.1 Systolic Blood Pressure

Figure 4.11 clearly shows that the control groups' systolic blood pressure decreased during the two-month duration of the trial. The experimental groups systolic blood pressure increased during this period.

The researcher observed that participants of the control group paid much more attention to their diet and followed an exercise programme more diligently than those participants in the experimental group. The same advice concerning diet and exercise was given to all participants, however some participants complied better than others. After statistical analysis it was noted that the control groups systolic blood pressure was better controlled than that of the experimental groups.

5.6.2.2 Diastolic Blood Pressure

As with the systolic blood pressure, the diastolic blood pressure of the control group showed a decrease during the research study. The experimental groups diastolic blood pressure decreased slightly between onset and month 1 but increased between month 1 and month 2 (Refer to Figure 4.12). At commencement of the trial the researcher advised participants to follow a 'diabetic diet' and to exercise regularly. Members of the control group adhered to a diet and exercise regimen whereas members of the experimental group did not. This could a contributing factor to the differences in blood pressure readings.

The increase and then decrease of the experimental groups diastolic blood pressure could also be due to "Aggravation". An aggravation is a homoeopathic term used to describe the 'brief cleansing' action that occurs when homoeopathic medication is taken (Lansky, 2003). During this aggravation period certain symptoms may increase in intensity before decreasing.

The systolic and diastolic blood pressure readings of the experimental group are within the normal range despite the increase in blood pressure.

Irrespective of the variations in both systolic and diastolic blood pressure readings, there were no significant statistical findings.

Bayne 1997, states that blood pressure is a "poor correlate of physiologic function". Bayne feels that blood pressure does not tell much about tissue perfusion. Blood pressure is the product of flow times resistance and does not allow clinical judgment about blood flow unless an assumption is made about systemic vascular resistance (Bayne, 1997).

Taking this into consideration and noting the statistical evidence, the researcher feels that the differences in blood pressure readings between groups is not such an important variable for this research.

5.6.3 Respiratory Rate

The respiratory rates of both the experimental and control groups were within the normal range of 12-18 breaths per minute.

Figure 4.13 does portray a slight decrease within the control groups' respiratory readings. The experimental groups respiratory rate decreased as well. This reason for the decrease in the experimental groups respiratory rate is unknown.

When statistically analysed results were non-significant.

5.6.4 Temperature

The temperature of both the control and experimental group remained almost constant during onset and month 1 (Refer to Figure 4.14). There was a deviation in readings during the time interval between month 1 to month 2.

A flaw in the data gathering could have resulted in the dramatic reduction of the control groups' temperature readings. However the temperature results were statistically non-significant.

5.6.5 Weight

The experimental and control groups weight decreased from the time of onset to month 2. However from month 1 to month 2 the control groups weight had decreased while the experimental groups increased slightly. The weight difference between month 1 and month 2 of the experimental group was only 0.69kg (Refer to Figure 4.15 for further details).

The marked reduction in the control groups weight could be due to the participants' diligence in following a healthy diet and exercising regularly. However results were statistically non-significant.

5.7 Summary

The data obtained and analysed shows that the homoeopathic remedy used for purposes of this research, was beneficial in the treatment of DM Type II. There was a significant decrease in the fasting and non-fasting glucose levels of the experimental group. However the fasting and non-fasting glucose level readings of the control were statistically non-significant.

There was no difference in the HbA_{1C} readings in both the experimental and the control group. The data signified a statistically non-significant result for both groups.

The results of the vital signs and weight measurements of the control and the experimental group were statistically non-significant.

CHAPTER SIX

CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

The statistical evidence with regard to the research conducted verified that the groups were compatible and suitable for comparison. It can be concluded from the results that the medicaments researched are suitable for the treatment of DM Type II in the selected potency. Furthermore, the research adds to data on and verifies that homoeopathic treatment is not based on the placebo effect but rather on scientific and statistically analysed trials.

6.1.1 Data obtained from Participant Form

No relevant findings could be statistically deducted from the Participant Form (Appendix B). The researcher did not gather further information of those symptoms asked in the participant form, during follow-up consultations.

According to the researcher a grading system should have been used for those symptoms, during the trial period. In this way further statistical data could have been captured and would have benefited the research.

6.1.2 Data obtained from Laboratory Tests

Information derived from the HbA_{1C} blood test revealed a statistically non-significant outcome. The P-Values for both the experimental and the control groups were >0,05 indicating no difference.

HbA_{1C} blood tests should be ideally taken quarterly (Griffin, 2003). However this was a two-month trial period. A longer research study could have demonstrated a more significant result.

6.1.3 Data obtained from Result Sheets

The Result Sheet (Appendix C) was used to collect data concerning the fasting glucose and the non-fasting glucose levels of the experimental and the control groups.

Statistical data revealed that this homoeopathic complex remedy containing *Arsenicum album 6CH*,

Phosphoricum acidum 6CH, Uranium nitricum 6CH, Lactic acid 6CH and *Insulinum 7CH*, was effective in decreasing the fasting glucose levels in DM Type II individuals.

A statistical significant decrease was also noted in non-fasting glucose levels of the experimental group. This is clear from the indicated P-Values.

6.1.4 Data obtained from Follow-up Consultations

During follow-up sessions participants' vital signs i.e. their pulse, blood pressure, respiratory rate and temperature were assessed. Their weight was also measured.

The data analysed proved statistically non-significant. Variations were seen in blood pressure readings of the control group. A slight decrease was noted. However there are many variables to consider therefore relevance to this data can be excluded. Moreover statistically speaking these results were rendered non-significant by the statistician.

6.2 Recommendations

Further research in this field could benefit from the following recommendations:

- The trial could be conducted on participants who are pre-diagnosed with DM Type II instead of post-diagnosed thus participants would not be on allopathic medication.

- A longer trial period would be beneficial in capturing more accurate HbA_{1C} data, preferably a trial duration of three months.

- When selecting participants, one could select only participants using the same allopathic medication.

- For further analyses of glucose levels, urine tests could be taken

- A healthy diet and exercise is essential for diabetic patients and these are two very important variables. It is suggested that participants could be divided into three groups one placebo group and two experimental groups. Of these experimental groups, one group follows a diet and exercise programme while the other does not.

- A trial could be conducted using the same complex remedy but adding a few more remedies that are used for DM Type II, such as S*yzygium jambolanum*.

- A larger sample group should prove beneficial for statistical purposes.

- During this study stress played an important role in fluctuating blood-glucose levels therefore stress is another variable and needs to be eliminated.

- A trial that would take into consideration the changes in thirst, appetite, urination, fungal infections etc, would improve the overall standard of the research. A grading system can be used for these symptoms in order to improve statistical data.

- A study that would observe the differences in opthalmoscopy, inspection of skin and the examination of sensory system between each consultation. A grading system may be used to witness the differences between each consultation. This could prove viable for statistical analysis.

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APPENDIX A

CONSENT FORM

Dear Applicant

The purpose of this study is to determine the effect of a homoeopathically prepared complex remedy in Diabetes Mellitus Type II. The complex remedy contains *Arsenicum album 6CH*, *Phosphoricum acidum 6CH, Uranium nitricum 6CH, Lactic acid 6CH and Insulinum 7CH.* You will be one of thirty participants suffering from Diabetes Mellitus Type II. The duration of the study will be two months.

You must be diagnosed with Diabetes Mellitus Type II and on any oral diabetic (conventional) medication. You still experience increased blood-glucose levels (> 11,1 mmol/L) despite being on medication. You occasionally suffer from symptoms indicative of diabetes mellitus type II i.e.:

- Increased thirst,
- Increased appetite,
- Increased urination,
- Urging to urinate during the evening,
- Weight gain or weight loss,
- Prone to fungal infections,
- Numbness and tingling in limbs.

During the trial period you will be advised to follow a sugar-free diet and to exercise regularly.

The remedy prescribed will be in liquid form and must be taken orally. You will be required to take one dose i.e. ten drops of the remedy three times daily, preferably two hours after meals.

Prior to the commencement of medication your glucose levels will be monitored using the blood-glucose finger prick test and your HbA_{1c} levels will be tested. You will be asked not to eat anything two hours prior to the test. Your vital signs, pulse, blood pressure, respiratory rate and temperature will also be assessed. On administration of medication you will assess your blood-glucose levels

twice daily. The first glucose test will be taken in the morning before eating anything, while the other test can be assessed after a meal.

Please note that your participation in this research study is voluntary and that you are at any stage free to refuse participation, or may withdraw from your consent. A copy of this consent form will be signed and made available to you. Any and all information submitted by you will be confidential and only I as the researcher will have access to it.

I, the volunteer, fully understand what this research entails and any questions that I have will be directed to the researcher. I understand the procedures to be followed and agree to abide by them. I agree that any information about my case may be used for discussion by the researcher and colleagues. I am aware that I may refuse participation at any time.

Date: _____ Signature: _____

Thank you

I, the researcher, have completely explained the techniques and purpose of the tests used in this research. Any questions that arise from the volunteers will be answered to the best of my ability.

Date:_____ Signature:_____

APPENDIX B

PARTICIPANT FORM

PARTICIPANT NUMBER: _____

(Please tick the appropriate option where applicable)

Title: Mr.____ Mrs. _____Miss _____Other _____ Please specify_____

Surname: _____ First Names: _____

Date of Birth: _____ Age: _____

Gender: Male _____ Female: _____

Occupation: _____

Address: _____

_____ Code:_____

Contact Details: (H)_____ (W)_____(Cell)_____

Please answer the following questions:

1. When were you diagnosed with Diabetes Mellitus Type II?

   _____

2. Are you on any medication for the above condition? Please specify? _____

   _____

   _____

3. Are you currently on any other medication? Please specify? _____

   _____

4. Do you suffer from any other illness/es? If so please state the condition/s _____

   _____

5. Are you presently experiencing any of the following conditions? (Please tick where applicable)
   - ❖ Increased thirst _____
   - ❖ Increased appetite _____
   - ❖ Increased urination _____
   - ❖ Urging to urinate during the evening _____
   - ❖ Prone to fungal infections _____
   - ❖ Numbness and tingling in limbs _____

How often do you take a blood-glucose reading? _____
_____

7. What was the reading of your last blood-glucose test? _____

Vital Signs

Pulse: _____ Blood Pressure: _____
Temperature: _____ Respiratory Rate: _____

Weight _____
Height_____
Body Mass Index: _____

Case Summary _____
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APPENDIX C

PARTICIPANT NUMBER: _____

RESULT SHEET

HbA_{1c} level: _____

DATE	TIME	WEEK	GLUCOMETER READING

DATE	TIME	WEEK	GLUCOMETER READING

DATE	TIME	WEEK	GLUCOMETER READING

DATE	**TIME**	**WEEK**	**GLUCOMETER READING**

DATE	TIME	WEEK	GLUCOMETER READING

HbA_{1c} level: _____

APPENDIX D
FOLLOW-UP SHEET

PARTICIPANT NUMBER: _____

Date: _____ Time: _____

Glucometer Reading: _____

Vital Signs

Pulse: _____ Blood Pressure: _____
Temperature: _____ Respiratory Rate: _____

Weight: _____
Length: _____
Body Mass Index: _____

Inspection of Skin

Hands: _____
_____
_____

Feet: _____
_____
_____

Examination

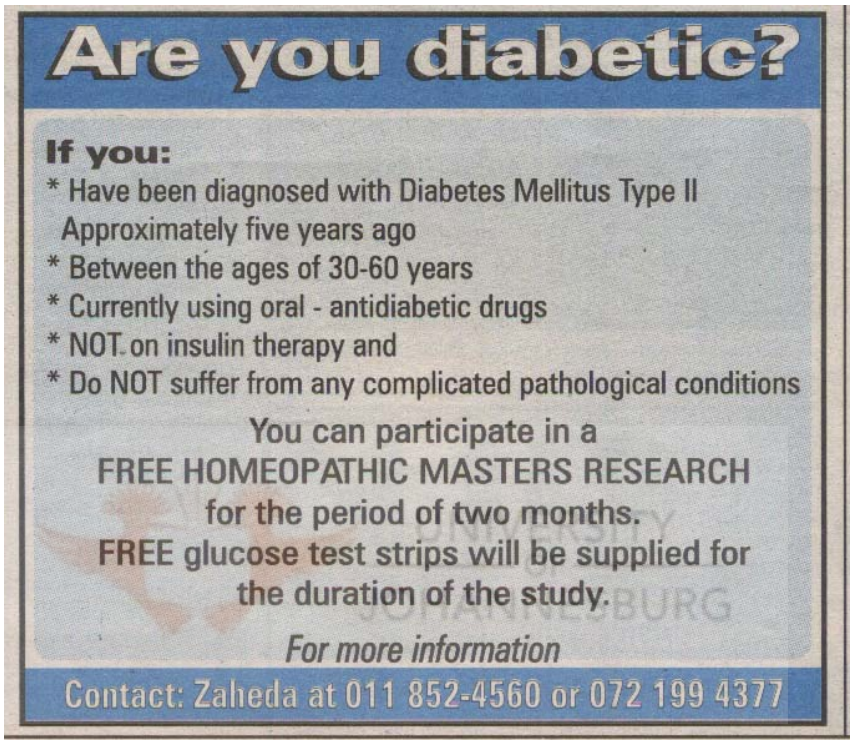
1. Opthalmoscopy: _____
_____
_____
_____

2. Sensory System:

2.1 Pain: _____
_____
2.2 Temperature: _____
_____
2.3 Light Touch: _____
_____
2.3 Vibration and Position: _____
_____

APPENDIX E

ADVERTISEMENT



APPENDIX F

DEMOGRAPHIC ANALYSIS

Case Processing Summary						
	Cases					
	Valid		Missing		Total	
	N	Percent	N	Percent	N	Percent
Group * age2	30	100.0%	0	.0%	30	100.0%
Group * Gender	30	100.0%	0	.0%	30	100.0%
Group * When diagnosed	30	100.0%	0	.0%	30	100.0%
Group * Medication A	30	100.0%	0	.0%	30	100.0%
Group * Medication B	30	100.0%	0	.0%	30	100.0%
Group * Medication C	30	100.0%	0	.0%	30	100.0%
Group * Medication D	30	100.0%	0	.0%	30	100.0%

Group: Age

Crosstab							
			age				Total
			30 to 39 years	40 to 49 years	50 to 59 years	60 or older	
Group	Control	Count	3	4	8	0	15
		% within Group	20.0%	26.7%	53.3%	.0%	100.0%
	Experimental	Count	1	6	7	1	15
		% within Group	6.7%	40.0%	46.7%	6.7%	100.0%
Total		Count	4	10	15	1	30
		% within Group	13.3%	33.3%	50.0%	3.3%	100.0%

Group: Gender

Crosstab					
			Gender		Total
			Male	Female	
Group	Control	Count	10	5	15
		% within Group	66.7%	33.3%	100.0%
	Experimental	Count	11	4	15
		% within Group	73.3%	26.7%	100.0%
Total		Count	21	9	30
		% within Group	70.0%	30.0%	100.0%

Group: When diagnosed

Crosstab									
			When diagnosed						Total
			1 to 12 months	24 months	36 months	48 months	60 months	72 months	84 months	
Group	Control	Count	2	3	2	2	3	2	1	15
		% within Group	13.3%	20.0%	13.3%	13.3%	20.0%	13.3%	6.7%	100.0%
	Experimental	Count	1	0	4	4	1	3	2	15
		% within Group	6.7%	.0%	26.7%	26.7%	6.7%	20.0%	13.3%	100.0%
Total		Count	3	3	6	6	4	5	3	30
		% within Group	10.0%	10.0%	20.0%	20.0%	13.3%	16.7%	10.0%	100.0%

APPENDIX G

T-TEST: CONTROL GROUP

HbA_{1c} level; Fasting glucose; Non-fasting glucose

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	HbA_{1c} Level - READING 2	9.5071	14	3.41545	.91282
	HbA_{1c} Level - READING 2	8.4571	14	2.22528	.59473
Pair 2	Fasting Glucose average month 1	10.4410	15	3.60524	.93087
	Fasting Glucose average month 2	10.0845	15	3.59879	.92920
Pair 3	Non-fasting glucose average month 1	10.4381	15	3.63250	.93791
	Non-fasting glucose average month 2	10.0928	15	3.60431	.93063

Paired Samples Correlations

		N	Correlation	Sig.
Pair 1	HbA_{1c} Level - READING 2 & HbA1c Level - READING 2	14	.287	.320
Pair 2	Fasting Glucose average month 1 & Fasting Glucose average month 2	15	.971	.000
Pair 3	Non-fasting glucose average month 1 & Non-fasting glucose average month 2	15	.970	.000

Paired Samples Test

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	HbA_{1c} Level - READING 2 - HbA_{1c} Level - READING 2	1.05000	3.50137	.93578	-.97163	3.07163	1.122	13	.282
Pair 2	Fasting Glucose average month 1 - Fasting Glucose average month 2	.35650	.86728	.22393	-.12378	.83679	1.592	14	.134
Pair 3	Non-fasting glucose average month 1 - Non-fasting glucose average month 2	.34524	.88388	.22822	-.14423	.83472	1.513	14	.153

APPENDIX H

T-TEST: EXPERIMENTAL GROUP

HbA_{1c} levels; Fasting Glucose; Non-fasting glucose

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	HbA_{1c} Level - READING 2	7.7923	13	1.51683	.42069
	HbA_{1c} Level - READING 2	7.6077	13	1.15935	.32155
Pair 2	Fasting Glucose average month 1	9.7074	14	2.23372	.59699
	Fasting Glucose average month 2	9.0607	14	1.95949	.52370
Pair 3	Non-fasting glucose average month 1	9.7219	14	2.24541	.60011
	Non-fasting glucose average month 2	9.0605	14	1.96752	.52584

Paired Samples Correlations

		N	Correlation	Sig.
Pair 1	HbA_{1c} Level - READING 2 & HbA_{1c} Level - READING 2	13	.519	.069
Pair 2	Fasting Glucose average month 1 & Fasting Glucose average month 2	14	.875	.000
Pair 3	Non-fasting glucose average month 1 & Non-fasting glucose average month 2	14	.861	.000

Paired Samples Test

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	HbA_{1c} Level - READING 2 - HbA_{1c} Level - READING 2	.18462	1.34898	.37414	-.63056	.99980	.493	12	.631
Pair 2	Fasting Glucose average month 1 - Fasting Glucose average month 2	.64666	1.08188	.28914	.02200	1.27132	2.236	13	.043
Pair 3	Non-fasting glucose average month 1 - Non-fasting glucose average month 2	.66136	1.14215	.30525	.00191	1.32082	2.167	13	.049

APPENDIX I
INDEPENDENT SAMPLE T-TESTS

T-Test

Group Statistics

	Group	N	Mean	Std. Deviation	Std. Error Mean
When diagnosed (months ago)?	**Control**	15	44.07	24.156	6.237
	Experimental	15	52.33	21.724	5.609
Pulse (onset)	**Control**	15	79.07	12.021	3.104
	Experimental	15	71.93	8.996	2.323
BP systolic (onset)	**Control**	15	120.93	12.803	3.306
	Experimental	15	124.40	13.442	3.471
BP diastolic (onset)	**Control**	15	81.33	9.817	2.535
	Experimental	15	81.87	9.643	2.490
Temperature (onset)	**Control**	15	36.480	.3121	.0806
	Experimental	15	36.480	.4021	.1038
Respiratory rate (onset)	**Control**	15	19.73	5.007	1.293
	Experimental	15	18.13	3.980	1.028
Weight (onset)	**Control**	15	76.00	14.702	3.796
	Experimental	14	83.24	13.902	3.715
Height (onset)	**Control**	15	1.6453	.07070	.01825
	Experimental	15	1.7047	.10453	.02699
Pulse	**Control**	12	79.42	12.199	3.521
	Experimental	14	70.17	19.268	5.149
BP Systolic (1 month)	**Control**	12	121.08	12.530	3.617
	Experimental	14	122.29	9.887	2.642
BP Diastolic (1 month)	**Control**	12	80.83	9.003	2.599
	Experimental	14	79.71	10.133	2.708
Temperature (1 month)	**Control**	10	36.54	.386	.122
	Experimental	14	36.47	.478	.128
Respiratory Rate (1 month)	**Control**	11	17.00	2.490	.751
	Experimental	14	18.36	4.431	1.184
Weight (1 month)	**Control**	11	77.43	14.518	4.377
	Experimental	13	81.23	11.952	3.315
Pulse (2 months)	**Control**	15	83.80	12.237	3.160
	Experimental	14	76.14	13.643	3.646
BP systolic (2 months)	**Control**	15	118.13	12.035	3.107
	Experimental	14	125.71	11.062	2.957
BP diastolic (2 months)	**Control**	15	77.73	10.222	2.639
	Experimental	14	83.86	9.231	2.467

Temperature (2 months)	**Control**	9	32.77	10.913	3.638
	Experimental	12	36.39	.584	.169
Respiratory Rate (2months)	**Control**	8	15.75	.707	.250
	Experimental	12	17.00	2.486	.718
Weight (2 months)	**Control**	14	75.21	15.106	4.037
	Experimental	13	81.92	14.459	4.010
HbA_{1c} Level - READING 2	**Control**	15	9.7667	3.44128	.88853
	Experimental	15	8.0933	1.62237	.41889
HbA_{1c} Level - READING 2	**Control**	14	8.4571	2.22528	.59473
	Experimental	13	7.6077	1.15935	.32155
Fasting Glucose average month 1	**Control**	15	10.4410	3.60524	.93087
	Experimental	15	9.8084	2.18773	.56487
Non-fasting glucose average month 1	**Control**	15	10.4381	3.63250	.93791
	Experimental	15	9.8187	2.19602	.56701
Fasting Glucose average month 2	**Control**	15	10.0845	3.59879	.92920
	Experimental	14	9.0607	1.95949	.52370
Non-fasting glucose average month 2	**Control**	15	10.0928	3.60431	.93063
	Experimental	14	9.0605	1.96752	.52584

Independent Samples Test

		Levene's Test for Equality of Variances		**t-test for Equality of Means**						
		F	**Sig.**	**t**	**df**	**Sig. (2-tailed)**	**Mean Difference**	**Std. Error Difference**	**95% Confidence Interval of the Difference**	
									Lower	**Upper**
When diagnosed (months ago)?	**Equal variances assumed**	.414	.525	-.986	28	.333	-8.267	8.388	-25.449	8.916
	Equal variances not assumed			-.986	27.691	.333	-8.267	8.388	-25.458	8.925
Pulse (onset)	**Equal variances assumed**	.503	.484	1.840	28	.076	7.133	3.877	-.807	15.074
	Equal variances not assumed			1.840	25.937	.077	7.133	3.877	-.836	15.103
BP systolic (onset)	**Equal variances assumed**	.073	.789	-.723	28	.476	-3.467	4.793	-13.285	6.352
	Equal variances not assumed			-.723	27.934	.476	-3.467	4.793	-13.286	6.353

BP diastolic (onset)	**Equal variances assumed**	.000	.984	-.150	28	.882	-.533	3.553	-7.811	6.745
	Equal variances not assumed			-.150	27.991	.882	-.533	3.553	-7.812	6.745
Temperature (onset)	**Equal variances assumed**	.999	.326	.000	28	1.000	.0000	.1314	-.2692	.2692
	Equal variances not assumed			.000	26.377	1.000	.0000	.1314	-.2700	.2700
Respiratory rate (onset)	**Equal variances assumed**	.002	.968	.969	28	.341	1.600	1.651	-1.783	4.983
	Equal variances not assumed			.969	26.644	.341	1.600	1.651	-1.790	4.990
Weight (onset)	**Equal variances assumed**	.001	.971	-1.361	27	.185	-7.243	5.322	-18.163	3.678
	Equal variances not assumed			-1.364	26.993	.184	-7.243	5.312	-18.142	3.656
Height (onset)	**Equal variances assumed**	3.098	.089	-1.821	28	.079	-.05933	.03258	-.12608	.00741
	Equal variances not assumed			-1.821	24.592	.081	-.05933	.03258	-.12650	.00783
Pulse	**Equal variances assumed**	.302	.588	1.432	24	.165	9.245	6.456	-4.079	22.569
	Equal variances not assumed			1.482	22.251	.152	9.245	6.238	-3.684	22.175
BP Systolic (1 month)	**Equal variances assumed**	.055	.816	-.273	24	.787	-1.202	4.397	-10.277	7.872
	Equal variances not assumed			-.268	20.850	.791	-1.202	4.479	-10.522	8.117
BP Diastolic (1 month)	**Equal variances assumed**	.118	.734	.295	24	.770	1.119	3.789	-6.701	8.939
	Equal variances not assumed			.298	23.957	.768	1.119	3.754	-6.629	8.867
Temperature (1 month)	**Equal variances assumed**	.091	.766	.374	22	.712	.069	.183	-.312	.449

	Equal variances not assumed			.388	21.577	.702	.069	.177	-.298	.436
Respiratory Rate (1 month)	**Equal variances assumed**	4.388	.047	-.907	23	.374	-1.357	1.496	-4.452	1.738
	Equal variances not assumed			-.968	21.116	.344	-1.357	1.402	-4.272	1.558
Weight (1 month)	**Equal variances assumed**	.371	.549	-.704	22	.489	-3.803	5.400	-15.002	7.395
	Equal variances not assumed			-.693	19.433	.497	-3.803	5.491	-15.279	7.672
Pulse (2 months)	**Equal variances assumed**	.959	.336	1.593	27	.123	7.657	4.806	-2.204	17.518
	Equal variances not assumed			1.587	26.158	.125	7.657	4.825	-2.257	17.572
BP systolic (2 months)	**Equal variances assumed**	.407	.529	-1.762	27	.089	-7.581	4.302	-16.408	1.246
	Equal variances not assumed			-1.767	26.996	.088	-7.581	4.289	-16.382	1.220
BP diastolic (2 months)	**Equal variances assumed**	.143	.708	-1.689	27	.103	-6.124	3.626	-13.564	1.316
	Equal variances not assumed			-1.695	26.975	.102	-6.124	3.613	-13.537	1.289
Temperature (2 months)	**Equal variances assumed**	6.017	.024	-1.159	19	.261	-3.625	3.129	-10.173	2.923
	Equal variances not assumed			-.995	8.034	.349	-3.625	3.641	-12.016	4.766
Respiratory Rate (2months)	**Equal variances assumed**	3.563	.075	-1.374	18	.186	-1.250	.910	-3.161	.661
	Equal variances not assumed			-1.645	13.518	.123	-1.250	.760	-2.886	.386
Weight (2 months)	**Equal variances assumed**	.022	.883	-1.177	25	.250	-6.709	5.700	-18.448	5.031
	Equal variances not assumed			-1.179	24.972	.250	-6.709	5.690	-18.429	5.012