

HYPERCHOLESTEROLAEMIA AND HOMOEOPATHY

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To David Kelham Standage for his endless help, support
and patience.

DECLARATION

I, Nerena Gillespie, do hereby declare that this research dissertation is my own work and has not been presented for any other diploma of another university or technikon.

Signed: *N. Gillespie*

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The work reported in this dissertation was performed in the Department of Homoeopathy, Technikon Natal, Durban.

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The object of the present research trial was to evaluate the efficacy of a single homoeopathic medication, Cholesterinum, in the ninth attenuation (9CH) in the treatment of hypercholesterolaemia. Special attention was paid to its effect on total cholesterol (TC) levels and the high-density lipoprotein cholesterol/ low-density lipoprotein cholesterol (HDL-C/LDL-C) ratio.

The design of the trial was as follows: A double - blind, placebo - controlled trial in which thirty two participants were randomly assigned to receive placebo or Cholesterinum 9CH twice daily for twelve weeks. Hypercholesterolaemic participants were chosen on a convenience sampling basis provided they had elevated TC and LDL-C levels. Blood samples were taken before treatment commenced and then once every four weeks for the duration of the study. A lipoprotein profile, which includes analysis of TC, HDL-C and triglycerides, was carried out on each blood sample by a commercial laboratory. The LDL-C levels were calculated using the Friedewald formula.

Results of the trial were as follows: It was calculated that 81.5% of the experimental group experienced an improvement in their TC levels compared to 68.75% of the control group. Cholesterinum 9CH produced a significant ($p=0.004$) reduction of 0.377mmol/l in the average TC of the experimental group compared to the non-significant

reduction of 0.118mmol/l that occurred in the control group. No significant change occurred in the HDL-C/LDL-C ratios of both groups.

Further statistical evaluation using unpaired T-tests revealed a significant difference between the initial TC reading of treated and placebo groups. (p=0.004) This significant difference was maintained after the first month of treatment (p=0.026) but decreased after the second and third months to non-significant levels. (p=0.199 and p=0.067 respectively)

The average TC readings of treated and placebo groups were compared before treatment and a 12.9% difference was calculated. This difference decreased to 9.6% by the end of the trial. As no significant difference existed between the initial and final TC readings of the placebo group, the assumption is made that the 3.3% decrease in the difference between both groups during the three month trial represents an improvement that took place largely in the treatment group.

This improvement does not seem to reach clinical significance although it was found to be statistically significant. The main argument in favour of its clinical insignificance being that the average change of 0.377mmol/l that occurred in the TC levels of the experimental group is not sufficient to change the coronary heart disease risk status of a patient.

It is recommended that further research be carried out on the use of the homoeopathic Simillimum in the treatment of hypercholesterolaemia, either on its own or in conjunction with Cholesterinum 9CH. It is also recommended that a larger sample group be used with a longer follow up period to increase reliability and validity of results and to allow for extrapolation of any findings to the general population.

Die doel van die studie was om die effek van die homopatiëse medisyne Cholesterinum, in die negende attenuasie (9CH) in die behandeling van hypercholesterolaemia te evalueer. Aandag is spesifiek geskenk aan die effek op die totale cholesterol (TC) vlak en die hoë-digtheid lipoproteïene cholesterol/lae-digtheid lipoproteïene cholesterol (HDL-C/LDL-C) verhouding.

Die was 'n dubbele-blinde plasebo-gekontroleerde studie waarin twee-en-dertig pasiënte willekeurig in twee groepe ingedeel was. Een groep is twee maal per dag vir twaalf weke plasebo toegedien en die ander Cholesterinum 9CH. Die deelnemers aan die studie is op steekproef basis gekies op voorwaarde dat hulle verhoogde TC en LDL-C vlakke gehad het. Bloedmonsters is voor die aanvang van die studie geneem en dan elke vier weke gedurende die projek. 'n Lipoproteïene profiel wat ontleding van die TC, HDL-C en trigliseriede ingesluit het, is op elke bloedmonster gedoen deur 'n plaaslike patologiese laboratorium. Die LDL-C vlakke is volgens die Friedewald formule bepaal.

Die uitslag van die studie is as volg: 81,5% van die eksperimentele groep het 'n verbetering in die TC-vlakke getoon teenoor die 68,75% in die kontrole groep. Die homopatiëse medisyne, Cholesterinum 9CH het 'n betekenisvolle verlaging van 0.377mmol/l ($p=0.004$) in die gemiddelde TC van die eksperimentele groep teweeg gebring

teenoor die verlaging van 0.118mmol/l in die kontrole groep. Geen betekenisvolle verandering word weerspieël in die HDL-C/LDL-C verhoudings van beide groepe nie.

Nog statistiese analises volgens die ongepaarde T-toets toon 'n betekenisvolle verskil in die aanvanklike TC lesing van die eksperimentele en kontrole groepe. ($p=0.004$) Die betekenisvolle verskil is volgehou na die eerste maand van behandeling ($p=0.026$) maar het gedaal na die tweede en derde maande. ($p=0.199$ en $p=0.067$ respektiewelik)

Die verskil tussen die aanvanklike gemiddelde TC lesings van die eksperimentele en kontrole groepe was 12.9%, en het verminder tot 9.6% teen die einde van die studie. Weens die feit dat geen betekenisvolle verskil bestaan tussen die aanvanklike en finale TC lesings van die kontrole groep nie, is die afleiding gemaak dat die 3.3% verlaging teen die einde van die studie 'n verbetering verteenwoordig wat meestal in die eksperimentele groep plaasgevind het.

Die verbetering het nie kliniese waarde nie, hoewel dit statisties betekenisvol is. Die belangrikste argument ten gunste van die kliniese waardeloosheid is dat die gemiddelde verandering van 0.377mmol/l wat in die TC vlakke van die eksperimentele groep plaasgevind het, nie genoegsaam is om die koronêre hart risiko status van die pasiënt te verander nie.

Dit word aanbeveel dat nog navorsing gedoen moet word na die gebruik van die homopatiiese Simillimum in die behandeling van hipercholesterolaemia, hetsy op sy eie of in samewerking met Cholesterinum 9CH. Nog 'n aanbeveling is dat 'n groter steekproefneming gedoen moet word, met 'n langer opvolgtydperk om ware en betroubare resultate te verkry en om voorsiening te maak vir die toepassing van resultate op die samelewing.

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CHAPTER ONETHE PROBLEM AND ITS SETTING1.1. IMPORTANCE OF THE STUDY

It has been documented in many studies that hypercholesterolaemia is associated with an increased risk of coronary heart disease, and that reduction of blood cholesterol levels will reduce the rate of coronary heart disease (Multiple Risk Factor Intervention Trial 1982; Castellli 1984; Lipid Research Clinics Coronary Primary Prevention Trial results 1 (LRC-CPPT 1) 1984; Consensus Development Conference 1985; Frick et al. 1987; Grover et al. 1992; Smith et al. 1992).

A number of risk factors, including cigarette smoking, hypertension and high blood cholesterol levels, have been identified as strongly associated with coronary heart disease (Castelli, 1984; Consensus Development Conference, 1985; Grundy et al. 1987; Wyndham et al. 1987).

Buhler et al. (1991) states that there are "diverse interactions" between the above risk factors and emphasizes alterations in serum lipoproteins, mainly elevated low-density lipoprotein cholesterol (LDL-C) and reduced high-density lipoprotein cholesterol (HDL-C) as the most

outstanding common denominator. The disturbed cholesterol homeostasis promotes the development of atherosclerosis and thrombo-embolic complications. He concludes that therapy aimed at reducing serum LDL-C and increasing HDL-C levels will have multifactorial beneficial effects on coronary heart disease.

Steyn et al. (1988) is of the opinion that hypercholesterolaemia may well be one of the most common coronary heart disease risk factors in South African populations with a typical Western lifestyle, which emphasizes the need for effective treatment of this condition.

Current allopathic treatment of hypercholesterolaemia involves dietary and other lifestyle changes as well as drug intervention (Report of the National Cholesterol Education Program (NCEP) 1988). Numerous clinical trials have demonstrated the efficacy of drug therapy for the treatment of hypercholesterolaemia (Frick et al. 1987; Bradford et al. 1993; Ferder et al. 1993; Miller et al. 1993; Schectman et al. 1993) with many investigating the effect of such treatment on the reduction of coronary risk (LRC-CPPT 1 1984; Lipid Research Clinics Coronary Primary Prevention Trial results 2 (LRC-CPPT 2) 1984; Frick et al. 1987; Manninen et al. 1988). The availability of highly effective drugs offers a simple pharmacologic answer to the control of hypercholesterolaemia and hence there has

recently been a surge of interest in cholesterol lowering drugs. Grundy (1986) expresses his concern in this upswing in interest. He states that all drugs have side effects or the potential for side effects, which sometimes do not become manifest for many years, and only after large numbers of patients have been treated.

The Council on Scientific Affairs (1983) comment on drug treatment which is supported by the expert panel of the NCEP (1988) is that because treatment must be pursued for a lifetime if risk factor reduction is to be maintained, and because any drug regimen may have undesirable side effects in some patients, drugs are not recommended except in patients whose lipid levels remain abnormal despite an adequate trial of diet therapy and weight reduction.

From research evaluated, the impression was gained that the efficacy of dietary therapy and the ability of patients to maintain the desired alteration in dietary habits for an extended period of time, is questionable. From the above considerations it becomes obvious that an alternative or supplementary method of treating hypercholesterolaemia would be beneficial, particularly if this treatment is simple enough for the patient to adhere to and does not involve too much of a change in lifestyle or have any undesirable side effects.

The use of homoeopathic medication in the treatment of hypercholesterolaemia has been poorly substantiated to date, but because it is a treatment modality that is believed to have limited adverse side effects, an investigation aimed at evaluating its efficacy would be advantageous.

The present study was therefore designed to attempt to evaluate the efficacy of a homoeopathic medicine in the treatment of hypercholesterolaemia.

1.2. PROBLEM STATEMENT

The purpose of this investigation is to evaluate the effect of Cholesterinum 9CH in the treatment of hypercholesterolaemic patients, in terms of fluctuations in total cholesterol (TC) levels and the HDL-C/LDL-C ratio, in order to determine the effect that Cholesterinum 9CH has on hypercholesterolaemia.

1.3. HYPOTHESIS

It is hypothesized that Cholesterinum 9CH will cause a reduction in the TC level and an increase in the HDL-C/LDL-C ratio.

1.4. ASSUMPTIONS

It is assumed that the participants of the study will take the medication as prescribed.

It is assumed that the medication will be prepared accurately as set out in the Homoeopathic Pharmacopoeia.

It is assumed that the participants will fast as requested for a period of twelve hours previous to having blood taken once every four weeks.

It is assumed that participants will not alter their lifestyle and dietary habits during the trial as requested by the researcher.

1.5. DELIMITATIONS

This study will not investigate the mechanism of action of Cholesterinum 9CH.

This study will not determine the aetiology of the hypercholesterolaemia prior to treatment.

This study will not investigate the triglyceride changes in the blood.

This study will not investigate the effect of dietary or lifestyle changes on cholesterol levels.

CHAPTER TWO

REVIEW OF THE RELATED LITERATURE

2.1. Low-density lipoprotein cholesterol

The guidelines developed by the expert panel of the NCEP identified LDL-C as the major atherogenic lipoprotein, and high levels of LDL-C as the primary target for cholesterol-lowering therapy (NCEP 1988).

The relationship between elevated serum cholesterol levels, especially LDL-C levels, and coronary heart disease is well established (Castelli 1984; LRC-CPPT 1 1984; LRC-CPPT 2 1984; Frick et al. 1987; Grover et al. 1992; Smith et al. 1992). This conclusion was also reached at a Consensus Development Conference held in 1985, the subject of which was lowering blood cholesterol levels to prevent heart disease, where a series of presentations was heard and available data reviewed by a panel of lipoprotein experts, cardiologists, primary care physicians, epidemiologists, biochemical scientists and experts in preventative medicine (Consensus Development Conference 1985).

The beneficial effects of reducing LDL-C to prevent coronary heart disease has been demonstrated in many clinical trials (LRC-CPPT 1 1984; Frick et al. 1987; Smith

et al. 1992). The LRC-CPPT 1 (1984) has been widely quoted as providing evidence of this nature. This randomised double-blind placebo controlled clinical trial tested the efficacy of lowering cholesterol levels for the primary prevention of coronary heart disease, using cholestyramine resin. This was carried out using a sample of 3806 middle-aged men who were at high risk for coronary heart disease because of elevated LDL-C levels. During treatment the cholestyramine group experienced plasma TC and LDL-C reductions of 13,4% and 20,3% respectively, which were 8,5% and 12,6% greater than those obtained in the placebo group. Both groups followed a moderate cholesterol-lowering diet. The cholestyramine group experienced 155 definite coronary heart disease deaths and/ or definite nonfatal myocardial infarctions, whereas the placebo group had 187 such events. On statistical evaluation, the incidence rate of coronary heart disease was estimated to be a statistically significant 19% lower in the treated than in the placebo group.

The results of this trial were critically evaluated and extended in a second article the LRC-CPPT 2 (1984). The researchers concentrated on internal and external consistency of the results and concluded that the trial clearly demonstrates that a reduction in coronary heart disease incidence is mediated chiefly by the lowering of cholesterol levels. It was also noted that an increase in the HDL-C levels among the cholestyramine treated group was

associated with an additional 2% reduction of coronary heart disease risk, but that the reduction of coronary heart disease incidence was mediated chiefly by the reduction of TC levels and LDL-C cholesterol levels.

Kronmal (1985) comments on the results of the LRC-CPPT 1 (1984) and expresses reservations at extrapolating the results to the general population, stating that the results should be confined to middle aged men with cholesterol levels above 6.85mmol/l.

The results of the LRC-CPPT 1 (1984) are qualitatively similar to the findings of the National Heart Lung Blood Institute(NHLBI) Type Two Coronary Intervention Study, which was carried out by Levy (1983). This was a secondary prevention trial that used the same drug but a different outcome measure in the form of angiographic assessment of change in coronary artery disease. In this study, changes in HDL-C levels seemed to be responsible for a larger portion of the treatment benefit than in the LRC-CPPT 1. However, both studies found that the combination of changes in HDL-C and LDL-C, expressed as a ratio of HDL-C to TC or LDL-C was sufficient to explain the observed benefit of cholestyramine treatment. For this reason, the HDL-C/ LDL-C ratio will be used in the present research trial to explain treatment benefit.

It was concluded at the Consensus Development Conference held in 1985, that the magnitude of the reduction in coronary heart disease can be estimated from the above two clinical trials, i.e. the LRC-CPPT 1 and NHLBI Type Two Coronary Intervention Study, which is that each 1% reduction in blood cholesterol levels yields approximately a 2% reduction in coronary heart disease rates (NHLBI Type Two Coronary Intervention Study 1983; LRC-CPPT 1 1984; Consensus Development Conference 1985).

The Helsinki Heart Study (Frick et al. 1987), a randomised double blind five year trial, tested the efficacy of simultaneously elevating serum HDL-C and lowering LDL-C with gemfibrozil, in reducing the risk of coronary heart disease in 4081 asymptomatic middle aged men with dyslipidaemia. All participants were free of coronary symptoms on entry into the trial but were at high risk of coronary heart disease because of abnormal concentrations of blood lipids. The subjects were examined at three month intervals for any symptoms or signs of myocardial infarction. It was concluded that the cumulative rate of cardiac end points at five years (with fatal and nonfatal myocardial infarction and cardiac death being the principal end points) was 27.3 per 1000 in the gemfibrozil group and 41.4 per 1000 in the placebo group. This represented a reduction of 34% in the incidence of coronary heart disease.

Manninen et al. (1988) deals with assessments of the lipid responses in the above trial in a more detailed fashion. He concludes that averaged over the five years, gemfibrozil therapy produced, compared with placebo, mean decreases of 10% in serum TC, 11% in LDL-C level, and a mean increase of 11% in HDL-C levels. It was concluded that both elevating HDL-C and lowering LDL-C levels are effective in the primary prevention of coronary heart disease as 50% of the protection can be attributed to the decrease in LDL-C and 50% to the increase in HDL-C. The 43% increase in triglycerides was shown to have no statistical significance to the incidence of coronary heart disease.

From the above considerations it becomes obvious that LDL-C plays a major role in the aetiology of coronary heart disease and should therefore serve as the primary target for cholesterol lowering therapy. For this reason an elevated concentration of this lipoprotein will be used as a criterion for entry of participants into the present research trial.

2.2. High-density lipoprotein cholesterol

A limited number of reports have indicated that HDL-C is inversely related to the incidence of coronary heart disease (LRC-CPPT 1 1984; LRC-CPPT 2 1984; Frick et al. 1987; Manninen et al. 1988; NCEP 1988) although according to Grundy et al. (1989) the pathophysiologic connection between reduced HDL-C levels and coronary heart disease is less secure than that of LDL-C.

Although the NCEP (1988) gave priority to the treatment of elevated LDL-C, it did not ignore the importance of low levels of HDL-C as a major risk factor for coronary heart disease, but not as a direct target of intervention. The expert panel does not advocate drug therapy specifically to raise HDL-C levels in patients without high cholesterol levels.

In several clinical trials the treatment used has resulted in slight or moderate elevations of HDL-C in addition to the sought for LDL-C reduction. These include the LRC-CPPT 1 (1984), NHLBI Type Two Coronary Intervention Trial (Levy et al. 1983) and the Helsinki Heart Study (Frick et al. 1987) as discussed previously. All three studies have been said, by Manninen et al. (1988) to jointly provide evidence for the role of high-density lipoprotein cholesterol in protection from coronary heart disease.

On evaluating the results of the LRC-CPPT1 (1984) the LRC-CPPT 2 (1984) states that although the 2% reduction in coronary heart disease risk (accompanying the rise in HDL-C) is a small percentage of the total 19% reduction in coronary heart disease risk in the treated group, the protection factor cannot be ignored.

Grundy et al. (1989) states that despite the results of various clinical trials, examples of which are discussed above, it would be desirable to design and implement a study in which an induced increase in HDL-C levels is the predominant lipoprotein change, before we can conclude with certainty that raised concentrations of HDL-C increase the risk of coronary heart disease.

Goldbourt et al. (1993) reports on the design of such a trial that he is currently running, in an attempt to establish whether the modification of HDL-C (and triglycerides) affects coronary heart disease incidence. He is making use of Bezafibrate, a fibric acid derivative that predominantly reduces the serum triglycerides and increases the HDL-C. The trial will be completed in 1998.

Grundy et al. (1989) is of the opinion that the available evidence suggesting that raised HDL-C levels contribute to a reduction of coronary heart disease risk is insufficient to recommend drug therapy for the express purpose of raising HDL-C levels in patients without high LDL-C levels

or other significant coronary risk factors. He states that the primary aim of therapy should be to reduce high risk levels of LDL-C, a guideline supported by the NCEP (1988), but that if this is accompanied by a rise in HDL-C levels so much the better.

Rossouw et al. (1985) and the Council on Scientific Affairs (1983) state that because plasma total cholesterol levels (of which LDL-C is the main subfraction) are directly proportional to, and HDL-C levels are inversely related to the incidence of coronary heart disease, it follows that the ratio of HDLC/TC or LDL-C is also inversely related to the risk of coronary heart disease and provides a good summary of lipid related risk. Since LDL-C transports cholesterol to the tissues and HDL-C is involved in the reverse pathway, they are of the opinion that the HDL-C/LDL-C ratio should theoretically have greater predictive power.

Due to the above considerations, therefore, for the purpose of this trial, although participants will be selected on the basis of a raised LDL-C level, the HDL-C/LDL-C ratio will be used to determine the effect of the medication on both lipoproteins and to monitor any treatment benefit.

2.3. Effect of dietary changes on cholesterol levels

Rossouw (1983) states in a review article on diet and heart disease, that the idea that food influences serum cholesterol levels and ultimately the incidence of coronary heart disease, received its major impetus from research conducted by Keys in the 1960's. He is of the opinion that the findings of Keys's international comparisons of fat intake, serum cholesterol levels and coronary heart disease, have precipitated a vast research effort and contradictory literature on this topic. Rossouw explains that Keys developed formulae predicting the effect of various dietary fat modifications on serum cholesterol levels. From these formulae he calculates that a decrease in total fat intake from 40% to 20% of energy intake, and an increase in the dietary polyunsaturated to saturated fat ratio from 0.4 to 1.0, will effectively lower the serum cholesterol level by 0.3- 0.5mmol/l with a major part of the benefit being obtained from the reduction in saturated fat intake. (Rossouw 1983.)

Numerous trials, including those carried out by Mensink and Katan (1989) and Grundy et al. (1986) which investigate the effect of substituting certain foodstuffs in an attempt to reduce cholesterol levels have been undertaken, but fail to produce consistent results.

The Consensus Development Conference (1985) concluded that there is no doubt that appropriate changes in diet will reduce blood cholesterol levels, and afford significant protection against coronary heart disease. Certain clinical trials have results that are concordant with this view, but there are also many that show this to be questionable.

For example, in the Oslo study (Hjermann et al. 1981) 1232 hypercholesterolaemic participants aged 40- 49 were treated with a cholesterol lowering diet and counselled to reduce their cigarette smoking. Mean serum cholesterol concentrations were approximately 13% lower in the intervention group than the control group during the five year trial. It was also concluded that 90% of the intervention group reduced their cholesterol levels, with the ratio of HDL-C/LDL-C being 66% higher four years after intervention in a subgroup of good diet responders. Along with the reduction in cholesterol levels there was an observed 47% lower incidence of coronary heart disease at the end of the five year treatment period, which was attributed to the dietary related reduction in TC, and to a lesser degree to smoking cessation.

In two reports, one by the Council on Scientific Affairs (1983) and the other by Rossouw (1983) it is stated that in carefully controlled metabolic ward situations, dietary change will result in a 30% or a 15% serum cholesterol reduction respectively. In the more generally applicable

free living subjects (as in the present research trial) the Council on Scientific Affairs (1983) states that the decrease is considerably less, since man's cholesterol levels are less sensitive to dietary fat and cholesterol manipulations than other species.

A further clinical trial, the Multiple Risk Factor Intervention Trial, (1982) was a randomised primary prevention trial designed to test the effect of a multi-factor intervention programme on mortality from coronary heart disease in 12866 high risk men aged between 35 and 57 years. The participants were randomly assigned either to a special intervention programme consisting of treatment for hypertension, counselling for cigarette smoking, and dietary advice for lowering blood cholesterol levels, or to a second group who were offered no intervention programme. Over an average follow-up period of seven years, risk factor levels declined in both groups but the observed 7.1% difference in coronary heart disease risk was statistically non-significant. Associated with this risk there was too small an overall difference of 2% between the cholesterol levels of the two groups to infer any benefit of the intervention methods.

The LRC-CPPT 1 (1984) previously discussed, was not designed to assess directly whether cholesterol lowering by diet prevents coronary heart disease. It states however that its findings, taken in conjunction with the large body

of evidence relating diet, plasma cholesterol levels and coronary heart disease, support the view that cholesterol lowering by diet would also be beneficial.

Kronmal (1985) commented on this conclusion of the above trial and states that it goes beyond what is reasonably justified on the basis of the actual results. He states that the placebo diet group experienced a 4.9% and a 7.7% reduction in TC and LDL-C levels respectively and that the effect on coronary heart disease was estimated even though the changes observed were relatively small. Kronmal concludes that this effect does not reach statistical significance.

The effects of dietary change on serum lipids is influenced not only by the composition of the diet but also by individual responsiveness, the type and genetic basis of the lipoprotein abnormality and compliance and palatability (Grundy et al. 1986; Hjermann et al. 1981). While some individuals may therefore respond favourably to dietary intervention, others will not.

The discordant nature of the above literature illustrates the need for further investigation into the diet-cholesterol issue and its potential benefits.

Because of the varied and unpredictable response of individual cholesterol levels to dietary change, all

participants in the present study were requested not to make any change in their dietary and lifestyle habits for the duration of the trial. The design of the study also includes a placebo group, and it is estimated that although participants in both groups may alter their dietary and lifestyle habits slightly these changes will be reflected in the placebo group, so that it will be possible to conclude what effect the medicine alone has had on the cholesterol levels.

2.4. Treatment of hypercholesterolaemia

2.4.1. Allopathic / Drug treatment

It is the view of the expert panel of the NCEP (1988) that patients whose LDL-C levels remain high despite a six month period of intensive dietary therapy (or three months if the level is above 5.82mmol/l) should be considered for drug treatment. The LDL-C levels that are considered to be high, and at which drug therapy should be considered are as follows:

>4.91mmol/l in patients without definite coronary heart disease or with two major coronary heart disease risk factors.

>4.14mmol/l in patients with definite coronary heart disease or two other coronary heart disease risk factors.

The above panel stressed that maximal efforts should be made in all patients to lower cholesterol levels and coronary heart disease risk by non-pharmacological means which includes lifestyle modifications such as diet, weight control, exercise and reduction of smoking.

The reason for the apparent reluctance in making the decision to treat with drug therapy is that it usually commits the patients to long-term therapy, for years or even for life, (NCEP 1988; Council on Scientific Affairs 1983) especially if risk factor reduction is to be maintained.

There is a wide variety of drugs available including the following categories, the effectiveness and side effects of each having been documented in many clinical trials as referenced below.

a) bile acid sequestrants eg cholestyramine (Council on Scientific Affairs 1983; LRC-CPPT 1 1984; Schectman 1993)

b) nicotinic acid (Canner, 1986)

c) HMG Co A reductase inhibitors eg lovastatin (Bradford et al. 1993; Ferder et al. 1993; Schectman et al. 1993)

d) fibric acid derivatives eg gemfibrozil (Frick et al. 1987; Manninen et al. 1988; Miller et al. 1993)

The choice of treatment depends on the nature of the lipid disorder and the likelihood of side effects in the particular patient. Side effects of hypolipidaemic drugs include nausea, indigestion, bloating, heartburn, constipation, alteration of hepatic and renal functioning, interference with absorption of other drugs, alopecia, impotence and cutaneous flushing which tend to preclude long term use.

From research evaluated it is evident that long term safety information for many of the hypolipidaemic drugs, especially the newer brands, is limited or not available, and their effects on the incidence of coronary artery disease not yet established.

A second consideration that precludes long term use of these drugs is the cost in terms of the medication as well as laboratory monitoring for response and side effects (Grundy 1986).

It was agreed by the Consensus Development Conference (1985) that further research should be encouraged to develop more effective, better tolerated, safer and more economical drugs (or other modes of treatment) for lowering blood cholesterol levels, which is therefore the subject of the present trial.

2.4.2. Homoeopathic treatment

Homoeopathic treatment is based on the principle "let likes be cured by likes" i.e. the same substance that causes a disease can cure it. This law formulates the parallel action between the toxicological power of a given substance and its therapeutic action. By extreme dilution and potentisation the curative properties of the medicines are enhanced and all poisonous side effects lost. Therefore homoeopathic treatment consists of giving the patient in weak doses the substance which, if given to a healthy individual, would cause symptoms similar to the patient's own pathological symptoms (Jouanny 1991). Because of the law of similars, almost any substance that has an effect on the human body can therefore be used in homoeopathy. Cholesterol, in excess, causes hypercholesterolaemia, and it follows from the above reasoning that cholesterol, given in homoeopathic potency to a patient suffering from this condition, would result in a cure.

Homoeopathic treatment of specific conditions has, however, been poorly substantiated to date, and it is therefore the purpose of the present research trial to investigate the effect of Cholesterinum 9CH (made from cholesterol, (5-cholesten-3B-ol) in the ninth attenuation) on hypercholesterolaemia, as suggested by Reckeweg (1983).

CHAPTER THREE

MATERIALS AND METHODS

3.1. Classification of participants

3.1.1. Initial classification based on total cholesterol levels:

Advertisements requesting participation in a clinical trial involving homoeopathic treatment of hypercholesterolaemia were placed in the internal mail system at Technikon Natal, Durban, as well as in the Natal Mercury newspaper.

Respondents were accepted providing they did not fall into one of the following categories:

- i) pregnant women (Cooper et al. 1992)
- ii) individuals who have undergone surgery (Cooper et al. 1992) or suffered a myocardial infarction in the past three months (NCEP 1988)
- iii) individuals on allopathic cholesterol reducing medication.

Participants were screened for an elevated TC level using as reference a graph of age-specific action limits for TC recommended by the Heart Foundation of Southern Africa (Rossouw et al. 1988). These action limits were derived

from reference values obtained in the coronary risk factor study baseline survey (Rossouw et al. 1985).

Cooper et al. (1988) discovered that there is a negligible difference between non- fasting and fasting TC levels, therefore when screening for hypercholesterolaemia was carried out in this study the participants were advised that fasting was not necessary. Screening was carried out by the researcher using the Reflotron dry chemistry analyzer, which uses a 30 micro liter capillary blood sample obtained by skin puncture. Sedor et al. (1988) evaluated the use of the Reflotron as a population screening device for cholesterol and concluded that it is reliable and suitable for this purpose. In order to ensure that the blood sample collection and analysis was carried out correctly, specific guidelines as outlined by Broughton et al. (1989) were adhered to.

3.1.2. Subsequent classification based on low-density lipoprotein cholesterol levels:

Those of the respondents with TC levels that placed them in the moderate or high risk category for coronary heart disease (Rossouw et al. 1988) were contacted.

An assessment of other non lipid risk factors, including hypertension and smoking, was made. Any allopathic medication that was being taken by respondents was

recorded. Studies have shown that it is difficult to determine the effect that drugs have on lipid measurements (Henkin et al. 1992) so people that were not on any allopathic medication were given preference as far as possible.

Those people that had TC levels in the high risk category plus hypertension and or smoking (which potentiates the risk of coronary heart disease) were not selected to participate in the trial and were referred to a medical doctor for further advice and treatment. It was decided that treating these people with a medicine that has not been demonstrated as effective as yet, or with a placebo would be unethical and dangerous. The selected participants each had a blood sample taken by a registered nurse at Technikon Natal.

The following conditions were adhered to in order to reduce pre- analytical variation of results:

- i) participants were asked to fast for an overnight period of twelve hours, since the LDL-C levels are estimated from measurements of other lipids including triglycerides and HDL-C that alter post prandially (Cooper et al. 1988; NCEP 1988)
- ii) venipuncture was carried out on participants who had been in a sitting position for at least five minutes,

to prevent the effect of posture or stasis on the cholesterol determination (Bachorik et al. 1982; Berger et al. 1988; NCEP 1988; Cooper et al. 1992)

iii) serum blood samples were obtained in a venoject tube, that was free of anticoagulant, since anticoagulants have been shown to dramatically affect the sample (Bachorik et al. 1982)

iv) application of a tourniquet was for as brief a period as possible (not longer than two minutes) (Bachorik et al. 1982; NCEP 1988)

A lipoprotein profile (lipogram) which includes analysis of triglycerides, HDL-C and TC levels was carried out on each blood sample by a commercial laboratory. Calculation of the LDL-C levels was according to the Friedewald formula (Friedewald et al. 1972).

Thirty two of those participants with an elevated LDL-C according to age- specific action limits as outlined by Rossouw et al. (1988) were identified and used further in the clinical trial.

Sixteen of the participants were given Cholesterinum 9CH twice a day for a period of three months and served as the experimental group, and the other sixteen served as a control group and received a placebo. The study was carried

out in a double blind manner, i.e. medicine was dispensed by an independent party, so that neither the researcher nor the participants knew in which group they had been placed.

Fasting blood samples were taken once every four weeks for a period of twelve weeks from date of commencement of treatment. Use was only made of one commercial laboratory to ensure uniformity of apparatus and analysis techniques. In addition to this, for two of the four battery of lipogram tests, one duplicate blood sample was sent in to the laboratory under a different name, to act as a control and ensure validity of the results. The above precautions were taken to reduce variation in the analytical stage of cholesterol determination, because as reported by Berger et al. (1988) there has recently been dissatisfaction at the levels of imprecision reported in laboratories carrying out routine tests using mainly enzymatic methods of cholesterol assay.

Participants were requested not to change their lifestyle (eg exercise, smoking) and eating habits during the trial in order to minimise sources of variation in serum lipids (Cooper et al. 1992).

CHAPTER FOUR

RESULTS

4.1. RESULTS OF THE PAIRED T-TEST

Table 1: Mean change and standard deviation (SD) after three months of treatment in the total cholesterol (TC) and ratio of treated and placebo groups.

	TC			RATIO		
	d	SD	95%CI	d	SD	95%CI
Treated	0.377	0.438	0.143 , 0.611	-0.003	0.055	-0.032 , 0.027
Placebo	0.118	0.518	-0.158 , 0.394	-0.020	0.010	-0.073 , 0.033

d= mean difference between initial reading and third reading after three month treatment period

CI= confidence interval

ratio=HDL/C/LDL (ie high density lipoprotein cholesterol/ low density lipoprotein cholesterol)

When comparing the initial TC reading of the placebo group with the third reading after three months of treatment no statistical difference was demonstrated. On the other hand a statistical difference ($p=0.004$) was noted between the initial and third TC readings of the treated group. No statistical difference was found between the initial and third ratios of treated or placebo groups.

4.2. RESULTS OF THE UNPAIRED T – TESTS

Table 2: Mean (x) and standard deviation (SD) of the initial readings of treated and placebo groups, before treatment commenced.

	TC			RATIO		
	x	SD	95%CI	x	SD	95%CI
Treated	6.654	0.828	0.289 , 1.432	0.298	0.087	-0.119 , 0.011
Placebo	5.793	0.752	0.289 , 1.432	0.352	0.092	-0.119 , 0.011

Comparison of the initial TC readings of both groups indicated that a statistical difference ($p=0.004$) occurred at this stage. No statistical difference existed between the initial ratios of both groups.

Table 3: Mean (x) and standard deviation (SD) of the first readings of treated and placebo groups, after one month of treatment.

	TC			RATIO		
	x	SD	95%CI	x	SD	95%CI
Treated	6.717	1.127	0.110 , 1.617	0.312	0.099	-0.147 , 0.015
Placebo	5.853	0.952	0.110 , 1.617	0.377	0.124	-0.147 , 0.015

When comparing the first TC readings of placebo and treated groups after one month of treatment, a statistical difference ($p=0.026$) again demonstrated. No statistical difference existed between the first ratios of both groups.

Table 4: Mean (x) and standard deviation (SD) of the second readings of treated and placebo groups, after two months of treatment.

	TC			RATIO		
	x	SD	95%CI	x	SD	95%CI
Treated	6.488	1.015	-0.266 , 1.219	0.327	0.103	-0.143 , 0.023
Placebo	6.011	1.040	-0.266 , 1.219	0.387	0.126	-0.143 , 0.023

No statistical difference was found between the second TC readings or ratios of the treated and placebo groups.

Table 5: Mean (x) and standard deviation (SD) of the third readings of treated and placebo groups, after three months of treatment.

	TC			RATIO		
	x	SD	95%CI	x	SD	95%CI
Treated	6.278	0.990	-0.045 , 1.249	0.301	0.071	-0.158 , 0.014
Placebo	5.675	0.792	-0.045 , 1.249	0.373	0.152	-0.158 , 0.014

No statistical difference was found between the third TC readings or ratios of the treated and placebo groups.

4.3. FREQUENCY TABLE

Table 6: Frequency table depicting changes in the TC levels for both the treated and placebo groups over the three month treatment period.

Group	TC LEVELS			Total
	Incr	Decr	No change	
Treated	3	0	13	16
Placebo	5	0	11	16

Incr = increased

Decr = decreased

4.4. GRAPHICAL REPRESENTATION

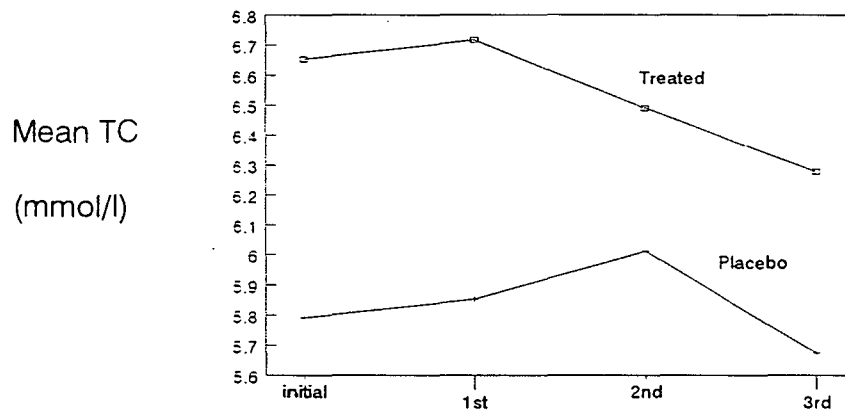


Figure 1: Mean TC readings of treated and placebo groups taken before treatment began, then once a month for three months.

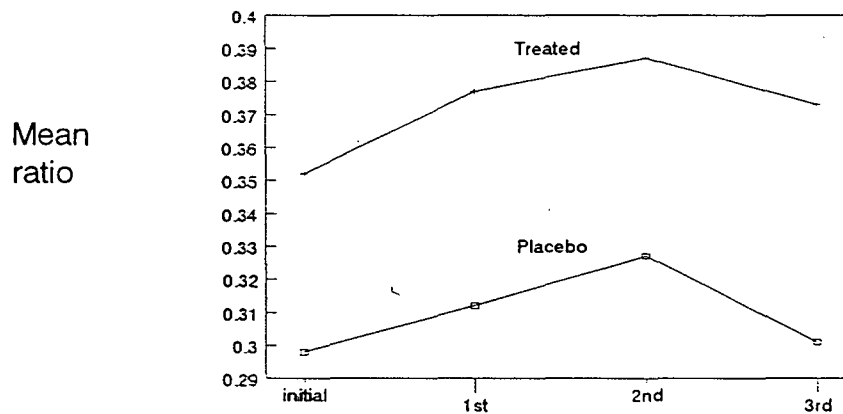


Figure 2: Mean ratio (HDL-C/LDL-C) of treated and placebo groups calculated before treatment began, then once a month for three months.

CHAPTER FIVEDISCUSSION AND RECOMMENDATIONS

The results of the paired T-test in Table 1 indicate that a significant decrease ($p=0.004$) occurred in the average TC reading of the sixteen participants in the treatment group after three months of treatment with Cholesterinum 9CH. The initial average TC reading of 6.654mmol/l compared to the final reading of 6.278mmol/l (Figure 1) represents a 5.7% reduction in the mean TC levels of these participants. (These percentage changes were computed for each participant and then averaged.)

The placebo group showed no significant change in its average TC level after the three month treatment period. (Table 1) Although a 0.118mmol/l decrease was noted between the initial and final readings of this group the change was a non-significant one, and represents a 2% reduction in the average TC levels of these participants.

In addition to the paired T-tests, the frequency table 6 further indicates the proportion of participants in both groups that experienced a favourable change in their TC level. It can be calculated from these results that 81.25% of the treatment group experienced an improvement in their TC compared to 68.75% of the placebo group. On the other hand 31.25% of the placebo group were found to experience

an increase in their TC as opposed to 18.75% of the treatment group.

The HDL-C/LDL-C ratio of both groups were compared before and after the treatment period and although an increase occurred in both groups it was too small to be considered significant. (Table 1 and Figure 2) The TC reading of an individual is largely an indication of the triglycerides, LDL-C and the HDL-C, with the concentration of the former two cholesterols being proportional to coronary heart disease risk and the concentration of the latter inversely proportional to coronary heart disease risk. It is therefore important to establish whether the reduction in TC level was as a result of a reduction in the LDL-C or HDL-C concentration. The effect of treatment on the ratio enabled us to conclude that the average LDL-C of the treated group decreased and the average HDL-C of the same group increased but neither sufficiently to be significant. It is therefore suggested that in further studies one should investigate the effect of treatment on each lipoprotein level individually, and in addition to this, investigate changes in the triglyceride levels, to determine the role that they play in the alteration in TC levels.

The unpaired T-tests compared the difference between the average TC readings of both groups at each successive reading. The initial average TC readings of treatment and

placebo groups were compared before the onset of treatment and a significant difference ($p=0.004$) existed between the two. (Table 2) The choice of participants who were to be part of the control or experimental groups was carried out on a strictly random basis so it is concluded that the higher TC average of the treated group was coincidental. It is possible, however, that this had an effect on the favourable results of the treated group. Participants were made aware of their initial TC values but not the subsequent readings until the trial was completed to prevent the knowledge of an improved or increased level affecting the outcome of treatment. It is argued that those participants with more severely elevated cholesterol levels, the majority of whom were in the experimental group, may have become concerned and endeavoured to change their lifestyle and eating habits despite having been requested not to. The participants were asked if they had made any changes in their habits and most replied that they had not. Those that had made changes admitted that the changes were not adhered to for more than a week. Figure 2 indicates that the average TC of the treated group in fact increased after one month of treatment so that the difference between the average TC readings of both groups remained significant. ($p=0.026$) (Table 3) It is therefore concluded that any changes that were made by the treated group as a result of the knowledge of their increased initial TC levels were not sufficient to affect the outcome of treatment.

After the second and third months, however, the significance levels had decreased to $p=0.199$ and 0.067 . (Table 4 and 5) indicating that some change took place in one or both groups. From the graph in figure 1 it is clear that this change occurred largely in the treatment group. During the second month of treatment the average TC reading of the treatment group improved by 0.229mmol/l , and the placebo by 0.158mmol/l which resulted in there no longer being a statistically significant difference between the two groups. In the third month of treatment both groups experienced slight reductions in TC levels resulting in the non-significant difference being maintained between both groups.

The difference between the mean TC readings of treated and placebo groups was calculated to be 12.9% before treatment began. This difference was maintained after the first month, but decreased to 9.6% by the end of the trial. As no significant difference was found between the initial and final TC readings of the placebo group we can assume that this 3.3% decrease of the difference between both groups after the three month trial indicates a 3.3% improvement in the average total cholesterol levels of the treatment group.

This improvement does not seem to compare favourably with results of the trials discussed in the literature review. It is difficult, however, to make comparisons between the

present research trial and other cholesterol lowering drug trials since the latter were carried out over a long period of time and on an extremely large scale. This increases validity of the results and the ability to extrapolate such results to the general population. For example the LRC-CPPT (1984) had a sample size of 3806 and a follow up period of 7-10 years, while the Helsinki Heart Study (Frick et al. 1987) ran over a five year period and made use of 4081 participants. A mean cholesterol reduction of 13.4% was recorded in the former trial and 10% in the latter.

Due to budget limitations in the present research trial, use was made of a sample size of thirty two and a follow up period of three months. In addition to this convenience sampling was carried out as opposed to random sampling, which further decreases the possibility of extrapolating the results to the general population.

The expert panel of the NCEP (1988) states that it is extremely important that more than one cholesterol measurement be obtained at the onset of treatment and an average calculated in order to assess the patient's cholesterol status accurately. The reason given for this is that cholesterol levels can fluctuate considerably from day to day in a given individual. This was not done in the present trial and is a suggestion for further research, as this will reduce the criticism that any recorded change occurred as a result of the diurnal variation in

cholesterol levels.

Although a statistically significant change occurred in average TC readings of the treatment group of the present research trial, this does not necessarily mean that the change was of clinical significance. The initial average TC (6.654mmol/l) of the experimental group indicated that the participants were at an increased risk of coronary heart disease, and after the treatment period the average (6.717mmol/l) remained in the moderate risk category. It is the opinion of the researcher that an average reduction of 0.377mmol/l in the TC of any group of patients, as occurred in the treatment group, particularly if it is not sufficient to change the coronary heart disease risk status of the group, does not represent a clinically significant reduction that could warrant recommending Cholesterinum 9CH as the homoeopathic treatment of choice for hypercholesterolaemia.

Further confounders that could have affected the results of treatment are as follows. Specific rules for taking the prescribed homoeopathic medication were outlined to the patient, and it was assumed that these were adhered to. It is possible, however, that the participants were unfamiliar with taking homoeopathic medicines, particularly twice a day for a three month period. A suggestion for further research would be to dispense the medicine in the form of tablets as opposed to pillules

and to monitor the taking of the medicine by requesting that the participants return the bottle of tablets at the end of each month so that they can be counted before the next months supply is dispensed. This was carried out in the LRC-CPPT 1 (1984).

In addition to this, the sensitivity of homoeopathic medicines to situations that antidote them (eg sunlight, camphor, toothpaste, taking of medicines with food etc) could have caused the medication in the treatment group to be less effective than if such conditions were strictly adhered to.

This research trial attempted to investigate the possibility of treating a specific condition with one specific medicine. This is not strictly in accordance with the principles of homoeopathy. Homoeopathy is based on the principle "let likes be cured by likes" which was previously discussed, but the concept of the Simillimum is an important aspect of homoeopathic prescribing that has not been dealt with in this trial. In short, this a method of prescribing a homoeopathic medication whose symptom picture (outlined in a Materia Medica) is as similar as possible to those symptoms that the patient is presenting with (Vithoulkas,1986). In this way the patient is treated on a holistic basis instead of one specific medication being prescribed for a specific condition.

It is suggested that further research trials be carried out on the treatment of hypercholesterolaemia using either the indicated Simillimum or a combination of Cholesterinum and the Simillimum, which according to Vithoulikas (1986) should be more effective.

CHAPTER SIXREFERENCES

Bachorik, P.S., Alberts, J.J., Ellefson, R.D. et al. 1982. Collection of blood samples for lipoprotein analysis. Clin Chem. 28:1375-8.

Berger, G.M.B., Christopher, K., Juritz, J.M., Liesegang, F. 1988. Accuracy and reproducibility of cholesterol assay in the western Cape. SAMJ. 74:490-5.

Bradford, R.H., Downton, M., Chremos, A.N. et al. 1993. Efficacy and tolerability of Lovastatin in 3390 women with moderate hypercholesterolaemia. Annals of Intern Med. 118:850-55.

Broughton, P.M.G., Bullock, D.G., Cramb, R. 1989. Quality of plasma cholesterol measurements in primary care. BMJ. 298:297-8.

Buhler, F.R., Tkachuk, V.A., Hahn, A.W.A., Resink, T.J. 1991. Low- and high-density lipoproteins as hormonal regulators of platelet, vascular endothelial and smooth muscle cell interactions: relevance to hypertension. Journal of Hypertension. 9(suppl 6):S28-S36.

Canner, P.L., Berge, K.G., Wenger, N.K., Stamler, J., Friedman, L., Prineas, R., Friedewald, W. 1986. Fifteen year mortality in Coronary Drug Project patients. J Am Coll Cardiol. 8:1245-1255.

Castelli, W.P. 1984. Epidemiology of coronary heart disease: The Framingham Study. Am J of Med. 4-12.

Consensus Development Conference. 1985. Lowering blood cholesterol to prevent heart disease. JAMA. 253:2080-86.

Cooper, G.R., Myers, G.L., Smith, S.J., Sampson, B.J. 1988. Standardisation of lipid, lipoprotein and apo-lipoprotein measurements. Clin Chem. 34:95-105.

Cooper, M.R., Myers, G.L., Smith, S.J., Schlant, R.C. 1992. Blood lipid measurements. JAMA. 267:1652-9.

Council on Scientific Affairs. 1983. Dietary and pharmacologic therapy for the lipid risk factors. JAMA. 250:1873-79.

Ferder, L.D., Bertolami, M.C., Gionnini, S.D. et al. 1993. A multicenter comparative trial of Lovastatin and Pravastatin in the treatment of hypercholesterolaemia. Am J of Cardiol. 71:810-5.

Frick, M.H., Elo, O., Happa, K. et al. 1987. Primary-prevention trial with gemfibrozil in middle aged men with dyslipidemia: The Helsinki Heart Study. NEJM. 317:1237-44.

Friedewald, W.T., Levy, R.I., Fredrickson, D.S. 1972. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem. 18:499-502.

Goldbourt, U., Behar, S., Reicher-Reiss, H. et al. 1993. Rationale and design of a secondary prevention trial of increasing serum high-density lipoprotein cholesterol and reducing triglycerides in patients with clinically manifest atherosclerotic heart disease. Am J of Cardiol. 71:909-15.

Grover, S.A., Abrahamowicz, M., Joseph, L., Brewer, C., Coupal, L., Suissa, S. 1992. The benefits of treating hyperlipidemia to prevent coronary heart disease. JAMA. 267:816-22.

Grundy, S.M. 1986. Cholesterol and coronary heart disease. JAMA. 256:2849-58.

Grundy, S.M., Greenland, P., Herd, A. et al. 1987. Cardiovascular risk factor evaluation in healthy American adults. Circulation. 75:1340-61.

Grundy, S.M., Goodman, D.S., Rifkind B.M., Cleeman, J.I. 1989. The place of HDL in cholesterol management. Arch of Intern Med. 149:505-9.

Henkin, Y., Como, J.A., Oberman, A. 1992. Secondary dyslipidaemia: inadvertant effects of drugs in clinical practice. JAMA. 267:961-7.

Hjermann, I., Holme, I., Byre, K.V., Loren, P. 1981. Effect of diet and smoking intervention on the incidence of coronary heart disease. Lancet. 1303-10.

Jouanny, J. 1991. The essentials of homoeopathic therapeutics. France: Editions Boiron.

Kronmal, R.A. 1985. Commentary on the published results of the Lipid Research Clinics Coronary Primary Prvention Trial. JAMA. 253:2091-3.

Levy, R.I. 1983. The influence of cholestyramine- induced lipid changes on coronary artery disease progression: The NHLBI Type Two Coronary Intervention Study. Circulation. 68(suppl 3):188.

Lipid Research Clinics Program: The Lipid Reasearch Clinics Coronary Primary Prevention Trial results:1. 1984. Reduction in the incidence of coronary heart disease. JAMA. 257:351-64.

Lipid Research Clinics Program: The Lipid Research Clinics Coronary Primary Prevention Trial results:2. 1984. The relationship of reduction in incidence of coronary heart disease to cholesterol lowering. JAMA. 251:365-74.

The Lovastatin Pravastatin Study Group: A Multicenter Comparative Trial of Lovastatin and Pravastatin in the treatment of Hypercholesterolemia. 1993. Am J of Cardiol. 71:810-15.

Manninen, V., Elo, M.O., Frick, H. 1988. Lipid alterations and decline in the incidence of heart disease in the Helsinki Heart Study. JAMA. 260:641-51.

Miller, M., Bachorik, P.S., Mc Crindle, B.W., Kwiterovich, P.O. 1993. Effect of gemfibrozil in men with primary isolated low-density lipoprotein cholesterol. Am J of Med. 94:7-12.

Mensink, R.P., Katan, M.B. 1989. Effect of a diet enriched with monounsaturated or polyunsaturated fatty acids on levels of low-density and high-density lipoprotein cholesterol in healthy women and men. NEJM. 436-41.

Multiple Risk Factor Intervention Trial Research Group: Multiple Risk Factor Intervention Trial. 1982. Risk factor changes and mortality results. JAMA. 248:1465-77.

Reckeweg, H.H. 1983. Materia Medica. Baden-Baden: Aurelia-Verlag.

Report of the National Cholesterol Education Program Expert Panel on detection, evaluation and treatment of high blood cholesterol in adults. 1988. Arch of Intern Med. 148:36-69.

Rossouw, J.E. 1983. Diet and heart disease in the 1980's. SAMJ. 64:437-41.

Rossouw, J.E., Jooste, P.L., Steyn, K., Benade, A.J.S. 1985. Serum total and high-density lipoprotein cholesterol-reference values obtained in the Coronary Risk Factor Study baseline survey. SAMJ. 67:533-8.

Rossouw, J.E., Steyn, K., Berger, G.M.B. et al. 1988. Action limits for serum total cholesterol. SAMJ. 73:693-700.

Schectman, G., Hiatt, J., Hartz, A. 1993. Evaluation of the effectiveness of lipid lowering therapy (Bile Acid sequestrants, Niacin, Psyllium and Lovastatin) for treating hypercholesterolaemia in veterans. Am J of Cardiol. 71:759-65.

Sedor, F.A., Holleman, C.M., Heyden, S., Schneider, K.A. 1988. Reflotron cholesterol measurements evaluated as a screening technique. Clin Chem. 34:2542-4.

Smith, G.D., Shipley, M.J., Marmot, M.G., Rose, G. 1992. Plasma cholesterol concentration and mortality: The Whitehall Study. JAMA. 267:70-5.

Steyn, K., Fourie, J., Van Vuuren, I., Marais, A.S., Opthof, J. 1988. Hypercholesterolaemia in a group of senior South African transport service employees. SAMJ. 73:701-3.

Vithoulkas, G. 1986. The science of Homoeopathy. London: Thorsons.

Wyndham, C.H., Seftel, H.C., Pilcher, G.J., Baker, S.G. 1987. Prevalence of hypercholesterolaemia in young Afrikaners with myocardial infarction: Ischaemic heart disease risk factors. SAMJ. 71:139-44.

APPENDIX A

RESULTS OF THE PLACEBO GROUP

NO	INITIAL READING			1ST READING			2ND READING			3RD READING						
	TC	LDL	HDL	R	TC	LDL	HDL	R	TC	LDL	HDL	R				
1	5.51	3.40	1.46	0.43	5.59	3.65	1.34	0.37	6.18	4.00	1.71	0.43	4.89	2.84	1.26	0.44
2	6.29	3.58	1.11	0.31	6.68	4.72	1.20	0.25	7.18	4.48	1.09	0.24	6.27	3.71	1.13	0.30
3	5.91	3.64	1.78	0.49	6.20	3.52	1.84	0.52	6.38	3.80	1.62	0.43	6.32	3.25	1.27	0.39
4	5.29	3.10	1.37	0.44	5.05	2.97	1.54	0.52	5.73	3.49	1.90	0.54	4.71	2.45	1.68	0.69
5	5.86	3.76	1.77	0.47	6.06	3.78	1.94	0.51	5.95	3.41	2.20	0.65	5.36	3.42	1.69	0.49
6	6.40	4.64	1.28	0.28	7.13	5.21	1.48	0.28	7.21	5.06	1.55	0.31	6.35	4.30	1.47	0.34
7	5.66	4.15	1.02	0.25	6.88	5.31	1.08	0.20	6.00	4.31	1.26	0.29	6.59	4.90	1.00	0.20
8	5.37	3.66	0.97	0.27	5.70	3.94	1.13	0.29	5.94	3.98	1.10	0.28	5.20	3.44	1.00	0.29
9	5.81	3.69	1.76	0.48	5.90	3.39	2.20	0.65	7.13	4.23	2.48	0.59	5.58	3.02	2.21	0.73
10	7.60	5.72	1.11	0.19	6.46	3.93	1.01	0.26	7.20	5.28	1.19	0.23	6.51	4.30	1.10	0.26
11	6.23	4.01	1.30	0.32	5.86	3.31	1.04	0.31	5.64	3.44	1.12	0.33	6.71	4.36	1.19	0.27
12	5.38	3.90	1.14	0.29	5.89	3.87	1.13	0.29	5.11	3.63	0.97	0.27	5.89	3.70	0.94	0.25
13	6.67	4.49	1.84	0.41	7.00	4.89	1.79	0.37	7.24	5.16	1.79	0.35	6.08	4.20	1.64	0.39
14	5.50	3.99	1.34	0.34	5.40	3.79	1.45	0.38	4.91	3.19	1.53	0.48	5.62	4.23	1.14	0.27
15	4.68	3.21	1.24	0.39	3.99	2.53	1.20	0.47	4.51	2.90	1.20	0.41	4.44	2.90	1.08	0.37
16	4.53	3.06	0.89	0.29	3.86	2.67	0.94	0.35	3.87	2.56	0.97	0.38	4.28	3.13	0.82	0.26

NO= patient number

R= ratio of high-density lipoprotein cholesterol/low-density lipoprotein cholesterol

TC= total cholesterol

LDL= low-density lipoprotein cholesterol

HDL= high-density lipoprotein cholesterol

INITIAL READING= before commencement of treatment

1ST READING= after one month of treatment

2ND READING= after two months of treatment

3RD READING= after three months of treatment

UNIT OF ALL READINGS IS MMOL/L

APPENDIX B

RESULTS OF THE TREATMENT GROUP

NO	INITIAL READING			1ST READING			2ND READING			3RD READING						
	TC	LDL	HDL	R	TC	LDL	HDL	R	TC	LDL	HDL	R				
1	8.15	6.70	0.64	0.10	8.64	7.48	0.63	0.08	9.33	7.84	0.71	0.09	7.97	6.79	0.68	0.10
2	6.64	4.84	1.20	0.25	6.72	4.92	1.07	0.22	6.56	4.69	1.10	0.23	5.93	4.26	0.97	0.23
3	4.92	2.93	1.15	0.39	5.97	3.68	1.70	0.46	5.48	3.86	1.30	0.34	4.32	2.71	1.03	0.38
4	6.40	4.51	1.54	0.34	6.19	4.53	1.46	0.32	5.96	3.76	1.85	0.49	5.46	3.49	1.47	0.42
5	6.49	4.76	1.41	0.30	6.09	4.07	1.27	0.31	5.91	3.59	1.48	0.41	6.01	3.98	1.27	0.32
6	6.19	3.86	1.39	0.36	5.95	3.99	1.36	0.34	6.25	4.00	1.45	0.36	5.79	3.57	1.30	0.36
7	6.46	4.69	1.32	0.28	6.26	4.38	1.36	0.31	7.13	4.96	1.63	0.33	6.83	4.95	1.48	0.30
8	7.82	5.36	2.12	0.40	7.46	4.81	2.38	0.49	7.11	4.51	2.23	0.49	7.01	5.26	1.56	0.30
9	6.61	4.39	1.23	0.28	7.78	5.18	1.27	0.25	5.49	3.57	1.10	0.31	6.09	3.72	1.06	0.28
10	8.03	6.13	1.27	0.21	9.50	7.19	1.60	0.22	6.85	4.90	1.36	0.28	7.89	5.52	1.48	0.27
11	7.25	5.69	1.16	0.20	6.52	4.85	1.27	0.26	7.72	6.06	1.28	0.21	7.41	5.90	1.78	0.30
12	6.35	4.14	1.74	0.42	7.23	4.93	1.93	0.39	6.40	4.25	1.79	0.42	6.83	4.87	1.72	0.35
13	6.25	4.13	1.67	0.40	6.07	4.12	1.48	0.36	6.45	4.44	1.53	0.34	6.15	4.35	1.43	0.33
14	5.78	4.50	1.11	0.25	5.82	4.38	1.20	0.27	5.23	3.75	1.13	0.30	5.23	3.75	1.13	0.30
15	6.40	4.32	1.35	0.31	5.73	3.77	1.16	0.31	6.20	4.35	1.17	0.27	5.46	3.93	1.06	0.27
16	6.72	4.91	1.40	0.29	5.54	3.59	1.35	0.38	5.73	3.76	1.28	0.34	6.05	4.27	1.27	0.30