BODY FAT MASS REDUCTION FROM SUPPLEMENTATION WITH MARINE OMEGA-3 AND L-CARNITINE VERSUS MARINE OMEGA-3 ALONE IN SUBJECT WITH FAT MASS ABOVE NORMAL LEVEL

KARNT WONGSUPHASAWAT

MASTER OF SCIENCE

PROGRAM IN ANTI-AGING AND REGENERATIVE SCIENCE

MAE FAH LUANG UNIVERSITY

2011

BODY FAT MASS REDUCTION FROM SUPPLEMENTATION WITH MARINE OMEGA-3 AND L-CARNITINE VERSUS MARINE OMEGA-3 ALONE IN SUBJECT WITH FAT MASS ABOVE NORMAL LEVEL

KARNT WONGSUPHASAWAT

THIS INDEPENDENT STUDY IS A PARTIAL FULFILLMENT OF THE REQUIEMENTS FOR THE DEGREE OF MASTER OF SCIENCE PROGRAM IN ANTI-AGING AND REGENERATIVE SCIENCE

MAE FAH LUANG UNIVERSITY

2011

BODY FAT MASS REDUCTION FROM SUPPLEMENTATION WITH MARINE OMEGA-3 AND L-CARNITINE VERSUS MARINE OMEGA-3 ALONE IN SUBJECT WITH FAT MASS ABOVE NORMAL LEVEL

KARNT WONGSUPHASAWAT

THIS INDEPENDENT STUDY HAS BEEN APPROVED
TO BE A PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF MASTER OF SCIENCE
PROGRAM IN ANTI-AGING AND REGENERATIVE SCIENCE
2011

EXAMINING COMMITTEE

.....CHAIRPERSON

(Lecturer Paisal Rummaneethorn)

.....COMMITTEE

(Prof. Dr. Thamthiwat Nararatwanch)

.....COMMITTEE

(Dr. Akkarach Bumrungpert)

ACKNOWLEDGEMENTS

The successful completion of this study was an aggregation of warmth, inspiration, advice and support from various valuable people and parties.

I would like to extend my sincere appreciation and thanks to Prof. Dr. Thamtiwat Nararatwanchai, my advisor, who had given me valuable advice and support throughout this study.

I would like to express my gratitude to the examining committee who, although being extremely busy with their duty and schedule, had spent their time and effort in advising and guiding me in this study.

I would like to thank my colleagues at the School of Anti-Aging and Regenerative Medicine, Mae Fah Luang University, for all their kind support and encouragement.

I would like to thank my dear friends, and colleagues, especially Ms. Prapatsorn Prakhunamnuey and Ms. Somporn Sitthipreechacharn at NutraMedica and P&F group of companies, who gave me full support at work, during this study.

My deepest gratitude was for my dearest parents who had always been my side, my wife who was always there for me and my lovely children for their lovely cheering.

Karnt Wongsuphasawat

Independent Study Title	Body Fat Mass Reduction from Supplementation with Marine omega-3 and L-Carnitine Versus Marine Omega-3 Alone in Subject with Fat Mass Above Normal Level
Author	Karnt Wongsuphasawat
Degree	Master of Science (Anti-Aging and Regenerative Science)
Supervisory Committee	Prof. Dr. Thamthiwat Nararatwanchai

ABSTRACT

Study on the effect of marine omega-3 comparing to omega-3 with L-carnitine was conducted in two similar groups of border line healthy to overfat or obese volunteer. Subjects were monitored at four weeks interval until the eighth week. Measurement parameters were the body composition, body weight and body fat percentage. These parameters were measured at the beginning of the study and at each monitoring interval, 4th week and 8th week. Study result showed no statistical significant weight reduction and body fat reduction between the two groups. Objectivity measurement of body fat, and weight in human could be hindered by environmental factors such as daily diet and short-term behavioral change. There was no serious side effect reported, except the commonly known adverse reactions such as nausea and fishy smell. Subject's self-assessment demonstrated satisfaction and positive attitude towards the treatment, with several effects such as body firmness, waste reduction and energizing effect felt within the first four weeks interval. Further human study in this area should be conducted in the rigidly control environment with control on diet and behavior.

Keywords: Omega-3 fish oil/L-carnitine/Fat burn/Body composition

TABLE OF CONTENTS

TABLE OF CONTENTS (continued)

TABLE OF CONTENTS (continued)

LIST OF TABLES

LIST OF FIGURES

CHAPTER 1

INTRODUCTION

1.1 Background and rationale of the study

Obesity and overweight are associated with a large number of medical complications that increase the burden for individuals directly and indirectly. The cultural perception of what a normal body should look like is closely linked to overweight. Although adipose tissue is responsible for creating smooth angles and grooves of the body, sometimes these cells do that job a little or too well and the body form becomes too round. Fat cells are essential to normal life. In a normal condition, fat cells, adipocytes, look like small, empty drops acting as reservoir for fat. However, in many circumstances, fat cells can be overloaded with fat, such as triglycerides. As adipocytes accumulate excess lipid, they start to degenerate and their normal function is distorted. Degeneration creates signal which attracts inflammatory cells, such as macrophages, to gather around cells. The macrophages releases cytokines, mainly TNF-α and Interleukin-1, into the systemic circulation, creating the so-called silent inflammation that can be detected in people who are obese or overweight. This chronic state of inflammation is a hallmark of the metabolic syndrome, adding to the increased risk profile of obese people. Cytokines may be fundamentally linked to the development of insulin resistance by inducing more production of hormone resistant that prompts other tissues such as muscles to resist insulin. In addition, overfilling of triglycerides leads to the deposition of fat in tissues that are not designed for lipid deposition, such as the liver and muscle, which is another important mechanism in the development of insulin resistance.

Even though overloading of fat cell with triglycerides can be prevented by eating less and exercising more, it is still not practical for many people. Another mechanism for preventing lipid accumulation is the activation of lipid oxidation or fat burning. Various pharmaceutical products and nutrients have been studied and used for the purpose of fat burning. Omega-3 fatty

acid is one of the widely known nutrients with many health benefits in cardiovascular health and anti-inflammation. It is one of the recommended supplements to fight the silent inflammation in metabolic syndrome. It would be of greater benefit if omega-3, while acting as anti-inflammatory agent also exerts the property to reduce fat deposit of the fat cells. Studies of the metabolic syndrome in an animal model have demonstrated that marine omega-3 fatty acid increased oxidation of fatty acids, probably through genetically-induced proliferation mitochondria and peroxisomes. Such findings and rationale ignites the interest to do further study of these effects in human and see the benefit of marine omega-3 in fat burning.

While marine omega-3 is hypothesized to have been demonstrated to have the ability to produce fat burning effect in rat model by increasing the proliferation of mitochondria and peroxisomes, it was also known that the transport of long-chain fatty acid through mitochondrial membrane requires carnitine as facilitator. Carnitine is essential in the conversion of long-chain fatty acid t acylcoA and acylcarnitine form, to make it able to enter mitochondria for eventual oxidation and involvement in energy production. This is another area of interest to see whether the additional supplementation of L-carnitine can enhance the fat burning effect expected from omega-3 fatty acid.

This research is designed based on the above rationale to study the effect of marine omega-3 on lipid oxidation, or fat burn, and to see whether L-carnitine when taking together with marine omega-3, can help to enhance the fat burning effect of marine omega-3 in subjects with slightly overweight to overweight problem.

1.2 Reasons for conducting human study

1.2.1 Since the main interest on supplementation with omega-3 and omega-3 plus L-carnitine are for the benefit of human's health, a good human research show be of true value for future medical application and further research.

1.2.2 The use of marine omega-3 and L-carnitine supplementation in human has already be widely accepted and approved by FDA in many countries including Thailand. No serious side effect has been reported and there should be least concern on the safety for subject in this study.

1.3 Research objectives

1.3.2 To study the effect of oral supplementation with marine omega-3 on lipid oxidation (fat burn) in subject with body fat composition higher than optimum level.

1.3.2 To compare the fat burning effect of marine omega-3 alone with marine omega-3 plus L-carnitine.

1.4 Research questions

1.4.1 Can marine omega-3 reduce excessive body fat composition?

1.4.2 Does the combination use of L-carnitine and marine omega-3 give better effect on the reduction of body fat composition than the use of marine omega-3 without combination?

1.5 Research hypothesis

1.5.1 Marine omega-3 supplement can help to reduce fat mass and % fat composition of the body.

1.5.2 L-carnitine enhances the effect of marine omega-3 on fat mass and % fat composition of the body, more than using marine omega-3 alone.

1.6 Conceptual framework

Excessive fat deposit in fat cell can lead to various complications that are detrimental to health. Normal intracellular lipid oxidation occurs in mitochondria. Short-chain fatty acid can enter mitochondria directly while long-chain fatty acid (LCFA) needs the help of L-carnitine to facilitate its transport through mitochondrial membrane. However, very long-chain fatty acid (VLCFA) has to be shortened in peroxisomes before it can enter mitochondria via the carnitine shuttle. L-carnitine is known to be essential in the transport of long-chain fatty acid through mitochondrial membrane for energy metabolism.

The conceptual framework for this study is based on the hypothesis that marine omega-3 can increase lipid oxidation or fat burning in fat cell by increasing the proliferation of mitochondria and peroxisomes. At the same time, as L-carnitine is known to be essential in the transport of long-chain fatty acid through mitochondrial membrane for energy metabolism, additional supplementation with L-carnitine should help to enhance the fat burning effect.

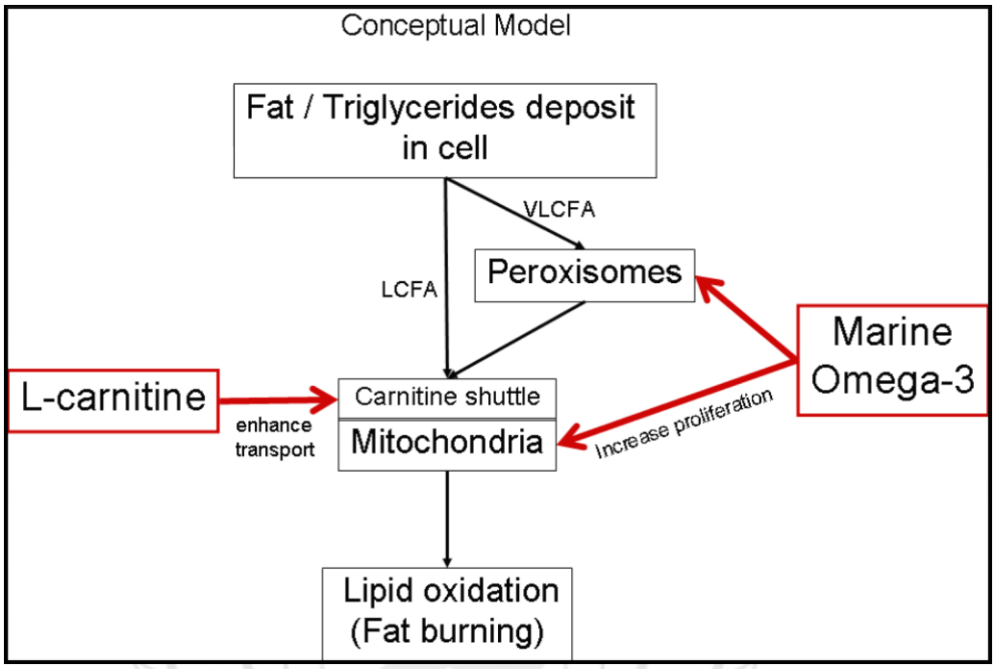


Figure 1.1 Conceptual model

A more elaborated illustration of the conceptual framework showing cell and its organelles can be demonstrated as follow:

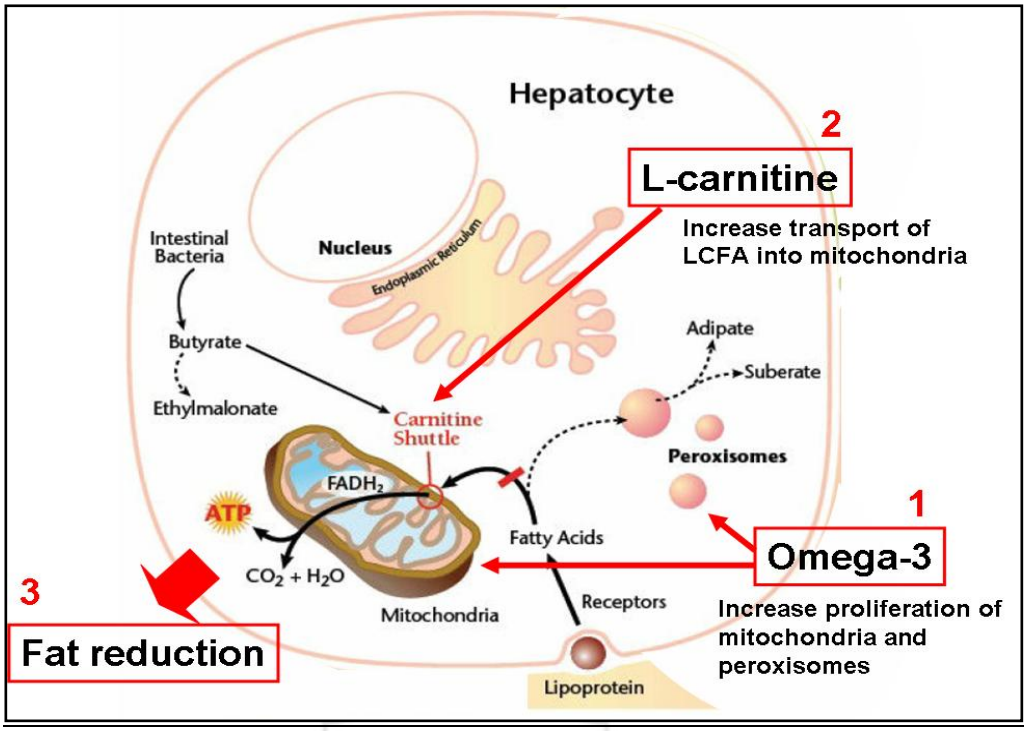


Figure 1.2 Graphic illustration of conceptual model

1.7 Contribution of the study

The study result will be of value in anti-aging practice to keep body fit and healthy by lowering the suboptimum fat composition, avoiding unwanted silent inflammation and other degenerative complications.

This study can also lead to further studies in this area such as dose response efficacy or the combination use with other supplements acting on energy metabolism.

1.8 Scope of research

Subject will be recruited from normal working people having fat composition above optimum level as analyzed by Body Composition Analyzer. Forty random subjects, male and female with the age of 25-55 will be recruited and divided into two groups, one group receiving marine

omega-3 alone, the other group receiving marine omega-3 with L-carnitine. Subjects will be required to come back to the Mae Fah Luang university hospital for follow-up after 4 weeks and 8 weeks of supplementation. Follow up measures will include general interview and Body Composition Analysis. Data on Fat composition will be analyzed and compared within group, at 4^{th} weeks, 8^{th} weeks, and between groups at the same period of investigation.

1.9 Terms and definition

1.9.1 Marine Omega-3

Omega-3 fatty acid from marine source e.g. fish and shell fish. Omega-3 fatty acid is a polyunsaturated fatty acid with many health benefits.

1.9.2 Essential Fatty Acid

Essential fatty acid is a fatty acid that cannot be synthesized in the body and must be obtained from food source. There two essential fatty acids, linoleic acid (LA) and alpha-linolenic acid (ALA). LA and ALA are widely distributed in plant oils. In addition, fish, flax, and hemp oils contain the longer-chain omega-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). Other marine oils, such as from seal, also contain significant amounts of docosapentaenoic acid (DPA), which is also an omega-3 fatty acid. Although the body to some extent can convert ALA into these longer-chain omega-3 fatty acids, the omega-3 fatty acids found in marine oils help fulfill the requirement of essential fatty acids

1.9.3 PUFA

Polyunsaturated fatty acid (PUFA) is the fatty acid that contains one or more double bond in the chemical structure, causing the fatty acid to exert different property from the saturated fatty acid, which is fatty acid without double bond.

1.9.4 LCFA

Long-chain fatty acids (LCFA) are fatty acids with aliphatic tails longer than 12 carbons. There are also other types of fatty acids categorized by the number of carbons in the structure as:

1.9.4.1 Short-chain fatty acids (SCFA) are fatty acids with aliphatic tails of fewer than six carbons.

1.9.4.2 Medium-chain fatty acids (MCFA) are fatty acids with aliphatic tails of 6–12 carbons, which can form medium-chain triglycerides.

1.9.4.3 Very-long-chain fatty acids (VLCFA) are fatty acids with aliphatic tails longer than 22 carbons

1.9.5 L-carnitine

L-carnitine is a protein that contains lysine and methionine amino acid. L-carnitine can be synthesized in human body as well as can be obtained from food source. It plays major role in the transport of long-chain fatty acid through mitochondrial member for lipid oxidation and energy production.

1.9.6 Lipid oxidation

Lipid oxidation is the process of degrading lipid. In general word, it is also known as fat burning.

1.9.7 Beta-oxidation

Beta oxidation is the metabolic process by which fatty acids are broken down in the mitochondria and/or in peroxisomes to generate acetyl-CoA. It is a catabolism of fatty acids in which the fatty acid chain is shortened by successive removal of two carbon fragments from the carboxyl end of the chain

CHAPTER 2

LITERATURE REVIEW

2.1 Marine omega-3

Fish oils were of great importance to human health because they contained special nutrient, omega-3 fatty acid or marine omega-3. Researchers believed that most people were getting too much of the wrong kinds of fats and needed the omega-3 from fish oil, marine omega-3 to balance the family of fat nutrients (Passwater, 1987). Recently, much attention had been given to the potential health benefits of omega-3 unsaturated fatty acids, particularly eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) from fish and fish oil (Zatsick & Mayket, 2007).

Polyunsaturated fatty acids (PUFAs) could be divided into two subcategories, the omega-3 and the omega-6 fatty acids. Both were considered as essential fatty acid, as they could not be synthesized by humans and must be obtained through diet or supplementation. Studies showed inverse relation between fish consumption and CHD death among population at higher risk of CHD. These studies indicated that 40-60g fish consumed per day could reduce the risk of death by 40% to 60%. Many clinical and epidemiologic studies had shown positive roles for omega-3 fatty acid in infant development, cancer, cardiovascular diseases, hyperlipidemia, various mental illnesses including depression, attention-deficit hyperactivity disorder and dementia (Riediger, Othman, Suh, Moghadasian, 2009). Omega-3 fatty acid was known to have effects against inflammation, platelet aggregation, hypertension and hyperlipidemia, of which the beneficial effect were exerted through several distinct mechanisms, including alterations in cell membrane composition and function, (Clandinin, Jumpsen & Suh, 1994) gene expression, or eicosanoid production (Simopoulos, 1999).

There were three major dietary omega-3 fatty acids: α-linolenic acid (ALA) (C18:3), eicosapentaenoic acid (EPA) (C20:5) and docosahexaenoic acid (DHA) (C22:6). Eicosanoids, produced by both omega-6 and omega-3 fatty acids were involved in the regulation of inflammation,

platelet aggregation and vasoconstriction/dilation. Both EPA and omega-6 arachidonic acid (ARA) (C20:4) competed for the common cyclooxygenase and lipoxygenase enzymes, making the ratio of omega-6: omega-3 fatty acid a determining factor for the outcome of the enzymatic pathway. As ARA produced more potent inflammatory and pro-aggregatory eisocanoids compared to EPA, it would be of particular importance when there was an abundance of omega-6 fatty acids and the scarcity of omega-3 fatty in our diet (Simopoulos, 2002).

Cardiovascular benefit of omega-3 fatty acid might be mediated through the modification of lipoprotein profile. Supplementation with 4g/day EPA decreased triglyceride levels by 23% (Mori et al., 2000) in subject with mild hyperlipidemia and by 12% (Grimsgaard, Bonaa, Hansen & Nordoy, 1997) in healthy subjects. Supplementation with DHA alone or in combination with EPA (1,252 mg total) in subjects with hypertriglyceridemia resulted in similar reductions in plasma triglyceride levels (21.8%) (Schwellenbach et al., 2006). Another study demonstrated the effect of 2 to 4 g/day EPA+DHA in lowering plasma triglyceride level by approximately 25% to 30% (Kris-Etherton, Harris, Appel, 2003). An increase in Apo lipoprotein B concentrations following omega-3 fatty acid supplementation had been observed in elderly subjects (Goyens & Mensink, 2006). Omega-3 fatty acid was also associated with the risk for cardiovascular diseases in healthy volunteers and patients with familial hyperlipidemia (Breslow, 2006). However, meta-analysis demonstrated that EPA + DHA intake produced a clinically significant dose-dependent reduction of fasting blood TAG but not total HDL or LDL cholesterol in hyperlipidemic subjects (Eslick, Howe, Smith, Preist & Bensoussan, 2009). The target EPA-DHA consumption should be at least 500 mg/day for individuals without underlying overt CV disease and at least 800 to 1,000 mg/day for individuals with known coronary heart disease and heart failure (Lavie, Milani, Mehra & Ventura, 2009). The American College of Cardiology (ACC) in conjunction with the American Heart Association (AHA) recommended the intake of 1 g/day of long chain omega-3 fatty acids for the prevention of cardiovascular disease (Eslick et al., 2009).

Omega-3 fatty acids from fish oil decreased the production of inflammatory cytokines and eicosanoids, acting both directly (replacing arachidonic acid as an eicosanoid precursor) and indirectly (altering the expression of inflammatory genes through effects on transcription factor activation). It was found to be a useful anti-inflammatory agents and could be of benefit in patients with chronic inflammatory diseases or at risk of hyperinflammation and sepsis (Calder, 2008).

Omega-3 fatty acid from fish oil significantly inhibited synthesis of TNF-α and IL-1 in severe heart failure and was found to improve body weight. The anabolic changes was found to be directly proportional to the magnitude of decrease in cytokine production (Mehra, Lavie, Ventura & Milani, 2006). Omega-3 fatty acid was recognized as a potential nutritional factor affecting fat distribution and abdominal fatness. It was found that feeding rats with fish oil, sunflower oil, and lard showed no significant difference in fat cell number, but adipocytes were significantly smaller in fish oil fed rats (Wahlqvist Hodgson, Ng, Hsu-Hage & Strauss, 1999). Supplementation with α-linoleic acid-rich diacylglycerol was found useful in the prevention of fatty liver formation. This effect could be related to the stimulation of lipid catabolism in the liver, increasing hepatic β-oxidation by 107% (Murase, Aoki & Tokimitsu, 2005).

Controlled clinical studies with marine omega-3 fatty acids containing DHA had demonstrated weight reduction and decreased serum levels of triglycerides and unesterified fatty acids, as well as positive effects on other cardiovascular effect, such as blood pressure. Animal studies demonstrated higher lipid oxidation and reduced abdominal fat volume, but not subcutaneous fat (Rossmeisl, 2009). Omega-3 fatty acid prevented weight gain and prevented glucose intolerance with shown lowered fasting glycemia, plasma insulin, triacylglycerols, and non-esterified fatty acids. The antiadipogenic effect of EPA/DHA might involve a metabolic switch in adipocytes which enhanced β-oxidation and upregulation of mitochondrial biogenesis (Flachs et al., 2005).

Dosage recommendations for omega-3 fatty acids and fish (Kris-Etherton, Grieger & Etherton, 2009).

For primary prevention of CVD

500 mg/day of EPA+DHA

(2 servings per week of oily fish would provide 400–500 mg/day of EPA+DHA) (Harris, Kris-Etherton & Harris, 2008).

For primary prevention of CVD

250 mg/day of EPA+DHA (Mozaffarian & Rimm, 2006).

For primary prevention of CHD death and after a coronary event

250–500 mg/day of EPA+DHA (Deckelbaum et al., 2008).

For women of child bearing age and nursing mothers,

consume 2 seafood servings/week, limiting intake of selected species (high in methyl mercury) (Mozaffarian & Rimm, 2006).

For vegans,

take 2–4 g of ALA per day, and 100–300 mg/day of DHA.

Some preliminary recommendations advised 2–3 servings/week of fish to lower risk of Alzheimer's disease, and cognitive decline with aging.

Omega-3 fatty acids could improve psychotic, depressive, and aggressive symptoms in severe patients. For postpartum depression and bipolar depression 0.15% of energy from EPA+DHA showed major benefits (Hibbeln, Nieminen, Blasbalg, Riggs & Lands, 2006).

The potential adverse effect of omega-3 fatty acid was minor and non-harmful since the main sources were fish or fish oil. Nausea and fishy burps might accompany regular use of supplements. Certain types of fish were high in methyl-mercury, e.g. shark, swordfish, king mackerel and tile fish, could lead to mercury poisoning with regular consumption of that type of fish. (Food and Drug Administration, 2004) Less mercury was found in fish oil alone compared to fish meat (Foran, Flood & Lewandrowski, 2003). Only little risk of excessive bleeding could be found with moderate omega-3 fatty acid intake (Harris, 2007).

2.2 L-Carnitine

Carnitine was first discovered by two Russian scientists in 1905 (Leibovitz, 1998), and was so named from the Latin caro, caronis (meaning fresh or meat). It was once named as vitamin BT by Fraenkel, who found that carnitine was necessary for the meal worm Tenebrio molitor. The important breakthrough was discovered in 1959 when Fritz discovered that carnitine stimulated the rate of fat burning (beta-oxidation) of long-chain fatty acid (LCFA) in the heart and other muscles (Fritz, 1959).

Carnitine is chemically termed 3-hydroxy-4-N-trimethyl amino butyric acid (Haeckel, Kaiser, Oellerich & Siliprandi, 1990). Human synthesized L-carnitine endogenously from L-lysine and L-methionine, and could also obtain from diet (Vaz, van Gool, Ofman, Ijlst & Wander, 1998). The endogenous synthesis of L-carnitine involved five separate enzymatic steps and required the two

amino acids, L-lysine and L-methionine together with the co-factors, ascorbic acid, iron, niacin and pyridoxine. Animal tissues such as beef and pork muscle generally contained high level of L-carnitine, while plant derived food are usually poor sources (Maher, 2001). Although mammals can synthesize some L-carnitine, eating strict vegetarian diet may deprive some tissues of the required amounts of L-carnitine, particularly during exercise, stress or various disease states.

The average adult body contained about 25 g of L-carnitine, of which 95% were found in muscles. L-carnitine was absorbed via a stereoselective active transport system located in the intestinal mucosa of duodenum and ileum (Hamilton, Li, Shug & Olsen, 1986). In addition, passive diffusion of L-carnitine had also been demonstrated in the intestine, but with significance only when it was ingested in large amount. The normal plasma carnitine concentration for healthy men was 59 μmol/L, and in healthy women was 51μmol/L, while children tended to have a lower range of 36-41 μmol/L. Bach found that after administering 2 g of L-carnitine orally to healthy volunteers, plasma levels increased to an average of 69 μmol/L (Bach, Schirardin, Sihr & Storck, 1983). It should also be noted that the unnatural D-isomer inhibited the absorption of the physiologically active L-isomer (Maher, 2001).

The tissue concentration of L-carnitine was generally several-fold higher than those in plasma. The concentration in skeletal muscle was approximately 70 times greater than plasma level. Skeletal muscle and heart held approximately 95% of total storage, with 4% in kidney and other tissues, and the remaining 1% in extracellular fluid (Maher, 2001). L-carnitine was mainly excreted via renal excretion, and was also highly conserved by kidney. Hyperthyroidism could increase the urinary excretion of carnitine, while hypothyroidism decreased excretion. The plasma half-life of L-carnitine was estimated to range from two to 15 hours in human. L-carnitine passed the placenta and could be delivered via breast milk.

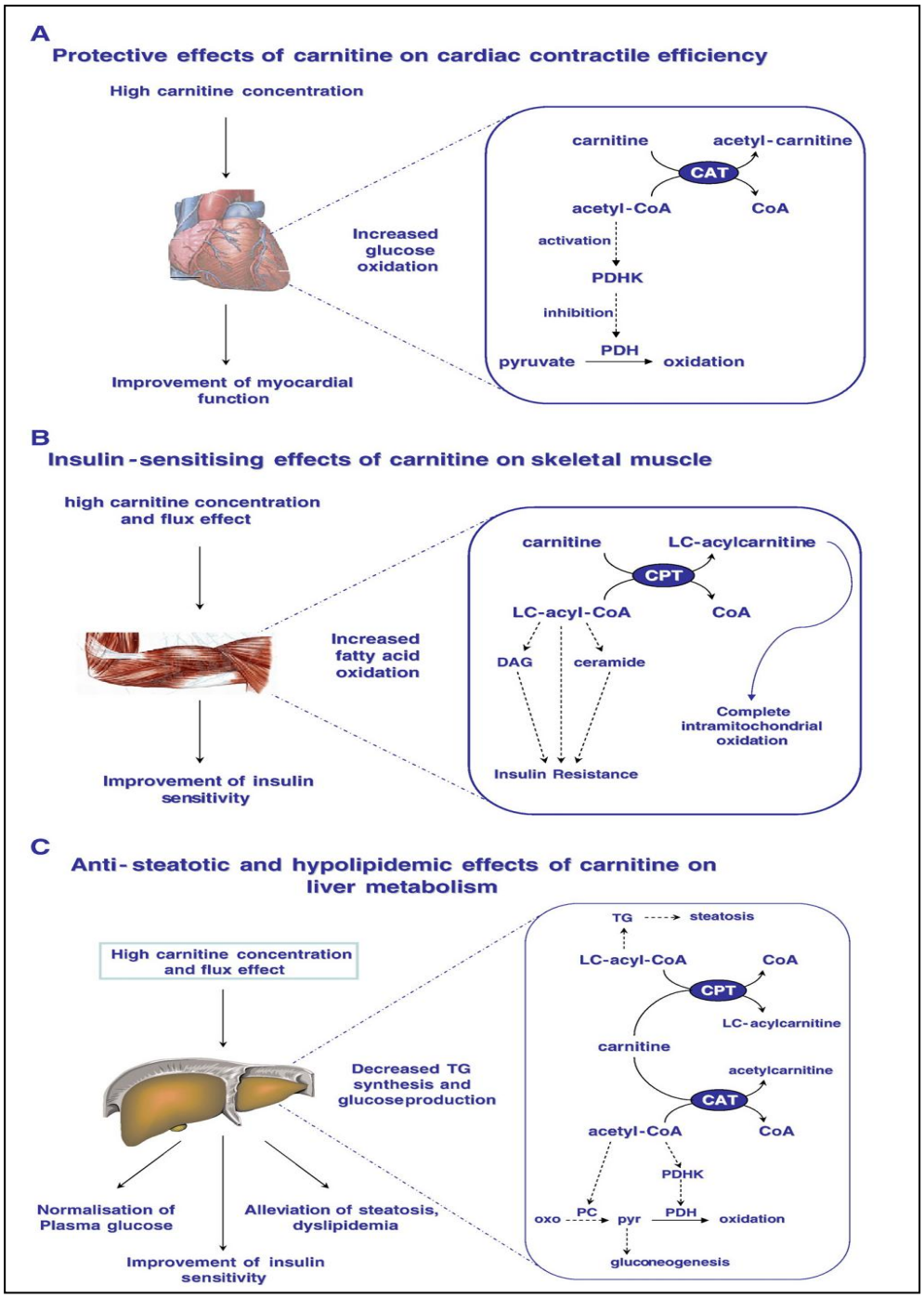
L-carnitine facilitated long-chain fatty acid (LCFA) transport through mitochondrial membrane for their oxidation and energy production. LCFAs could not traverse the mitochondrial membrane by it self. LCFAs activated on the outer mitochondrial outer membrane by long-chain acyl-CoA synthetase (LCAS) were still not permeable through the mitochondrial inner membrane. These beta-oxidative chain-shortening were preceded by the carnitine-dependent transport of activated fatty acids into the mitochondrial matrix. This transport system consisted of three proteins, carnitine palmitoyltransferase I (CPT-I), acylcarnitine:carnitine translocase (CACT), and carnitine palmitoyltransferase II (CPT-II), each

with a different submitochondrial outer membrane. (Steiber, Kerner & Hoppel, 2004) The pharmacologic action of L-carnitine could be described as (1) metabolic action, such as the role in lipid and glucose metabolism, and (2) biophysical action, such as those stemming from physico-chemical interactions between L-carnitine and plasma membrane lipid components. (Arduini, Bonomini, Savica, Amato & Zammit, 2008)

The role of carnitine in long-chain fatty acid oxidation was well defined. Evidences showed supported a role for the voltage-dependent anion channel in the transport of acyl-CoAs through the mitochondrial outer membrane. (Steiber et al., 2004) Recent reported data had also shown the role of carnitine and the carnitine transport system in the interplay between peroxisomes and mitochondrial fatty acid oxidation. There were also reports showing L-carnitine's buffering of acyl-CoA/CoA that reflects intracellular metabolism.

A detailed study on metabolic effect of L-carnitine in the heart of normal working rat had shown the effect of L-carnitine to enhance glucose consumption by stimulating flux through pyruvate dehydrogenase (Broderick, Qunney & Lopaschuk, 1992). Studies demonstrated conclusive evidence that L-carnitine stimulated fatty acid oxidation in healthy (Muller, Seim, Kiess, Loster & Richter, 2002) or overweight subjects (Wutzke & Lorenz, 2004). Researcher also found that supra-physiological levels of L-carnitine might alleviate impairment of the proximal components of the insulin signaling cascade in the skeletal muscle of insulin-resistant or Type-2 diabetic patient (Arduini et al., 2008) (Figure 1.1). Other roles of L-carnitine included buffering of the acyl coenzyme A (CoA)-CoA ratio, branched chain amino acid metabolism, removal of excess acyl groups and peroxisomal fatty acid oxidation (Hoppel, 2003).

The administration of L-carnitine in aged rats at the dose of 300mg/kg body weight, demonstrated time –dependent normalization of the abnormally elevated lipid peroxides. It was also shown to reduce lipid peroxidation, elevation of glutathione peroxidase activity and ascorbic acid content (Kalaiselvi & Panneerselvam, 1998). In human, disorders of fatty acid oxidation and metabolism such as increased lipolysis, increased lipid peroxidation, accumulation of acylcarnitines, and altered membrane permeability, were found to be typically associated with primary and secondary form of carnitine deficiency (Hoppel, 2003). Therapeutic administration of carnitine showed promise in treating selected groups of patients having altered carnitine homeostasis, resulting complications.



From Arduini, A., Bonomini, M., Savica, V., Amato, A. & Zammit, V. (2008). Carnitine in metabolic disease: Potential for pharmacological intervention. **Pharmacology & Therapeutics, 120**(2), 149-156.

Figure 2.1 Effects of L-carnitine

L-carnitine (2g per day in two equally divided dose, morning and evening) was found to significantly lower the plasma lipoprotein(a) level compared to placebo in 94 selected hypercholesterolemic patients with newly diagnosed type-2 DM, after 3 and 6 months (Derosa et al., 2003).

Evidence were reported that L-carnitine improves sperm motility, with increased relationship between PHGPx (phospholipid hydroperoxide glutathione peroxidase) content and sperm motility after carnitine supplementation (Garolla et al., 2005).

The observed safe level (OSL) risk assessment method indicated that strong safety evidence for the intakes of up to 2000 mg per day of L-carnitine equivalents for long-term supplementation. Although much higher doses had been tested without showing adverse effect and might be safe, the data were still not sufficient for confident conclusion of long-term safety at higher dose level (Hathcock & Shao, 2006).

2.3 Fat and adipose tissue

Fat tissue serves a series of functions that are important for normal life, its primary role being to act as a depot when too little food is available. As a part of our immune system, fat cells are protecting us from developing Type 2 diabetes. This function only occurs, however, when they are small and not distended by fat overloading. Abdominal fat cells are the most dynamic ones and experiments have demonstrated that the omega-3 fatty acid DHA (docosahexaenoic acid) can reduce fat cell size even without body weight reduction.

The main storage compartment for fatty acid in human was adipose tissue which was currently found to hold many key roles in metabolism and signaling (Mohamed-Ali, Pinkney & Milani, 1998). A lean man has approximately 18% body weight as fat compared to 30% in an obese man (Jensen, 2002). Recent research showed that t1/2 of adipose tissue fatty acid, demonstrated by stable isotope technology to be between 6 and 9 months, reflects an integrated measure over 1-1.5 years intake (Strawford, Antelo, Christiansen & Hellerstein, 2004). Since approximately 99% of adipose tissue was Triacylglycerols (TAG) in healthy adults, with cholesterol (0.3%) and phospholipid (<0.1%) making minor contribution, the total or (TAG) fatty acid composition of adipose tissue is typically measured (Hirsch, Farquhar, Ahrens Jr, Peterson

& Stoffel, 1960). In general, the fatty acid composition of subcutaneous adipose tissue taken from sites such as buttock, abdomen, or upper arm appeared to be similar. However, a few studies reported small (between 2%-10% differences in the proportions of saturated fatty acid (SFA) and monounsaturated fatty acids (MUFA) with abdomen having higher SFA and MUFA than the buttock (Hodson, Skeaff & Fielding, 2008).

Fatty acids were released from adipose tissue TAG stores bye the action of lipases into the venous effluent and were transported in plasma as a complex with albumin. A TAG molecule was formed from a glycerol backbone with three fatty acids attached. The majority of TAG in fasting plasma was usually carried in very low density lipoprotein (VLDL) particles. The fatty acid composition of plasma TAG had been reported to represent dietary intake from the preceding day(s) (Hodson et al., 2008).

2.4 Bioelectrical Impedance Analysis (BIA)

Bioelectrical impedance analysis (BIA) was a method of measuring body composition e.g. fat mass, predicted muscle mass, etc., by measuring bioelectrical impedance in the body. Fat within the body allowed almost no electricity to pass through, while electricity passed rather easily through water, much of which was found in muscles (Tanita, 2008). BIA was based upon the relationship between the volume of the conductor (i.e., the human body), the conductor's length (i.e., the subject's height), the components of the conductor (i.e., fat or FFMs) and its impedance. BIA assumed that volume of a conductor could be deducted from measurements of its length and resistance. The overall conductivity of human body was closely related to lean tissue and had been validated with criterion methods such as hydrodensitometry and skinfold measurement. It had been used in a range of specific groups including the elderly, children and adolescents, the overweight, middle-aged, malnourished, dialysis patients, infants for nutritional analysis, during growth, in eating disorders, for cancer patients, in ethnic groups and in patients with cystic fibrosis. Although the standard error of estimates was at best reported as 2.5% in humans, its advantages such as speed of operation, safety, probability and lack of intrusion made it an ideal tool for epidemiological investigations (Brodie, Moscrip & Hutcheon, 1998).

Body fat percentage is the amount of body fat as a proportion of your body weight.
Reducing excess levels of body fat has shown to reduce the risk of certain conditions such as high blood pressure, heart disease,diabetes and cancer. The chart below shows the healthy ranges for body fat.

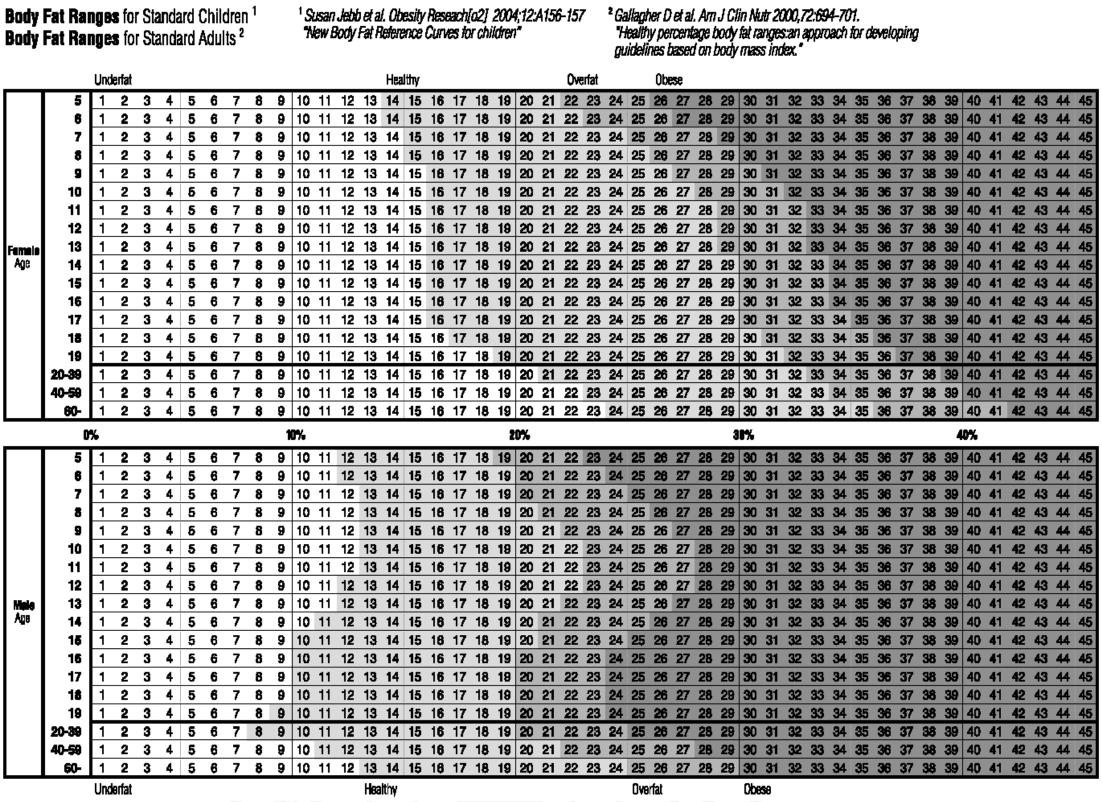


Figure 2.2 Standard nody fat ranges measured by BIA

CHAPPTER 3

RESEARCH METHODOLOGY

3.1 Population and sample size

Study population

Normal working people in Bangkok, male and female, between 25-55 years of age, who agreed to join the study voluntarily and were analyzed as having % fat composition above optimum, 18% in male and 22% in female.

3.2 Sample size calculation

Sample size is defined by the following formula

$$n_0 = \frac{Z_\alpha^2}{4d^2}$$

Set confident interval at 95 % $\alpha = 0.05$

(P = 0.5 Q = 0.5 : PQ = 0.25 = ¼)

d = 20%

n = 17 subjects per group

Set allowance for 20% drop out rate: Sample size will be 20 subjects per group. Hence, total sample size is 40 subjects; 20 per group.

3.3 Type of research

3.3.1 Experimental research: Human, randomized, controlled, clinical trial. 8th weeks follow up for result.

3.3.2 Study variables

3.3.3 Independent variables are the treatment given.

3.3.4 Dependent variable is the change in body fat composition.

3.4 Selection of sample

Sample will be randomly recruited from working people in the business area, shopping malls and office building in Bangkok. After subjects have been clearly explained on the purpose of the study, subjects will be given a preliminary test using Body Composition Analyzer to see if inclusion criteria are met. After being enrolled into the study, subject will be randomly assigned to each group of the two treatment groups, one group receiving Marine omega-3 and the other group having Marine omega-3 plus L-carnitine.

3.4.1 Inclusion criteria

3.4.1.1 Male or female at the age of 25-55 years.

3.4.1.2 Each subject voluntarily agrees to participate in the research and signs informed consent form at the beginning of the study.

3.4.1.3 Subject has fat composition above 18% in male, and 22% in female, or BMI above 22.

3.4.1.4 Subject can attend follow-up visit that will be set at the end of 4th week and 8th week.

3.4.1.5 Subject will stop taking all other medication or supplements that can affect the lipid and energy metabolism during the 8 weeks period.

3.4.2 Exclusion criteria

3.4.2.1 Subject of known allergic to fish, sea food, omega-3 and L-carnitine.

3.4.2.2 Subject who is taking drugs acting on energy and fat metabolism e.g. patients who are under weight loss medication, patient with thyroid hormone medication.

3.4.2.3 Subject with known abnormality of thyroid, and liver function.

3.4.2.4 Pregnant women and breast feeding mother are excluded from the study.

3.4.2.5 Professional athletes will be excluded.

3.5 Research tools

3.5.1 Marine omega-3 licap (double strength; 500 mg capsule containing 300 mg omega-3)

3.5.2 L-carnitine tablets (L-carnitine 250mg + alpha lipoic acid 125 mg)

3.5.3 Body Composition Analyzer – TANITA Model SC331-S

3.5.4 Research protocol declaration

3.5.5 Informed consent form

3.5.6 Investigator record form

3.5.7 Volunteer's Self-assessment form

3.6 Research procedure

3.6.1 Recruit subject into the research using the inclusion criteria as guideline.

3.6.2 Investigator explains purpose and procedure of the research to subjects in detail

3.6.3 Investigator gets subject to sign inform consent form and fill in the personal data in research record form.

3.6.4 Investigator checks subject's body composition and interviews subjects on general information, lifestyles, medical history. Investigator keeps records of all data obtained in research record form.

3.6.5 Investigator randomly assigns subject into group of study protocol, and gives subject the supplement to take.

3.6.6 Investigator explains the proper use of the supplement, its benefit and possible side effect to subject. The supplement given will be enough for the period of 4 weeks, when subject are required to come back for follow up.

3.6.7 Subject comes back at the end of the 4th week and 8th week for follow up. At each follow-up visit, investigator will interview subject on diet and daily behavior for the past 4 weeks together with performing body composition test, and make record.

3.6.8 At the end of 8th week, subjects are also required to fill up a self-assessment questionnaire.

3.7 Criteria to withdraw from the study

3.7.1 Subject wants to withdraw from the study with personal reason.

3.7.2 Subject encounters severe side effect from the medication used in the study.

3.7.3 Subject becomes sick from disease with moderate to severe degree that may interfere with the study result.

3.7.4 Subject fails to follow-up on the preset schedule.

3.8 Result Evaluation

3.8.1 Measurement of fat composition

Fat mass and % Fat composition will be measured by Body Composition Analyzer (TANITA Model SC331-S: Tetra polar Bioelectrical Impedance Analysis) BMI will be calculated using the formula: Weight (kg.) divided by Height^2 (m^2)

3.8.2 General assessment by researcher

Evaluation by volunteer using self-assessment questionnaire

3.9 Data collection

Investigator will perform data collection upon each follow-up visit.

3.10 Statistics used for data analysis

3.10.1 Use descriptive statistics to demonstrate data characteristics

3.10.2 Compare mean of Fat composition and BMI at T0 and T2 (8th week) in each group by using paired t-test, if there is normal distribution in the data, other wise Wilcoxon matched pair sign rank test will be used.

3.10.3 Compare the mean of change in Fat composition and BMI during T0 and T2, between the two groups using repeated measure ANOVA.

3.10.4 Analyze self-assessment evaluation by descriptive statistics

CHAPTER 4

RESULT

Result of the study is analyzed and report in three section, subject charactereristics data, study result and patient satisfaction.

Table 4.1 Subject characteristics at start

		N	Mean	SD	Minimum	Maximum
Age	Omega-3 (ω3)	22	35.68	6.1130	24.00	48.00
	ω3+Carnitine	20	35.25	7.0550	26.00	52.00
	Total	42	35.48	6.5000	24.00	52.00
Weight	Omega-3 (ω3)	22	67.56	11.5578	53.60	100.80
	ω3+Carnitine	20	71.40	12.3159	54.90	104.50
	Total	42	69.39	11.9362	53.60	104.50
Body Fat	Omega-3 (ω3)	22	34.53	7.4389	15.90	50.20
	ω3+Carnitine	20	33.33	8.5107	19.00	50.00
	Total	42	33.96	7.8918	15.90	50.20
Visc Fat	Omega-3 (ω3)	22	7.46	2.4442	4.00	13.00
	(3+Carnitine	20	8.85	3.4834	5.00	18.00
	Total	42	8.12	3.0300	4.00	18.00

Subjects were mostly female, 78.6 %. Age range were in range of 24-52 years of age, with a mean of 35.48 years of age. All subjects were working people having lifestyle and work habit that could be classified as active type, walking around or standing, 76.2%, and passive type,

sitting, 33.8%. Initial weight was in the range of 53.6 – 104.5 kg, with the mean of 69.39 kg. Body fat ranged from 15.90 – 19.00 % of body weight, with the mean of 33.96 %. Visceral fat was also measured for all subjects, ranging from 4.0 – 12.0, with the mean of 8.12

Table 4.2 Subject characteristics 2

Group	Sex		Total	Action		Total
	Male	Female		Active	Passive	
Omega-3 (w3)	3	19	22	17	5	22
w3+Carnitine	6	14	20	15	5	20
Total	**9**	**33**	**42**	**32**	**10**	**42**

Group	Physical Rating					Total
	Obese1	Obese2	Obese3	Health5	Health6	
Omega-3 (w3)	4	5	2	5	6	22
w3+Carnitine	4	5	3	4	4	20
Total	**8**	**10**	**5**	**9**	**10**	**42**

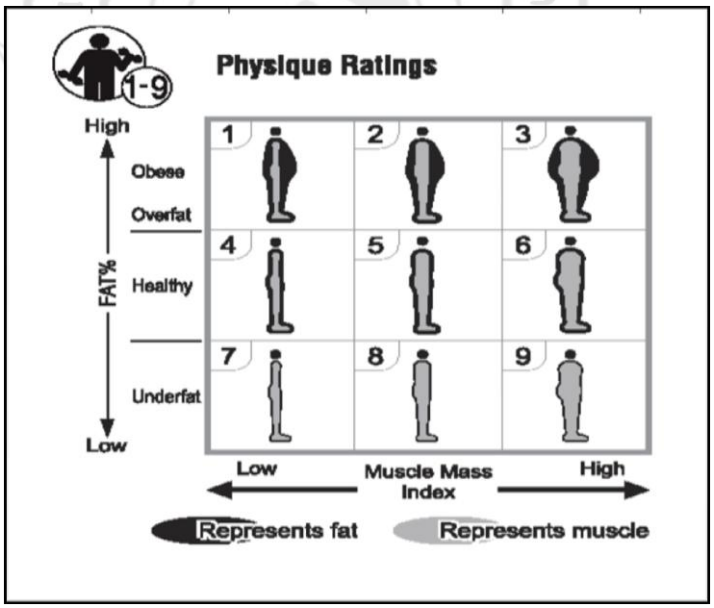


Figure 4.1 Physical rating guide

The analysis of subject characteristics between the two groups, group taking Omega-3 only and group taking Omega-3 with L-carnitine showed that there was no significant difference in the characteristics in term of age, weight, body fat and visceral fat of subjects between the two groups. Subject characteristics on gender, lifestyle action and physical rating were also collected and shown on table 4.2

During the study, subjects were advised to take Omega-3 or Omega-3 plus L-carnitine daily while keeping normal lifestyle. All parameters were evaluated at the end of 4th week and 8th week. Data on body fat percentage and visceral fat were shown in table 4.3

Table 4.3 Parameter monitoring of the Omega-3 group at T0 (starting point), T1 (4th week) and T2 (8th week)

		Omega-3 Group				
		N	**Mean**	**SD**	**Minimum**	**Maximum**
Body Fat	T0	22	34.53	7.4389	15.90	50.20
	T1	22	34.28	7.5483	14.00	49.30
	T2	22	34.90	7.6089	13.00	48.80
Weight	T0	22	67.56	11.5578	53.60	100.80
	T1	22	67.55	11.2847	53.90	99.10
	T2	22	67.75	10.9411	54.40	98.00
Visceral Fat	T0	22	7.45	2.4442	4.00	13.00
	T1	22	7.41	2.4623	4.00	13.00
	T2	22	7.45	2.4636	4.00	13.00

Table 4.4 Parameter monitoring of the Omega-3 plus L-carnitine group at T0 (starting point), T1 (4th week) and T2 (8th week)

		Omega-3 plus L-carnitine Group				
		N	**Mean**	**SD**	**Minimum**	**Maximum**
Body Fat	T0	20	33.33	8.5107	19.00	50.00
	T1	20	33.31	8.6229	20.20	51.30
	T2	20	33.44	8.7540	19.90	50.80
Weight	T0	20	71.40	12.3159	54.90	104.50
	T1	20	71.61	12.5601	54.60	106.40
	T2	20	71.61	12.5703	54.90	106.30
Visceral Fat	T0	20	8.85	3.4834	5.00	18.00
	T1	20	8.80	3.3966	5.00	18.00
	T2	20	8.85	3.4378	5.00	18.00

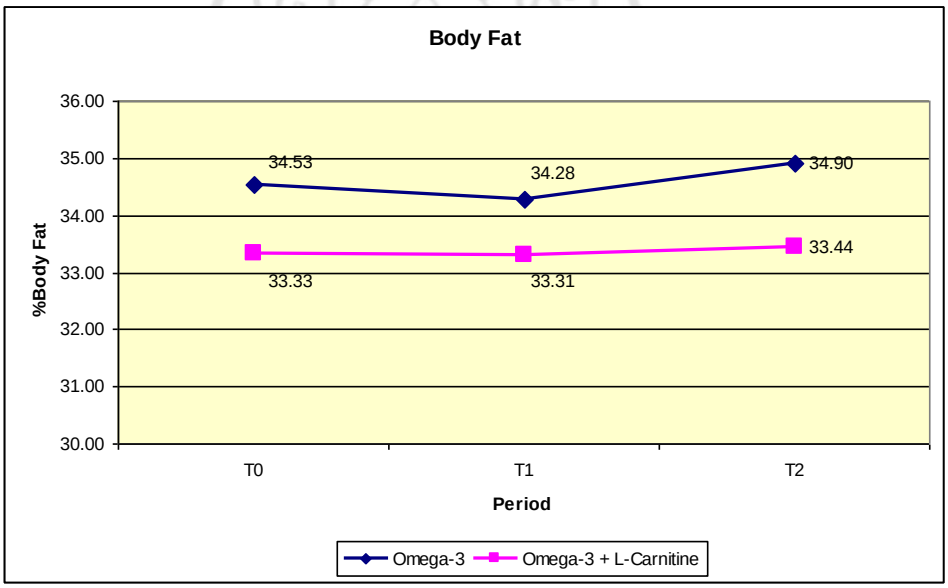


Figure 4.2 Mean body fat comparison within group and between group

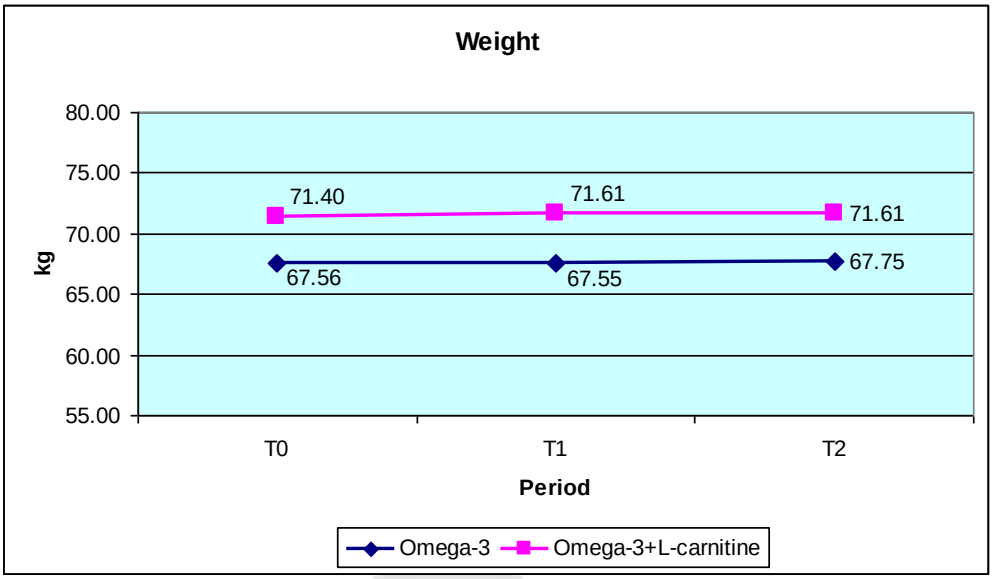


Figure 4.3 Mean weight comparison within group and between group

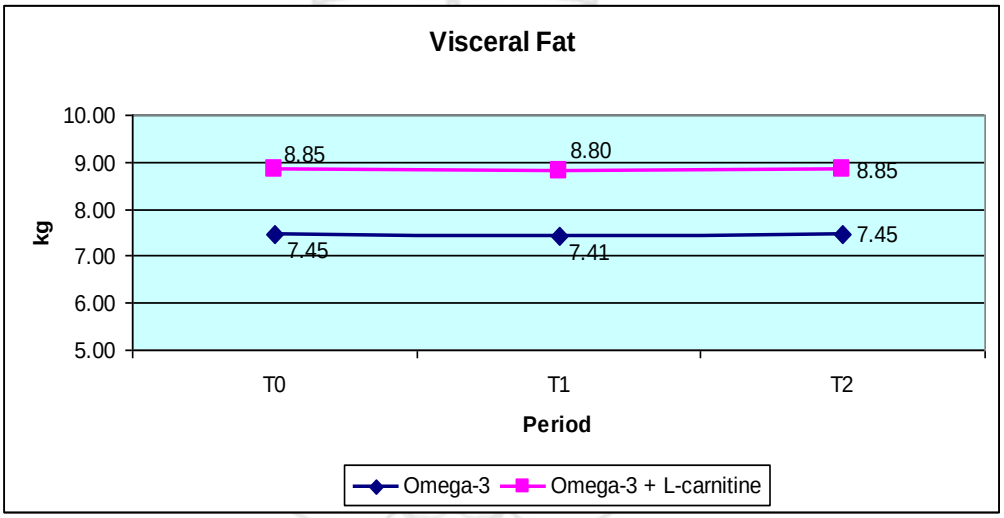


Figure 4.4 Mean visceral fat comparison within group and between group

Result from eight weeks of administration with the two regimens of supplement demonstrated minimal change in all three parameters measured at T0, T1 and T2 in both group. Statistical analysis showed that there was no statistical signifant in % Body Fat between T0 and T2 of the group receiving Omega-3. The other group receiving Omega-3 with L-carnitine also

showed no statistical difference in % Body Fat between T0 and T2. There were also no statistical significant difference in weight between T0 and T2 in both groups.

Table 4.5 Body fat change in male versus female

		N	Mean	SD	Minimum	Maximum
Body Fat Change	Male	9	-0.3111	1.35411	-2.90	1.30
T0-T2	Female	33	0.4697	0.84502	-1.80	1.60
	Total	42	0.3024	1.01007	-2.90	1.60

An interesting observation was that there was a statistically signicant difference in the Body Fat Change between different gender. From the overall data of both groups combined Male subjects showed significant reduction in Body Fat when compare to female subjects ($p<0.038$).

Self-assessment data were grouped into the compliance & safety parameters, effectiveness and overall attitude towards the treatment as shown in figure 9, 10, 11. Comparative analysis between the two groups showed no significant difference in all parameters from the questionnaire.

Table 4.6 Comparative self-assessment data on safety between the two groups

	Group	N	Mean	SD
Nausea	Omega-3 (ω3)	21	1.24	0.625
	ω3+Carnitine	18	1.06	0.236
Vomit	Omega-3 (ω3)	21	1.14	0.478
	ω3+Carnitine	18	1.00	0.000
Constipation	Omega-3 (ω3)	21	1.29	0.717
	ω3+Carnitine	18	1.50	0.857
Loose stool	Omega-3 (ω3)	21	1.33	0.730
	ω3+Carnitine	18	1.33	0.686
Oily skin/hair	Omega-3 (ω3)	21	1.57	0.746
	ω3+Carnitine	18	1.61	0.979

Table 4.6 (continued)

	Group	N	Mean	SD
Loss appetite	Omega-3 (ω3)	21	1.14	0.478
	ω3+Carnitine	18	1.28	0.752
Appetite	Omega-3 (ω3)	22	2.23	1.193
	ω3+Carnitine	18	2.44	1.199
Itching	Omega-3 (ω3)	21	1.05	0.218
	ω3+Carnitine	18	1.00	0.000
Headache	Omega-3 (ω3)	21	1.33	0.796
	ω3+Carnitine	18	1.11	0.323
Arrhytmia	Omega-3 (ω3)	22	1.27	0.631
	ω3+Carnitine	18	1.11	0.323

Table 4.7 Comparative self-assessment data on effectiveness between the two groups

	Group	N	Mean	SD
Body Firmness	Omega-3 (ω3)	22	2.36	1.002
	ω3+Carnitine	18	2.56	1.149
More active	Omega-3 (ω3)	22	2.91	0.921
	ω3+Carnitine	18	2.78	1.003
Endurance	Omega-3 (ω3)	22	2.86	1.125
	ω3+Carnitine	18	3.00	1.138
Smaller waist	Omega-3 (ω3)	21	2.33	0.913
	ω3+Carnitine	18	2.61	0.850
Energized	Omega-3 (ω3)	22	3.05	0.899
	ω3+Carnitine	18	3.06	1.259
Overall Satis	Omega-3 (ω3)	22	3.95	0.722
	ω3+Carnitine	18	3.89	0.758
Satis Rate	Omega-3 (ω3)	21	6.76	0.889
	ω3+Carnitine	16	6.94	1.302
Will continue	Omega-3 (ω3)	22	3.86	0.889
	ω3+Carnitine	18	3.67	1.029

In order to evaluate subject assessment on overall treatment containing Omega-3, data analysis based on all subjects was conducted. Almost all subjects, 98.5%, reported ease of taking the supplement provided and 77.5% reported convenience to carry along. Noticable adverse reaction was nausea which was reported by 2 cases (5.1%) as moderate, and another 2 cases as slightly. Fishy smell was reported by 17.5%, while 35% reported as having slight smell after taking the supplement. Constipation was felt by 25.6% of subject while lose stool was also reported by 20.5%.

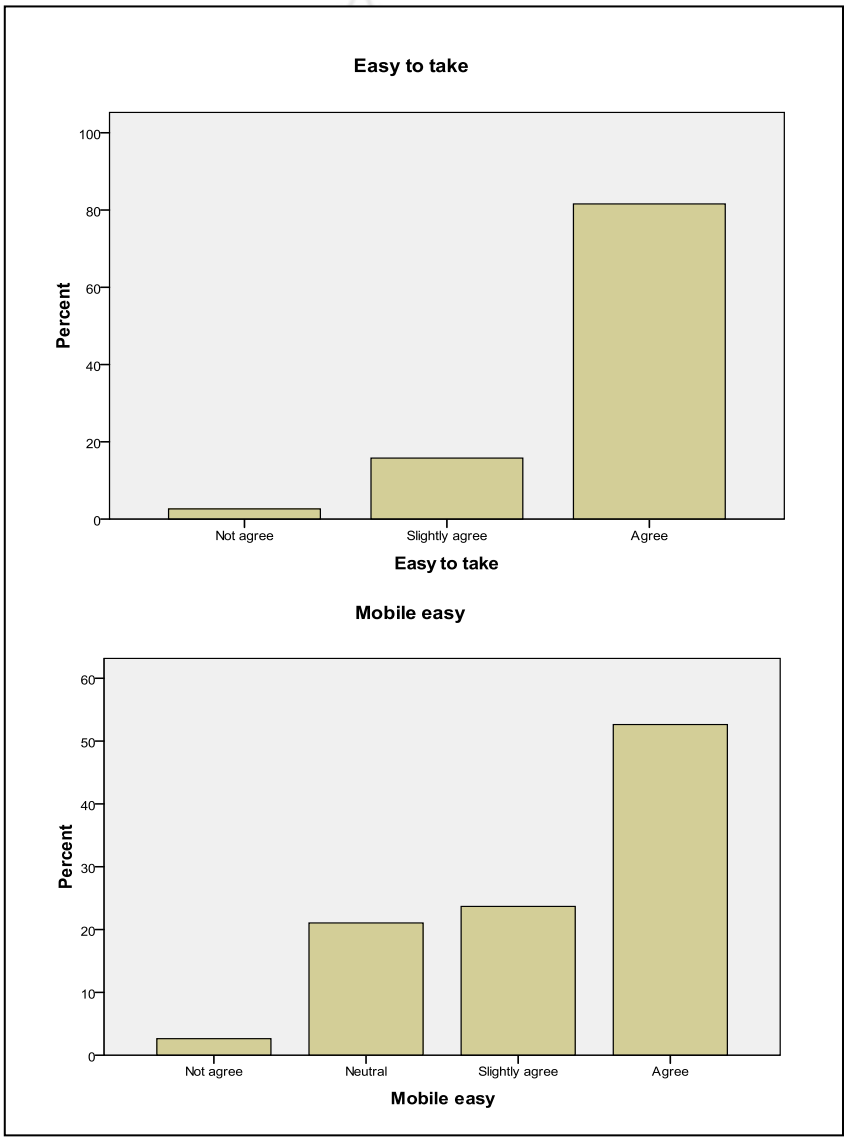


Figure 4.5 Self-assessment on compliance

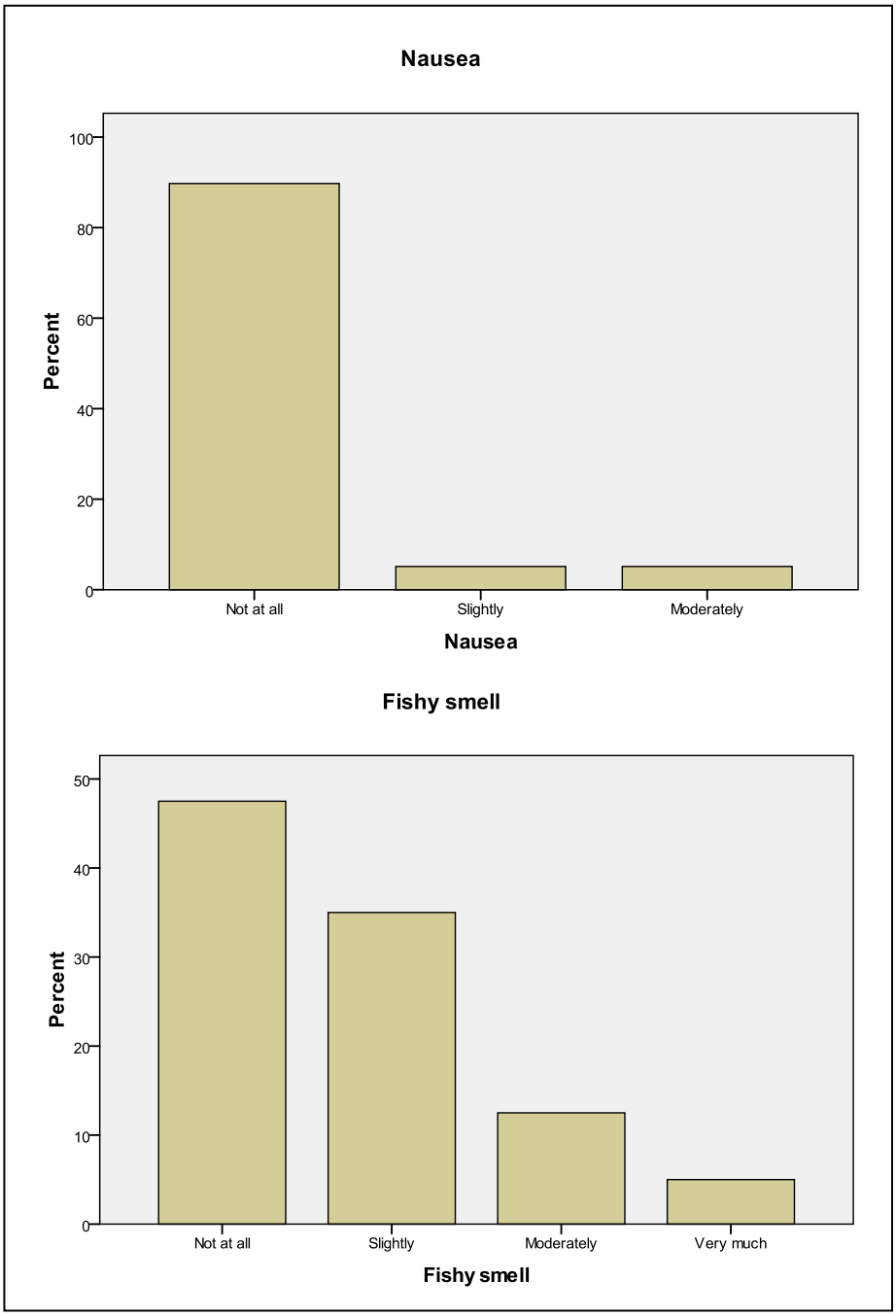


Figure 4.6 Self-assessment on compliance (2)

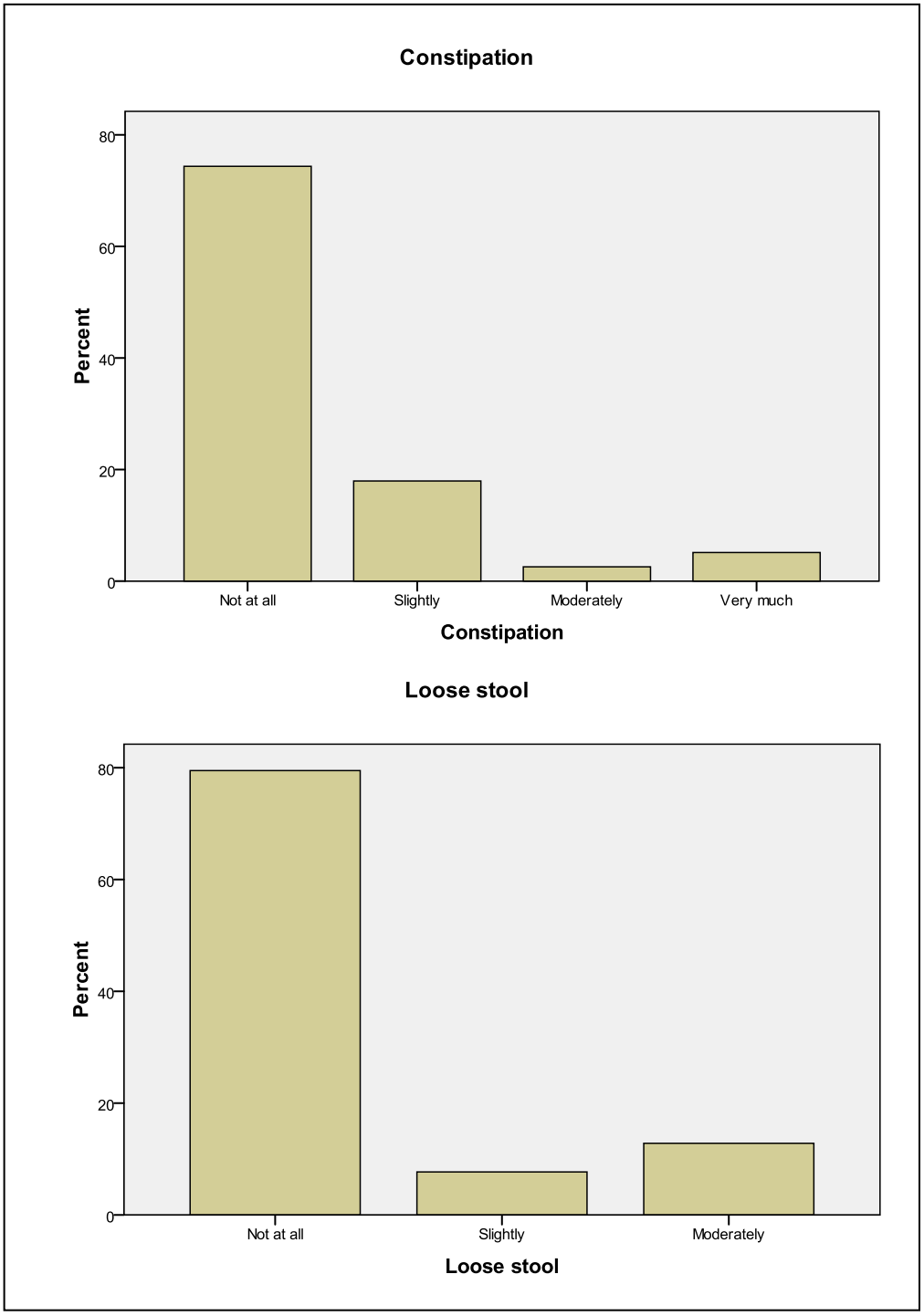


Figure 4.7 Self-assessment on adverse reaction

Oily skin and hair was also reported by 38.5% of subject. Two subjects reported having accelerated heart rate.

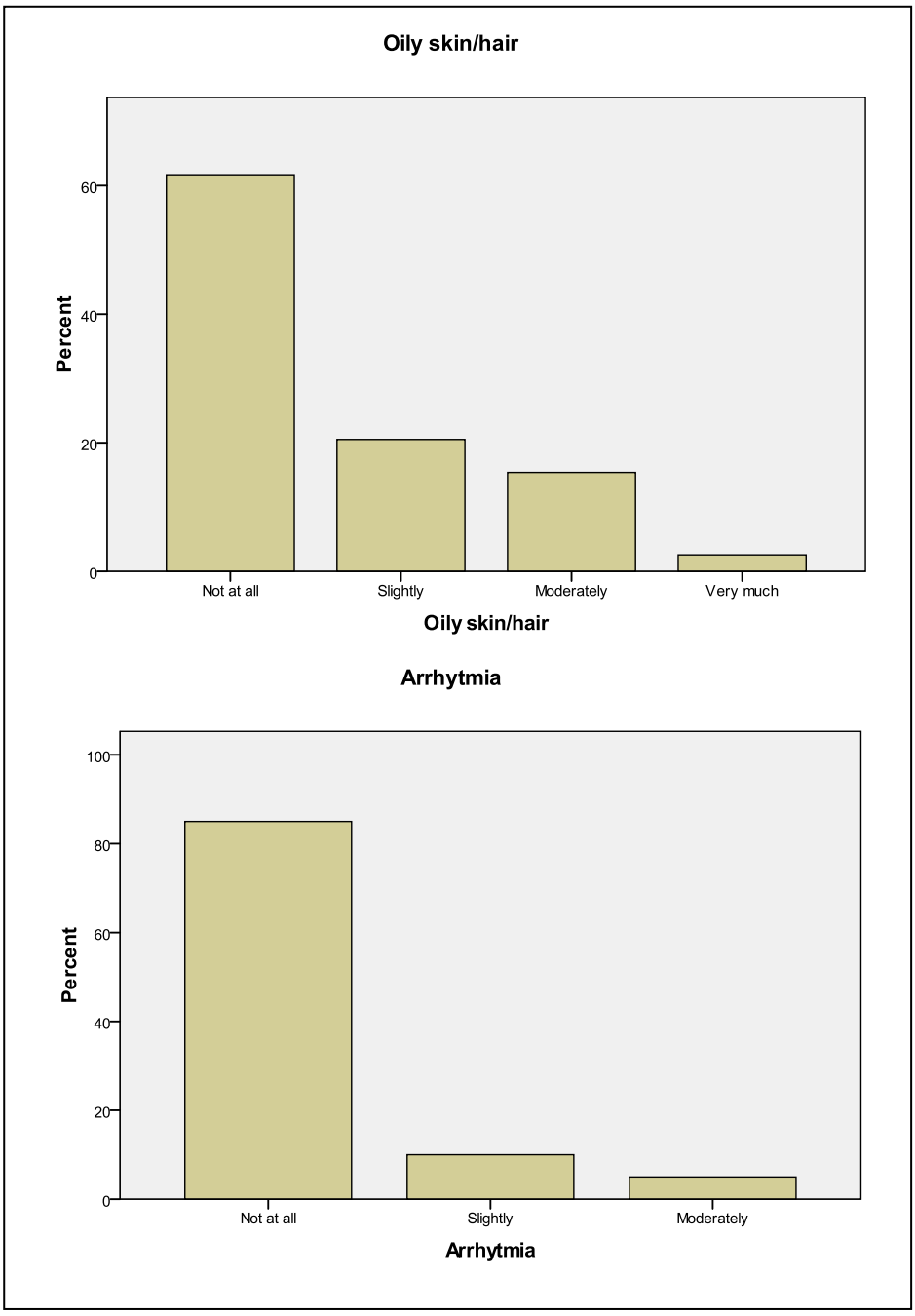


Figure 4.8 Self- assessment on adverse reaction (2)

45.0% of subjects felt that they better digestion and freshing feeling after taking the supplements causing them to have better appetite, while 20% felt only slightly appetite. Two cases reported loss of appetite, and 3 cases felt slightly loss of appetite.

63.5% reported that they feel more active while 45% felt that they have better endurance.

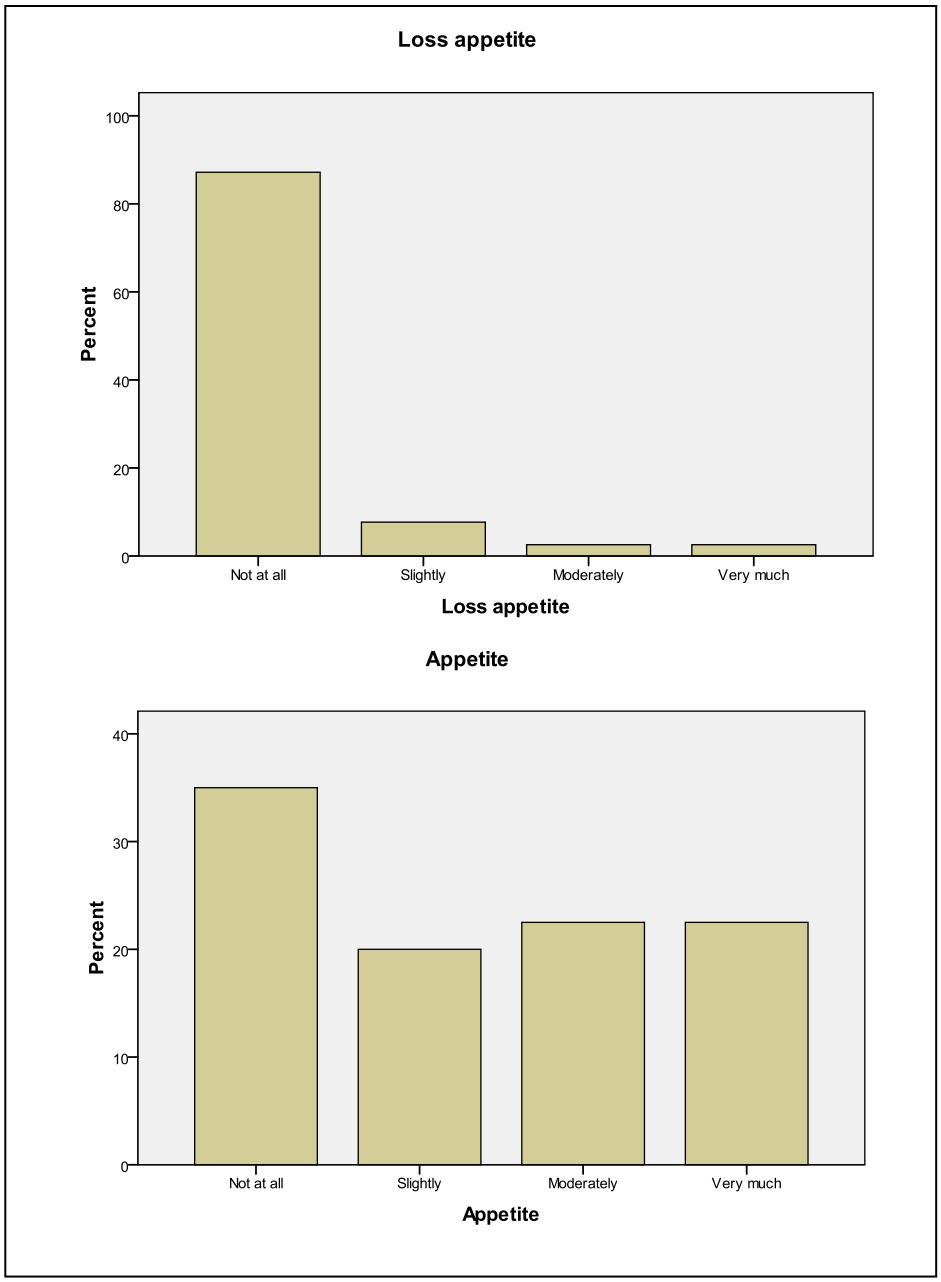


Figure 4.9 Self-assessment on appetite

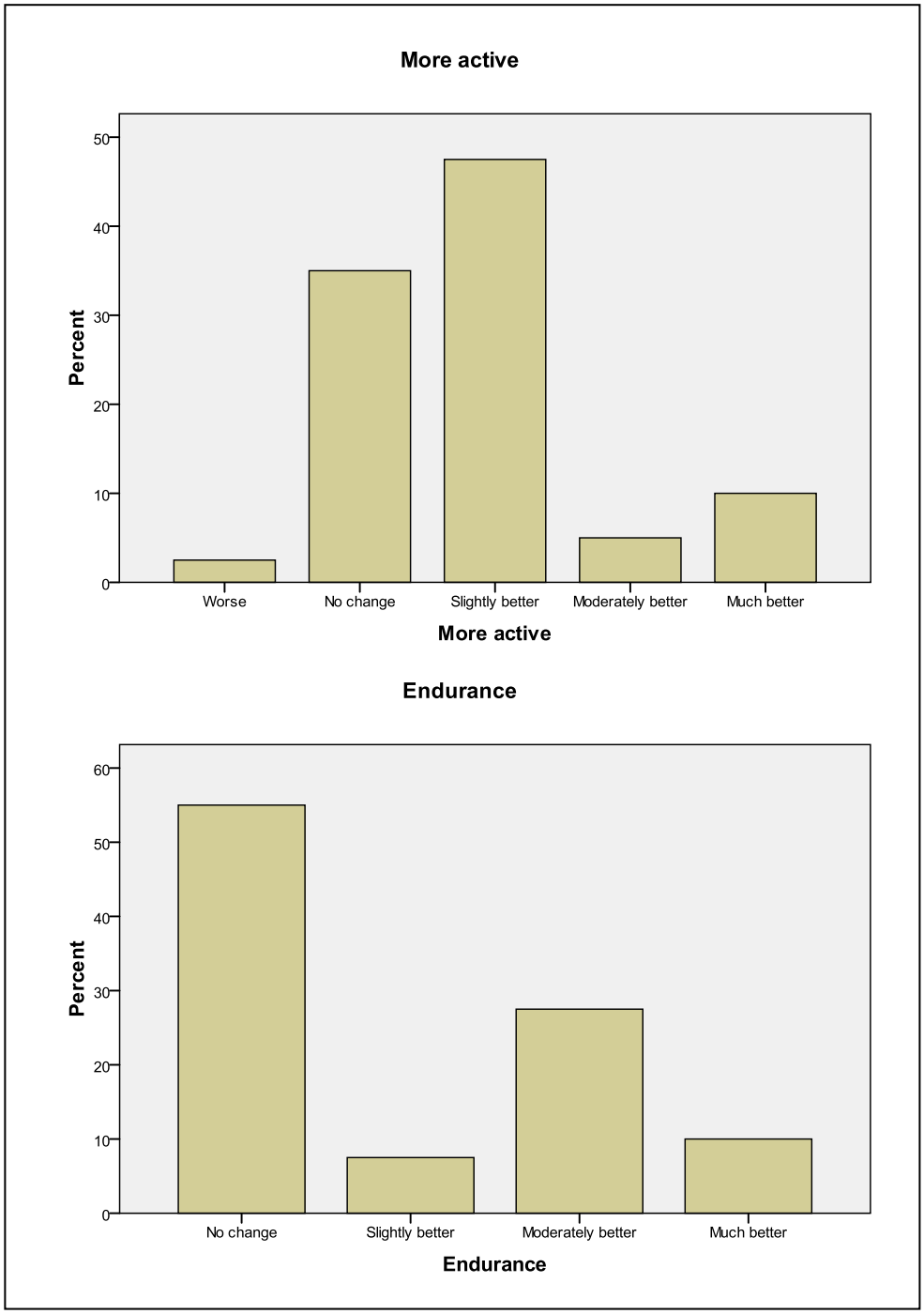


Figure 4.10 Self-assessment on performance

Subjects were asked to assessment body firmness and shape. 55% of subjected felt that their bodies were more firm which 83.8% could be noticed from the 4th week, while 6.5% noticed from the first week and 9.7% noticed from the second week of treatment.

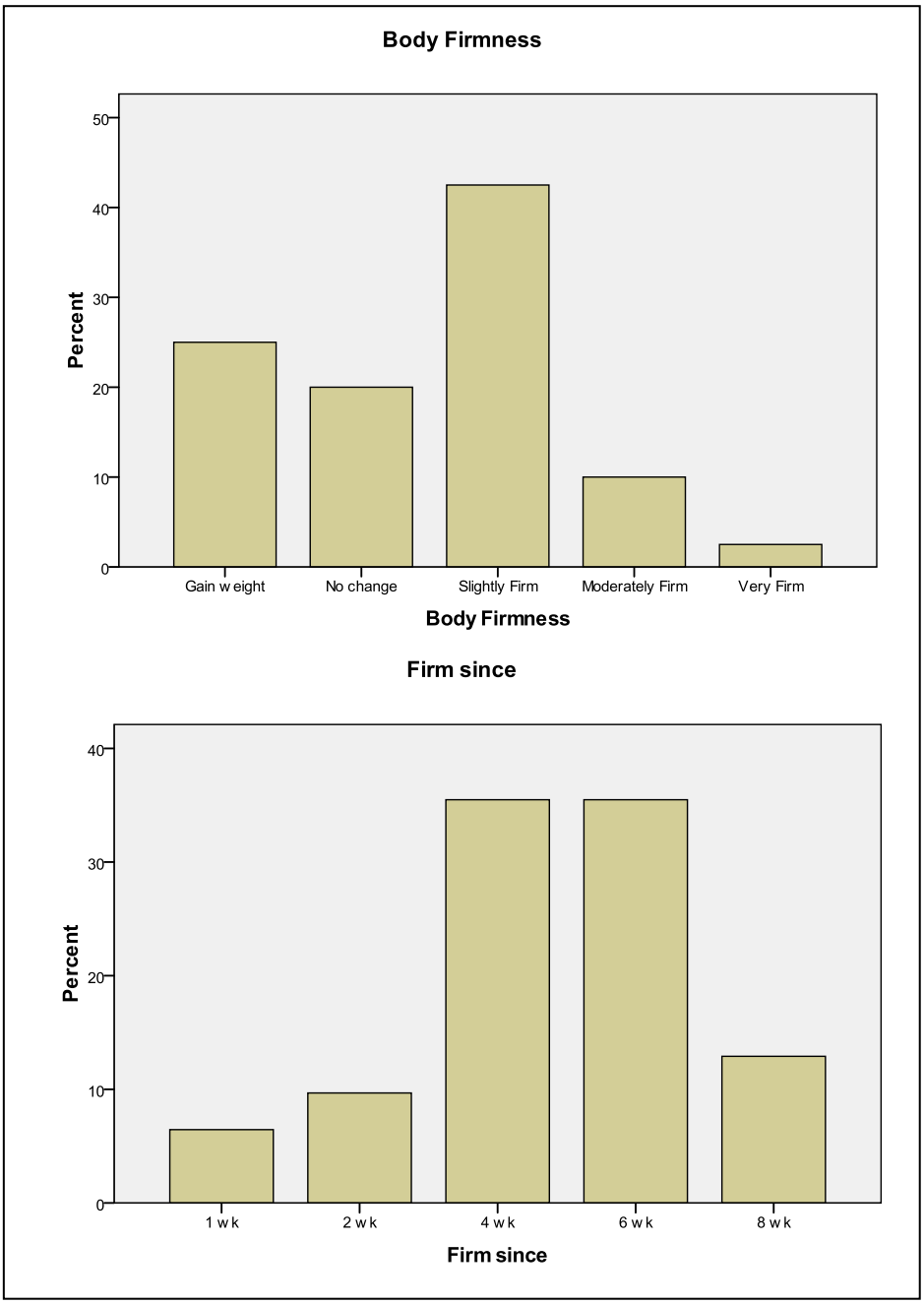


Figure 4.11 Self-assessment on body firmness

43.6% of subjects felt that they have smaller waist from slightly smaller to much smaller. Smaller waist could be felt from the second week of treatment in 96.4% of subjects.

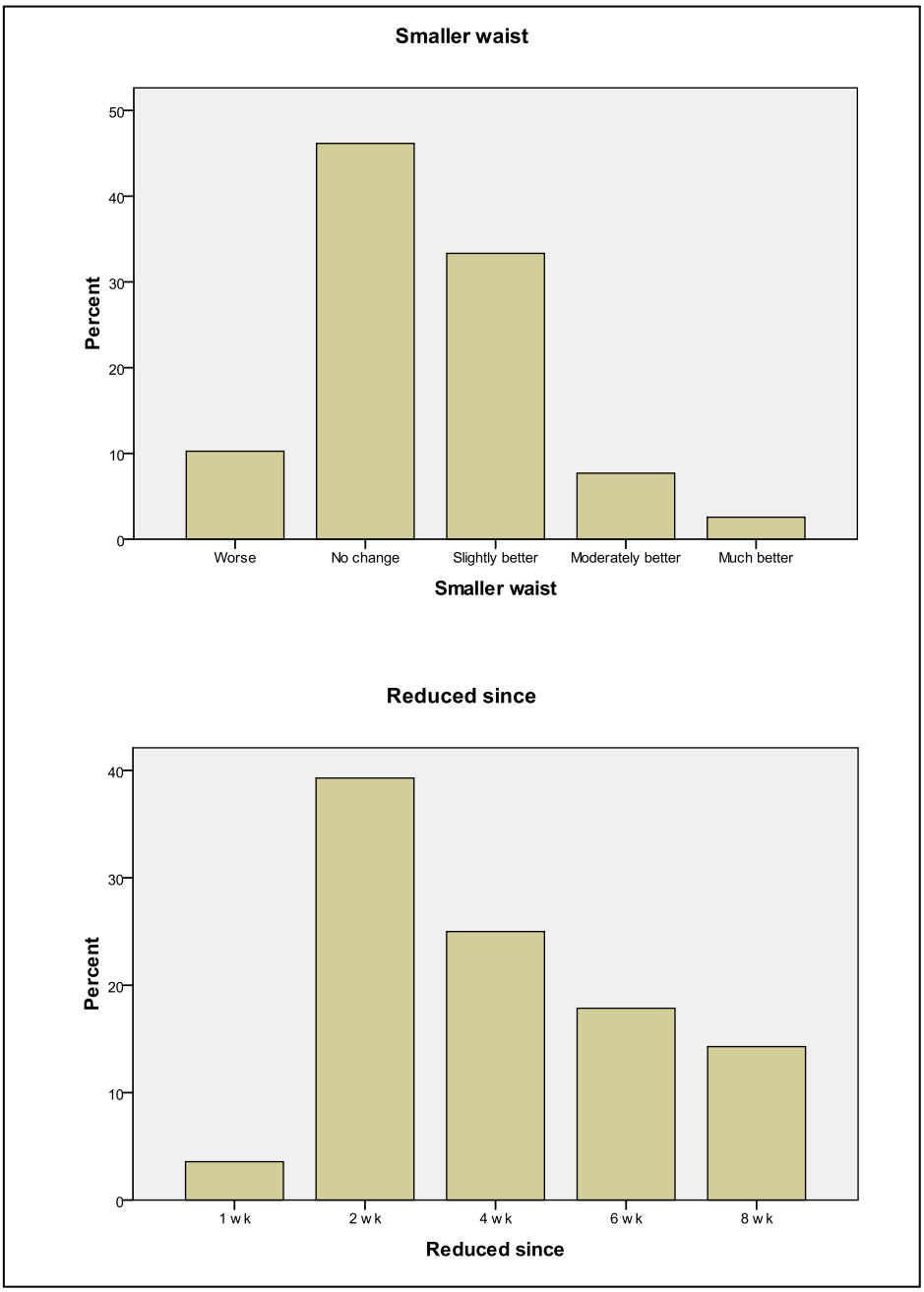


Figure 4.12 Self-assessment on waist size

62.5% of subjects reported elevated energy level, of which 77.4% of those who noticed elevated energy level could felt from the forth week of treatment, while 6.5% felt from the first week and 16.1% could felt from the second week.

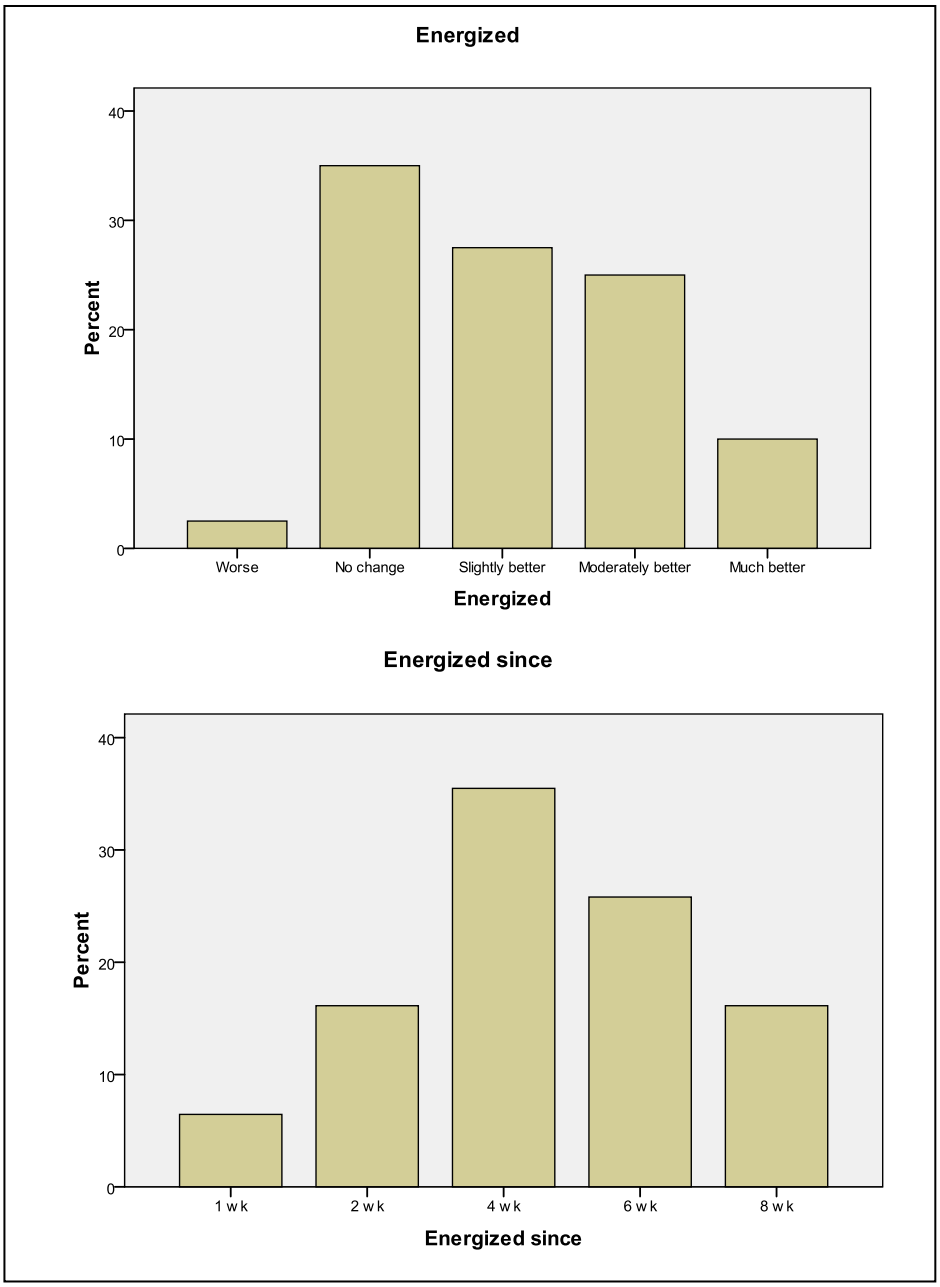


Figure 4.13 Self-assessment on effectiveness energy

Upon the questions whether subject would continue to take the supplement, 70% expressed the willingness to continue, and 20% answered that they might consider to continue.

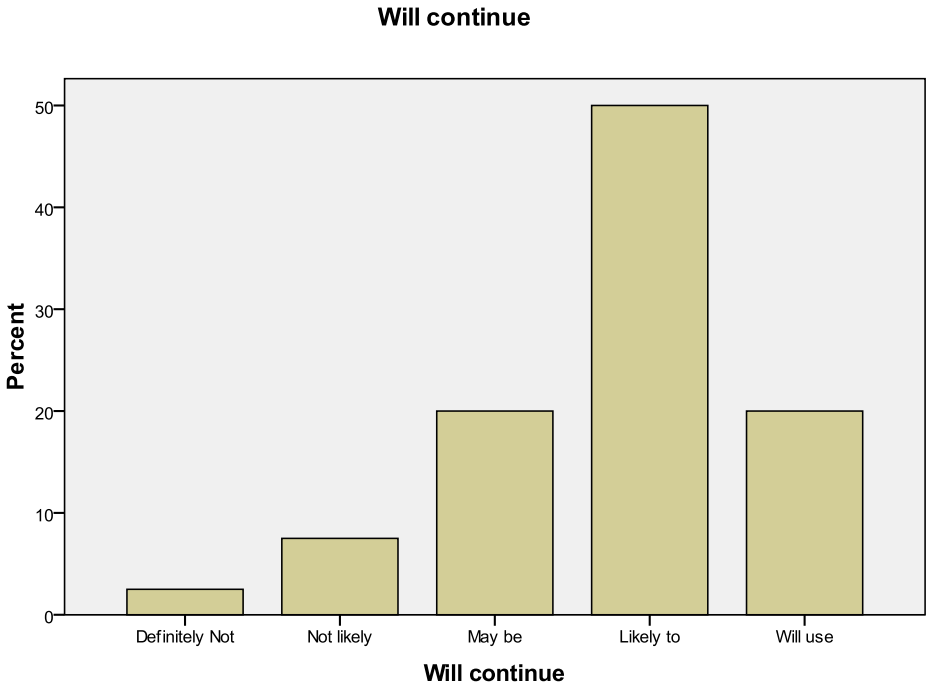


Figure 4.14 Subject willingness to continue to take the supplements

CHAPTER 5

CONCLUSION AND DISCUSSION

5.1 Discussion

Marine omega-3 had been demonstrated to promote higher lipid oxidation and reduced abdominal fat volume (Rossmeisl, 2009). It was also shown to prevent weight gain and glucose intolerance with the mechanism that might involve a metabolic switch in adipocytes which enhanced β-oxidation and upregulation of mitochondrial biogenesis (Flachs et al., 2005).

Our study in normal subject with body fat percentage level in the range between healthy borderline level to overfat and obese was conducted to compare the effect of marine omega-3 alone to the effect of marine omega-3 in combination with L-carnitine, given on a daily basis for eight weeks. Result of the study did not demonstrate statistically significant change in body fat percentage, weight or visceral fat mass before the treatment either with the marine omega-3 group or marine omega-3 in combination with L-carnitine group. There was also no statistically significant different in the degree of change between the two groups. Since subjects in the study were normal working people having normal lifestyle, the diet control could be an important factor that might affect the efficacy of the treatment given. However, it was the intention of the investigator to measure the effect of the two regimens of treatment in normal lifestyle. It was also noticeable that previous studies done on the lipid oxidation and reduction of body fat (Rossmeisl, 2009) or the prevention of weight gain by marine omega-3 (Flachs et al., 2005) were all conducted in animal model. The animal model study could provide better control on interfering environmental factors, especially diet and daily activities, so that measurement of the treatment result could be seen more precisely. In human study there can be more confounding factors such as diet control, daily time schedule and meal time and level of daily activities. Moreover, external environment might also affect the personal factors such as weather change, seasonal holidays which can greatly affecting

lifestyles and diet during the period. Since the purpose of this study was to compare the effect of omega-3 versus omega-3 in combination with L-carnitine, no placebo control group was assigned. It might be interesting to see how placebo group would respond to the same regimen in the same period of study, as there were quite a number of seasonal holidays during the study which might affect the body fat percentage and weight directly.

Despite the non-significant different in the objective measurement on body fat percentage and weight change in the two groups of subjects, self-assessment questionnaire revealed interesting feeling and perception of the subjects towards treatment received. Strong response on body change, body firmness (55% response with 83.8% felt from 4th week) and waist reduction (43.6% response with 96.4% felt from 2nd week), as well as the response on performance, feel more active (63.5% more active, 45% better endurance), energized (62.5% more energized 83.8% noticed from the 4th week), could lead to further study in a controlled environment. The contradicting response on appetite (45% better appetite, 12.8% loss appetite) could also lead to further investigation on appetite effect that could be caused by the action omega-3 and L-carnitine individually. The overall satisfaction especially the willingness to continue, 90% overall, could demonstrate subjects attitude towards the treatment received as strongly positive and could be viewed as safe.

Human research on the effect of marine omega-3 were shown to increase basal fat oxidation and negatively impact BMI in obese women under controlled environment, being inpatient and consumed very low carolie diet (Kunesova et al., 2006). These studies suggested that long-chain omega-3 fatty acid could induce weight loss in obese female treated with very low carolie diet. Omega-3 fish oils was also shown to decrease TNF-α production in heart failure patient and also improve body weight at the same time (Mehra et al., 2006)

Omega-3 was known to be quite safe to use as dietary supplement. Finding from this study, based on self-assessment questionnaire, showed that adverse reaction were relatively low to none. The adverse reactions found were of no serious concern. Reported adverse reaction included nausea, fishy smell, oily skin and hair, palpitation, constipation and loose stool. The incidences of these adverse reactions were not different between the two groups in the study, leading to the implication that these effects, if it was from the treatment, might be from omega-3 rather than L-carnitine. Previous studies and reviews on omega-3 also showed that side effects were uncommon but might include a fishy aftertaste and gastrointestinal disturbances such as nausea, bloating, and belching

(Zatsick & Mayket, 2007). L-carnitine administration in humans had been reported to cause very few side effects. In studies that involved doses as high as 15 g daily, research reported excellent tolerance and only occasional gastric upset and diarrhea. When 2 g of L-carnitine was administered for one year to more than 4,000 patients, the incidence of gastric upset, nausea, and diarrhea was 6 percent, 5 percent, and 2 percent, respectively (Maher, 2001).

The effect of L-carnitine when added to omega-3 had not been clearly indicate from this study result as there was no significant difference between the two groups in the study. A similar result was reported in a study on the effect of carnitine on fat oxidation and body composition showing that carnitine induce fat oxidation, while the body composition parameters, Body Fat Mass, Total Body Water, Lean Body Mass and Body Weight remained unchanged. (Wutzke & Lorenz, 2004).

5.2 Conclusion

This study had not shown different effect of marine omega-3 comparing to omega-3 plus L-carnitine in body fat percentage and weight. Neither had the effect been observed in each group of treatment when comparing before and after the study. While omega-3 and L-carnitine were still commonly used for various heatlh benefit, more study might be needed to demonstrated the benefit of omega-3 in human body fat reduction. Environmental interference might be one of the concerned factors, which lead to suggestion on tight environmental control and behavioral control in future study of such effect. Despite the non-significant objective measurement, subject's satisfaction and self-assessment were quite positive on the effectiveness of the treatment. With such response, a double blind, placebo control study was also suggested for further study.

REFERENCES

REFERENCES

Arduini, A., Bonomini, M., Savica, V., Amato, A. & Zammit, V. (2008). Carnitine in metabolic disease: Potential for pharmacological intervention. **Pharmacology & Therapeutics, 120**(2), 149-156.

Bach, A. C., Schirardin, H., Sihr, M. O. & Storck, D. (1983). Free and total carnitine in human serum after oral ingestion of L-carnitine. **Diabet Metab, 9**(2), 121-124.

Breslow, J. (2006). N-3 fatty acids and cardiovascular disease. **Am J Clin Nutr, 83**(6), 1477S-1482S.

Broderick, T. L., Qunney, H. S. & Lopaschuk, G. D. (1992). Carnitine stimulation of glucose oxidation in the fatty acid perfused isolated working rat heart. **J Biol Chem, 267**(6), 3758-3763.

Brodie, D., Moscrip, V. & Hutcheon, R. (1998). Body composition measurement: A review of hydro densitometry, anthropometry, and impedance methods. **Nutrition, 14**(3), 296-310.

Calder, P. C. (2008). The 2008 ESPEN Sir David Cuthbertson lecture: Fatty acids and inflammation - from the membrane to the nucleus and from the laboratory bench to the clinic. **Clinical Nutrition, 29**(1), 5-12.

Clandinin, M. T., Jumpsen, J. & Suh, M. (1994). Relationship between fatty acid accretion, membrane composition and biologic functions. **J Pediatr, 125**(5 Pt 2), S25-S32.

Deckelbaum, R. J., Leaf, A., Mozaffarian, D., Jacobson, T. A., Harris, W. S. & Akabas, S. R. (2008). Conclusions and recommendatinos from the symposium, beyond cholesterol: Prevention and treatment of coronary heart disease with omega-3 fatty acids. **Am J Clin Nutr, 87**(6), 2010-2012.

Derosa, G., Cicero, A. F. G., Gaddi, A., Mugellini, A., Ciccarelli, L. & Fogari, R. (2003). The effect of -carnitine on plasma lipoprotein(a) levels in hypercholesterolemic patients with type 2 diabetes mellitus. **Clinical Therapeutics, 25**(5), 1429-1439.

Eslick, G. D., Howe, P. R. C., Smith, C., Priest, R. & Bensoussan, A. (2009). Benefits of fish oil supplementation in hyperlipidemia: A systematic review and meta-analysis. **Int J Cardio, 136**(1), 4-16.

Flachs, P., Horakova, O., Brauner, P., Rossmeisl, M., Pecina, P., Franssen-Van Hal, N., Ruzickova, J., Sponarova, J., Drahota, Z., Vlcek, C., Keijer, J., Houstek, J. & Kopecky, J. (2005). Polyunsaturated fatty acids of marine origin upregulate mitochondrial biogenesis and induce [beta]-oxidation in white fat. **Diabetologia, 48**(11), 2365-2375.

Food & Drug Administration. (2004). **What you need to know about mercury in fish and shellfish?.** Retrieved July 1, 2010, from http://www.fda.gov/food/foodsafety/product-specificinformation/seafood/foodbornepathogenscontaminants/methylmercury/ucm115662.htm

Foran, S. E., Flood, J. G. & Lewandrowski. K. B. (2003). Measurement of mercury levels in concentrated over-the-counter fish oil preparations: Is fish oil healthier than fish?. **Arch Pathol Lab Med, 127**(12), 1603-1605.

Fritz, I. B. (1959). Action of carnitiine on long-chain fatty acid oxdation by liver. **Am J Physiol, 197**(2), 297-304.

Garolla, A., Maiorino, M., Roverato, A., Roveri, A., Ursini, F. & Foresta, C. (2005). Oral carnitine supplementation increases sperm motility in asthenozoospermic men with normal sperm phospholipid hydroperoxide glutathione peroxidase levels. **Fertility and Sterility, 83**(2), 355-361.

Goyens, P. L. & Mensink, R. P. (2006). Effects of alpha-linolenic acid vs those of EPA/DHA on cardiovascular risk markers in healthy elderly subjects. **Eur J Clin Nutr, 60**(8), 978-984.

Grimsgaard, S., Bonaa, K. H., Hansen, J. B. & Nordoy, A. (1997). Highly purified eicosapentaenoic acid and docosahexaenoic acid in humans have similar triacylglycerol-lowering effects but divergent effects on serum fatty acids. **Am J Clin Nutr, 66**(3), 649-659.

Haeckel, R., Kaiser, E., Oellerich, M. & Siliprandi, N. (1990). Carnitine: Metabolism function and clinical implication. **J Clin Chem Clin Metab, 28**, 291-295.

Hamilton, J. W., Li, B. U., Shug, A. L. & Olsen, W. A. (1986). Carnitine transport in human intestinal biopsy specimens. **Gastroenterology, 91**(1), 10-16.

Harris, W. S., Kris-Etherton, P. M. & Harris, K. A. (2008). Intake of long-chain fatty acids associated with reduced risk for death from coronary heart disease in healthy adults. **Curr. Atheroscler. Rep, 10**(6), 503-509.

Harris, W. S. (2007). Expert opinion: Omega-3 fatty acids and bleeding--cause for concern?. **The American Journal of Cardiology, 99**(6, Supplement 1), S44-S46.

Hathcock, J. N. & Shao, A. (2006). Risk assessment for carnitine. **Regulatory Toxicology and Pharmacology, 46**(1), 23-28.

Hirsch, J., Farquhar. J., Ahrens, E. H. Jr., Peterson, M. L. & Stoffel, W. (1960). Studies of adipose tissue in man. A microtechinc for sampling and analysis. **Am J Clin Nutr, 8**, 499-511.

Hodson, L., Skeaff, C. M. & Fielding, B. A. (2008). Fatty acid composition of adipose tissue and blood in humans and its use as a biomarker of dietary intake. **Progress in Lipid Research, 47**(5), 348-380.

Hoppel, C. (2003). The role of carnitine in normal and altered fatty acid metabolism. **American Journal of Kidney Diseases, 41**(Supplement 4), S4-S12.

Hibbeln, J. R., Nieminen, L. R., Blasbalg, T. L., Riggs, J. A. & Lands, W. E. (2006). Healthy intake of omega-3 and omega-6 fatty acids: Estimations consdering worldwide diversity. **Am J Clin Nutr, 83**(6), 1483-1493.

Jensen, M. (2002). Adipose tissue and fatty acid metabolism in humans. **J Royal Soc Med 95**(42), 3-7.

Kalaiselvi, T. & Panneerselvam, C. (1998). Effect of l-carnitine on the status of lipid peroxidation and antioxidants in aging rats. **The Journal of Nutritional Biochemistry, 9**(10), 575-581.

Kris-Etherton, P. M., Harris, W. S. &Appel, L. J. (2003). Fish consumption, fish oil, omega-3 fatty acids and cardiovascular disease. **Arterioscler Thromb Vasc Biol, 23**, 20-30.

Kris-Etherton, P. M., Grieger, J. A. & Etherton, T. D. (2009). Dietary reference intakes for DHA and EPA. **Prostaglandins, Leukotrienes and Essential Fatty Acids, 81**(2-3), 99-104.

Kunesova, M., Braunerova, R., Hlavaty, P., Tvrzicka, E., Stankova, B., Skrha, J., Hilgertova, J., Hill, M., Kopecky, J., Wagenknecht, M., Hainer, V., Matoulek, M., Parizkova, J., Zak, A. & Svacina S. (2006). The influence of n-3 polyunsaturated fatty acids and very low calorie diet during a short-term weight reducing regimen on weight loss and serum fatty acid composition in severely obese women. **Physiological Research, 55**(1), 63-72.

Lavie, C. J., Milani, R. V., Mehra, M. R. & Ventura, H. O. (2009). Omega-3 polyunsaturated fatty acids and cardiovascular diseases. **Journal of the American College of Cardiology, 54**(7), 585-594.

Leibovitz, B. E. (1998). **L-Carnitine: The energy nutrient.** Los Angeles: Keats Publishing.

Maher, T. J. (2001). L-Ccarnitine. In M. C. o. P. a. h. Sciences (Ed.), **Natural healing track** (p. 8). Maryland: The NIH campus.

Mehra, M. R., Lavie, C. J., Ventura, H. O. & Milani, R. V. (2006). Fish oils produce anti-inflammatory effects and improve body weight in severe heart failure. **The Journal of Heart and Lung Transplantation, 25**(7), 834-838.

Mohamed-Ali, V., Pinkney, J. H. & Coppack, S. W. (1998). Adipose tissue as an endocrine and paracrine organ. **Int J Obes Relat Metab Disord, 22**(12), 1145-1148.

Mori, T. A., Burke, V., Puddey, I. B., Watts, G. F., O'Neal, D. N., Best, J. D. & Beilin, L. J. (2000). Purified eicosapentaenoic and docosahexaenoic acids have differential effects on serum lipid and lipoproteins, LDL particle size, glucose, and insulin in mildly hyperlipidemic men. **Am J Clin Nutr, 71**(5), 1085-1094.

Mozaffarian, D. & Rimm, E. B. (2006). Fish intake, contaminants, and human health: evaluating the risks and the benefits. **JAMA, 296**(15), 1885-1899.

Muller, D. M., Seim, H., Kiess, W., Loster, H. & Richter, T. (2002). Effects of oral L-carnitine supplementation on in-vivo long-chain fatty acid oxidation in healthy adults. **Metabolism, 51**(11), 1389-1399.

Murase, T., Aoki, M. & Tokimitsu, I. (2005). Supplementation with [alpha]-linolenic acid-rich diacylglycerol suppresses fatty liver formation accompanied by an up-regulation of [beta]-oxidation in Zucker fatty rats. **Biochimica et Biophysica Acta (BBA) - Molecular and Cell Biology of Lipids, 1733**(2-3), 224-231.

Passwater, R. A. (1987). **Fish oil update.** New Canaan: Keats Publishing.

Riediger, N. D., Othman, R. A., Suh, M. & Moghadasian, M. H. (2009). A systemic review of the Rroles of n-3 fatty Acids in health and disease. **Journal of the American Dietetic Association, 109**(4), 668-679.

Rossmeisl, M. (2009). Obesity and diabetes; new findings reported from M. Rossmeisl and co-authors describe advances in obesity and diabetes. **Health Risk Factor Week,** p. 411.

Schwellenbach, L. J., Olson, K. L., McConnell, K. J., Stolcpart, R. S., Nash, J. D. & Merenich, J. A. (2006). The triglyceride-lowering effects of a modest dose of docosahexaenoic acid alone vs in combination with low dose eicosapentaenoic acid in pateients with coronary artery disease and elevated triglycerides. **J Am Coll Nutr, 25**(6), 480-485.

Simopoulos, A. P. (2002). The importance of the ratio of omega-6/omega-3 essential fatty acids. **Biomedecine & Pharmacotherapy, 56**(8), 365-379.

Simopoulos, A. P. (1999). Essential fatty acids in health and chronic disease. **Am J Clin Nutr, 70**(3), 560S-569S.

Steiber, A., Kerner, J. & Hoppel, C. L. (2004). Carnitine: A nutritional, biosynthetic, and functional perspective. **Molecular Aspects of Medicine, 25**(5-6), 455-473.

Strawford, A., Antelo, F., Christiansen, M. & Hellerstein, M. K. (2004). Adipose tissue triglyceride turnover, de novo lipogenesis and cell proliferation in humans measured with $2H_2O$. **Am J Physiol Endocrinol Metab, 286**(4), E577-E588.

Tanita, C. (2008). **Technical notes.** Tokyo: Tanita corporation.

Vaz, F. M., van Gool, S., Ofman, R., Ijlst, L. & Wanders, R. J. (1998). Carnitine biosynthesis: Identification of the cDNA encoding human [gamma]-butyrobetaine hydroxylase. **Biochemical and Biophysical Research Communications, 250**(2), 506-510.

Wahlqvist, M. L., Hodgson, J. M., Ng, F. M., Hsu-Hage, B. H-H. & Strauss, B. J. G. (1999). The role of nutrition in abdominal obesity. **Nutrition Research, 19**(1), 85-101.

Wutzke, K. D. & Lorenz, H. (2004). The effect of L-carnitine on fat oxidation, protein turnover, and body ompostionon in slightly over weight subjects. **Metabolism, 53**(8), 1002-1006.

Zatsick, N. M. & Mayket, P. (2007). Fish oil: Getting to the heart of it. **The Journal for Nurse Practitioners, 3**(2), 104-109.

APPENDIXS

APPENDIX A

INFORMED CONSENT FORM

หนังสือให้ความยินยอมเข้าร่วมในโครงการวิจัย

เขียนที่.....

วันที่.....

ข้าพเจ้า.....อายุ.....ปี อยู่บ้านเลขที่..... ถนน.....หมู่ที่.....
แขวง/ตำบล.....เขต/อำเภอ.....จังหวัด.....

ขอทำหนังสือนี้ให้ไว้ต่อหัวหน้าการวิจัยเพื่อเป็นหลักฐานแสดงว่า

ข้อ 1 ข้าพเจ้าได้รับทราบถึงโครงการวิจัยของ นาย กานต์ วงศ์ศุภสวัสดิ์ และ คณะ เรื่องการศึกษาประสิทธิผลการเผาผลาญไขมันสะสมจากการใช้ มารีน โอเมก้า-3 และ แอล คาร์นิทีน เทียบกับมารีน โอเมก้า-3ในคนที่มีไขมันมวลรวมสูงกว่าปรกติ

ข้อ 2 ข้าพเจ้าได้รับการอธิบายเกี่ยวกับวัตถุประสงค์ วิธีการวิจัยถึงประสิทธิภาพความปลอดภัย อาการหรืออันตรายที่อาจเกิดขึ้นรวมทั้งประโยชน์ที่จะได้รับจากการวิจัยโดยละเอียดแล้ว

ข้อ 3 ข้าพเจ้าได้รับรองจากผู้วิจัยจะเก็บข้อมูลส่วนตัวของผู้ถูกทำวิจัยเป็นความลับจะเปิดเผยเฉพาะผลสรุปเท่านั้น

ข้อ 4 ข้าพเจ้าได้รับทราบจากผู้วิจัยแล้วว่าหากมีอันตรายใดอันเกิดขึ้นจากการวิจัยดังกล่าว ผู้ถูกทำการวิจัยจะได้รับการรักษาพยาบาลโดยไม่มีค่าใช้จ่าย

ข้อ 5 ข้าพเจ้าได้รับทราบว่ามีสิทธิในการบอกเลิกการร่วมโครงการวิจัยนี้ และไม่มีผลกระทบต่อการดูแลรักษาที่จะพึงได้รับต่อไป

ข้อ 6 ผู้ดำเนินการวิจัยได้อธิบายเกี่ยวกับรายละเอียดต่างๆประโยชน์ที่จะได้รับจากการวิจัย รวมทั้งความเสี่ยงที่อาจเกิดขึ้นให้ได้รับทราบ

ข้อ 7 ข้าพเจ้ายินดี เข้าร่วมการวิจัยนี้ ตามเงื่อนไขและวิธีการที่กำหนดและชี้แจงแล้วโดยผู้ดำเนินการวิจัยโดยไม่มีข้อเรียกร้องอื่นใด

ข้าพเจ้าได้อ่านและเข้าใจข้อความในหนังสือนี้ทั้งหมดแล้วเห็นว่าถูกต้องตามเจตนาของข้าพเจ้า จึงได้ลงลายมือชื่อไว้เป็นสำคัญพร้อมหัวหน้าโครงการวิจัยและต่อหน้าพยาน

ลงชื่อ..... ลงชื่อ.....

(.....) (.....)

ผู้ยินยอม หัวหน้าโครงการวิจัย

ลงชื่อ..... ลงชื่อ.....

(.....) พยาน (.....) พยาน

APPENDIX B

PATIENT RECORD FORM

Patient Record Form Omega-3 Fat Burn

แบบบันทึกข้อมูลโครงการวิจัย

เรื่อง ประสิทธผลการเผาผลาญไขมันสะสมจาการใช้ มารีนโอเมก้า-3 และแอล คาร์นิทีน เทียบกับ มารีนโอเมก้า-3 ในคนที่มีไขมันมวลรวมสูงกว่าปรกติ

ชื่อคนไข้ _____ **นามสกุล** _____ **HN**

วัน/เดือน/ปี เกิด _____ **เพศ** ☐ ชาย ☐ หญิง **SN**

ที่อยู่ เลขที่ _____ หมู่ / ซอย _____ อาคาร _____ ชั้น _____

ถนน _____ เขต/อำเภอ _____

แขวง/ตำบล _____ จังหวัด _____

โทรศัพท์ _____ โทรมือถือ _____

ประวัติแพ้ยา ☐ ไม่เคยแพ้ยา

☐ เคยแพ้ยา ได้แก่

โรคประจำตัว

สถานภาพ ☐ โสด ☐ สมรส ☐ หม้าย **จำนวนบุตร/ธิดา** _____ **คน**

การศึกษา ☐ มัธยม ☐ ปวช-ปวส ☐ ปริญญาตรี ☐ ปริญญาโท

☐ สูงกว่าป.โท ☐ อื่นๆ (โปรดระบุ) _____

อาชีพ ☐ นักศึกษา ☐ แม่บ้าน ☐ เกษียณ ☐ ข้าราชการ ☐ พนักงานบริษัท ☐ เจ้าของกิจการ

ใส่หมวกประจำ ☐ ใช่ ☐ ไม่ใช่

การดูแลเส้นผม ☐ ใช้แชมพูป้องกันผมร่วง

ความบ่อย ☐ทุกวัน ☐สัปดาห์ละ ครั้ง ☐ อื่นๆ _____

☐ ใช้ Conditioner หรือ Rinsing

ความบ่อย ☐ทุกวัน ☐สัปดาห์ละ ครั้ง ☐ อื่นๆ _____

☐ ทำทรีทเมนต์เส้นผม (Hair treatment)

ความบ่อย ☐ทุกวัน ☐สัปดาห์ละ ครั้ง ☐ อื่นๆ _____

วิธีสระผม ☐ สระเอง ☐ ไปร้านสระผม

เคยใช้ยารักษาผมร่วง ☐ ไม่เคย

☐ เคย ใช้ยา 1 _____ ใช้ครั้งสุดท้ายเมื่อ _____

2 _____ ใช้ครั้งสุดท้ายเมื่อ _____

3 _____ ใช้ครั้งสุดท้ายเมื่อ _____

ประวัติครอบครัว มีสมาชิกครอบครัวที่มีปัญหาโรคอ้วน เบาหวาน หรือ โรคหัวใจต่อไปนี้

☐ พ่อ ☐ แม่ ☐ พี่-น้อง

☐ อื่นๆ _____

น้ำหนักคนไข้ กก.	**ส่วนสูง** ซม.	**อายุ** ปี

โรคเกี่ยวกับ metabolic ที่เคยเป็น _____

Patient Record Form Omega-3 Fat Burn

T 0	จำนวนยาที่เหลือ	
วันที่	A แคปซูล	B เม็ด
	รับยาเพิ่ม ชุด	
General assessment		
		By

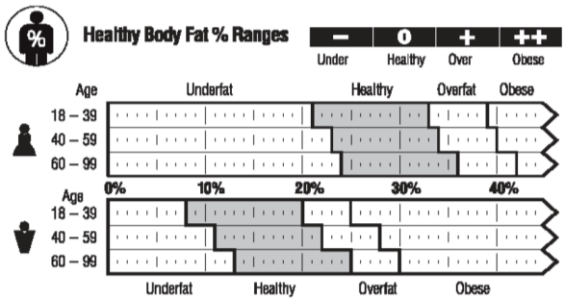
T 1	จำนวนยาที่เหลือ	
วันที่	A แคปซูล	B เม็ด
	รับยาเพิ่ม ชุด	
Safety & Tolerance ☐ ปรกติดี ไม่แพ้	มีอาการแพ้ ☐ เล็กน้อย ☐ ปานกลาง ☐ มาก-แพ้รุนแรง	☐ อื่นๆ
รายงานการใช้ยาโดยคนไข้	การรับประทาน	
	Side effect	
	Other	
General assessment		
		By

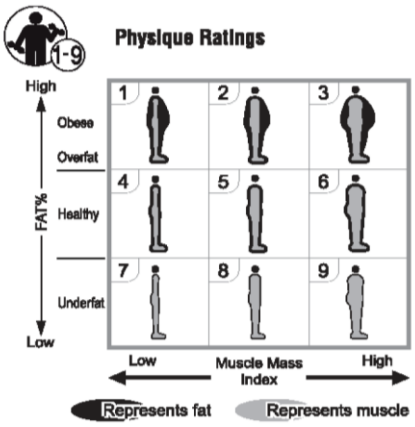
T 2	จำนวนยาที่เหลือ	
วันที่	A แคปซูล	B เม็ด
	รับยาเพิ่ม ชุด	
Safety & Tolerance ☐ ปรกติดี ไม่แพ้	มีอาการแพ้ ☐ เล็กน้อย ☐ ปานกลาง ☐ มาก-แพ้รุนแรง	☐ อื่นๆ
รายงานการใช้ยาโดยคนไข้	การรับประทาน ☐	
	Side effect ☐	
	Other	
General assessment		
		By

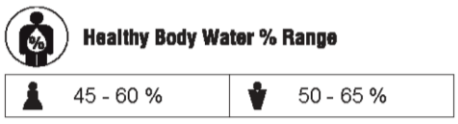
Patient Record Form

Omega-3 Fat Burn

	DATE	TIME	Weight	Body Fat %	Body Water %	Muscle Mass	Physique Rating	Bone Mass	DCI / BMR	Metabolic Age	Visceral Fat
T0											
T1											
T2											







Bone Mass Ranges

Average of estimated bone mass (lb)

	Weight		
	Less than 110 lb	110 lb - 165 lb	165 lb and up
	4.3 lb	5.3 lb	6.5 lb
	Less than 143 lb	143 lb - 209 lb	209 lb and up
	5.9 lb	7.3 lb	8.1 lb

Visceral Fat Rating

Healthy level	0	1 - 12
Excess level	+	13 - 59

Project Completion	การประเมินผลโดยคนไข้	☐ ทำเรียบร้อยแล้ว
	ค่าตอบแทนอาสาสมัคร	☐ จ่ายแล้ว

APPENDIX C

% BODY FAT COMPOSITION TABLE

Body fat percentage is the amount of body fat as a proportion of your body weight.
Reducing excess levels of body fat has shown to reduce the risk of certain conditions such as high blood pressure, heart disease,diabetes and cancer. The chart below shows the healthy ranges for body fat.

Body Fat Ranges for Standard Children [1]
Body Fat Ranges for Standard Adults [2]

[1] *Susan Jebb et al. Obesity Research[o2] 2004;12:A156-157 "New Body Fat Reference Curves for children"*

[2] *Gallagher D et al. Am J Clin Nutr 2000;72:694-701. "Healthy percentage body fat ranges:an approach for developing guidelines based on body mass index."*

APPENDIX D

SELF-ASSESSMENT QUESTIONNAIRE

แบบประเมินหลังการใช้ยา

แบบประเมินหลังการใช้ยา / การรักษา

HN | SN

สำหรับผู้ที่ร่วมศึกษาผลการใช้มาเป็นเวลา **8** สัปดาห์ (2 เดือน) ยาหมายเลข | วันที่

ได้รับยา ☐ 1 ชนิด ☐ 2 ชนิด

ส่วนที่ 1 ความเห็นเกี่ยวกับลักษณะผลิตภัณฑ์

กรุณาทำเครื่องหมาย ☑ ในช่องที่ตรงกับความเห็นของท่าน
ท่านเห็นด้วยหรือไม่ กับคุณสมบัติ ในข้อต่อไปนี้

		ไม่ เห็นด้วย	ไม่ค่อยเห็นด้วย	เห็นด้วยเล็กน้อย	เห็นด้วย
1	ยาที่ได้รับ รับประทานง่าย				
2	ยาที่ได้รับ พกสะดวก				

	หลังรับประทานยาแล้ว ข้าพเจ้ามีอาการต่อไปนี้	ไม่เป็นเลย	เล็กน้อย	ปานกลาง	มาก
3	คลื่นไส้				
4	มีกลิ่นคาวเมื่อหายใจออก				
5	ท้องผูก				
6	อุจจาระเหลว				
7	ร้อนวูบวาบ				
8	ผื่นขึ้น				
9	เบื่ออาหาร				
10	ผิวมัน ผมมัน				
11	อาเจียร				
12	อยากอาหารมากขึ้น				
13	คัน				
14	ปวดศีรษะ				
15	ใจสั้น				

ส่วนที่ 2 ความเห็นเกี่ยวกับยาที่ใช้รักษา

กรุณาทำเครื่องหมาย ☑ ในช่องที่ตรงกับความเห็นของท่าน

B1	ฉันรู้สึกได้ว่ายาที่ได้รับทำให้ เริ่มรู้สึกว่ารูปร่างกระชับขึ้น	อ้วนมากขึ้น	ไม่เปลี่ยนแปลง	รูปร่างกระชับเล็กน้อย	รูปร่างกระชับปานกลาง	รูปร่างกระชับขึ้นมาก
B2	ฉันรู้สึกได้ว่ายาที่ได้รับทำให้ เริ่มรู้สึกรูปร่างกระชับขึ้น ตั้งแต่ เมื่อไร	ใน 1 สัปดาห์	ใน 2 สัปดาห์	ใน 4 สัปดาห์	ใน 6 สัปดาห์	ใน 8 สัปดาห์
B3	ฉันรู้สึกได้ว่ายายาที่ได้รับทำให้ ทำกิจกรรมคล่องแคล่วขึ้น อืดอัดน้อยลง	อืดอัดมากขึ้น	เหมือนเดิม	อืดอัดน้อยลงเล็กน้อย	อืดอัดน้อยลงปานกลาง	อืดอัดน้อยลงมาก
B4	ฉันรู้สึกได้ว่ายาที่ได้รับทำให้ ทำงานได้ทน นานขึ้น เหนื่อยช้าลง	ไม่ทนงานขึ้นเลย	ไม่เปลี่ยนแปลง	ทนงานเล็กน้อย	ทนงานปานกลาง	ทนงานขึ้นมาก
B5	ฉันรู้สึกว่ายาที่ได้รับ ทำให้ รอบเอวบางลง	รอบเอวใหญ่ขึ้น	ไม่เปลี่ยนแปลง	เอวบางลงเล็กน้อย	เอวบางลงปานกลาง	เอวบางลงมาก
B6	ฉันสังเกตุได้ว่ายาที่ได้รับ ทำให้ เอวเริ่มบางลง ตั้งแต่เมื่อไร					

แบบประเมินหลังการใช้ยา

	ใน 1 สัปดาห์	ใน 2 สัปดาห์	ใน 4 สัปดาห์	ใน 6 สัปดาห์	ใน 8 สัปดาห์
B7 ฉันรู้สึกได้ว่ายาที่ได้รับทำให้ มีความกระปรี้กระเปร่าขึ้น					
	แย่ลง	เหมือนเดิม	ดีขึ้น เล็กน้อย	ดีขึ้น ปานกลาง	ดีขึ้น มาก
B8 ฉันสังเกตุได้ว่ายาที่ได้รับทำให้ กระปรี้กระเปร่าขึ้น ตั้งแต่เมื่อไร					
	ใน 1 สัปดาห์	ใน 2 สัปดาห์	ใน 4 สัปดาห์	ใน 6 สัปดาห์	ใน 8 สัปดาห์

ส่วนที่ 3 ความเห็นทั่วไปเกี่ยวกับการรักษา

กรุณาทำเครื่องหมาย ☑ ในช่องที่ตรงกับความเห็นของท่าน

C1 โดยรวมแล้ว ฉันมีความพอใจกับการรักษานี้...เพียงใด					
	ไม่พอใจ อย่างยิ่ง	ไม่ค่อย เล็กน้อย	เฉยๆ	พอใจ เล็กน้อย	พอใจมาก
C2 ฉันเริ่มรู้สึกว่า เห็นผลจากการใช้ตั้งแต่...เมื่อใด					
	ใน 1 สัปดาห์	ใน 2 สัปดาห์	ใน 4 สัปดาห์	ใน 6 สัปดาห์	ใน 8 สัปดาห์
C3 ฉันคิดว่า ผลรวมของยาที่ได้รับเป็น..อย่างไร					
	อ้วนมาก ขึ้น	ไม่เปลี่ยน แปลง	รูปร่าง กระชับ เล็กน้อย	รูปร่าง กระชับ ปานกลาง	รูปร่าง กระชับ ขึ้นมาก
C4 ถ้าคะแนนเต็มคือ 10 คะแนน ฉันจะให้คะแนนการรักษานี้ เท่าใด			(กรุณาเติมตัวเลขคะแนน ในช่อง)		
C5 ฉันคิดว่า ต่อไปจะใช้ยาที่ได้รับนี้ต่อไป..หรือไม่					
	ไม่ใช้	ไม่น่าจะใช้	เฉยๆ	คิดว่า น่าจะใช้	ใช้ แน่นอน

D1 ความเห็นต่อผลิตภัณฑ์ที่ฉันได้ใช้ เกี่ยวกับคุณสมบัติต่อไปนี้อย่างไร	ไม่ เห็นด้วย	เฉยๆ	เห็นด้วย เล็กน้อย	เห็นด้วย อย่างยิ่ง
มีประสิทธิภาพ ใช้ได้ผล				
เห็นผลเร็ว				
รับประทานง่าย				
ให้ความรู้สึกที่ดี เมื่อใช้				
ปลอดภัย / ไม่แพ้				

ส่วนที่ 4 ข้อมูลพื้นฐาน

กรุณาทำเครื่องหมาย ☑ ลงในช่องสี่เหลี่ยมที่ท่านคิดว่าตรงกับคำตอบที่ท่านต้องการที่สุด หรือเติมข้อความในช่องว่าง

A เพศ ☐ หญิง ☐ ชาย

B อายุ ☐ ปี (เติมเลขอายุในช่อง)

C การศึกษา
☐ มัธยม ☐ ปริญญาโท
☐ ปวช-ปวส ☐ สูงกว่า ป. โท
☐ ปริญญาตรี ☐ อื่นๆ (โปรดระบุ) _____

D อาชีพ
☐ นักศึกษา ☐ เจ้าของกิจการ
☐ แม่บ้าน ☐ ข้าราชการ
☐ เกษียณ ☐ พนักงานบริษัท ☐ วิชาชีพอิสระ

E ตำแหน่งหน้าที่
☐ เจ้าของ ☐ ผู้จัดการ / หัวหน้างาน
☐ พนักงานชั่วคราว ☐ ผู้บริหารระดับสูง
☐ พนักงานประจำ ☐ ไม่ได้ทำงาน

F รายได้ส่วนตัวต่อเดือน (บาท)
☐ < 10,000 ☐ 10,001-20,000
☐ 20,001-40,000 ☐ 40,001-60,000 ☐ > 60,000

CURRICULUM VITAE

CURRICULUM VITAE

NAME	Mr. Karnt Wongsuphasawat
DATE OF BIRTH	17 September 1960
ADDRESS	17 Soi Yenjitr 6, Chan 24 Road, Sathorn, Bangkok 10120, Thailand.

EDUCATION BACKGROUND

1986	Master Degree in Business Administration, Thammasart University
1983	Bachelor Degree in Pharmaceutical Science, Chulalongkorn University

WORKING EXPERIENCE

2010-Present	Lecturer at School of Anti-Aging and Regenerative Medicine, Mae Fah Luang University
1996-2010	Executive Director-P&F-NutraMedica Group of Companies.
1994-1996	Managing Director-Dentsply (Thailand) Limited
1988-1994	Marketing Director-Upjohn Company Limited.

PUBLICATION

Karnt Wongsuphasawat, Tanattha Kittisopee, Samart Powpaka. (2008). The relative importance of store attributes on consumer's response towards drug store: The moderating effect of buying purpose. **Thai journal of Hospital Pharmacy, 18**(1),11-25.