# PROFESSORIAL INAUGURAL LECTURE SERIES

# FOOD IS OUR MEDICINE

**Professor Dr. Mohamad Roji Sarmidi**

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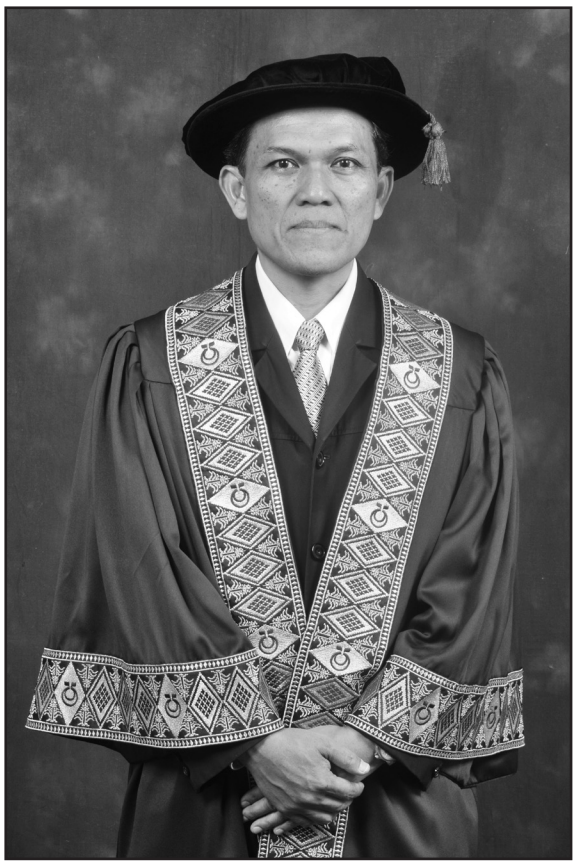

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*by*
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## INTRODUCTION

The paper describes the role of foods and nutrition in the promotion of human health. The relationship between foods, metabolism, homeostasis and metabolic disorders are briefly described. The aim of the paper is to highlight a simple strategy based on biochemistry, process engineering, human physiology and foods to achieve cellular homeostasis and health.

### Early Views on Health and Diseases

The issue of health and on how to stay free from debilitating diseases up to the ripe old age is increasingly getting more attention by the public. The subject had been deliberated by a long list of renown scholars, doctors and philosophers such as Hippocrates [1-3], Musa Al Maimon (Moses Maimonides) [4], Louis Pasteur [5-6], Claude Bernard [7], Robert M'carrison [8], John Tilden [9], Herbert Sheldon [10], Weston Price [11] and Walter Canon [12]. A number of the ideas and approaches to health and wellbeing had been put forward however not all withstand to the scrutiny of modern sciences. The earlier doctors and scholars such as Hippocrates and Musa Al Maimon (Moses Maimonides) advocated a balance way of life as the ultimate means to keep ourselves healthy. Louis Pasteur and his followers on the other hand promoted the germ theory, the idea that diseases are cause by external agent such as microbes and viruses. John Tilden and Herbert Shelton from the school natural hygiene emphasized human diseases is an adaptation response of the body in its effort to expel toxic substances. As a consequence detoxification was central in the treatment of any diseases. Physiologist Claude Bernard [7] and Walter Canon [12]

expounded on the importance of internal environment (milieu interieur) or homeostasis of the body in promoting health. Robert M'carrison, Thomas Cleave [13] and Weston Price are well known for their work on the debilitating effect of depleted process on health and proved that pristine wholesome food is a prerequisite for health. However we are well aware the current dominant thinking by the medical community is by following the legacy of Louis Pasteur the germ theory [5, 6] and the genetic predisposition paradigm.

**Modern Human Diseases**

At present the knowledge in the area of health sciences and medicine has increased leap and bound. The advances in clinical sciences, anatomy and physiology, biochemistry, genetic engineering, nutrition science, microbiology, immunology, endocrinology and other areas of medical knowledge contributed a lot to the understanding of health and diseases. The life expectancy throughout the world is substantially increased. At the same time most of the infectious diseases have been eradicated. Public health infrastructure such as comfortable housing, potable water supply, sewerage system and access to modern healthcare facilities are widely available. In spite of these improvements in the healthcare amenities, humans are still burden with chronic metabolic diseases and their associated effect. Chronic metabolic diseases such as diabetic type 2, cancer, cardiovascular disease, hypertension and autoimmune disorder are on the increase [14] and the cure is elusive for most doctors. The search for the answer by the mainstream medical community is mainly targeted toward finding a magic bullet for the cure of chronic metabolic disorders. The prognosis is highly unlikely since metabolism consist of thousands of metabolites and metabolic pathways [15,16]. In a metabolic disorder such as hypertension and diabetes aggressive lowering the blood pressure and sugar levels by inhibiting specific metabolic pathways jeopardised the long-term health of the patient considerably [14]. A similar trend was noted in the treatment of all types of cancer using chemotherapy in which the recorded success rate was less than 3% for 5-year survival [17]. A treatment with success rate of 3% for 5 years is carrying unacceptable risk.

**Food and Nutrients as Medicine Revisited**

One of the fundamental concepts in process engineering is the principle of material balance. The principle states that the material input is equal to the accumulation and output from the system [18]. In order for an accumulation of material in the system to occur the input should be higher than output. The understanding of the principle is crucial in nutrition as human requires nutrients from external source. In material balance the availability and proportion of each nutrient component is important to ensure appropriate supply. Any omission, inadequacy or excess of a particular nutrient component will lead to disturbance in metabolism in the long run. Hippocrates (460-377 BC) the father of Western medicine

was quoted to have written the most precise aphorism on food and health “thy food shall be thy medicine” [1-3]. The saying is deceptively simple as it was an affirmation on the use of food for nourishing and medicating the body. From material balance point of view, the validity of the aphorism is obvious. However for the general public it is not that simple to convince them despite the simplicity of the concept [19-21]. The reason is that they have been conditioned to resort to pharmaceutical even for slight health symptom such as runny nose, cough or elevated body temperature. As for the medical community the challenge is even greater as they are not familiar with the used of nutrient to address any health disorder. This is due to limited nutrition component in any modern medical teaching curriculum [22-24]. As a consequence they require extensive supporting scientific evidence even before contemplating on the use of food and nutrients as health promoting agents. They insist for evidence in the form the standard clinical trial similar to pharmaceutical products as well. However it is obvious that no pharmaceutical company is willing to carry out such study since nutrient molecules are not patentable.

**Issues with Modern Healthcare**

The advances in biochemistry, metabolomics and system biology contribute tremendously in elucidating the role of nutrition in health maintenance and disease prevention. Epidemiological evidence also indicated that communities consuming indigenous natural wholesome food are known to stay free from chronic debilitating illnesses [8, 9]. Hence the consumption of wholesome unadulterated indigenous diet is a crucial component in any community to preserve health and prevent the onset metabolic diseases. The implication of this concept is far reaching to the healthcare provider and general public as it touches the core belief on how to keep ourselves healthy. The use of food as medicine is simple to implement and in many ways it empower the society to proactively look after themselves. Accordingly the cost is much lower and the benefit is higher. Modern medicine seems to keep distance from the Hippocrates idea on food as medicine and health since they focus mainly on treating disease symptoms with pharmaceutical drug and surgical procedures. Let there is no moment of doubt, pharmaceutical drug and surgical procedures are crucial as lifesaving intervention in emergency situation such as physical trauma, injury and acute infection. However the outcome for the treatment of metabolic disorder using pharmaceutical drug and surgery is less than desired [6, 58, and 59]. To date not a single pharmaceutical drug is known to reverse or cure any metabolic health disorder. They are intended to alleviate and manage the symptom. As a result the patients are often required to take the medication for the illness as well as to address the drug side effect for the rest of his life [6].

In medical practice, health conditions are assessed by blood chemistry evaluation on common metabolites represented by sugar level, cholesterol, triglyceride, uric acid and organ function such as liver. The obsession in lowering cholesterol in blood for example

defies biochemical and physiological logic. Elevated cholesterol is merely the body response to drive the metabolism toward homeostasis to compensate the lack of adequate vitamin C [25, 26]. There is a clear discordance between biochemistry and medical practice. More than 300 scientific and clinical studies have been published highlighting the danger of cholesterol lowering drug statin [27]. The latest study published on 8th of August 2012 in the journal of diabetes care [27] reported that diabetic type 2 patients taking statin drug showed a higher coronary artery calcification (CAC) than the less frequent user. In addition the progression of CAC and aortic artery calcification (AAC) was significantly increased in frequent statin user [27, 28]. Furthermore statin used by postmenopausal women increased the risk of getting diabetes mellitus [29]. Statin also been shown to accelerate the progression of age-related cataract in diabetes patients [29, 78]. The mechanism of nutrient deficiency in causing health degeneration and chronic metabolic disorder is not well understood by the general public.

## NUTRIENT DEFICIENCY DISORDERS

### Scurvy and Vitamin C

The era of dreadful nutrient deficiency diseases such as, scurvy, beriberi, pellagra, rickets, anaemia and many others are classic disorder caused by single nutrient deficiency has long gone [31]. The current public are not cognisant of the terrible human disease such scurvy. Scurvy is a health condition characterized by the body literally falling-apart due to impairment in collagen synthesis as a result of vitamin C deficiency [30]. The inability of the body to synthesize sufficient collagen and connective tissues caused the swelling and bleeding of the gum that eventually lead the teeth to fall out, offensive mouth odour, ruptured of small blood vessel and loosening of the limb. The word scurvy is derived from Latin word scorbutus means a disease that ruptures or lacerates the belly. Early symptom of scurvy according to James Lind, a Scottish physician in the mid-1700s who was attributed to propose lemon as the cure stated the following: “a listlessness to action, lazy inactive disposition that generate into a universal lassitude”. The other early signs of scurvy are lack of energy and decreased in endurance in exercise. These early pre-scorbutic sign are not uncommon amongst the present general population and the trend is disturbing [32].

In fact osteoporosis [33, 34] is also a type of scurvy so is cardio vascular disease [35, 61]. Osteoporosis is strongly associated with scurvy of the bone as it is a result of collagen synthesis impairment and imbalance between osteoclast and osteoblast due to vitamin C deficiency.

Human shares a similar biochemistry trait with guinea pig, primate and fruit bat in their inability to synthesize ascorbic acid from glucose [50] due to inactivity of L-gulonolactone oxidase gene. L-gulonolactone oxidase deficiency is considered a public inborn error

in metabolism as it affects all human regardless of their race and age [32]. We have to compensate this inborn error with appropriate dietary adjustment by consuming plenty of vitamin C rich wholesome foods. Inadequate consumption of vitamin C containing food constitutes a health risk as the long-term consequence is deadly.

**Beri Beri and Vitamin B1 (Thiamine)**

Beri beri on the other hand is a disease characterized by polyneuritis (inflammation of nerves) where the symptoms include paralysis and numbness of the limb, cardiac and respiratory disorder followed by severe muscular atrophy that often lead to death. [32, 34]. Beriberi is a disease due to deficiency of thiamine vitamin B1. Thiamine is a coenzyme for the metabolism of carbohydrates, lipid and protein. Therefore vitamin B1 is essential in maintaining the health of the heart, muscle and nervous system. By designed, all food items in their natural state contain traces of vitamin and other cofactors needed for cellular uptake and metabolism of that particular food. Only unprocessed natural food contain mineral such as magnesium, calcium, sodium and potassium are in the right ratio. The problem lies in the way foods are processed to render them more stable, convenient and appealing to human taste. For example polished rice is more stable and palatable, however most of its thiamine content is removed together with the bran during the processing. So are white flour, white sugar and the processed foods derived from them.

**Suboptimal Nutrients Intake and Metabolic Disorders**

It is now known that suboptimal nutrients supply above the levels causing classic vitamin deficiency is a contributing factor for chronic metabolic disorders [32]. Most of the existing chronic metabolic disorders such as type 2 diabetes, hypertension, obesity, coronary vascular disease, osteoporosis, osteoarthritis and even cancer are cause by the compounding effect of multiple suboptimal nutrients level. For example, hypertension in not a simple elevation blood pressure, it is a systemic metabolic disorder in every cell due to the malfunction of the sodium-potassium pump enzyme [37]. The malfunction is due to chronic exposure to processed food with inappropriate mineral ratio due to excessive addition of sodium. It is regrettable under the present circumstances the relationship between health disorder and nutrition deficiency is seldom highlighted.

**Modern Healthcare Solution for Metabolic Disorders**

The public is more often told that most of the chronic diseases are hereditary in nature or cause by yet to be determined factors. It is also often highlighted as a result of excess of certain food component such as salt, fat and sugars. The public is continuously subjected to

misinformation on the negative effect calorie dense food, saturated fat, butter, cholesterol, eggs, food supplements and other nutritious natural foods. The obsession with heart friendly polyunsaturated oil, low cholesterol foods, low fat alternative, low salt, low sugar, high fibre and low calorie sweeteners denies the public with essential nutrients in the right form. Omission of nutritious foods and the promotion of nutrient depleted processed foods in our society constitute a major health risk.

In addition the used of blockbuster drug to treat symptom such as high cholesterol, hypertension and diabetes on top of nutrient depleted food further exacerbate the health condition [39]. These prescription drugs are known to deplete further the availability of nutrient to the body. Thus the combination of nutrient depleted food and prescription drug is a real health buster in modern society. The widely prescribed drug such as statin drug and beta-blockers is known to inhibit the production of coenzyme Q10. Coenzyme Q10 is crucial for the mitochondrial function in the production adenosine triphosphate (ATP). In addition beta-blocker inhibits the production of melatonin and may disturb our sleep pattern. The common diuretic is known to deplete mineral such as calcium, magnesium, potassium, zinc and water soluble vitamin including ascorbic acid, thiamine and pyridoxine [39]. Even the frequently prescribed antibiotics are known to deplete most of the vitamins and minerals. We have to take the problem of nutrient depletion into consideration whenever drug taking is inevitable.

## THE ROLE OF FOOD AND NUTRIENT IN METABOLISM

In recent years however, the issue of food and health is beginning to get a wider attention by the public as the incidence of chronic metabolic disorder is on the rise and the cure is nowhere near. From material balance point of view, chronic metabolic disorder is a suboptimal nutrition deficiency health condition which cannot be reversed by the used of pharmaceutical agent such as drug [32]. The elaborate metabolic pathways are driven by nutrients derived from food, enzyme cofactors and coordinated by our endocrine system. Metabolism, metabolic pathways, nutrients and food are closely linked and interrelated [40]. The basis of food as medicine and medicine as food rest on fact that metabolism is the fundamental process of life. The feedstocks of cellular metabolism are nutrients, oxygen, water and sunlight in the case of production of vitamin D and never involve any prescription drugs. Prescription drugs mainly act as metabolic pathways inhibitors that posed additional burden to the liver detoxification duty. Unlike nutrients any xenobiotic chemical introduced is treated as foreign material and the liver will initiate detoxification process to remove from the body to protect its cellular function. For the liver detoxification to function, a range of nutrients such as the whole range of vitamin B and sulphur containing amino acids should be available [41]. In the phase 1 detoxification reaction the xenobiotic compounds are converted into more reactive intermediates by the microsomal cytochrome

P450 monooxygenase enzyme family. These reactive intermediates undergo conjugation reaction with acetate, glucuronate, glycine or sulphate to form water soluble metabolites and excreted through urine and bile [41]. Therefore a proper understanding on how our body function and regenerate at cellular level is crucial.

**Soil Health and Metabolism**

Every single cell of our body is ultimately made up of atoms and molecules originating from food material and water we consume and assimilate. The metabolites, enzymes, cofactors, antibodies and hormones involve in the cellular metabolism are all synthesized from food substance we consumed. The nutritive value of food material such as meat, dairy and poultry depend on the nutrient content of the feed material. At the same time nutritive value of the feed material such as grass, soya bean, corn, wheat and barley in turn depend on the soil health on which they are grown. Eventually soil chemistry and biology determine the health of human that subsist on it [42]. At the end of the day human, plant and animal health is the manifestation of soil health as rightly stated by the material balance principle. In simple term, the atoms and molecules for the structure and function of human cell are originally from the soil making their way through the food chain and food we consumed. The exception is oxygen and carbon that originate from carbon dioxide during photosynthesis and hydrogen from water molecules [43, 44].

A wholesome nutritious food is produced from rich and fertile soil. Fertile soil provides with the macro and micro mineral nutrients for plant growth. Plant material contains about 45% carbon atoms by mass [43]. The carbon and oxygen are derived from carbon dioxide in air while the hydrogen is from water. The higher is carbon dioxide in the air the higher is the photosynthesis rate of both C3 and C4 plants. As a result more oxygen is released to the atmosphere [44]. It seem the low carbon advocator could not accept the intensification of life sustaining natural carbon cycle as beneficial to the planet Earth. Their obsession to lower carbon dioxide in the atmosphere is a distraction from the real sustainability issue such as air pollution, soil health, clean water, wholesome food production and human health. In this regard carbon dioxide can be considered as atmospheric fertilizer. The sunlight supplies the energy to drive the photosynthesis for the production of simple sugar. The simple sugar is then used to provide the cell with substrate for glycolysis and aerobic respiration for the production of ATP and precursor molecules for cellular metabolic activities similar to mammalian cell. It is therefore important to appreciate the fundamental life support role of photosynthesis by plant and phototropic bacteria to the earth biotic system. Without adequate sunlight, fertile soil, water, carbon dioxide and appropriate temperature life based on carbon will not flourish on earth. We have to preserve and enhance the biotic earth capability to support photosynthesis in plant and phototropic bacteria. Our biological life depends on photosynthesis reaction as the true primary transformer of abiotic into biotic resource. In the age of smart phone and internet, human still have to depend on

plants, coral, algae, phototropic bacterial and animal for his nourishment. Every carbon and oxygen atom in our bodies originates from carbon dioxide in the atmosphere through the food we consumed [43].

**Metabolism and Cellular Turnover**

In the growing phase of our life food is used as the material to build and maintain our body. As we reached maturity where physical growth ceases our bodies continue to regenerate and repair without stopping. It is a dynamic balance between cell death and cellular regeneration. The lifespan of cells lining of the gastrointestinal organ is 5 days while the epidermis cells of the skin last about 14 days. The red blood cells are replaced every 120 days and the liver has turnover time of 300 to 500 days. Skeletal muscle turnover time is much higher in the order of 15 years. On the average the age of the cells in adult's body is 7 to 10 years [45]. From material balance point of view our new cell is made of new material as well as well from recycled cellular material. We have to continuously provide high quality nutrient as building block so that it can be incorporated into the new cellular structure.

**Metabolism and Energy Conversion**

In addition, the energy needed to drive the metabolism is also derived from food. 1 mole of glucose under aerobic condition undergoes a series of reaction in glycolysis and Krebs cycle to produce maximum of 38 moles of ATP. Glycolysis takes place in the cytosol bring in a net of 2 ATP and Krebs cycle in the mitochondria generates 36 ATP. At the same time a range of metabolites for cellular component and function are synthesized in the Krebs cycle [31]. ATP is a high-energy molecule that stores energy to drive metabolic activities of the cells. For metabolism to take place the cellular apparatuses should be functioning and the relevant metabolites as well as enzyme cofactors are available. Enzyme cofactors are generally in the form of vitamins and minerals. Glycolysis reaction requires thiamine, niacin and magnesium as the enzyme co-factors. The conversion of pyruvic acid, fatty acid and amino acids into an intermediate for the Krebs cycle acetyl co-enzyme A requires additional co-factor pyridoxine and pantothenic acid. The Krebs cycle needs thiamine, riboflavin, niacin, ubiquinone (CoQ10), magnesium as the co-factors and oxygen. Ideally we should be able to obtain energy from a mixture of carbohydrates, proteins and fats. For the reaction to be efficient these vitamins and minerals have to be obtained from external sources in the form of food [31]. Therefore to qualify food as medicine it must be wholesome containing the appropriate ratio of macro and micronutrients required for cellular metabolism and regeneration of the cellular components. A depleted processed food devoid of essential micronutrients and laden with food adulterant is potentially detrimental to the health in the long run.

## HUMAN NUTRITION AT A GLANCE

Food material, water and oxygen are the feedstock for the cellular metabolism. Water serve as aqueous solvent involve in digestion, absorption and metabolism as well as in all physiological and structural function. Human cannot live more than 5 days without water intake. The average man needs in the range of 1.2-2.5 litres of water per day depending of the physical activity, environment and food intake. Consuming food high in salt require a higher water intake to ensure electrolytes balance is maintain [46].

Most of natural food exist as complex food materials in the form of bio-polymers and bio-composites containing water, proteins, carbohydrates, lipids, minerals, vitamins, enzymes in raw food and a range of bioactive molecules and microbe and viruses. Microbes acting as probiotic is an important component of human nutrition as they assist digestion and production of nutrient such as vitamins and short chain fatty acids. They are also important as part of human immune system in the gastrointestinal tract and reproductive system especially in women. Human is in fact a human-bacterial hybrid as the body contain more than 500 species of bacteria. Microbes outnumbered human cells by 100 to 1. Most microbes inhabit human body as commensal microorganisms sharing nutrients and living along with human [47, 48]. In fact according to recent publication in Journal of Medical Microbiology viruses are also a member of the beneficial microorganism in our body [49]. Therefore it is important to consume adequate prebiotics in our diet to support probiotic microbes proliferation and avoid in taking unnecessary antibiotics that suppresses them.

Most of the food materials from plants and animals origin require cooking and digestion to reduce them into their simplest form for cellular uptake. Protein rich food such as meat is digested into its constituent amino acids. The essential amino acids for adult are lysine, leucine, isoleucine, histidine, methionine, phenylalanine, threonine, tryptophan and valine [40]. For children additional amino acid arginine is required for growth. These amino acids have to be obtained exclusively from food sources as human are unable to synthesize any of them [40]. Starch is hydrolysed into glucose and triglycerides into fatty acid and glycerol. Essential fatty acids are the omega-6 linoleic and omega-3 alpha-linolenic acids [40]. The completely digested protein and triglyceride are for the building blocks of cellular components whereas glucose is use as substrate for glycolysis and citric acid cycle for the production of ATP. At the same time their micronutrient content such as vitamin and mineral are released for absorption by the gastrointestinal tract. To date there are 10 water soluble vitamin specifically B1 (thiamine), B2 (riboflavin), B3 (niacin), B5 (pantothenic acid), B6 (pyridoxine), B7 (biotin), B8 (adenosine monophosphate), B9 (folic acid), B12 (cyanocobalamin) and vitamin C, and 4 fat soluble vitamin D, E, A and K identified as essential for human metabolism. The macro-mineral for instance calcium, phosphorus, iron, sulphur, iodine, sodium, potassium, magnesium, chlorine and micro mineral such as copper, cobalt, zinc, chromium and selenium, manganese, molybdenum, fluoride and ultra-trace elements are released in the gastrointestinal tract for absorption [50, 51]. Any deficiency of these essential nutrients jeopardises the whole organism in the long run.

**Gastrointestinal Function and Nutrition**

One of the main issues in food digestion in modern society is the inefficiency of the gastrointestinal tract in carrying out the process. This is due to the digestion efficiency is dependent on the health status and the overall cellular metabolism itself. Low metabolism is known to slow down the transit time of food in the gastrointestinal tract, promote constipation, bloating, irritable bowel syndrome (IBS), diverticulitis and other digestive distress [45]. Chronic constipation with bulky, dry and abrasive stools is common in society that consumes nutrient deficient processed food. It is a clear sign of digestive distress, malnutrition and low metabolism. IBS and diverticulitis are indication of chronic inflammation of the digestive tract and chronic inflammation lowers the metabolic rate. As observed, inefficient digestion compromises the health of gastrointestinal tract with dire consequent to the overall metabolism. Thus the key to an effective digestion is to have a high basal metabolic rate. A low metabolic rate is causing inefficient digestion and slowing down the bowel movement as indicated by longer transit time of digested foods. At the same time inefficient digestion lowers the metabolic rate. It is a catch-22 situation. Therefore, we have to solve these issues simultaneously to have any chance to improve our health.

**Indigestion and Metabolism**

Efficient digestion is more than about consuming high fibre foods. High fibre foods may even aggravate a compromised the digestive system. The long-term solution is to stimulate the metabolism by addressing the factors that contribute to low metabolism such hypothyroidism, inflammation, nutrition deficiency and elevation of stress hormone. At the same time we have to deal with the physical aspect of constipation by consuming only easily digestible wholesome low fibre fruits and vegetables until regular bowel movement is achieved. Once the constipation subsided, the focus is to follow a diet that enhances metabolic rate. Such diet primarily consisted of wholesome, nutritious and minimally processed food that excludes refined sugar, fructose, white flour, polyunsaturated vegetable oil and trans fatty acid containing oils and margarines and caffeinated drinks. Liberal intake of easily digested complex carbohydrate and saturated fats and minimized the protein component help to speed up metabolism. Hypothyroidism is made worst by a higher intake of protein and polyunsaturated vegetable oil. On the other hand, saturated fat such as dairy butter and coconut oil are known to enhance cellular metabolism due to the presence of the short chain fatty acid [52]. Butter contains butyric acid while coconut oil is contains capric, caprylic and lauric acid [53]. In addition, high fat and low residue nutrient dense food is known to promote regular bowel movement.

Digested and assimilated food materials in the form of simple sugar, fatty acids and amino acids are the substrates of the enzymatic reaction in the metabolism. Vitamin and

mineral ions act as the enzyme co-factors and water as the aqueous medium of the reaction. The products of metabolism are chemical energy in the form of ATP, building block of the cellular components and metabolic regulator such as neurotransmitters and hormones. In simple term, metabolism is a set of biochemical reaction in the cells to generate energy and production of metabolites for cellular function and component from food material we consumed. It is an enzyme-controlled reaction coordinated by the endocrine system to maintain cellular homeostasis under varying body activities and environments. Cellular homeostasis is achieved by the orchestration of thousands of metabolic pathways forming a fine tuned biological system. A finely tuned biological system requires a complete cellular nutrient to be presence and the absence of contaminant in the form of endocrine disruptor and metabolic inhibitors. The importance of metabolism to any living organism cannot be overstated as it signifies life itself.

Therefore to maintain the metabolism to be in the tiptop condition the consumption of suitable nutritious wholesome food that contains all the essential nutrients throughout our live is crucial.

## THE CHOICE OF FOOD AND METABOLISM

The influence of the choice of food on metabolism is beginning to get the attention of health expert. The fact is food choices and life style influence the hormone secretion that regulates our mood, satiety, hunger, craving and eventually the metabolism. Secretion of hormone cortisol, glucagon, insulin, leptin, adiponectin, ghrehlin, thyroid hormone, testosterone, serotonin, melatonin, growth hormone and neurotransmitters such as, dopamine,gamma-aminobutyric acid (GABA), epinephrine and many others are directly influence by our relationship with food [54, 55, 65]. Hormonally balance nutrition is food that contains the nutrients the body need without triggering the unnecessary negative hormone adaptive response. As such the food should be in the appropriate form with desirable sensory profile and non-stimulatory. The form and sensory attribute of food is crucial to meet the physiological requirement such as satiety, pleasant feeling of fullness minus the undesirable food craving. Food satiety is regulated by the hormone leptin and its circulatory level is a function of energy stored in the adipose tissue. A higher level of leptin promotes a reduction of food intake and increase in energy expenditure to regulate the amount of fat stored in adipose tissue. Hormone leptin control the long-term energy balance while ghrehlin operate at much shorter term on hourly basis. Food such as boiled potatoes is filling and satisfying by keeping hunger at bay longer. In term of satiety index, boiled potatoes scored 323% while croissant 47% and white bread 100% [56,57]. Dysregulation of energy balance such as in obese individual is always linked to leptin resistance. Leptin resistance is the down regulation of leptin receptors attributed to a sustain elevation of leptin. The continuous elevated leptin level caused the receptor to be fewer in number and less responsive to leptin signal [60].

**Food Craving and Metabolism**

Another widespread concern in modern society is a condition called food craving. Food craving is mainly due to excessive stimulation of neurotransmitter dopamine receptors by highly flavoured food products. Over production of dopamine by consumption of highly flavoured processed food lead to over stimulation of dopamine receptors. The overstimulation results in down regulation of dopamine receptor that is compensated by consuming even more addictive food to achieve similar satiety level of normal individual. For food addicts, the release of more dopamine is becoming the priorities in selection of food choice. Thus, highly flavoured processed food is designed to target hedonic eaters rather than providing nutrition. In short, it is to maximize pleasure, consumption and profit to the food manufacturers and not health. At present, hedonic food leads to food addiction, overconsumption, malnutrition and health matters such as obesity and metabolic disorder. One of the most common food ingredients that stimulate appetite and triggers craving and addiction is monosodium glutamate (MSG). In laboratory rat study MSG is shown to down regulates hypothalamic appetite suppression. In addition MSG promotes the secretion of insulin and adrenalin thus inducing hunger and fat storage. The linked between MSG and obesity through the induction of fat storage and overconsumption is well documented. This is why after finishing a large packet of intensely flavoured crisp laden with MSG makes us even hungrier than before. In addition, MSG is an excitotoxin that over stimulate the nervous system that can lead to neurodegenerative disorder. MSG is ubiquitous in processed food products and becoming harder to avoid.

**Low Metabolism, Inflammation, and Nutrition**

Another major issue related to metabolism in modern society is the prevalent of low metabolic rate as mentioned briefly earlier. Hypothalamic-Pituitary-Adrenal (HPA) and Hypothalamic-Pituitary-Thyroid (HPT) axis that interact in many ways with diet, nutrition and lifestyle regulate metabolism. The availability of appropriate amino acids in the diet, the building block of the neurotransmitter and hormone is important in maintaining a balance metabolism. For example L-phenylalanine an essential amino acid and L-glutamine a conditionally essential amino acid are the building block of neurotransmitter that regulate metabolism must be obtained from food. Any deficiency of these amino acids in our diet especially during period of stress disturbs the balance of metabolism. Imbalance metabolism such as low metabolic rate is link to a number of metabolic disorders such as autoimmune disorder, constipation, frequent infection, dry skin, lethargy, diminish libido, cold hand and feet, excessive fat deposition, low blood pressure and many others. Thus the HPA and HPT-axis regulates homeostasis by controlling metabolic activities of the body. Low metabolic activity is a manifestation of systemic biological adaptation due to elevation

of stress hormone as a result of stressful factors whether physical or psychological. Factors such as nutrition deficiency as a result of dieting, prolong strenuous exercise, lack of sleep, exposure to environmental allergens and pollutants, traumatic event such as death of the love one, major surgery and anything else that trigger the elevation of stress hormone such as cortisol and dehydroepiandrosterone (DHEA). Elevated stress hormone cortisol causes the body to breakdown muscle protein, insulin resistance and suppresses the thyroid function [61-63]. In addition, the thyroid function is significantly suppressed by inflammation. Thus thyroid function is both suppressed by stress hormone as well as systemic inflammation. Depleted processed food and inflammatory food such as polyunsaturated vegetable oil and fructose are known to suppressed thyroid function. A suppressed thyroid function can result in a low metabolism that is prevalent in modern society.

It is acknowledged, metabolism plays a vital role in health and sickness. Healthy state is a condition where the metabolism is at its peak level in every single cell. In chronic sickness, there is metabolic impairment especially in the energy generation by the mitochondria.

Once again the choice of wholesome nutritious foods to support cellular function that is free from appetite stimulating and hormone disrupting chemicals is essential to ensure good metabolic health. We have to re-establish our relationship with food to promote ideal metabolism level, optimal health and happiness. Metabolic health is about providing the every single cell with its metabolic requirement.

## METABOLISM, MITOCHONDRIA, AND METABOLIC DISORDERS

The most important organelle in human cell responsible for metabolism is mitochondria. Mitochondria are the “powerplant” that is responsible for energy conversion and metabolites generation using nutrients and oxygen. The majority of the respiratory oxygen in the region of 85% is used in mitochondria in oxidative phosphorylation to form ATP. Mitochondria generate about 95% of the energy generated in the cell. In addition, mitochondria produce mitochondrial protein responsible for the electron transport chain in the Krebs cycle as well. Every cell with a few exceptions such as red blood cells contains 200-2000 mitochondria. Mitochondria metabolism impairment has been associated with a long list of seemingly unrelated chronic metabolic disorders and diseases of ageing [66-69]. Metabolic disorders such as chronic fatigue syndrome, hypertension, diabetic type 2, cancer, cardiovascular disease, cardiomyopathy, Parkinson’s disease, Alzheimer and autoimmune such as rheumatoid arthritis, multiple scelerosis are known to be related to mitochondria impairment [70-75]. Otto Warbug reported that a mere 30% impairment in mitochondria function in its energy generation is sufficient to create cellular condition suitable for the cancer cell to proliferate [64].

**Mitochondria, Reactive Oxygen Species, and Nutrition**

Impairment of mitochondria is caused mainly by reactive oxygen species (ROS) produced by the mitochondria. ROS such as superoxide ($O_2^-$) radical is converted to hydrogen peroxide by manganese superoxide dismutase and to water by glutathione peroxidase. However in the event of accumulation of superoxide radical due to slow conversion into water, oxidative damage occurs. Glutathione is one of most efficient antioxidant produced by the body and it is a tripeptide consists of glutamine, glycine and cysteine. Glutathione peroxidase requires selenium as a cofactor. In addition the nitric oxide generated in the cytosol and mitochondria react with ($O_2^-$) to form peroxynitrite ($ONOO^-$) another radical. These 2 radicals are recognised to cause injury to the mitochondria and cellular components. An inflammatory mediator such as tumor necrosis alpha (TNF-$\alpha$) is known to cause mitochondrial damage and increase in ROS generation.

**Mitochondria and Krebs Cycles Inhibitors**

Metabolic impairment due to deficiency of Krebs cycle nutrients and cofactors and the present of metabolic inhibitors such as mercury, arsenic, fluoride and other heavy metals is also known to impair the mitochondrial function. Arsenic inhibits Krebs cycle enzymes such as isocitrate dehydrogenase, alpha-ketoglutarate dehydrogenase, succinate dehydrogenase and cytochrome C oxidse with dire consequences.

**Mitochondria and Omega-6 Linoleic Acid**

Another important factor in mitochondrial metabolic function is the integrity of its inner membrane cardiolipin [78]. The alteration of cardiolipin structure is known to cause impairment of mitochondrial function. Cardiolipin is tetra-acyl phospholipid with linoleic acid as the fatty acid component. The functional property of cardiolipin is important for its ability to interact with the mitochondrial protein and maintaining the inner membrane integrity in term of fluidity and osmotic stability [78]. The crucial acyl component is the linoleic acid an essential omega-6 fatty acid. The problem with obtaining adequate linoleic acid is its stability. Linoleic acid is prone to undergoes free radical lipid peroxidation in the presence of heat. Therefore the availability of non-damage linoleic acid is important for the structure and function of cardiolipin and mitochondrial function. In order to ensure the structure and function of the mitochondria a simple material balance strategy should be adopted. All the essential nutrients, cofactors, mineral and phytonutrients should be made available to the cell. The effect of ROS on the mitochondria should be minimised by consuming high anti-oxidant phytonutrients. Avoidance mitochondria oxidative phosphorylation inhibitor such as heavy metal and pesticides is crucial for optimum function of mitochondria. Optimum

functions of mitochondria are essential for health and prevention of most of metabolic disorders including cancer.

**$Na^+/K^+$-ATPase AND HYPERTENSION**

Metabolic disorder such as hypertension is an indicator that there is an imbalance in the metabolism throughout the whole body. The nature of the imbalance is in common with other metabolic disorder such diabetes type 2. Hypertension is associated with elevated metabolite such as glucose and triglyceride [75-77]. In addition, there is high level of insulin, stress hormone and inflammation markers. The hypertension has to do with the electrical system driven by an enzyme the $Na^+/K^+$-ATPase simply known as sodium-potassium pump as well as impairment in mitochondrial function. Sodium-potassium pump is responsible of moving sodium out of the cell and potassium into the cell. In one cycle the enzyme move 3 sodium ions out of the cell and 2 potassium ions into the cell with one net positive charge. In fact sodium-potassium pump acts as microscopic electrical generator providing electricity for the cellular need such as for the muscles and nerves system. Sodium-potassium pump uses about 25% of energy produce by the mitochondria and its function has a significant effect on the cellular metabolism. A reduction in Na/K pumps efficiency lead to a series of metabolic event in order to maintain metabolic equilibrium. The immediate effect is the elevation of sodium ions in the cells. The increase of sodium leads to an increase of calcium ions in the cells. Elevated calcium ions trigger the contraction of muscle around the small arteries that make them narrower. A smaller diameter artery offers a higher resistance to blood flow hence the higher is the blood pressure [37]. In addition the increase in calcium ions in the cell gives rise to the lowering of magnesium ions that lead to a lower sensitivity of insulin. As a result more insulin is released bringing about elevated level of insulin hormone in the extracellular fluid. Elevated insulin hormone on the other hand stimulate kidney to retain more sodium ions and the process reinforces the hypertension.

Blood pressure could also be caused by the sympathetic nervous system, renin-angiotensin system stimulation and the proliferation of vascular smooth muscle.

In order for sodium-potassium pump to work as it should be appropriate ratio of potassium, sodium, calcium and magnesium ions should be made available to the cells by consuming unprocessed natural food. Most natural unprocessed foods contain mineral in the appropriate ratio for cellular metabolism. Magnesium ions are also acting as the co-factor for the potassium-sodium pump enzyme. Hypertension that is caused by inappropriate ratio of mineral intake should be reversible by adopting wholesome natural foods diet as they contain a balanced mineral profile.

## CONCLUSION

In order to use foods as our medicine, we have to have an appropriate, happy and sustainable relationship with them. A well prepared wholesome nutritious food is nourishing to the cells and promotes overall wellbeing to the whole body and uplifts our mood. From material and energy balance point of views all the essential nutrients carbohydrates, proteins, lipids, vitamins, minerals, water, phytochemicals and their corresponding derivative molecules crucial for food digestion and cellular metabolisms should be made available in the proper quantity as the ingredients of our food. Wholesome nutritious foods should be obtained from a healthy and nutrient rich agriculture soil that in turn produced healthy plants and animal and microbes. The foods are appropriately process to maintain the form and their nutrients content. The selection of foods for nourishment should be based on wholesomeness to satisfy the material balance requirement beyond suboptimal level. In addition the prepared food should be in the right form, texture and desirable sensory attribute to facilitate digestion and elicit appropriate hormonal response and minimised craving. It is also important to minimise the present of metabolic inhibitors and antimicrobial agents in food to maintain the integrity of the mitochondrial function and viability of commensal and symbiotic microbes in the gastrointestinal tract. Bon appetite!

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**Professor Dr. Mohamad Roji Sarmidi**
Research Alliance Biotechnology
d/a Institut Pembangunan Bioproduk (IBD)
Universiti Teknologi Malaysia
Johor Bahru

Dr. Mohamad Roji Sarmidi is a Professor of Bioprocess Engineering and the Dean of Biotechnology Research Alliance at the Universiti Teknologi Malaysia (UTM). Born on the 18th of June 1960 in the town of Banting, Selangor, Malaysia, he received his early education at Sekolah Kebangsaan Sungai Lang, Banting and continued his secondary education at the renowned Sekolah Tuanku Abdul Rahman (STAR), Ipoh. Dr. Mohamad Roji spent his tertiary education in the United Kingdom by obtaining his A-Levels at the North Devon College, Devon and later on graduating in Chemical Engineering from the University of Surrey. He pursued his Masters degree in Biochemical Engineering at the University of Birmingham and subsequently completed his Ph.D. at Aston University in Chemical Engineering in 1993.

His research interests are in the applications of bioprocessing and bioproduct development relating to human health. His research themes focuses on the development of products and services for the wellness industry, promoting wellness as a multidisciplinary strategy for health enhancement based on system biology, where the main goal is to promote cellular homeostasis by using metabolites and nutrients.

He is currently leading an R&D team developing soil health nutrients, nutraceutical and regenerative cosmetics. Realizing the importance of transferring research outputs and scientific knowledge for the benefit of human wellness, Dr. Mohamad Roji diversifies himself as a nutritional medicine practitioner at the Institute of Bio-product Development, UTM, providing consultations mainly in addressing chronic metabolic disorders to members of the university and the general public.

Prior to his present position, he headed the Bioprocess Engineering Department (1994-1997) and appointed as the R&D Manager of CEPP, UTM (1999-2008). He has authored and co-authored more than 65 refereed journals and articles. He is an active participant in bioproduct development activities and has also accumulated a number of patents and research awards. His interest and research expertise has led him to be the Founding Chairman of the International Conference on Biotechnology for the Wellness Industry (ICBWI) since 2008 and the Chief Editor of International Journal of Biotechnology for the Wellness Industry. Furthermore, Professor Dr. Mohamad Roji is an Associate Member of

Institute of Chemical Engineers (IChemE) and also the Deputy President of the Association of Nutritional Medicine Practitioners Malaysia (MNMedP).

Prof. Dr. Mohamad Roji enjoys tending to his own biotic garden and is an active advocate of children's education and the younger generation. He is the Chairman of Governors of Sekolah Rendah Islam (SRI), Johor Bahru.

**Professor Dr. Mohamad Roji Sarmidi**
Research Alliance Biotechnology
d/a Institut Pembangunan Bioproduk (IBD)
Universiti Teknologi Malaysia
Johor Bahru

Dr. Mohamad Roji Sarmidi merupakan Profesor Kejuruteraan Bioproses dan Dekan Penyelidikan Research Alliance di Universiti Teknologi Malaysia (UTM). Beliau dilahirkan pada 18 Jun 1960 di Banting Selangor. Mendapat pendidikan awal di Sekolah Kebangsaan Sungai Lang, Banting dan kemudiannya melanjutkan pelajaran ke peringkat menengah di Sekolah Tuanku Abdul Rahman (STAR), Ipoh. Beliau menamatkan pengajian di peringkat A-Level dari The North Devon College, Devon dan seterusnya memperoleh Ijazah dalam bidang Kejuruteraan Kimia dari University of Surrey. Kemudian, beliau telah menyambung pengajian ke peringkat Ijazah Sarjana dalam bidang Kejuruteraan Biokimia di University of Birmingham dan seterusnya menamatkan pengajian di peringkat Doktor Falsafah di Aston University dalam bidang Kejuruteraan Kimia pada tahun 1993.

Penyelidikan beliau lebih menjurus kepada pengaplikasian bioproses dan pembangunan bioproduk terhadap kesihatan manusia. Tema kajian beliau memberi tumpuan kepada pembangunan produk dan perkhidmatan untuk industri kesejahteraan, membangunkan kesejahteraan sebagai strategi pelbagai disiplin untuk meningkatkan kesihatan berdasarkan biologi sistem, di mana matlamat utama adalah untuk menggalakkan homeostasis selular dengan menggunakan metabolit dan nutrisi.

Kini, beliau mengetuai satu pasukan R&D dalam membangunkan produk kesihatan tanah, nutraseutikal, dan produk kosmetik. Beliau juga merupakan seorang pengamal perubatan menerusi pemakanan di Institut Pembangunan Bio-produk UTM. IBD juga turut memberikan khidmat perundingan terutamanya dalam menangani masalah berkaitan penyakit-penyakit kronik kepada ahli-ahli Univerisiti dan orang awam.

Sebelum beliau menyandang jawatan sebagai Dekan Penyelidikan, beliau merupakan Ketua Jabatan Kejuruteraan Bioproses (1994-1997) dan menjadi Pengurus R&D CEPP, UTM (1999-2008). Beliau telah mengarang dan menjadi pengarang bersama lebih daripada 65 jurnal berwasit dan artikel. Beliau merupakan seorang yang aktif dalam aktiviti pembangunan bioproduk dan juga telah berjaya mengumpulkan beberapa paten dan menyandang beberapa Anugerah Penyelidikan. Beliau juga merupakan Pengerusi Pengasas Persidangan Antarabangsa Bioteknologi untuk Industri Kesihatan (ICBWI) sejak tahun 2008 dan juga merupakan Ketua Editor Jurnal Antarabangsa Bioteknologi untuk

Industri Kesihatan. Selain itu, Profesor Dr. Mohamad Roji adalah Ahli Bersekutu Institut Jurutera Kimia (IChemE) dan juga Timbalan Presiden Persatuan Pengamal Perubatan Nutrisi Malaysia (MNMedP).

Di samping itu, beliau juga minat berkebun secara biotik dan giat dalam pendidikan kanak-kanak dan generasi muda. Beliau merupakan Pengerusi Lembaga Pengarah Sekolah Rendah Islam (SRI), Johor Bahru.