Mahabaleshwar V. Hegde
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Sharad P. Adekar *Editors*

Omega-3 Fatty Acids

Keys to Nutritional Health

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Preface

This book, "*Omega-3 Fatty acids: Keys to Nutritional Health*," is the product of our sincere effort, to provide scientific evidence for the extraordinary power of nature's wonder molecules —omega-3-fatty acids. Chapters by experts in different specific aspects of omega-3 fatty acids for human health, have been presented to our wide spread readers, nutritionists, dieticians, clinicians, and all health conscious readers and health professionals. There is no exaggeration if we state that man owes his very existence on this planet to omega-3 fatty acids, as these molecules are largely responsible for the creation human brain. It is the brain that gives man the extraordinary power to sense the nature and its environment and enable him to adapt, to live in more comfort. Omega-3 fatty acids, besides being the hardware of the brain, take active part in almost every aspect of life reactions in health and disease.

Our Chap. 1 on "*Nutrition, Life, Disease, and Death*" narrates the importance of supply of all essential nutrients in adequate quantities including omega-3 fatty acids and Chap. 36 of Dr. M. Jeganathan on "*Role of Antioxidants*" which are also needed not only as anti-stress, anti-aging nutrient, but also to prevent oxidation of omega-3 fatty acids in human body's hostile environment.

It is unequivocally established that recent rise in the incidences and severity of several diseases, including diabetes, heart disease, obesity, pregnancy complications, alzheimer, psoriasis and aging, can be primarily attributed to the paucity of omega-3 fatty acids in modern human diet. Hence, "*Bring Back Omega-3 Fatty acid into Food Chain*" has been aglobal cry. Therefore, our Chap. 2 on "*Flax Biovillage*" and Chap. 3, "*Linseed Agriculture*" by Dr. P.K Singh aim at unleashing the power of linseed, for omega-3 nutritional security. Chap. 21 by Dr. Scott Doughman presents a case of "*Microalgae oil*" and Dr. Rafael Zarate's in Chap. 9, that of "*marine algae*,"as safe and effective vegetarian food. Authors argue that different biotechnological approaches can boost fatty acid yield in microalgae, and thereby, microalgae may become important attractive, continuous, sustainable good omega-3 source, to satisfy the increasing world demand. In Chap. 34, Georgia Lenihan-Geels discusses the prospects of bioengineering of plant seed oils for docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), algae aquaculture and enhancement of LC-PUFA in meat, and dairy products through plant-derived livestock feeds. In addition to increase the world omega-3 supply, for actually attaining omega-3 nutritional security and better health for one and all, another attractive complementary strategy is to fortify food, resourcing omega-3 fatty acid from flaxseed, marine algae, or fish oil sources. Manohar Panse in Chap. 8, while discussing the "*Omega-3 fatty acid Food Fortification*," also highlights the importance of compliance of regulatory guidelines, required for marketing such products. Further, Manohar Panse has also discussed *Development of omega-3 eggs* in Chap. 5 and *World Market of Omega 3 Fatty Acids* in Chap. 7. Most importantly, the *pharmacokinetics of safety of omega-3 fatty acids* has been reviewed by Dr. Juan Tamargo in Chap. 39. Dr. Puranik in Chap. 10 describes *omega-3 oil emulsion* that prevents lipid peroxidation and also offers not only increased stability and shelf life but also better bioavailability. In our Chap. 4 on "*Omega-3 Milk*," with our colleague Dr. P.B. Ghorpade and Dr. S.L. Bodhankar, we narrate the importance of incorporating omega-3 fatty acid in milk and its utility for human health.

The major problem today is the severe imbalance of the two essential fatty acids namely omega-3 and omega-6 fatty acids. Omega-3 fatty acids being primarily anti-inflammatory and omega-6 being proinflammatory, too much omega-6 and very little of omega-3 fatty acids in modern human diet, the disease-prone inflammatory pathway is dominant in the modern man. Dr. Kadooin in Chap. 15 discusses how omega-3 to omega-6 ratios can be manipulated in oilseeds to achieve balance of omega-3 and omega-6 fatty acids.

Most interesting thought-provoking chapters (Chaps. 27–32) have been provided by Robert Brown. His concern about the linoleic acid/alpha-linolenic acid imbalance and its influence on various aspects of ill health today is evident from the inferences drawn by him.

One of the major well-acknowledged effects of omega-3 fatty acids are their ability to prevent heart diseases. Dr. Manohar Garg in Chap. 6 discusses how omega-3 fatty acids control *hyperlipidemia*; Dr. Jubbin Jacob in Chap. 37, *cardiovascular disorder*; Dr. Quian Gao in Chap. 25, *cardiovascular events*; and Dr. Sang Lee in Chap. 33, *Myocardial Infarction*.

Dr. Sayed Ahmed in Chap. 11, discusses the mechanism by which EPA- and DHA-derived eicosanoids and lipid mediators contain chronic inflammation and prevent degenerative diseases.

Effects of omega-3 fatty acids on immune system in reducing the pathological manifestation especially in diseases related to inflammation, allergy, and autoimmunity have been discussed by Dr. Sudha Gangal in Chap. 26.

Dr. Vikas Kumar in Chap. 38 on *Psoriasis*, a multifaceted autoimmune disorder discusses the potential benefits of omega-3 fatty acid, their metabolites, and the mechanisms involved in psoriasis treatment.

Role of omega-3 fatty acids in mitochondrial diseases and its profound effects on muscle, brain, heart, liver, nerves, eyes, ears, kidney functions, involvement in CVD, and diabetes have been discussed by Dr. S. Katyare in Chap. 17. Dr. Katyare in chapter on diabetes shows the link between omega-3 fatty acids in diabetic complications, neuropathy, retinopathy, nephropathy, and angiopathy, and the beneficial effect of omega-3 fatty acid supplementation in Chap. 16, and Dr. Katyare further in Chap. 18 on Alzheimer argues that omega-3 fatty acid supplementation may be safe and prophylactic for Alzheimer's disease.

Oxidative stress and inflammation are the major mechanism that contributes to the pathogenesis of degenerative diseases including neurotraumatic, neurodegenerative, and neuropsychiatric diseases. Dr. Akhlaq A. Farooqui, in Chap. 19, concludes that increased consumption of omega-3 fatty acids may result in retardation of oxidative stress and neuroinflammation due to the production of resolvins, neuroprotectins, and maresins.

Dr. Tassos Georgiou in Chap. 20 on the role of omega-3 fatty acids on eye health describes how omega-3 fatty acid supplementation can result in regression in some type of retinopathies, including age-related macular degeneration, macular dystrophies, and also some form of drying eye.

Importance of omega-3 fatty acids in maternal nutrition in growing fetus, reducing the risk of adverse pregnancy outcome, has been reviewed in Chap. 35, by Dr. Sadhana Joshi.

Dr. Gabriel Fernandes, in Chap. 40, describes effect of fish oils on pain resolution, achieving prolonged disease free life.

Obesity leads to several chronic morbidities including type 2 diabetes, atherosclerosis, and hypertension, which are major components of the metabolic syndrome. In chapter 14, Dr. Maria J. Morena Aliaga reviews randomized controlled trials that evaluate the effect of supplementation of EPA and DHA on weight loss, insulin sensitivity, lipid metabolism, blood pressure, and inflammation in subjects with metabolic syndrome characteristics. Dr. Lindsay Brown in Chap. 13 describes linseed as a functional food for the management of obesity. He concludes that there is considerable evidence that the constituents in flaxseed especially ALA and probably also secoisolariciresinol diglucoside and fiber to a lesser extent, either separately or combined, can be defined as functional food, as they may improve the multiorgan changes induced by obesity.

Decrease in the brain DHA content causes number of neurobiological effects including depression. Dr. Beth Levantin in Chap. 22 discusses the evidences that support the involvement of decreased brain omega-3 fatty acids in the etiology of postpartum depression and other depressive disorders and their implications in prevention and treatment.

Dr. Julio Ochoa in Chap. 23 summarizes the role of omega-3 fatty acids in bone health and turnover. In Chap. 24, Dr. Julio Ochoa summarizes the interactive role of Fe and DHA in physiologicaland nutritional deficiency situations, revealing that DHA stimulates Fe metabolism.

In Chap. 12 on cancer, we discuss the anticancer action of omega-3 fatty acids that may counter the proinflammatory, proangiogenic, and prometastaic and cell proliferative actions of AA eicosanoids and induce apoptosis.

It is no wonder that omega-3 fatty acids are very crucial for our health as they constitute the functional structural component of the membrane and also the precursors of hundreds of eicosanoids and lipid mediators controlling thousands of reactions in human body. Therefore, it is not surprising that the omega-3 deficiency has wide range of adverse effects on different organs and tissues aggravating each and every disease. Therefore, the book also focuses on the means of urgently bringing back omega-3 fatty acids into food chain. These aspects have been very well illustrated by the contributory authors and co-authors of the chapters of the book. We would like to profusely thank them all, being the part of this useful exercise.

Finally, volume editors would like to extend their appreciation to Springer and their staff for providing professional platform for communication with the experts in the field.

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About the Editors

Prof. Mahabaleshwar V. Hegde earned his B.Sc. (Biology), B. Sc. (Hons) (Chemistry), M.Sc. (Biochemistry), and Ph.D. (Enzymology), all from University of Pune. India. Dr. Hegde gained molecular biology research experience at Prof. Julius Marmur's Laboratory at Albert Einstein College of Medicine, New York. He was visiting scientist at the Virology Department of Sloan Kettering Cancer Center, New York.

He taught biochemistry at postgraduate level as demonstrator, lecturer, reader, and professor of biochemistry for 33 years at University of Pune and retired as the Head of the Department of Chemistry.

Thereafter, he was coordinator of omega-3 projects at Biochemical Division of National Chemical Laboratory, Pune, for three years.

Dr. Hegde later shifted to Bharati Vidyapeeth Deemed University's (BVDU) Interactive Research School for Health Affairs (IRSHA), to continue focused research on "Role of Omega-3 Fatty acids in Human Health." Realizing the adverse effects of precariously low levels of omega-3 fatty acids on human health, Dr. Hegde developed "Flax Biovillage concept." The idea was validated with the help of two National Agricultural Innovation Projects funded by Indian Council of Agricultural Research, on flaxseed, 1) Linseed Agriculture for Rural Livelihood Security, 2) Linseed Value Addition, for providing better price and buy back guarantee to the farmers. Dr. Hegde's team developed many omega-3-enriched products including omega-3 egg, omega-3 milk, and omega-3 chicken with the aim of achieving omega-3 nutritional security in the country, to reduce morbidity and mortality. In order to take the initiative forward and for promoting linseed agriculture, ICAR instituted Linseed Value Addition Center at BVDU, to connect to the remaining 13 ICAR linseed research centers for promoting Linseed Agriculture in the country.

Currently, Dr. Hegde is the director for Center for Innovation in Nutrition Health Disease established within IRSHA. He has also established Real World Nutrition Laboratory Foundation, a not-for-profit company, for validating the omega-3-enriched products in the market and gets industrial linkage for scaling up.

Dr. Hegde has guided 16 students for Ph.D., several M.Phil., M.Pharm., M.D., M.S., and M.D.S. dissertations. He has published over 75 papers in diverse fields and authored textbook in biochemistry for undergraduates, written several chapters in books. Dr. Hegde is member of several scientific societies, society of biological chemists, microbiology, nutrition, and poultry science, and fellow of society of Indian Agriculture Biochemists.

Dr. Hegde is recipient of DST-Lockheed Martin Innovation gold medal and received Rs. one lakh cash award and special appreciation award of Bharati Vidyapeeth for conducting research program, directly relevant to society.

Dr. Hegde is also recipient of research grants from several funding agencies, besides ICAR, Department of Science and Technology, Department of Biotechnology, BIRAC Biotechnology Ignition Grant (BIG), Council of Scientific and Industrial Research, Khadi Village Commission, etc.

In the last 15 years, Dr. Hegde has focused his research efforts to establish the role omega-3 fatty acids in health and disease, to verify and confirm the efficacy of omega-3 fatty acids and antioxidant supplementation in disease outcome along with usual treatment regimen, to develop technologies/protocol to enrich egg, milk, and chicken with omega-3 fatty acids, and to stabilize omega-3 fatty acids in omega-3 enriched functional foods.

Dr. Anand Arvind Zanwar M. Pharma,. Ph.D. is currently working as scientist at Interactive Research School for Health Affairs, Bharati Vidyapeeth Deemed University, India. The main research focus includes preclinical pharmacology and toxicology. He has been working mainly on pharmacological and nutritional aspects of flaxseed and omega-3 fatty acid. Further fortification of various kinds of food with omega-3 fatty acid and its pharmacological evaluation has been his important focus. Dr. Zanwar is currently scientist in charge for the newly established ICAR-AICRP-Linseed Value Addition Centre at Bharati Vidyapeeth Deemed University, India.

Dr. Zanwar worked on various projects related to anti-inflammatory, antidiuretic, immunomodulatory, hepatoprotective, diabetes, wound healing, antihypertensive, cardioprotective activities, and complication of cardiovascular disease in preclinical screening of various medicinal plants/herbal extracts. He has experience in evaluating drug safety and efficacy as well as surgical techniques necessary for animal model research of cardiovascular pharmacology. Further, he has experience in various techniques related to phytochemistry and natural product in order to isolate the active compound from extract.

Dr. Zanwar received Ph.D. in pharmaceutical sciences form Bharati Vidyapeeth Deemed University, Pune, India. He has recently received, "Young Investigator Award" by the Asia Pacific Federation of International Atherosclerosis Society at Hong Kong and "International Travel Grant Award" from Science and Engineering Research Board, Department of Science & Technology, New Delhi. He has also received best paper award by Indian Atherosclerotic Society.

Dr. Zanwar has several publications and patents to his credit. He has authored several book chapters published by Humana press-Springer Science and Academic Press-Elsevier publisher. He is currently acting as reviewer board member for many peer-reviewed international journals.

Dr. Sharad P. Adekar M.D., Ph.D. is a physician scientist with experience in Immunology, Infectious diseases, and antibody discovery. Currently, he is working as medical vice chair at WIRB, Puyallup, WA, USA. Prior starting at WIRB, Dr. Adekar was working as consultant in antibody discovery and development area. He also worked as director of antibody research at Immunome, Inc., in Pennsylvania. He received his medical degree (M.B.B.S., MD) from B.J. Medical College, Pune, and worked on his Ph.D. thesis at Thomas Jefferson University, Philadelphia, PA ,and received final Ph.D. from University of Pune, India. In India, he also worked as scientist at IRSHA, Bharati Vidyapeeth Deemed University's, Medical College Campus, Dhankawadi,

Pune 411043, India, where he was involved in omega-3 fatty acid research in health and diseases.

Dr. Adekar has invented a novel method to make human monoclonal antibodies and **received US patent for `Fusion partner cell line that are used for preparation of hybrid cells that express human antibodies" in October 2013**. He has also applied patents for antibody technology as well as number of human antibodies.

Dr. Adekar has extensive experience in human antibodies in terms of discovery and leads optimization and preclinical development of monoclonal antibody therapeutics. **He has created human monoclonal antibodies in oncology, infectious diseases, and autoimmune and neurological diseases.**

He has published various peer-reviewed articles and participated in several conference presentations that include panel discussions, invited presentations, and peer-reviewed oral presentations. He has also served as Principal Investigator on SBIR grant applications and generated funds.

Dr. Adekar has demonstrated ability to develop and optimize novel research approaches and successful implementation of those ideas while collaborating with different groups. He has skills in translating business objectives into action plans and scientific methods necessary to drive a team.

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Nutrition, Life, Disease, and Death

1

Mahabaleshwar V. Hegde, Anand Arvind Zanwar, and Sharad P. Adekar

Introduction

The main aim of the chapter was to emphasize the extraordinary importance of omega-3 fatty acids for human health today. However, we cannot undermine the importance of the rest of the essential nutrients. All the essential nutrients in adequate quantities and their bioavailability have also to be ensured for good health. It is also important to be conscious of anti-nutrients [1, 2] including long-term use of drugs, tobacco, toxic pollutants, heavy metals and our ability to completely detoxify and protect our body from any harmful effects [3]. In this chapter, we will attempt to briefly discuss these confounding factors on which the ultimate beneficial effects omega-3 fatty acids actually rests.

We Are What We Eat

The living organisms are unique in that they are self-replicating, self-adjusting, self-repairing, and self-evolving systems. We are what we eat. Daily what we eat makes our body, robust or fragile. So it is obvious that we have to pay proper attention to what we eat. For this, we have to fully understand and appreciate what our body daily needs are. You must know whether or not you are providing in your daily diet all that you need. Eat right and stay healthy and fit. More often than not our health problems originate because we have not given proper attention to what we eat. Often the question is asked are we living to eat or we are eating to live. We often blame our genes that we inherited from our parents. None of us have any choice of choosing our parents. Like it or not, we have to live with it. Accept it as our fate. No one is born with perfect set of all healthy genes. There will be some defect somewhere which might crop up and start affecting our health sooner or later. If the defect happens to be in some vital genes, one can be born within born errors [4] that become apparent almost immediately. If detected early and attended early, for some, it may be possible to control and reduce the sufferings [5]. But there are many so-called diseases of civilization [6] that do not become apparent immediately but show up later in life and become a chronic degenerative disease. All of us know that these types of health problems that manifest as chronic diseases, such as heart disease, diabetes, arthritis, mental illness, and cancer because of sudden drastic lifestyle changes, are now surfacing sooner than later. Again one can blame our genes that we inherited from our parents. Although we can do nothing about the imperfect genes that we may have inherited, we have to blame ourselves for having precipitated the disease early, mostly due to unhealthy diet and partly due to lifestyle. It is therefore now these degenerative diseases are being regarded as lifestyle disease. Modern stressful lifestyle, junk food, pollutants, tobacco, overuse of drugs, alcohol, along with total negligence to the actual nutritional needs of the body, all cumulatively contribute to the early occurrence and increase in severity of degenerative diseases. It is our wrong lifestyle, bad eating habits that make us vulnerable to get the genetically predisposed disease, early and more aggressively. We must understand and appreciate that genes do not function on their own. Genes need basic ingredients, essential nutrients, incessantly supplied from our food, to do their assigned job properly. Genes can work efficiently, only if we supply these basic ingredients adequately, daily in our food, only then they are capable of giving us a healthy body.

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Of the many essential nutrients, the deficiency of omega-3 fatty acids, a crucial nutrient in modern man's diet, and also the ratio of omega-6/omega-3 [7] are largely responsible for our health problems, hence the emphasis on omega-3 fatty acids in this book.

Our body is dynamic; it continuously renews itself from the food that we eat. Different parts of the body are programmed by the genes to be renewed at different rates. Old cells die by a natural process called apoptosis and are replaced by new cells. This creation of new cells happens with the help of ingredients provided by food constituents. Old cells must die as they are no longer able to carry out their functions efficiently and have to be replaced by new cells. So it becomes apparent that without the continuous supply of proper and complete nutrients through our food, body cannot create optimally functional new healthy cells in each and every part of our body. So it is clear that perfect understanding of body's needs and their adequate supply through food is basic to our good health. Improper and incomplete nutrients in our food will result in creation of unhealthy new cells, ultimately resulting in unhealthy body. Conversely, if one gives good food, complete in all respects in quantity and quality, we can transform our body from ill health to good health.

Human Body Knows no Pathies but Understands Nutrition

Allopathy, ayurveda, unani, homeopathy, and traditional or modern medicines are different pathies or different modes of treatment. However, each one of these pathies just provides chemicals resourced from natural or synthetic sources to treat diseases through their unique treatment modalities. These chemicals have to interact with abnormal metabolism, characteristic of the disease, in a favorable way to normalize metabolism and to bring about curing process. However, human body knows no pathies but understands nutrition. These chemicals, being not natural and not normal constituent of our metabolism, can have some side effects. On the other hand, nutrients are part and parcel of the normal metabolism and hence nutrients are primary for the maintenance of good health. Actually, in most of the times, inadequate or improper intake of nutrients is the root cause of our disturbed metabolism and illness. Obviously medicines coming from modern medicine or alternative complimentary medicine cannot constitute a substitute for essential nutrients needed by the human body, in the food. This being the case, it is nearly impossible to normalize the metabolism by the chemicals coming from traditional or modern medicines, unless supported by the judicious nutritional support of essential nutrients.

Entropy and Nutrition

According to the second law of thermodynamics, cosmic force drives the whole universe toward increasing entropy, to move toward disorder and destruction. Life is order. Death is disorder. Life is defeating entropy and death is victory of entropy [8]. Hence, death is imminent and more natural. Life is therefore a miracle, and aging, disease, and death are certainty.

Thus, eating is as much a way of acquiring order, as it is a way of gaining energy for defeating entropy, to sustain life. Living organisms are not in equilibrium, rather they require a continuous influx of free energy to maintain order in a universe bent upon maximizing disorder. Metabolism is an overall process through which living systems acquire and utilize the energy they need to carry out their various functions. They do so by coupling the exergonic reaction of nutrient oxidation to the endergonic reactions, required to maintain the living state [8].

It is very difficult to imagine how life could have been formed on our planet, against all odds. It is more difficult to imagine that the life continues and evolve on this planet. However, by some miracles of circumstances, the life got formed and has sustained over four billion years. For creating and sustaining life, the life forces have to work against the nature's law of entropy, the ever increasing disorder (entropy), and against the basic laws of thermodynamics. However, not surprisingly therefore, the nature has the last laugh and ultimately entropy wins and death ensues (Fig. 1.1). What all this simply means is that for the life to sustain well, remain in a healthy state, we have to continuously help our body to manage to work against the second law of thermodynamics. So the nutrition has to fulfill two independent functions: firstly, to provide all the ingredients needed to feed our body (with basic macro and over 40 essential micronutrients) daily to renew our body (Fig. 1.2);

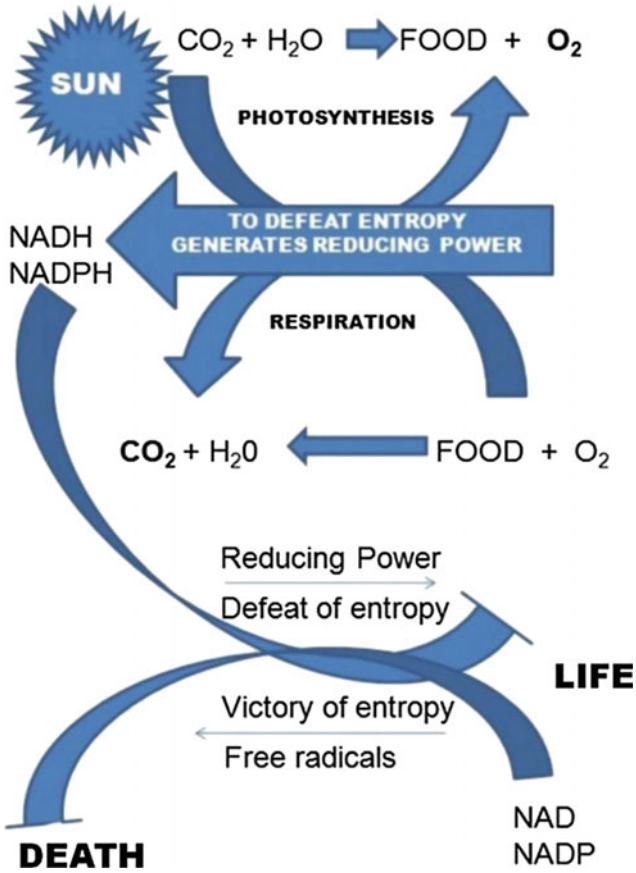

Fig. 1.1 Life is created and sustained by reducing power, defeating entropy

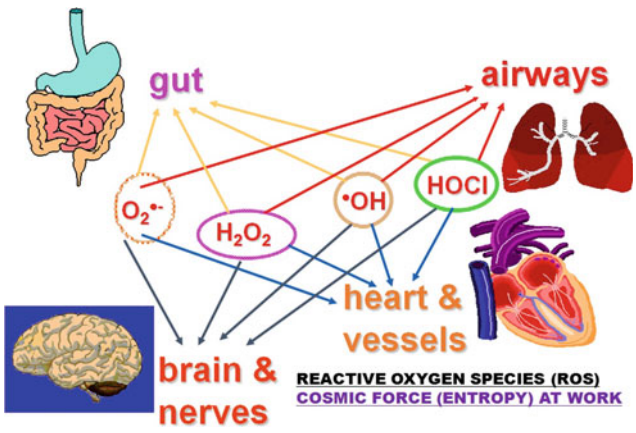

Fig. 1.2 Oxygen for life and oxygen for death

secondly, to provide enough antioxidants from food along with antioxidant defense of the body to neutralize the inevitable entropy forces such as oxidative stress and free radicals (Fig. 1.3), to protect us from disease and death. So it becomes obvious that first we have to understand the basics of nutrition and the basis on which we can live a long healthy life.

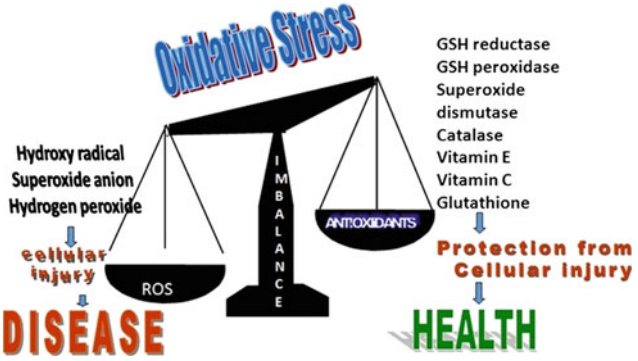

Fig. 1.3 Managing oxidative stress

Origin of Life, Chemical and Early Biological Evolution

Before we discuss the basics of nutrition and the philosophy of living, healthy long life, it may be prudent to discuss how and under what circumstances life got formed on this planet, overriding the second law of thermodynamics and the subsequent biological evolution that led to the creation most astonishing life-form, we the human being.

It is reliably estimated that life originated on our planet about four billion years ago [9], when there was no oxygen in earth's atmosphere. Carbon, hydrogen, oxygen, and nitrogen were the chosen primary elements by nature to create life on this planet. Primordial earth had all these four basic elements, carbon, hydrogen, oxygen, and nitrogen in reduced form, carbon as methane CH_4, hydrogen as H_2, oxygen as water OH_2, and nitrogen as ammonia NH_3. Urey made the case that reducing atmosphere was ideal for the origin of life [10]. Perhaps this was an ideal condition for life to originate. Oparin and Haldane [11] and Urey and Miller, by mimicking the primordial condition of the earth [12] in their laboratory, showed that CH_4, H_2, H_2O, and NH_3 can generate the fundamental life-forming molecules, amino acids, sugars, fatty acids nucleotides, which is the basis of chemical evolution, to later initiate biological evolution [13] (Fig. 1.4).

There are two main characteristics of living state that distinguishes it from lifeless state, viz. growth and replication. Today we know that deoxyribonucleic acid (DNA) has attained that ability not only to store all the information of a life-form, but also to express the information, transmit to the next generation, and evolve to survive and adapt to any environment to the extent possible. The information stored in DNA is expressed through the formation of variety of very versatile protein molecules that can take up several responsibilities to keep the life in healthy living state, including the function of replication of DNA. So it is very intriguing whether DNA has to be replicated by the DNA polymerase, a protein, the product of DNA itself. So

Fig. 1.4 Important ingredients needed in food for good health

naturally we wonder, what came first DNA or protein? DNA that codes for protein or protein that replicates DNA? This leads to famous dilemma chicken or egg what came first? However, this riddle has been fairly well resolved by assuming that RNA is the first living molecule, a molecule that had originally the ability to replicate and grow. Initially, RNA [14] could take up the responsibility of both, of a genetic material, that can store information and also transfer information to next generation, as well as act as an enzyme replicase. However, RNA could not carry out either of these functions very efficiently. Therefore, the nature evolved two distinct more efficient molecules, deoxyribonucleic acid (DNA) as genetic material and protein as enzyme, to act as catalytic agent to carry out all life reactions.

Originally, under primordial conditions, the energy was derived from the reduced molecules, but soon a way was found to derive the energy from the sunlight, through a process of photosynthesis, that again produced reduced molecules $NADH^+$ and $NADPH^{+,}$ to provide the most basic support to sustain life, for maintaining reducing conditions within each and every cell. $NADH^+$ is primarily used for generating ATP, a universal ubiquitous energy currency of all life-forms on this planet. On the other hand, $NADPH^+$ is the driving force to build up our body matter from the building blocks supplied by food ingredients. It seems this initial process of photosynthesis became so overwhelming and self-perpetuating that whole earth got engulfed by green plantation. The process also led to the evolution of large amount of oxygen by splitting water. The oxygen later converted into O_3 (ozone) and formed the outermost cover of the earth that filtered some radiations, and the photosynthesis was modified to suit this new situation. Animal forms were later evolved to keep the life in balance. Photosynthesis and respiration are same reactions but occurring in reverse. While in respiration process, glucose and oxygen yield carbon dioxide and water. In photosynthesis, organic carbon (glucose and starch) are produced from inorganic carbon (carbon dioxide). On the one hand in respiration, NADPH and ATP are derived via oxidation of organic carbon (food), and on the another hand, the photosynthesis generates fundamental reduced molecules NADH, NADPH, and ATP by capture of sun energy and manufacture food and in respiration NADH, NADPH, and ATP are produced, via oxidation of food. Ultimately it is the reduced internal cellular environment that supports life, although differently produced in plants and animals. All these discussions are to emphasize the importance of antioxidants (reduced molecules) in our food besides essential nutrients.

Vegetarianism Is Healthier

It can be noted that the plant forms derive energy from the sun through photosynthesis and by fixing carbon dioxide CO_2 from air, by reductive synthesis form biomolecules and evolve oxygen. This became a perfect platform set for the nature to experiment and to develop very complementary animal life-forms that can derive energy from biomolecules in plant forms by oxidation process that uses oxygen from atmosphere and evolves carbon dioxide. The nature thereby acquired balance between the two opposing ways of living. We the human, the animal forms, derive energy by oxidative process that uses oxygen and evolves carbon dioxide. The oxidation–reduction process produces again the same reduced molecules NADH and NADPH. So it seems the reducing power is the driving force for the life that defeats

the entropy. This oxidation process also inevitably produces some highly reactive oxygen species (ROS), free radicals. ROS are primarily now recognized as agents of aging disease and death. So these free radicals can be considered as agents of entropy at work. Therefore, the major approach to protect ourselves from disease and death would be to effectively neutralize the free radicals by consuming sumptuous amount of food rich in antioxidants. Between the vegetarian and non-vegetarian, obviously the vegetarian would be rich in reduced molecules (antioxidants) as during the process of photosynthesis oxygen evolves and more reduced molecules are left behind. It is understandable that vegetarian food has more power of neutralizing free radicals defeating entropy and can support healthy long life.

Man Is Crippled in Evolution

Everyone is aware of human genome project [15]. The project on which very huge amount of money was spent to get the nucleotide sequence of all 23 pairs of human chromosomes. The project was completed ahead of time. When the project started, it was thought that man is the most complex organism on the planet and possibly has more than hundred thousand genes. But at the end of the project, it became evident that man has less than twenty thousand genes [16]. This is very much off the expected mark, particularly when even the simple-looking rice plant has forty-five thousand genes [17], twice that of human genome. Although this finding seems paradoxical, it is not surprising if we recognize the fact that man is crippled in evolution. Now this seemingly paradoxical situation can be explained by the difference in synthetic capabilities of rice versus man. Rice has ability to synthesize all its needs, namely all vitamins, all 20 amino acids, and the two essential omega-3 and omega-6 fatty acids from carbon dioxide from the air, minerals, and water from the soil with the help of energy obtained from sunlight. However, man is not endowed with this extraordinary synthetic power. He has lost them during evolution. He is not provided with the genes to make these nutrients. He is crippled in evolution. Therefore, he needs to obtain these nutrients, which are regarded as essential nutrients, readymade, daily from the food. However, we have been provided with the brain instead, with the ability to think. Now that we know that we are deprived of these genes and have lost the genes and as we have no ability to synthesize these nutrients, it should be our endeavor to ensure that our daily diet has the quality proteins that can provide all the essential amino acids adequately, all the vitamins, minerals, and also two essential omega-3 and omega-6 fatty acids. Only if we take care of these, we can have healthy body and any ill health that arises out of this negligence or ignorance may possibly be managed to some extent, for some time, by medicines, but cannot be corrected. Nutrition is vital and primary for good health; this seems to be the hidden message from the human genome project. Food for thought, think of food, seems to be a revelation from the human genome project [18].

Essential Micronutrients in Human Nutrition

Human food must contain six categories of ingredients: water, proteins, carbohydrates, fats, vitamins, and minerals. Although fiber cannot be regarded as required food ingredient, but is extremely important in prevention of diseases as it is helps in digestion and absorption and the bioavailability of micronutrients, about 60 % of the human body is composed of water. Nearly all the life-sustaining chemical reactions are carried out in aqueous medium. All the three bulk foods, namely proteins, carbohydrates, and fat can be sources of caloric energy. Carbohydrates and proteins provide four calories per gram. Carbohydrates are primary source of energy, and proteins and fat are used sparingly as source of energy or under emergency. Fat provides nine calories per gram. The human body is capable of manufacturing saturated and monosaturated fats, but not the essential omega-3 and omega-6 polyunsaturated fat.

Given enough calories, human body is capable of manufacturing thousands of chemical compounds from the food ingredients called metabolites by a process called metabolism to sustain life. However, unlike plants, as mentioned above, human body is incapable of synthesizing several nutrients, and hence they are called essential. These are some 40 micronutrients (Fig. 1.2).

Digestion Absorption, Critical in Nutrition

For the bioavailability of the nutrients, proper digestion and absorption are the critical factors. The diet is largely determined by the availability, processing, and palatability of foods. A healthy diet includes preparation of food and storage methods that preserve nutrients from oxidation, heat or leaching, and that reduce risk of food-borne illnesses. Bioavailability of nutrients is very vital as it actually determines the proportion of a nutrient that is absorbed from the diet and used for normal body functions. There are several steps in the metabolic pathway that can affect the ultimate nutrient bioavailability. Nutrients are first processed in mouth by process of chewing and get mixed with acid and enzyme in gastric juice. Finally released into small intestine.

Here with action of more enzymes, supplied by the pancreatic juice, food matrix is broken down to make the nutrients bio-accessible. Bioavailability is influenced by minerals and other ingredients in food. For example, vitamin C can enhance iron absorption, and phytosterols [19] can inhibit cholesterol absorption. The host factors, for example, intrinsic factor (IF), are needed for the absorption of vitamin B_{12} in lower intestine [20].

Survival of the Sickest

The two guiding force of evolution is to survive and reproduce. All kinds of environmental factors, weather patterns, changing food supplies, and even dietary preferences, have affected our evolution. In the course of evolution, mutations that are bad do not survive; when they are good, they lead to the evolution of a new trait through the process of natural selection. Obviously, DNA does not determine life, it shapes it; environment and your choice of environment and food surely does. Referring to Triage theory put up by Bruce Ames, we stated that nature favors short-term survival over the long-term survival. This aspect is discussed at length in the book entitled "Survival of the Sickest" by Maolem [21]. This very nature of nature selects you to suffer from deadly disease (thalassemia) to save you from deadly disease (malaria), immediate death, and suffering for long time.

Similar principle also seems to be true even with respect to nutrition. This aspect has been convincingly demonstrated by the Triage theory put up by Bruce [22]. The theory is based on the fact that "nature favors short-term survival over long-term survival." Nature strives to keep you alive today, even if the action taken is responsible for your long-term suffering later.

Very important aspect of nutrition, that we often tend to neglect, is the need of completeness, need of every essential nutrient in adequate quantity. All nutrients are important in its own right. Every one of the 40 nutrients mentioned has a well-defined role in the metabolism. If the diet is deficient in any one of them, body will not be able to function optimally and it is certain to have adverse effect on health. According to Bruce Ames, our body prioritizes the supply of micronutrients to vital organs (heart, for example) and for vital functions (blood coagulation) to ensure our immediate survival. In the event of suboptimal supply of micronutrients, only vital organs and vital functions will get the micronutrients on priority. The rest of the organs (liver, kidney, and the organs that are not as important as heart for immediate survival) get starved of these nutrients and eventually succumb to this continued discrimination, so also less vital functions not important for immediate survival such as DNA repair gets compromised. Not surprisingly, inability of our body to repair the DNA damage that inevitably occurs because of the want of enough micronutrients can be the primary cause for developing cancer later.

Triage literally means sorting out patients based on the possibility of their survival and prioritizes treatment, particularly during war. Bruce Ames worked with vitamin K [23] as micronutrient to prove his triage theory. Vitamin K works in our body with five gene products to control blood coagulation, a vital function for our immediate survival. Vitamin K also works with 12 more gene products for bone health, not vital, not so important for immediate survival. Knocking vital blood coagulation genes in mice experiment was lethal and knocking out bone health genes was not lethal. In the event of suboptimal supply of vitamin K, vitamin K would be prioritized for blood coagulation function and vitamin K availability for bone health gene functions will be compromised. This suboptimal vitamin K supply can eventually lead to bone diseases. Bruce Ames further suggests that our present recommended daily allowance for micronutrients must be reviewed in light of triage theory. The present RDA for vitamin K, 90 mcg per day, may be just enough for managing blood coagulation function and not enough for bone health. The take away home message from the theory is that we must ensure the adequate intake of all the 40 essential nutrients daily for good health.

Omega-3 Fatty Acid Crucial Nutrient

We have above argued that intake of all 40 nutrients daily is a must to keep the human body in a healthy state. Available evidence from recent published meta-analyses indicates that omega-3 fatty acids plays a crucial role in the prevention of non-communicable diseases such as cardiovascular disease, breast cancer, and colorectal cancer. [24].

Detailed account of the role of omega-3 fatty acids in health and disease has been mentioned in a number of chapters that follow. Here, it is suffice to say that because of paucity of omega-3 in the modern diet and also because of excessive omega-6 fatty acid intake, there is an imbalance, resulting in highly inflammatory conditions, prevailing globally in modern man. The recent rise of degenerative diseases is attributed to this imbalance and dominance of inflammatory condition in modern man.

Omega-3 Index

The omega-3 index is the combined percentage of eicosopentanoic acid and docosohexanoic acid of total fatty acids in red blood cell membrane [25]. It is inferred that man

as hunter–gatherer consumed almost equal amount of omega-3 fatty acid; the omega-3 index was close to 1:1. But in recent times, his food has very little of omega-3 and is excessively loaded with omega-6 fatty acid; the omega-3 index is 1:10, 1:20, or even 1:50, but ideally the healthy omega-3 index suggested to be 1:5. This ratio 1:5 has been thought to be ideal because omega-3 fatty acid (ALA) and omega-6 fatty acid(LA) are processed by the same set of elongase and desaturases to highly unsaturated fatty acids (HUFA), EPA and DHA (both omega-3), and AA (omega-6). Five times higher levels of omega-6 do not affect the conversion of omega-3 PUFA to omega-3 HUFA. This is because the elongases and desaturases have higher affinity to omega-3 than omega-6 fatty acids. Therefore, even at five times less level of omega-3 fatty PUFA's can be equally converted. Omega-3 fatty acids are one of the most sought after essential nutrient. In order to cut down omega-6 fatty acid consumption, omega-9 (MUFA olive oil) oleic acid is being promoted all over the world [26].

Free Radicals

Free radicals are molecules, such as reactive oxygen species (ROS), that have lost an electron and have become very unstable and become highly reactive and can rob electrons from neighboring vital molecules [27]. They act as terrorists in the body, attack vital protein, DNA, leading to dysfunction, mutation, and cancer. They attack proteins and enzymes, inactivate them, and thereby disrupt the normal activities they perform. Free radicals attack cell membranes, in cells that line our blood vessels, and hardening and thickening of the arteries eventually resulting in heart attacks and strokes. Free radicals attack on collagen can cause cross-linking, resulting in the stiffness of joints. Thus, ROS contributes to both initiation and promotion of many major diseases [27]. This constant attack of ROS is also referred to as oxidative stress [28]. Actually, the clinical presentation of various diseases, the way illness finally appears, can be the representation of variation in the individualistic protection provided by the body's antioxidant defenses [29] and also the antioxidants in the food. Under oxidative stress, the weakest link in the body may be the first to give way to a specific disease, partly determined by genetic predisposition.

It would be wrong to infer that free radicals are always bad. Free radicals and antioxidants play a dual role both toxic and beneficial compounds, since they can be either harmful or helpful to the body [30]. However, free radicals may create a chain reaction that can damage the body. It must be noted that the production of free radicals in the body is continuous and inescapable.

Oxidative Stress

It is well known that chronic, persistent stress triggers numerous illnesses. However, exactly how that occurs is, although, not fully understood; there are some ideas and theories explaining the stress and its relation to illness. Oxidative stress is a condition wherein ROS is in excess of the available antioxidant buffering capacity [30].

Human body has trillions of cells of over 200 different kinds as a part of various organs, heart, brain, kidney, liver, and lungs. performing various important functions and working in unison to keep our body in healthy state. In every cell, there are numerous smaller organelles, mitochondria, power house of the cell. Every cell generates ROS if it cannot neutralize it effectively with its available antioxidant buffering capacity; oxidative stress will be induced potentially injuring the cell and inevitably can initiate disease process [31].

Autophagy

Autophagy is a self-degradative process that is important for balancing sources of energy, in response to nutrient stress. Free radicals change cellular responses. At low level, they may act like signaling molecules but at high levels can damage the organelles, particularly mitochondria [32]. Associated mitochondrial dysfunction may result in energy depletion, redox changes, and cell death. Autophagy (or self-eating) is a lysosome-mediated degradation process for nonessential or damaged cellular constituents. Physiologically autophagy serves to preserve the balance between organelle biosynthesis, protein synthesis, and their clearance. Oxidative stress is inseparably linked to mitochondrial dysfunction. Oxidative stress normally implies that ROS/RNS are toxic species because of their highly reactive nature. Similarly, autophagy may be regarded as bad for the cell since an unhealthy cell has multiple vesicles. However, under some situations, "self-cleansing" can be good for the cell. Generally, autophagy can be regarded as the activity that decreases ROS/RNS damage, as autophagy plays an important role in both sensing oxidative stress and removing oxidatively damaged proteins and organelles.

Integrating Homeostasis Allostasis and Stress

Homeostasis [33] means staying the same. The enzymes work best at optimum temperature and pH. Internal conditions allowed to vary within narrow limits. Human body temperature, for example, varies between 36.1 and 37.8 °C.

So a better definition of "homeostasis" is the maintenance of the internal environment within narrow limits. Homeostasis consist of number of cooperating mechanisms acting simultaneously or successively. Homeostasis is the result of organized self-governance. Actually many pharmaceutical interventions work for homeostasis by suppressing extreme reaction. Although body tries to keep metabolites normally within normal limits by the process of homeostasis, sometimes the body may need to readjust and cross the normal limits and remain stable by changing to maintain stability by a process called allostasis [34]. Allostasis is an adoptive change, usually temporary, to deal with emergency situations. However, in the long run, allostatic change, so-called allostatic load, may fail to be adaptive as the maintenance of allostatic changing over a long period may result in wear and tear. Human body is adaptable, but it cannot maintain allostatic overload for very long time, without consequence of adverse effect on health.

Life, Disease, Cancer, and Death: Simple Play of Redox

Redox homeostasis [35] actually governs the life, disease, death, and cancer. Cell maintains redox balance under physiological conditions. This is achieved through generation and elimination of free radical. Free radical includes reactive oxygen species (ROS) such as superoxide, hydroxyl radical and non-radical species such as hydrogen peroxide and nitrogen species (RNS) comprised of nitric oxide, peroxynitrite. For maintaining redox homeostasis cells are equipped with enzymatic and non-enzymatic antioxidant system. Superoxide dismutase is major class of enzymatic antioxidant system that catalyses dismutation of O_2 to H_2O_2. H_2O_2 is further broken down by catalase. H_2O_2 can also be eliminated by glutathione peroxidase by converting reduced to oxidized glutathione.

There is a view that cancer is an epigenetic disease. Normal cells in response to chronic stress, in desperate attempt to survive, undergo many different adaptive mutations, to bring about malignant transformation, to survive and multiply indefinitely. It must be noted that the cancer cells have abnormal energy metabolism that depends heavily on aerobic glycolysis, known as Warburg effect.

Telomers and the Lifespan

Telomers are repeated nucleotide sequences located at the ends of linear chromosomes. It is believed that telomers shorten with each somatic cell replication. Telomers are essential for the chromosomal stability and replication. Enzyme telomerase is important in telomere formation, restoration, and maintenance [36]. Telomers can be maintained or lengthened [37] by adding telomeric DNA to shortened telomers [38]. Telomere length is also linked to and likely regulated by exposure to pro-inflammatory cytokines and oxidative stress [39]. Higher n-6 intake is associated with shorter telomere length [40] Inflammation triggers T cell proliferation, one known cause for T cell shortening [41]. Oxidative stress promotes telomere erosion during replication. Oxidative stress stimulates the synthesis of pro-inflammatory cytokines. Although telomers shorten with aging, shortening is not inevitable. PUFAs in blood may prevent telomere shortening. Omega-3 fatty acids can reduce inflammation and decrease oxidative stress [42]. Lower n-6/n-3 ratios were associated with longer telomere length. N-3 supplementation lowered F-2 isoprostane (oxidative stress). Although shortening of telomers with age is a natural phenomenon, the dietary intervention that reduces the joint burden of oxidative stress and inflammation can have positive impact on telomere length within few months [43]. Circulating PUFA levels are not always correlated with dietary intake that depends on absorption and metabolism. There is a compelling evidence that lower n-6/n-3 ratio slows biological aging. It is obvious that omega-3 fatty acids, possibly other essential nutrition, provide long healthy life.

Role of DHA in Human Brain, Adaptability to the Diverse and Adverse Environment for Survival

We now refer to ground-breaking, courageous, and visionary book of Bruce Lipton "Biology of Belief" [44] that provides solid evidence that membrane directly in contact with internal microenvironment or with external macroenvironment decides and dictates the fate of the cell and it is not the DNA, decorated master molecule that governs life. All function that our body carries out are also carried out by every single cell in our body and these cells also learn from their microenvironment and create their own cellular memories.

Most importantly, Bruce Lipton vehemently argues that it is the membrane, may it be of a prokaryote without any organelles or an eukaryotic cell with nucleus, mitochondria, and other well-defined organelles, with well-defined functions within the cell, which governs life within the cell, as dictated by the environment, and therefore, it can be regarded as the brain of the cell.

Fossil evidence reveals that single-celled life-forms originated within 600 million years after the earth was first formed, and for the next 2.75 billion years, only free-living single-celled organisms—bacteria, algae, protozoans populated the earth. However, around 750 million years ago,

these single-celled organisms became smarter, intelligently chose to live as community of cells, socially interactive millions, billions, and even trillion cells, as biological compulsion to survive. For efficient living and to survive in harmony, individual cells became tissues, assumed specialized task, and became organs. These organized collection of cellular communities formed organism: plants, animals including most sophisticated complicated humans.

Bruce Lipton surmises that "*the cells operations are primarily molded by its interaction with the environment not by its genetic code.*" Although the DNA in the nucleus are remarkable molecules and carry the blueprint of all life-forms, however, they do not control the operations of the cell. Therefore, the membrane with their receptors, interacting intelligently with the environment and efficiently governing the life functions inside the cell, constitute the true brain.

Darwin's theory of evolution proposes that animals well suited to their environment survive. It is clear now that environment is driving force behind evolution, which in turn decided by ability of organism to process information about its environment. Therefore development of brain that has ability to receive, process, respond to environmental challenges faster has increased chances of survival [44–46]. Therefore, a complex human brain that contains about 100 billion neurons, more than 100,000 km of interconnections, and having an estimated storage capacity of 1.25×10^{12} bytes [47] was evolved.

Omega-3 fatty acid, particularly DHA, has an important role in the development of human brain. If you regard human brain as super computer, it would be appropriate to regard DHA as the hardware of the brain.

DHA has special significance in evolution of human brain [48, 49].

DHA is abundantly present in the human brain and is an essential requirement in every step of brain development such as neural cell proliferation, migration, differentiation, and synaptogenesis. The multiple double bonds and unique structure of DHA allows imparting special membrane characteristics for effective cell signaling. Evidences indicate that DHA accumulates in areas of the brain associated with learning and memory. Many development disorders such as dyslexia, autism spectrum disorder, attention deficit hyperactivity disorder, and schizophrenia are causally related to decreased level of DHA.

Therefore it is clear that Omega-3 fatty acids have not only played a major role in evolution of man, providing him the smartest brain, but also have provided with increased ability to interact with the environment and better adaptability to very diverse, adverse, environment and survive.

Concluding Remarks

Although we regard omega-3 fatty acids as most crucial nutrient today, we do not in any way wish to undermine the importance of other nutrients. In fact, we advocate that our diet should be complete in all essential nutrients, free of anti-nutrients, and high in antioxidants to ensure good health.

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Flax Bio-village Concept

2

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Introduction

The Flax Bio-village Concept (FBC) was formulated with holistic approach, its primary objective being to attain omega-3 nutritional security, at the same time promote flaxseed (linseed) agriculture. FBC researches and develops methods, to add value to linseed, by resourcing omega-3 fatty acid from linseed and enriching commonly consumed food, including egg milk chicken, for public health.

Functional Foods and Public Health

The focus of public health has to be to improve health and quality of life through prevention and treatment of disease and other physical and mental health conditions. Food is one of the most important and modifiable lifestyle determinants of human health. Under-nutrition and over-nutrition are both crucial determinants of morbidity and mortality and therefore nutritional interventions are needed to reduce morbidity and mortality through dietary changes. There are two approaches for micronutrient intervention, direct supplementation, or fortification (functional foods). Supplementation involves supplying the essential micronutrient nutrients in capsule form and requires a commitment of the consumer to take them regularly and religiously. On the other hand, functional foods provide the essential micronutrients as natural ingredients of the food. The latter, functional food approach is particularly suitable for developing countries like India, wherein a sea of illiterate masses divided on caste, religion, and regional basis, no one would understand the language of reason. Better way to tackle the problem is to provide functional foods that simultaneously attain food security as well as nutritional security.

There is a distinction between nutritional problems of developing and developed countries. Developed countries may suffer from over-nutrition and developing countries mostly with under-nutrition. Today, industrialized societies are characterized by increase in energy intake and decrease in energy expenditure; excessive increase in saturated fat, omega-6 unsaturated fat, and trans fat, along with drastic decrease in omega-3 fat intake; a decrease in complex carbohydrate and fiber; an increase in cereal grains; and a decrease in fruits and vegetables. On the other hand, developing countries, while struggling to catch up with developed world, have not only got the health problems of industrialized world, associated with affluent lifestyle, but at the same time a large section of the society face the problems of under-nutrition, malnutrition, with associated health problems like low birthweight, premature birth, infant mortality, and other pregnancy complications. Humans evolved on a diet in which the ratio of omega-6 to omega-3 essential fatty acids (EFAs) was about 1, whereas it is now become 15:1 or more [1], because the modern human diet is precariously low in omega-3 and harmfully excessive in omega-6 fatty acid. The phenomenon of omega-3/omega-6 imbalance exists in almost all parts of the world, equally in both developed and developing countries. Omega-3 functional food intervention would benefit both developed and developing countries.

Therefore, "bring back omega-3 fatty acids into food" chain has been a global cry.

These functional foods are responsible for overall well being and also protects from several disorders such as cancer, cardiovascular, inflammation, diabetes and many other degenerative diseases. It is well established that there is strong correlation between active constituent in food and its efficacy in controlling the progression or prevention of disease [2]. For the maximum reach, it is desirable to

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incorporate the most crucial omega-3, functional components, in daily consumed foods, such as egg, milk, and chicken.

Crucial Role of Omega-3 Fatty Acids in Public Health Today

Our health is very largely governed by nutrition in food. Health of our people is closely linked to our economy and progress. Today, we are faced with a very peculiar situation of malnutrition, under-nutrition, and over-nutrition. It is becoming increasingly evident from recent research that our health problem primarily originates from the inadequate supply of essential nutrient to our body. We need over 40 essential nutrients—vitamins, essential amino acids, minerals, and omega fatty acids. Of these essential nutrients, deficiency of omega fatty acids in modern human diet is responsible in a very major way to our disease-prone health status today.

Why omega-3 is so important? Omega-3 is part of cell membrane. They are responsible for hormonal regulation that regulates blood clotting, contraction and relaxation of artery walls, and inflammation. Both omega-6 and omega-3 are essential. However, most of us get too much omega-6 and very little of omega-3 fatty acid. Here is a situation of over-nutrition of omega-6 and under-nutrition of omega-3 fatty acid. This imbalance is largely the root cause of the increase in severity and incidences of several diseases, including heart disease, diabetes, arthritis, cancer, mental disorders, pregnancy complications, infant mortality, and child health. Role of omega-3 in well known during pregnancy in particular for infant nerve and eye function. Therefore it is critical to provide adequate supply of omega-3-poly unsaturated fatty acid during last trimester. It is therefore important to ensure adequate and balanced supply of EFAs, particularly to the nations with emerging economies and this would be the most prudent public health strategy for improving the health of the populations [3].

The ratio of omega-6 to 3 2.3:1 is recommended so as to maximize ALA to DHA conversion. This is because both omega-3 and omega-6-fatty acid compete for the same desaturase and elongase. Higher than this ratio of omega-6 (Linoleic acid) in the diet can affect ALA to EPA, DHA conversion in vivo. Kinetic studies conducted in vivo [4] have shown that ≈15 % of dietary ALA is converted to the long-chain omega-3 fatty acids, of which eicosapentaenoic acid (EPA; 20:5) and docosahexaenoic acid (DHA; 22:6) predominate at typical intakes of both linoleic acid (LA; 18:2), 15 g/d (5 % of energy) and alpha-linolenic acid (ALA; 18:3) 2 g/d (0.6 % of energy). Quantitatively, this conversion results in ≈300 mg of n-3 long-chain fatty acids being derived via conversion from ALA. When dietary linoleic acid is increased to 30 g/d, conversion of ALA to the long-chain omega-3 fatty acids is reduced by ≈40 % [5]. Thus, the conditions that favor maximal conversion of ALA to EPA and DHA are critically dependent on the amount of linoleic acid in the diet [6].

Inuit metabolism study revealed fish derived omega-3-fatty acids are protective. It seemed that Inuit were protected from cardiovascular disease and low incidence was attributed to their fat rich in traditional marine mammal diet. This findings led to recommendation, resulting in millions of westerners consuming fish oil to prevent heart disease. The rarity of ischemic heart disease in Greenland Inuits, once known as Eskimos, may partly be explained by the antithrombotic effect of the long-chained diets rich in marine oils [7]. On their traditional diet, rich in fat from marine mammals, Inuit seemed to be quite healthy with a low incidence of cardiovascular disease, so fish oil must be protective. Those conclusions eventually led to the recommendation that Westerners eat more fish to help prevent heart disease and sent tens of millions scrambling for fish oil pills.

Recently, it has been shown that Greenland Inuits show genetic signatures of diet and climate adaptation [8]. The adverse health effects of a high-fat diet are counterbalanced by high omega-3 (EPA and DHA) diet. They have unique mutations, nearly in 100 % of the Inuit, which is only 2 % in Europeans and 15 % in Han Chinese. The strongest signal of signature of adaptation was found on chromosome 11 in the cluster of fatty acid desaturases. Two genes FADS1 and FADS2, coding for delta 5 and delta 6 desaturase (D5D, D6D), are rate limiting steps and have been selected for adaptation to Inuit diet. It seems obvious that this mutation is vital for their survival of Inuit on high-fat diet. It was also noted that the mutation was found to be strongly associated with height because growth is in part regulated by person's fatty acid profile, which also affect the regulation of growth hormones. So it seems that what is true for Inuit, high EPA, and DHA fish diet may not be straightaway true for everyone else. Difference in the type omega-3 intake of vegetarian and non-vegetarian is depicted in Fig. 2.1.

Fish oils provide a source of EPA and docosahexaenoic acid (DHA), two fatty acids now recognized to be important for human health [9]. The increasing demand for EPA and DHA containing fish oils is putting pressure on fish species and numbers [10]. Fisheries provide fish for human consumption and supplement production, at a maximal historical rate, suggesting mass-scale fishing is no longer sustainable. High rate of fishing is resulting in a substantial effect on fish levels with the possibility of extinction [11]. The world's fish stocks are fast declining and it has been estimated that 100 % of the world's fish taxa will have collapsed by 2048 [12]. The major sources of these omega-3 fatty acids are oily fish species including salmon, mackerel, and herring [13].