

$\omega-3$

Fatty acids

$\omega-6$



हर कदम, हर डगर
किसानों का हमसफर
आज की कृषि, अजुगुन पथिक
AgriSearch with a human touch

Therapeutic Value of Fish

$\omega-3$

PUFAs

PUFAs

EPA + DHA

$\omega-6$

EPA + DHA

B. P. Mohanty
D. Sudheesan
T. V. Sankar
M. K. Das
A. P. Sharma

$\omega-6$

PUFAs

PUFAs

$\omega-3$

EPA + DHA

EPA + DHA

PUFAs

EPA + DHA

$\omega-6$

EPA + DHA

$\omega-3$

PUFAs



Central Inland Fisheries Research Institute

(Indian Council of Agricultural Research)

Barrackpore, Kolkata - 700 120, West Bengal





INDIAN COUNCIL OF AGRICULTURAL RESEARCH
FISHERIES DIVISION, KAB-II

**Nutrient Profiling and Evaluation of Fish
as a Dietary Component**

Outreach Activity Consortium # 3



Central Inland Fisheries Research Institute, Barrackpore
Lead Institute

2008 - 2012



CIFRI
Barrackpore



CIFT
Cochin



CMFRI
Cochin



CIBA
Chennai



CIFA
Bhubaneswar



CIFE
Mumbai



DCFR
Bhimtal



Therapeutic Value of Fish

B. P. Mohanty
D. Sudheesan
M. K. Das
A. P. Sharma



Bulletin No. 170

March, 2011

Central Inland Fisheries Research Institute

(Indian Council of Agricultural Research)

Barrackpore, Kolkata - 700 120, West Bengal

Therapeutic Value of Fish



B. P. Mohanty
D. Sudheesan
T. V. Sankar
M. K. Das
A. P. Sharma

B. P. Mohanty, D. Sudheesan, M. K. Das, A. P. Sharma
CIFRI, Barrackpore
T. V. Sankar, CIIT, Cochin

ISSN 0979-616X

© CIFRI, Barrackpore. March 2011

A Contribution from ICAR Outreach Activity (#3) Consortium: Nutrient Profiling and Evaluation of Fish as a Dietary Component.

Material contained in this Bulletin may not be reproduce, in any form, without the permission of the publisher

Declaration: The pharmaceutical preparations and Brand Names mentioned in the bulletin are just to show the readers the wide use of the fish oils and other materials across the globe. The authors declare no conflict of interest in this regard.

Published by:
Director,
CIFRI, Barrackpore

Printed at
Eastern Printing Processor
93, Dakshindari Road, Kolkata - 48

Therapeutic Value of Fish

B. P. Mohanty
D. Sudheesan
T. V. Sankar
M. K. Das
A. P. Sharma



Bulletin No. 170

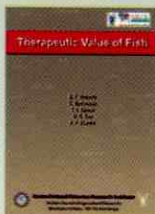
March, 2011

Central Inland Fisheries Research Institute

(Indian Council of Agricultural Research)

Barrackpore, Kolkata - 700 120, West Bengal

Therapeutic Value of Fish



B. P. Mohanty
D. Sudheesan
T. V. Sankar
M. K. Das
A. P. Sharma

B. P. Mohanty, D. Sudheesan, M. K. Das, A. P. Sharma
CIFRI, Barrackpore
T. V. Sankar, CIFT, Cochin

ISSN : 0970-616X

© CIFRI, Barrackpore.
March 2011

A Contribution from ICAR Outreach Activity (#3) Consortium : Nutrient Profiling and Evaluation of Fish as a Dietary Component.

Materials contained in this Bulletin may not be reproduced, in any form, without the permission of the publisher.

Declaration : The pharmaceutical preparations and Brand Names mentioned in the bulletin are just to show the readers the wide use of the fish oils and other materials across the globe. The authors declare no conflict of interest in this regard.

Published by :
Director,
CIFRI, Barrackpore

Printed at :
Eastern Printing Processor,
93, Dakshindari Road, Kolkata - 700 048



डा. एस. अय्यप्पन
सचिव एवं महानिदेशक

DR. S. AYYAPPAN
SECRETARY & DIRECTOR GENERAL

भारत सरकार

कृषि अनुसंधान और शिक्षा विभाग एवं

भारतीय कृषि अनुसंधान परिषद्

कृषि मंत्रालय, कृषि भवन, नई दिल्ली - 110 114

GOVERNMENT OF INDIA

DEPARTMENT OF AGRICULTURAL RESEARCH & EDUCATION
AND

INDIAN COUNCIL OF AGRICULTURAL RESEARCH

MINISTRY OF AGRICULTURE, KRISHI BHAVAN, NEW DELHI - 110 114

TEL: 23382629; 23386711 FAX: 91-11-23384773

e-Mail: dg.icar@nic.in

FOREWORD

Fish is a health food and is available as an affordable protein source. It has been known since long that fish possess therapeutic values and is being used for treating many diseases. Since fish is a cheap source of protein, it can go a long way to reduce protein calorie malnutrition prevailing in the underdeveloped and developing countries. Fish is a rich source of polyunsaturated fatty acids; omega-3 fatty acids are effectively being used in nutraceuticals for reducing coronary diseases, osteoarthritis, dementia, age-related macular degeneration, asthma and depression. Many fish species are used in Ethnomedicine all over the world. *Channa striatus* is known for its medicinal value and is commonly used as a remedy for healing wounds and post-operative recovery; the rich content of amino acids and fatty acids in this species accounts for its therapeutic ability. Many studies have been conducted to understand the species' medicinal properties. A recent trend is the fish spas for ichthyotherapy using *Garra rufa* and it is claimed that the treatment is useful in reducing skin diseases like psoriasis. Including fish in diet is recommended by the health experts and nutritionists for ensuring a sound health for the mankind.

It is expected that this bulletin on 'Therapeutic Value of Fish' under the ICAR Outreach Activity-3 Consortium on 'Nutrient Profiling and Evaluation of Fish as a Dietary Component' will provide a complete outlook on the therapeutic benefits of fishes. Further research on the therapeutic value of important fishes like *Clarias batrachus*, *Anabas testudineus* and *Heteropneustes fossilis* could also explain the scientific basis of the perceived therapeutic value of these fishes. Such new information can be generated and incorporated and this document can be revised to serve as a 'Handbook on Therapeutic values of fish'.

The authors deserve appreciation for their efforts in preparation of this bulletin that may prove to be a source of valuable information for diverse users.

(S. Ayyappan)

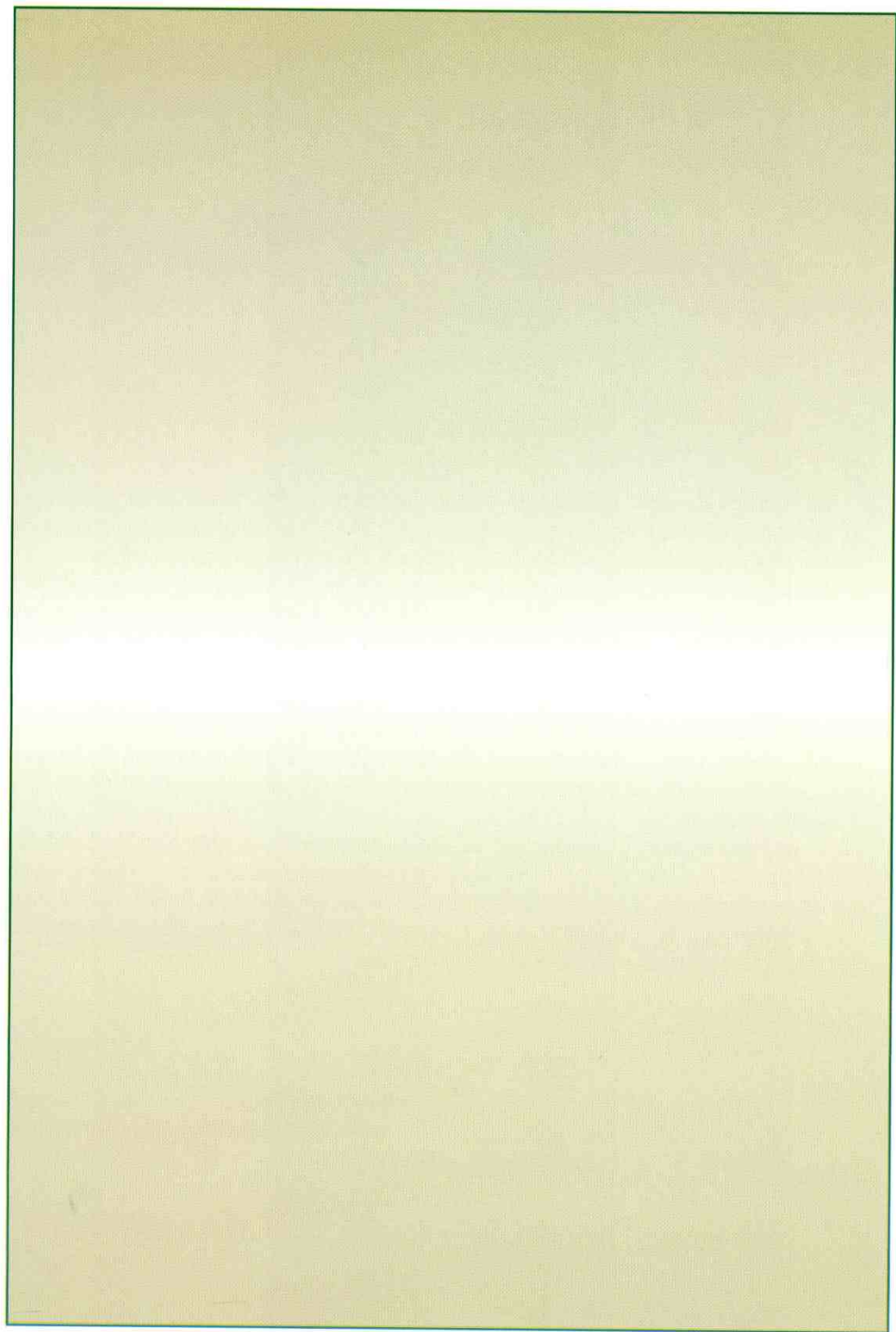
Dated the 31st March, 2011
New Delhi

FOREWORD

Fish is a rich source of nutrients like polyunsaturated fatty acids, amino acids, vitamins and minerals and therefore, it has therapeutic values. Fish plays a major role in preventing and curing coronary diseases, asthma, mental illness, eye diseases, low birth weight, nutrient deficiencies. It is important to include fish in our daily diet to maintain a healthy life. Many products are available in market like the fish oil, omega-3 tablets, fish oil enriched food products; they are commonly prescribed by physicians, nutritionists, dieticians for patients recovering from diseases, injuries and wounds. Fish is considered a cheap source of protein and can be consumed to combat the protein-calorie malnutrition in children. There are fish species with established therapeutic values like the *Channa striatus*, which is commonly used for curing diseases. Then there is the fish spa, which has come up recently, used for skin treatments. Many fishes are used in traditional system of medicines, which are being used for years. It is worth mentioning the role of small indigenous fishes in providing a healthy nutrient rich diet.

I have immense pleasure to acknowledge the efforts of the authors in bringing out the bulletin on 'Therapeutic Value of Fish' as a part of the ongoing ICAR Outreach Activity-3 Consortium on 'Nutrient Profiling and Evaluation of Fish as a Dietary Component'. I am sure that this project will help in furthering research on the medicinal qualities of fishes and as a result, a detailed documentation of therapeutic values of many fish species could be possible.

(B. Meenakumari)
Deputy Director General (Fisheries),
Fisheries Division, Indian Council of Agricultural Research,
Krishi Anusandhan Bhavan-II, Pusa Campus,
New Delhi-110012

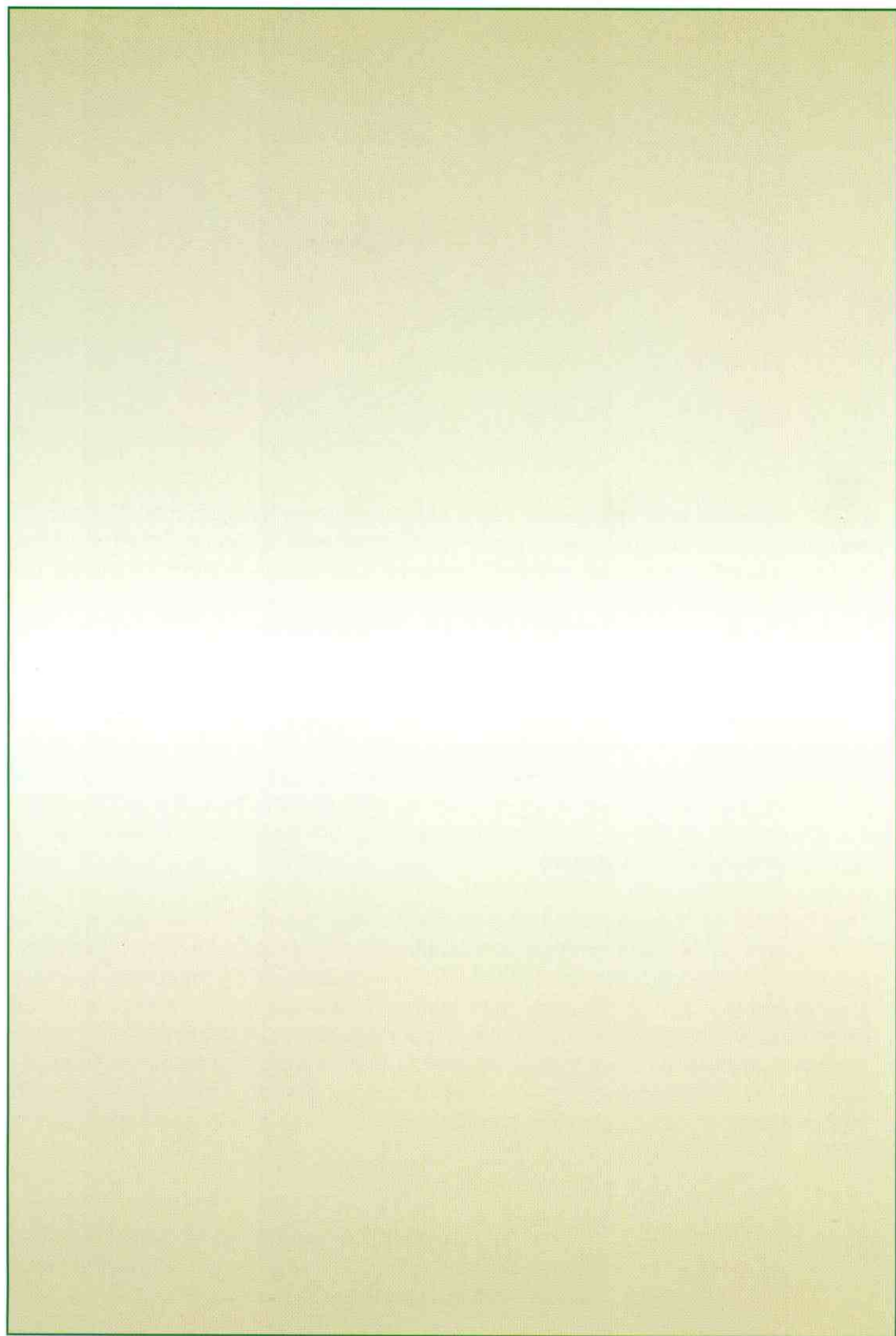


FOREWORD

The medicinal and therapeutic value of fish is known for centuries. The medicinal quality of fish is harnessed to prevent and cure heart diseases, arthritis, asthma and various other ailments, thereby, maintaining an overall health for humans. Our country, as well as other countries, has a rich traditional knowledge of fishes being used as medicines. This bulletin has given comprehensive information on the therapeutic values of fishes including detailed accounts of clinical correlations of fish components and its effectiveness against certain preventable human diseases. It also mentions about present day trends like fish spas. The importance of small indigenous fishes in providing nutritious and healthy diet to common man is also highlighted. Therapeutic properties of *Channa striatus* are also being studied. This document provides a proof of the increasing awareness among the people about the importance of fish in providing the essential nutrients and its role in fighting against diseases and disorders.

This bulletin on 'Therapeutic Value of Fish' under the ICAR Outreach Activity-3 Consortium on 'Nutrient Profiling and Evaluation of Fish as a Dietary Component' is an appreciable compilation of the importance of fishes in therapeutics. I appreciate the efforts made by the authors for gathering a wealth of information and publishing this worthwhile document. I hope that more scientific studies about role and applications of food fishes to fight against human hunger and diseases from perspective and prospective angles will be conducted and an inventory of fishes for therapeutic and medicinal value is brought out for better health of common people.

(S. D. Singh)
Assistant Director General (Inland Fisheries)
Fisheries Division, Indian Council of Agricultural Research
Krishi Anusandhan Bhavan-II, Pusa, New Delhi-110012



Acknowledgements

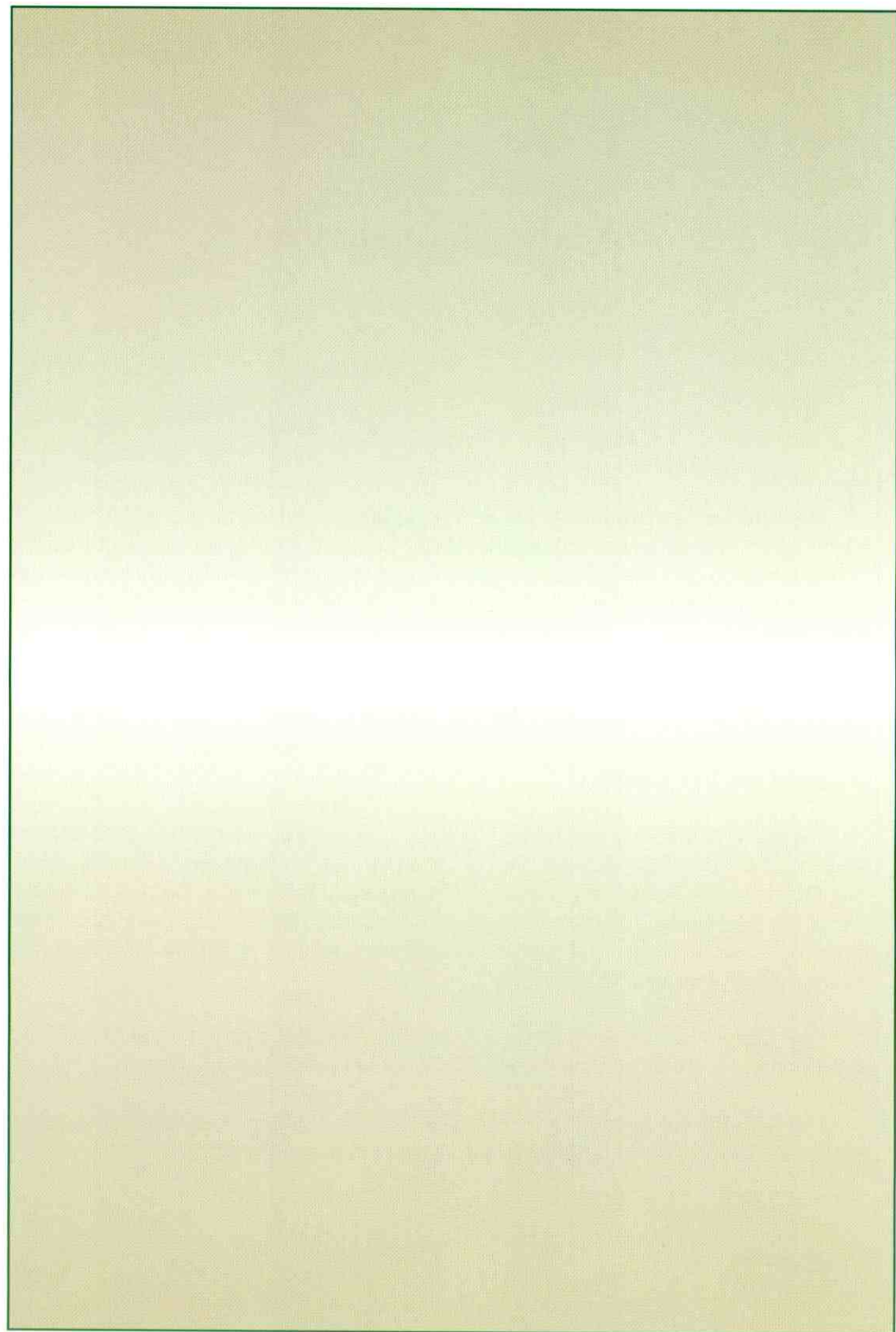
The authors are grateful to Dr. S. Ayyappan, Secretary, DARE and DG, ICAR for his keen interest in the Outreach Activity Consortium (#3) on 'Nutrient Profiling and Evaluation of Fish as a Dietary Component' involving seven out of the eight Research Institutes under the Fisheries Division of Indian Council of Agricultural Research.

The authors are thankful to Dr. B. Meenakumari, DDG (Fisheries) and Dr. S. D. Singh, ADG (Inland Fisheries) who has played an important role in formulation, planning and implementation of this project. For their keen *intrest* in the project and guidance and supervision.

The authors are very much thankful to Dr. T.V. Sankar, Senior Scientist & Head, Division, Dr. Susheela Mathew, Senior Scientist ; Dr. R. Anandan, Senior Scientist and Dr KK Asha, Scientist, Division of Biochemistry & Nutrition, Central Insitute of Fisheries Technology (Indian Council of Agricultural Research), Cochin for their help in sample analysis. The Authors are also thankful to Dr. Sajina A.M., Scientist for the help in manuscript editing.

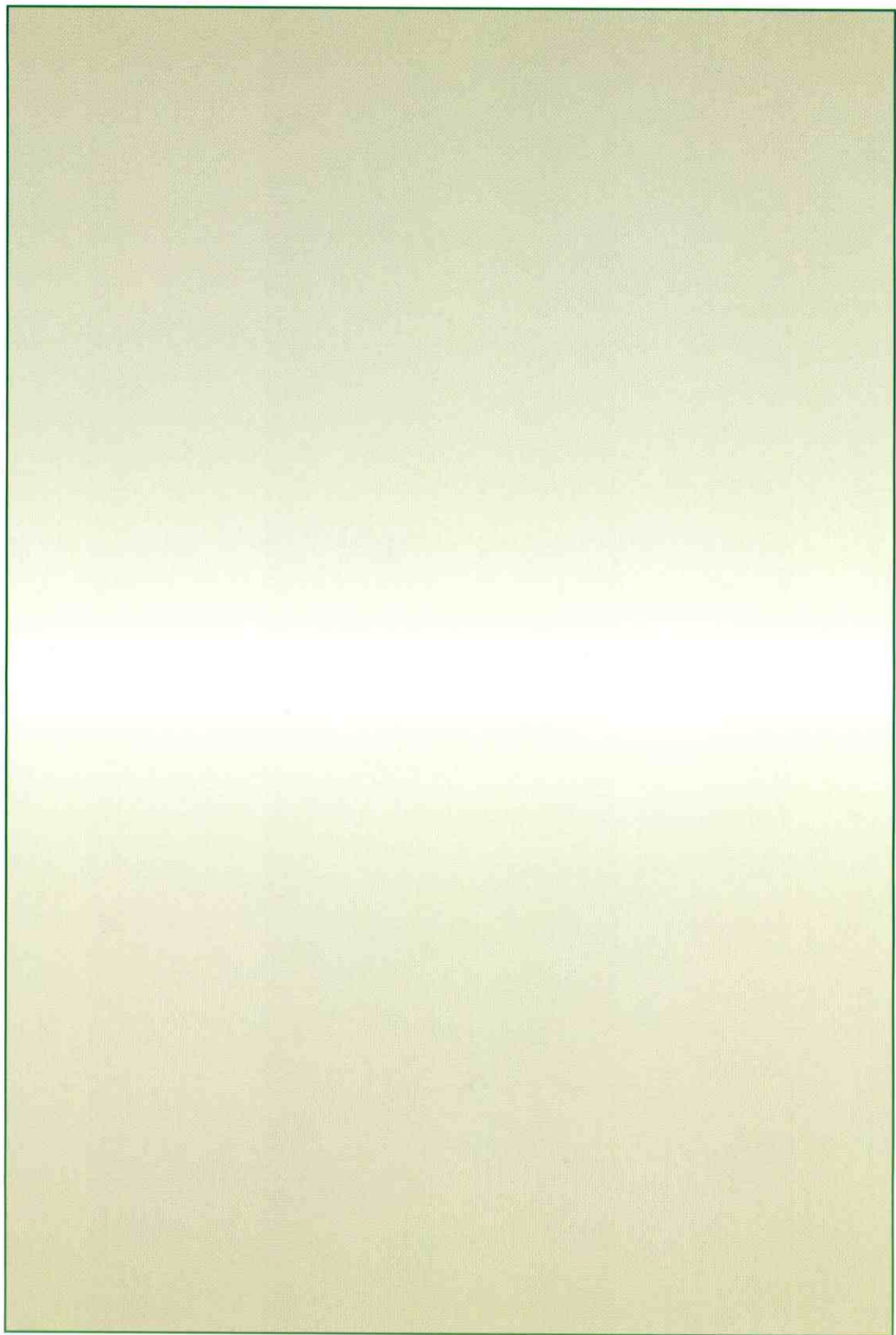
The authors are thankful to Dr P.K. Katiha, Principal Scientist and I/C, Project Monitoring and Documentation Cell, CIFRI for faciliating the publication.

The authors are highly thankful to M/s Eastern Printing Processor, Kolkata for the cover design and for printing the document in a short time.



Contents

SL. No.	Chapters	Page No.
1	Introduction	1
2	Therapeutic value of fish	3
3	Proteins for preventing protein-calorie malnutrition	7
4	Fish fats and oils	10
5	Fish as a rich source of vitamins A and D and other vitamins	23
6	Fish as a rich source of minerals and trace elements	28
7	Fish with established therapeutic values	32
8	Fishes in spas for Ichthyotherapy	41
9	Fishes in folklore medicine	44
10	References	52



1 Introduction

Therapy is the systematic application of remedies to effect a cure for diseases, ailments, pain or injury and the branch of science that deals with the treatment of disease or art and science of healing is known as therapeutics. Therapies can be of various types, namely, chemotherapy, biotherapy, hormone therapy, gene therapy, light therapy, physiotherapy, psychotherapy and many more depending upon the tools (drugs, surgery, radiation, mechanical devices, diet, psychiatry) used in treatments. Preventive or prophylactic therapies are taken to prevent the occurrence of diseases, e.g. vaccines. Treatments may be active, i.e. to cure a disease and no further treatment is required after recovery; long term, in case of wound healing; supportive, to keep the body functioning till the disease clears; symptomatic, to relieve the symptoms until the immune system heals the body; or palliative, minimizing discomfort for patients. Many chemical substances having medicinal properties are used for therapeutic purposes and are known as pharmaceuticals. These are derived either from natural products or synthesized through chemical processes. Those which are derived from life forms are called biopharmaceuticals.

When food and food products are used for treating diseases owing to its medical and health benefits, it is called nutraceuticals. They include the nutrients like vitamins, minerals, fatty acids, dietary supplements, specific diets, genetically engineered foods, herbal products, processed foods, etc. The Indians, Egyptians, Chinese, and Sumerians are just a few civilizations that have provided evidence suggesting that foods can be effectively used as medicine to treat and prevent disease. Ayurveda have mentioned the benefits of food for therapeutic purpose. Documents hint that the medicinal benefits of food have been explored for thousands of years. Hippocrates said that people should “Let food be thy medicine.” Until just recently, analysis of food was limited to the flavor of food (sensory taste and texture) and its nutritional value (composition of carbohydrates, fats, proteins, water, vitamins and minerals). However, there is growing evidence that other components of food may play an integral role in the link between food and health. Awareness regarding foods and the importance of nutrients playing a role in therapeutic healing is increasing among consumers.

Fish is an important source of vital nutrients like the proteins and fats (macronutrients) and vitamins and minerals (micronutrients). It is considered as the ‘cheapest source of

animal proteins' and 'rich food for poor people'. It represents a unique source of long chain polyunsaturated fatty acids (PUFA) of the n-3 family, mainly the eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), and fat soluble vitamins, which play an essential role in human health. Several studies indicate that fish is also perceived as a healthy food by consumers, particularly compared with meat – the main substitute for animal proteins. More and more people are turning towards seafood as a healthy source of digestible high quality protein (all the nine essential amino acids that the body cannot synthesize are provided by fish/seafood). Both freshwater and marine finfish and shellfish contain nutrients essential for the proper growth and development of humans. It is required in adequate amount in all stages of human life. From infancy to old age, consumption of fish along with a balanced diet ensures a healthy life, with minimal susceptibility to diseases.

2 Therapeutic Value of Fish

The therapeutic values of fish have been established since long. Several compounds have been extracted from fish and these are employed as remedies in the official medicine (Hamada and Nagai, 1995). Some of these compounds are important as tools for biochemical research or as new leads for the development of anticancer and antiviral drugs (Higa, 1996). Agosta (1996) says that the new chemical compound derived from dogfish sharks (*Squalus acanthias* Linnaeus 1758) is one of the most promising discoveries of the 1990s, that kills parasites, fungi, and bacteria. This chemical helps prevent infections in wounded sharks, and someday it may be used for humans. Finkl (1984) refers to *Eptatretus stoutii* (Lockington 1878), and *Dasyatis sabina* (Lesueur 1824) as sources of cardiac stimulants, antitumors, and analgesic, respectively. Oily fish, like cod, herring, salmon, and turbot, have great medicinal value to human beings due to the presence of n-3 polyunsaturated fatty acids. This helps the prevention of arthritis (Adeodato, 1997). The presence of an anticoagulant system in the plasma of Atlantic salmon (*Salmo salar* Linnaeus 1758) and rainbow trout (*Oncorhynchus mykiss* [Walbaun 1792]) has been confirmed, that supports similarities with the protein C anticoagulant system in mammals (Salte *et al.*, 1996). Tetrodotoxin (TTX), a water-soluble guanidinium derivative, is a bioactive compound produced by puffer fish that resembles procaine in its ability to inhibit transmission of nerve cell (Colwell, 1997). When diluted it acts as an extraordinary narcotic and analgesic (Bisset, 1991).

Regular fish consumption and the intake of n-3 PUFA play an important role in the primary and secondary prevention of coronary heart disease and stroke (Sidhu, 2003; Gezondheidsraad, 2004; Kris-Etherton, 2002). Possible mechanisms involved in this protective action of n-3 PUFA relate mainly to their antiarrhythmic, antithrombotic, anti-inflammatory and antiatherogenic effects. n-3 PUFA also have a beneficial effect on endothelial function and the immune system, and can help in lowering blood pressure in hypertensive individuals.

Various studies suggests that consumption of fish or fish oil lowers risk of CHD death and sudden death. Comparing different types of fish, lower risk appears more strongly related to intake of oily fish (e.g., salmon, herring, sardines), rather than lean fish (e.g., cod, catfish, halibut). Fish intake may modestly affect other cardiovascular outcomes (Table-1). n-3 PUFAs influence several cardiovascular risk factors. Effects occur within weeks of intake and may result from altered membrane fluidity and

receptor responses following incorporation of n-3 PUFAs into cell membranes and direct binding of n-3 PUFAs to intracellular receptors regulating gene transcription. The heterogeneity of the effects of fish or fish oil intake on cardiovascular outcomes is likely related to varying dose and time responses of effects on the risk factors (Figure 1).

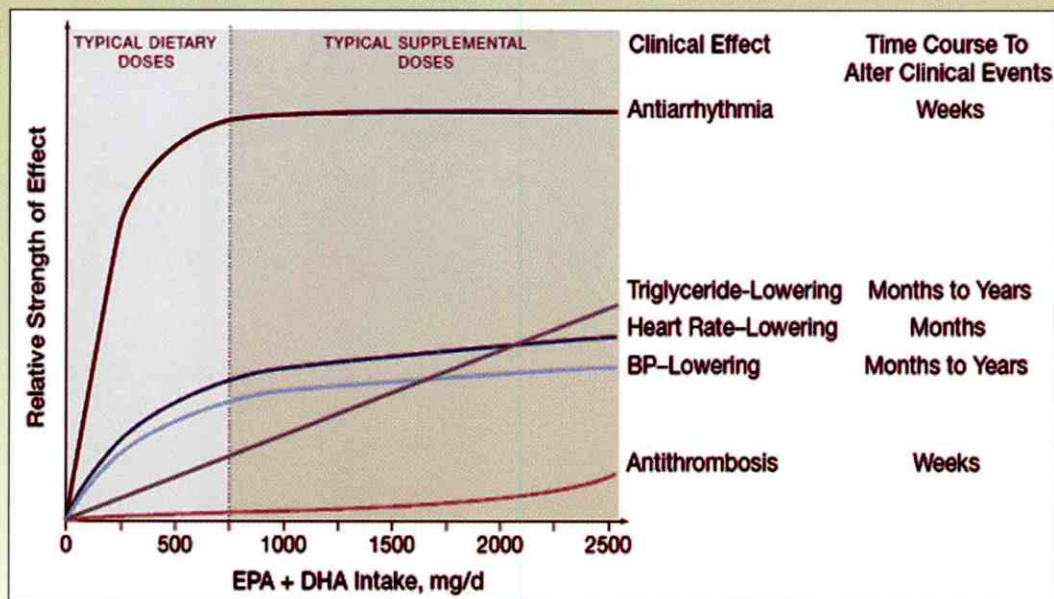
Table 1. Summary of Evidence for Effects of Consumption of Fish or Fish Oil on Cardiovascular Outcomes

Outcome	Clinical Effect	Strength of Evidence	Comment
CHD mortality CHD death Sudden death	~ 35% decrease ~ 50% decrease	Strong Strong	Probable threshold of effect- most risk reduction occurs with modest intake (~250 mg/d EPA+DHA), with little additional benefit with higher intakes
Ischemic stroke	~ 30% decrease	Moderate	Strong evidence from prospective cohort studies; no RCTs
Nonfatal CHD Nonfatal MI Progression of atherosclerosis Postangioplasty restenosis	Modest benefit Modest benefit Modest benefit	Equivocal Equivocal Equivocal	Possible benefits at very high intakes (~ 2 g/d n-3 PUFAs) Mixed results in cohort studies and RCTs Possible benefits in a meta-analysis of RCTs
Recurrent ventricular tachyarrhythmias	Modest benefit	Equivocal	Mixed results in 3 RCTs
Atrial fibrillation	~ 30% decrease	Limited	Mixed results in 2 cohort studies; benefit in 1 RCT
Congestive heart failure	~ 30% decrease	Limited	Benefit in 1 prospective cohort study

Abbreviations: CHD, coronary heart disease; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; MI, myocardial infarction; n-3 PUFA, n-3 polyunsaturated fatty acid; RCT, randomized clinical trial.

Source: Mozaffarian, D. and Rimm, E. B., 2006.

Figure 1. Schema of potential dose responses and time courses for altering clinical events of physiologic effects of fish or fish oil intake



Source: Mozaffarian, D. and Rimm, E. B., 2006.

The presence of DHA may be one of the probable causes that regular fish consumption stimulates brain development. It has been known since the 1960s that DHA is one of the major components of the grey matter of the nervous system (brain) and the phospholipids of the retina of the human eye (vision). It appears to play a vital role in the development of these organs and systems. Therefore, the maintenance of an adequate level of DHA in both the brain and the retina is important for proper functioning of the nervous system and visual functions.

Increased blood levels of n-3 fatty acids like EPA and DHA is found to lower incidence of obesity thereby indicating the importance of fish oils in weight management (Micallef et al., 2009).

Regular fish consumption can improve the development of bones, owing to the content of vitamin D in fish. Vitamin D is essential for proper bone mineralisation; its intake is especially important for young children to prevent rickets and for elderly people, who are at risk for osteoporosis and osteomalacia.

Scientific data also indicate that the consumption of fish or fish oil containing n-3 PUFAs lowers the incidence of diabetes, and appears to alleviate symptoms of rheumatoid arthritis (Sidhu, 2003).

Fish tissues constitute a potential source of anticancer molecules to be explored. For example, squalamine, an aminosterol isolated from the liver of the dogfish shark *Squalus acanthias* (Moore et al., 1993), was demonstrated to be a potent inhibitor of angiogenesis and tumour growth in several animal models (Sills et al., 1998; Cho and Sharks, 2002).

Alkylglycerols, natural etherlipids abundant in shark liver oil, were recently described as inhibitors of tumor vascularization (Pedrono et al., 2004). Picot et al (2005) demonstrated in their study that some fish protein hydrolysates (FPH), obtained by controlled enzymatic hydrolysis of muscle proteins, exert a significant antiproliferative activity on human cancer cell lines in vitro.

In Hyderabad, the Bathini Goud family has been administering fish medicine to lakhs of people suffering from asthma. They give the patients to swallow a 2-inch to 3-inch long murrel fish which carry a drop of the secret formula. The fish carrying the medicine slips down the throat easily and enters the alimentary tract clearing the mucus and phlegm which is supposed to be the contributing factor to asthma. It is administered on a particular day, Mrigashira karthi. However, there is some skepticism involved as the fish might be carrying parasites and pathogens which can affect human health and also, conditions may be worse when people allergic to fish consume this. There has been no scientific research or clinical trials under medical supervision done on this particular medicine (www.lifepositive.com; www.ayurvedic-medicines.org).

3 Proteins for Preventing Protein-Calorie Malnutrition

Proteins are the most abundant macromolecules found in biological systems; they are present in diverse forms such as the enzymes, hormones, antibodies, etc., having specific biological functions. They are polymers of amino acid residues, bonded together by peptide bond between the carboxyl and amino groups of the adjacent amino acid residues. A basic set of 20 amino acids, in various combinations, are involved in the formation of proteins. The structure of proteins can be explained in four levels. The basic sequence of amino acid residues of a protein is its primary structure. Secondary structure refers to the spatial arrangement of amino acid residues in the linear sequence. Tertiary structure describes all aspects of the three-dimensional folding of a polypeptide. When a protein has two or more polypeptide subunits, their arrangement in space is referred to as quaternary structure.

The function of a protein largely depends on its structure. Many vital functions of the body are performed by proteins. Almost all the chemical reactions are catalyzed by enzymes (a form of protein). Proteins play an important role in the transport and storage of many small molecules and ions. Haemoglobin transports oxygen in erythrocytes, myoglobin transports oxygen in muscle, iron is carried in the blood plasma by transferrin and stored in the liver as a complex with ferritin. Proteins are the major component of muscle. Muscle contraction is made possible by the sliding actions of two proteins, actin and myosin. Collagen, a fibrous protein provides the mechanical support for skin and bones. Antibodies are specialized proteins that give immune protection against foreign substances. Receptor proteins help in generation and transmission of nerve impulses. Rhodopsin is the photoreceptor protein in retinal rod cells. Growth and differentiation of cells are controlled and coordinated by hormones. Likewise, there are many types of proteins crucial for the proper functioning of body (stryer 1995).

As mentioned earlier, amino acids are the building blocks of proteins. Out of the twenty amino acids, nine cannot be synthesized by the human body and have to be acquired through diet. They are known as the essential amino acids (EAA) - histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan and valine. A balanced diet is necessary to get all the nutrients in correct amounts for maintaining a sound health. Since proteins and amino acids are indispensable for the human body, deficiencies of these nutrients can cause many diseases.

Protein-calorie malnutrition (PCM) is a nutritional disease commonly found in the developing and underdeveloped countries of Asia, Africa, Latin America where poverty, drought, famine, political inconsistency, etc., are the major causes that lead to poor nutrition among the people. It is also associated with other infections and micronutrient deficiencies.

Kwashiorkor and marasmus are the extreme conditions of PCM, mostly found in children, caused due to lack of protein and energy (Fig - 2). Kwashiorkor results from a chronic deficiency of protein, whereas marasmus is caused by a chronic calorie deficiency and along with protein insufficiency. In kwashiorkor, early symptoms include fatigue, irritability, and lethargy. As protein deprivation continues, growth failure, loss of muscle mass, generalized swelling (edema), and decreased immunity can be observed in the patient. A large, protuberant belly is common in those having the disease. On the other hand, marasmus is characterized by growth retardation in weight more than height so that the head appears quite large relative to the body. There is a progressive wasting of subcutaneous fat and muscle (emaciation) so that the skin appears loose. Severe prolonged marasmus may result in permanent retardation (Table - 2). PCM also occurs in adults, who are under chronic nutritional deficiency.



Fig - 2. (a) A normal, healthy baby (b) A child suffering from marasmus (c) A child having Kwashiorkor

Table 2: Symptoms of Kwashiorkor and Marasmus

Feature	Kwashiorkor	Marasmus
Growth failure	Present	Present
Wasting	Present	Present, marked
Oedema	Present (sometimes mild)	Absent
Hair changes	Common	Less common
Mental changes	Very common	Uncommon
Dermatitis, flaky paint	Common	Does not occur
Appetite	Poor	Good
Anaemia	Severe (sometimes)	Present, less severe
Subcutaneous fat	Reduced but present	Absent
Face	May be oedematous	Drawn in, monkey-like
Fatty infiltration of liver	present	absent

Source : Latham, 1997

PCM can be treated by providing the patients a complete balanced diet. Protein-rich food is essential in curing malnutrition. Fish is considered as an inexpensive source of protein, and is a potential source to meet the protein demand. The protein content in fish varies from 15-20% of the live body weight. Fish contains all the essential amino acids and provides quality protein in human diet. As fish is available in variable prices, common man can afford to meet the dietary requirement of proteins. Intake of fish proteins can be helpful in mitigating protein-calorie malnutrition, kwashiorkor and marasmus. In many Asian countries, rice is the main source of food; along with rice, fish makes a healthy diet to combat the protein-calorie deficiency.

There are studies indicating the hypocholesterolemic effect of fish proteins in albino rats. The fish protein demonstrated a reduction in cholesterol levels in blood by reducing the activity of acyl - CoA: cholesterol acyltransferase (Ammu et al., 1989; Bergeron and Jacques, 1989; St. John and Eoll, 1991; Zhang and Beylan, 1993; Devadasan and Gopakumar, 1997; Hege et al., 2004)

4 Fish Fats and Oils As a Rich Source of PolyUnsaturated Fatty Acids (PUFAs), ω -3 Fatty Acids EPA and DHA

Lipids are water-insoluble macro-biomolecules that are soluble in organic solvents and have a variety of biological roles ranging from fuel molecules, energy stores to components of membranes. Lipids in body are divided into two groups: storage lipids and structural lipids. Storage lipids are the reserve storehouse of fuel for the body while structural lipids form the essential parts of cell structure such as the cell membranes. There are three major types of lipids are phospholipids, glycolipids and cholesterol. Phospholipids form the integral part of cell membranes, glycolipids are the markers for cellular recognition and cholesterol plays an important role in fat transport, key regulator of membrane fluidity and is the precursor of steroids.



Biological membranes (Biomembranes)

Biological membranes are organized sheet-like assemblies made up of mainly proteins and lipids. Phospholipids are the major class of membrane lipids. The fatty acid chains in phospholipids usually contain even number of carbon atoms, most commonly the 16- and 18-carbon fatty acids. The levels of unsaturation of fatty acid chains in membrane lipids have a profound effect on membrane fluidity. Membrane lipids contain both hydrophilic (polar head) and hydrophobic (hydrocarbon tail) groups. In membranes these lipids are arranged in a bimolecular sheet or bilayer, with the hydrophilic unit face outward and the hydrophobic unit towards the core of the bilayer (Fig - 3). Proteins are embedded in the core of the

bilayer, held by the hydrophobic interactions between the lipids and hydrophobic groups of the proteins. Some proteins protrude from only one side of the membrane; others have domains exposed on both sides, giving a functional asymmetry to the membrane. The individual lipids and proteins in a membrane form a fluid mosaic pattern that is free to change. The fluidity of the membrane is due to the noncovalent bonds existing between the membrane components. This fluid mosaic model of cell membranes (Fig - 4) was proposed by singer and nicolson (1972).

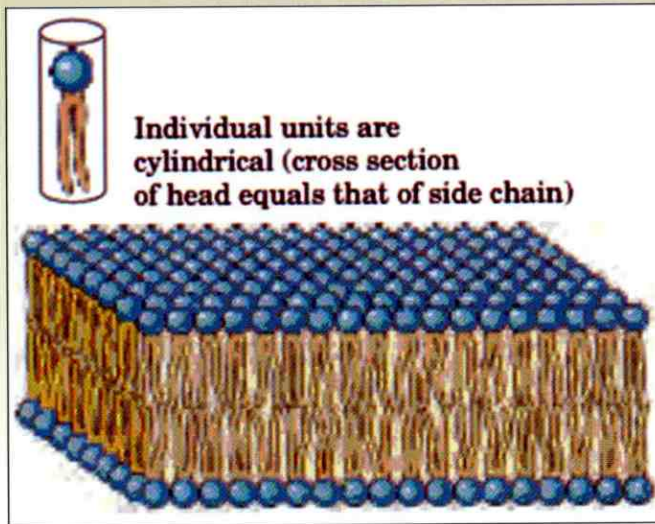
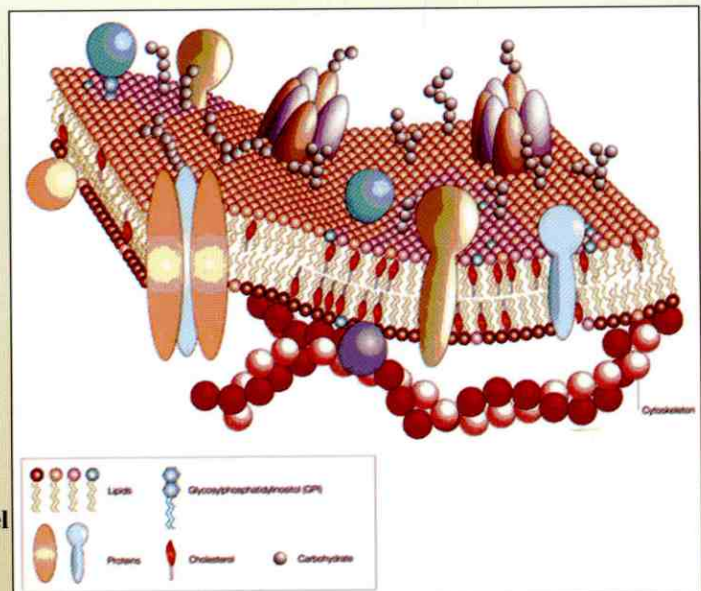
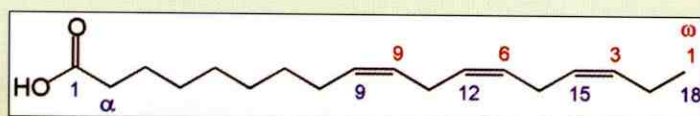


Figure 3: Lipid Bilayer
(Source: Nelson and Cox, 2004)

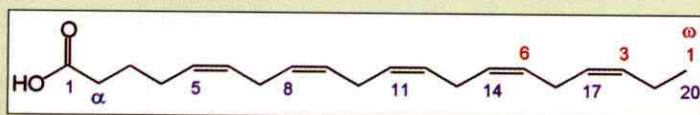


At the cell surface, transporters move specific organic solutes and inorganic ions across the membrane; receptors sense extracellular signals and trigger molecular changes in the cell; adhesion molecules hold neighboring cells together. Within the cell, membranes organize cellular processes such as the synthesis of lipids and certain proteins, and the energy transductions in mitochondria and chloroplasts. In humans, at least 60 different sphingolipids have been identified in cellular membranes. Many of these are especially prominent in the plasma membranes of neurons, and some are clearly recognition sites on the cell surface. The carbohydrate moieties of certain sphingolipids define the human blood groups and therefore determine the type of blood that individuals can safely receive in blood transfusions. Gangliosides are concentrated in the outer surface of cells, where they present points of recognition for extracellular molecules or surfaces of neighboring cells. The kinds and amounts of gangliosides in the plasma membrane change dramatically during embryonic development. Sterols have four fused rings and a hydroxyl group. Cholesterol, the major sterol in animals, is both a structural component of membranes and precursor to a wide variety of steroids (Lehninger, 1982; Lehninger et al., 2005).

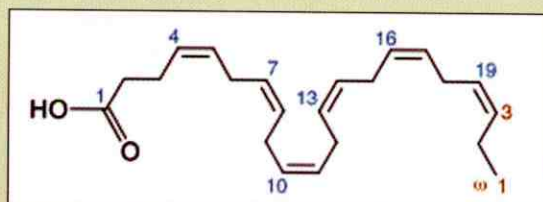
The fatty acids are grouped into saturated and unsaturated fatty acids, based on number of double bonds in them. The latter group consists of mono-unsaturated (MUFA) and poly-unsaturated fatty acids (PUFA) (Fig -5). PUFAs include the essential fatty acids, viz., α -linolenic acid (18:3, n-3; ALA) and linoleic acid (n-6 fatty acid) and are highly important for human health. They form the starting point for the creation of long-chain polyunsaturated fatty acids (LC-PUFA) like the eicosapentaenoic acid (20:5, n-3; EPA) and the docosahexaenoic acid (22:6, n-3; DHA). Some of the major sources of n-3 and n-6 fatty acids are the fish and shellfish (Table - 3).



α -linolenic acid (ALA), an essential n-3 fatty acid



Eicosapentaenoic acid (EPA)



Docosahexaenoic acid (DHA)

Figure 5. Chemical structure of some PUFAs

Table 3: Various Sources of EPA and DHA

Fish/Seafood	Total EPA/DHA (mg/100 g)
Mackerel	2300
Chinook salmon	1900
Herring	1700
Anchovy	1400
Sardine	1400
Coho salmon	1200
Trout	600
Spiny lobster	500
Halibut	400
Shrimp	300
Catfish	300
Sole	200
Cod	200

Source: Logan, 2004

In the body, essential fatty acids serve multiple functions. In each of these, the balance between dietary ω -3 and ω -6 strongly affects function. They are modified to make: (1) the classic eicosanoids (affecting inflammation and many other cellular functions); (2) the endocannabinoids (affecting mood, behavior and inflammation); (3) the lipoxins from ω -6 EFAs and resolvins from ω -3 (in the presence of aspirin, down regulating inflammation); (4) the isofurans, neurofurans, isoprostanes, hepoxilins, epoxyeicosatrienoic acids (EETs) and Neuroprotectin D; (5) they form lipid rafts (affecting cellular signaling); (6) they act on DNA (activating or inhibiting transcription factors such as NF κ B, which is linked to pro-inflammatory cytokine production).

Omega-3 Fatty Acids

Pioneering research conducted by Danish scientists indicated that in spite of a large intake of fat and cholesterol, the consumption of fish protected Greenland Eskimos against heart disease (Dyerberg et al., 1975; Bang and Dyerberg, 1980; Sidhu, 1993). Greenland Eskimos who consumed 700mg/day cholesterol from high-fat marine foods, had significantly lower plasma low density lipoproteins (LDL) and very low density lipoproteins (VLDL) compared to Denmark Eskimos consuming Western European diets (Bang and Dyerberg, 1980; Dyerberg et al., 1975; Sidhu, 1993). EPA and DHA are known to reduce the risk of coronary heart diseases, protect against diabetes mellitus and exhibit anti-inflammatory action, as

well as being associated with brain development, vision and reproduction (Kim and Mendis, 2006; Sidhu, 2003). They are important in treatment of atherosclerosis, cancer, rheumatoid arthritis, psoriasis and diseases of old age such as Alzheimer's and age-related macular degeneration (AMD). Research suggests that high intakes of fish and omega-3 fatty acids are linked to decreased rates of major depression. Low plasma concentrations of DHA predict low concentrations of cerebrospinal fluid 5-hydroxyindoleacetic acid (5-HIAA), which in turn is associated with depression and suicide (Logan, 2004; Rees et al., 2005).

As the importance of omega-3 fatty acids to health has received increasing awareness, the number of food products enriched in omega-3 fatty acids has increased. Many manufacturers add fish oil into their final product to enrich it in omega-3 fatty acids. Some animal products, such as milk and eggs, can be naturally enriched for omega-3 fatty acids by feeding the animals a diet that is rich in omega-3 fatty acids.

DHA

DHA is an omega 3 PUFA (Fig - 6) which has very limited synthesis in the body. In the human body, DHA is derived from eicosapentaenoic acid (EPA) via docosapentaenoic acid (DPA) as an intermediate by desaturase enzyme and beta oxidation in peroxisomes. During early life, there is limited metabolic capacity to convert ALA to DHA. Thus in fetal life, infancy and early childhood, DHA should be acquired from dietary sources to maintain optimal health.

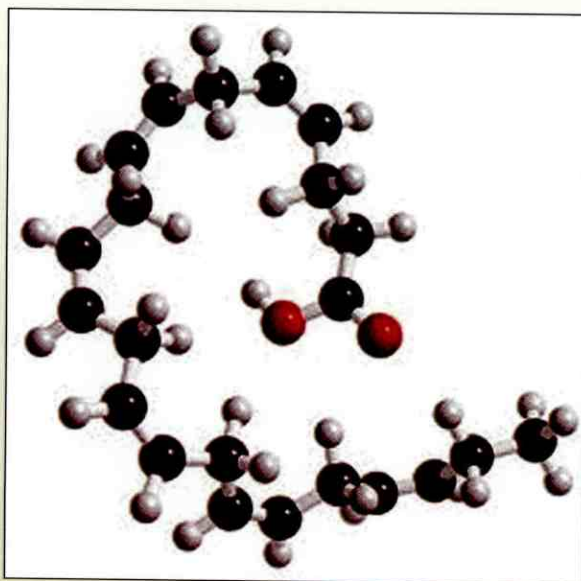


Figure 6: Structure of DHA

(source: www.3dchem.com)

Role of docosahexaenoic acid (DHA) in children: DHA is an omega -3 polyunsaturated essential fatty acid. The development of visual and neurological functions in infants has been demonstrated in various DHA studies. In a randomized controlled trial in USA, it has been found that toddler formula supplemented with DHA improved RBC DHA status and lowered incidence of respiratory illness ($p=0.024$) compared to formula without DHA in children less than 3 years of age. Thus role of DHA in infants and toddlers seems to be defined and adequate intake needs to be ensured.

Intake of DHA in children: Eicosapentaenoic acid (EPA) and DHA intake is often low in 2-12 years old children relative to intake in breast fed infants and adult intake. It has been found that large proportions of children have low levels of intake of n-3 omega fatty acids with >97% of all groups consuming less than 1% energy from this fats due to poor intake of EPA & DHA.

Consumption of healthy diets that contribute with adequate amounts of fat and fatty acids is needed to children. Dietary intakes in childhood should support future adult health such as prevention of metabolic disorders & cardiovascular disease, support immune function and maintain healthy reproductive system.

DHA is predominant in fish and seafood and consumption of these foods in Indian children is virtually lacking. In vegetarians the predominant polyunsaturated fatty acid is linolenic acid (LA) - an omega 6 fatty acid. Alpha linolenic acid (ALA) which is an omega 3 fatty acid is not so abundant in vegetarian diets. (5) ALA is a precursor of EPA and DHA. The ideal ratio of LA to ALA should be 3:1 in the diet, however most diets have a ratio of 10:1 or 15:1. Under these circumstances, omega 6 fatty acids inhibit the conversion pathway of omega 3 fatty acids. Thus decreasing LA content has been found to increase the ALA conversion to EPA and DHA.

(<http://www.pediatriconcall.com>)

EPA

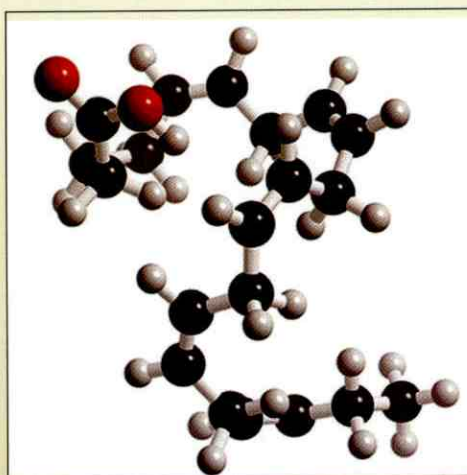


Figure 7: Structure of EPA

(source: www.3dchem.com)

Eicosapentaenoic acid (EPA or also icosapentaenoic acid) is an omega-3 fatty acid (Fig - 7). EPA and its metabolites act in the body largely by their interactions with the metabolites of arachidonic acid. It acts as a precursor for prostaglandin-3 (which inhibits platelet aggregation), thromboxane-3, and leukotriene-5 groups (all eicosanoids). It is obtained in the human diet by eating oily fish or fish oil— e.g, cod liver, herring, mackerel, salmon, menhaden and sardine. The human body can also convert alpha-linolenic acid (ALA) to EPA, but this is much less efficient than the resorption of EPA from food containing it, and ALA is itself an essential fatty acid, an appropriate supply of which must be ensured. Because EPA is also a precursor to docosahexaenoic acid (DHA), ensuring a sufficient level of EPA on a diet containing neither EPA nor DHA is harder both because of the extra metabolic work required to synthesize EPA and because of the use of EPA to metabolize DHA. Medical conditions like diabetes or certain allergies may significantly limit the human body's capacity for metabolization of EPA from ALA.

EPA in particular may possess some beneficial potential in mental conditions, such as schizophrenia (Peet et al., 2001; Song and Zhao, 2007). Several studies report an additional reduction in scores on symptom scales used to assess the severity of symptoms, when additional EPA is taken. Recent studies have suggested that EPA may affect depression, and importantly, suicidal behavior. One such study (Huan et al., 2004), took blood samples of 100 suicide-attempt patients and compared the blood samples to those of controls and found that levels of eicosapentaenoic acid were significantly lower in the washed red blood cells of the suicide-attempt patients. EPA has inhibitory effect on CYP2C9 and CYP2C19 hepatic enzymes. At high dose, it may also inhibit the activity of CYP2D6 and CYP3A4, important enzymes involved in drug metabolism (Yao et al., 2006). Research suggests that EPA improves the response of patients to chemotherapy, possibly by modulating the production of eicosanoid (Hardman, 2004). It might also reduce the risk of developing certain types of cancer, including multiple myeloma (Fernandez, 1999).

Omega-6 Fatty Acids

Like n-3 fatty acids, n-6 fatty acids (such as α -linolenic acid and arachidonic acid) play a similar role in normal growth. n-6 is "better" at supporting dermal integrity, renal function, and parturition. The biological effects of the n-6 fatty acids are largely mediated by their conversion to n-6 eicosanoids that bind to diverse receptors found in every tissue of the body. The conversion of tissue arachidonic acid (20:4n-6) to n-6 prostaglandin and n-6 leukotriene hormones provides many targets for pharmaceutical drug development and treatment to diminish excessive n-6 actions in atherosclerosis, asthma, arthritis, vascular disease, thrombosis, immune-inflammatory processes and tumor proliferation. Competitive interactions with the n-3 fatty acids affect the relative storage, mobilization, conversion and action of the n-3 and n-6 eicosanoid precursors. This competition was recognized as

important when it was found that thromboxane is a factor in the clumping of platelets, which leads to thrombosis. The leukotrienes were similarly found to be important in immune/inflammatory-system response, and therefore relevant to arthritis, lupus, and asthma. These discoveries led to greater interest in finding ways to control the synthesis of n-6 eicosanoids. The simplest way would be by consuming more n-3 and fewer n-6 fatty acids.

Table -4: List of common n-3 and n-6 fatty acids found in nature

Common name	Lipid name	Chemical name	Abbr.
Common n-3 (ω-3) Fatty Acids			
α -Linolenic acid	18:3 (n-3)	<i>all-cis</i> -9,12,15-octadecatrienoic acid	ALA
Stearidonic acid	18:4 (n-3)	<i>all-cis</i> -6,9,12,15-octadecatetraenoic acid	STD
Eicosapentaenoic acid	20:5 (n-3)	<i>all-cis</i> -5,8,11,14,17-eicosapentaenoic acid	EPA
Docosapentaenoic acid	22:5 (n-3)	<i>all-cis</i> -7,10,13,16,19-docosapentaenoic acid	DPA
Docosahexaenoic acid	22:6 (n-3)	<i>all-cis</i> -4,7,10,13,16,19-docosahexaenoic acid	DHA
Common n-6 (ω-6) Fatty Acids			
Linoleic acid	18:2 (n-6)	9,12-octadecadienoic acid	LA
Arachidonic acid	20:4 (n-6)	5,8,11,14-eicosatetraenoic acid	AA
Docosadienoic acid	22:2 (n-6)	13,16-docosadienoic acid	DDA
Docosapentaenoic acid	22:5 (n-6)	4,7,10,13,16-docosapentaenoic acid	DPA

Some medical research suggests that excessive levels of n-6 fatty acids, relative to n-3 fatty acids, may increase the probability of a number of diseases and depression. Modern Western diets typically have ratios of n-6 to n-3 in excess of 10 to 1, some as high as 30 to 1. The optimal ratio is thought to be 4 to 1 or lower. Excess n-6 fats interfere with the health benefits of n-3 fats; in part because they compete for the same rate-limiting enzymes. A high proportion of n-6 to n-3 fat in the diet shifts the physiological state in the tissues toward the pathogenesis of many diseases: prothrombotic, proinflammatory and proconstrictive. Chronic excessive production of n-6 eicosanoids is associated with heart attacks, thrombotic stroke, arrhythmia, arthritis, osteoporosis, inflammation, mood disorders and cancer. Many of the medications used to treat and manage these conditions work by blocking the effects of the potent n-6 fat, arachidonic acid. Many steps in formation and action of n-6 hormones from n-6 arachidonic acid proceed more vigorously than the corresponding competitive steps in formation and action of n-3 hormones from n-3 eicosapentaenoic acid. The Cyclooxygenase (COX)-1 and COX-2 inhibitor medications,

used to treat inflammation and pain, work by preventing the COX enzymes from turning arachidonic acid into inflammatory compounds. Many of the anti-mania medications used to treat bipolar disorder work by targeting the arachidonic acid cascade in the brain. Linoleic acid (18:2, n-6), the shortest-chained n-6 fatty acid, is an essential fatty acid. Arachidonic acid (20:4) is a physiologically significant n-6 fatty acid and is the precursor for prostaglandins and other physiologically active molecules.

Some of the important n-3 and n-6 fatty acids found in nature are listed out in Table - 4

Fish Oils and PUFAs for Human Health- Some Clinical Correlations

1. Omega-3 fatty acids have been shown in epidemiological and clinical trials to reduce the incidence of Coronary Heart Disease (CHD). Studies have indicated decreases in total mortality and cardiovascular incidents (i.e. myocardial infarctions) associated with the regular consumption of fish and fish oil supplements. Similar to those who follow a Mediterranean diet, Arctic-population - who consume high amounts of n-3 fatty acids from fatty fish - also tend to have higher proportions of n-3, increased HDL cholesterol and decreased triglycerides (fatty material that circulates in the blood) and less heart disease. Administration of purified EPA from fish oil improves the thickness of carotid arteries along with improving blood flow in patients with unhealthy blood sugar levels. Non-fatal coronary events are also significantly reduced in the people fed with EPA and they have superior cardiovascular function. Thus, EPA is a promising treatment for prevention of major coronary events, especially non-fatal coronary events. Recommendations made by American Heart Association (AHA) Dietary Guidelines include at least two servings of fish per week (particularly fatty fish) (Kris-Etherton et al., 2002). The structure of human heart is given in Fig - 8

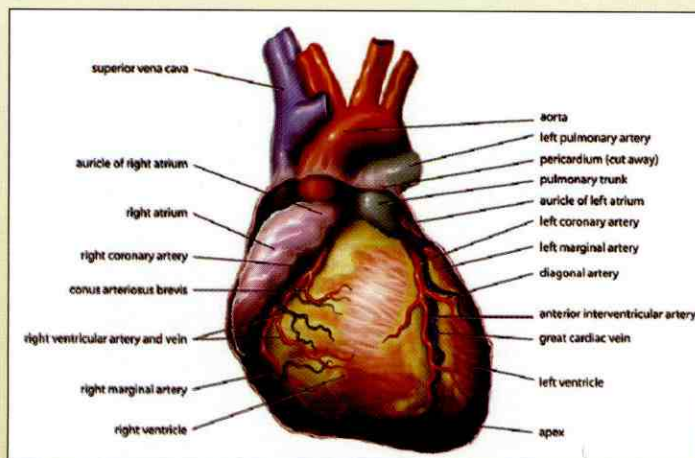


Figure 8: Human heart

(Source: www.wikipedia.org)

2. Lack of essential fatty acids causes behavioural problems in the pediatric population which is known as Attention-Deficit Hyperactivity Disorder (ADHD). Children suffering from ADHD are inattentive, impulsive and hyperactive and often experience comorbidity with other behavioural disorders including anxiety, conduct, oppositional and/or mood disorders and antisocial personality. The prevalence rates are estimated at 4–15%; boys are more commonly diagnosed with ADHD than girls. Studies have reported that children with ADHD had significantly lower levels of arachidonic (AA), eicosapentaenoic (EPA) and decosahexaenoic acids (DHA) in their blood and these hyperactive children suffered more from symptoms associated with essential fatty acid deficiency (thirst, frequent urination, and dry hair and skin) and were more likely to have asthma (Stevens et al., 1995). Problems associated with ADHD also persist into adulthood, changes in some symptoms occur with age (Kooij et al., 2005). The aetiology of ADHD appears to be multifactorial with genetic and environmental influences. Focus has also been placed on diet, including emerging evidence that ADHD may be



associated with low levels of dietary and erythrocyte long-chain n-3 PUFA (LC n-3 PUFA). The LC n-3 PUFA, including EPA and DHA, can be converted from α -linolenic acid by endogenous desaturation and elongation; however, only negligible amounts are converted. LC PUFAs are critical in normal brain and nervous system development and function. DHA is highly concentrated in brain and retina, while LC n-6 arachidonic acid together with DHA plays a major structural role in neuronal membranes. Therefore, there has been growing interest in the role of n-3 PUFA in psychiatric illness across the lifespan. It has been well established that DHA is critical for infant brain development, and it may be associated with enhanced cognitive performance in childhood. A number of studies have found lower blood n-3 levels in children with ADHD compared with

control groups and there is evidence for alleviation of ADHD symptoms with n-3 PUFA supplementation. Studies have reported improvement in ADHD symptoms in children following supplementation with 732 mg/d of LC n-3 PUFA and 60 mg/d of α -linolenic acid (18: 3n-6) over 24–30 weeks. Given the overall current evidence for the role of LC n-3 PUFA in ADHD symptoms and the lower consumption of foods rich in LC n-3 PUFA, children with ADHD are encouraged to consume more LC n-3 PUFA containing foods for mental health benefits (Ng et al., 2009).

3. Children who consume fresh, oily fish have significantly lower risk of developing asthma (airway hyper responsiveness). Omega-3 fatty acids, EPA and DHA, especially EPA is reported to prevent development of asthma or reduce its severity. Studies have suggested long-term fish oil supplementation may reduce asthma severity. Major dietary sources of DHA are fish and fish oils. (Hodge et al., 1996; Broughton et al., 1997).
4. Low dietary intakes and plasma concentration of n-3 fatty acids are associated with dementia (memory loss), cognitive decline and age-related macular degeneration (AMD) risk. These are some of the major cause of disability in the elderly population. AMD is a disease associated with aging that gradually destroys sharp, central vision (Fig - 9). Central vision is needed for seeing objects clearly and for common daily tasks such as reading and driving. AMD affects the macula (located in the center of the retina, the light-sensitive tissue at the back of the eye), the part of the eye enables to see fine detail. AMD causes no pain. In some cases, AMD advances so slowly that people notice little change in their vision. In others, the disease progresses faster and may lead to a loss of vision in both eyes. AMD occurs in two forms: wet and dry. 'Wet AMD' occurs when abnormal blood vessels behind the retina start to grow under the macula. These new blood vessels tend to be very fragile and often leak blood and fluid. The blood and fluid raise the macula from its normal place at the back of the eye. Damage to the macula occurs rapidly. With wet AMD, loss of central vision can occur quickly. Wet AMD is also known as advanced AMD. It does not have stages like dry AMD. An early symptom of wet AMD is that straight lines appear wavy. 'Dry AMD' occurs when the light-sensitive cells in the macula slowly break down, gradually blurring central vision in the affected eye. As dry AMD gets worse, you may see a blurred spot in the center of your vision. Over time, as less of the macula functions, central vision is gradually lost in the affected eye. The most common symptom of dry AMD is slightly blurred vision. There may be difficulty in recognizing faces and more light is needed for reading and other tasks. Dry AMD generally affects both eyes, but vision can be lost in one eye while the other eye seems unaffected. AMD is a leading cause of vision loss in people over 60 years of age. It has been reported that n-3 Fatty acids, particularly DHA delay the progression of dementia and AMD (Johnson and Schaefer, 2006). Major dietary sources of DHA are fish and fish oils.

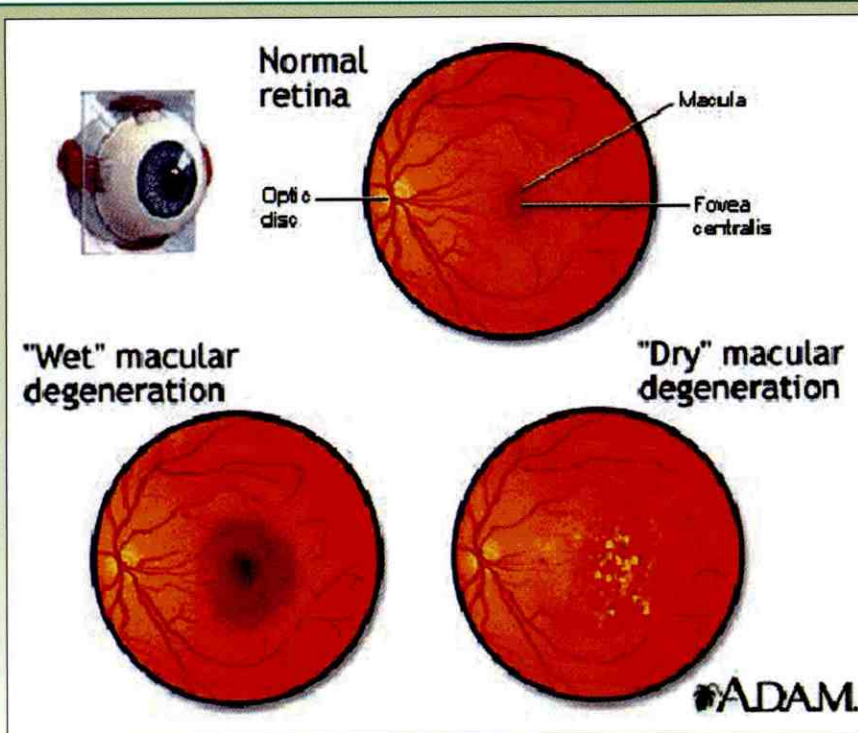


Figure 9: Age-related Macular Degeneration

(Source: www.adam.com)

5. In a study of nearly 9,000 pregnant women, researchers found women who ate fish once a week during their first trimester had 3.6 times less risk of low birth weight (LBW) and premature birth than those who ate no fish. Low consumption of fish was a strong risk factor for preterm delivery and low birth weight. However, attempts by other groups to reverse this increased risk by encouraging increased pre-natal consumption of fish were unsuccessful.



6. Omega-3 fatty acids are known to have membrane-enhancing capabilities in brain cells. One medical explanation is that n-3 fatty acids play a role in the fortification of the myelin sheaths. A benefit of n-3 fatty acids is helping the brain to repair damage by promoting neuronal growth. In the prefrontal cortex (PFC) of the brain, low brain n-3 fatty acids are thought to lower the dopaminergic neurotransmission in this brain area, possibly contributing to the negative and neurocognitive symptoms in schizophrenia. This reduction in dopamine (a neurotransmitter) system function in the PFC may lead to an over activity in dopaminergic function in the limbic system of the brain which is suppressively controlled by the PFC dopamine system, causing the positive symptoms of schizophrenia (a psychiatric diagnosis that describes a mental disorder characterized by abnormalities in the perception or expression of reality). This is called the n-3 polyunsaturated fatty acid/dopamine hypothesis of schizophrenia. This mechanism may explain why n-3 supplementation shows effects against both positive, negative and neurocognitive symptoms in schizophrenia (Ohara, 2007).
7. Several epidemiological studies suggest covariation between seafood consumption and rates of 'mood disorders' (where a disturbance in the person's mood is hypothesized to be the main underlying feature). Long term disturbances of mood such as depression and bipolar disorder are considered mood disorders. Biological marker studies indicate deficits in omega-3 fatty acids in people with depressive disorders, while several treatment studies indicate therapeutic benefits from omega-3 supplementation. A similar contribution of omega-3 fatty acids to coronary artery disease may explain the well-described links between coronary artery disease and depression. Deficits in omega-3 fatty acids have been identified as a contributing factor to mood disorders and offer a potential rational treatment approach.



5 Fish as a rich source of vitamins: A, D and other vitamins

Vitamins are micronutrients essential for the human health; these cannot be synthesized in the body and so have to be obtained through diet. Vitamin A and D are fat-soluble vitamins, isoprenoid compounds synthesized by the condensation of multiple isoprene units, and serve as hormone precursors.

Vitamin A

Vitamin A was first isolated from fish-liver oil. There are two natural forms, vitamin A₁ (retinol) (Fig - 10), obtained from marine fish livers, and vitamin A₂, from freshwater fish livers. Vitamin A in its various forms functions as a hormone and as the visual pigment of the vertebrate eye. Acting through receptor proteins in the cell nucleus, the vitamin A derivative retinoic acid regulates gene expression in the development of epithelial tissue, including skin. In vertebrates, β -carotene, the pigment that gives carrots, sweet potatoes, and other yellow vegetables their characteristic color, can be enzymatically converted to vitamin A. Vitamin A is stored in the liver in sufficient amounts. The livers of coldwater fish are very rich in preformed vitamin A.

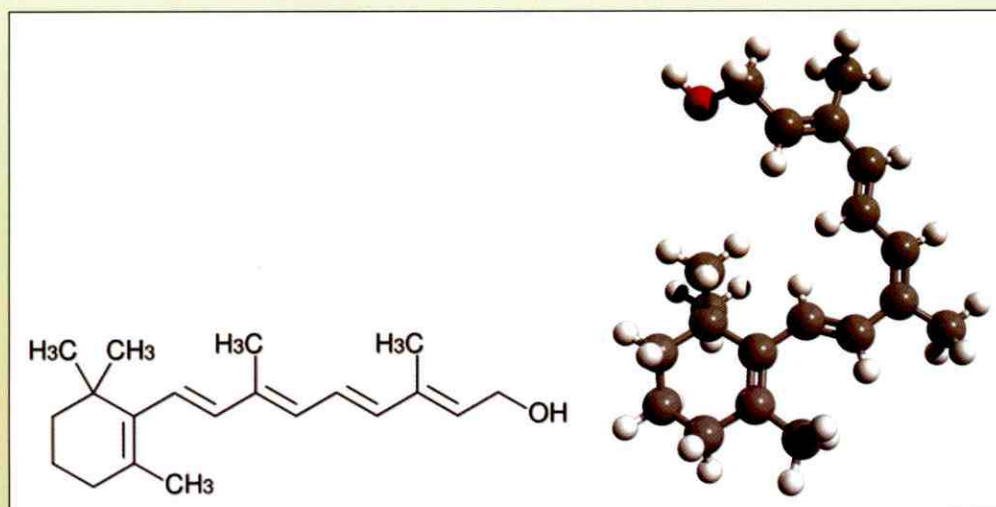


Figure 10: Structure of vitamin A₁ (retinol)

Deficiency of vitamin A leads to a variety of symptoms in humans, including xerophthalmia (dryness of the eyes), keratomalacia (excessive keratin formation in the skin and the cornea of the eye), retarded development and growth; and night blindness, an early symptom commonly used in diagnosing vitamin A deficiency. Children having protein-calorie malnutrition are especially prone to vitamin A deficiency. It also occurs in people with intestinal or pancreatic diseases in which there is defective fat absorption, as such people fail to absorb vitamin A or carotene, both of which are fat soluble. The early stage of xerophthalmia is manifested as night blindness, owing to deficient synthesis of the visual pigment, rhodopsin, which contains retinal, for which vitamin A is the precursor.

Vitamin D

Vitamin D₃, or cholecalciferol (Fig - 11), is normally formed in the skin from 7-dehydrocholesterol in a photochemical reaction promoted by the UV component of sunlight. It is also abundant in fish liver oil. Vitamin D₃ itself is not biologically active, but it is converted by enzymes in the liver and kidney to 1, 25-dihydroxycholecalciferol, a hormone that regulates calcium uptake in the intestine and calcium levels in kidney and bone. Another common form is vitamin D₂ (ergocalciferol). Normally, vitamin D is not required in the diet so long as there is enough exposure of the skin to sunlight, which causes the production of vitamin D. however, when the skin is not exposed to sunlight regularly, vitamin D should be provided in diet. Although Eskimos are not exposed to sunlight in Arctic winter, they obtain ample vitamin D from fish (Lehninger, 1982)

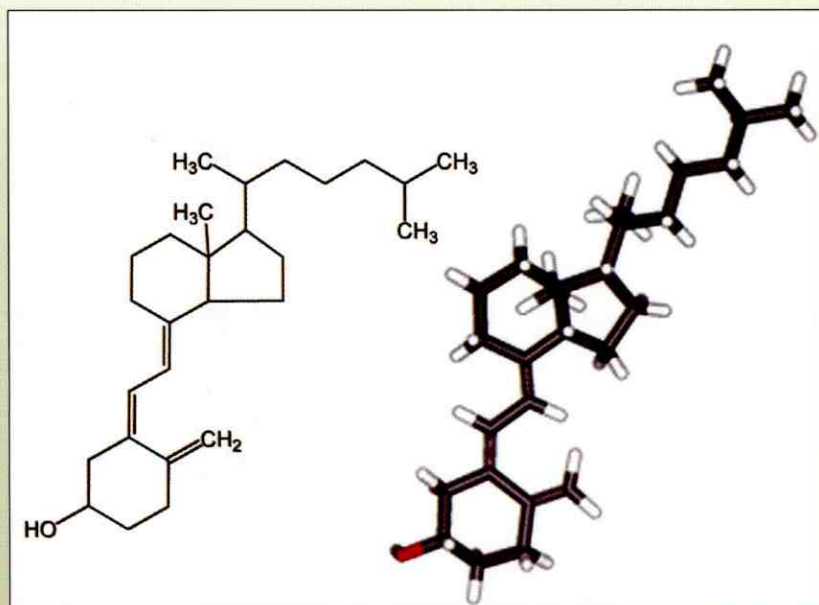


Figure 11: Structure of vitamin D₃

Deficiency of this vitamin leads to abnormal calcium and phosphorus metabolism and defective bone formation in the children's disease rickets (Fig - 12(a)), resulting in bowlegs (Fig - 12(b)) and pigeonbreast. Deformations of bones appear in skull, chest, and spine. Osteomalacia is the deficiency disease of vitamin D in adults. Child-bearing women fed on marginal diets are susceptible to vitamin D deficiency.



Figure 12(a): A 2½-year-old boy with severe rickets (Source: Lehninyer et al., 2005)



Figure (b): Radiograph of a two-year old rickets sufferer, with a marked genu varum (bowing of the femurs) and decreased bone opacity,

In developing countries, fish and fisheries play an important role in the diets, livelihoods, and income of many poor population groups who suffer from vitamin and mineral deficiencies (Roos et al., 2007). Fishes are rich sources of vitamin A and D. Small indigenous fishes traditionally occupy an important link in the life, livelihood, health and the general well being of the rural mass, especially the poor. It has been reported that some species such as mola (*Amblypharyngodon mola*) (Fig - 13(a)), darkina (*Esomus danricus*) (Fig - 13 (b)), dhela (*Osteobrama cotio cotio*) (Fig - 13 (c)) and kaski (*Corica soborna*) contain high amount of vitamin A and other micronutrients and minerals (Thilsted et al., 1997, Roos et al., 2002). They have high levels of preformed vitamin A compounds, mainly as retinoids (vitamin A1), dehydroretinoids (vitamin A2), **all-trans retinol and 13-cis retinol** found predominantly in the eyes and viscera (Sivell et al., 1984; Stancher & Zonta, 1984). **Small amounts of β -carotene may be present.** The proportions of vitamin A-1 and vitamin A-2 vary considerably between species. For example, in chanda (*Parambassis baculis*), vitamin A-1 accounts for 90% of the total vitamin A content, expressed as retinol activity equivalent (RAE), and 20% in darkina (*Esomus danricus*) (Table - 5) (Roos et al., 2007). The study also indicated that vitamin A accumulation is more in pelagic microphagous fishes.

Molluscs are also rich in vitamins. The foot of *Pila* sp., *Bellamya* sp., *Lamellidens* sp., and *Parreysia* sp. is rich in vitamins A, B, D (Prabhakar and Roy, 2009). These are used as traditional medicines by tribal people to cure many diseases.

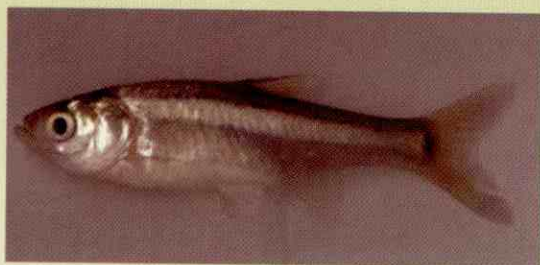


Figure 13 (a): *Amblypharyngodon mola*



Figure 13 (b): *Esomus danricus*



Figure 13 (c): *Osteobrama cotio cotio*

Table 5: Categories of commonly consumed fish species according to vitamin A content

Category	Vitamin A content ^a (RAE/100 g raw, cleaned parts)	Common Name ^b	Scientific name
Very high	>1,500	Mola	<i>Amblypharyngodon mola</i>
		Chanda	<i>Parambassis baculis</i>
High	500–1,500	Dhela	<i>Osteobrama cotio cotio</i> ^c
		Darkina	<i>Esomus danricus</i>
		Chanda	<i>Parambassis ranga, Chanda nama</i>
		Koi	<i>Anabas testudineus</i>
Medium	100–500	Tengra	<i>Mystus vittatus</i>
		Taki	<i>Channa punctatus</i>
		Chela	<i>Chela cachius</i>
		Kachki	<i>Corica soborna</i>
		Baim/Chikra	<i>Macrognathus aculeatus, Masta cembelus pancalus, M. amatus</i>
		Puti	<i>Puntius sophore, P. chola, P. ticto</i>
		Gutum	<i>Lepidocephalus guntea</i>
		Chapila	<i>Gudusia chapra</i>
		Kolisha	<i>Colisa fasciatus</i>
Low	< 100	Shing	<i>Heteropneustes fossilis</i>
		Magur	<i>Clarias batrachus</i>
		Chata	<i>Colisa lalia</i>
		Tilapia	<i>Oreochromis niloticus</i>
		Mrigal	<i>Cirrhinus cirrhosus</i>
		Rui	<i>Labeo rohita</i>
		Silver carp	<i>Hypophthalmichthys molitrix</i>
		Hilsha	<i>Tenuulosa ilisha</i> ^d

RAE, retinol activity equivalent

a. A single sample of some species and replicate samples of other species were analyzed.

b. The fish species are listed in order of decreasing vitamin A content.

c. One sample of dhela was analyzed in a minor study conducted at the Department of Human Nutrition, The Royal Veterinary and Agricultural University, Denmark, in 1993. Dhela was not available for sampling at the time when this study was conducted.

d. An alternative scientific name is *Hilsa ilisha*.

(Source: Roos et al., 2002)

6 Fish As A Rich Source of Minerals and Trace Elements

Minerals are the other group of micronutrients required by humans for proper growth and biological function. They can be classified into bulk elements and trace elements depending upon their amount of requirement (Table - 6). Bulk elements include calcium, magnesium, sodium, potassium, phosphorus, sulfur, and choline. The trace elements essential for human health are iron, copper, manganese, iodine, fluorine, molybdenum, selenium, and zinc. The most of the trace elements function as enzyme cofactors or prosthetic groups (Table - 7).

Calcium is the structural component of bone and teeth mineral and free Ca^{2+} serves as regulatory agent in cell cytosol. Calcium together with phosphorus forms the insoluble crystalline mineral calcium hydroxyapatite. Calcium is highly important in human nutrition as it is required during infancy and childhood, when the skeleton is growing and also during pregnancy and lactation. Phosphorus in the form of phosphate is a vital component of the bones, nucleic acids, nucleotide coenzymes and ATP-ADP- energy transferring system.

Iron is required for the synthesis of iron-porphyrin (Fig - 14) proteins haemoglobin, myoglobin, cytochromes and cytochrome oxidase. It is carried in the blood bound to the plasma protein transferrin, and stored in the tissues in the form of ferritin (protein containing ferric hydroxide and ferric phosphate). Liver, spleen and bone marrow contain enough ferritin. Iron is absorbed only as ferrous ions (Fe^{2+}). Deficiency of iron leads to iron-deficiency anaemia. Iron deficiency is most frequent in children, adolescent girls and women.

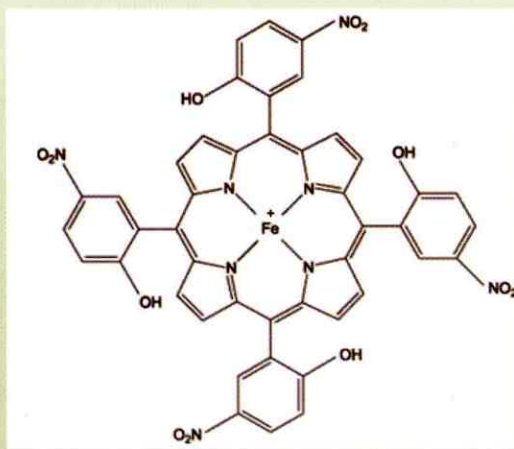


Figure 14: Iron-porphyrin complex
(Source: www.scielo.br)

Copper is essential in the diet as it is required for the proper utilization of iron and synthesis of cytochrome oxidase, which contains both iron and copper. Copper is also necessary for the development of connective tissues and blood vessels.

Zinc forms an important part of enzymes as their prosthetic groups. These include alcohol dehydrogenase, carbonic hydrogenase, DNA and RNA polymerases and carboxypeptidase. Zinc is found in high concentrations in the prostat gland, sperm cells, and eyes. Zinc deficiency leads to small stature, anaemia, low serum albumin and retarded development of reproductive system.

Many small indigenous fish species (SIS) (Fig - 15) contain high amount of minerals like calcium, iron, and zinc (Roos et al., 2007). Two species from the genus *Esomus* (*E. danricus*, *E. longimanus*) are rich in high iron content (Thilsted 2010). Many SIS are eaten whole, including the bones, and are, therefore, a rich calcium source. The 2 species from the genus *Esomus*, *darkina* from Bangladesh and *trey changwa plieng* from Cambodia, have high iron content. Iron in fish is present in the forms of heme iron, a high-molecular subpool of complexbound nonheme iron, and inorganic iron, the proportions varying with fish species. According to the study conducted by Roos et al. (2007), it was estimated that SIS contributed 40% and 31% of the total recommended intakes of vitamin A and calcium, respectively, at household level in the peak fish production season.

Table 6: Elements Required in Human Nutrition

Bulk Element:
Calcium
Chlorine
Magnesium
Phosphorus
Potassium
Sodium
Trace Element:
Copper
Fluorine
Iodine
Iron
Manganese
Molybdenum
Selenium
Zinc

Other Trace Element known to be essential in animals and very likely essential for Human

Arsenic

Chromium

Nickel

Silicon

Tin

Vanadium

Table 7: Some important minerals that Serve as Cofactors for Enzymes

Minerals	Enzymes
Cu 2+	Cytochrome oxidase
Fe2+ or Fe3+	Cytochrome oxidase Catalase, peroxidase
K+	Pyruvate kinase
Mg2+	Hexokinase Glucose 6- phosphate Pyruvate kinase
Mn2+	Arginase Ribonucleotidase reductase
Mo	Dinitrogenase Nitrate reductase
Ni2+	Urease
Se	Glutathione peroxidase
Zn2+	Carbonic anhydrase Alcohol dehydrogenase Carboxypeptidases A & B DNA polymerase






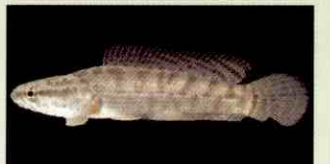









		
<i>Chanda ranga</i>	<i>Amblypharyngodon mola</i>	<i>Mystus tengra</i>
		
<i>Ailia coila</i>	<i>Anabas testudineus</i>	<i>Channa punctatus</i>
		
<i>Xenentodon cancila</i>	<i>Salmostoma bacaila</i>	<i>Esomus danricus</i>
		
<i>Gudusia chapra</i>	<i>Puntius sophore</i>	<i>Puntius chola</i>
		
<i>Rhinomugil corsula</i>	<i>Glossogobius giuris</i>	<i>Eutropiichthys vacha</i>

Figure 15: Some Freshwater Small Indigenous Fishes (SIF) of India

7 Fish with established therapeutic values

Channa striatus

Channa striatus (striped snakehead) is a carnivorous, air-breathing freshwater fish, indigenous to many tropical and subtropical countries of Asia. It is a highly nutritious fish and known to have medicinal values and used as a cure for many ailments. It is widely consumed in Asia-Pacific region as a rich source of protein and to induce wound healing in post-operative as well as post-delivery, especially among caesarean mothers (Sabto, 1998). The haruan based cream is effective for exfoliation dermatitis, such as psoriasis, eczema and ichthyosis (Mat Jais et al., 1997). *C. striatus* helps in wound healing by the increase in tensile strength. It is hypothesised that this effect may be due to its high content of arachidonic acid, glycine and polyunsaturated fatty acids (Baie and Sheikh, 2000). The extract from *C. striatus* has potent anti-inflammatory and analgesic properties (Somchit et al., 2004; Zakaria et al., 2004) and has been in use for centuries to reduce pain, inflammation and enhance wound healing (Zuraini et al., 2006).



It is reported that *C. striatus* contains all the essential amino and fatty acids for wound healing, particularly glycine (Mat Jais et al., 1994; Mat Jais et al., 1998). The studies indicated high content of arachidonic acid in fresh haruan fillet and the presence of oleic acid (C18:1) and linoleic acid (C18:2) in mucous extract. Studies have revealed that extract from haruan has antinociceptive activity and the extract has provided 100% block on peritoneal pain receptor and enhanced morphine, suggesting that it can be seen as a potential source of useful drugs (Mat Jais et al., 1997; Mat Jais, 2007). Amino acids and fatty acids are important for the wound healing process and their deficiency can hinder the recovery. Glycine is the most important component of human skin collagen and together with alanine, arginine, proline, leucine, isoleucine, serine, and phenylalanine, will combine with aspartic acid and glutamic acid to form a polypeptide that is associated or responsible for tissue growth and wound healing (Heimann, 1982; Chyun and Griminger, 1984; Westaby, 1985; Greenhalgh and Gamelli, 1987). Arachidonic acid is a precursor for prostaglandins that may induce platelet aggregation and adhesion in endothelial tissue, thereby initiating blood clotting (Bowman and Rand, 1980). Prostaglandins, known to be involved in pain sensation, inflammation and wound healing, are released when tissues are injured or wounded. The prostaglandins,

PGE1 and PGE2, possess antinociceptive activity (Fan and Chapkin, 1998; Hosoi et al., 1999; Stock et al., 2001). Huang et al. (2001) reported on the presence of lipo-amino acid, N- arachidonylglycine in bovine and rat brain and other tissues that is capable of suppressing inflammatory pain. The high amount of glycine and the presence of arachidonic acid are believed to be the precursors for the formation of arachidonylglycine. According to Griffin et al. (2000), fatty acid derivative palmitoylethanolamide is capable of binding to cannabinoid receptors, which are known to mediate the antinociceptive effects of marijuana; the high content of palmitic acid in Haruan may also help explain its antinociceptive activity. Moreover, the presence of stearic acid and oleic acid in haruan may also explain the anti-inflammatory activity of the extract, because these fatty acids have been reported to attenuate the activity of polymorphonuclear leucocytes and suppress inflammatory processes (Crocker et al., 2001). Glutamate and aspartate, which are the excitatory amino acids and found in high amounts in Haruan, have also been found to be involved in endogenous pain inhibition (Aimone and Gehart, 1986; Jacquet, 1988).

Al-saffar et al. (2011) studied the therapeutic effect of *C. striatus* extract against osteoarthritis. Osteoarthritis (OA), also known as degenerative arthritis or degenerative joint disease, is an age-related joint disease characterized by degradation of joints, articular cartilage associated with subchondral response and inflammation of the synovial membranes and chronic pain. Occasionally, the joints may also be filled with fluid. As the disease progresses, the affected joints appear larger, are stiff and painful. In smaller joints, such as at the fingers, hard bony enlargements, called Heberden's nodes (on the distal interphalangeal joints) and/or Bouchard's nodes (on the proximal interphalangeal joints), may form, and limit the movement of the fingers significantly. Osteoarthritis at the toes leads to the formation of bunions, rendering them red or swollen.



Figure 16: Medial side OA of the knee shows radiographic evidence that includes medial side joint space narrowing, subchondral bone sclerosis, osteophyte formation, and sharpening of tibial spines (Source: Phillips et al., 2010)

The causes of primary OA probably are multifactorial: altered biomechanics, cytokine abnormalities, and genetic factors may combine to initiate a cascade of changes that become self-perpetuating as damage accumulates (Mankin and Lippiello, 1970). The main risk factor for OA is age; more than 80% of persons older than 75 years are affected. However, OA is not a natural consequence of aging. The knees are most frequently involved in primary OA (Figure - 16), followed by the hips and hands. The mechanical forces experienced across weight-bearing joints clearly play a role; therefore, obesity is a strong risk factor for OA (Phillips, 2010).

The study by Al-Saffar et al. (2011) (Fig - 17) demonstrated that oral administration of haruan extract reduced the global pathological score of the articular cartilages and synovial membranes of the OA joints. The extract can enhance the proliferation of collagen fibres in the matrix substance of the articular cartilage. This alleviation may decrease and suppress the fibres from being destructed and prevent subsequent matrix degradation. The high amounts of n-3 PUFAs in haruan extract is known to play a role in synthesis of collagen fibre (Mat Jais et al., 1998). It can strengthen the matrix through remodeling of collagen fibres via the synthesis of inter- and intramolecular protein cross-linking (Chithra et al., 1998) and thereby minimizing the degradation and inflammation.

Another property of the extract is its ability to enhance the production of glycosaminoglycans and hyaluronic acid (Baie and Sheikh, 2000) for matrix healing. Inflammatory events at the OA joints are mainly due to the fragmentation of the degrading articular cartilage into the synovium which subsequently triggers the inflammatory process by producing prostanoids and pro-inflammatory mediators such as IL-1 and TNF- α which in turn stimulates the generation of oxygen free radical species (Cahue et al., 2007). These oxygen free radical compounds can cause and enhance chondrocytes degeneration at the articular cartilage. Anti-inflammatory property of the extract inhibits some of the inflammatory process and its earlier therapeutic application reflects the importance of earlier treatment on the disease progression.

Other fish species which are known to have medicinal values are *Clarias batrachus* (Magur) *Heteropneustes fossilis* (Singhi) and *Anabas testudineus* (Koi) (Fig - 18). These fishes are traditionally used to cure infections, reduce pain and usually given to patients recuperating from operations, injuries and wound. But much research had to be conducted on these species to have a better understanding on the therapeutic components and their effects on diseases. The proximate composition of these species is given in Table - 8, mineral content in Table - 9, and fat soluble vitamin content in Table - 10.

Radiographs showing changes in Femoral (F) and tibial (T) parts of the knees. (A, B): Normal knees showed clear radiolucent joint space (arrows) and distinct sub-patellar opacity (thick arrow). (C, D): Knees post 15 days of OA showed decreased joint space, roughened articular surfaces (arrows) and less distinct sub-patellar opacity (thick arrow). (E): HII group post 2 days of OA showed swelling of the joint (doubled head arrow) with still prominent joint space (arrow). Post euthanasia, right knees of HI and HII revealed no progressed changes in femoral and tibial parts with somewhat clear joint space (F, G) whereas, changes progressed severely in CEL and NS groups: complete loss of joint space with distinct dystrophic changes (thin arrows), rough articular surfaces and indistinct subpatellar opacity (thick arrow) (H-L).
 (Source: Al-Saffar et al. 2011. Journal of Animal and Veterinary Advances 10 (4): 460-469.)

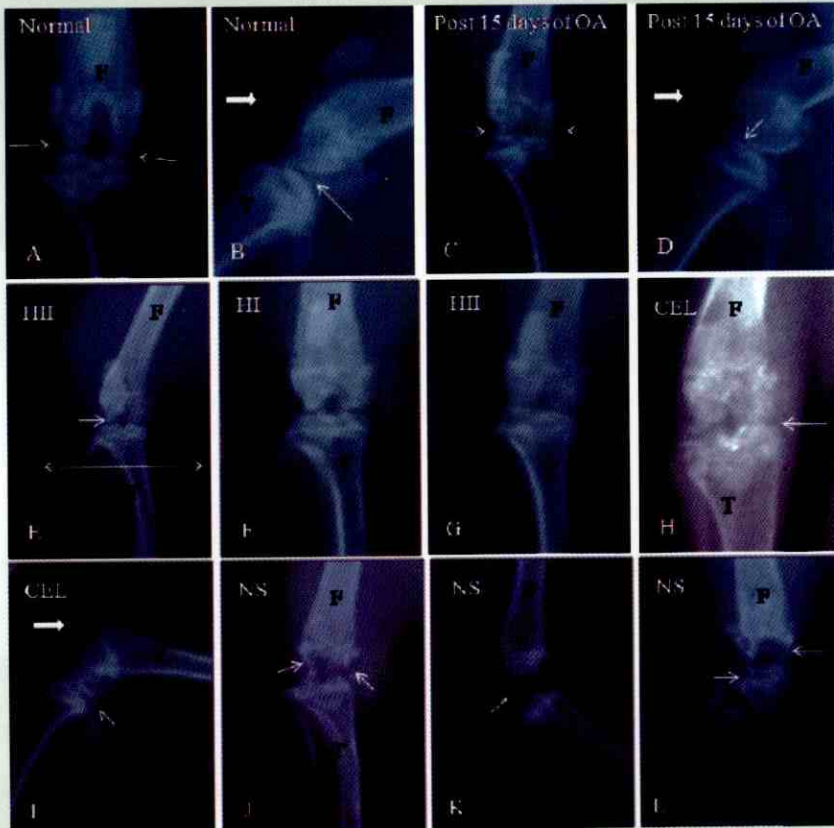
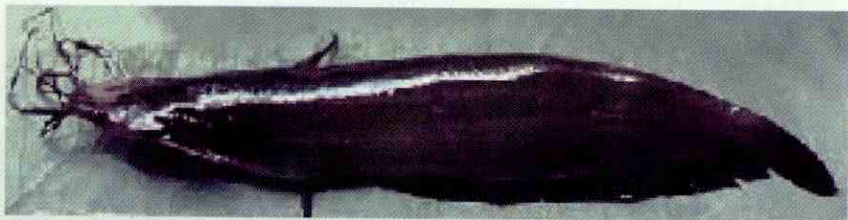




Fig - 18 (a) *Clarias batrachus* (Magur)



(b) *Anabas testudineus* (Koi)



(c) *Heteropneustes fossilis* (Singhi)

Table 8: Proximate composition of Magur, Singhi and Koi (% w/w basis)

Fish Species	Weight (g)	Moisture	Crude Protein	Fat	Ash
<i>Clarias batrachus</i>	≤ 50	62.39-78.06	15.27-17.38	2.91-3.77	1.77-2.42
	> 50	73.94-78.10	15.17-17.52	0.7-6.62	2.09-2.59
<i>Heteropneustes fossilis</i>	≤ 50	70.17-79.34	14.43-19.5	2.26-5.52	1.79-3.07
	> 50	65.43-81.48	13.21-20.26	1.3-8.64	2.24-3.5
<i>Anabas testudineus</i>	≤ 50	62.72-77.02	14.29-18.97	1.92-18.97	2.71-7.59
	> 50	61.94-67.65	12.67-17.49	7.35-14.52	3.82-7.16

Table 9: Mineral content Magur, Singhi and Koi (mg/100g w/w basis)

Fish Species	Weight (g)	Na	K	Ca	Fe	Mn	Zn	Se
<i>Clarias batrachus</i>	≤ 50	149.39-205.48	216.35-241.99	7.56-7.98	0.25-1.29	0.1-0.16	0.39-0.47	0.22-1.19
	> 50	152.42-223.7	205.27-259.97	8.01-85.32	0.61-2.64	0.08-0.7	0.54-1.35	0.16-2.34
<i>Heteropneustes fossilis</i>	≤ 50	154.36-231.75	189.93-309.35	13.26-110.31	2.83-7.53	0.24-1.03	0.17-1.53	0.02-1.33
	> 50	131.25-217.73	161.67-375.46	52.72-274.78	1.21-5.49	0.31-0.95	0.46-2.69	0.15-1.2
<i>Anabas testudineus</i>	≤ 50	156.06-252.88	75.89-218.54	135.95-271.09	2.16-12.01	0.3-1.24	0.1-2.06	0.11-1.4
	> 50	138.52-199.28	192.07-256.31	117.73-268.57	1.33-4.61	0.32-1.17	0.11-1.21	0.05-1.91

B. N. Paul, Co-PI, Outreach Activity - 3 CIFA (ICAR) Bhubaneswar
(personal communication)

Table 9: Fat soluble vitamin content in Koi and Singhi (w/w basis)

<i>Fish species</i>	Weight (g)	A (I.U./ 100g)	D (I.U./ 100g)	E (I.U./ 100g)	K (µg/ 100g)
<i>Anabas testudineus</i>	≤ 50	85.77	121.6	0.7	0.53
	> 50	93.9	43.12	1.997	1.16
<i>Heterop- neustes fossilis</i>	> 50	0.86	13.6	0.16	3.8

SHARK LIVER OIL

Shark liver oil is obtained from sharks that live in cold, deep oceans are caught for food purposes. The liver oil from sharks has been used by fishermen for centuries as a folk remedy for general health. It is purportedly useful for healing wounds, sores, irritations of the respiratory tract and the alimentary canal and for lymph node swelling. It is one of the active ingredients in hemorrhoid creams such as Preparation H.



Shark liver oil is rich in alkylglycerols, which are naturally found in mother's milk and in bone marrow. It also contains pristane, squalene, vitamins A, D, omega-3 fatty acids, triglycerides, glycerol ethers, and fatty alcohols.

Most shark liver oil supplements have not been tested to find out if they interact with medicines, foods, or other herbs and supplements. Even though some reports of interactions and harmful effects may be published, full studies of interactions and effects are not often available. Because of these limitations, any information on ill effects and interactions below should be considered incomplete.

Although many people have taken shark liver oil, the issue of potential toxicity at the usual doses has not been well studied. Some mild digestive problems such as nausea, upset stomach, and diarrhea have been reported. Some animal studies have found that shark liver oil and its components may raise blood cholesterol levels. A Japanese study (Akutsu et al., 2006) found some shark liver oil supplements to be contaminated with Polychlorinated

biphenyls (PCBs) and Polybrominated diphenyl ethers (PBDEs). PCBs can have harmful effects in humans, and may increase the risk of some types of cancer. People with seafood allergies may also react to shark liver oil.

COD LIVER OIL

Cod liver oil is a nutritional supplement derived from liver of cod fish. It has high levels of the omega-3 fatty acids, EPA and DHA, and very high levels of vitamin A and vitamin D. It is widely taken to ease the symptoms of arthritis and for other health benefits. It was once commonly given to children, because the high levels of vitamin D in cod liver oil have been shown to prevent rickets and other symptoms of hypovitaminosis D (Rajakumar, 2003).



Depending on the quality of the oil, the flavor and aroma range from a mild sardine-like flavor, to an intense odor of fish and oil. High quality cod liver oil is a pale-yellow, thin, oily liquid, having a slightly fishy and bland taste. Manufacturers sometimes add flavorings, such as citrus or mint essence, to cod liver oil to make it more palatable. While taking the capsules as well as the liquid form, one may experience a rancid fishy aftertaste during belching.

Medicinal Use

Cod liver oil is widely taken to ease the pain and joint stiffness associated with arthritis (Gruenwald et al., 2002) and has also been clinically proven to have a positive effect on heart (von Schacky,

2000), bone (Akpede, 1999) as well as helping to repair wounded skin (Terkelsen et al., 2000), hair, and nails. Cod liver oil and fish oil are similar, but cod liver oil has much higher levels of vitamins A and D. Many adults do not meet the RDA for Vitamin D (Reginster, 2005; Calvo et al., 2004; Peterlik and Cross, 2005; Cantorna and Mahon, 2004). Cod liver oil may be an effective complementary measure for long-term treatment of multiple sclerosis (Swank and Barbara, 1987). Use of cod liver oil during pregnancy is associated with lower risk of Type I diabetes in the offspring (Stene et al., 2000). This effect was found only in mothers taking cod liver oil, not in mothers taking multivitamin supplements. Cod liver oil taken by nursing mothers improves the breast milk by increasing the amount of fatty acids, which promotes brain development, and the amount of vitamin A, which helps prevent infections, but the level of vitamin D is unchanged. A Norwegian study of more than 68,000 women reported that female cancer patients who took daily cod-liver oil supplements had significantly reduced mortality (25% for all cancers, 45% for lung cancer) compared to women who did not take such supplements (Lund, et al., 2007; Skeie, 2009).

Adverse Effects

Because cod liver oil has a very high level of vitamin A, it is possible to exceed the Recommended Dietary Allowance (RDA) of vitamin A. Vitamin A accumulates in body fat, and can reach harmful levels sufficient to cause hypervitaminosis A (Lips, 2003). Pregnant women may want to consider consulting a doctor when taking cod liver oil because of the high amount of natural forms of vitamin A such as retinol. High doses of synthetic vitamin A (retinoids) have been shown to cause birth defects (Myhre et al., 2003). The risks of hypervitaminosis and of exposure to environmental toxins such as mercury, polychlorinated biphenyls, dioxins, and other contaminants, are reduced when purification processes are applied to produce refined fish-oil products, which consequently contain raised levels of omega-3 fatty acids, such as EPA and DHA (Bays, 2007). A high intake of cod liver oil by pregnant women is associated with a nearly fivefold increased risk of gestational hypertension (Olafsdottir et al., 2006), although this study did not control for mercury, which can be present in harmful amounts in fish and which is another cause of hypertension (Horowitz et al., 2002). Some urge caution when taking cod liver oil and other fish-based supplements since they may contain elevated levels of toxins such as mercury and PCBs found in fish (Bays, 2007). Some supplement companies regularly test cod liver oil for purity.

8

Fishes in Spas for Ichthyotherapy

Ichthyotherapy is the treatment of skin wound/condition with fish. The fish nibbles or feed on the affected skin removing the dead skin and avoid the healthy skin. The fish is maintained in hygienic pools and sparsely fed. The most commonly used fish in Ichthyotherapy is *Garra rufa*, popularly known as the 'doctor fish', 'nibble fish' or Kangal fish'. The treatment initially started in the Kangal hot springs of Turkey (Mossman, 2007). They are used to help treat patients suffering from various skin disorders, including psoriasis and eczema, since the fish will eat and remove any dead skin. Spa therapy under observation of a dermatologist may be effective and useful for psoriasis vulgaris patients (Ozçelik et al., 2000; Grassberger, and Hoch, 2006).



Garra rufa (Doctor Fish)
(Source: www.fishbase.org)

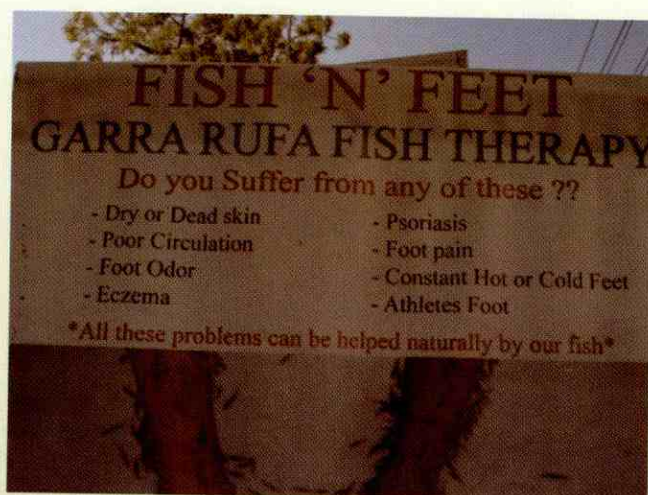
In 2006, doctor fish spa resorts opened in Japan, and Croatia, where the fish are used to clean the bathers at the spa. There are also spas in resorts in China, Belgium, the Netherlands, South Korea, Singapore, Bosnia & Herzegovina, Hungary, Slovakia, India, Thailand, Indonesia, Malaysia, Philippines, Hong Kong, Bucharest, Romania, Barcelona, Spain and France. In 2008, the first widely known doctor fish pedicure service was opened in the United States Virginia. In 2010 the first UK spa opened in Sheffield. In India, the spa treatment is available in metro cities like Mumbai, Delhi and Bangalore. Kenko Reflexology and Fish Spa uses the fish therapy for guests to experience natural exfoliation of the feet to produce healthy, glowing skin and healing them from even the most crusty or diseased epidermis. The water in the Fish Spa treatment sinks is changed daily and the water is treated with 2000W Ultra Violet Sterilization to kill virus and bacteria in water. The temperature is controlled at approximately 30°C (www.mybangalore.com).



Fish nibbling on feet. Source: www.mybangalore.com

Benefits:

- Natural exfoliation of dead skin – Smoother and healthy glowing skin with easy moisturizer absorption
- Promote blood circulation – Micro massage sensation from these ‘little masseurs’
- Lightening of minor scars
- Easing of psoriasis and minor eczema
- Release stress and tension



Claims made by fish spa (Source: <http://hubpages.com/hub/Fish-Spa-Phenomena>)

But concerns have been raised that infections could be spread through open wounds. Fish spa pedicures have already been banned in some U.S. states for health and safety reasons. The fish tanks and the water are sterilized after each customer use and utmost care is taken to sanitize the spa. Still, the concerns remain as the expensive fish itself is not thrown away after each use. Therefore, the officials are skeptical about the safety of the fish therapy.



9

Fishes in Folklore Medicine

A number of fish species are reported to being used in India as traditional medicine for various ailments (Table - 11, 12). The Ao tribe of Nagaland uses *Amphipnous cuchia* (Eel) to treat asthma and general weakness; fresh blood of the fish is drunk (Kakati et al., 2006).

Table 11: List of fishes commonly used in folklore medicine

Species	Common Name
<i>Monopterus cuchia</i> (Hamilton, 1822)	Cuchia eel
<i>Monopterus albus</i> (Zuiew, 1793)	Eel
<i>Schizothorax richardsonii</i> (Gray, 1832)	Snow trout
<i>Tor putitora</i> (Hamilton, 1822)	Mahseer
<i>Channa punctata</i> (Bloch, 1793)	Spotted snakehead
<i>Labeo gonius</i> (Hamilton, 1822) carp fish	Kuria labeo
<i>Labeo rohita</i> (Hamilton, 1822)	Rohu
<i>Eusphyra blochii</i> (Cuvier, 1816)	Hammer head shark

Source: Mahavar and Jaroli, 2008

Table 12: Fishes used in Brazilian traditional medicine

Family/Species/common Name	Conditions to which remedies are prescribed
Auchenipteridae	Umbilical hernia, asthma, sexual impotence
<i>Trachelyopterus galeatus</i> (Linnaeus, 1766) - “Cumbá”	
Anostomidae	
<i>Schizodon knerii</i> (Steindachner, 1875) - “Piau-branco”	Leucoma, edema
Ariidae	
<i>Bagre bagre</i> (Linnaeus, 1766) - Coco sea catfish, “bagre-fidalgo”	Injuries caused by itself
<i>Genidens barbatus</i> (Lacepède, 1803) - White sea catfish, “bagre-do-mangue”	Pain relief caused in injuries by the species' sting

Genidens genidens (Cuvier, 1829)

– catfish, “bagre”

Injuries caused by itself

Sciadeichthys luniscutis (Valenciennes, 1837) – “bagre-urutu”

Pain relief caused in injuries by the species’ sting

Aspredinidae

Aspredo aspredo (Linnaeus, 1758)

Asthma

– Banjo catfish, “banjo”, “viola”

Aspredinichthys tibicen (Valenciennes, 1840)

- Ten barbed banjo, “viola”

Balistidae

Balistes vetula (Linnaeus, 1758)

Stroke, asthma, thrombosis, earache, pain relief caused in injuries by the species’ sting, haemorrhage, ascites, schistosomiasis, appendicitis, menstrual cramps, gastritis

- Queen triggerfish, “cangulo”, “capado”, “peroá”

Batrachoididae

Thalassophryne nattereri

Pain relief caused in injuries by the species’ sting

(Steindachner, 1876) -Venomous toadfish, “niquim”

Callichthyidae

Callichthys callichthys (Linnaeus, 1758) – “cascarudo”, “caboge”

Asthma, umbilical hernia

Carcharhinidae

Carcharhinus limbatus (Müller &

Osteoporosis

Henle, 1839) – Blackfin shark,

“sucuri preto”

Carcharhinus porosus (Ranzani, 1840)

Asthma, rheumatism, wounds, inflammations, osteoporosis, anaemia

-Smalltail shark, “junteiro”, “cação-gaiapreta”

Galeocerdo cuvier (Péron &

Osteoporosis

Lesueur, 1822)

- Tiger shark, “jaguara”

Rhizoprionodon lalandii (Müller & Henle,

Rheumatism

1839) - Brazilian sharpnose shark, “cação”

Rhizoprionodon porosus (Poey, 1861)

- Sharpnose shark, “cação”

Sphyrna lewini (Griffith & Smith, 1834) Asthma, wounds, rheumatism,
 -Scalloped hammerhead, “peixe-martelo”, inflammation
 “cação-panã”, “cação-chapéu”

Centropomidae

Centropomus parallelus Poey, 1860 Nephritis

Centropomus undecimalis (Bloch, 1792)
 -Common snook, “rubalão” Edema in the legs

Characidae

Astyanax bimaculatus (Linnaeus, 1758) Alcoholism, leishmaniosis, skin burns,
 -Twospot astyanax, “piaba-mirim”, wounds, rheumatism
 “machadinha”, “piaba chata”

Brycon nattereri Günther, 1864
 -“pirapitinga”, “matrinchá” Flu

Clupeidae

Opisthonema oglinum (Lesueur, 1818)
 -Atlantic thread herring, “sardinha” Alcoholism

Dasyatidae

Dasyatis guttata (Bloch & Schneider, 1801)
 - Longnose stingray, “raia branca” Asthma, pain relief caused in injuries by
Dasyatis marianae (Gomes, Rosa & the species' sting, burns
 Gadig, 2000) - Brazilian large-eyed
 stingray, “raia mariquita”

Doradidae

Franciscodoras marmoratus (Reinhardt, Injuries caused by itself
 1874) – “Urutu” Swelling
Lithodoras dorsalis (Valenciennes, 1840)

Echeneidae

Echeneis naucrates Linnaeus, 1758
 - Live shark sucker, “rêmora”, “pegador” Asthma, bronchitis

Electrophoridae

Electrophorus electricus (Linnaeus, 1766) Sprains, bruises, insect bites,
 -Electric eel, “poraquê” snake bite, asthma, flu, pain in general,
 muscle strain, rheumatism, osteoporosis,
 deafness, pneumonia, itching

Erythrinidae

Erythrinus erythrinus (Bloch & Schneider, 1801) – “Matrôe” Asthma

Hoplias malabaricus (Bloch, 1794)
-Trahira, “traíra”

Ophthalmological problems, rheumatism, cataracts, wounds, snake bite, conjunctivitis, stroke, thrombosis, asthma, toothache, fever, earache, diarrhoea, deafness, boils, bleedings, alcoholism, tetanus, sore throat, itching, sprains, leucoma

Hoplias lacerdae Miranda Ribeiro, 1908
- Giant trahira

Leucoma

Gadidae

Gadus morhua Linnaeus, 1758
– Atlantic cod, “bacalhau”

Boils

Ginglymostomatidae

Ginglymostoma cirratum (Bonnaterre, 1788)
- Nurse shark, “cação-lixá”

Rheumatism

Heptapteridae

Pimelodella brasiliensis (Steindachner, 1876)
– “mandim”

Injuries caused by that fish species

Rhamdia quelen (Quoy & Gaimard, 1824)
– Mole, Catfish

Weakness

Megalopidae

Megalops atlanticus (Valenciennes, 1847)
-Tarpon, “camurupim”, “cangurupim”

Stroke, headache, asthma, shortness of breath, thrombosis, chest pain, injuries caused by bang

Muraenidae

Gymnothorax funebris Ranzani, 1840
–Green moray, “moréia verde”

Gymnothorax moringa (Cuvier, 1829)
–Spotted moray, “moréia pintada”

Bleeding (wounds)

Gymnothorax vicinus (Castelnau, 1855)
-Purplemouth moray, “moréia”

Myliobatidae*Aetobatus narinari* (Euphrasen, 1790)

-Spotted eagle ray, "raia- chita"

Asthma, pain relief caused in injuries by the species' sting, burns, haemorrhage

Narcinidae*Narcine brasiliensis* (Olfers, 1831)

-Brazilian electric ray, "raia elétrica"

Toothache

Ogcocephalidae*Ogcocephalus vespertilio* (Linnaeus, 1758)

-Batfish, "Peixe morcego"

Asthma, bronchitis

Pimelodidae*Pseudoplatystoma corruscans* (Spix &

Agassiz, 1829) - Spotted sorubim,

"surubim"

Flu

Prochilodontidae*Prochilodus argenteus* Spix & Agassiz,

1829- "curimatá-pacú", "curimatá"

To avoid swelling of the breast feeding, mycosis

Serrasalminidae*Serrasalmus brandtii* (Lütken, 1875)

-White piranha, "pirambeba"

Inflammations, sexual impotence

Sciaenidae*Cynoscion acoupa* (Lacepède, 1801)

-Acoupa weakfish, "pescada amarela"

Renal failure

Cynoscion leiarchus (Cuvier, 1830)

-Smooth weakfish, "pescada branca"

Renal failure

Micropogonias furnieri (Desmarest, 1823)

-Whitemouth croaker, "corvina"

Pain relief caused in injuries by the species' sting, cough, asthma, bronchitis

Pachyurus francisci (Cuvier, 1830)

- San Francisco croaker, "cruvina-de-bico"

Asthma, urinary incontinence, backache

Sparidae*Calamus penna* (Valenciennes, 1830)

-Sheepshead porgy, "peixe-pena"

Asthma

Synbranchidae*Synbranchus marmoratus* Bloch, 1795

-Marbled swamp eel, "muçum"

Bronchitis

Syngnathidae*Hippocampus erectus* Perry, 1810

-Horsefish, "cavalo-marinho"

Asthma

Hippocampus reidi (Ginsburg, 1933)

-Longsnout seahorse, "cavalo-marinho"

Asthma, edema, bronchitis, haemorrhage, haemorrhage in women, disorders after parturition (to accelerate recovery after parturition), gastritis, tuberculosis, to prevent abortion

Tetraodontidae*Colomesus psittacus* (Bloch &

Schneider, 1801) -Banded puffer, "baiacu"

Breast cancer, backache, warts

Sphoeroides testudineus (Linnaeus, 1758)

-Checkered puffer, "baiacu"

Rheumatism

Trichiuridae*Trichiurus lepturus* Linnaeus, 1758

-Largehead hairtail

Asthma

Urolophidae*Urotrygon microphthalmum*

(Delsman, 1941) -Smalleyed round stingray, "raia"

Asthma, pain relief caused in injuries by the species' sting, burns

Source: Alves, R. R. N., 2009

Species belonging to *Paratelphusa*, *Macrobrachium*, *Bellamya*, *Pila*, *Achatina*, *Lamelidens*, *Novaculina* and *Parreysia* are edible to aboriginal people and particularly they have been used as medicines for the cure of a number of ailments such as rheumatism, cardiac diseases, controlling blood pressure, asthma, rickets, calcium metabolism, nervousness, giddiness and also providing missing vitamins and minerals (Mahata, 2002). Many species of shell fishes are being used as ethno-medicine for the cure of a number of diseases by the people of Kosi river basin in the region of North-Bihar (Prabhakar and Roy, 2009) (Table - 13).

Table 13: Shell fishes used as ethno-medicine by people of Kosi River Basin of North-Bihar, India

Diseases	Species used to cure diseases	Method of application for cure of diseases
Asthma Arthritis Joint pain Rheumatism Conjunctivitis	<i>Bellamya sp.</i> <i>Bellamya bengalensis</i>	Soup prepared from the foot of <i>Bellamya sp</i> is used to cure these diseases. To get cured from conjunctivitis, <i>Bellamya bengalensis</i> are collected from pond and are kept in clean fresh water in a earthen pot for night and the water is used like eye drop. This method is considered best for the cure of this disease in this region.
Rickets	<i>Pila sp</i>	Soup prepared from the eggs of <i>Pila</i> is used to cure rickets in children.
Cardiac ailments	<i>Lamellidens sp.</i>	Soup prepared from the foot of <i>Lamellidens Sp.</i> and <i>Parreysia sp.</i> Is used to cure the cardiac ailments and to control blood pressure.
Blood pressure	<i>Parreysia sp.</i> -do-	
Giddiness and dehydration	<i>Lamellidens sp.</i>	The shell powder of <i>Lamellidens sp.</i> mixing with honey is used for the remedy of giddiness and dehydration.
Nervousness	<i>Lamellidens sp.</i>	-do-

Night blindness	<i>Bellamya sp.</i> <i>Pila sp</i>	Curry of the foot of <i>Bellamya sp</i> is eaten regularly by aboriginal people of Kosi region to cure night blindness and for better eye sight.
Anaemia	<i>Macrobrachium sp.</i> <i>Paratelphua sp.</i>	Soup and curry prepared from these shell fishes helpful in the cure of anaemia and vitamin deficiencies; cure paralysis, promote strength; cure arthritis.

Source: Prabhakar and Roy, 2009

- Adeodato, S., 1997. Os santos remédios do mar. Globo Ciência, Abril: 20-25.
- Agosta, W., 1996. Bombardier beetles and fever trees: a close-up look at chemical warfare and signals in animals and plants, New York: Addison-Wesley Publishing Company, 224 p.
- Aimone, L. D. and Gebhart, G. F., 1986. Stimulation-produced spinal inhibition from the midbrain is mediated by an excitatory amino acid neurotransmitter in the medial medulla. J. Neurosci., 6: 1803–13.
- Akpede, G. O., Omotara, B. A., Ambe, J. P., 1999. Rickets and deprivation: a Nigerian study. J. R.Soc.Health, 119 (4): 216–22
- Akutsu, K., Tanaka, Y., Hayakawa, K., 2006. Occurrence of polybrominated diphenyl ethers and polychlorinated biphenyls in shark liver oil supplements. Food Addit Contam.: 23 (12): 1323-1329
- Alves, R. R. N., 2009. Fauna used in popular medicine in Northeast Brazil. Journal of Ethnobiology and Ethnomedicine, 5:1 doi:10.1186/1746-4269-5-1
- Ammu, K., Stephan, J. and Devadasan, K., 1989. Influence of dietary protein on cholesterol levels in A albino rats. Fishery Technology, 26, 125-130.
- Baie, S. H. and Sheikh, K. A., 2000. The wound healing properties of Channa striatus-cetrimide cream — tensile strength measurement. Journal of Ethnopharmacology : 93–100
- Bang, H. O. and Dyerberg, J., 1980. Lipid metabolism in Greenland Eskimos. Adv. Nutr. Res., 31: 1–32.
- Bays, H. E., 2007. Safety Considerations with Omega-3 Fatty Acid Therapy. American Journal of Cardiology, 99 (Supplement 1) (6): S35–S43
- Bergeron, N. and Jacques, H., 1989. influence of fish protein as compared to casein and soy protein on serum and liver lipids, and serum lipoprotein cholesterol levels in the rabbit. Atherosclerosis, 78: 113 - 121. (medline).

- Bisset, N. G., 1991. One man's poison, another man's medicine? *J. Ethnopharm.*, 32: 71-81.
- Bowman, W. C., Rand, M. J., 1980. *Textbook of Pharmacology*, 2nd edn. Blackwell Scientific Publications, London.
- Broughton, K. S., Johnson, C. S., Pace, B. K., Liebman, M. and Kleppinger, K. M., 1997. Reduced asthma symptoms with n-3 fatty acid ingestion are related to 5-series leukotriene production. *Am J Clin Nutr.*, 65: 4 1011-1017
- Calvo, M. S., Whiting, S. J. and Barton, C.N., 2004. Vitamin D fortification in the United States and Canada: current status and data needs. *Am J Clin Nutr.*, 80:1710S-1716S.
- Cantorna, M. T. and Mahon, B. D., 2004. Mounting evidence for vitamin D as an environmental factor affecting autoimmune disease prevalence. *Exp Biol Med (Maywood)* 229:1136-1142.
- Chithra, P., Sajithlal, G. B., Chandrakasan, G., 1998. Influence of aloe vera on the healing of dermal wounds in diabetic rats. *Journal of Ethnopharmacology*, 59: 195-201.
- Cho, J. and Sharks, K. Y., 2002. A potential source of antiangiogenic factors and tumor treatments. *Mar. Biotechnol.*, 4(6): 521-5.
- Chyun, J. H. and Griminger, P., 1984. Improvement of nitrogen retention by arginine and glycine supplementation and its relation to collagen synthesis in traumatized mature and aged rats. *J. Nutr.*, 114: 1697-704.
- Colwell, R. R., 1997. Microbial biodiversity and biotechnology. In: Reaka-Kudla ML et al. (Ed), *Biodiversity II: understanding and protecting our biological resources*, Washington, D.C.: Joseph Henry Press, p. 77-78.
- Crocker, I. P., Lawson, N., Baker, P. N. and Fletcher, J., 2001. The anti-inflammatory effects of circulating fatty acids in obstructive jaundice: Similarities with pregnancy-induced immunosuppression. *Q. J. Med.*, 94: 475-84.
- Cunningham, S., 2009. Foot-nibbling garra rufa fish risks and health benefits of turkish "doctor fish" spas. <http://www.suite101.com>

- Devadasan, K. and Gopakumar, K., 1997. Nutritional significance of dietary fish lipids and proteins in patients with cardiovascular problems. Asia Pacific Fishery Commission Summary report of papers presented at the 10th session of the Working Party of Fish Technology and Marketing. Colombo, Sri Lanka, 4-7 June 1996. pp. 155-165. (FAO Fish Rep.).
- Dickinson, P. Fish spa phenomenon <http://hubpages.com/hub/Fish-Spa-Phenomena>
- Dyerberg, J., Bang, H. O. and Hjorne, N., 1975. Fatty acid composition of the plasma lipids in Greenland Eskimos. *Am. J. Clin. Nutr.*, 28: 958-966.
- Fernandez, E. Chatenoud, L., La Vecchia, C., Negri, E. and Silvia Franceschi 1999. Fish consumption and cancer risk . *Am J Clin Nutr* , 70: 85-90.
- Finkl, C. W., 1984. Os medicamentos do mar. In: Cousteau, J. Y. (Ed), *Enciclopédia dos Mares*, v. 1, Rio de Janeiro: Salvat, p. 74-75.
- Grassberger, M. and Hoch, W., 2006. Ichthyotherapy as alternative treatment for patients with psoriasis: a pilot study. *eCAM*, 3(4): 483-488.
- Greenhalgh, D. G. and Gamelli, R. L., 1987. Is impaired wound healing caused by infection or nutritional depletion? *Surgery*, 102: 306-12.
- Griffin, G., Tao, Q. and Abood, M. E., 2000. Cloning and pharmacological characterization of the rat CB2 cannabinoid receptor. *J. Pharmacol. Exp. Ther.*, 292: 886-94.
- Gruenwald, J., Graubaum, H. J. and Harde, A., 2002. Effect of cod liver oil on symptoms of rheumatoid arthritis. *Adv. Ther.*, 19: 101-107.
- Hamada, M. and Nagai, T., 1995. Inorganic components of bones of fish and their advanced utilization. *J. Shimonoseki Univ. Fish.*, 43: 185-194.
- Hardman, W. E., 2004. (n-3)Fatty Acids and Cancer Therapy . *Journal of Nutrition*, 134 (12): 3427S
- Hege, W., Bjørn, L., Gudbrandsen, O. A., Ild, E., Espe, M., Muna, Z., Mørk, S. and Berge, R.K., 2004. Fish protein hydrolysate reduces plasma total cholesterol increases the proportion of HDL cholesterol, and lowers seyl - COA: cholesterol seyltransferase activity in liver of zucker rats. *J. Nutr.*, 134: 1320 - 1327.

- Heimann W., 1982. Fundamentals of Food Chemistry. AVI Publishing, Connecticut.
- Higa, T., 1996. Introduction. *J. Toxicology – Toxin Reviews*, 15: vii.
- Hodge, L., Salome, C. M., Peat, J. K., Haby, M. M., Xuan, W. and Woolcock, A. J., 1996. Consumption of oily fish and childhood asthma risk. *Medical Journal of Australia*, 164: 137-140
- Horowitz, Y., Greenberg, D., Ling, G. and Lifshitz, M., 2002. Acrodynia: a case report of two siblings. *Arch Dis Child*, 86: 453
- Hosoi, M., Oka, T., Abe, M. Hori, T., Yamamoto, H., Mine, K., Kubo, C., 1999. Prostaglandin E (2) has antinociceptive effects through EP(1) receptor in the ventro medial hypothalamus in rats. *Pain*, 83: 221–7.
- Huan, M., Hamazaki K., Sun, Y., Itomura, M., Liu, H., Kang, W., Watanabe, S., Terasawa, K., Hamazaki T., 2004. Suicide attempt and n-3 fatty acid levels in red blood cells: a case control study in China. *Biological psychiatry*, 56 (7): 490-6.
- Huang, S. M., Bisogno, T., Petros, T. J. Chang, S. Y., Zavitsanos, P. A., Zipkin, R. E., Sivakumar, R., Coop, A., Maeda, D. Y., De Petrocellis, L., Burstein, S., Di Marzo, V. and Walker, J. M., 2001. Identification of a new class of molecules, the arachidonyl amino acids, and characterization of one member that inhibits pain. *J. Biol. Chem.*; 276: 42 639–44.
- Jacquet, Y. F., 1988. The NMDA receptor: Central role in pain inhibition in rat periaqueductal gray. *Eur. J. Pharmacol.*, 154: 271–6.
- Johnson, E. J. and Schaefer, E. J., Potential role of dietary n 3 fatty acids in the prevention of dementia and macular degeneration. *Am J Clin Nutr*, 83(suppl):1494S–8S.
- Kakati, L. N., Bendang, Ao and Doulo, V., 2006. Indigenous Knowledge of Zootherapeutic Use of Vertebrate Origin by the Ao Tribe of Nagaland *J. Hum. Ecol.*, 19(3): 163-167
- Kim, S. K. and Mendis, E., 2006. Bioactive compounds from marine processing byproducts- a review. *Food Research International*, 39: 383-393

- Latham, M. C., 1997. Protein energy malnutrition. In: Human nutrition in the developing world. Food and Agriculture Organization of the United Nations. 127-146 pp.
- Lehninger, A. L., 1982. Principles of biochemistry. Worth Publishers, New York
- Lehninger, A. L., Nelson, D. L. and Cox, M. M., 2005. Lehninger principles of biochemistry, Volume 1. Fourth Ed. W.H. Freeman.
- Lips, P. 2003. Hypervitaminosis A and fractures. N. Engl J. Med., 348 (4): 1927–1928
- Logan, A. C., 2004. Omega-3 fatty acids and major depression: a primer for the mental health professional. Lipids in Health and Disease, 3 (1): 25.
- Lund, E.; Dumeaux, V., Braaten, T., Hjartåker, A., Engeset, D., Skeie, G., Kumle, M., 2007. Cohort Profile: The Norwegian Women and Cancer Study—NOWAC—Kvinner og kreft. International Journal of Epidemiology, 37(1): 36–41.
- Mahata, M. C., 2002. Edible Shell Fish (Molluscs) of Chotanagpur Plateau, Jharkhand (India). Baripada, Orissa: Bio-publications, pp. 1-133
- Mahawar, M. M. and Jaroli, D. P., 2008. Traditional zootherapeutic studies in India: a review. Journal of Ethnobiology and Ethnomedicine, 4:17 doi:10.1186/1746-4269-4-17
- Mankin, H. J. and Lippiello, L., 1970. Biochemical and metabolic abnormalities in articular cartilage from osteo-arthritic human hips. J Bone Joint Surg.; 52A: 424-434
- Mat Jais, A. M., Dambisya, Y. M. and Lee, T. L., 1997. Antinociceptive activity of *Channa striatus* (Haruan) extracts in mice. J. Ethnopharmacol., 57: 125-130
- Mat Jais, A. M., Matori, M. F., Kittakoop, P. and Suwanborirux, K., 1998. Fatty acid composition in mucus and roe of Haruan, *Channa striatus*, for wound healing. Gen Pharmacol., 30: 561-563
- Mat Jais, A. M., McCulloch, R. and Croft, K., 1994. Fatty acid and amino acid composition in Haruan as a potential role in wound healing. Gen Pharmacol., 25: 947-950

- Micallef, M., Munro, I., Phang, M. and Garg M., 2009. Plasma n-3 fatty acids are negatively associated with obesity. *Br. J. Nutr.*, 102 (9): 1370-4.
- Moore, K. S., Wehrli, S., Roder, H., Rogers, M., Forrest Jr, J. N., McCrimmon, D., et al. 1993. Squalamine: an aminosterol antibiotic from the shark. *Proc Natl Acad Sci USA*, 90(4):1354-8.
- Mossman, M., 2007. Fish that go skin-deep. *Scientific American*, June.
- Mozaffarian, D. and Rimm, E. B., 2006. Fish intake, contaminants, and human health evaluating the risks and the benefits. *JAMA*, 296, (15):1885-1899.
- Myhre, A. M., Carlsen, M. H., Bøhn, S. K., Wold, H. L., Laake, P., Blomhoff, R., 2003. Water-miscible, emulsified, and solid forms of retinol supplements are more toxic than oil-based preparations. *Am. J. Clin. Nutr.* 78 (6): 1152-9.
- Roos, N., Md. A. Wahab, Chamnan, C. and Thilsted, S. H., 2007. The role of fish in food-based strategies to combat vitamin a and mineral deficiencies in developing countries. *J. Nutr.*, 137 (4): 1106-1109.
- Ng, K., Meyer, B. J., Reece, L. and Sinn, N., 2009. Dietary PUFA intakes in children with attention-deficit/hyperactivity disorder symptoms. *British Journal of Nutrition*, 102: 1635-1641
- Ohara K., 2007. The n-3 polyunsaturated fatty acid/dopamine hypothesis of schizophrenia. *Prog Neuropsychopharmacol Biol Psychiatry*; 31:469-474.
- Olafsdottir, A. S., Skuladottir, G. V., Thorsdottir, I., Hauksson, A., Thorgeirsdottir, H. and Steingrimsdottir, L., 2006. Relationship between high consumption of marine fatty acids in early pregnancy and hypertensive disorders in pregnancy. *BJOG* 113:301-309
- Ozçelik, S., Polat, H. H., Akyol, M., Yalçın, A. N., Ozçelik, D. and Marufihah, M., 2000. Kangal hot spring with fish and psoriasis treatment. *J. Dermatol.*, 27(6): 386-90.
- Pedrono, F., Martin, B., Leduc, C., Le Lan, J., Saiag, B., Legrand, P., et al, 2004. Natural alkylglycerols restrain growth and metastasis of grafted tumors in mice. *Nutr Cancer*; 48(1): 64-9.
- Peet, M., Brind, J., Ramchand, C. N., Shah S., Vankar, G. K., 2001. Two double-blind placebo-controlled pilot studies of eicosapentaenoic acid in the treatment of

schizophrenia. *Schizophrenia Research*, 49 (3): 243–51

- Peterlik, M. and Cross, H. S., 2005. Vitamin D and calcium deficits predispose for multiple chronic diseases. *Eur J Clin Invest*, 35: 290-304. DOI: 10.1111/j.1365-2362.2005.01487
- Phillips, C. R., Brasington Jr., R. D., 2010. Osteoarthritis treatment update: Are NSAIDs still in the picture? *Journal of Musculoskeletal Medicine*, 27 (2) www.musculoskeletalnetwork.com
- Prabhakar, A. K. and Roy, S. P., 2009. Ethno-medicinal Uses of Some Shell Fishes by People of Kosi River Basin of North-Bihar, India. *Ethno-Med*, 3 (1): 1-4.
- Rajakumar, K., 2003. Vitamin D, Cod-Liver Oil, Sunlight, and Rickets: A Historical Perspective. *Pediatrics*, 112(2):132-135.
- Rees, A. M., Austin, M. P., Parker, G., 2005. Role of omega-3 fatty acids as a treatment for depression in the perinatal period. *The Australian and New Zealand Journal of Psychiatry*, 39 (4): 274–80
- Reginster, J. Y. 2005. The high prevalence of inadequate serum vitamin D levels and implications for bone health.. *Curr Med Res Opin*, 21: 579-586. DOI: 10.1185/030079905X41435
- Roos, N., Leth, T., Jakobsen, J., Thilsted, S. H., 2002. High vitamin A content in some small indigenous fish species in Bangladesh: Perspectives for food-based strategies to reduce vitamin A deficiency. *Int J Food Sci Nutr*, 53: 425–37.
- Roos, N., Thorseng, H., Chamnan, C., Larsen, L., Gondolf, U. H., Thilsted, S. H., 2007. Iron content in common Cambodian fish species: perspectives for intake in poor, rural households. *Food Chemistry*, 104 (3): 1226-1235
- Sabot, A., 1988. Environmental physiological studies of Haruan in Sabah. BSc Thesis, Universiti Kebangsaan Malaysia.
- Salte, R., Norberg, K. and Odegaard, O. R., 1996. Evidence of a protein c-like anticoagulant system in bony fishes. *Thromb. Res.*, 83: 389-397.
- Sidhu, G.S., 1993. Lipids in Food and Their Role in Human Health: Assessment of Some Nutritional and Technological Aspects of Fats and Cholesterol Modified Foods. Division of Food Science and Technology, CISRO, North Ryde, Australia. pp. 1–139.

- Sidhu, K. S., 2003. Health benefits and potential risks related to consumption of fish or fish oil. *Regulatory Toxicology and Pharmacology*, 38: 336-344
- Sills Jr, A. K., Williams, J. I., Tyler, B. M., Epstein, D. S., Sipos, E. P., Davis, J. D., McLane, M. P., Pitchford, S., Cheshire, K., Gannon, F. H., Kinney, W. A., Chao, T. L., Donowitz, M., Laterra, J., Zasloff, M. and Brem, H., 1998. Squalamine inhibits angiogenesis and solid tumor growth in vivo and perturbs embryonic vasculature. *Cancer Res*, 58(13): 2784-92.
- Singer, S.J. and Nicolson, G. L., 1972. The fluid mosaic model of the structure of cell membranes. *Science*, 175:720-731.
- Sivell, L. M., Bull, N. L., Buss, D. H., Wiggins, R. A., Scuffam, D., and Jackson, P. A., 1984. Vitamin A activity in foods of animal origin. *Journal of the Science of Food and Agriculture*, 35, 931-939.
- Skeie, G., Braaten, T., Hjarta, A., Brustad, M. and Lund, E., 2009. Cod liver oil, other dietary supplements and survival among cancer patients with solid tumors. *Int J Cancer* 125: 1155-60.
- Stancher, B., and Zonta, F., 1984. Quantitative high-performance liquid chromatographic method for determining the isomer distribution of retinol (vitamin A1) and 3-dehydroretinol (vitamin A2) in fish oils. *Journal of Chromatography*, 312, 423-434.
- Stene, L. C., Ulriksen, J., Magnus P, et al., 2000. Use of cod liver oil during pregnancy as associated with lower risk of Type I diabetes in the offspring. *Diabetologia* 43:1093-1098. DOI: 10.1007/s001250051499
- Song, C., Zhao, S., Oct 2007. Omega-3 fatty acid eicosapentaenoic acid. A new treatment for psychiatric and neurodegenerative diseases: a review of clinical investigations. *Expert Opin Investig Drugs*, 16 (10): 1627-38
- St. John, L. C. and Bell, F. P., 1991. Arterial lipid biochemistry in the spontaneously hyperlipidemic Zucker rat and its similarity to early atherogenesis. *Atherosclerosis*, 86:139-144. (medline).
- Stock, J. L., Shinjo, K., Burkhardt, B. et al. The prostaglandin E2 EP1 receptor mediates pain perception and regulates blood pressure. *J. Clin. Invest.* 2001; 107: 325-31.

- Stryer, L., 1995. Biochemistry. 5th Ed, W. H. Freeman & CO., New York. 1089p. ISBN: Q71671843-x.
- Swank, R. L., and Duggan, B. B., 1987. The Multiple Sclerosis Diet Book: A Low-Fat Diet for the Treatment of MS. New York: Doubleday
- Terkelsen, L. H., et al. 2000. Topical application of cod liver oil ointment accelerates wound healing: an experimental study in wounds in the ears of hairless mice. J Plast. Reconstr. Surg., 34 (1): 15–20
- von Schacky, C., 2000. n-3 Fatty acids and the prevention of coronary atherosclerosis". Am J Clin Nutr, 71 (1 Suppl): 224S–7S
- Westaby S. Wound Healing, 2nd edn. Macmillan Press, New York. 1985.
- Yao, H. T., Chang, Y. W., Lan, S. J., Chen, C. T., Hsu, J. T., Yeh, T. K., 2006. The inhibitory effect of polyunsaturated fatty acids on human CYP enzymes. Life Sci., 79 (26): 2432–40.
- Zhang, X. and beymen, A. C., 1993. influence of dietary fish proteins on plasma and liver cholesterol concentrations in rats. Br. J. Nutr., 69:767-777. (medline).
- www.adam.com
- www.ayurvedic-medicines.org
- www.fishbase.org
- www.mybangalore.com
- www.pediatriconcall.com
- www.scielo.br/img/revistas/jbchs/v19n2/a22fig02.gif
- www.wikipedia.org
- www.3dchem.com
- <http://hubpages.com/hub/fish-spa-phenomena>

Paul, B. N., Co-PI, Outreach Activity - 3 CIFA (ICAR) Bhubaneswar (personal communication)

Publications from Outreach Activity (#3):

Nutrient Profiling and Evaluation of Fish as a Dietary Component

Contribution No.	Publication details
1.	Fish as Health-Food (Folder), CIFRI, Barrackpore, 2010
2.	Nutritional Significance of Small Indigenous Fishes in Human Health. B. P. Mohanty, B. K. Behera and A. P. Sharma. Bulletin No. 162, CIFRI, Barrackpore. p.73. 2010. ISSN 0970-616X.
3.	Nutrient Profiling of Fish. T. V. Sankar, S. Mathew, R. Anandan, K. K. Asha and B. P. Mohanty. CIFT, Cochin. p.61. 2010. ISBN 978-81-905878-3-9.
4.	<i>Tenualosa Ilisha</i> : A Rich Source of ω -3 PUFAs. B. P. Mohanty, Soma Das, U. Bhaumik and A. P. Sharma. Bulletin No. 171. CIFRI, Barrackpore. 2011. ISSN 0970-616X.

