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Spirulina in combating Protein Energy Malnutrition (PEM) and Protein Energy Wasting (PEW) - A review

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Abstract

Spirulina, is a simple extract of blue-green algae, which is now used worldwide as a food product and as a dietary supplement. It contains, essential amino acids, lipids, vitamins, minerals and anti-oxidants and can be considered as a wholesome food supplement. *Spirulina* contains, approximately, 65% to 71% protein by dry weight and is claimed to be non toxic nutritious food with exceptional properties. A large amount of scientific literature available about *Spirulina* and its usage in treatment of child malnutrition, nutrition rehabilitation of HIV-infected, cancer patients, hepato-protective effects etc. However, there is no specific review available which gives more emphasis on the protein and energy content and its effects. In the present work, we reviewed several papers and reports and paid more attention on protein content, which is the major constituent of *Spirulina* and its effect on various disease conditions and possibility of using *Spirulina* in combating against Protein Energy Malnutrition (PEM) and Protein Energy Wasting (PEW). This work is of certain significance for nutritionists, doctors and public health workers involved in combating malnutrition. The risks involved and optimal intake level for humans and animals are discussed in detail.

Keywords: Protein Energy Malnutrition (PEM):Protein Energy Wasting (PEW):*Spirulina*¸ Toxicity.

Introduction

It is not accurately known when people started using microalgae as food source or food supplement but the first recorded evidence is from Bernal Diaz del Castillo, a member of Heman Cortez's (Spanish conquistador) troops, reported in 1520, in Tenochtitlan (today Mexico City):that *S. maxima* was harvested from the lake Texcoco, dried and sold for human consumption. Native Mexicans called it as Tecuitlalt, meaning "excrements of stones". The topic of the Tecuitlalt, which was earlier discovered in 1520, was not mentioned again until 1940, the French phycologist Pierre Dangeard mentioned about a cake called "*dihe*", consumed by Kanembu tribe, African Lake Chad, Kanem (Chad, Africa). Dangeard studied the "*dihe*" samples and found that it is like a puree of spring form blue algae (Sánchez et al. 2003).

The first unialgal culture achieved by Beijerinck in 1890 and cultivation only started in 1919 by Otto Warburg's (Richmond 2008). Otto Warburg is well known for his work on *Chlorella* and his aim is to understand and use them as a model for physiology and photosynthesis research and not as a potential food source. He used microalgae, Chlorella, because of its fast growing, non-motile and simple life cycle properties. Warburg's study was important because he was able to understand the number of quantas required to possess photosynthesis and he also proposed the concept of light utilization efficiency and conversion of light to chemical energy (Richmond 2008).

During 1964 and 1965, the botanist Jean Leonard, during his Belgian Trans-Sabaran Expedition, confirmed that *dihe* is made up of *Spirulina* and thus chemical analysis was started on *Spirulina* (Sanchez, 2003). During that time, Léonard received a request from Sosa-Texcoco Ltd, Mexico to study a bloom of algae in their sodium hydroxide production facility. As a result, the first systematic and detailed study of the growth requirements and physiology of *Spirulina* was performed. This study, which was a part of Ph.D. thesis by Zarrouk (1966):was the basis for establishing the first large-scale production plant of *Spirulina* (Habib et al. 2008).

A single cell protein, which is nothing but a protein derived from culture of single celled organisms, has gained popularity as alternative food source during World War 1 and World War II. After the formation of United Nations in the post war period, hunger and malnutrition problems were highlighted by the Food and Agriculture Organization of United Nations and has introduced the concept of protein gap and reported that 25% of

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Table 1: Nutrition profile of spirulina powder from various companies including Earthrise Nutrionals, USA (Gershwin and Belay 2007):DIC LIFETEC Co. Ltd. Japan (Hainan-DIC Microalgae Co. Ltd China) (http://www.dlt-spl.co.jp/business/en/spirulina/elements.html):Parry Nutraceuticals (A Division of E.I.D.Parry (India) Ltd.):India (www.parrynutraceuticals.com/PDF/Parry_Organic_Spirulina_powder.pdf): Nutrex Hawaii, USA (Moorhead et al. 2011) and Foundation Antenna Technologies, Geneva, Switzerland (Falquet 1997)

Composition Per 100 g	**Companies**				
	Earthrise Nutrionals, USA	**DIC LIFETEC Co. Ltd. Japan (Hainan-DIC Microalgae Co. Ltd. China)**	**Parry Nutraceuticals, India**	**Nutrex Hawaii, USA**	**Foundation Antenna Technologies, Switzerland**
1. Macronutrients					
Calories (kcal)	373	386	410	333	
Total fat	5.6 g	8.2 g	5 to 6 g	5 g	4 - 7 g
Myristic (C 14:0)	10 mg	16.4 mg	10-30 mg	40 mg	
Palmitic (C 16:0)	2440 mg	3632 mg	2000 - 2500 mg	6100 mg	1032 - 1806 mg
Palmitoleic (C 16:1)	330 mg	237.8 mg		594 mg	152 - 266 mg
Heptadecanoic (C17:0)	20 mg	24.6 mg			
Stearic (C18:0)	80 mg	90.2 mg	10 - 50 mg	250 mg	68 - 119 mg
Oleic (C18:1)	120 mg	246 mg	100 - 200 mg	51 mg	664 - 1162 mg
Linoleic (C18:2)	970 mg	2000 mg	750 -1200 mg	3300 mg	480 - 840 mg
Gamma-Linolenic (C18:3)	1350 mg	1238 mg	1000 - 1500 mg	3200 mg	1604 - 2807 mg
Others (C20)	140 mg	715 mg			
Total carbohydrate	17.8 g	12.7 g	15 to 25 g	16 g	15 - 25 g
Dietary fiber	7.7 g	8.3 g		7 g	4 - 7 g
Sugars	1.3 g	4.4		9 g	
Lactose	<0.1 g	-			
Protein	63 g	69.4 g	56 to 69 g	67 g	55 - 70 g
Ash	< 9 %	5.6 %	6 to 9 g	8 - 13 g	7 - 13 g
Moisture	< 7 %	< 4.1 %	2.5 to 4.5 %	3 - 6 g	3 - 7 g
Essential amino acids					
Histidine	1000 mg	1170 mg	500 - 1500 mg	1500 mg	1000 mg
Isoleucine	3500 mg	3480 mg	3000 - 4000 mg	3260 mg	3500 mg
Leucine	5380 mg	5610 mg	3000 - 5000 mg	4890 mg	5400 mg
Lysine	2960 mg	3080 mg	3000 - 6000 mg	2620 mg	2900 mg
Methionine	1170 mg	1590 mg	1000 - 6000 mg	1330 mg	1400 mg
Phenylalanine	2750 mg	2870 mg	2500 - 3500 mg	2610 mg	2800 mg
Threonine	2860 mg	3300 mg	1500 - 3000 mg	2810 mg	3200 mg
Tryptophan	1090 mg	1100 mg	1000 - 2000 mg	8500 mg	900 mg
Valine	3940 mg	3900 mg	1000 - 3000 mg	3740 mg	4000 mg
Nonessential amino acids					
Alanine	4590 mg	4910 mg	4000 - 5000 mg	4660 mg	4700 mg
Arginine	4310 mg	4190 mg	3000 - 5000 mg	4760 mg	4300 mg
Aspartic acid	5990 mg	6180 mg	1500 - 3000 mg	7280 mg	6100 mg
Cystine	590 mg	700 mg	500 - 750 mg	5600 mg	600 mg
Glutamic acid	9130 mg	9290 mg	6000 - 9000 mg	8440 mg	9100 mg
Glycine	3130 mg	3210 mg	2000 - 4000 mg	3190 mg	3200 mg
Proline	2380 mg	2400 mg	2000 - 3000 mg	2470 mg	2700 mg
Serine	2760 mg	3210 mg	3000 - 4500 mg	2650 mg	3200 mg
Tyrosine	2500 mg	2740 mg	1000 - 2000 mg	2380 mg	3000 mg
2. Vitamins					
Vitamin A	352000 IU	18000mcg		11250 IU	
Vitamin K	1090 mcg	2220 mcg	0.90 - 1.05 mg	2500 mcg	2.24 mg
Vitamin C	0 mg	0 mg	-	0 mg	traces
Vitamin E	10 IU	10.6 mg		9500 mcg	10 mg
Vitamin B1 (Thiamine HCl)	0.5 mg	4.82 mg	0.15 - 0.30 mg	117 mcg	3.5 mg
Vitamin B2 (Riboflavin)	4.53 mg	3.93 mg	4.0 - 7.0 mg	4667 mcg	4 mg
Vitamin B3 (Niacin)	14.9 mg	39.3 mg	10.0 - 25.0 mg	13330 mcg	14 mg
Vitamin B6 (Pyridox. HCl)	0.96 mg	0.91 mg	0.5 - 1.5 mg	1000 mcg	0.8 mg
Vitamin B12	162 mcg	0.24 mg	0.10 - 0.30 mg	300 mcg	0.32 mg
Biotin	5 mcg	32.3 mcg		17 mcg	0.005 mg
Folic acid	10 mcg	73 mcg	0.05 - 0.30 mg	206 mcg	0.01 mg
Phantothenic acid	100 mcg	1.23 mg		150 mcg	0.1 mg
Inositol	64 mg	103 mg	70 - 90 mg	57 mg	64 mg
3. Minerals					
Calcium	468 mg	70.5 mg	60 - 110 mg	334 mg	1000 mg
Iron	87.4 mg	83.3 mg	25 - 100 mg	217 mg	180 mg
Phosphorus	961 mg	921 mg	700 - 1000 mg	1100 mg	800 mg
Iodine	142 mcg		0.2 - 0.4 mg	500 mcg	
Magnesium	319 mg	278 mg	200 - 300 mg	500 mg	400 mg
Zinc	1.45 mg	1.04 mg	1.0 - 3.0 mg	3 mg	30 mg
Selenium	25.5 mcg	-	0.003 - 0.010 mg	0.03 mg	0.01 - 0.04 ppm

Copper	0.47 mg	0.26 mg	0.2 - 0.4 mg	0.67 mg	1.2 mg
Manganese	3.26 mg	3.81 mg	1.0 - 3.0 mg	13.3 mg	5 mg
Boron	1000 mcg			0.733 mg	
Chromium	<400 mcg	0.39 mg	0.1 - 0.3 mg	1.34mg	0.28 mg
Molybdenum	1000 mcg			< 400 mcg	
Potassium	1660 mg	1520 mg	1000 - 1500 mg	2000 mg	1400 mg
Sodium	641 mg	210 mg	700 - 1000 mg	1000 mg	900 mg
4. Phytonutrients					
Phycocyanin	14000 mg	6550 mg	14000 - 16000 mg	8000 mg	15000 mg
Chlorophyll	1000 mg	1220 mg	1100 -1500 mg	1000 mg	1100 mg
Superoxide dismutase (SOD)	531000 IU	1000unit/g		3600 units	
Gamma linolenic acid (GLA)	1080 mg			1067 mg	1300 mg
Total carotenoids	504 mg		360 - 500 mg	500 mg	370 mg
β-carotene	211 mg	216 mg	140 - 200 mg	227 mg	140 mg
Other Carotenes	30 mg				
Zeaxanthin	101 mg	114 mg	125 - 200 mg	300 mg	
Xanthophylls	170 mg		180 - 300 mg		
Myxoxanthophyll	70 mg				
Zeaxanthin	60 mg				
Cryptoxanthin	10 mg				
Echinenone	10 mg				
Other Xanthophylls	20 mg				
Sulfolipids	100 mg				
Glycolipids	2000 mg				
5. Other Minerals					
Arsenic	< 1 ppm	-	< 0.50 ppm	< 0.5 ppm	0.06 - 2 ppm
Cadmium	< 0.5 ppm		< 0.20 ppm	<0.2 ppm	0.01 - 0.1 ppm
Mercury	< 0.05 ppm		< 0.05 ppm	<0.025 ppm	0.01 - 0.2 ppm
Lead	< 2.5 ppm	-	< 0.2 ppm	<0.2 ppm	0.6 - 5.1 ppm
Germanium	60 mcg				
Silicon		743 ppm			
Sulfur		0.69 g			
Cobalt		0.30 ppm			
Fluorene					112-630 ppm

world's population has a deficiency of protein intake in their diet. Many research projects on yeast, chlorella, *Spirulina*, some bacteria and moulds for large scale production of "single cell proteins" were launched. In 1950, the United States and Japan began the experimental cultivations of this microorganism to investigate its chemical composition and industrial applications. Studies were accelerated after the release of the book, *Algal Culture from Laboratory to Pilot Plant* (Burlew, 1953):which triggered research work around the globe (Richmond, 2008). Japan was the first country to produce *Chlorella* based diet food (Sanchez, 2003). *Spirulina*, in 1967 was established as a "wonderful food source" by the International Association of Applied Microbiology.

The first pilot plant which produced 150 tonnes of dry *Spirulina* biomass per year started production in 1973; its production capacity was thereafter raised to 300 tonnes of medium-grade product per year from 12.0 hectares of natural ponds by Sosa-Texcoco Ltd, Mexico. The annual value of *Spirulina* production represented a third of the company's income from the manufacture of powdered soda from the lake deposits. In 1995, Sosa-Texcoco ceased production of *Spirulina*. The only remnant today, Lake Texcoco, still has a living algae *Spirulina* population.

From 1970, the nutritional and medicinal studies on *Spirulina* have been extensively studied along with its applications in water treatment. According to the national report received by Food and Agriculture Organization (FAO):United Nation, the production of algae culture was greater than 68000 tons in 2008 and major contribution from China and Chile. China started to produce *Spirulina* through factories in 1990 and there were more than 80 factories by 1997 (Habib et al. 2008). *Spirulina* is produced in at least 30 countries (Australia, Bangladesh, Benin, Brazil, Burkina Faso, Chad, Chile, China, Costa Rica, Côte d'Ivoire, Cuba, Ecuador, France, India, Israel, Italy, Japan, Madagascar, Martinique, Mexico, Myanmar, Philippines, Peru, Portugal, Spain, Thailand, Togo, United States of America and Vietnam) (Habib et al. 2008).

Benefits of Spirulina

Spirulina does not need fertile land and has an advantage of having rapid growth within 20 days, takes less energy input and less water per kilo than soya, corn proteins and is environmental friendly as there is possibility of recycling water after harvesting and produce more oxygen than trees per acre by consuming carbon dioxide (H.E. Remigio M. Maradona 2008).

Very few studies were found to describe the actual respiration rate of *Spirulina sp.* and in the below analysis, we could able to collect some information to prove *Spirulina* produces more oxygen than trees per acre. The notations used to measure trees size is "dbh". *dbh* refers to the tree diameter measured at 4.5 feet above the ground and based on a study conducted on trees and their oxygen release rates by David et al. (2007):trees with 1 - 3 inch - dbh produce 2.9 kg O_2/per year; 9-12 inch dbh: 22.6 kg O_2/year; 18-21 inch dbh: 45.6 kg O_2/year; 27-30 inch dbh; 91.1 kg O_2/year and greater than 30 inch dbh 110.3 kg/O_2 year. With reference to the data reported by Dinesh et al. (2010):after calculations, 42 ft^2 area with 1000 L can produce approx. 20.717 kg oxygen per year with cell concentration varying from $1 * 10^5$ to $5 * 10^5$ cells per ml and 200 ft^2 area with 4000 L, can produce approx. 100 kg oxygen per year, if cell concentration per ml increases, still increase in the rate of oxygen release can be achieved. With reference to the respiration rate reported by Rym (2012):115.89 kg O_2 per year and as per Ohira et al. (1998):5.676 kg O_2 per year per 150 grams dry weight *Spirulina*, can be

produced. It is quite evident based on the above scientific data that *Spirulina* produce more oxygen than trees per acre.

Spirulina and its nutritional composition

The common name, *Spirulina*, refers to the dried biomass of *Arthrospira platensis*, (Gershwin and Belay 2007):which belongs to the oxygenic photosynthetic bacteria that cover the groups *Cyanobacteria* and *Prochlorales*. These photosynthetic organisms, *Cyanobacteria*, were first considered as alge until 1962 and for the first time, these blue green algae were added to prokaryote kingdom and proposed to call these microorganisms as *Cyanobacteria* (Stanier and Van Neil 1962):where algae is considered to be a very large and diverse group of eukaryotic organisms. This designation was accepted and published in 1974 by the Bergey's Manual of Determinative Bacteriology, which is worldwide considered as a bible for biologists (Sánchez et al. 2003). Scientifically, there is a quite distinction between *Spirulina* and *Arthrospira* genus. Stizenberger, in 1852 gave the name *Arthrospira* based on the septa presence, helical form and multicellular structure and Gomont in 1892, confirmed aseptate form of the *Spirulina* genus. Geitler in 1932, reunified both members designating them as *Spirulina* without considering the septum. The worldwide research on microalgae was carried out in the name of *Spirulina*, but the original species exploited as food with excellent health properties belongs to genus *Arthrospira*. This common difference between scientists and customers is difficult to change (Sánchez et al. 2003). These *Arthrospira* genus, constitute a helical trichomes of varying size and with various degree of coiling including tightly coiled morphology to even straight uncoiled form. The filaments are solitary and reproduce by binary fission and the cells of the trichomes vary from 2 µm to 12 µm and can sometime reach up to 16 µm. Species of the genus *Arthrospira* have been isolated from alkaline brackish and saline waters in tropical and subtropical regions. Among the various species included in the genus *Arthrospira, A. platensis* is the most widely distributed and is mainly found in Africa but also in Asia. *Arthrospira maxima* is believed to be found in California and Mexico (Gershwin 2007).

Since, 1970, *Spirulina* was analyzed physically and chemically and numerous properties were evaluated. Based on the nutrition profile listing of various multi-national global players (Table 1), *Spirulina* contains approximately 65 to 70% proteins, 15 to 25% carbohydrates, 4 to 9 % fats and remaining vitamins, minerals, pigments and very few toxic contaminations. In this article, the main focus is review of all the works carried out on protein content for combating against Protein Energy Malnutrition (PEM) and Protein Energy Wasting (PEW) around the globe is discussed in detail.

Comparision of protein content in Spirulina with other foods

Spirulina contains more natural proteins when compared with other natural foods (Table 2). The true protein digestibility and the biological activity of *Spirulina* protein calculated by Narasimha et al. (1982) is 75.5 and 68 respectively. The Recommended Dietary Allowance (RDA) for protein consumption is 0.8g/kg body weight and for athletes, RDA ranges from 1.2 to 1.4 g/kg/day (Otten et al. 2006). The advantage of *Spirulina* protein can withstand without denaturating up to 67^0C (Sánchez et al. 2003).

Table 2: Comparision of protein content of other foods with *Spirulina* (Henrikson 1994)

Food Type	**Crude Protein (%)**
Spirulina powder	65 to 70
Whole Dried egg	47
Skimmed powdered milk	37
Whole soybean flour	36
Peanuts	26
Chicken	24
Fish	22
Beef meat	22
Cereal flours	<12
Vegetables	< 5

Risk assessment of Spirulina

Extensive care should be taken while consuming or prescribing *Spirulina* as a protein source. *Spirulina* has more vitamin A, in terms of beta carotenes, when compared with any natural foods and care should be taken while administrating *Spirulina* that it should not exceed the Recommended Dietary Allowance (RDA) of 400 mcg to 900 mcg for normal adult male or female, where as lactation stage, it can go up to 1300 mcg per day. Daily intake of Vitamin A >25,000 IU for >6 years an >100,000 IU for >6 months are considered toxic (Penniston and Tanumihardjo 2006; Fairfield and Fletcher 2002). 100 grams of *Spirulina*, contains greater than 353000 IU (Gershwin and Belay 2007) and based on the recommended dietary allowance of Vitamin A, it is recommended to consume only 7 grams of *Spirulina* per day which contains 25000 IU and children less than 6 years to 6 months can take 25 grams of *Spirulina* per day.

Excessive consumption of vitamin K, up to 0.2 g/kg body weight does not show any toxic effect on rats (Molitor and Robinson 1940) and recommended RDA for vitamin K is >19 years, 90 mcg per day and >6 months to 12 months, 2.5 mcg per day and it varies between 30 mcg to 60 mcg for 1 to 19 years. With reference to these values, <1 year to 6 months kids, it is recommended to give 4 grams of *Spirulina* per day for adults which contributes about 90 mcg vitamin K and < 2 grams for 1 year to 6 months kids. Based on the composition, other vitamins are within RDA limit per 10 grams of *Spirulina* powder. After observing, RDA for adults for minerals, calcium (1300 mg):iron (10 mg):iodine (150mcg): phosphorus (700mg):Magnesium (420 mg):Zinc (11 mg):Selenium (0.055 mg):Copper (0.9 mg):Manganese (2.3 mg):Boron (1000 to 10000 mcg):Germanium (1.5 mg) (Schauss 1991):Potassium (4700 mg) and Sodium (1500 mg):most of them are within the range for consumption of 100 grams of *Spirulina*. Based on RDA values for chromium (35 mcg) and molybdenum (45 mcg) are safe for 10 grams of *Spirulina* per day. Coming to the pigments, phycocyanin at 0.25 to 5.0 g/kg body weight have not shown any toxic effect in rats (Naidu et al. 1999) and GLA can be consumed up to 1.6 g per day. RDA recommends 30 to 45 grams of carbohydrates per meal and maximum of 195 grams per day and maximum of 40 % of calories coming from carbohydrates and fats about 20 to 60 g per day for an average adult (Dietary Reference Intakes, 2004).

Overall, based on the complete nutritional assessment, normal healthy adult can take < 4 grams of *Spirulina* per day. But, it is found that there is no toxic effect on rats, when consumed greater than 0.8 g/kg of pure *Spirulina* powder (Krishnakumari et al. 1981). Based on the nutritional facts and composition and RDA values, it is recommended to take < 4 grams of *Spirulina* per day for healthy adult due to the presence of excess Vitamin A and not

more than 10 grams as it exceeds the RDA values of heavy metals (Table 3).

We believe that the above Table 3 will give basic idea about *Spirulina* and risks involved in consumption and

Table 3: Risk assessment of spirulina based on US-RDA values for healthy adults (19 to 50) years and the black color indicates excess than RDA

Nutrients	US - RDA (RDI, 2004)	Consumption pattern (per day)						
		4 gram	10 grams	15 grams	25 grams	100 grams	200 grams	500 grams
Total fat	20-35 g	0.224 g	0.56 g	0.84 g	1.4 g	5.6 g	11.2 g	28 g
Linoleic (C18:2)	10-17 g	0.0388 g	0.097 g	0.1455 g	0.2425 g	0.97 g	1.94 g	4.85 g
Total carbohydrate	130 g	0.712 g	1.78 g	2.67 g	4.45 g	17.8 g	35.6 g	89 g
Fibre	38 g	0.308 g	0.77 g	1.155 g	1.925 g	7.7 g	15.4 g	**38.5 g**
Protein	46-56 g	2.52 g	6.3 g	9.45 g	15.75 g	**63 g**	**126 g**	**315 g**
Vitamin A (Upper Limit: 7500 mcg)	700-900 mcg	4224 mcg	**10560 mcg**	**15840 mcg**	**26400 mcg**	**105600 mcg**	**211200 mcg**	**528000 mcg**
Vitamin K (Upper Limit: No adverse effect)	90 -120 mcg	43.6 mcg	109 mcg	**163.5 mcg**	**272.5 mcg**	**1090 mcg**	**2180 mcg**	**5450 mcg**
Vitamin C	75-90 mg	0 mg	0 mg	0 mg	0 mg	0 mg	0 mg	0 mg
Vitamin E	15 mg	0.36 mg	0.9 mg	1.35 mg	2.25 mg	9 mg	**18 mg**	**45 mg**
Vitamin B1	1.1 - 1.2 mg	0.02 mg	0.05 mg	0.075 mg	0.125 mg	0.5 mg	1 mg	**2.5 mg**
Vitamin B2	1.1-1.3 mg	0.1812 mg	0.453 mg	0.6795 mg	1.1325 mg	**4.53 mg**	**9.06 mg**	**22.65 mg**
Vitamin B3	14-16 mg	0.596 mg	1.49 mg	2.235 mg	3.725 mg	14.9 mg	**29.8 mg**	**74.5 mg**
Vitamin B6	1.3-1.7 mg	0.0384 mg	0.096 mg	0.144 mg	0.24 mg	0.96 mg	**1.92 mg**	**4.8 mg**
Vitamin B12 (Upper Limit: No adverse effect)	2.4 -2.6 mcg	6.48 mcg	**16.2 mcg**	**24.3 mcg**	**40.5 mcg**	**162 mcg**	**324 mcg**	**810 mcg**
Biotin	30 mcg	0.2 mcg	0.5 mcg	0.75 mcg	1.25 mcg	5 mcg	10 mcg	25 mcg
Folic acid	400 mcg	0.4 mcg	1 mcg	1.5 mcg	2.5 mcg	10 mcg	20 mcg	50 mcg
Phantothenic acid	5 mg	0.004 mg	0.01 mg	0.015 mg	0.025 mg	0.1 mg	0.2 mg	0.5 mg
Inositol	Not available	2.56 mg	6.4 mg	9.6 mg	16 mg	64 mg	128 mg	320 mg
Calcium	1000-1200 mg	18.72 mg	46.8 mg	70.2 mg	117 mg	468 mg	936 mg	**2340 mg**
Iron	8-18 mg	3.496 mg	8.74 mg	13.11 mg	**21.85 mg**	**87.4 mg**	**174.8 mg**	437 mg
Phosphorus	700 mg	38.44 mg	96.1 mg	144.15 mg	240.25 mg	**961 mg**	**1922 mg**	**4805 mg**
Iodine	150 mcg	5.68 mcg	14.2 mcg	21.3 mcg	35.5 mcg	142 mcg	**284 mcg**	**710 mcg**
Magnesium	310-420 mg	12.76 mg	31.9 mg	47.85 mg	79.75 mg	319 mg	**638 mg**	**1595 mg**
Zinc	8-11 mg	0.058 mg	0.145 mg	0.2175 mg	0.3625 mg	1.45 mg	2.9 mg	7.25 mg
Selenium	55 mcg (Upper Limit - 400 mcg)	1.02 mcg	2.55 mcg	3.825 mcg	6.375 mcg	25.5 mcg	51 mcg	127.5 mcg
Copper	900 mcg	18.8 mcg	47 mcg	70.5 mcg	117.5 mcg	470 mcg	**940 mcg**	**2350 mcg**
Manganese	1.8-2.3 mg	0.1304 mg	0.326 mg	0.489 mg	0.815 mg	**3.26 mg**	**6.52 mg**	**16.3 mg**
Boron	Not available	40 mcg	100 mcg	150 mcg	250 mcg	1000 mcg	2000 mcg	5000 mcg
Chromium	20-35 mcg	16 mcg	**40 mcg**	**60 mcg**	**100 mcg**	**400 mcg**	**800 mcg**	**2000 mcg**
Molybdenum	45 mcg	16 mcg	40 mcg	**60 mcg**	**100 mcg**	**400 mcg**	**800 mcg**	**2000 mcg**
Potassium	4.7 g	0.0664 g	0.166 g	0.249 g	0.415 g	1.66 g	3.32 g	**8.3 g**
Sodium	1.2-1.5 g	0.02564 g	0.0641 g	0.09615 g	0.16025 g	0.641 g	1.282 g	**3.205 g**
Germanium	1.5 mg /day (Schauss 1991)	0.0024 mg	0.006 mg	0.009 mg	0.015 mg	0.06 mg	0.12 mg	0.3 mg
Cobalt	25-600 mcg (Mucklow et al. 1990)	NA	NA	NA	NA	NA	NA	NA
Fluorene	3 - 4 mg	NA	NA	NA	NA	NA	NA	NA

The black color in the Table 3 shows that the particular nutrient exceeds the RDA value. It was not colored black at 4 grams at Vitamin A and Vitamin B, even though they are exceeding the RDA values as the Vitamin A, upper limit is 7500 mcg and Vitamin B, there is no upper limit (Dietary Reference Intakes, 2004). Chromium and vitamin A are exceeding RDA values at 10 grams of *Spirulina* and at 15 grams consumption, molybdenum, vitamin K is exceeding and at 25 grams, Iron was exceeding RDA value and at 100 grams, protein, manganese, phosphorous, vitamin B2 are exceeding and at 200 grams, vitamin E, B3, B6, copper, iodine and magnesium are exceeding and at 500 grams, calcium, vitamin B1, potassium and sodium are exceeding RDA and it is strongly recommended to consume less than 4 grams per day for an average healthy adult to avoid any toxic effect based on the above scientific data. Care should be taken while consuming and data related to cobalt and fluorine in water used for *Spirulina* production was not reported by many companies and these contents will also affect the quality of *Spirulina* along with arsenic, lead, cadmium, mercury and silicon concentrations. industries should take care while preparing formulations or food fortification products using *Spirulina*.

Protein Energy Malnutrition (PEM)

The World Health Organization (WHO) defines malnutrition as ‘‘the cellular imbalance between the supply of nutrients and energy and the body’s demand for them to ensure growth, maintenance, and specific functions” and Protein Energy Malnutrition (PEM) refers to a form of malnutrition, where there is inadequate calorie or protein intake. Malnutrition is present in both developed as well as under developing nations. Due to lack of adequate food supply caused by socio-economical, political and environmental factors, malnutrition was prevalent in developing countries and in developed countries 6 to 51% of hospitalized children were found to be malnourished (Grover and Ee 2009).

Protein Energy Wasting (PEW)

Wasting refers to the process by which a debilitating diseases cause's muscle and fat tissue to waste "away" and it is also referred to acute malnutrition. Protein Energy Wasting (PEW): term was coined by the "International Society of Renal Nutrition and Metabolism (ISRNM)" to address the syndromes of muscle wasting, malnutrition and inflammation during Chronic Kidney Diseases (CKD) orAcute Kidney Injury (AKI) and it also means loss of body protein mass and fuel reserves (Fouque et al. 2008).

Table 4: Production of *Spirulina* and its social acceptance, cost effectiveness studies for hunger alleviation in developing countries

Country	Summary of Results	Subject	Reference
Chile	Mass cultivation, process optimization and economic analysis for growth of spirulina in 30 ponds (1120 m^2) was carried out at Santaigo production facility, Chile	Production	Valderrama et al. 1987
India	Spirulina (Arthrospira) fusiformis was grown in small mud pots to provide food supplements for a family has been developed and acceptability of the method as a family enterprise was evaluated.	Production	Jeeji and Seshadri 1988
USA	Earthrise Farms, USA tried popularizing spirulina by preparing granola bar and various kinds of pasta	Product development	Henrikson 1989
Vietnam	*Spirulina platensis* culture was bought from France to Institute of Biology, Hanoi, Vietnam. In 1977, a pilot pond of 12 m^2 was started in Thuanha, Vietnam and in 1980, it is expanded to 3000 m^2 and all process parameters were optimized to suite Vietnam atmosphere.	Production	Kim 1990
Bangladesh	*Spiruilna* cultivation in pilot plant was started by Applied Botany Section, Biological Research Division, Bangladesh Council of Scientific and Industrial Research Laboratories (BCSIR):Dhaka. A technology was developed to suite Bangladesh environment.	Production	(Nahar and Begum 1991)
France	The use of *Spirulina* as a possible feed for aqua culture was demonstrated in the study by growing tilapia, small pelagic fishes, shrimp, and mollusks in a series of artificial canals.	Aqua culture	Fox 1999
Kenya	Five spirulina cultivation sites were selected and the possibility for further development and promotion were evaluated in the project. It is found that is Significant efforts need to be made to improve the scope of production, bringing nutrition experts and NGO's at national level.	Production	Harris 2010
Brazil	Spirulina was proved to be an adequate protein source for recovery of body weight and muscle protein of protein malnourished rats.	Rats	Voltarelli 2011
India	Value added extruded product with 5% Spirulina + 95% Wheat flour + 5% Corn flour was developed and sensory parameters like taste, odour, texture, color, appearance were found to be at acceptable level.	Product development	Vijayarani et al. 2012
Brazil.	Different formulations of cassava cake were developed varying the concentration of *Spirulina platensis* and cassava bran. Based on the sensory tests, the product received excellent acceptance level.	Product development	Navacchi et al. 2012
Chad	Detailed explanation about the Spirulina and its development in Chad since 1988 and initiatives of the BIEP (Interminestrial Bureau of Studies and Programing):in collaboration with the BECMA (Bureau of Studies and Culture of Microalgae) were outlines in this paper along with the production technology.	Production	Halawlaw 2013
Iran	The *Spirulina platensis* and *Chlorella vulgaris* were incorporated into probiotic fermented milks to increase the functional properties.	Product development	Beheshtipour 2013
Indonesia	The aim of the work is to develop a product for local production of *Spirulina* in Indonesia and promoting amoung uneducated Indonesian fishermen.	Production	Van Koolwijk 2014
Egypt	Sixteen food formulas were prepared for as complementary food babies (1-3 years age) by using spirulina at 0, 2.5 0.5 and 7.5% for the production of two types of baby food one of them is ready to eat by using some fruits and vegetables and evaluated.	Product development	Sharoba 2014
Algeria	The product formulation composed by 2/3 of jujube syrup, 1/6 Spirulina water extract and 1/6 natural lemon juice was found to be best and further analysis of nutrients was done. The formulation reveals satificatory microbiological quality and also allows exploration of the *Ziziphus jujuba* fruit which is in extinction in Algeria.	Product development	Benahmed et al. 2014
Arab League	Five blends were prepared with one control and other blends with varying spirulina concentration from 2.5 to 10% and properties like taste, texture, odour, nutritional composition, physical and functional properties and microbiological properties were evaluated.	Product development	Morsy et al. 2014
France	The phenomenon of social conversion by farmers from traditional agricultural systems to Spirulina production was explained in detail along with the impact on conversion.	Production	Stéfanini 2015
India	High saline (0.4M NaCl) and low nitrogen (<0.01 M $NaNO_3$) significantly increased the carotenoid production in *Spirulina platensis*, which may be resulted due to excessive formation of free radicals under stress.	Production	Sujatha and Nagarajan 2013
Spain	Supercritical fluid extraction (SFE) was used to enrich Vitamin E in spirulina and 29.4 mg/g vitamin E was achieved.	Production	Mendiola et al. 2008

***Spirulina*: PEM and PEW**

The idea of using *Spirulina* to combat against malnutrition i.e. hunger alleviation, was conceived in 1984 by Fox RD, in his work on fighting against malnutrition with *Spirulina* with various available technologies. He also promoted villagers to grow *Spirulina* from recycled village wastes and proposed to use *Spirulina* as concentrated nutritional food supplement to increase immuno-resistance against infectious diseases (Fox 1985). Henrikson (1989):in his book on "Earth food *Spirulina*", explained various nutritional properties, clinical studies and in recent updated edition released in 2010, he has also included chapters on alge for bio-fuel production and interesting recipes. *S. platensis* is described as a good source of complementary diet to prevent malnutrition in developing countries (Kim 1990). The idea of cultivation of *Spirulina* or any other alternative protein source, for reducing the incidents off hunger, starvation, and malnutrition was suggested by Rodulfo (1990). Bucaille (1990) studied the effectiveness of *Spirulina* algae as food for children with protein-energy malnutrition. Many experiments were done on rats to prove the renoprotective properties of *Spirulina* (Table 10).

PEM due to hunger

There are two types of hungers, one is hunger due to lack of food and other is lack of micronutrients, "hidden hunger" (Bindu and Channarayappa, 2014). Lack of adequate food sources in under developing countries and lack of proper nutritional awareness in developed countries, resulted in micronutrient deficiency and malnutrition. The self sufficiency in some developing countries was achieved by increasing the production of cereal crops but it resulted in decrease in the production of pulses which are main sources of protein (Babu and Rajasekaran 1991). This may be the prime cause of malnutrition in developing countries.

Table 5: Clinical studies for combating malnutrition using *Spirulina* in developed and in under developing countries.

Country	Summary of Results	Subject	Reference
France	At the Hôpital Bichat, France, *Spirulina* (80-90 grams/day) was administrated to undernourished children. Adsorption of *Spirulina* protein was found to be good and also observed that in spite of heavy dosage, there is no noteworthy increase in blood uric acid.	Children	Santillan 1974
Mexico	Administration of 2 to 3 grams of protein (in terms of either *Spirulina*/Cow's milk/Soya) per body weight for four days was given to 10 children aged 5 to 10 months and it found that the relative retention of *Spirulina* is high when compared with cow's milk and soya.	Children	Proteus Inc. (1975)
China	27 children aged 2-6 years old were administrated with 1.5 g *Spirulina* mixed with 12 g baked barley sprout, Vitaimn B1 and Zinc. The children in a short period recovered from diarrhea and constipation at Nanjing Children Hospital, China.	Children	Miao 1987
Democratic Republic of the Congo	Spirulina was administrated to 28 children suffering from protein-energy diseases. The parameters measured during the study, showed a positive effect of *Spirulina* on patients.	Children	Bucaille 1990
Austria	Suggested to use C^{13} stable isotope as tracer to assess the impact of infection in undernourished people and on kinetics of protein breakdown and synthesis.	Malnourished population	IAEA (1992)
India	1 gram of dried *Spirulina fusiformis* was given every day as nutritional supplement to 5000 pre-school children for a period of 6 to 13 months and clinical parameters were evaluated. Based on the survey at the end of the study, 4% reduction in incidence of Bitot's spots was observed.	Children	Seshadri 1993
Burkina-Faso	The effectiveness of giving 5 g/day of *Spirulina* to 182 children for 90 days, suffering from malnutrition does not resulted in any change in weight gain.	Children	Branger et al. 2003
Burkina-Faso	*Spirulina* + Misola (millet, soja, peanut) based food was given to 550 undernourished children suffering from malnutrition at the Centre Medical St. Camille, Uagadougou, Burkina Faso. This study confirms that *Spirulina* plus Misola are good food supplements for undernourished children.	Children	Simpore et al. 2006
Brazil	Young Wistar rats (30 days old) were fed for 60 days with 17% protein from *Spirulina* and compared to rats fed 17% protein casein. The body weight, length, soleus muscle total protein, protein degradation and DNA were similar in both groups but The muscle protein synthesis rates were increased in rats fed with Spirulina diet.	Rats	Voltarelli and de Mello 2008
Brazil	Spirulina was proved to be an adequate protein source for recovery of body weight and muscle protein of protein malnourished rats.	Rats	Voltarelli 2011
India	900 mg of Spirulina was administrated to 100 girls with age 11 to 13 years for 6 months and significant improvement anthropometric measurements and hemoglobin, serum ferrtin, serum zinc, serum protein and serum albumin levels was observed.	Children	Ramesh et al. 2013
Brazil	23 Wistar rats were given *Spirulina* based diet in malnutrition phase for 30 days and significant nutrition recovery of animals was observed. The study proved that low *Spirulina* percentage diet (Spirulina 8.8% + casein 5.0%) are better than high Spirulina percentage diet (Spirulina 17.6% + casein 0.15% or Spirulina 26.4%).	Rats	Moreira et al. 2013
Zambia	60 children (18 to 36 months) were divided into two equal groups and one group was given 10 g *Spirulina* daily intake and other group without *Spirulina* intake were monitored for 9 months and the *Spirulina* treated children showed larger improvement in height for age Z score.	Children	Masuda et al. 2014
India	200 adolescent girls (13-15 years):from Shimla were divided into equal groups and one group was given 1 gram Spirulina + 40 grams wheat basan ladoo (an Indian recipe) for 6 days a week for two months and other group was given placebo for the same period. The group with *Spirulina* supplementation showed less prevalence of common ailments (paleness of skin, conjunctiva, dental caries, fatigue) when compared with other group.	Children	Dewan 2014

Spirulina can be considered as a best source of protein in terms of gram protein per cultivatable land ratio but major problem faced in developing countries is the acceptance level of this super food into daily recipes. Various studies from 1991 on social acceptance of algal supplements as alternative food, cost effectiveness in growing *Spirulina* in developing countries, field and clinical studies on human population were done by many researchers (Table 4 and Table 5) to understand and alleviate hidden hunger and malnutrition (Babu and Rajasekaran 1991) and provide food security. Few studies on each and every micro nutrient were tabulated in Table 6 and *Spirulina* as an alternative cheap feed for animals and aqua culture was also tabulated in Table 7.

In 1989, Earthrise Farms, USA, tried popularizing granular bars. Mass cultivation, process optimization and economic analysis for growing *Spirulina* was done at Santaigo production facility, Chile (Valderrama et al. 1987). In 1988, Jeeji and Seshadri tried popularizing mud pot cultivation in India i.e. 30 to 40 L capacity open culture vessel to produce 2 grams of *Spirulina* per day per person and 3 pots are sufficient to produce enough *Spirulina* for a family with 3 to 4 members. Mass production in Vietnam was started from 1980 (Kim 1990). Pilot scale plants in 1980's were started in Bangladesh by Applied Botany Section, Biological Research Division, Bangladesh Council of Scientific and Industrial Research Laboratories (BCSIR):Dhaka and later extended to rural communities (Habib et al. 2008). Detailed experimentation about *Spirulina* since 1988 was done by BIEP (Interminestrial Bureau of Studies and Programing):in collaboration with the BECMA (Bureau of Studies and Culture of Microalgae in Chad (Halawlaw 2013). In China, *Spirulina*

Table 6: Various studies on micronutrients and role of *Spirulina* in human health

Micronutrient	Summary of Results	Subject	Country	Reference
Vitamin A	The experiments done on rats showed that the biological values of alga were acceptable and also established in his work that dried spirulnia contain more β-carotene (pro-vitamin A).	Rats	France	Clement et al. 1967
	Spirulina (0 to 26.7%) was fed to male rats for 6 weeks. At low levels of *Spirulina* feed (<2.7) and high level (>10.7%) caused reduction in plasma, liver and heart α-tocopherol. Liver retinoid levels decreased when fed with >10.7% and < 10.7 % there is in increase in retinoids. *Spirulina* was found to significantly alter the storage and utilization of Vitamin A.	Rats	USA	Mitchell et al. 1990
	The absorption of β-carotene in *Spirulina* fed rats was found to be low when compared with rats fed with synthetic β-carotene. *Spirulina* fed rats have not shown dosage related increase in Vitamin A in liver and serum but the vitamin A storage was found to be much higher than expected.	Rats	India	Annapurna et al. 1991
	The initial loss of beta-carotene on spray drying were between 7 to 10% and on storage in colored bottles containing air, more than 50% loss was observed in <45 days. Flakes (>20 mesh size) retain 52% and spray dried fine powder (100 mesh) retained 34%. The authors recommended producing dry alga in the form of flakes or granules to retain beta carotene. Sodium metabisulphite (0.1 to 1.0%) as an antioxidant can be used to retard degradation rate of beta carotene. The opened containers should be exhausted within 15 days of purchase and minimum air/oxygen access is required to retain beta-carotene.	Storage and loss	India	Seshadri et al 1991
	Spirulina based on β - carotene level (equivalent to 60 µg/d and 120 µg/d) was fed to vitamin A depleted rats for 10 days. The *Spirulina* fed group showed better growth.	Rats	India	Kapoor and Mehta 1993
	Hexachlorocyclohexane (HCH) (1000 ppm) was mixed with *Spirulina* (0.0628% and 3.18%) and fed to male albino rats for 7 weeks. Growth rate reduced but body weight increased at the end of seventh week. The ameliorating effects of alga on the dietary toxicity of HCH in retinol deficient albino rats were established.	Rats	India	Venkataraman et al. 1994
	Spirulina (30 g/Kg) was fed to female shrimps with Pigment Deficiency Syndrome (PDS) for 4 weeks and the study confirms that the bioavailablity of carotenoids is high and inclusion in diet to is recommended for shrimps with precluded carotenoid deficiency related problems.	Shrimp	India	Regunathan and Wesley 2006
	In a group of well-nourished, normal-weight Chinese men following low-vitamin A diets, 4.5 mg *Spirulina* β-carotene consumed with 22 g fat has the same Vitamin A activity as does 1 mg retinyl acetate.	Human	China	Wang et al. 2008
	Neuroprotective effects of a Spirulina 0.1% supplemented diet in the G93A SOD1 mouse model of ALS beginning at 5 weeks of age and continuing for 10 weeks. Spirulina dietary supplement significantly maintained body weight and extension reflex, and reduced inflammatory markers and motor neuron degeneration in G93A mice.	Rats	USA	Garbuzova-Davis and Bickford 2010
	Spirulina (2 grams and 4 grams) was fed to 228 children (6-11 years) for 5 days per week for 10 weeks. The total body vitamin storage increased significantly with a median increase of 0.160 mmol in the children taking 2 grams and 0.279 mmol for children taking 4 grams Spirulina.	Human	China	Li et al. 2012
Vitamin B Complex	Spirulina produce non-cobalamin Vitamin B-12 analogues that are unavailable to humans and even block Vitamin B-12 metabolism.	Human	USA	Herbert and Drivas 1982
	The bioavailability of the Vitamin B-12 in children with B12 deficiency was checked by feeding them 0.1 to 2.7 mcg Vitamin B-12/day (Algal equivalent) for 2 months. There is an increase in plasma vitamin B-12 level but change in Mean Corpuscular Volume (MCV) is not significant suggesting that low bioavailablity of Vitamin B-12 from *Spirulina*.	Human	The Netherlands	Dagnelie et al. 1991
	No difference in body weight gain, relative liver, or relative kidney weight could be found in male weaning Wistar rats fed with *Spirulina* for four weeks. The rats were initially feed for 6 weeks, vitamin B-12 deficient diet. These data illustrate that cobalamins from algae are indeed absorbed by the rat but distribution pattern over liver and kidneys indicates that at least part of the cobalamins, measured by a specific radioassay, may actually be analogues.	Rats	The Netherlands	Van den Berg 1991
Vitamin E	*Spirulina* (1500 mg/kg/day) and Vitamin E (50mg/kg/day) was fed to adult female albino rats of wistar strain weighting between 180 and 220 grams for 6 weeks. The lens soluble protein, glutathione and water content profiles show the preventive role of *Spirulina* and Vitamin E in naphthalene-induced cataract in rats.	Rats	India	Haque and Gilani 2005

Calcium	Novel sulfated polysaccharide (named calcium spirulan (Ca-SP)) alga *Spirulina platensis* was extracted using hot water by bioactivity-directed fractionation. The unique polysaccharide was composed of rhamnose, ribose, mannose, fructose, galactose, xylose, glucose, glucuronic acid, galacturonic acid, sulfate, and calcium. Ca-SP was found to inhibit the replication of several enveloped viruses, including Herpes simplex virus type 1, human cytomegalovirus, measles virus, mumps virus, influenza A virus, and HIV-1.	Inhibitor	Japan	Hayashi et al. 1996
	These results suggest that Ca-SP, a novel sulfated polysaccharide, could reduce the lung metastasis of B16-BL6 melanoma cells, by inhibiting the tumor invasion of basement membrane probably through the prevention of the adhesion and migration of tumor cells to laminin substrate and of the heparanase activity.	Inhibitor	Japan	Mishima et al. 1998
	Ca-SP after further purification, found to contain rhamnose, 3-O-methylrhamnose (acofriose):2,3-di-O-methylrhamnose, 3-O-methylxylose, uronic acids, and sulfate. The backbone of Ca-SP consisted of 1,3-linked rhamnose and 1,2-linked 3-O-methylrhamnose units with some sulfate substitution at the 4-position. The polymer was terminated at the nonreducing end by 2,3-di-O-methylrhamnose and 3-O-methylxylose residues.	Inhibitor	Japan	Lee et al. 1998
	Ca-SP at 20 µg/ml or less may retard the repair process of damaged vascular endothelium through inhibition of vascular endothelial cell proliferation by induction of a lower ability to respond to stimulation by endogenous basic fibroblast growth factor.	Inhibitor	Japan	Kaji et al. 2002
Iron	Ingestion of daily dose of *Spirulina* (10 g) recommended for human consumption by the commercial source would provide up to 1.5 to 2 mg absorbed iron.	Rats	USA	Johnson and Shubert 1986
	The absorption of iron from Spirulina was significantly lower than that of ferrous sulphate and whole egg but significantly greater than that from whole wheat.	Rats	India	Kapoor and Mehta 1992
	Spirulina might promote the growth rate of Iron Deficiency Anemia (IDA) rats and there was an repletion effect of Spirulina on IDA rats.	Rats	China	Jiangming et al. 1994
	The pregnant and lactating rats fed with *Spirulina* + wheat gluten (22% protein equivalent) showed significant higher iron storage and hemoglobin content then casein + wheat gluten diet.	Rats	India	Kapoor and Mehta 1998
	In vitro digestion/Caco-2 cell culture system was used to measure the iron Spirulina availability. 6.5-fold increase in iron content using *Spirulina* digest in comparison with meat was observed.	Iron Availability	France	Puyfoulhoux et al. 2001
	Spirulina (3 grams/day) is supplemented for 12 weeks to 40 people with >50 years age both male and female. Increase in hemoglobin is found after 12 weeks and increase in Complete cell count (CCC) and indoleamine 2,3-dioxygenase (IDO) enzyme activity was observed. Spirulina may ameliorate anemia and immunosenescence in older subjects.	Human (>50 years)	USA	Selmi et al. 2011
Iodine	*Spirulina* was grown in 10^{-8} to 10^{-4} g/l Potassium Iodide (KI) and 0.5 to 15 mg/L Selenious acid (H_2SeO_3) and bioaccumulation was observed for pharmaceutical formulation purpose. The increase of selenium and iodine accumulation is observed at maximum 13 mg/L and 500 mg/L concentrations respectively and polynomial equation to explain the accumulation was also developed. If iodine content in medium is 500mg/L, then iodine concentration in biomass 2 mg/L, total lyophilized biomass is 0.8 g/l and iodine enrichment coefficient is 0.4%.	Formulation	Russia	Mosulishvili et al. 2002
Magnesium	Mg-fortification of *Spirulina* does not improve Mg availability and that crude spirulina represents an adequate source of Mg as efficient as all bran and Banania.	Formulation	France	Planes et al 2002
Zinc	The highest bioenrichment of *Spirulina platensis* to Zn and Se were 371.2µg/g and 752.7µg/g under the concentration of 4mg/L Zn and 200mg/L Se was found and above that the growth speed changed.	Bio-enrichment	China	Wang and Songgang 1998
	Spirulina extract (250 mg) plus zinc (2 mg) twice daily for 16 weeks may be useful for the treatment of chronic arsenic poisoning with melanosis and keratosis.	Human	Bangladesh	Misbahuddin et al. 2006
Selenium	Se-deficient rats were then repleted for 56 days with Se (75 µg/kg of diet) supplied as sodium selenite and Selenium enriched spirulina. The bioavailabilities of Se in retentate, as assessed by slope ratio analysis using selenite as a reference Se, were 89 and 112% in the tissue Se content and 106 - 133% in the glutathione peroxidase activities.	Rats	France	Cases et al. 2002
	In vitro antioxidant and antiproliferative activities of selenium-containing phycocyanin (Se-PC) purified from selenium-enriched Spirulina platensis was investigated and the results indicated that Se-PC exhibited stronger antioxidant activity than phycocyanin by scavenging ABTS, DPPH, superoxide anion, and 2,2′-azobis-(2-amidinopropane)dihydrochloride free radicals and have potential applications in chemoprevention.	Bio-enrichment	China	Chen and Wong 2009

industries are supported by State Science and Technology Commission (SSTC) as a National Strategic Programme since 1986. The SSTC developed various technologies related to medium optimization, downstream processing, practical use and strain selection and there were approximately 80 factories in China in 1997 cultivating about 10^6 m^2 producing 400 tons *Spirulina* powder per year (Li and Qi, 1997). Promotion of *Spirulina* in five cultivation sites in Kenya was done by Harris 2010. A value added food products were developed by Vijayarani et al. (2012) and Navacchi et al. (2012):India, Beheshtipour (2013):Iran, Sharoba (2014):Egypt, Benahmed et al. (2014):Algeria, Morsy et al. (2012):Arab League, and Van Koolwijk (2014):Indonesia and social conversion by farmers from traditional agro systems to *Spirulina* production was studied in France (Stefanini 2015).

Spirulina proved to recover malnourished rats (Volatrelli and De Mello 2008;Voltarelli 2011) and another study on malnourished rats for 30 days, proved that low *Spirulina* diet (8.8%) is more effective than high *Spirulina* diet (>17.6%). In one study, *Spirulina* fed 5 g/day to malnourished children does not result in any change in weight gain (Branger et al. 2003) (Table 5).

Spirulina was administered up to 90 g/day to under nourished children at the Hôpital Bichat, France and in spite of heavy dosage, absorption levels of proteins were found good (Santillan 1974). *Spirulina* was administered 2 to 3 grams per kg body weight to 5 to 10 month's old children and observed that the protein retention rate is high (Proteus Inc. 1975). 1.5 grams of *Spirulina* mixed with 12 g baked barley sprout, vitamin B1 and zinc recovered children from diarrhea and constipation (Miao 1987). Many such studies on children with protein energy diseases (Bucaille 1990):malnutrition (Simpore et al. 2006):Vitamin A deficiency (Seshadri 1993):nutrition for healthy children (Ramesh et al. 2013;Masuda et al. 2014;Dewan 2014) were done along with special studies like using C^{13} stable isotope along with *Spirulina* to understanding the kinetics of protein breakdown (IAEA 1992). Still further studies on *Spirulina* are required to establish the optimal concentration level for each disease conditions and malnutrition. Various studies on micronutrients and role of *Spirulina* in human body is listed in Table 6.

According to IIMSAM (Intergovernmental Institution for the use of Micro-algae *Spirulina* against Malnutrition):recognized by United Nations (UN) and consultative observer of The United Nations Economic and Social Council (ECOSOC):UN, there are 178 million globally estimated stunned children. IIMSAM works to promote the use of *Spirulina* against acute malnutrition and global food security by promoting its mandate and collaborating with various countries (H.E. Remigio M. Maradona 2008).

Since 1967, many researchers tried establishing *Spirulina* as a major source of vitamin A with highest bioavailability of beta-carotene in rats (Clement et al. 1967; Mitchell et al. 1990; Annapurna et al. 1991; Kapoor and Mehta 1993; Venkataraman et al. 1994; Garbuzova-Davis and Bickford 2010):humans (Wang et al. 2008; Li et al. 2012) and aqua culture (Regunathan and Wesley 2006). The studies on loss of beta-carotene during storage, spray drying and other unit operations was done by Seshadri et al (1991). The studies for increasing the productivity of beta-carotene by changing the medium composition of *Spirulina* were also done (Sujatha and Nagarajan 2013).

Based on their studies on bioavailability of Vitamin B12 in humans (Herbert and Drivas (1982) and Dagnelie et al. (1991)) it is suggested not to use it as a source of vitamin B12 for children with B12 deficiencies as it contain non-cobalamin Vitamin B-12 analogues that are unavailable to humans. Similar results were also supported by Van den Berg (1991). Studies on Vitamin K, were not available and studies on Vitamin E are found to be less (Haque and Gilani 2005; Mendiola et al. 2008). Calcium spirulan (Ca-SP)) from *Spirulina platensis* was isolated in Japan in 1998 and since then enormous amount of research was done on it, against various diseases including HIV, measles virus, mumps virus, influenza A virus, and cancer (Hayashi et al. 1996;Mishima et al. 1998; Lee et al. 1998; Kaji et al. 2002). Research on *Spirulina* as a source of iron for healthy and anemic rats were done since 1986 (Johnson and Shubert 1986; Kapoor and Mehta 1992; Jiangming et al. 1994; Kapoor and Mehta 1998; Puyfoulhoux et al. 2001) and aged population in 2011 (Selmi et al. 2011) and exact bioavailability values were also established (Table 6).

Magnesium fortification of *Spirulina* does not improve the magnesium bioavailability (Planes et al 2002) but further studies on this area are required and bioenrichment of *Spirulina* with high concentrations of iodine (Mosulishvili et al. 2002):zinc and selenium (Wang and Songgang 1998) significantly improved the mineral concentrations. *Spirulina* with zinc can be used for treatment of chronic arsenic poisoning with meelanosis and keratosis (Misbahuddin et al. 2006). The bioavailability values of selenium were available in Table 6 (Cases et al. 2002). Purified selenium from *Spirulina* can be used as strong antioxidant and have potential applications in chemoprevention (Chen and Wong 2009). Large corporations are required to promote research on *Spirulina* for establishing exact bioavailability values of micronutrients so that *Spirulina* can be used for enteral nutrition in malnourished patients. Overall, based on the above data, *Spirulina* can be used as a source for alleviating hidden hunger or micronutrient deficiencies in children but care should also be taken while administrating *Spirulina* to the patients by referring to Table 3.

Spirulina as an alternative feed for animals and aquaculture

Spirulina as an alternative feed for animals and aqua was reported in Table 7. Cyanobacteria as a source of food for aqua culture were established by Fox (1999). A system including *Spirulina*, *Artemia* and mangrove fauna was used for producing tilapia, small pelagic fishes, shrimp, and mollusks in artificial canals with circulating filtered sea water. *Spirulina* was used as a feed for poultry, pig, cattle and many other animals and aqua culture. Various studies on Spirulina as an alternative feed for animals and aquaculture were listed in Table 7.

After considering the listed facts in Table 7, *Spirulina* can be fed up to 10 % for poultry (Ross and Dominy 1990) and less than 4% for Quail (Ross et al. 1994). Increase in the *Spirulina* content up to 40g/kg for 16 d in 21 day old boiler male chicks, resulted in yellow and red coloration of flesh and this may be due to the accumulation of the yellow pigment, zeaxanthin (Toyomizu et al. 2001). Pigs (Nedeva et al. 2014):rabbits (Peiretti and Meineri 2008) and lambs (Holman et al. 2012) can receive up to 10% of the feed and increase in the *Spirulina* content in cattle resulted in increase in milk yield and weight (Stanley and Jones 1976; Kulpys et al. 2009; Heidarpour et al 2011). *Spirulina* as an alternative feedstock and immune booster for various types of fish including big mouth buffalo, (Stanley and Jones 1976):milk fish (Santiago et al. 1989):cultured striped jack (Shigeru et al. 1991):carp (Ayyappan 1992; Ramakrishnan et al. 2008):red sea bream (Mustafa et al. 1994):tilapia (Olvera-Novoa et al.

Table 7: Various studies on *Spirulina* as an alternative feed for animals and aquaculture for alleviating hunger and for providing food security

Country	Summary of Results	Subject	Reference
USA	Bigmouth buffalo Ictiobus cyprinellus (Valenciennes):was fed with 29 g dry weight per kg body weight Spirulina for 28 days and an increase of 14 g/Kg body weight was observed.	Big mouth buffalo	Stanley and Jones (1976)
French Polynesia	Spirulina (0 to 8 %) in pelletized form was fed to shrimps. The growth, survival and pigmentation were considerably more when compared with single cell ingredient sources like lactic yeast.	Shrimp	Cuzon et al. 1981
The Philippines	Wild milkfish fry ($90/m^2$):were fed with Spirulina and formulated diet. The stocking rate was $92.5/m^2$ after 7 weeks and the Spirulina fed fish gave weight increment (0.881±0.140 g).	Milkfish	Santiago et al. 1989
USA	*Spirulina* (0 to 20%) was fed to poultry and found that day old chicks, after 3 weeks, the growth rate reduced for 10% and 20% spirulina feed and >12% diet receiving Hubbard male boiler chicks after 41 days, a slight decrease in growth was observed but there is no significant difference due to the *Spirulina* and concentration level up to 10% except increase in color of yolk and fertility rate.	Poultry	Ross and Dominy 1990
Japan	The levels of carotenoids were increased by supplementation of *S. maxima* 5 to 10% diet to Cultured striped Jack *Caranx delicatissimus*.	Cultured Striped Jack	Shigeru et al. 1991
India	10% Spirulina in basal diet improved specific growth rates and live weight	Carp	Ayyappan 1992
Japan	The red sea bream were fed with 2% Spirulina for 95 days and elevated protein assimulation and increased stromal fraction was observed.	Red sea bream	Mustafa et al. 1994
USA	There was a consistent increase in yolk color with increase in concentration from 0% to 4% of freeze dried spirulina in quails fed for 8 weeks. Yolk color increased more in freeze-dried *Spirulina* when compared with extruded *Spirulina*.	Quail	Ross et al. 1994
USA	Spirulina and its potential applications as an animal feed were reviewed.	Aqua Culture	Belay et al. 1996
South Africa	Juvenile Haliotis midae, Port Alfred, South Africa, were fed red alga (*Pfocamium corallorhiza*) for 3 months before the experiment. Spirulina based diet (19% protein) was fed for 124 days along with 4 other feeds (casein, fishmeal, soya oil cake and torula yeast). fishmeal and Spirulina spp. algae are found to be most suitable proteins for inclusion in practical diets for H. midae.	Abalone	Britz 1996
México	Spirulina (20 to 100%) diet along with animal protein was given 6% of their body weight to tilapia in a closed recirculating system. After a 9 week feeding period, the growth rate and protein utilization increased in 20% and 40% spirulina diet. Further increase in Spirulina, decreased the growth.	Tilapia	Olvera-Novoa et al. 1998
Italy	40 crossbred rabbits were given Spirulina platensis (5% to 15%) for 24 days and found no obvious health problems. The final weight gain and feed efficiency did not alter significantly but rabbits receiving >10% spirulina showed highest feed intake.	Rabbits	Peiretti and Meineri 2008
India	*Spirulina maximus* at 3% diet to common carp (Cyprinus carpio - 4.59±0.95 g) produced the specific growth rate (1.27±0.02%/d):feed conversion ratio (0.71±0.08):and , protein efficiency ratio 1.96±0.03.	Carp	Ramakrishnan et al. 2008
Lithuania	The Lithuanian black and white cows in their early lactation period were fed with 200 g of spirulina per day for 90 days. The cow's receiving *Spirulina* became 8.5 to 11 % fatter and gave 34 kg milk per day in the beginning of their lactation and it is found to be 6 kg more than those of the control group.	Cow	Kulpys et al. 2009
Taiwan	White shrimp (Litopenaeus vannamei):were given Spirulina (6 to 20 µg/g):which is earlier hot water extracted and compared with normal spirulina (200 to 600 mg/L) for 24 to 96 hours. Shrimp that received the hot-water extract of S. platensis had enhanced innate immunity and increased resistance against V. alginolyticus infection.	Shrimp	Tayag et al 2010
Iran	Twenty four Holstein calves were given *Spirulina platensis* 0 g to 25 g per day for 57 days. The results showed that treatment effect was not significant on the final weight, daily gain; daily feed intake, feed efficiency and digestibility coefficient below 25 g. Increase in the level up to 25 grams, decrease in digestibility in terms of crude protein, dry matter, neutral detergent fiber, and organic matter were observed. However, reduction in plasma cholesterol, LDL, HDL concentration was found and there is no effect on other blood parametters like BUN, albumin and globulin.	Holstein calves	Heidarpour et al 2011
Thailand	Spirulina (3% and 5%) was fed to African Sharptooth Catfish (*Clarias gariepinus*) with initial size 30.63-32.47 g for 60 days. The immunity (1.70 Units/mL) for 5% *Spirulina* feed was found to be higher.	Catfish	Promya and Chitmanat 2011
Turkey	Spirulina (0 to 10%) was fed to fish (3.75±0.02g) for 12 weeks. The specific growth rate, feed intake, total egg production, hatching rate of eggs was found to be higher. The yellow and blue coloration of the yellow tail cichlid and carotenoid in skin was enhanced.	Yellow tail	Güroy et al. 2012
Australia	24 weaned lambs (purebred Merino dams sired by Dorset, White Suffolk, Black Suffolk and Merino rams lamb) weighing 37.5±5.2 kg, 42 days old were fed with 0 to 20 wt/vol *Spirulina* for 6 weeks. Lambs on Spirulina levels of 10% recorded the highest mean live weight of 41.9 ± 0.7 kg and lambs with 20% did not significantly improve when compared to the control group (0%).	lamb	Holman et al. 2012
France	Spirulina platensis was given as a sole food for zebrafish broodstock, egg production was found to be lower but survival rate (73%) was higher when compared with commercial feed (55%). No difference in egg and larval weight and size was observed and the larval survival rate of 69% at 31 days post fertilization was observed. The spirulina based diet is recommended for zebrafish larvae in the first few days of life.	Zebrafish	Geffroy 2013
Bangladesh	Studies were done on the growth performance, feed utilization and body composition of fiingerlings of stinging cat fish and effect of spirulina.	Cat fish	Ali 2014
Bulgaria	48 Danube white pigs, weighing 12.15 to 12.471 kg were given 2 to 3 g per day for 47 days. The weight increased to 30.9 to 33.9 kg and significant increase in growth intensity from 12.50% to 14.25% was observed. The number of erythrocytes and hemoglobin are 15% and 13 % higher in 3 g fed pigs. There are relatively small number of sick animals (<2.40%) when compared with control group (5.40%).	Pigs	Nedeva et al. 2014

Table 8: Various studies on *Spirulina* for nutrition rehabilitation patients suffering from cancer

Country	Summary of Results	Subject	Reference
USA	Spirulina algae extract along with 0.1% 7, 12-dimethylbenz[a]anthracene in mineral oil when applied tropically for 3 times per week for 28 weeks found to remove gross tumors in Hamster. However, microscopic sections of the buccal pouch in the Spirulina fed group showed localized areas of dysplasia and early carcinoma-in-situ undergoing destruction. β carotene and mineral oil fed group of hamsters also showed considerable decrease in tumors.	Hamster	Joel Schwartz 1988
India	1g/day of Spirulina was fed to oral leukoplakia patients in Kerala, India and complete regression of lesions was observed in 20 of 44 subjects supplemented and within one year of discontinuing supplements, 9 out of 20 reponders within spirulina fed developed recurrent lesions. Patients did not result in increased serum concentration of retinol or β-carotene, nor was it associated with toxicity.	Human	Babu et al 1995
China	Spirulina platensis (12, 30 an 60 mg/kg) was administrated for 21 days to mice and dogs, which were damaged by injecting cyclophosphamie annd ^{60}Co-γ irradiation. 30 and 60 mg/kg increased the level of white cells in blood and nucleated cells and DNA in bone marrow but no effect in red cells in mice but 12 mg/kg increased the level of red cells, white cells and hemoglobin in blood and nucleated cells in bone marrow in dogs. *Spirulina* has chemo-protective and radio protective capabilities.	Mice and Dog	Zhang et al. 2001
India	Spirulina was administered orally for 3 days, twice daily for 7 weeks to mouse, which were earlier treated with doxorubicin (DOX) for 4 weeks. In vitro cytotoxic studies using ovarian cancer cells demonstrated that Spirulina did not compromise the anti tumor activity of doxorubicin.	Mouse	Khan et al. 2005
México	Spiruina (0 to 800mg/kg body weight) was given to mice for 2 weeks. Protective effects of spirulina in relation to cyclophosphamide -induced genetic damage to germ cells was found.	Mice	Chamorro-Cevallos et al. 2008
Japan	Syngeneic tumor-implant mice (C57BL/6 *versus* B16 melanoma) were fed with spirulina to elucidate the mechanism of raising antitumor NK (Natural Killer) activation. Orally administered Spirulina enhances tumoricidal NK activation through the MyD88 pathway. Spirulina and BCG–cell wall skeleton synergistically augmented IFN-γ production and antitumor potential in the B16D8 *versus* C57BL/6 system. We infer from these results that NK activation by Spirulina has some advantage in combinational use with BCG–cell wall skeleton for developing adjuvant-based antitumor immunotherapy.	Mice	Akao et al. 2009
USA	Spirulina (1%) against dibutyl nitrosamine (DBN) precursors were studied on rats (120±5g). The study indicates that the liver tumor was reduced from 80% to 20% by Spirulina. Immunohistochemical results show that PCNA and p53 were reduced by spirulina supplementation. Spiruilna inhibited cell prolifeation, increased p21 and decreased the expression levels at 48 hrs post treatment.	Rat	Ismail et al. 2009
Czech Republic	Spirulina inhibited the pancreatic cancer growth rate since the third day of treatment. Decrease in the generation of mitochondrial ROS and glutathione redox status was observed.	Human pancreatic cancer cell lines	Konícková et al. 2014

1998):catfish (Promya and Chitmanat 2011; Ali 2014):yellow tail (Güroy et al. 2012):Zebrafish (Geffroy 2013): and shrimps (Cuzon et al. 1981; Tayag et al 2010) and Abalone (Britz 1996) was established and up to 2% *Spirulina* per day in feed can be safely recommended for fish, shrimps and abalone (Table 7).

Effect of Spirulina in combating against Protein Energy Malnutrition (PEM) in patients with various chronic diseases

PEM in cancer patients

Protein calorie under nutrition is seen in advanced cancer patients with loss of adipose tissue, visceral protein and skeletal muscle varying unpredictably from patient to patient. Good nutrition may increase the survival rate of the patients (Nixon et al. 1980). Table 8 shows the list of clinical studies on *Spirulina* and its benefits for alleviating protein energy malnutrition in cancer patients.

Spirulina algae extract, when applied tropically for 3 times per week for 28 weeks along with 0.1% 7, 12-dimethylbenz[a]anthracene in mineral oil, removed tumors in hamsters (Joel Schwartz 1988). This study promoted many scientists to explore the antitumor immunotherapy potential of *Spirulina*. Extensive studies including human trails (Babu et al 1995):cell lines (Konícková et al. 2014) and on rats (Zhang et al. 2001;Khan et al. 2005; Chamorro-Cevallos et al. 2008; Akao et al. 2009 and Ismail et al. 2009) were done to prove the cancer inhibitory properties of *Spirulina*.

PEM in HIV patients

After the discovery of calcium spirulan (Ca-Sp) by Hayashi et al. (1996):extensive research has been done to inhibit the replication of several enveloped viruses, including (human immunodeficiency virus) HIV-1. Studies on peripheral blood mononuclear cells (Ayehunie et al 1998) and humans (Simpore et al 2005; Yamani et al. 2009; Azabji-Kenfack 2011) were done along with structural modification studies on calcium spirulan (Lee et al. 2001). *Spirulina* was fed up to 25 g/day to HIV patients and considerable improvement in weight loss, anaemia, karnofsky score, CD4 cell count was observed along with decrease in the HIV viral load (Simpore et al 2005; Yamani et al. 2009;Azabji-Kenfack 2011) (Table 9).

Protein Energy Wasting

Protein energy wasting describes the increase of mechanisms causing syndromes of wasting, malnutrition, inflammation, and their interrelationships in individuals with chronic kidney disease (CKD) or acute kidney injury (AKI) (Fouque et al. 2008). Studies on abrupt loss of kidney function due to exposure to mercury to the kidney and its failure in rats was studied by Fukino et al. (1990). *Spirulina* was administered along with mercury to rats which were alive up to 10 days, where the control group which were fed only mercury died within 4 days. The study confirms the protective effect of *Spirulina* against renal failures and reduction of general renal dysfunctions. Extensive research was done on

Table 9: Various studies on *Spirulina* for nutrition rehabilitation patients suffering from HIV patients

Country	Summary of Results	Subject	Reference
USA	Spirulina (0.3 to 1.2 µg/ml):reduced viral production by approximatly 50% in peripheral blood mononuclear cells (PBMC). Fractionation of the extract revealed antiviral activity in the polysaccharide fraction and also in a fraction depleted of polysaccharides and tannins.	Peripheral blood mononuclear cells (PBMC)	Ayehunie et al 1998
Japan	Calcium ion binding with the anionic part of the molecule was replaced with sodium and potassium ion in Calcium Spirulan. The replacement of calcium ions with sodium and potassium maintained the antiviral activity but divalent and trivalent metal ions decreased the antiviral activity.	Structural modification Calcium Spirulan	Lee et al. 2001
Italy	Spiurlina 15 to 25 g/day was fed to 84 children with HIV infection for 8 weeks and compared with 86 undernourished children. Level of anaemia decreased during the study and 81.8% of undernourished children and 63.6% of HIV infected children were recuperated. Spirulina can be effective for weight loss and anaemia for HIV and HIV negative undernourished children.	Children	Simpore et al 2005
Central African Republic	79 patients with HIV were given 10 grams of Spirulina per day for six months. No difference was found in patients receiving *Spirulina* and the control group but there was an increase in protidemia, creatinemia and Karnofsky score.	Human	Yamani et al. 2009
Cameroon	Food supplements, calculated as per 1.5 g/Kg body weight proteins and spirulina (25%) was given to malnourished HIV infected adults with age 18 to 35 years for 12 weeks. HIV viral load significantly decreased and increase in CD4 cell count was observed at the end of the study.	Human	Azabji-Kenfack 2011

Table 10: Various studies on spirulina and protein energy wasting in renal problems

Country	Summary of Results	Subject	Reference
USA	Approximately 5 to 30% protein hydrolysate prepared from protein source *Spirulina*, fish, and macroronus with 70 to 95% of natural bee honey can be used to patients with chronic renal insufficiency or other protein metabolic disorders.	Human	Stoilov et al. 1999
India	Effect of urinary oxalate and uric acid level on high spirulina diet and risk of nephrolithiasis was found by Spirulina (1500 mg/kg and 0;75% in drinking water) for 4 weeks. The crystal deposition and damage in renal cells was observed. During hyperoxaluric conditions the *Spirulina* diet must possibly be avoided and can be considered in normal subjects checked for family history of renal stone deposition.	Rats	Farooq et al. 2005
India	Renoprotective potential of Spirulina (500 too 1500mg/Kg) against Gentamicin (100mg/kg) was evaluated on rats. Treatment with *Spirulina* significantly restored renal functions, reduced lipid peroxidation and enhanced reduced glutathione levels, superoxide dismutase and catalase activities.	Rats	Kuhad et al. 2006
India	*Spirulina (*1,000 mg/kg) was administered orally for 8 days and Cisplatin treatment was given on day 4 and Nephrotoxicity was assessed after 6 days. There is decrease in the levels of superoxide dismutase, catalase and glutathione peroxidase and increase in lipid peroxidation, plasma urea, creatinine, urinary β-NAG, plasma and kidney tissue malondialdehyde. Spirulina significantly protected the Cisplatin induced nephrotoxicity through its antioxidant properties.	Rats	Mohan et al. 2006
Saudi Arabia	Rats were fed with 0.75% ethylene glycol in drinking water for three weeks and after that they were fed with Spirulina (20 mg/kg body weight) for another three weeks. The rats fed with spirulina recovered from nephrolithiasis or renal stone disease and completely from hepatotoxicity induced by ethylene glycol.	Rats	Al-Attar 2010
India	Oral pretreatment with *Spirulina* to rats, prevented 4-nitroquinoline-1-oxide induced hepato and nephrotoxicity. The antioxidant properties mediated by Spirulina in eliminating reactive free radicals were established.	Rats	Viswanadha et al. 2011
Mexico	Phycobiliproteins and C-phycocyanin extracted from Spirulina were fed to rats with mercury (5 mg/Kg Intraperitoneal). All doses of phycobiliprotein and C-phycocyanin prevented enhancement of oxidative markers and protected against mercuric cholirde caused cellular damage in the kidneys.	Rats	Rodríguez-Sánchez et al. 2012
Egypt	Hepatonephroprotective and antioxidant potential of *Spirulina* against deltamethrin toxicity in rats was assessed. Spirulina normalized the elevated serum levels of AST, ALT, APL, uric acid, urea and creatinine. Furthermore, it reduced deltamethrin-induced lipid peroxidation and oxidative stress in a dose dependent manner.	Rats	Abdel-Daim et al. 2013

rats but very few studies were available on human population (Table 10).

Stoilov et al. (1999) proposed the idea of using 5 to 30% protein hydrolysate from *Spirulina*, fish and macroronus along with natural bee honey can be used to patients with chronic renal insufficiency. High *Spirulina* diet should be avoided for patients with renal stone deposition problems (Farooq et al. 2005). Renoprotective potential against Gentamicin (Kuhad et al. 2006):Cisplatin (Mohan et al. 2006):ethylene glycol (Al-Attar 2010):4-nitroquinoline-1-oxide (Viswanadha et al. 2011):mercury (Rodríguez-Sánchez et al. 2012):deltamethrin (Abdel-Daim et al. 2013) was established in rats and still human trails are required to find the exact dosage of *Spirulina*. The above summary of results, presented in the Table 9, from various sources confirms that *Spirulina* can be used to combat against protein energy wasting.

Conclusions

The present review had revealed that significant studies were done on *Spirulina* to establish its potential use as a food supplement, food additive, animal or aqua feed and to combat against all forms of Protein Energy Malnutrition (PEM) and Protein Energy Wasting (PEW). But many studies are required on human population to find the exact clinical dosage of this super food to patients with different protein-calorie or renal disease conditions. The above review also suggests to use *Spirulina* not greater than 4 grams per day for normal healthy adults, <25

grams/day for HIV patients, <2 % for aqua culture and <10% for poultry and animal feed. Exact dosage has to be developed for cancer patients and patients with renal problems. *Spirulina* is not recommended as a source of vitamin B12 for vitamin B12 deficiency children (Herbert and Drivas 1982;Dagnelie et al. 1991) and low dosage of *Spirulina* (5g/day) does not showed any significant increase in weight in malnourished children (Branger et al. 2003) and it is also not recommended for patients with family history of renal stone depositions. Extensive studies on Vitamin K, Vitamin B1, Vitamin B2, Vitamin B3, Vitamin B6, improvement of cobalamin Vitamin B-12 in *Spirulina* strains using genetic modification, clinical potential of calcium-spirulan against HIV and other viral diseases, antitumor and renoprotective properties of *Spirulina* on human population are required for further understanding the clinical potential of *Spirulina* to combat against PEM and PEW. Specific mechanisms should be developed by industries to remove vitamin A, vitamin K, vitamin B12, molybdenum and chromium to increase the consumption level up to 100 grams of *Spirulina* per day. Development of various *Spirulina* fortified foods are required to create nutritional awareness and increase the acceptance level in developing countries.

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