



As nutrient-rich whole foods, microalgae are moving from juice bars and excipient status to the clinical setting as active ingredients. Profs Marc Cohen and Jenny Jamison provide an overview.

# Single-cell food

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**N**utritionists and public-health authorities agree that the Australian population needs to increase its dietary intake of plant-based foods. Many would also encourage the consumption of organically produced ‘whole foods’ involving minimal processing, including those at the base of the food chain so as to reduce bio-accumulation of environmental toxins.

Several ‘living foods’ that have gained popularity are the nutrient-dense microalgae species chlorella, spirulina and, more recently, dunaliella. These microalgae are deemed to be functional foods due to their high concentrations of

whole-food nutrients, containing significant amounts of lipids, protein, chlorophyll, carotenoids, vitamins, minerals, and unique pigments.<sup>1</sup>

## Spirulina

Spirulina is a blue-green cyanobacteria with a long tradition of human use, having been harvested as a food source for possibly thousands of years by Mexican Aztecs and by the Kanembu people of central Africa.<sup>2</sup> There are

several species of spirulina, although *Spirulina platensis* and *S. maxima* (recently reclassified as *Arthrospira maxima*, *A. platensis* by the TGA<sup>3</sup>) are the most commonly used in nutritional supplements, for which they are grown in tanks under controlled conditions or harvested from lakes.

Spirulina is rich in nutrients, containing up to 70 per cent protein, B-complex vitamins, chlorophyll, beta-carotene, numerous minerals, high levels

**Composition of microalgae vs. carrots (per 100 g)**

	Spirulina <sup>a</sup>	Chlorella <sup>a</sup>	Dunaliella <sup>c,d,e</sup>	Carrots <sup>b</sup>
Protein	57 g	67 g	35.4 g	1 g
Total fats	8 g	12.9 g	7 g	0
Carbohydrates	24 g	1.1 g	29.7 g	10 g
Energy	1214 kJ	1600 kJ	1893 kJ	180 kJ
Fibre	4 g	8.7 g	0.4 g	3 g
Chlorophyll	1 g	3.9 g	1.54 g	NA
Betacarotene	0.34 mg	119 mg	8800 mg	8.3 mg
Lutein/zeaxanthin	0.0 mg	503 mg	97.6 mg	0.26 mg

a. Japan Food Research Labs, no. 102042170, 21 May 2002; 103044178002, 20 May, 2003

b. USDA National Nutrient Database for standard references (release 18), 2005

c. National Measurement Institute, Australia, 2005

d. Craft Technologies Inc, US

e. National Institute of Oceanography, Israel, 2005



of the essential polyunsaturated fatty acid  $\gamma$ -linolenic acid, vitamin E and unique pigments, including phycocyanin.<sup>1</sup> Animal experiments suggest spirulina provides a biologically useful but differently metabolised form of selenium.<sup>4</sup>

Remarkable claims have been made regarding spirulina, which is reputed to have anti-oxidant, antiviral, antineoplastic, lipid-lowering, hypocholesterolaemic, hepatoprotective, anti-allergic and immune-modulatory activities, and has been promoted as a weight-loss aid.

However, while preliminary research has shown some promise for some of these indications and the safety of spirulina, human evidence is lacking.

#### Indications

Spirulina has shown some antiviral activity in laboratory and animal studies, and preclinical evidence also suggests immunomodulatory, hepatoprotective, anti-allergic and hypocholesterolaemic effects.<sup>2</sup>

Following from animal studies that found spirulina effective in lowering serum **cholesterol** and **triglyceride** levels, some clinical trials suggest possible efficacy in humans.<sup>5-7</sup> However, these trials are methodologically flawed or poorly reported.

A small trial involving **type 2 diabetic** patients found beneficial effects on lipids and fasting blood sugar after two months

of oral spirulina (Multinal, New Ambadi Estate P/L, Algal Division, Madras, India) supplementation.<sup>6</sup>

Despite being promoted for **weight loss**, spirulina was trialled 20 years ago for this indication, and found to have no benefit over placebo.<sup>8</sup>

One weak randomised trial reported beneficial effects on precancerous **oral leukoplakia** lesions in 115 patients receiving 1 g *S. fusiformis* (New Ambadi Estates, Madras, India) over 12 months.<sup>9</sup>

A randomised double-blind trial published last year compared 1 g and 2 g daily doses of spirulina (Earthise Nutritionals Inc, Irvine, California) with placebo in individuals with **allergic rhinitis**. The higher dose significantly reduced interleukin-4 levels by 32 per cent from phytohaemagglutinin-stimulated peripheral blood mononuclear cells.<sup>10</sup>

#### Dosage

Spirulina may be sold in capsule, tablet, flake or powdered form, or as a component of 'green food' products containing chlorella, barley grass and wheatgrass, in daily doses ranging from 250 mg to 5 g.<sup>11</sup>

#### Adverse effects

Spirulina is well tolerated, with headache, muscle pain, facial flushing and sweating being the only adverse effects reported after oral consumption.<sup>2</sup>

#### Precautions and contraindications

Theoretically, the phenylalanine content of cyanobacteria may exacerbate phenylketonuria. There is also potential for heavy-metal contamination of spirulina harvested naturally from contaminated waters; this is more likely with non-spirulina species, such as *Anabaena*, *Aphanizomenon* and *Microcystis*.<sup>2</sup>

#### Pregnancy and lactation

Data are insufficient to safely recommend the use of spirulina during pregnancy or breastfeeding. A diet of up to 30 per cent spirulina did not cause any toxic effects in a mouse study.<sup>12</sup>

#### Interactions

Small but statistically significant increases in alkaline phosphatase and serum calcium were observed in a four-week weight-loss study of 15 volunteers receiving 200 mg/day spirulina tablets.<sup>8</sup>

#### Chlorella

Chlorella (*Chlorella pyrenoidosa*, *C. vulgaris*) is a freshwater green alga containing 60 per cent protein in the form of amino acids, and betacarotene, vitamin D, vitamin B12, folate, iron and enzymes such as pepsin. Chlorella provides more bioavailable vitamin B12 than spirulina, provided large amounts are consumed.<sup>13</sup> It is also an extremely rich source of the carotenoid lutein, which is found in the macula of the eye.

Promoted as a health tonic, anecdotal reports claim chlorella provides diverse benefits through increasing the level of albumin in the bloodstream, ranging from improved digestion to accelerated wound healing, retarded ageing processes and enhanced immunity.<sup>14</sup> Claims concerning anticarcinogenic activities are based on animal studies of an extract isolated from chlorella, not the whole plant.<sup>15</sup> Similarly, there is no evidence to support claims about the chelating effect

### Minerals in whole-food supplements

	Ca	Mg	Na	K	Cu	Zn	Fe
Dunaliella	178	540	823	5	0.4	4	23.5
Spirulina	547	330	>999	5	1.1	2	50.5
Chlorella	201	211	106	5	0.1	1	214
Kelp powder	1443	796	>999	7	0.2	3	27
Wheatgrass	937	83	315	6	0.4	2	13.7
Green barley	384	186	818	6	0.6	2	8.4

SOURCE: TRACE ELEMENTS INC, US; NATIONAL OCEANOGRAPHIC INSTITUTE, ISRAEL



of chlorella on heavy metals in humans.

**Indications**

A pilot study suggested chlorella reduced or stabilised sitting diastolic blood pressure in people with mild-to-moderate **hypertension**.<sup>16</sup> A review of double-blind, placebo-controlled, randomised clinical trials concluded that daily dietary supplementation with chlorella may indeed reduce high blood pressure, lower serum **cholesterol** levels, accelerate **wound healing** and enhance **immune functions**.<sup>17</sup> The authors also recommended that the potential of chlorella to relieve symptoms, improve quality of life and normalise body functions in patients with **fibromyalgia**, hypertension or **ulcerative colitis** justified performing larger, more comprehensive clinical trials.

One randomised, double-blind, placebo-controlled trial in 124 healthy adults undergoing **influenza vaccination** found that chlorella-derived dietary supplementation, although failing to increase the antibody response to influenza vaccine in the overall study population, increased the antibody response of participants aged 50–55 years<sup>18</sup> — an interesting finding given our ageing population.

**Dosage**

Capsules, tablets and granules are available, as is the stand-alone powder. The daily dose of dietary supplements of chlorella provides 500–3000 mg of the intact organism. The therapeutic dose is unknown.<sup>15</sup>

**Adverse effects**

Allergic reactions and photosensitivity have been reported in some consumers of chlorella.<sup>19</sup>

**Precautions/contraindications**

Some products may be rich in vitamin K and may affect the INR of patients using warfarin.<sup>19</sup>

Super foods comparison: trace elements (mg/100 mg)									
	Mn	Cr	Se	B	Co	Mo	S	Li	Rb
Dunaliella	1.8	0.2	1.02	25.4	0.022	0.041	<2000	0.9	0.66
Spirulina	2.6	0.53	0.03	0.25	0.13	0.11	<2000	0.093	0.13
Chlorella	4	0.06	0.01	0.03	0.038	0.042	<2000	0.01	0.066
Kelp powder	3.8	0.23	0.69	11.1	0.045	0.094	2426	0.068	0.85
Wheatgrass	5.1	0.09	0.04	0.33	0.005	0.05	<2000	0.008	1.0
Green barley	3.9	0.11	0.15	1.05	0.004	0.066	<2000	0.023	0.51

**Pregnancy and lactation**

Data are insufficient to safely recommend the use of chlorella during pregnancy or breastfeeding.

**Interactions**

Animal studies suggest some constituents may reduce side-effects of 5-fluorouracil.<sup>20</sup>

**Dunaliella**

Dunaliella is a soft-celled microalga found in many coastal waters and saltwater lakes. Dunaliella is one of the most salt-tolerant life forms known, and is adapted to extremely high ultra-violet radiation. To cope with these extreme environments, dunaliella produces very high levels of osmotic glycerol and the anti-oxidant molecule betacarotene.

On a per-gram basis, dunaliella has more than twice the chlorophyll and over 6000 times the anti-oxidant content of spirulina (see table, p 85). Furthermore, dunaliella's soft-cell membrane makes it easily digestible compared to other microalgae with hard cell walls.<sup>21</sup>

While dunaliella contains many different carotenoids, it is highest in natural betacarotene, which can make up to 10 per cent of its dry weight.<sup>21</sup> The US Department of Agriculture deems dunaliella to be the richest known source of this important fat-soluble anti-

oxidant, so it is commonly used as a source of natural betacarotene in nutritional supplements (Nutrient database for standard references, release 18).

**Indications**

Recent advances in production technology have allowed the whole dried dunaliella biomass to become commercially available.<sup>41</sup> To date, most of the clinical research on dunaliella has been on betacarotene-rich whole organism. Human studies, however, suggest that dunaliella can protect against **exercise-induced asthma**<sup>31,32</sup>, normalise high LDL oxidation in patients with **diabetes**<sup>33</sup> and male hyperlipidaemic smokers<sup>34</sup>, as well as protect the skin from **sun damage**<sup>35</sup> and protect against **radiation damage**, as demonstrated by its use in children exposed to the Chernobyl disaster.<sup>36</sup>

Animals studies further suggest that the natural betacarotene-rich dunaliella protects against GI inflammation<sup>37</sup>, water-immersion stress<sup>38</sup>, whole-body irradiation<sup>39</sup> and CNS oxygen toxicity.<sup>40</sup>

**Dosage**

Whole dunaliella is sold as 250–500 mg capsules containing approximately eight per cent betacarotene. The recommended dose is 1–3 g/day, taken with meals or other dietary fat to increase the bioavailability of carotenoids.

SOURCE: TRACE ELEMENTS INC., US



### Betacarotene in profile

While vitamin A is toxic in high doses, betacarotene is only converted into vitamin A as required by the body and is considered to be non-toxic even when given in doses as high as 180 mg/day.<sup>22</sup>

Not all betacarotene is the same. Synthetic betacarotene comprises the all-trans isomer, while natural betacarotene also contains the 9-cis isomer. All-trans betacarotene is converted to vitamin A, which plays an essential role in vision, growth, reproduction, immune function and maintenance of the skin and mucous membranes. The 9-cis isomer contained in natural betacarotene also acts as a powerful anti-oxidant.<sup>23</sup>

High intake of betacarotene-containing foods has consistently shown benefits, including prevention of cancer<sup>24</sup> and heart disease<sup>25</sup>, as well as age-related macular degeneration and cataract.<sup>26</sup> Supplementation with synthetic betacarotene, however, has produced mixed results, with two studies finding an increased lung-cancer risk in heavy smokers or those with high asbestos exposure.<sup>27,28</sup> This association, however, has not been found with natural betacarotene and authorities continue to recommend intake of betacarotene-rich foods.

At doses above 30 mg/day, betacarotene may cause an orange-yellow colouration of the skin (carotenoderma), which is harmless and reversible on reducing carotenoid consumption<sup>29</sup> and may even be considered desirable.<sup>22</sup> This effect is utilised in tanning tablets to produce a natural-looking skin tan.<sup>30</sup>



**Mudflats in Western Australia, where betacarotene is farmed from *Dunaliella salina* for commercial use. This area is believed ideal for dunaliella farming, as it has clean seawater supplies, high UV radiation, an optimal temperature range with very low rain fall**

#### Adverse effects

No adverse effects from consumption of the whole dunaliella have been reported. Carotenoderma may become evident after a few months of consumption but is harmless and reversible on discontinuation.

#### Precautions and contraindications

None known.

#### Pregnancy and lactation

Data are insufficient to recommend the use of dunaliella during pregnancy or breastfeeding.

#### Interactions

None known.

#### Clinical implications

On a gram-for-gram basis, microalgae may be the most nutrient-dense food on earth<sup>42</sup>, with minimal indigestible structures in contrast to higher plants or animals, which typically have less than half their dry weight being nutritionally useful.<sup>43</sup>

Microalgae contain a range of macro- and micronutrients, including chlorophyll, carotenoids, phytonutrients, amino acids, polysaccharides, essential fatty acids, carbohydrates, vitamins and bioavailable minerals. Thus, in contrast to the reductionist or pharmaceutical approach to nutrition that leads to supplementation with only a few (often synthetically produced) nutrients, microalgae provide a holistic mix of nutrients developed over millions of years of evolution. While research is accumulating that suggests microalgae has many health benefits, further research is required to determine their clinical applications. ▀

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