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## Food, Nutrition and Diet Therapy in Psoriasis

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### 1. Introduction

Diet has been suggested to play a role in the etiology and pathogenesis of psoriasis (Araujo et al., 2009; Wolters, 2005). Periods of fasting, a hypocaloric and vegetarian diet have been associated with an improvement in symptoms due to changes in the metabolism of polyunsaturated fatty acids (PUFAs) and an influence on the profile of eicosanoids, leading to suppression of the inflammatory process (Lithell et al., 1983; Rucevic et al., 2003; Wolters, 2005). The consumption of alcoholic beverages is prevalent among patients with psoriasis and is the greatest cause of the high mortality rate among individuals with moderate to severe forms of the disease and should therefore be avoided (Chistophers, 2001; Poikolainen et al., 1990; Smith & Fenske, 2000; Wolters, 2005). According to several authors, calcitriol (the active form of vitamin D) and its analogs have anti-proliferation, pro-differentiation and immune-regulating properties that may inhibit the growth and maturation of keratinocytes, with oral supplementation often suggested for patients who do not topically use calcitriol (Andorini, 2002; Holick, 2003; Wolters, 2005).

The skin acts as an interface between the body and surrounding environment, thus the skin is constantly exposed to both endogenous and exogenous pro-oxidants, leading to the generation of harmful oxidant species. Oxidative stress and the generation of excessive free radicals have been related to skin inflammation in psoriasis. Patients with this condition have reduced plasma levels of  $\beta$ -carotene and  $\alpha$ -tocopherol as well as a decline in serum selenium and high concentrations of malondialdehyde, which is a marker of lipid peroxidation in the plasma and red blood cells (Briganti & Picardo, 2003; Azzini et al., 1995; Serwin et al., 2003).

Data from literature indicates that the topical application or oral administration of antioxidants is suggested as preventive therapy for the natural aging of the skin and cancer caused by ultraviolet rays (Briganti & Picardo, 2003). With regard to lipids, studies have demonstrated the anti-inflammatory effect of fish oil in individuals with psoriasis, as diets rich in omega 3 modify the metabolism of PUFAs, thereby influencing the profile of eicosanoids, which leads to the suppression of the inflammatory process (Smith & Fenske, 2000). A number of authors report an association between latent sensitivity to gluten (pre-celiac disease state) and different skin diseases, including psoriasis, suggesting a gluten-free diet may provide beneficial effects (Duggan, 2004; Humbert et al., 2006; Leffler et al., 2003; Michaelsson et al., 2003; Nelson, 2002; Wolters, 2005).

The aforementioned data underscore the importance of studies on psoriasis, especially with regard to the influence of nutrition on the etiopathogenesis and treatment of this condition.

## **2. Influence of calorie intake, periods of fasting and vegetarian diet**

A number of studies report that symptoms of inflammatory disease, such as rheumatoid arthritis, can improve with a hypocaloric diet or during periods of fasting (Muller et al., 2001; Palmblad et al., 1991). Similarly, the prevalence and severity of psoriasis were shown to improve during periods of fasting and a hypocaloric diet, suggesting diet to be an important consideration for the prevention and treatment of the moderate non-pustular form of the disease (Rucevic et al., 2003; Wolters, 2005).

While various mechanisms have been discussed, the direct cause of these positive effects on the symptoms of psoriasis remains unknown (Wolters, 2005). The most important reason is likely a reduction in arachidonic acid (AA) intake, resulting in a lower production of inflammatory eicosanoids. During the fasting state, a reduction in the activation of TCD4 cells and an increase in the number and/or function of the anti-inflammatory cytokine interleukin 4 have been observed; Calorie restriction leads to a reduction in oxidative stress (Fraser et al., 1999; Wolters, 2005). However, the few studies that have addressed the effect of caloric restriction on psoriasis offer inconsistent data on the benefits of this conduct over a long period of time (Lithell et al., 1983; Rucevic et al., 2003). The results of evaluations carried out during World War I revealed that individuals with psoriasis experienced significant improvement during calorie restriction, with the recurrence of skin lesions after the reintroduction of a normal diet (Ricketts et al., 2010).

A vegetarian diet may be beneficial to all patients with psoriasis due to the reduction in AA intake and consequent reduction in the formation of inflammatory eicosanoids (Fraser et al., 1999).

## **3. Polyunsaturated fatty acids**

Lipids are macronutrients that perform energy, structural and hormonal functions in organisms. Fatty acids are monocarboxylic acids with a hydrocarbon chain of variable size and double bonds between carbon atoms. These substances are classified as monounsaturated and polyunsaturated, depending on the number of double bonds they contain. Fatty acids are integral compounds of nearly all lipids. Two series of PUFAs are differentiated, depending on the location of the first double carbon bond at the methyl radical. Linoleic acid, which is an essential fatty acid, belongs to the omega 6 family and is found in a large quantity of oleaginous seeds; this acid can be converted into AA, which is principally derived from meat and egg sources (Dutra-de-Oliveira, 2000). Eicosapentaenoic acid (EPA) and docosahexaenoic acid are the most abundant omega 3 fatty acids in food and are found mainly in cold-water fish, such as mackerel, sardine, salmon, herring, etc. (Wolters, 2005).

Besides their function in the phospholipid membrane, PUFAs are needed for the formation of eicosanoids, which are metabolic regulators (Jones & Papamandjaris, 2001). AA is a precursor of prostaglandins, leukotrienes and other compounds that have important functions in inflammation and the regulation of immunity, whereas EPA derivatives exhibit anti-inflammatory properties (Calder, 2001). High concentrations of AA and its pro-

inflammatory metabolites have been observed in psoriatic lesions as well as in other auto-immune and inflammatory disorders. Therefore, one treatment option for psoriasis may be the replacement of AA with an alternative fatty acid, especially EPA, which is metabolized through the same enzymatic pathways as AA (Mayser et al., 2002; Wolters, 2005).

Fish oil (omega 3), has been observed to change the serum and lipid composition of epidermal and blood cell membranes, which rationalizes its use in the treatment of psoriasis. High levels of AA are found in psoriatic lesions and it is believed that its metabolite, leukotriene B<sub>4</sub>, may be the mediator of inflammation in psoriasis (Ricketts et al., 2010). Thus, when omega 3 fatty acids are metabolized by cyclooxygenase or lipoxygenase in place of AA in the cell membranes, these substances may assist in reducing inflammation (Ricketts et al., 2010).

Conflicting results are reported regarding the effect of the oral supplementation of omega 3 on this disease and there are no clear findings regarding the dose to be employed (Mayser et al., 2002; Wilkinson, 1990). In vitro studies report that the addition of fish oil to the diet of individuals with psoriasis leads to an increase in EPA in relation to AA in the plasma and platelets, with a significant reduction in the synthesis of leukotriene B<sub>4</sub> (Ricketts et al., 2010).

Initial studies involving different amounts of EPA ranging from 3.6 to 14 grams per day for periods of six weeks to six months report some clinical improvement with minimal side effects; however, lower doses for a shorter period of time are reported to offer no significant improvement (Maurice et al., 1987; Ziboh et al., 1986; Kragballe & Fogh, 1989; Kojima et al., 1989). The majority of studies report positive results; however, less effective results are reported in randomized, controlled trials (Wolters, 2005). Despite the inconsistent results, the consumption of fish rich in omega 3 is recommended. Moreover, parenteral infusions of omega 3 may be beneficial to patients hospitalized with acute psoriasis (Wolters, 2005).

#### 4. Gluten

Celiac disease is an enteropathy associated with different extra-intestinal manifestations, such as anemia, transaminase elevation, osteopenia, neurological conditions, emotional and psychiatric disorders, auto-immune disease and dermatological problems. This disease is characterized by an allergy to gluten (a protein found in wheat, oats, rye and barley), leading to malabsorption and atrophy of the intestinal villi, which improves with a gluten-free diet (Abenavoli et al., 2006).

This gluten-sensitive enteropathy tends to be mildly symptomatic and even asymptomatic, which may explain the association between latent gluten sensitivity and psoriasis (Wolters, 2005). A number of studies report an association between celiac disease and psoriasis (Michaelsson et al., 2000; Woo et al., 2004). According to some authors, however, this association is controversial due to currently limited data (Addolorato et al., 2003; Collin & Reunal, 2003). Since both celiac disease and psoriasis are related to T helper 1 (Th1) cytokines, this association could be caused by the activation of Th1 by the interleukins IL1 and IL8, stemming from the rapid division of keratinocytes (Ojetti et al., 2003).

There is no consensus among current literature regarding the high prevalence of patients with psoriasis and antibodies associated to celiac disease (Ricketts et al., 2010). Thus, there

is a need for prospective studies in order to determine the incidence of celiac disease and the real percentage of increased levels of antigliadin, antiendomysial and anti-tissue transglutaminase antibodies in patients with psoriasis (Ricketts et al., 2010).

A gluten-free diet can improve skin lesions even in patients without celiac disease but with the antigliadin antibodies IgA and IgG, which are important to the diagnosis of celiac disease (Michaelsson et al., 2003). Likewise, studies indicate that a gluten-free diet leads to an improvement in rheumatoid arthritis, which is another chronic inflammatory disease (Hafstrom et al., 2001). Data remains scarce in regards to the mechanisms involved in the association between celiac disease, psoriasis and a gluten-free diet in skin lesions. A number of hypotheses have been raised, such as an alteration in intestinal permeability, immune mechanisms and vitamin D deficiency (Abenavoli et al., 2006).

## 5. Oxidative stress and antioxidants

The skin is constantly exposed to oxidants, which leads to the formation of harmful reactive oxygen species (Briganti & Picardo, 2003). Oxidative stress and the increased formation of free radicals have been related to skin inflammation and are reported to be among the most important factors in the pathogenesis of psoriasis (Kiyamat et al., 2003; Rocha et al., 2004; Relhan et al., 2002; Wolters, 2005). Studies demonstrate that individuals with psoriasis have high concentrations of malondialdehyde, a lipid peroxidation marker, and is compromised antioxidant status, with reduced levels of  $\beta$ -carotene,  $\alpha$ -tocopherol and selenium (Azzini et al., 1995; Briganti & Picardo, 2003; Serwin et al., 2003).

High alcohol intake (stemming from the psychosocial impact of the disease) and either active or passive smoking are among some of the factors that can increase oxidative stress and reduce levels of natural antioxidants in individuals with a history of the disease for more than three years (Lecomte et al., 1994; McKenzie, 2000; Monk & Neil, 1986; Naldi et al., 1992). The consumption of fruit and vegetables may be beneficial to such individuals due to the high antioxidant content, such as carotenoids, flavonoids and vitamin C, as an adequate antioxidant status is considered useful to the prevention of imbalance between oxidative stress and antioxidant defense (Naldi et al., 1996; Wolters, 2005). However, few studies have investigated the effects of antioxidant supplementation on the symptoms of psoriasis (Wolters, 2005).

## 6. Selenium

Selenium is an essential trace element with immune-modulating and anti-proliferative properties, with an influence over the immune response whether through a change in the expression of cytokines and respective receptors or by making immune cells more resistant to oxidative stress (Celerier et al., 1995; Roy et al., 1992; Spallholz et al., 1990). Moreover, data indicates that patients with inflammatory skin diseases, skin cancer, malignant melanoma and cutaneous T-cell lymphoma have low concentrations of selenium (Clark et al., 1984; Deffuant et al., 1984; Hinks et al., 1987; Michaelsson & Edqvist, 1984).

The low concentration of selenium found in patients with psoriasis may be a risk factor for the development of the disease. However, there are few studies on the role of this element in the pathogenesis (Hinks et al., 1987; Fairris et al., 1989; Michaelsson et al., 1989; Harvima et



al., 1993; Pinton et al., 1995; Azzini et al., 1995). Low levels of selenium are related to the severity of psoriasis and may occur due to low food intake or excessive flaking of the skin (Serwin et al., 2003). Serwin et al. (2003) found that selenium levels were significantly lower in patients with a diagnosis of psoriasis for more than three years in comparison to healthy volunteers (38.69 vs 48.41;  $p < 0.05$ ).

Kharaeva et al. (2009) demonstrated for the first time that the combination of conventional therapy and supplementation with vitamin E, co-enzyme Q10 and selenium resulted in an improvement in the clinical condition of patients with severe psoriasis as well as a reduction in oxidative stress. Supplementation using inorganic forms of selenium (sodium selenite and selenate) is also reported to lead to clinical improvement in patients with psoriasis (Fairris et al., 1989; Pinton et al., 1995).

## 7. Vitamin D

Vitamin D is a pro-hormone that can be produced from 7-dehydrocholesterol through the exposure of skin to ultraviolet B rays of the sun. Besides its importance in the homeostasis of calcium and bone metabolism, calcitriol (the active form of vitamin D) has effects on more than 30 types of tissue, including skin (Wolters, 2005). Vitamin D plays an important role in reducing the risk of a number of chronic diseases, such as auto-immune diseases, infectious diseases, cardiovascular diseases and some forms of cancer (breast, colon-rectal and prostate cancer) (Fu & Vender, 2011).

Vitamin D plays an essential role in cell proliferation, differentiation, apoptosis and angiogenesis. Vitamin D also has beneficial effects on inflammatory diseases mediated by Th1 lymphocytes, such as diabetes, psoriasis, Crohn's disease and multiple sclerosis (Cantorna et al., 2004; Holick, 2007; Ikeda et al., 2010). Vitamin D has proven to be highly effective in the treatment of psoriasis, as patients having received vitamin D for the treatment of osteoporosis exhibited an improvement in psoriasis (Abramovits, 2009; Smith et al., 2009; Van De Kerkhof, 2005). Due to the function of calcitriol and its analogs in psoriasis, oral supplementation with vitamin D should be considered in patients who do not make use of topical treatment with this vitamin, as vitamin D deficiency is frequent in these individuals (Holick, 2003; Wolters, 2005).

## 8. Vitamin B12

Data from the literature demonstrates the efficacy of using intramuscular and systemic vitamin B12 in patients with psoriasis in addition to the positive effects of topical vitamin B12 (Ricketts et al., 2010).

## 9. Zinc

Zinc deficiency has been associated with the presence of psoriatic plaque (Smith et al., 2009). However, there is little evidence on the benefits of oral supplementation as of yet (Burrows et al., 1994). Moreover, there are no recommendations regarding the amount or chemical form that offers the best beneficial effects.

## 10. Alcoholic beverages

The first studies on the association between psoriasis and the consumption of alcoholic beverages emerged in 1963. While some investigations have failed to demonstrate such an association, recent studies have shown a significant correlation (Wolf et al., 1999). Besides contributing to the development of psoriatic plaque, alcohol intake is involved in triggering periods of exacerbation, associated with a reduced response to treatment and the risk of liver toxicity associated to the use of methotrexate (Gupta et al., 1993; Higgins et al., 1994; Liu et al., 2010; Qureshi et al., 2010; Smith & Fenske, 2000).

The exact mechanism by which alcohol causes or aggravates psoriasis is not yet fully clarified. Some authors propose that alcohol induces immunological dysfunction, leading to immunosuppression, and increases the production of inflammatory cytokines and cell cycle activators, such as cyclin D1 and keratinocyte growth factor, which could lead to epidermal over-proliferation (Farkas et al., 2003; Ockenfels et al., 1996; Smith & Fenske, 2000). Moreover, the greater susceptibility to superficial infection observed in alcoholics, such as those caused by *Streptococcus* and trauma, has also been suggested in the development of psoriasis (Farkas et al., 2003).

Data from literature indicates that alcohol is a risk factor for psoriasis in young and middle-aged men and, while not a risk factor in women, alcohol intake aggravates the condition in this gender (Poikolainen et al., 1994). Patients with psoriasis are recommended to exercise with caution when consuming alcohol, especially during periods of exacerbation. Moreover, due to all possible effects, a number of authors recommend abstention (Behnam et al., 2005; Wolters, 2005). Thus, identifying this risk factor in patients with psoriasis could contribute toward a reduction in episodes of exacerbation, thereby achieving better treatment results (Kazakevich et al., 2011).

## 11. Obesity

The first associations between psoriasis and obesity were reported in large epidemiological studies carried out in Europe (Duarte et al., 2010). A pioneering American study conducted in the state of Utah reports a 34% prevalence of obesity among individuals with psoriasis, which is much higher than the 18% reported in the general population (Herron et al., 2005).

Obesity is known to cause a state of chronic inflammation, with high levels of TNF- $\alpha$ , IL-6 and C-reactive protein, which are associated to the progressive increase in body mass index (BMI). In this state of chronic inflammation, alterations in resistance/sensitivity to insulin and greater oxidative stress, with the production of free radicals, lead to a greater likelihood of the development of diabetes and metabolic syndrome as well as the influence of these pro-inflammatory cytokines in the course and presentation of psoriasis (Hamminga et al., 2006; Wakkee et al., 2007). The association between obesity and psoriasis has been well established, as obesity can increase the risk of developing psoriasis and preexisting psoriasis can increase the risk of patients becoming obese (Farías et al., 2011).

Non-pharmacological treatment aimed at changes in lifestyle should be offered to all patients, especially those with a BMI  $\geq 25$  kg/m<sup>2</sup>, for whom the goal is controlled, healthy weight loss (Farías et al., 2011). A low-calorie diet is recommended, following the Step I diet (Obesity Society, 2000) (Table 1), with a calorie restriction of 500 to 1000 kilocalories per day, based on the patient's energy expenditure, which can be determined through measurement

techniques such as indirect calorimetry or through mathematical formulas such as the Harris-Benedict equation (Table 2) (Frankenfield et al., 1998). For greater compliance to treatment and patient follow up, the participation of a nutritionist is needed to individualize the treatment, considering all socioeconomic and cultural aspects. Farías et al (2011) suggests the recommendations of the Nutrition Committee of the American Heart Association (Table 3 e Table 4).

Nutrient	Recommendation intake
Reducing calories	Approximately 500 to 1,000 kilocalories / day
Total fat	< 30% of total calories
Saturated fat	8 a 10% of total calories
Monounsaturated fat	≤15% of total calories
Polyunsaturated fat	≤10% of total calories
Total cholesterol	<300 mg / day
Proteins	Approximately 15% of total calories
Carbohydrates	At least 55% of total calories
Sodium	100 mmol / day (approximately 2.4 g of sodium)
Calcium	1.000 to 1.500 mg/Day
Fiber	20 a 30 g/Day

Table 1. Diet Step 1 (Obesity Society, 2000).

Women	$BMR = 655 + (4.35 \times \text{weight in pounds}) + (4.7 \times \text{height in inches}) - (4.7 \times \text{age in years})$
Men	$66 + (6.23 \times \text{weight in pounds}) + (12.7 \times \text{height in inches}) - (6.8 \times \text{age in years})$

Table 2. Basal metabolic rate according to the Harris Benedict formula.

Balance calorie intake and physical activity to achieve or maintain a healthy body weight.
Consume a diet rich in vegetables and fruits.
Choose whole-grain, high-fiber foods
Consume fish, especially oily fish, at least twice a week.
Limit your intake of saturated fat to _7% of energy, <i>trans</i> fat to _1% of energy, and cholesterol to _300 mg per day by <ul style="list-style-type: none"><li>-Choosing lean meats and vegetable alternatives;</li><li>– Selecting fat-free (skim), 1%-fat, and low-fat dairy products; and</li><li>– Minimizing intake of partially hydrogenated fats.</li></ul>
Minimize your intake of beverages and foods with added sugars.
Choose and prepare foods with little or no salt.
If you consume alcohol, do so in moderation.
When you eat food that is prepared outside of the home, follow the AHA Diet and Lifestyle Recommendations.

Table 3. Diet and Lifestyle Recommendations for Cardiovascular Disease Risk Reduction (American Heart Association Commitee Nutrition, (AHA) 2006).



<b>Lifestyle</b>	<ul style="list-style-type: none"><li>• Know your caloric needs to achieve and maintain a healthy weight.</li><li>• Know the calorie content of the foods and beverages you consume.</li><li>• Track your weight, physical activity, and calorie intake.</li><li>• Prepare and eat smaller portions.</li><li>• Track and, when possible, decrease screen time (eg, watching television, surfing the Web, playing computer games).</li><li>• Incorporate physical movement into habitual activities.</li><li>• Do not smoke or use tobacco products.</li><li>• If you consume alcohol, do so in moderation (equivalent of no more than 1 drink in women or 2 drinks in men per day).</li></ul>
<b>Food choices and preparation</b>	<ul style="list-style-type: none"><li>• Use the nutrition facts panel and ingredients list when choosing foods to buy.</li><li>• Eat fresh, frozen, and canned vegetables and fruits without high-calorie sauces and added salt and sugars.</li><li>• Replace high-calorie foods with fruits and vegetables.</li><li>• Increase fiber intake by eating beans (legumes), whole-grain products, fruits, and vegetables.</li><li>• Use liquid vegetable oils in place of solid fats.</li><li>• Limit beverages and foods high in added sugars. Common forms of added sugars are sucrose, glucose, fructose, maltose, dextrose, corn syrups, concentrated fruit juice, and honey.</li><li>• Choose foods made with whole grains. Common forms of whole grains are whole wheat, oats/oatmeal, rye, barley, corn, popcorn, brown rice, wild rice, buckwheat, triticale, bulgur (cracked wheat), millet, quinoa, and sorghum.</li><li>• Cut back on pastries and high-calorie bakery products (eg, muffins, doughnuts).</li><li>• Select milk and dairy products that are either fat free or low fat.</li><li>• Reduce salt intake by<ul style="list-style-type: none"><li>- comparing the sodium content of similar products (eg, different brands of tomato sauce) and choosing products with less salt;</li><li>- choosing versions of processed foods, including cereals and baked goods, that are reduced in salt; and</li><li>- limiting condiments (eg, soy sauce, ketchup).</li></ul></li><li>• Use lean cuts of meat and remove skin from poultry before eating.</li><li>• Limit processed meats that are high in saturated fat and sodium.</li><li>• Grill, bake, or broil fish, meat, and poultry.</li><li>• Incorporate vegetable-based meat substitutes into favorite recipes.</li><li>• Encourage the consumption of whole vegetables and fruits in place of juices.</li></ul>

Table 4. Practical Tips to Implement AHA 2006 Diet and Lifestyle Recommendations.

## 12. Psoriasis and metabolic syndrome

Metabolic syndrome is a set of metabolic alterations, particularly insulin resistance, which, together, lead to a greater risk of pro-inflammatory and pro-thrombotic alterations. A number of studies have suggested an increase in the prevalence of the components of metabolic syndrome in patients with psoriasis (Cohen et al., 2008; Neimann et al., 2006; Sommer et al., 2006).

Patients with psoriasis have a greater prevalence of metabolic syndrome in comparison to those with other dermatological conditions (30.1% vs 20.6%; OR: 1.65; 95%CI: 1.16 to 2.35) (Gisondi et al., 2007). However, few studies have considered the possibility of associating the treatment for psoriasis with the components of metabolic syndrome (Fu & Vender, 2011). A case report of a patient with psoriasis and metabolic syndrome suggests that the treatment program designed by nutritionists and endocrinologists through the modification of diet and treatment of comorbidities provided an improvement in blood glucose, cholesterol and BMI, along with a clinical improvement in psoriasis (Saraceno et al., 2008).

## 13. Conclusion

Diet is an important factor in the etiology and pathogenesis of psoriasis. Low-calorie and vegetarian diets may be beneficial to the treatment of this condition. Although the results regarding the oral supplementation of fish oil are inconsistent, patients are recommended to consume fish rich in omega 3 PUFAs and parenteral infusions of PUFAs are recommended for patients hospitalized with acute psoriasis. Further studies are needed to clarify the role of a gluten-free diet, which may improve the severity of the disease in patients with IgA and/or IgG antigliadin antibodies. Moreover, the consumption of fruit and vegetables may be beneficial due to their high antioxidant content. Vitamin D is an important treatment option due to its immuno-regulating and anti-proliferation activity. Patients with psoriasis should not consume alcoholic beverages in order to avoid exacerbation of the disease.

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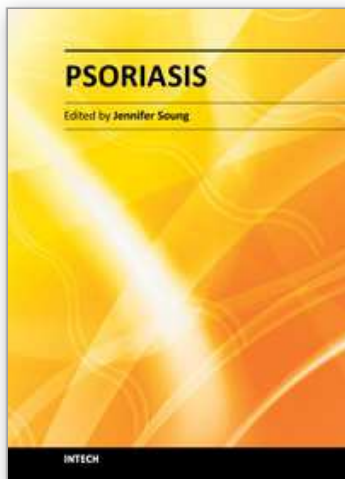
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Edited by Dr. Jennifer Soung

ISBN 978-953-307-878-6

Hard cover, 372 pages

**Publisher** InTech

**Published online** 15, February, 2012

**Published in print edition** February, 2012

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Maria Lucia Diniz Araujo, Paulla Suylane Santos Fernandes Costa and Maria Goretti Pessoa de Araujo Burgos (2012). Food, Nutrition and Diet Therapy in Psoriasis, Psoriasis, Dr. Jennifer Soung (Ed.), ISBN: 978-953-307-878-6, InTech, Available from: <http://www.intechopen.com/books/psoriasis/food-nutrition-and-diet-therapy-in-psoriasis>

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