Antioxidants in vegan diet and rheumatic disorders

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Abstract

Plants are rich natural sources of antioxidants in addition to other nutrients. Interventions and cross sectional studies on subjects consuming uncooked vegan diet called living food (LF) have been carried out. We have clarified the efficacy of LF in rheumatoid diseases as an example of a health problem where inflammation is one of the main concerns. LF is an uncooked vegan diet and consists of berries, fruits, vegetables and roots, nuts, germinated seeds and sprouts, i.e. rich sources of carotenoids, vitamins C and E. The subjects eating LF showed highly increased levels of beta and alfa carotenes, lycopen and lutein in their sera. Also the increases of vitamin C and vitamin E (adjusted to cholesterol) were statistically significant. As the berry intake was 3-fold compared to controls the intake of polyphenolic compounds like quercetin, myricetin and kaempherol was much higher than in the omnivorous controls. The LF diet is rich in fibre, substrate of lignan production, and the urinary excretion of polyphenols like enterodiol and enterolactone as well as secoisolaricirecinol were much increased in subjects eating LF. The shift of fibromyalgic subjects to LF resulted in a decrease of their joint stiffness and pain as well as an improvement of their self-experienced health. The rheumatoid arthritis patients eating the LF diet also reported similar positive responses and the objective measures supported this finding. The improvement of rheumatoid arthritis was significantly correlated with the day-to-day fluctuation of subjective symptoms. In conclusion the rheumatoid patients subjectively benefited from the vegan diet rich in antioxidants, lactobacilli and fibre, and this was also seen in objective measures.

Keywords: Antioxidants; Living food; Lactobacilli and fibre

1. Introduction

Plant materials constitute the main part of our normal food. At present various vegetarian diets are gaining more interest in western societies on ethical and/or nutritional basis.

Some populations live exclusively on plant items (vegans) (Dwyer, 1991). Most Seventh Day Adventists prefer a lacto-vegetarian diet, and they have often been examined as a model population in studies of health and diet (Mills et al., 1994).
Epidemiological studies have shown that the consumption of several plant foods have statistically significant association with lessened coronary heart disease risk (Fraser, 1994). The high levels of both water and lipid phase antioxidants diminish the risk of lipid peroxidation. The oxidized lipids increase the risk of cardiovascular diseases, and vegetarians have significantly less oxidized LDL as well as an increased total antioxidant status and molar ratio vitamin E/cholesterol, which all indicate a more effective protection of lipoproteins against oxidation (Nagyova et al., 1998). In addition, the populations that eat mostly vegetarian diets may also have a lower risk for constipation, diverticular disease, gallstones and appendicitis (Key et al., 1999). Cancer is related to the radical reactions. The risk to die in some forms of cancer may be lowered by vegetable rich diets (e.g. Steinmetz and Potter, 1991). Vegetarian men have lower incidence of prostate cancer than omnivorous males (Denis et al., 1999).

Plants face heavy load of light. UV light generates radicals in their tissues. Furthermore during photosynthesis oxygen in statu nascendi is generated in their chloroplasts. When the plants are oxidizing nutrients, their mitochondria are releasing oxygen-derived radicals like in the animal cells. All this means that plants must be very well prepared to meet the challenges of the oxygen radical stress and contain a broad variety of antioxidant chemicals. Plants have also antioxidant enzymes (e.g. Roy, 1994).

Metabolic radicals are either the cause or outcome of several disease processes. The plants in diet thus provide many kinds of compounds to help the antioxidant defence in patients.

Living food is an extreme uncooked vegan diet developed by Wigmore (1990) in United States. The diet consists of vegetables, roots, fruits, berries, germinated seeds, cereals, sprouts and nuts. The diet contains no coffee, tea, alcohol or table salt. Diet has thus very low Na content. It contains no cholesterol, and its lipids are rich in unsaturated fatty acids (Hänninen et al., 1992; Ågren et al., 1995).

Vegetable rich diets contain much fibre. Fibre promotes the gut function. Both these elements significantly affect the gut microflora. We have shown that intestinal microflora is much changed when people adopt LF diet, and when they switch back to their omnivorous diet the changes are reversed (Peltonen et al., 1992). Several LF items are fermented, and they contain a lot of lactobacilli (Mantere-Alhonen and Ryhänen, 1994). As one could expect the number of lactobacilli increased also in the faecal samples, when the people started to eat the LF diet (Ryhänen et al., 1993).

Microflora uses fibre components also as substrates. Not only short-chain fatty acids, but also beneficial lignans (Adlercreutz, 1998) and less harmful phenolic compounds are produced (Hänninen et al., 1992).

Rheumatoid disorders disable significant numbers of people by pain and other symptoms. The pathophysiology of rheumatoid disorders is poorly understood. Inflammation is, however, one of the features. Some rheumatoid patients had spontaneously adopted the living food diet, and they had provided anecdotal evidence on benefits in their problems. We have been able to confirm the subjective benefits and provide objective support, too.

The aim of the present paper was to examine the effectiveness of the living food on the symptoms of fibromyalgia and rheumatoid arthritis patients and discuss the relation of the symptoms to the antioxidants and other diet components.

2. Subjects and methods

We studied the health parameters of 20 volunteered long term users (up 14 years) of LF diet and their controls (n = 20) as well as 33 fibromyalgic subjects (divided into living food intervention and omnivorous controls) and 42 rheumatoid arthritis patients (divided again into LF intervention lasting 3 months and omnivorous control groups). The patient intervention groups returned back to their previous omnivorous diets after the experiments. The study plan was approved by the Ethics Committee of the University of Kuopio and the Helsinki City Hospitals.
The long-term LF users and the fibromyalgic subjects prepared their diets themselves after learning that in special courses. The rheumatoid arthritis subjects obtained, however, their food premade in a specialized kitchen. The compliance of the subjects was followed by analyzing their daily urinary sodium excretion, which should drop to a fraction when subjects consume LF.

All the subjects reported their food behaviours using questionnaires and if necessary diet specialist helped them. The intakes of nutrients were calculated using specialized data banks containing the living food analysis data and Nutrica program, which contains the data of Finnish conventional foods. The flavonols of Finnish berries were analyzed using methods described in detail in Hääkkinen et al. (1999).

The qualified specialized clinicians evaluated the health of the subjects during the studies. Patients reported their subjective symptoms using standardized questionnaires with the help of the clinicians. To estimate the activity of rheumatoid arthritis we created a relative activity index (RAI), which highly correlates \( r = 0.92, P = 0.0001 \) with DAS index (Scott et al., 1993). To estimate the amount of subjective adaptation symptoms we followed daily estimates of our test group on visual analogue scales. A similar composite index was calculated by summarizing the day-to-day changes (absolute values) of following variables: feeling of effectiveness, feeling of energy, mood, tiredness and amount of hours slept. The higher the sum of changes in each variable was, the more fluctuation the person had experienced. These sums were transformed into normalized rank scores and summarized in analogous manner with RAI (Nenonen, 1995; Nenonen et al., 1998).

The biochemical parameters of the subjects were analyzed using standard methods of clinical chemistry. Serum carotenoids were extracted using the method described by Folch et al. (1957) and the quantitation was made using the method described by Nellis and De Leenheer (1983). The analysis of the daily urinary lignans and related compounds was carried out as described by Adlercreutz et al. (1995).

### 3. Results

#### 3.1. Antioxidant and lignan levels

Food items like berries and vegetables are rich in antioxidants such as carotenoids and flavonoids. Fig. 1. gives the flavonol contents of some berries eaten by the LF users in significant amounts.

The subjects eating LF diet can get very high amounts of quercetin, kaempherol and myricetin in their diet, and intake can exceed the Finnish average values (1.24 mg/day, Hääkkinen et al., 1999) more than 10-fold Table 1.

All the plants contain high amounts of antioxidant vitamins C and E. Serum vitamin C levels cannot much increase in subjects on vegan diets due to fast urinary excretion of this vitamin, but
Table 1
Daily consumption of berries and calculated daily intakes of flavonols quercetin, kaempherol and myricetin (calculated from their 5-day dietary records); three typical examples of living food users

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<tr>
<th></th>
<th>HH</th>
<th>AH</th>
<th>MR</th>
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<tbody>
<tr>
<td>Amount berries eaten</td>
<td>240</td>
<td>207</td>
<td>199</td>
</tr>
<tr>
<td>g/day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No berry species</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Quercetin mg/day</td>
<td>2.35</td>
<td>4.22</td>
<td>17.90</td>
</tr>
<tr>
<td>Kaempherol mg/day</td>
<td>1.53</td>
<td>0.51</td>
<td>0.41</td>
</tr>
<tr>
<td>Myricetin mg/day</td>
<td>1.18</td>
<td>3.94</td>
<td>2.50</td>
</tr>
<tr>
<td>Total mg/day</td>
<td>5.05</td>
<td>8.68</td>
<td>20.80</td>
</tr>
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</table>

* Berries consumed were black currant (*Ribes nigrum*), red currant (*Ribes x pallidum*), blueberry (*Vaccinium myrtillus*), raspberry (*Rubus idaeus*), rowanberry (*Sorbus aucuparia*), sea buckthorn berry (*Hippophae rhamnoides*) and strawberry (*Fragaria x ananassa*).

still the increase was statistically significant as was also vitamin E cholesterol ratio (Rauma et al., 1995b). The subjects on LF diet obtained significantly higher amounts of various carotenoids, too. The serum levels of beta and alfa carotenes as well as those of lycopene and lutein were, in contrast to above mentioned vitamins, several folds higher in long term users of the living food than in the omnivorous controls (Fig. 2).

When the subjects were on the living food diet the daily urinary excretion of lignans like enterodiol and enterolactone was about ten fold and that of secoisolariciresinol about three times higher than in the omnivorous controls (Table 2).

3.2. Rheumatoid symptoms

The rheumatoid patients reported significant subjective alleviation of their symptoms, when they started to eat living food diet, and the symptoms got worse, when they returned back their previous omnivorous diet. The composite indices of objective measures showed also improvement of the rheumatoid arthritis patients during the intervention (Nenonen, 1995; Nenonen et al., 1998). In a closer examination we found that there was a significant correlation of the degree of subjective adaption and the decrease in the activity of rheumatoid arthritis ($P = 0.03$). The correlation coefficient was negative depicting that those persons with highest value of day-to-day fluctuation of subjective symptoms linked with the diet had also the greatest decrease of disease activity. On the other hand, both the patients on LF diet and their omnivorous controls behaved in the same manner (Fig. 3).

When the fibromyalgic subjects adopted the LF diet, a number of positive results were recorded. The results on their joint stiffness ($P = 0.001$) (Fig. 4A) and pain (visual analogue scale) ($-0.38, P = 0.003$) (Fig. 4B) as well as their general health improved.

4. Discussion

The present results showed that the subjects on vegan diet called living food obtained a lot of various antioxidants in their food compared to their omnivorous controls. The blood and urine analyses showed that the antioxidants like carotenoids and some polyphenolic compounds were also absorbed and very high levels were found in their sera or daily urine. Also vitamin C and E (related to cholesterol) were increased in blood. These compounds are known to damp down the propagation of the radical chain reactions. The SOD activity in the red cells was increased, too (Rauma et al., 1995b).

The rheumatoid disorders are typical chronic inflammatory diseases. LF diet seems to be associated with both subjective and objective improvements of rheumatoid symptoms (Nenonen, 1995; Nenonen et al., 1998). The significant subjective alleviation of the symptoms could be due to increased levels of antioxidants in the blood and most probably also in the affected tissues, and the action of radicals is dimished.

The advocates of LF diet link the positive effects of the diet with the so called subjective adaptation symptoms experienced during the first weeks to months on the new diet. The present analysis does not support this hypothesis. The relations between these mental symptoms and disease activity seems not to be linked with the diet, because it was seen both in intervention and control groups. What comes to gastrointestinal
adaptation symptoms, the situation is different. Here the change in the intestinal microflora is linked with the improvement of rheumatoid symptoms (Peltonen et al., 1997). Thus it seems probable that the positive effects of the diet are mediated more by its microbiologic effects than its subjective and mental effects.

The chemical loading of the body increases the metabolism of xenobiotics in the liver and other tissues. Thus also the production reactive metabolites from these substrates as well as also reactive oxygen metabolites increases. Gut bacteria convert aromatic amino acids of both exogenous and endogenous proteins to phenols. Phenols are generally toxic. The adoption of the LF diet caused a drop of both phenol and para-cresol levels in blood as well as in the daily urinary output (Hänninen et al., 1992). This alleviates the radical load of the subjects and may also contribute to the lessened symptoms in rheumatoid patients.

The highly increased fibre intake promotes the gut mobility and lessen the time available for absorption of harmful compounds from the gut, too. This may contribute to the lowered availability of substrates, fall in serum levels as

![Graph showing serum carotenoids](image)

**Fig. 2.** The serum carotenoids (lutein, lycopene, alfa carotene and beta carotene) of eight long term users of living food (A) and their omnivorous controls (B) presented so that all the high pressure liquid chromatograms detected at 445 nm wavelength, arbitrary absorbance units) are exposed over each other. The runs show that the level of some so far unidentified carotenes show also much higher levels in the sera of vegans.
Table 2
Urinary excretion of lignans and isoflavonoids in middle-aged women eating living food and their omnivorous controls

<table>
<thead>
<tr>
<th>Compounds</th>
<th>Mixed food</th>
<th>Living food</th>
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<tbody>
<tr>
<td>Lignans</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Matairesinol (nM/day)</td>
<td>65 ± 2</td>
<td>62 ± 2</td>
</tr>
<tr>
<td>(31–181)</td>
<td>(13–148)</td>
<td></td>
</tr>
<tr>
<td>Secoisolariciresinol (nM/day)</td>
<td>224 ± 2</td>
<td>603 ± 2</td>
</tr>
<tr>
<td>(117–360)</td>
<td>(110–2486)</td>
<td></td>
</tr>
<tr>
<td>Enterodiol (nM/day)</td>
<td>933 ± 4</td>
<td>13,490 ± 10</td>
</tr>
<tr>
<td>(273–6010)</td>
<td>(129–65,416)</td>
<td></td>
</tr>
<tr>
<td>Enterolactone (µM/day)</td>
<td>4 ± 4</td>
<td>46 ± 3</td>
</tr>
<tr>
<td>(0.3–32)</td>
<td>(6–214)</td>
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<tr>
<th>Isoflavonoids</th>
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<tr>
<td>Daidzein (nM/day)</td>
<td>347 ± 8</td>
<td>245 ± 4</td>
</tr>
<tr>
<td>(20–8398)</td>
<td>(12–662)</td>
<td></td>
</tr>
<tr>
<td>O-Demethylangolensin (nM/day)</td>
<td>17 ± 12</td>
<td>9 ± 4</td>
</tr>
<tr>
<td>(0–1634)</td>
<td>(0–36)</td>
<td></td>
</tr>
<tr>
<td>Equol (nM/day)</td>
<td>63 ± 2</td>
<td>5 ± 5</td>
</tr>
<tr>
<td>(32–130)</td>
<td>(0–38)</td>
<td></td>
</tr>
<tr>
<td>Genistein (nM/day)</td>
<td>93 ± 2</td>
<td>76 ± 3</td>
</tr>
<tr>
<td>(9–2986)</td>
<td>(33–225)</td>
<td></td>
</tr>
</tbody>
</table>

Table 2: Urinary excretion of lignans and isoflavonoids in middle-aged women eating living food and their omnivorous controls.

compounds can promote the general health of rheumatoid subjects. When the subjects started to eat LF diet, we observed also a radical change in the faecal urease activity, which dropped to about one third of the previous level and returned back to it after the readoption of the omnivorous diet. Urease hydrolyzes urea to ammonia, which is quite toxic. Also the faecal beta-glucuronidase activity fell. This enzyme hydrolyzes various glucuronides, and the lipophilic aglycones are absorbed to increase the chemical loading of the body (Ling and Hänninen, 1992).

The dramatic change of the intestinal microflora and its metabolism may also significantly contribute to the diminution of the rheumatoid symptoms. The results obtained indicated that the greater was the change in the microflora the better was the condition of rheumatoid arthritis patients (Peltonen et al., 1997). Lactobacilli are generally considered healthy, and their number increased one order of magnitude in the faeces of living food eaters (Ryhänen et al., 1993).

The intestinal mucosa is not completely impermeable to macromolecules. Some components of
Fig. 4. The subjective self evaluation of the symptoms (morning stiffness (A) and pains at rest (B), visual analogue scale) and their alleviation in fibromyalgic subjects and their alleviation during the living food period and reagravation afterwards compared to their fibromyalgic controls. (Light columns the intervention and dark columns the omnivorous control group of fibromyalgic subjects.)
the microbial structures pass through the barrier and find their way into the blood stream. One theory suggests that these fragments initiate the formation of antibodies that attack also the normal components of the tissues because they are so similar with the bacterial glycopolysaccharides (e.g. Peltonen, 1994). Therefore the extensive change of the intestinal microflora could lower the antigenic stimulus and lessen the autoimmune side reactions.

Even if the LF diet provides equal amounts of energy than the omnivorous diet, its physiological availability appears to be poorer than of the conventional diet. For instance the fibromyalgic subjects who adopted LF diet and were eating it ad libitum lost weight (Kaartinen et al., 2000). Rheumatoid patients have locomotor problems. Weight loss is therefore positive, if the subject is overweight.

Food is one of the basic matters in the physiological health promotion. The different vegetarian diets are getting popular among people who are becoming more aware of their potential health advantages. Some adopt the vegetarian diets also from ethical reasons, because in the meat production the conversion of feed to product is usually poor and deterioration of nature is of general concern. Plant foods are often much richer in taste. The vegan diets may cause, however, also problems.

It is well documented that vegan diet poses especially infants and young children to vitamin B-12 deficiency. However, this risk is relevant also for adult vegans. Manifestation of symptoms depend on several personal factors including time on vegan diet, the size of stores and the efficiency of the enterohepatic circulation (Herbert, 1994).

In our studies the subjects having eaten living food for several years showed quite variable levels of serum vitamin B-12 (Rauma et al., 1995a). None of the subjects had any clinically detectable problems of vitamin B-12 deficiency even, when the measured serum level was low. Some subjects who had been on this diet for years showed normal vitamin B-12 levels (Rauma et al., 1995a). In spite of this living food eaters should not rely on living food as a sole source of vitamin B-12, but supplement their diet with this vitamin.

Pain and other symptoms tend to immobilize rheumatoid patients. Low physical activity means a risk of osteoporosis. Another problem in vegan diet is the scanty supply of calcium combined to low dietary intake of vitamin D (Outila et al., 1998). This is especially harmful for growing children but also for vegans of all ages. Hence, careful individual dietary planning combined to calcium and vitamin D supplementation is recommended. The rather low intake of calcium in vegetarian diet increases the osteoporosis risk. The low intake of calcium can be compensated by the low intake of sodium chloride in the living food diet, because the sodium excretion in urine is related to the calcium output, i.e. the lower sodium excretion can save the calcium stores in the body (Cirillo et al., 1997).

One can conclude from our studies that the patients of rheumatoid diseases appear to benefit both subjectively and objectively from the vegan diet rich in various antioxidants, fibre and lactobacilli.

References


