Chapter 25

Seabuckthorn Oils, Mucous Membranes and Sjögren's Syndrome with Special Reference to Latest Studies

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SUMMARY

The beneficial effects of the oils from the seeds, fruit flesh and peel of seabuckthorn (*Hippophae rhamnoides*) on the mucous membranes have been widely reported. The latest studies have shown positive effects of orally taken seabuckthorn oil capsules on chronic inflammation of female genital tract mucosa. Dry mouth, dry eyes, dry and inflammatory mucosa in the female genital tract and problems in the gastro-intestinal mucosa are typical symptoms of Sjögren's syndrome. Medicinal solutions to these problems are scanty. Supplementation of seabuckthorn oil may present an effective way of dietary management of Sjögren's syndrome. Largely due to different origins of raw material and processing technologies, compositional variation among seabuckthorn oils of different sources is extremely high. Carefully optimized and standardized composition is of vital importance for achieving optimal and stable health effects of seabuckthorn oils.

Keywords: *Seabuckthorn oil, Hippophaë rhamnoides, mucous membranes, Sjögren's syndrome.*

INTRODUCTION

Seabuckthorn berry is rich in oil both in seeds (seed oil) and in the fruit soft parts *i.e.* flesh and peel (pulp oil). Seeds contain typically around 10 per cent oil, whereas the oil content in the soft parts

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varies over a much wider range from 0.5 to 10 per cent (f. w.), largely depending on origins and varieties. Seabuckthorn seed oil and pulp oil differ considerably in fatty acid composition (Table 25.1). While linoleic (18:2n-6) and α-linolenic (18:3n-3) acids are the major fatty acids in the seed oil, the high level of palmitoleic acid (16:1n-7, up to 50 per cent) differentiates seabuckthorn pulp oil from most other oils of plant origin. Both the seed and pulp oils are rich in tocopherols, tocotrienols and plant sterols. In addition, the pulp oil contains especially high level of carotenoids (Table 25.1).

Table 25.1: Composition of Oils from Seed and Soft Parts of Seabuckthorn Berry (1, 2)

	Fatty Acids (Weight %)						
	Palmitic	*Palmitoleic*	*Stearic*	*Oleic*	*Vaccenic*	*Linoleic*	*α-Linolenic*
	16:0	16:1n-7	18:0	18:1n-9	18:1n-7	18:2n-6	18:3n-3
Seed oil	6-10	< 0.5	2-4	15-20	2-4	35-40	20-35
Pulp oil	15-40	15-50	1-2	10-20	5-10	5-15	5-10

	Carotenoids (mg/100 g)	*Plant Sterols (Weight %)*	*Tocopherols and Tocotrienols (mg/100 g)*
Seed oil	10-50	1-2	100-200
Pulp oil	100-400	2-3	100-400

SEABUCKTHORN OIL AND HEALTH OF MUCOUS MEMBRANES

Mucous membranes cover the digestive, respiratory, and urogenital tracts and the inner surface of eyes. Mucous membranes are important channels for interactions and substance exchanges between human body and the environment. They are often the major routes for pathogens and external toxins and allergens to enter the body. Health condition of mucous membranes plays an important role in the general well-being of the whole body. Mucous membranes are constantly under the challenges of genetic deficiencies, diseases, stress, ageing, side effects of medical treatments and environmental factors such as air and water pollutes. As a result, people often suffer from irritated mucous membranes. Dryness, high sensitivity and inflammation of mucous membranes are commonly found even among those generally considered as healthy. Furthermore, medical solutions for problems of mucous membranes are rather limited and often unsuccessful.

Dietary management with food supplements and nutraceuticals providing nutritional supports are initial measures to maintain the health of mucous membranes. Nutrients such as lipids and proteins are essential for the normal structure and function and regeneration of mucous membranes. Antioxidants protect membrane lipids from oxidation. Seabuckthorn seed and pulp oils combine high levels of beneficial fatty acids, natural antioxidants and vitamins as well as plant sterols. Clinical studies and animal experiments have shown multiple beneficial effects of the oils on mucous membranes (Table 25.2). Promoting tissue regeneration, improving immune function and reducing lipid peroxidation are clearly the fundamentals of these effects.

Gastric Mucosa

In a clinical experiment involving thirty cases of peptic ulcer (3), the patients took orally twelve seabuckthorn oil capsules daily for one month. A cure rate of 76.6 per cent and a total effective rate of 96.7 per cent were reported. Seabuckthorn oil was also used as an adjuvant treatment of 116 peptic ulcer patients, 71 with duodenal ulcer and 45 with gastric ulcer. Oral application of seabuckthorn oil

relieved pain and accelerated the repair process of gastric and duodenal epithelial tissue and mucosa (4). Protective and curative effects of seabuckthorn seed and pulp oils against gastric ulcer have been extensively investigated using animal models.

Table 25.2: Effects of Seabuckthorn Oils on Mucous Membranes (1)

Effects	*Study*	*Comments*
Gastric and duodenal mucosa	· Clinical trials	· Clear effects
· Protect and strengthen mucosa	· Animal experiments	· More studies on biochemical mechanism needed
· Cure ulcers		
· Reduces gastric secretion		
Urogenital mucosa	· Clinical practice	· Mostly case reports and clinical practice
· Cure cervicitis	· Case reports	
· Antiinflammation		
Mouth mucosa	· Clinical trials	· Mostly case reports and clinical practice
· Speed up recovery and reparation of stomatitis and esophagitis	· Animal experiments	
· Improve symptoms of dry mouth		
Anti-inflammation	· Clinical trials	· Results of studies support health claims from traditional use and clinical practice
· Heal burns, wounds, scalds	· Animal experiments	
· Promote tissue regeneration	· Clinical practice	
· Antiinflammatory and analgesic effects		
Anti-oxidation	· Animal and *in vitro* studies	· Well designed experiments with promising results.
· Reduce peroxidation of cell membrane	· *In vivo* studies in man	· Maybe a fundamental mechanism related to most beneficial effects
· Maintain membrane structure and functions.		
· More effective than pure vitamin E		
Improve immune function	· Animal experiments	· Well designed experiments,
· Improve specific and nonspecific immune functions	· Clinical studies	· Conclusions based on results of animal experiments and clinical study
· Antagonise the effects of immune suppressants		
Safety	· Animal studies	· Isolated from an edible berry
· No side effects reported	· Clinical experience	· Safe to use

Intragastric seed oil protected rat gastric mucosa from reserpine-, water-immersion- and pylorus-ligation-induced ulcer (5-7). Seed oil speeded up the healing of acetic-acid- and reserpine-induced ulcers (7, 8). In these studies, seabuckthorn oil treatment decreased the ulcer index by 40-60 per cent. Similar studies showed ulcer preventive and curative effects of oils from pulp/peel (7-9) and whole berries of seabuckthorn (7, 10). Oil isolation technology may have an impact on the antiulcerative efficacy of seabuckthorn oils by influencing the oil compositions. Figure 25.1 presents antiulcerative effects of seabuckthorn seed oil and pulp oil extracted by supercritical CO_2 (7).

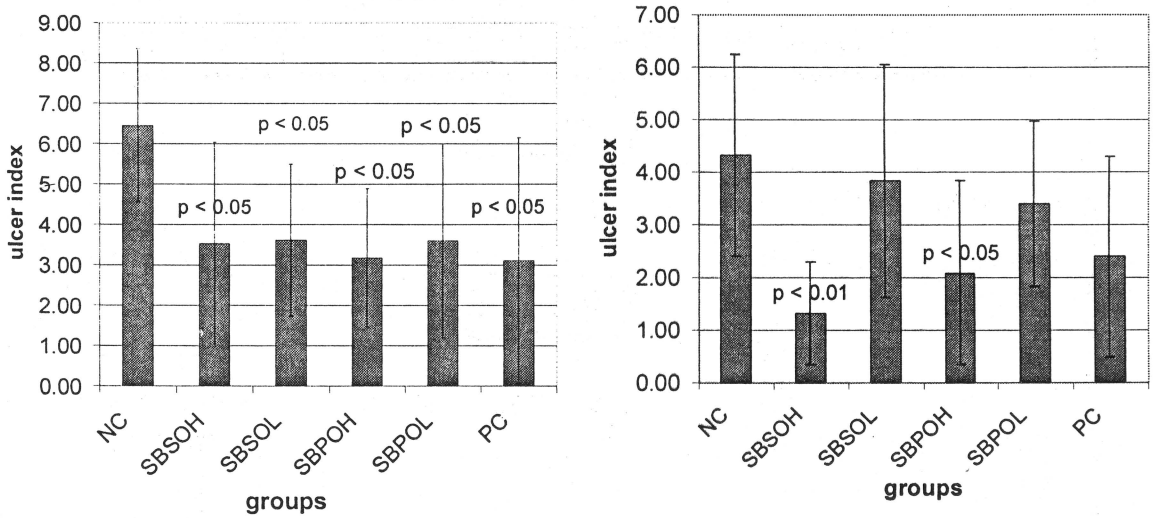

Figure 25.1: Anti-ulcerative Effects of Seabuckthorn Seed and Pulp Pils (7)

A, protective effects against reserpine-induced gastric ulcer; B, curative effects on acetic-acid-induced gastric ulcer. NC, negative control (4 per cent Tween 80 solution, 7.0 ml/kg per day); SBSOH, seabuckthorn seed oil high dose (7.0 ml/kg per day); SBSOL, seabuckthorn seed oil low dose (3.5 ml/kg per day); SBPOH, seabuckthorn pulp oil high dose (7.0 ml/kg per day); SBPOL, seabuckthorn pulp oil low dose (3.5 ml/kg per day); PC, positive control (Cimetidine, 80 mg/kg per day). The treatment lasted for seven days, before the ulcer induction in the reserpine model, after the ulcer induction in the acetic acid model. P values shown in the figure indicate difference between treatments and negative control.

The antiulcerative mechanism of seabuckthorn oils was related to promoting the regeneration of mucous membranes and the epithelialisation of ulcer areas (10). Seabuckthorn oil also inhibited gastric secretion (8) and proteolytic activity within gastric mucosa (10). Furthermore, increasing the hydrophobicity of the surface of mucosa and retarding gastric emptying was suggested to be among the mechanisms involved. b-sitosterol and b-sitosterol-b-D-glucoside in seabuckthorn oils are important for the antiulcerative activity (11-13). The efficacy of the two compounds may differ depending on the cause of ulcer formation (14).

Urogenital Mucosa

In topical application seabuckthorn oils and preparations containing seabuckthorn oil improve the health of mucous membranes of urogenital tract. Antiinflammatory and analgesic effects of seabuckthorn oils have been reported (15-17). In topical treatment of patients with cervicitis, seabuckthorn seed oil and a suppository 'Shayoushuan' (containing 50 per cent seabuckthorn seed oil and other herbal ingredients) were reported to be effective (15). Wang (17) treated 30 patients suffering from partial erosion of the cervix with topically sprayed seabuckthorn seed oil, once a day. All the 30 cases were cured after three months of treatment.

Cervicitis and vaginal inflammation is often associated with decreased tissue levels of carotenoids and vitamin E, compounds enhancing differentiation and regeneration of epithelial cells (18, 19). The

positive effect reported of seabuckthorn oil and Shayoushuan suppository was probably related to the high content of natural carotenoids and vitamin E.

Mouth Mucosa

Seabuckthorn seed oil was topically used (3-4 times a day) to treat sixty children (4 months–12 years old) with ulcerative stomatitis (20). All the sixty cases significantly improved after two days of treatment. Fifty-five cases were cured after 3-5 days of treatment, and two severe cases were cured after 8 days of treatment. Topical application of seabuckthorn seed oil was effective in treating stomatitis of patients with leukemia (21). Orally taken seabuckthorn seed oil, pulp oil and a mixture of seed and pulp oils improved esophagitis caused by irradiation therapy (22). High level of carotenoids and vitamin E in the oils were suggested to be responsible for the clear tissue-regenerative effects observed. A synergistic effect between some herbal components and seabuckthorn oil in experimental models of irradiation esophagitis was highlighted by Li and colleagues (23).

Dry mouth (xerostomia) is a common clinical complaint affecting up to 40 per cent of adults, mainly women and the elderly. Dry mouth, often a symptom of salivary gland dysfunction, provokes unpleasant oral symptoms such as burning mouth, difficulty in speaking, chewing and swallowing. Oral treatment with seabuckthorn oil (standardized SBA24 extract comprising a mixture of pulp oil and seed oil) capsules (5 g oil per day) for four weeks effectively relieved the dry mouth symptoms and improved the general condition of mouth mucosa (24)

Anti-oxidative Activity

The strong antioxidative activity of seabuckthorn oils is due to the high content of tocopherols and tocotrienols and carotenoids. All the natural isomers of vitamin E are present in seabuckthorn oils; α-tocopherol is the major one in pulp oil and γ-tocopherol in seed oil. Lycopene, α-, β-, and γ-carotenes are the main carotenoids in seabuckthorn oil. The natural isomers of vitamin E and carotenoids are more efficient antioxidants than single synthetic isomers. Working synergistically, vitamin E and carotenoids protect lipids and membrane structure from oxidation damage. Malondialdehyde (MDA) is a product of lipid peroxidation. Interactions between MDA membrane components result in disturbed structure and function of cell membranes.

An increased level of MDA and a decreased level of tocopherols in plasma were found in patients with gastric ulcer compared with healthy subjects (25). Oral supplementation of seabuckthorn oil for two weeks improved the ulcer symptom, decreased the MDA level and increased the level of tocopherols in plasma. Intragastric administration of seabuckthorn berry oil had preventive and curative effects against gastric ulcer in rats. The antiulcerative effects were clearly associated with a decreased MDA level and an increased level of a-tocopherol in gastric mucosa (26).

In animal models, addition of seabuckthorn oils into feed inhibited lipid oxidation and damage of cellular structure induced by cold-exposure and chemicals. The effect was reflected as the suppression of MDA formation as well as the maintenance of normal cellular structure and activities of membrane-bound enzymes such as glutathione peroxidase, Na/K-ATPase, and superoxide dismutase (SOD) (1).

Immune Function

Seabuckthorn oils are known to regulate immune functions and antagonise the effects of immune suppressants (1). Feeding seabuckthorn oil to mice increased the phagocyticity of abdominal macrophages and spleen NK cell activity as well as SRBC (sheep red blood cell)-primed antibody

production in normal and cyclophosphamide (an immune-suppressant)-treated mice. In clinical cancer treatment, oral seabuckthorn oil has been used to reduce the immuno-suppressive and hemotoxic effects of chemotherapy and irradiation therapy.

STANDARDISED SEABUCKTHORN OIL CAPSULE REDUCED CHRONIC VAGINAL INFLAMMATION: A CASE STUDY

Background

Gynecologists, dermatologists, and general practitioners all recognize a female patient who presents with recalcitrant vulvar itching and/or burning, a tale of many physicians she has seen, and a long list of medications she has used.

It is sometimes very difficult to make a differential or exact diagnosis of these conditions. Sometimes they are reflections of general skin diseases or systemic diseases. Into the first category belong *e.g.* lichen sclerosus and atrophicus (LSA), lichen ruber, lichen planus, psoriasis, erythema multiforme etc. Diseases as lupus erythematosus and Sjogren's syndrome are included into the second category. Furthermore, many chronic infectious condititions as desquamative inflammatory vaginitis and chronic viral, bacterial and parasitic inflammations may mimic the other above mentioned conditions.

Some common features of these conditions are itching, burning, reddening and increased vaginal discharge. Also pain at vulvar area, either vulvodynia or vulvar vestibulitis may be typical symptoms. Sometimes the conditions may lead to synechiae and strictures of the vagina. LSA appears as firm, flat pink-white, or translucent plaques which later coalesce, constricting the vulva and perineal areas in a crinkled white parchment-like skin. Atrophy of labia minora, phimosis of the clitoris, fissuring and traumatic ecchymoses often become prominent features. Treatment options have been systemic and local estrogens, local testosterone, systemic and local corticosteroids, retinoids, and antiinflammatory ointments, sometimes even surgery. Treatment has often been empirical and, in many cases, inefficient. Therefore there is a need to develop and investigate alternative possibilities to deal with these conditions.

Study Design and Subjects

Topical application seabuckthorn oils and preparations containing seabuckthorn oil have been shown to improve the health of mucous membranes of urogenital tract. Therefore we decided to design a trial by using orally administered seabuckthorn oils for the treatment of patient who had suffered from conditions described above, and had experienced a multitude of treatments. The patients took orally capsules of standardised SBA24 Omega 7 Seabuckthorn Oil (extracted by supercritical CO_2, Aromtech Ltd, Finland), a mixture of oils from seeds and berry soft parts at an optimized ratio, 6 capsules a day (3 g seabuckthorn oil per day) for 12 weeks. The committee of ethics accepted the study plan.

Five subjects recruited are described in Table 25.3. The vaginal conditions of all the cases had shown resistance to the treatments given before. Four of the five cases had been receiving high dose HRT and local corticoids earlier, but with poor results.

Evaluation Methods

Health history was taken before the treatment. Clinical investigation was performed, and plasma estrogen (estradiol) level was measured at 0, 6 and 12 weeks after initiating the treatment. Patients' subjective assessment of the condition was also asked by applying visual analogue scale (VAS) at the same time points, as shown in Figure 25.2.

Table 25.3: Description of Study Subjects

No. of Subject	Age (yrs)	Duration of Condition (yrs)	Diagnosis
1	65	7	Lichen ruber
2	58	3	Rheumatoid arthritis, Sjögren's syndrome
3	79	15	LSA
4	75	>20	Lichen ruber
5	35	10	Lichen ruber

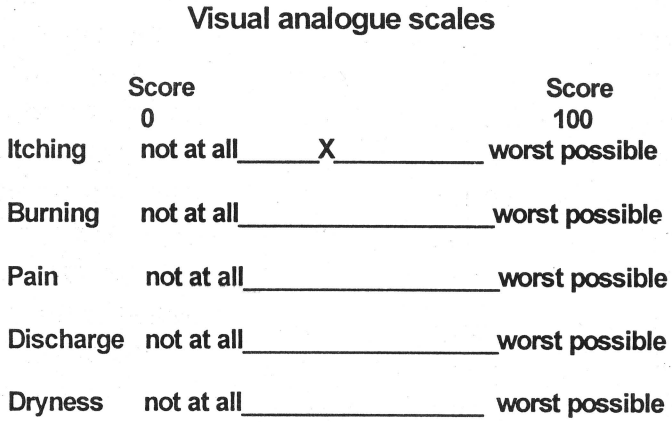

Figure 25.2: Visual Analogue Scale (VAS)

RESULTS

All the women were able to continue through the trial. Table 25.4 presents an overview of the total scores representing the sum of the scores of all the symptoms followed. Significant improvement after seabuckthorn oil treatment was seen in three severe cases. The best improvement was seen in patient no.3 representing as much as 66 per cent decreases of the total VAS score. The average total score value was decreased by 46 per cent, from 185 to 100 by seabuckthorn oil treatment. Estrogen levels at the end of trial were equal to the pretreatment measurements. None of the subjects reported any side effects. Figure 25.3 gives examples of the VAS assessment before and at the end of trial.

Table 25.4: VAS Scores and Subjective Assessment

No. of the Subject	Before Treatment	At the End of the Study	Subjective Improvement
1	86	127	No
2	15	15	Slight
3	378	127	Great
4	240	103	Good
5	204	127	Good
Average	185	100	

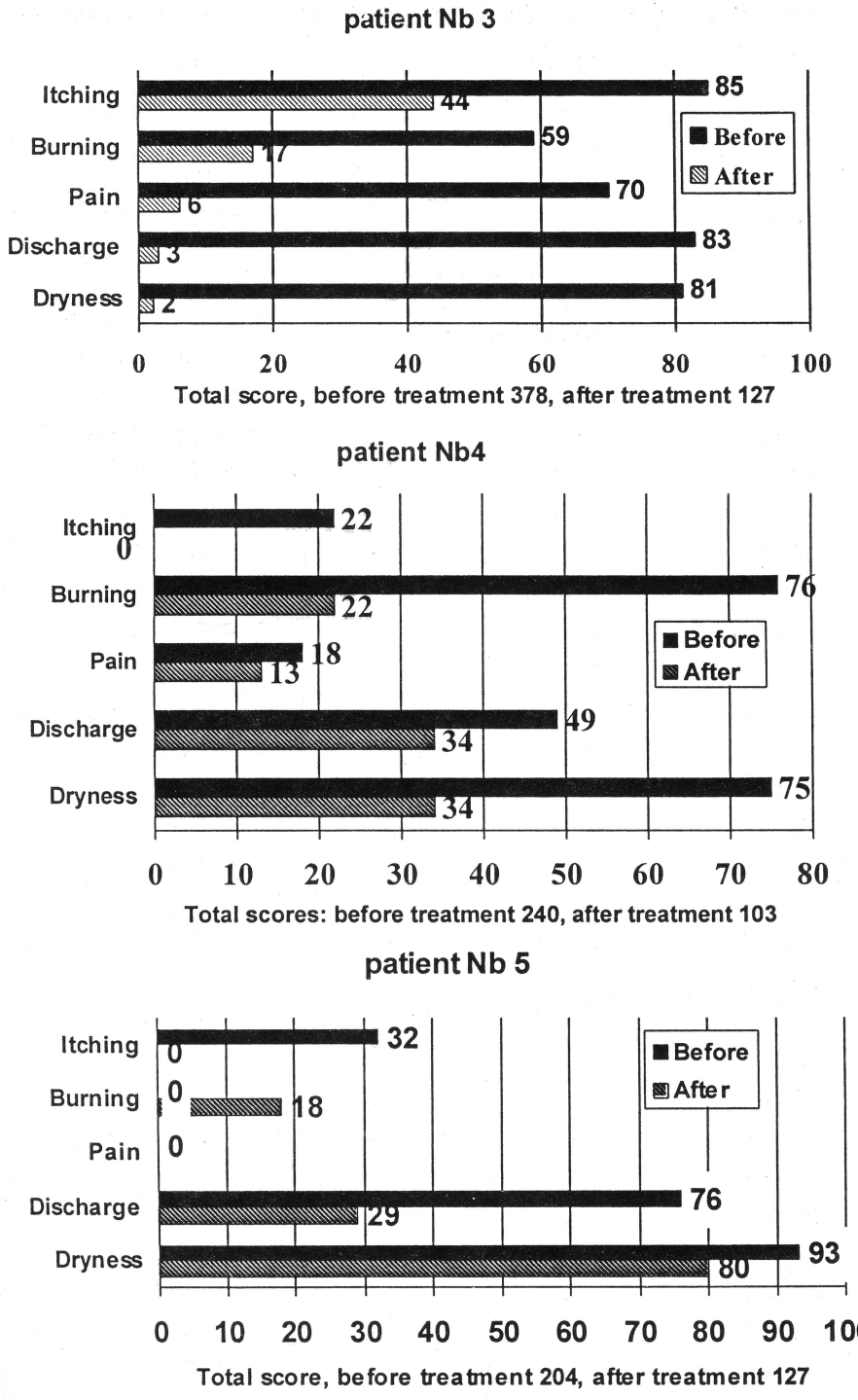

Figure 25.3: Examples of Individual Assessment of VAS Before and After the Treatment

CONCLUSIONS

From this open 12-week trial we can summarize:

1. Oral application of standardised SBA24 Omega 7 seabuckthorn oil capsules considerably improved chronic vaginal inflammation in three severe cases. In the two less severe cases, the improvement was less obvious.
2. The positive effect observed did not take place through increase of circulating estrogen level.
3. Based on the results of the present study and the effects shown in studies documented in literature, oral administration of SBA24 Omega 7 seabuckthorn oil presents a promising alternative for treating chronic vaginal inflammation.
4. Clinical trials with larger number of patients are justified to more accurately pinpoint the conditions which may benefit from treatment with seabuckthorn oils.

EFFECTS OF SEABUCKTHORN OIL CAPSULE ON SJÖGREN'S SYNDROME: A DOUBLE BLIND, CROSS OVER STUDY

Background

Sjögren's syndrome (SS) is a slowly progressive, inflammatory, autoimmune diseases affecting primarily the exocrine glands. Histologically, it is characterized by lymphocytic infiltrates replacing functional epithelium and leading to decreased exocrine secretions. Serologically, Ro/SSA and La/SSB auto-antibodies are present in the serum (27, 28). Problems in mucous membranes are the central symptoms of Sjögren's syndrome (SS). Dryness, pain and inflammation in mucosa in the mouth, eyes, and nose and urogenital tracts are typically complaints of SS patients. Often, gastric mucosa is also affected by the diseases (29, 30). These symptoms deteriorate with age and certain types of medications.

In the present state of art, artificial tear drop is the major treatment of dry eyes. No single method is consistently effective in the treatment of xerostomia, though stimulation of salivary gland with highly flavoured lozenges is often used. Lubricant gels and moisturizing lotions are used for dry vagina and skin. None of these measures offers a fundamental solution to the problems of Sjögren's syndrome.

Dietary factors may contribute to the etiology and progressions of SS. Abnormalities have been reported in both the intake and metabolism of polyunsaturated fatty acids of SS patients (31, 32). A proper ratio between Omega 3 and 6 fatty acids in the diet may be associated with lower risk of SS (32, 33). Dietary intake of minerals and vitamins may also a significant impact on the manifestation of SS (31, 34). There are indications that nutritional interventions may help to relieve the symptoms of SS (31, 35-37).

Seabuckthorn lipids have beneficial effects on the mucous membranes and skin (1, 2). Oral supplementation with SBA 24 Omega 7 Seabuckthorn Oil Capsule improved dry mouth conditions of Sjögren's syndrome patients (24) and reduced inflammation in the vagina of postmenopausal women. The aim of the present study was to investigate the effects of SBA 24 Omega 7 Seabuckthorn Oil Capsule on female patients of Sjögren's syndrome with special attention to the possible effects on the mucous membranes of the mouth, eyes and genital tract.

Subjects and Study Design

Twenty-five female Sjögren's syndrome patients of age 37-66 (average age 52.2) with typical symptoms of itching, burning, liquid secretion and dryness in the genital tract mucosa were recruited

through the Finnish Sjögren's Syndrome Association. Thirteen of the patients were postmenopausal. In the double blind, placebo-controlled, cross-over study, the patients took randomly capsules of SBA 24 Omega 7 Seabuckthorn Oil (Aromtech Ltd, Finland) or capsules of fractionated coconut oil (as placebo), six capsules (3.0 g oil) per day; administration period lasted for three months for each product. The symptoms of SS were evaluated using a visual analogue scale and by verbal description at three different time points: the baseline (before treatment), the end of the first period of three months and the end of the second period of three months. The study design was approved by the Ethical Committee of Turku University Central Hospital. The study was carried out at the Gynecology Center of Turku, Finland.

Statistical Data Analysis

Statistical analysis program SPSS 12.0 for Windows was used for the data analysis of the study. Non-parametric comparisons between the frequency of improvement and score values of improvement after taking Omega 7 and the use of the placebo was carried out using Mann-Whitney U-tests. Differences reaching a confidence level of 95 per cent ($P < 0.05$) were considered as statistically significant, whereas those reaching a confidence level of 90 per cent ($P < 0.1$) were considered close to statistically significant.

RESULTS

Twenty-three patients finished the study with good compliance. Five symptoms in genital mucosa and seven other typical symptoms of Sjögren's syndrome were followed during the whole study. Improvements in conditions of the mucous membranes reflected as decrease in the visual analogue scale of the followed symptoms occurred both after the use of Omega 7 and the placebo (fractionated coconut oil). To some extent, this might have been due to the beneficial effect of both products as well as some placebo effects. Clear differences were recognized between Omega 7 and the placebo (fractionated coconut oil) in the following aspects.

Overall Improvement in Sjögren's Syndrome

Comparing the percentage of the patients that experienced improved or worsened conditions of mucosa during the treatments, we found an overall better rate of improvement after use of Omega 7 compared with the placebo after the first three months (Figure 25.4). This difference is statistically highly significant ($P < 0.01$). Some patients experienced worsened symptoms during the study period, which might have been due to multiple reasons. It is also noteworthy that the percentage of such patients was generally much smaller in the Omega 7 group compared with the placebo group. In other words, during the first three months of the study, Omega 7 gave a much better chance of improvement in the conditions of genital mucosa and typical SS symptoms including dry mouth, dry eyes, fatigue, joint pain, pale finger, and atopic skin.

Improvement in Genital Tract Mucosa

The effect of the seabuckthorn oil capsules on genital tract mucosa was clearly seen during the whole study period. Figure 25.5 shows a significantly higher percentage of improved patients in symptoms in genital mucosa especially itching and burning ($P < 0.01$). The overall comparison including all the five symptoms showed a statistically better effect of Omega 7 compared with the placebo ($P < 0.01$).

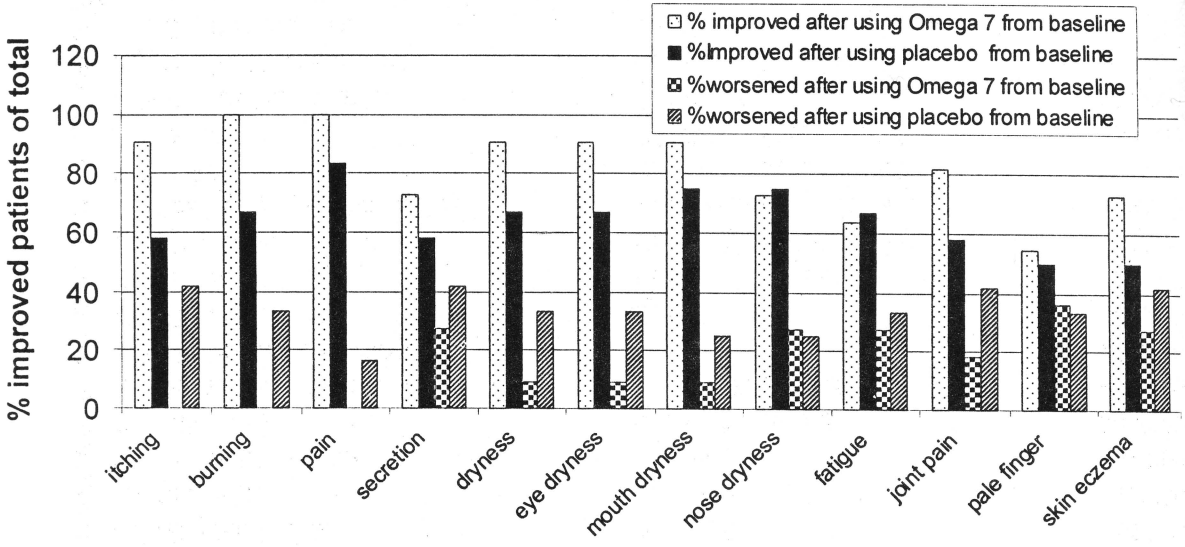

Figure 25.4: Percentage of Improved Patients and Worsened Patients After Use of Omega 7 and the Placebo as the Treatment for the First Three Months

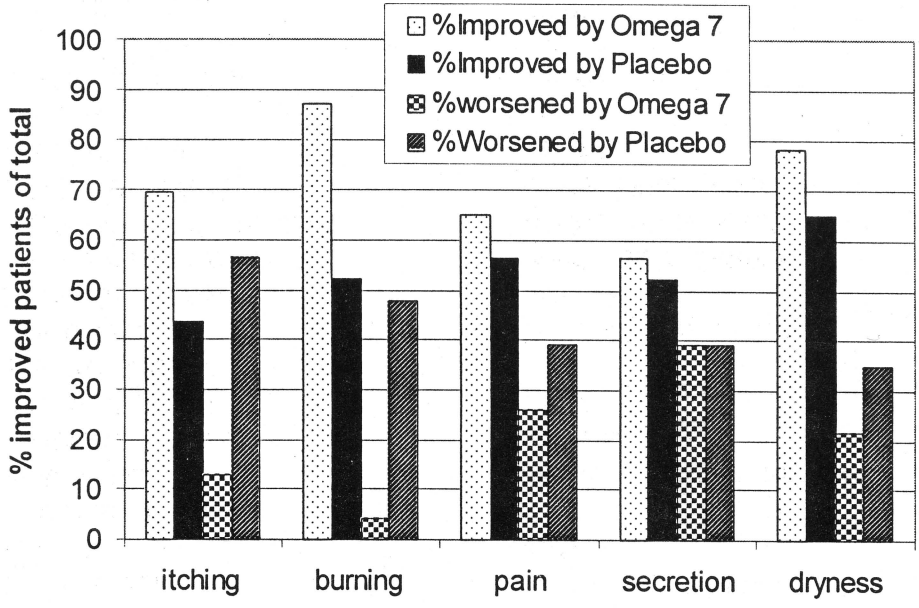

Figure 25.5: Percentage of Patients with Improved or Worsened Conditions of Genital Mucosa after Use of Omega 7 and Placebo

CONCLUSIONS

The double-blind, placebo-controlled cross-over study demonstrated clear beneficial effect of SBA 24 Omega 7 Seabuckthorn Oil Capsule on condition of genital tract mucosa of female patients of Sjögren's syndrome. The results of the first three months of the study indicated overall positive effects of Omega 7 on typical symptoms of Sjögren's syndrome including dry mouth, dry eyes, fatigue, joint pain, pale finger, and atopic skin, which encourages further study in this field.

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