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Original research

Marked improvement of thyroid function and autoimmunity by *Aloe barbadensis* miller juice in patients with subclinical hypothyroidism

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ABSTRACT

Some natural compounds decrease serum levels of thyroid autoantibodies, but results are inconsistent and thyroid function has been evaluated infrequently; moreover, the effects of *Aloe* on thyroid autoimmunity and function have been examined in very few studies. This study stems from the observation of one co-author, who has Hashimoto's thyroiditis (HT)-related subclinical hypothyroidism (SCH). Upon checking her biochemical thyroid panel when taking daily *Aloe barbardensis* Miller juice (ABMJ) for thyroid-unrelated reasons, she noticed a decrease in serum thyroperoxidase autoantibodies (TPOAb) and thyrotropin (TSH) and an increase in serum free thyroxine (FT4). Based on this observation, we enrolled 30 consecutive HT women with levothyroxine-untreated SCH and high TPOAb levels. All of them took ABMJ (50 ml daily) for nine months and were tested for serum TSH, FT4, free triiodothyronine (FT3) and TPOAb. Measurements were performed at baseline and at months 3 and 9. TSH, FT4 and TPOAb improved significantly already at month 3 and further (−61%, +23% and −56%) at month 9. However, FT3 decreased significantly at month 3 (−16%) with no further decrease at month 9, so that the FT4:FT3 ratio increased significantly (+33% and + 49%). At baseline, 100% of women had TSH > 4.0 mU/L and TPOAb > 400 U/ml, but frequencies fell to 0% and 37%, respectively, at month 9. In contrast, a control group (namely, 15 untreated SCH women of comparable age and baseline levels of TSH, FT4, FT3 and TPOAb) had no significant changes in any index. We conclude that the daily intake of 100 ml ABMJ for 9 months in women with HT-related SCH decreases the burden of thyroid autoimmune inflammation. In addition, ABMJ rescues thyrocyte function, with decreased need for conversion of the prohormone T4 into the more active T3 through ABMJ-induced inhibition of T4 deiodination.

Introduction

Aloe is a very old plant with medicinal properties that was discovered by the ancient Egyptians, who called it "the plant of immortality" [1]. The botanical name of *Aloe vera* is *Aloe barbadensis* Miller. It belongs to the *Asphodelaceae* (*Liliaceae*) family, and is a shrubby or arborescent, perennial, xerophytic, succulent, pea-green color plant. It grows mainly in the dry regions of Africa, Asia, Europe and America [1]. Records of its use were engraved in tablets thought to be from 2100 B.C. *Aloe* then travelled to various parts of the globe, and starting from the 17th century it had become a common medicinal plant [2]. The name *Aloe vera* derives from the Arabic word "*Alloeh*" meaning "shining bitter substance" and from the Latin word "*vera*" meaning "true." Two millennia ago, Greek scientists regarded *Aloe vera* as the universal panacea [1]. Egyptian queens Nefertiti and Cleopatra used *Aloe* as part of their regular beauty regimes. Alexander the Great and Christopher Columbus used it to treat soldiers' wounds. The first reference to *Aloe vera* in the English literature dates back to 1655, when John Goodyer translated the Dioscorides' Medical treatise *De Materia Medica*. By the early 1800s, *Aloe vera* was in use as a laxative in the United States, and in the mid-1930s it was successfully employed to treat chronic and severe radiation dermatitis [1].

Aloe Barbadensis leaf juice is extracted from the leaves of the aloe plant. *Aloe Barbadensis* leaves contain over 200 nutritional substances, including 20 minerals (particularly iron, chromium, zinc, selenium, copper, manganese, magnesium, sodium, potassium, and calcium), 20

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amino acids, a dozen vitamins (A, B1, B2, B3, B5, B6, B12, C, E, choline, and folic acid), active enzymes (alkaline phosphatase, amylase, bradykinase, carboxypeptidase, catalase, cellulase, lipase, and peroxidase), anthraquinones (mostly known for their laxative effects), sterols, lignin, saponins, salicylic acids and others [1]. Interestingly, the thyroid hormone-forming tyrosine is the rarest amino acid present in *Aloe Barbadensis* leaves (28 μmol/100 g), while arginine is the main one (449 μmol/100 g) [3]. The anti-oxidant and/or anti-inflammatory properties of *Aloe vera* are explained by its content in vitamin A, C and E, in the glycoprotein C-glucosyl chromone, in certain sterols (campesterol, β-sitosterol and lupeol), vegetal hormones (auxins and giberrelins) and bradykinase. Campesterol, β-sitosterol, lupeol and two anthraquinones (aloin and emodin) act as analgesics and antiseptics [1]. These sterols are also found in shea butter and sabal/saw palmetto (*Serenoa repens*) [4,5]. Further details can be found in the Volume 1 of WHO (World Health Organization) Monographs on Selected Medicinal Plants [6]. As reviewed elsewhere [1], some uses of *Aloe vera* are based on scientific evidence in humans and/or animals, while other uses are based on tradition. Scientific-based therapies for *Aloe vera* include seborrheic dermatitis, psoriasis vulgaris, genital herpes, skin burns, wound healing, pressure ulcers, mucositis, radiation dermatitis, acne vulgaris, lichen planus, frostbite, aphthous stomatitis, type 2 diabetes mellitus, HIV infection, cancer prevention, ulcerative colitis and constipation. Traditional-based therapies for *Aloe vera* include alopecia, bacterial and fungal skin infections, parasitic infections, chronic leg wounds, systemic lupus erythematosus, arthritis and tic douloureux.

A number of natural compounds/nutraceuticals are being used to treat autoimmune thyroid diseases (AIT), namely Graves' disease (GD), GD-associated ophthalmopathy, HT and postpartum thyroiditis (PPT) [7–29]. Though an exhaustive list of these substances goes beyond the scope of the present paper, examples of them include omega-3-fatty acid-rich small oily fish [7,8], L-carnitine [9–11], selenium [12–29], and myoinositol [27–29]. However, the observation that prompted the present study stemmed from a fortuitous observation (Table 1). One of the authors of the present paper, who has a history of HT-associated initial, mild hypothyroidism (also called subclinical hypothyroidism [SCH]), decided to take *Aloe Barbadensis* Miller juice (ABMJ), at the dose of 50 ml every morning on an empty stomach, as a skin soother and laxative. No other medications or over-the-counter compounds were taken. She checks thyroid function and thyroperoxidase autoantibodies [TPOAb] semiannually, since in one relative progression to overt hypothyroidism was preceded by a frank fall in FT4 and increase in both TSH and TPOAb approximately six months earlier. At the biochemical check performed three months after having started taking ABMJ, she was struck by the remarkable improvement of all indices (Table 1). The improvement was even more impressive six months later (Table 1).

Table 1
Summary of the *Aloe vera barbadensis* Miller juice-induced changes in the biochemical thyroid profile of one author of the present paper and that prompted the study described herein.[a]

	Follow-up			
	Before use of Aloe juice		During use of Aloe juice	
	Range (min - max)	Last value	First value	Last value
TSH, mU/L [0.2–4.0]	4.3–5.5	5.14	3.22	1.83
FT4, pmol/L [7–19]	7.9–8.3	8.3	8.9	11.44
FT3, pmol/L [2.7–6.4]	5.0–5.25	5.22	5.0	4.78
TPOAb, U/ml [0–35]	1,256–1875	1875	778	246

[a] Follow-up prior to use of the aloe juice (50 ml twice a day) spans 14 months, respectively. The first value of each thyroid index under the juice regimen was recorded 3 months after having started taking the juice; the last value was recorded 9 months after having started taking the juice. Numbers in brackets are the reference ranges.

Based on this positive experience, we decided to test the effects of ABMJ administration in HT women with levothyroxine-untreated SCH and high levels of TPOAb.

Materials and methods

Materials

The ABMJ taken by all patients was *Aloe Vera*[2] by ZUCCARI (Trento, Italy). Each 100 ml preparation of ABMJ, which has an energetic value of 7.40 kcal (31.20Kj), contains nonpasteurized and noncarbon filtered *Aloe vera* leaf juice and pulp (49.8 g), 0.2 g fats (0% saturated), 1.2 g carbohydrates, zero proteins, and 0.06 g minerals (of which, 0.02 g sodium). The juice also contains citric acid as an acidifier and sodium benzoate and potassium sorbate as typical preservatives with biocidal properties. Noteworthy, *Aloe Vera*[2] is free of aloin, a substance primarily contained in the outer cuticles of the leaves that is irritating to the intestinal mucosa. Once opened, the one-liter bottle has to be stored in the refrigerator, as recommended by the producer.

Patients

Based on the observations summarized in Table 1, we aimed to recruit women, aged 30 to 55 years and with HT-associated SCH (TSH > 4.0 mU/L; high levels of TPOAb), who had never been treated with L-T4 and/or supplements. In addition to past and current treatment with L-T4 and/or supplements, exclusion criteria were: (i) concurrent diseases, including diabetes mellitus and other autoimmune diseases; (ii) use of any nutraceuticals/drugs that affect the hypothalamic-pituitary-thyroid axis and autoimmunity. These criteria were verified with the family physicians.

Patients were informed of the aforementioned initial observation and enrolled upon signing an informed consent form. Thirty women, aged 20 to 55 years, were enrolled and all of them completed the study. They were treated with 50 ml ABMJ (*Aloe Vera*[2]), which was taken in the morning on an empty stomach. To minimize confounding factors, all patients were directed to the same natural product health store where the said co-author bought ABMJ. The natural product health store personnel informed us that each patient had bought enough bottles to complete the study. Paralleling the initial observation, the duration of study was 9 months, with serum TSH, FT3, FT4 and TPOAb measured at baseline (time zero), and 90 ± 3 days (3 months) and 180 ± 3 days (9 months) later. Measurement of FT3 was added for sake of completeness.

For the purpose of comparison with a group of Hashimoto's thyroiditis women who were under no thyroid hormone replacement therapy and no supplementation with nutraceuticals, we took advantage of a database on patients with Hashimoto's thyroiditis (Interdepartmental Program of Molecular & Clinical Endocrinology and Women's Endocrine Health, University hospital of Messina). Based on age and levels of the fundamental indices (serum TSH and TPOAb) at time zero, the 30 Aloe-treated women could be matched to 15 women with SCH of comparable age (21–57 years) and baseline levels of serum TSH and TPOAb that had been measured with the same corresponding kits.

Assays

Serum TSH, FT4, FT3 and TPOAb were assayed using electrochemilumiscent kits (Roche, Mannheim, Germany). Reference values were 0.27–4.2 mU/L for TSH, 9.3–17.1 pg/ml (12–22 pmol/L) for FT4, 2.0–4.4 pg/ml (3.1–6.8 pmol/L) for FT3, and 0–100 U/ml for TPOAb. To avoid intra-assay variations, sera were stored at −20 °C, and all 90 sera for each analyte (30 patients × 3 time points) were assayed in one