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The Safety and Efficacy of a Sustainable Marine Extract for the Treatment of Thinning Hair: A Summary of New Clinical Research and Results from a Panel Discussion on the Problem of Thinning Hair and Current Treatments

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ORIGINAL ARTICLE

The Safety and Efficacy of a Sustainable Marine Extract for the Treatment of Thinning Hair: A Summary of New Clinical Research and Results from a Panel Discussion on the Problem of Thinning Hair and Current Treatments

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Panel Discussion with Vivian W. Bucay MD,[c] Wendy E. Roberts MD,[d] Heidi A. Waldorf MD,[e] and Steven H. Dayan MD[f]

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ABSTRACT

Alopecia and thinning hair are highly prevalent conditions affecting a large proportion of men and women. Diffused hair loss is often more difficult to diagnose in women, mostly due to over-reliance on the assumption of hormonal influences, and it is commonly treated with a multi-therapy approach. Clinical studies have demonstrated the effectiveness of a nutraceutical supplement to provide essential nutrients that aid in stimulating existing hair growth and reducing hair shedding. The supplement Viviscal® contains a proprietary blend of proteins, lipids, and glycosaminoglycans derived from sustainable marine sources. We present here a summary of studies that have examined the safety and efficacy of this nutraceutical; as well as discussions on hair loss and current therapies from a recently convened expert panel in dermatology and plastic surgery.

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INTRODUCTION

Alopecia is one of the most prevalent dermatologic conditions. In the United States alone, 50% of women will suffer from hair loss at some point in their lives and 50% of men experience hair loss before the age of 50.[1] Furthermore, it has been reported that 20% of women under the age of 50 and 42% of women over the age of 70, who presented at a dermatology clinic for non-hair concerns, exhibited diffused hair loss that was diagnosed at greater than Ludwig stage II.[2] By the age of 30, 25% of Caucasian men show signs of androgenic balding; and by the age of 60, 67% are bald or balding.[3]

Various factors can lead to hair loss. While androgenic alopecia is generally the most common type of hair loss in men, the involvement of androgens in patterned or non-patterned hair loss is not as well established in women. Identifying the causes of hair loss or thinning hair has proven especially complex in women; and factors such as diet, medications, past and existing medical conditions, and a family history of alopecia are considered. For example, telogen effluvium, a common source of hair loss in women, can result from a variety of factors such as stress, diet, hormonal changes, or medications.[4-7]

Current treatment options for alopecia and thinning hair include topical formulations, prescription medications, and oral supplements (Table 1).[8-18] These are often used in combination as no one treatment has proven fully effective when used alone.[19,20] Moreover, both topical and prescription medications can entail unwanted side effects.[19-21] Hair transplantation is also a treatment option, but the procedure is invasive and can be costly. Hence, currently, a fully safe and effective therapy for hair loss does not exist.

Furthermore, as our understanding of the impact of alopecia and thinning hair has increased, the negative influence they can play in human social interactions has also increasingly come to light. In addition to aesthetic concerns, hair loss has been illustrated to have adverse psychological effects on patients, such as low self-esteem and poor self-confidence.[3,13-17]

TABLE 1.

Current Treatment Options for Hair Loss/Thinning Hair	
FDA Approved	Minoxidil, finasteride (men only)
Non-FDA Approved	Anti-androgens (women): spironolactone, flutamide, cyproterone acetate, cimetidine 5-α reductase inhibitors (women): finasteride, dutasteride estrogens (women): 17 α-estradiol estrogen, receptor antagonists Melatonin
Dietary	Millet extract, pantothenic acid, cytochrome P450 (CYP)- complex, biotin, L-cystine, B-complex vitamins

FDA, US Food and Drug Administration.

It has been reported that 52% of women and 28% of men are very-to-extremely upset by their hair loss.[16,17] Therefore, novel therapies that would provide effective relief, without unwanted adverse effects (AEs), are of great significance.

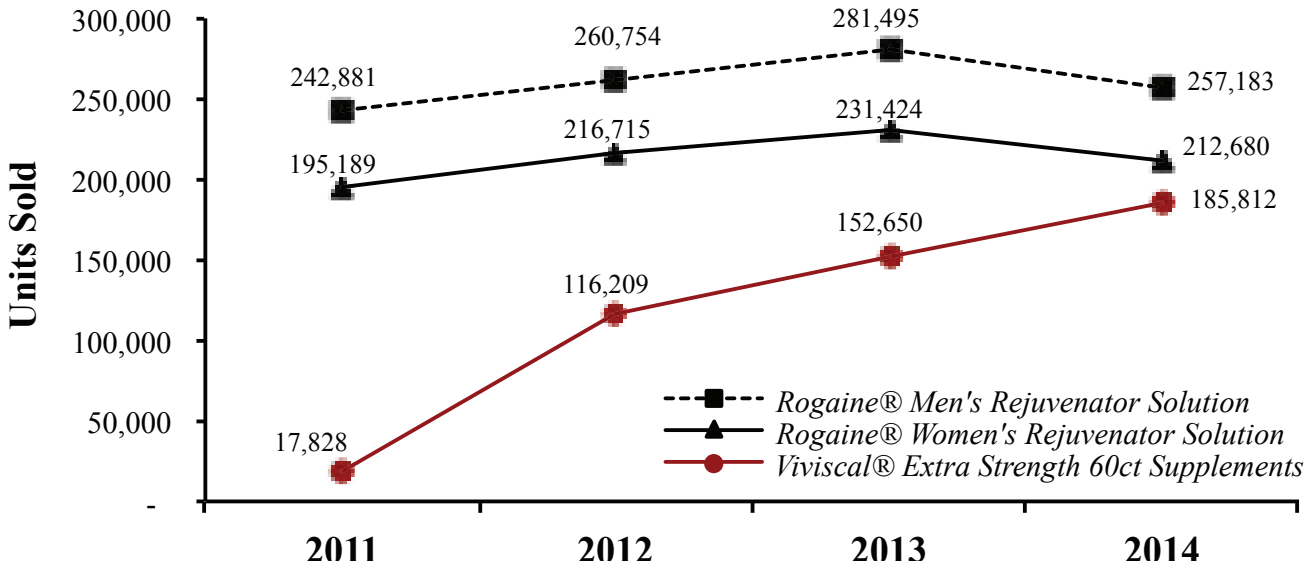
As elucidated above, one of the factors that can influence hair condition is diet or nutrition. Whereas there are examples of the AEs of severe malnutrition on hair,[22-24] little systematic attention has been paid to the impact of average Western diets on hair growth. Isolated reports have evaluated the influence of various dietary supplements such as millet extracts, biotin, L-cystine, and B-complex vitamins on hair.[8] More recently, the impact of supplements containing omega-3 and omega-6 fatty acids, and a mixture of antioxidants including lycopene[9] and pantothenic acid,[10] has also been studied.

Viviscal

Viviscal® (Lifes2good, Inc., Chicago, IL) is a dietary supplement that contains as its primary active ingredient a combination of proteins, lipids, and glycosaminoglycans (GAGs) of marine origin, as well as several of the ingredients noted above.[11] While there is a paucity of studies examining the dietary benefits of GAGs on hair growth, their impact on skin health and photoaging has been documented.[12] Patients with facial photoaging who received an oral supplement containing collagen, chondroitin sulfate, and other constituents displayed increased serum levels of hyaluronic acid and fibronectin compared with baseline, which, subsequently, was associated with improved appearance of the skin.[12]

In the past decade an increasing number of reports have provided support for nutraceuticals as effective and safe treatment options.[25,26] Furthermore, as patients search for options to support and enhance their hair, there seems to be a growing trend toward supplementation compared with prescription or over-the-counter (OTC) medications (Figure 1). Since the early 1990's, numerous studies have examined and established the safety and efficacy of Viviscal in promoting existing hair growth and reducing hair shedding. Here we review the results of recent clinical studies and provide a discussion among experts in the field regarding the problem of hair loss and its available treatments.

FIGURE 1. Annual unit volume of Rogaine® and Viviscal®.



Source: IRI US Multi-Outlet, Unit Measurement, Calendar Year 2011-2014.
Rogaine® is a trademark of Johnson & Johnson, New Brunswick, NJ.

TABLE 2

Changes in Hair Count and Shedding After Three Months of Treatment

	Baseline	Month 3
Terminal Hair	178.3 ± 7.8	235.8 ± 14.4[a]
Vellus Hair	19.6 ± 2.1	21.2 ± 2.2[a]
Shed Hair	27.1 ± 26.6	16.5 ± 14.4[b]

See Ablon, 2015[30]
Mean and standard deviations are reported (n=30)
[a]*P*<.0001
[b]*P*=.002
Measurement area was 4 cm^2

A Novel Nutraceutical for Treating Thinning Hair

The main component of Viviscal, the marine complex AminoMar®, was originally identified from the fish- and protein-rich diet of the Scandinavian Inuits in the late 1980's.[27,28] In the 25-year period since then, its efficacy and safety have been demonstrated through a multitude of clinical studies (Table 4). Early studies demonstrated the beneficial effects of Viviscal on both male and female subjects with alopecia areata and alopecia totalis,[29] as well as on young men with hereditary androgenic alopecia.[28]

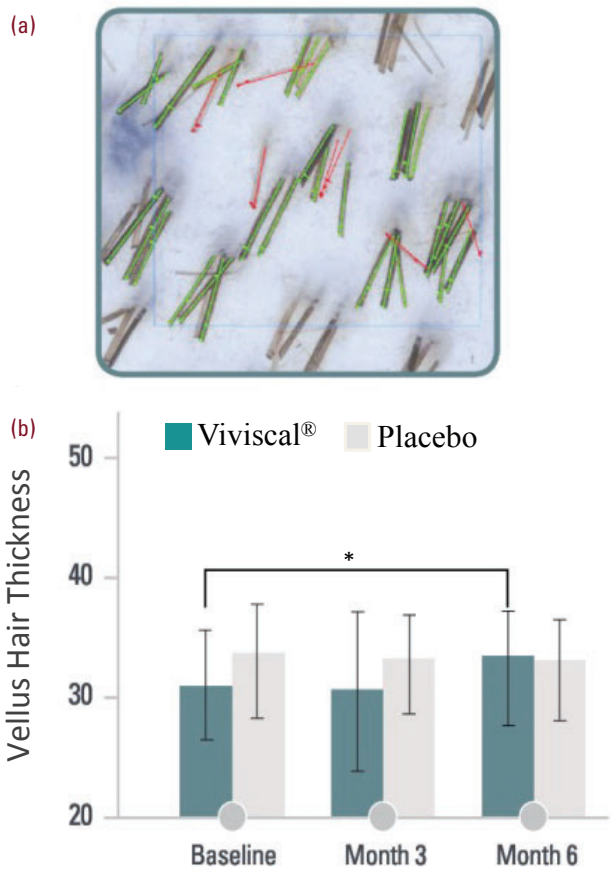
The use of Viviscal, specifically for women with thinning hair, was pioneered at the Ablon Skin Institute Research Center in Manhattan Beach, CA. In a randomized, double-blind, placebo-controlled pilot study, healthy women between the ages of 21 and 75 with self-perceived thinning hair were randomized to receive Viviscal (n=10) or placebo (n=5) twice daily for 6 months.[11] The change in hair count was assessed on a 4 cm^2 area of scalp by using phototrichogram imaging. In the treatment group, the mean number of terminal hairs increased by 211% after 3 months of treatment and by 225% after 6 months. Subjects in the treatment group also reported improvements in overall hair volume and scalp coverage, as well as in hair shine and body thickness. Moreover, improvements in skin moisture retention and smoothness were also observed in the treatment group. No AEs were reported.

A follow-up study enrolled 60 women with a mean age of 48.6 ± 10.0 years (range 24-65) who had self-perceived thinning hair associated with poor diet, stress, hormonal influences, or abnormal menstrual cycles.[30] Subjects were randomized in a double-blind fashion to receive either a twice-daily dose of Viviscal (n=30) or a placebo (n=30) for 3 months. The change in hair count was assessed on a 4 cm^2 area of scalp using phototrichograms. Changes in hair shedding were also measured.

In subjects treated with Viviscal, the mean number of terminal hairs increased by 32% (*P*<.0001) after 3 months. Moreover, the mean number of vellus hairs also increased by 8.2% (*P*<.0001) and the shed hair count decreased by 39% (*P*=.002) (Table 2). Hair type was defined by hair shaft diameter as vellus-like (≤40 µm) or terminal (>40 µm). Subjects in the treatment group also had significant increase in the quality of life and self-assessment scores, whereas there was no change among the placebo-treated subjects.[30] This is in agreement with previous reports,[13-17] elucidated above, that subjects' self-assessment of the quality and quantity of hair can negatively impact confidence and self-esteem if thinning hair is perceived.

A similar randomized, placebo-controlled study further examined the benefits of Viviscal in reducing the shedding and increasing the diameter of hair in women with subclinical hair thinning or loss. Seventy-two subjects with a mean age of 44

FIGURE 2. Mean thickness and caliber of the vellus hair was significantly higher in subjects receiving daily treatments of Viviscal® for 6 months.
(a) The blue trichogram/count measure 0.5 cm x 0.5 cm (0.25 cm^2). Under the conditions of digital analysis 1 pixel = 5.411 µm.
(b) The thickness of vellus hair increased by 7.4% after 6 months of dietary supplement.



n=33 for the Viviscal group and n=30 for the placebo group.
Mean and standard deviations are reported.
A student t-test was used to determine significance.
*P<.05

TABLE 3.

Viviscal® Significantly Enhances Existing Hair Growth and Diameter					
	Group	Baseline	Day 90	Day 180	Significance[b]
Terminal Hair	Viviscal[a]	189.9 ± 15.24	297.4 ± 96.09	341.0 ± 60.92	*P*<.0001
	Placebo[a]	190.3 ± 20.69	189.2 ± 19.89	192.7 ± 24.11	NS[c]
Vellus Hair	Viviscal	19.9 ± 1.71	20.2 ± 5.40	22.8 ± 2.29	*P*=.0001[c]
	Placebo	21.8 ± 5.37	22.2 ± 6.71	22.5 ± 6.42	NS
Hair Diameter (mm)	Viviscal	0.060 ± 0.0070	0.066 ± 0.0085	0.067 ± 0.0085	*P*=.006
	Placebo	0.061 ± 0.0092	0.060 ± 0.0092	0.061 ± 0.011	NS

[a]n=17 in the Viviscal group and n=19 in the placebo group.
[b]Repeated measures analysis of variance across study days contrasts per treatment group.
[c]Baseline vs day 180 only.
NS, not significant.

(range 24-55) and self-perceived thinning hair were enrolled and randomized in 2 groups.[31] Changes in hair growth were measured using phototrichogram imaging of a 0.25 cm^2 area of scalp. Hair type was defined by hair shaft diameter as vellus-like (≤40 µm) or terminal (>40 µm). Furthermore, hair shedding was assessed using a validated protocol that collected shed hairs during in-clinic shampooing.

After 6 months, Viviscal-treated subjects demonstrated a significant increase in mean vellus-like hair caliber (diameter; Figure 2). This observation suggests that vellus hairs were transitioning towards terminal hair classification, a process that may continue to develop over the course of the treatment. Moreover, subjects displayed a significant reduction (18.3%) in hair shedding after 3 months of daily treatment.

In yet another recent multi-site, double-blind, placebo-controlled study, 40 women, 20 to 65 years of age, were randomized to receive either daily doses of Viviscal or a placebo for 6 months.[32] Subjects' scalps were photographed at baseline and after 6 months, and evaluated by an independent third party (Figure 3). An increase of 57% in hair count was observed in the treatment group after 3 months. Remarkably, the hair count further increased by 80% after 6 months of daily intake of Vivis-

FIGURE 3. Continuous use of Viviscal® for 90 and 180 days promotes visible hair growth.
Top row: Macrophotographs of the target area at baseline (left), 90 days (center), and 180 days (right).
Bottom row: Digital images of the target area at baseline (left), 90 days (center), and 180 days (right).

cal. There was no significant change in hair count in the placebo group. Furthermore, the hair diameter also increased by 12% in the treatment group (Table 3). There were also no reported AEs.

Ongoing studies are also seeking to establish the molecular mechanism by which Viviscal promotes hair growth. Results from early in vitro studies have demonstrated that its polysaccharide complexes have greater bioavailability than similar products (unpublished results). Furthermore, Viviscal has been shown to enhance the proliferation of dermal papilla (DP) cells, which have been shown to play an important role in orchestrating the hair growth cycle.[33,34] Preliminary studies have illustrated that Viviscal increases the alkaline phosphatase (AP) levels in DP cells (unpublished results). As AP is a key marker of the anagen phase, an increase in its expression suggests an increase in the number of DP cells that are actively growing during the anagen phase.[34-36] Thus, in vitro examination of the molecular mechanisms of Viviscal is consistent with the results

TABLE 4.

Clinical Studies Examining the Effects of Viviscal® on Hair Growth

Study	Duration of Study (months)	Double-Blind	Placebo-Controlled	Participants	Key Results
Ablon and Dayan, 2015[32]	6	Yes	Yes	40 females[a]	Statistically significant results were observed in the active group[b]: • 57% increase in terminal hairs after 3 months • 80% increase in terminal hairs after 6 months • 12% increase in hair diameter after 6 months
Ablon, 2015[30]	3	Yes	Yes	60 females	Statistically significant results were observed in the active group[b]: • 32% increase in terminal hairs after 3 months. • 39% reduction in hair shedding after 3 months
Bloch, 2014[37]	6	No	No	52 females	The self-assessment questionnaires revealed improvements after 6 months: • 94% in hair volume • 92% hair thickness • 91% in nail growth rate • 92% in nail strength • An increase of 237 strands in 90 days and 772 strands in 180 days • A decrease of 90 telogen hair strands in 90 days and 181 hair strands in 180 days
Pinski, 2014[c,38]	N/A	No	No	20 males	• Hair qualities showing the greatest improvement were scalp coverage and hair fullness
				20 females	•The quality of life questionnaire showed an increase in perceived personal attractiveness and confidence
Thomas J. Stephens & Associates et al, 2013[31]	6	Yes	Yes	72 females	Statistically significant results were observed in the active group[b]: • 7.4% increase in hair diameter after 6 months • 8.3% reduction in hair shedding after 3 months
Ablon, 2012[11]	3	Yes	Yes	15 females	• 111% increase in terminal hairs after 3 months vs no change in the placebo subjects • 125% increase in terminal hairs after 6 months vs no change in the placebo subjects
Jackson, 2011[39]	4	No	No	16 African-American females	Following treatment with Viviscal, the greatest change in hair growth and hair quality occurred during the initial 2 months of treatment. Increased changes continued to occur after that time, except for a very slight decrease in the number of hairs lost on an average day.
Thomas J. Stephens & Associates, 2010[40]	10 weeks	No	No	16 females	• An average 46% reduction in hair loss was reported • 75% of subjects reported an increased thickness in the body of the hair • 75% of subjects reported an increase in overall hair volume

Study	Double-Blind	Placebo-Controlled	Participants	Key Results
The following studies were conducted prior to Lifes2good, Inc.'s involvement with Viviscal				
Pereira, 1997[41]	No	No	200 males[d]	• 75.3% of patients observed a significant decrease in hair loss • 14.6% of patients showed partial regrowth
Majass et al, 1996[42]	No	No	23 males	After 6 months of treatment:
			61 females	• 92% of areata, 83.3% of totalis, and 31.8% of universalis groups showed signs of growth.
Lassus et al,1994[28]	No	No	30 males	• Hair loss decreased for 100% of subjects after 2 months of treatment • 92% of patients showed signs of hair growth.
Lassus and Eskelinen, 1992[27]	Yes	Yes	40 males[e]	• Mean increase in non-vellus hair of 38.1% was recorded in patients after 6 months of treatment • 95% of subjects showed both clinical and histological improvements
Lassus and Santalahti, 1992[29]	No	No	20 males 20 females	• 85% of subjects with alopecia areata showed improvement • 45% of subjects with alopecia totalis showed significant improvement

[a]3 withdrew from the treatment and 1 from the placebo group before study completion.
[b]Using phototrichogram measuring system.
[c]This trial was conducted on the Viviscal Hair Filler Fibers.
[d]178 completed the study.
[e]3 withdrew from placebo group before study completion.

of our clinical studies, where daily intake promotes existing hair growth.

Hair loss is a prevalent and often emotionally disturbing condition that affects a significant proportion of men and women. Multiple randomized, double-blind, placebo-controlled studies have demonstrated the safety and efficacy of Viviscal – a dietary supplement containing a proprietary blend of proteins, lipids, and GAGs – in promoting existing hair growth. Considering the limitations of the current treatments for alopecia and thinning hair, there is a need for alternative therapy options. In our studies, treatments with Viviscal alone led to an increase in existing hair growth. Therefore, as further discussed below, Viviscal may be an effective treatment option both alone and in combination with other pharmaceutical therapies such as minoxidil.

EXPERT ROUNDTABLE DISCUSSION

In August 2014, a group of aesthetic experts in dermatology and plastic surgery convened in Chicago, IL. The goal of this meeting was to initiate an interactive dialogue among clinicians on the topic of treatments for hair loss and thinning hair. Physicians reviewed the key findings from clinical studies examining the effects of a nutraceutical on hair growth, and shared their experiences with the supplement for treating hair loss and thinning hair in their patients. The participating physicians were **Vivian Bucay** MD (San Antonio, TX), **Wendy Roberts** MD (Palm Springs, CA), **Heidi Waldorf** MD (New York, NY), and **Steven Dayan** MD (Chicago, IL).

The Prevalence of Hair Loss

What percentage of your patients is concerned about their hair, including but not limited to loss, thinning, or texture?
Dr. Bucay: *Probably between 20% and 30%.*

Dr. Roberts: *Approximately 30%.*

Dr. Waldorf: *Fewer than 10% discuss it. Probably 25% of those who take supplements are on some hair/nail supplement.*

Among patients concerned with the condition of their hair, what is the percentage of male vs female?
Dr. Bucay: *I would say that of the ones who bring up hair loss, 80% to 90% are women, probably because the male patients usually present for androgenic alopecia and there is so much in the marketplace that also addresses the issue.*

Dr. Roberts: *Males 40% and females 60%.*

Dr. Waldorf: *90% female, but most of my cosmetic patients are female.*

Treatment Options

List the treatments that you currently recommend for hair concerns. Please include over-the-counter (OTC), prescription, and other treatments.

Dr. Bucay: *I recommend Viviscal, topical minoxidil, bimatoprost off-label mixed in with minoxidil solution, Ducray Neoptide® Spray (Ducray Laboratoires Dermatologiques, Boulogne, France) if appropriate, oral spironolactone, which acts as a 5-α reductase inhibitor, oral finasteride, and oral dutasteride.*

Dr. Roberts: *I recommend finasteride, minoxidil, spironolactone, tretinoin, vitamins, supplements, laser, platelet-rich plasma, and hair transplantation.*

Dr. Waldorf: *I recommend OTC conditioners/prewashes to protect/improve the condition of the hair, Latisse® (Allergan, Inc., Irvine, CA), RevitaLash® (Athena Cosmetics, Inc., Ventura, CA) for hair and brows, minoxidil, and, for men only, Propecia® (Merck & Co., Inc., Kenilworth, NJ).*

Do you believe there is a need for an effective oral hair supplement?

Dr. Bucay: *Absolutely!*

Dr. Roberts: *Absolutely, yes.*

Dr. Waldorf: *For an effective hair* and *nail supplement. Many patients are on "hair/nail" supplements.*

Several reports describe the use of combination therapy for the treatment of hair loss, such as topical minoxidil with finasteride for male pattern hair loss,[23] or topical minoxidil with spironolactone for female pattern hair loss.[24] Others describe the use of topical minoxidil with herbal products such as red ginseng[25] or nutritional supplements containing antioxidants, vitamins, iron, folic acid, biotin, calcium, minerals, and amino acids.[26]

How about combining supplement use with topical minoxidil?

Dr. Waldorf: *Minoxidil doesn't compete with supplementation. They would use them at the same time.*

Dr. Roberts: *Yes, they do 2 different things. That's synergy…it's a different approach.*

Dr. Waldorf: *Who do you have use it?*

Dr. Bucay: *For every patient who comes in complaining of hair loss or thinning hair, they realize they don't have as much hair as they used to. I don't see anything clinically wrong, but I think as we get older a lot of people do notice their hair.*

Review of Viviscal Clinical Results

After reviewing the data, how do you see Viviscal fitting into a treatment regimen for your patients?

Dr. Bucay: *I think that Viviscal is an excellent option either as a stand alone supplement or as part of a comprehensive hair restoration plan. This may include prescription medications or even the recommendation for hair transplantation, which I do not do.*

Dr. Roberts: *Viviscal should be used by hair loss patients who do not have shellfish allergies or contraindications.*

Dr. Waldorf: *The data were persuasive. I am currently doing an anecdotal "trial" on myself and a patient to see if we notice the difference.*

Dr. Dayan: *All of the patients from my study are on Viviscal. Every single one of them continued on, and they're thrilled.*

DISCLOSURES

The opinions expressed in this supplement are solely those of the authors. Carl S. Hornfeldt PhD RPh has received honoraria fees as a consultant for Lifes2good. Mark Holland is an employee of Lifes2good. Steven H. Dayan MD was an advisor to Viviscal and an investigator in the clinical studies. Heidi A. Waldorf MD, Vivian W. Bucay MD, Wendy E. Roberts MD, and Steven H. Dayan MD all received an honorarium for their participation in the roundtable discussion.

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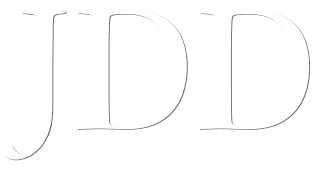

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