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DIRECTOR'S MESSAGE



Devon Powell,
Executive Director

The holidays are behind us, and we're full steam ahead into 2012, although around here we're hard pressed to tell if it's winter, with temperatures in the 40s, 50s and even the 60s. But we know it's not over yet. I haven't heard of any freeze issues this year for crop growers in the northern Mexico/Texas ranges—knock on wood—but as the cliché goes: “It's not over 'til the fat lady sings.” I'm certain everyone is looking forward to spring as much as I am.

There are a lot of goings-on with the IASC at the moment, including international activities and internal projects that will be completed in the very near future. Chief among the internal projects are the IASC Market Survey, the aloe vera leaf juice monograph, and the finalization of the initial round of aloin testing of all products within the certification program.

IASC Market Survey

This project was undertaken as part of the IASC's efforts to protect the aloe vera industry as a direct result of the National Toxicology Program's (NTP) study on “non-decolorized whole leaf extract of aloe barbadensis Miller.” One of the requests from the Food and Drug Administration (FDA) made following the release of the NTP draft technical report was for industry to provide details on what type(s) of aloe raw ingredients are in aloe vera products in the U.S. marketplace. The IASC stated that the primary ingredients found in marketplace materials are dissimilar to the ingredient tested by the NTP and that it would collect and provide data to support this hypothesis.

Subsequently, IASC staff requested that all members provide information on the raw materials used in any finished products sold in the United States and then compiled this information along with the specification sheets for those raw materials. This packet of information is nearing readiness for a final review, at which time it will be presented to the FDA.

Aloe Vera Leaf and Inner Leaf Juice Monograph

The IASC board approved the development of a monograph on aloe vera leaf and inner leaf juice in 2009, which was supported in part by a special assessment of the membership. The project has reached the high draft level, and the finished standards and compliance monograph is expected to be released in the coming months.

The board subsequently approved the addition of a scientific compendium, which was sponsored in part by Herbalife, with the other half of the funding coming from the IASC general funds.

Aloin Testing of Certification Program Products & Raw Materials

The IASC board approved the adoption of the testing of products within the program for compliance with the ≤ 10 ppm aloin (at single strength) standard, which was implemented October 2010. The process has included the development of an high-performance liquid chromatography method, which will soon undergo AOAC Single Laboratory Validation of Chemical Methods for Dietary Supplements and Botanicals. The program's products, which included more than 450 at the time, have all now been tested using this new method, and the results, including chromatograms, will be sent to all participants shortly.

Out of the 450+ products analyzed, almost all were in compliance with the IASC standard. In fact, the vast majority of those products tested had far less than the ≤ 10 ppm standard. The industry should be proud to have supported

the production of this data and having it available to clearly demonstrate and clarify industry's stance that our products contain very little aloin. This will assist our efforts greatly going forward.

I'll personally be looking forward to seeing these projects finalized and available to the industry. There's great satisfaction in continuing to serve this group, and I'll look forward to seeing many of you next month in Anaheim at Natural Products Expo West!



Devon Powell
Executive Director



Regulation of Dietary Supplement Claims and Substantiation

By Marc Ullman and Linda Dougherty

Any dietary supplement manufacturer making a claim on a product's label or labeling that the product affects the structure or function of the body is required under the Federal Food, Drug, and Cosmetic Act (FDCA) to have adequate substantiation that the structure/function claim is truthful and not misleading (FDCA Section 403(r)(6)). In addition, the Federal Trade Commission (FTC) regulates claims made in dietary supplement advertising and also requires that claims be substantiated, truthful, and not misleading. This article discusses the Federal Drug Administration's (FDA) enforcement of the FDCA's substantiation requirement and information FDA has provided through guidance documents concerning and explaining this requirement.

Determining whether the Product is a Dietary Supplement

The Dietary Health and Education Act of 1994 (DSHEA) recognizes dietary supplements as a special category of "food" products, which may qualify to

make structure/function claims. It is important to note that dietary supplements are statutorily defined by DSHEA as products that are orally ingested; thus, topical products (e.g., lotions and creams) cannot be marketed as "dietary supplements." Such products may be marketed as cosmetics, which are defined as "articles intended to be rubbed, poured, sprinkled, or sprayed on, introduced into, or otherwise applied to the human body or any part thereof for cleansing, beautifying, promoting attractiveness, or altering the appearance." However, cosmetic products are limited to making cosmetic claims (i.e., claims that the product will cleanse, beautify, promote attractiveness, or alter the appearance). Cosmetic products are prohibited from making structure/function claims or drug claims.

Determining whether there is Adequate Substantiation for a Dietary Supplement

The FDCA requires that any structure/function claim being made by a dietary supplement be adequately substantiated. While the term "substantiation" is not statutorily defined, FDA has modeled its substantiation requirement on FTC's requirement that a manufacturer have "competent and reliable scientific evidence" for claims made in advertisements. Whereas FDA has primary jurisdiction over claims made in labeling for dietary supplements, FTC's requirement applies to any claims made about dietary supplements in advertising.

In December 2008, FDA issued a guidance document titled “Substantiation for Dietary Supplement Claims Made Under Section 403(r)(6),” in which FDA sets forth its interpretation of what constitutes adequate substantiation. In this guidance document, FDA outlines the factors a manufacturer should consider in determining whether it has adequate substantiation for claims made in labeling.

The first factor discussed by FDA is identifying the meaning of a claim. FDA notes that a manufacturer must have adequate substantiation for all implied claims as well as for all expressed claims. Moreover, a manufacturer must have substantiation for any reasonable interpretation of statements made on labeling, whether or not the statement was intended to constitute a structure/function claim.

The second factor is considering the relationship of the evidence to the claim. For example, FDA recommends that the studies being used as substantiation for dietary supplement claims identify a specific dietary supplement or ingredient and be relevant to the actual serving size and conditions of use of the dietary supplement product.

The third factor to consider is the quality of the evidence. One criteria to consider is the study design. For example, the so-called “gold” standard study would be a randomized, double blind, placebo-controlled clinical trial on humans. FDA notes, however, that such

studies are not always practical or possible.

The fourth factor involves considering how well the totality of evidence supports the structure/function claim being made. FDA states that the strength of the entire body of evidence should be considered, including the quantity of studies and the consistency and replication of findings.

In addition to reviewing FDA’s guidance document, it is advisable to review FTC’s guidance document titled “Dietary Supplements: An Advertising Guide for Industry.”

FDA’s Enforcement of the Substantiation Requirement

The first step FDA will generally take to enforce the substantiation requirement is issuance of a Warning Letter, in which FDA states its conclusion that a claim made on labeling is not supported by reliable scientific evidence. Manufacturers or marketers receiving a Warning Letter have 15 days to respond. These letters are published on FDA’s website and are publicly accessible.

Dietary supplement marketers are required to submit a 30-day notification letter to FDA outlining the structure/function claims being made in labeling. FDA may, but is not required to, respond to such letters with a Courtesy Letter stating FDA’s belief that the products claims constitute drug claims rather than structure/function claims. However, FDA’s failure to send a Courtesy Letter does not constitute tacit approval of the claims being made, and FDA may thereafter send a Warning Letter after the product is on the market.

In the event that a manufacturer does not adequately address FDA’s concerns listed in a Warning Letter, FDA may seek an injunction in federal court and may execute a seizure of the products making an impermissible claim. In certain cases, the manufacturer or marketer may be found criminally liable.

FTC, on the other hand, does not issue Warning Letters, but rather files administrative complaints or complaints in federal court, which carry the potential of significant financial penalties, injunctions, and 20-year consent decrees.



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It is important to note that an additional consequence may be a consumer class-action lawsuit against the manufacturer and marketer for making unsubstantiated claims. Warning Letters issued by FDA have been used to support plaintiffs' claims in product liability and consumer fraud litigations.

Conclusion

Whether you are marketing a dietary supplement product or a cosmetic product, it is important to confirm that all claims being made are appropriate for the relevant product category and that any structure/function claims being made for dietary supplements are supported by adequate substantiation. It is highly advisable that any manufacturer or marketer with questions as to whether its product claims are appropriate seek the advice of counsel prior to marketing the product.

* * *

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SCIENCE & ALOE: LITERATURE CITATIONS BY STEVEN DENTALI, PH.D.

40 Marker Compounds in an Herbal Formula Quantified by One Method

- ◆ Liu M, Liu S, Shi X, Liu M, Zhang YD, Wang Q. [Quality evaluation of a herbal prescription through quantification of 40 components by HPLC-ESI-MS/MS.](#) *Phytochem Anal.* 2011 Oct 21. doi: 10.1002/pca.1366. [Epub ahead of print]

This study reported the successful measurement of 40 marker compounds in an herbal formula and the use of the method for analysis of 10 manufactured product batches.

Heavy Metal Analysis of Herbal Materials

- ◆ Yuan X, Chapman RL, Wu Z. [Analytical methods for heavy metals in herbal medicines.](#) *Phytochem Anal.* 2011 May-Jun;22(3):189-198. Available for free [download](#).



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This review, available for free download, discusses contemporary methods of heavy-metal analysis that are applied to herbal materials, including the commonly used technologies of atomic absorption spectrometry and inductively coupled plasma mass spectrometry.

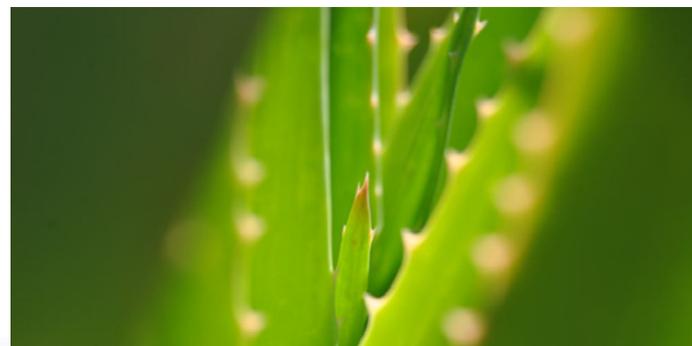
No Toxicity Seen from Aloe Vera Gel CO₂ Extract

- ◆ Tanaka M, Yamada M, Toida T, Iwatsuki K. [Safety evaluation of supercritical carbon dioxide extract of Aloe vera gel.](#) *J Food Sci.* 2011 Nov 10. doi: 10.1111/j.1750-3841.2011.02452.x. [Epub ahead of print]

Safety studies were performed on a supercritical carbon dioxide extract, prepared from washed aloe vera inner leaf material. Testing for genotoxicity was negative and no adverse effects were seen in single dose or 90-day dosing with administration of 150 mg/kg in rats.

IASC AND ALOE IN THE NEWS

- ◆ [Ingredient innovation central to global soft drink growth](#) – [Beveragedaily.com](#)
- ◆ [Water Board to distribute rare medicinal saplings](#) – [The Times of India](#)
- ◆ [Many uses makes Aloe Vera a must](#) – [The Fort Bend \(Texas\) Sun](#)
- ◆ [The miracle of Aloe Vera](#) – [examiner.com](#)
- ◆ [Super food beauty smoothie](#) – [University News, University of Missouri-Kansas City](#)



LEGAL & LEGISLATIVE NEWS

Capitol Hill Update: A Look Ahead

By Peter Evich, Vice President, Van Scoyoc Associates, and AHPA National Legislative Consultant

For its final act of 2011, Congress gave us another round of high-stakes political theater. In this act, however, the House Republicans were the ones who blinked when they agreed to accept the Senate's compromise to extend for two months the current holiday that lowers workers' Social Security payroll taxes from 6.2 percent to 4.2 percent. The House's acceptance of this stopgap measure averted a January tax increase for 160 million Americans.

Also part of the short-term payroll-tax package was a 60-day extension of unemployment benefits and a continuance of the current Medicare reimbursement rates for doctors, who were facing the prospect of a 27 percent rate cut starting Jan. 1, 2012. In addition, the bill adopted an expedited approval process for the controversial Keystone XL pipeline to bring Canadian tar sands oil to Texas refineries.

Unfortunately, the partisan rancor over the payroll-tax-extension legislation overshadowed bipartisan congressional approval of the fiscal year (FY) 2012 omnibus spending measure (H.R. 2055), which occurred mid-December. While the passage of this multi-bill budget package occurred two and a half months into the new fiscal year, the enactment of the FY12 annual federal budget stands in stark contrast to the protracted congressional fight that occurred over the FY11 appropriations measures, which Congress and the president weren't able to agree on until six and half months into the fiscal year for which the measures were meant to cover.

Second Session of the 112th Congress: Outlook for 2012

Even as rancor and legislative uncertainty dominated the final days of the first session of the 112th Congress, House Republican leaders have been working on an agenda for 2012 that is designed to portray a majority

party eager to find common ground on pressing national issues.

Moreover, the inability of the joint-deficit committee to produce legislation last fall offers an added incentive for Congress to enact targeted pieces of legislation. A shift to more routine legislation could give Speaker of the House John Boehner, R-Ohio, a chance to deliver on his promise to allow legislation to emerge from congressional committees. The erosion of “regular order” in the 112th Congress has been an overriding concern of serious congressional observers, but look to see a real effort by both House and Senate leaders to return to a deliberative legislative process this year.

Above all, though, the major dynamic at play is that 2012 is both a presidential and congressional election year. Inevitably, the presidential campaign will influence both the agenda and the tenor of debate in Congress. Just as President Obama has been coordinating his campaign themes with his party’s legislative efforts, congressional Republicans are also likely to take some cues from their nominee.

Prescription Drug User Fee Act Reauthorization

Many congressional committees have already begun to make plans for this year, and some legislative priorities are clear. One guaranteed agenda item that the House Energy and Commerce and Senate HELP Committees will be considering in the coming months is the reauthorization of the Prescription Drug User Fee Act (PDUFA). Originally passed in 1992, PDUFA authorized the Food and Drug Administration (FDA) to begin collecting fees from drug sponsors to expand FDA staff so that new drugs could be reviewed more quickly. Since the existing PDUFA law expires on Sept. 30, 2012, the congressional objective is to get PDUFA reauthorization passed before the current law lapses.

Obviously, prescription-drug user fees do not impact the supplement industry. However, this must-pass legislation is always a magnet for other provisions that address issues and items within FDA purview. For instance, federal lawmakers who have been following reports of tainted drugs have signaled that they will attempt to use PDUFA reauthorization to enact measures that will add more layers of requirements to address what they believe are safety issues and other

deficiencies in the pharmaceutical supply chain. A supply shortage of certain drugs is another major issue, so it is expected that some legislators will look to tuck on provisions to deal with inadequate supplies of critical medicines.

In years past, the supplement industry was on watch to thwart harmful provisions that were being considered by our congressional detractors as possible “add-ons” to PDUFA reauthorization. While we will of course be on the lookout for efforts to add language to PDUFA that undermines the trade (for example, new or existing legislation from Sen. Richard Durbin, D-Ill.), we may need to view PDUFA as a vehicle that provides an opportunity to achieve our objectives. Reasonable questions to ask at this juncture are: Why? How? I’ll address both of these questions, but in reverse order.

NDI Guidance and FSMA Reinspection Fees: Legislative Relief?

The industry has a potential opportunity to be proactive as it relates to PDUFA because supplement champion Sen. Tom Harkin, D-Iowa, serves as the chairman of the Senate HELP Committee. As chairman, Harkin will be spearheading the PDUFA reauthorization effort on the Senate side. Our other top Senate champion, Sen. Orrin Hatch, R-Utah, also sits on the HELP Committee. Looking at the House, our major detractors, Reps. Henry Waxman, D-Calif., and John Dingell, D-Mich., are in the minority party, and therefore their influence on shaping or amending this legislation is greatly diminished.

In light of the deeply troubling (to put it mildly!) new dietary ingredient (NDI) draft guidance document, there may be a compelling need to look at PDUFA reauthorization as a vehicle for our congressional champions to give FDA very clear direction on the Dietary Supplement Health and Education Act’s intent regarding the agency’s regulatory authority related to NDIs. In short, if we come to believe that FDA does not intend to make significant changes in its final NDI guidance, a legislative remedy must be on the table.

Another issue that may require the supplement trade’s attention is FDA’s pending implementation of reinspection fees under the Food Safety Modernization Act (FSMA). The American Herbal Products

Association (AHPA) has formally submitted comments to FDA calling on the agency to publish guidance, as required under law, before assessing reinspection fees on small businesses (see the Dec. 1, 2011, *AHPA Update: AHPA Submits Comments to FDA on FSMA Fees*). If FDA does not provide small businesses relief related to FSMA reinspection fees, congressional intervention might need to be pursued on this issue.

At some point this year, the supplement industry may conclude that, without legislative intervention, FDA will take actions that will harm this class of goods, restrict consumer access to supplements, and negatively impact the economy. If so, we will need to orchestrate our efforts, harness our congressional strengths, and seize upon the finite opportunities that will be available in the coming months to achieve our goals.

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Senators Hatch and Harkin Urge FDA to Withdraw NDI Draft Guidance

In a [letter](#) to Food and Drug Administration (FDA) Commissioner Margaret Hamburg, M.D., Sens. Orrin Hatch, R-Utah, and Tom Harkin, D-Iowa—the principal authors of the Dietary Supplement Health and Education Act (DSHEA)—asked Hamburg to immediately withdraw the agency’s controversial draft guidance on new dietary ingredients (NDI) and begin work on “a new draft that will provide needed clarification on what constitutes an NDI, but does not undermine the balance Congress struck in DSHEA to provide consumers with access to safe, affordable dietary supplement products.”

Saying that the draft guidance “serves to undermine DSHEA in a number of important aspects,” the senators listed their “significant” concerns with the current draft guidance, including:

- The requirement that manufacturers submit an NDI notification for every dietary supplement containing



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an NDI; The contention that synthetic copies of botanicals can never be dietary ingredients;

- The limit on the types of physical modifications that do not result in “chemically altering” a dietary supplement by “incorrectly construing the list in DSHEA legislative history as an exclusive rather than illustrative list.”
- The limit on physical modifications diverges from Congressional intent by “including only ingredients that were marketed before enactment of DSHEA in the form of dietary supplements as ‘old dietary ingredients.’”

Because of these and “other concerns,” the senators asked Hamburg to direct her staff to meet with their staffs in early January to discuss their concerns in more detail. The meeting was held on Jan. 26, but any outcomes have not been made public.

“The American Herbal Products Association is pleased that Senators Hatch and Harkin have requested that FDA withdraw the draft NDI guidance,” said AHPA President Michael McGuffin. “This request is in alignment with the position AHPA stated in our comments submitted to the agency in December. We look forward to working with FDA to create new guidance that is consistent with DSHEA and ensures that consumers will continue to have access to safe, affordable dietary supplement products.”

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Durbin, Waxman Ask GAO to Review Adverse Events Reporting System

On November 8, Sen. Richard Durbin, D-Ill., and Rep. Henry Waxman, R-Calif., sent a [letter](#) to the Government Accountability Office (GAO) asking it to examine whether the Food and Drug Administration

(FDA) is effectively executing the Adverse Events Reporting (AER) process for dietary supplements.

In place since 2007, the AER system allows FDA to track issues associated with dietary supplements by mandating that manufacturers, packers, and distributors report any supplement-related adverse health effects to FDA. Established by the Dietary Supplement and Over the Counter Drug Consumer Protection Act of 2006, also sponsored by Durbin, the system was intended to increase transparency within the industry and to facilitate FDA’s ability to act upon any impending health threats linked to supplements.

Durbin and Waxman claim in their letter, however, that FDA’s management of this system is murky. Although FDA created an Internet-based portal, [MedWatchPlus](#), to give manufacturers, health care providers, and consumers a single place to report adverse health effects, Durbin and Waxman challenge how often the system is being used and how frequently, efficiently, and effectively FDA reviews and acts upon inputted information. The letter outlines seven specific questions for GAO to pose to FDA in order to solicit a precise rundown of usage and to determine what types of AERs are being filed.

Durbin purports that such clarification is necessary in order to better protect consumers against potentially harmful supplements. “Most products labeled as dietary supplements are legitimate health aids,” Durbin said in a statement November 8. “But that is not the case for all of them, and consumers deserve to know that the FDA is looking out for their health and safety by keeping unsafe supplements off the shelves. The FDA has the tools necessary to determine which supplements can cause and have caused severe health problems—they should use them effectively.”

However, according to news reports, industry trade associations contend that such a review will prove that the AER process is indeed functioning properly and therefore offering adequate consumer protection. According to the American Herbal Products Association (AHPA), of the first 598 AERs submitted on supplements, 59 percent came from manufacturers, 29 percent from consumers, and 10 percent from health care professionals. AHPA President Michael McGuffin

asserted in a 2009 report that the industry was complying with this process.

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Anti-hyperglycemic and Anti-hypercholesterolemic Effects of Aloe vera Leaf Gel in Hyperlipidemic Type 2 Diabetic Patients: A Randomized Double-Blind Placebo-Controlled Clinical Trial.

Abstract

Diabetes mellitus type 2 with dyslipidemia is a common disease. Previous studies suggest that *aloe* (*ALOE VERA* L.) leaf gel may positively affect the blood glucose and lipid levels in dyslipidemic type 2 diabetic patients. Thus, in this randomized double-blind placebo-controlled clinical trial with hyperlipidemic (hypercholesterolemic

and/or hypertriglyceridemic) type 2 diabetic patients aged 40 to 60 years not using other anti-hyperlipidemic agents and resistant to daily intake of two 5 mg glyburide tablets and two 500 mg metformin tablets, the efficacy and safety of taking *aloe* gel (one 300 mg capsule every 12 hours for 2 months) combined with the aforementioned drugs in treatment of 30 patients were evaluated and compared with the placebo group (n = 30). The *aloe* gel lowered the fasting blood glucose, HbA1c, total cholesterol, and LDL levels significantly (p = 0.036, p = 0.036, p = 0.006, and p = 0.004, respectively) without any significant effects on the other blood lipid levels and liver/kidney function tests (p > 0.05) compared with the placebo at the endpoint. No adverse effects were reported. The results suggest that *aloe* gel may be a safe anti-hyperglycemic and anti-hypercholesterolemic agent for hyperlipidemic type 2 diabetic patients.

Clinical and Microbiological Effects of Commercially Available Dentrifice Containing Aloe vera: A Randomized Controlled Clinical Trial.

Abstract

BACKGROUND: Certain plants used in folk



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medicine serve as a source of therapeutic agent by having antimicrobial and other multi-potential effects. This prospective, randomized, placebo and positively controlled clinical trial was designed to evaluate the clinical and microbiological effects of a commercially available dentifrice containing *Aloe vera* in the reduction of plaque and gingival inflammation in subjects with gingivitis.

MATERIAL AND METHODS: Ninety subjects diagnosed with chronic generalized gingivitis were selected and randomly divided into three groups: Group 1 ? placebo toothpaste, Group 2 ? *Aloe vera* containing toothpaste and Group 3 ? triclosan containing toothpaste with polymer and fluoride. Clinical evaluation was undertaken using the gingival index of L?e and Silness and plaque was assessed using the Tureskey et al. modification of Quigley Hein Index and microbiological counts were assessed at baseline, 6 weeks, 12 weeks and 24 weeks. A subjective evaluation was also undertaken by questionnaire.

RESULTS: *Aloe vera* containing toothpaste showed significant improvement in gingival and plaque index scores as well as microbiologic counts compared to placebo dentifrice. These improvements were comparable to triclosan containing toothpaste.

CONCLUSIONS: *Aloe vera* containing toothpaste may be a useful herbal formulation for chemical plaque control agent and improvement in plaque and gingival status.

Clinicopathological Studies on Vitamin D(3) Toxicity and Therapeutic Evaluation of Aloe vera in Rats.

Abstract

A study was conducted to examine the clinical signs, hematological, biochemical and histopathological changes in vitamin D(3) toxicity at a dose rate 2 mg/kg b.wt. of vitamin D(3) and to assess the protective effect of *Aloe vera* in vitamin D(3) toxicity. The clinical signs observed were anorexia, progressive weight loss, difficulty in movement and respiration, diarrhea, epistaxis, subnormal body temperature and nervous signs before death. Mortality was observed in treated rats between day 10 and day 19 of treatment. The gross postmortem changes observed were severe emaciation,

white chalky deposits on epicardial surface of heart, pin point white deposits on cortical surface of kidneys with pale yellow discoloration and diffused white deposits on serosal surface of stomach and intestine with bloody ingesta in lumen. The hematological changes included non-significant increase in hemoglobin and total leukocyte count and significant increase in relative neutrophil count. The biochemical changes observed were significant increase in plasma concentration of calcium, phosphorus and blood urea nitrogen, whereas a significant decrease in the concentration of albumin and total plasma protein was observed. The histopathological lesions included calcification of various organs, viz., tongue, stomach, intestines, kidney, heart, aorta, larynx, trachea, lungs, spleen, choroid plexus arteries of brain and vas deferens. The *Aloe vera* juice (2.5% in drinking water) has no protective effect on vitamin D(3) toxicity (2 mg/kg b.wt.).

Comparison of aloe vera mouthwash with triamcinolone acetonide 0.1% on oral lichen planus: a randomized double-blinded clinical trial.

Abstract

INTRODUCTION: Corticosteroids are the mainstay for treatment of oral lichen planus (OLP) and have their own side effects. The aim of this study was to compare the therapeutic effects of *aloe vera* (AV) mouthwash with triamcinolone acetonide 0.1% (TA) on OLP.

METHODS: A total of 46 patients with OLP were enrolled in this study. The patients were randomly divided into 2 groups. Each group was treated with received AV mouthwash or TA. The treatment period for both groups was 4 weeks. The basement data were recorded for each patient. Patients were evaluated on days 8, 16 and after completing the course of treatment (visit 1-3). The last follow-up was 2 months after the start of treatment (visit 4). Visual analogue scale was used for evaluating pain and burning sensation and Thongprasom index for clinical improvement and healing. In addition, lesion sizes were measured and recorded at each visit using a grid.

RESULTS: Baseline characteristics, including pain and burning sensation score, size and clinical characteristics of the lesions according to Thongprasom index, were

not different between the 2 treatment groups. Both AV and TA significantly reduced visual analogue scale score, Thongprasom score and size of the lesions after treatment ($P < 0.001$) and after 2 months of discontinuation of the treatment ($P < 0.001$). In the AV group, 74% of patients and in the TA group 78% of patients showed some degrees of healing in the last follow-up.

CONCLUSIONS: AV mouthwash is an effective substitute for TA in the treatment of OLP.

Computer aided screening and evaluation of herbal therapeutics against MRSA infections.

Abstract

Methicillin resistant *Staphylococcus aureus* (MRSA), a pathogenic bacterium that causes life threatening outbreaks such as community-onset and nosocomial infections has emerged as 'superbug'. The organism developed resistance to all classes of antibiotics including the best known Vancomycin (VISA). Hence, there is a need to develop new therapeutic agents. This study mainly evaluates the potential use of botanicals against MRSA infections. Computer aided design is an initial platform to screen novel inhibitors and the data finds applications in drug development. The drug-likeness and efficiency of various herbal compounds were screened by ADMET and docking studies. The virulent factor of most of the MRSA associated infections are Penicillin Binding Protein 2A (PBP2A) and Panton-Valentine Leukocidin (PVL). Hence, native structures of these proteins (PDB: 1VQQ and 1T5R) were used as the drug targets. The docking studies revealed that the active component of *Aloe vera*, β -sitosterol (3S, 8S, 9S, 10R, 13R, 14S, 17R) -17- [(2R, 5R)-5-ethyl-6-methylheptan-2-yl] -10, 13-dimethyl 2, 3, 4, 7, 8, 9, 11, 12, 14, 15, 16, 17- dodecahydro-1H-cyclopenta [a] phenanthren-3-ol) showed best binding energies of -7.40 kcal/mol and -6.34 kcal/mol for PBP2A and PVL toxin, respectively. Similarly, Meliantriol (1S-1-[(2R, 3R, 5R)-5-hydroxy-3-[(3S, 5R, 9R, 10R, 13S, 14S, 17S)-3-hydroxy 4, 4, 10, 13, 14-pentamethyl-2, 3, 5, 6, 9, 11, 12, 15, 16, 17-decahydro-1H-cyclopenta[a] phenanthren-17-yl] oxolan-2-yl] -2- methylpropane-1, 2 diol), active compound in *Azadirachta indica* (Neem) showed the binding energies of -6.02 kcal/mol for PBP2A and -8.94 for PVL toxin. Similar studies were conducted with

selected herbal compound based on pharmacokinetic properties. All in silico data tested in vitro concluded that herbal extracts of *Aloe-vera*, Neem, Guava (*Psidium guajava*), Pomegranate (*Punica granatum*) and tea (*Camellia sinensis*) can be used as therapeutics against MRSA infections.

Concomitant herbal medicine and Antiretroviral Therapy (ART) use among HIV patients in Western Uganda: A cross-sectional analysis of magnitude and patterns of use, associated factors and impact on ART adherence.

Abstract

Abstract use of herbal medicines among patients receiving Anti-retroviral Therapy (ART) remains by far an uncharacterised phenomenon in Africa and Uganda specifically. We evaluated the use of herbal medicines among patients on ART at the HIV clinic of Mbarara Regional Referral Hospital (MRRH), examined factors associated with their concomitant use and their impact on ART adherence. This was a cross-sectional study among 334 systematically sampled patients receiving ART at the HIV clinic of MRRH from February to April 2010. We collected data on patient demographics, clinical characteristics, perceptions of quality of care received, self-perceived health status, information on ART received, herbal medicines use and ART adherence. Study outcomes were concomitant herbal medicine and ART use, and ART adherence. Descriptive analysis and logistic regression were conducted using Stata10.0. Close to half, 155 (46.4%) reported concomitant herbal medicines and ART use, with 133 (39.8%) using herbal medicines at least once daily. Most (71.6%) used herbal medicines to treat HIV-related symptoms. A majority (92.3%) reported that the doctors were unaware of their use of herbal medicines, 68.5% citing its minimal importance to the attending physician. Most frequently used herbs were *Aloe vera* (25%) and *Vernonia amygdalina* (21%). Time since start of ART (OR 1.14 95% CI: 1.01-1.28, for each one year increase), number of ART side effects reported (≥ 3 vs. ≤ 1 , OR 2.20 95% CI 1.13-4.26) and self-perceived health status (Good vs. Poor, OR 0.31 95% CI 0.12-0.79) were independently associated with concomitant herbal medicine and ART use. Concomitant herbal medicine and ART use was not

associated with poor ART adherence (OR 0.85 95% CI 0.47-1.53). There is widespread concomitant herbal medicines and ART use among our patients, with no association to poor ART adherence. Patients appear to use these therapies to complement as opposed to substituting ART.

Cytogenetic toxicity of *Aloe vera* (a medicinal plant).

Abstract

The cytogenetic toxicity of the crude leaf extract of *Aloe vera*, a medicinal plant, was evaluated in two test systems, onion and Swiss albino mice, using their root tip meristematic and bone marrow cells, respectively. No significant increase in structural abnormalities in chromosomes was observed, but a marked increase in cells with chromosome-number anomalies was found. The extract, however, significantly increased the mitotic index of both cell types.

Evaluation of wound-healing formulation against sulphur mustard-induced skin injury in mice.

Abstract

Sulphur mustard (SM) is a bifunctional alkylating agent that causes cutaneous blisters in human and animals. Remedies to SM-induced dermatotoxicity are still in experimental stage. Due to inevitable requirement of a wound-healing formulation against SM-induced skin lesions, efficacy of formulations including povidone iodine, *Aloe vera* gel, betaine or framycetin sulphate was evaluated in present study. SM was applied percutaneously (5 mg/kg) once on back region of Swiss albino mice; and after 24 hours, DRDE/WH-02 (Defence Research and Development Establishment/ Wound Healant- 02, containing polyvinylpyrrolidone [PVP], *A. vera* gel and betaine), Ovadine, Soframycin or *A. vera* gel were applied topically, daily for 3 or 7 days in different groups. Skin sections were subjected to histopathology, histomorphologic grading, tissue leukocytosis, terminal deoxynucleotidyl transferase dUTP nick end labelling (TUNEL) assay and immunohistochemistry of inflammatory-reparative biomarkers. DRDE/WH-02 treated mice received highest score on the basis of histomorphologic scale and lowest number of TUNEL-positive cells compared to other groups. DRDE/WH-02 showed better wound

healing as evidenced by widespread re-epithelialization, homogenous fibroplasias well supported by the expression of transforming growth factor- α , endothelial nitric oxide synthase (eNOS) and fibroblast growth factor. Upregulation of interleukin 6 in DRDE/WH-02-treated mice skin resulted in increased tissue leukocytosis and an early removal of tissue debris that initiated reparative process at faster rate compared to other groups. In conclusion, DRDE/WH-02 provided better healing effect and can be recommended as an effective wound healant against SM-induced skin injury.

Floral traits mediate the vulnerability of aloes to pollen theft and inefficient pollination by bees.

Abstract

Background and Aims Pollen-collecting bees are among the most important pollinators globally, but are also the most common pollen thieves and can significantly reduce plant reproduction. The pollination efficiency of pollen collectors depends on the frequency of their visits to female(-phase) flowers, contact with stigmas and deposition of pollen of sufficient quantity and quality to fertilize ovules. Here we investigate the relative importance of these components, and the hypothesis that floral and inflorescence characteristics mediate the pollination role of pollen collection by bees. Methods For ten *Aloe* species that differ extensively in floral and inflorescence traits, we experimentally excluded potential bird pollinators to quantify the contributions of insect visitors to pollen removal, pollen deposition and seed production. We measured corolla width and depth to determine nectar accessibility, and the phenology of anther dehiscence and stigma receptivity to quantify herkogamy and dichogamy. Further, we compiled all published bird-exclusion studies of *aloes*, and compared insect pollination success with floral morphology. Key Results Species varied from exclusively insect pollinated, to exclusively bird pollinated but subject to extensive pollen theft by insects. Nectar inaccessibility and strong dichogamy inhibited pollination by pollen-collecting bees by discouraging visits to female-phase (i.e. pollenless) flowers. For species with large inflorescences of pollen-rich flowers, pollen collectors successfully deposited pollen, but of such low quality (probably self-pollen) that they made almost no contribution to seed set. Indeed, considering

all published bird-exclusion studies (17 species in total), insect pollination efficiency varied significantly with floral shape. Conclusions Species-specific floral and inflorescence characteristics, especially nectar accessibility and dichogamy, control the efficiency of pollen-collecting bees as pollinators of *aloes*.

Herbal medicine in the treatment of ulcerative colitis.

Abstract

Ulcerative colitis (UC) is a refractory, chronic, and nonspecific disease occurred usually in the rectum and the entire colon. The etiopathology is probably related to dysregulation of the mucosal immune response toward the resident bacterial flora together with genetic and environmental factors. Several types of medications are used to control the inflammation or reduce symptoms. Herbal medicine includes a wide range of practices and therapies outside the realms of conventional Western medicine. However, there are limited controlled evidences indicating the efficacy of traditional Chinese medicines, such as *aloe vera* gel, wheat grass juice, *Boswellia serrata*, and bovine colostrum enemas in the treatment of UC. Although herbal medicines are not devoid of risk, they could still be safer than synthetic drugs. The potential benefits of herbal medicine could lie in their high acceptance by patients, efficacy, relative safety, and relatively low cost. Patients worldwide seem to have adopted herbal medicine in a major way, and the efficacy of herbal medicine has been tested in hundreds of clinical trials in the management of UC. The evidences on herbal medicine are incomplete, complex, and confusing, and certainly associated with both risks and benefits. There is a need for further controlled clinical trials of the potential efficacy of herbal medicine approaches in the treatment of UC, together with enhanced legislation to maximize their quality and safety.

Herbs in dentistry.

Abstract

Herbs have been used for centuries to prevent and control disease. Herbal extracts are effective because they interact with specific chemical receptors within the body and are in a pharmacodynamic sense, drugs themselves. By using herbal medicines, patients have

averted the many side effects that generally come with traditional medicines, but this does not mean that side effects do not occur. Only knowledgeable practitioners can prescribe the right herb and its proper dosage. Herbal medicines had been considered in every culture, however, pharmaceutical companies overturned this type of thinking. Now, pharmaceuticals are called traditional and herbs are libeled as the 'alternative'. The biggest challenge and problem is lack of information about the effect of herbs in oral tissues, mechanism of effect, and side effects. *Several* popular conventional drugs on the market are derived from herbs. These include aspirin (from white willow bark), digitalis (from foxglove), and sudafed (modelled after a component in the plant ephedra). Herbal products can vary in their potency. Therefore, care must be taken in selecting herbs, even so, herbal medicines have dramatically fewer side effects and are safer to use than conventional medications. The herbs described in this article are Bloodroot, Caraway, Chamomile, Echinacea, Myrrh, Peppermint, Rosemary, Sage, Thyme, *Aloe Vera*, Propolis, and a summary of other herbs that are useful in dentistry. Herbs may be good alternatives to current treatments for oral health problems but it is clear that we need more research.

Immunomodulatory effects of Aloe vera and its fractions on response of macrophages against *Candida albicans*.

Abstract

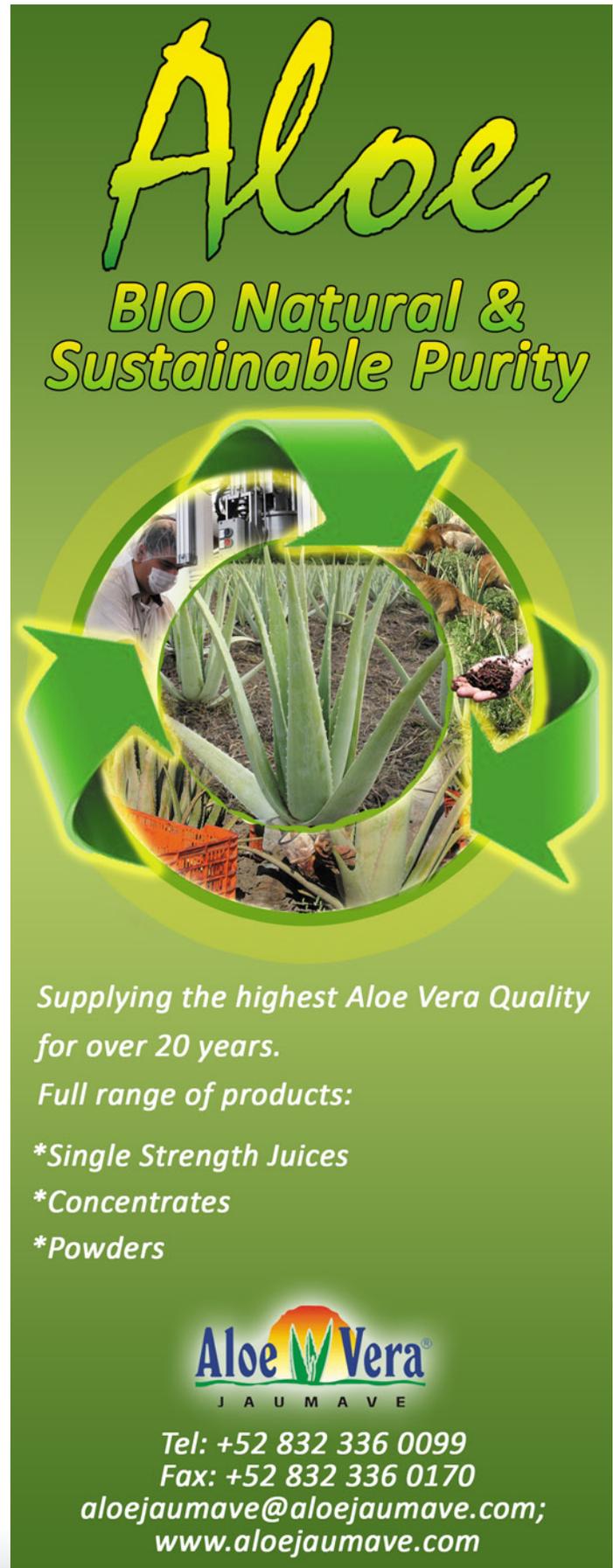
Natural products are important resources in traditional medicine and have been long used for prevention and treatment of many diseases. Medicinal plants have immunomodulatory properties. *Aloe* is one of the herbal medicines widely used in natural treatment and alternative therapy for various types of diseases. *Aloe vera* has been shown to modulate the immune response. Macrophages have been shown to play an essential role as the first line of defense against invading pathogen. *Candida albicans* is a communal and opportunistic pathogen in humans. In this study, we investigated the effect of *A. vera* extract and its fractions on infected macrophages with *C. albicans*. Viability of intraperitoneal macrophages was evaluated by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) test. Cell viability of infected

macrophages was increased by the extract and dose of some isolated fractions dependently. The extract as well as R100, R50, R30, and R10 fractions of *A. vera* significantly increased cell viability of macrophages in most doses. R5 and F5 fractions showed no significant difference in comparison with control group. Further studies in animal models and human are necessary to clarify the modulatory effects of *A. vera* on macrophage function. Isolation and purification of *A. vera* components are also needed to find out the effective molecules.

Immunostimulatory and protective effects of *Aloe vera* against coccidiosis in industrial broiler chickens.

Abstract

This paper reports the immunostimulatory and protective effects of *Aloe vera* extracts (aqueous and ethanolic) against coccidiosis in industrial broiler chickens. The study was divided into two experiments. Experiment-I was conducted for the evaluation of immunostimulatory activity of *A. vera* and experiment-II demonstrated the protective efficacy of *A. vera* extracts against coccidiosis in chickens. Results of the experiment-I revealed significantly higher ($p < 0.05$) lymphoproliferative responses in chickens administered with ethanolic extract of *A. vera* as compared to those administered with aqueous extract and control group. Microplate haemagglutination assay for humoral response on day 7th and 14th post primary and secondary injections of sheep red blood cells (SRBCs) revealed significantly higher ($p < 0.05$) anti SRBC antibody (total Igs, IgG and IgM) titers in chickens of experimental groups as compared to the control group. None of the extracts, however, demonstrated significant effects on the development of lymphoid organs. Results of experiment-II revealed maximum protection (60%) in chickens administered with aqueous *Aloe* extract as compared to the ethanolic extract administered chickens (45%). Mean oocysts per gram of droppings in the control group was significantly higher ($p < 0.05$) as compared to the chickens in both the experimental groups. Chickens administered with aqueous *Aloe* extract showed a minimal mean lesion score (2.3) followed by those administered with ethanolic *Aloe* extract (2.6) and control chickens (3.05) for caeca,



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and a similar pattern was observed for intestinal lesion scoring. Further, significantly higher weight gains and antibody titers ($p < 0.05$) were observed in chickens administered with *A. vera* extracts as compared to those in the control group. It was concluded that *A. vera* may be a potential and valuable candidate to stimulate the immune responses and can be used successfully as an immunotherapeutic agent against coccidiosis in industrial broiler chickens.

Interventions for treating oral lichen planus.

Abstract

BACKGROUND: Oral lichen planus (OLP) is a common chronic inflammatory disease associated with cell-mediated immunological dysfunction. Symptomatic OLP is painful and complete healing is rare. Objectives. To assess the evidence for the efficacy and safety of treatments for symptomatic OLP. Methods: Cochrane Oral Health Group Trials Register, the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE and EMBASE were searched in January 2011 to identify all randomized controlled trials evaluating any intervention for the treatment of symptomatic OLP. Results: 28 trials were included in this Cochrane review. There is no evidence from 3 RCTs that topical pimecrolimus is better than placebo in reducing pain from OLP. There is weak evidence from 2 RCTs that topical *aloe vera* may be associated with a reduction in pain compared to placebo. There is weak and unreliable evidence from two small trials, at high risk of bias, that topical ciclosporin may reduce pain and clinical signs of OLP. There is no evidence (from 5 trials each evaluating a different steroids and/or calcineurin inhibitors) that there is a difference between treatment with topical corticosteroids (TCSs) compared to topical calcineurin inhibitors with regard to reducing pain associated with OLP or that any specific steroid therapy is more or less effective at reducing pain.

CONCLUSIONS: Although TCSs are considered to be first line treatment, we identified no RCTs that compared TCSs with placebo in patients with symptomatic OLP. From the 28 trials included in this systematic review, the wide range of interventions compared means there is insufficient evidence to support the effectiveness of any specific treatment as being superior.

Investigating the Effect of Aloe vera Gel on the Buccal Permeability of Didanosine.

Abstract

The buccal mucosal route offers several advantages but the delivery of certain drugs can be limited by low membrane permeability. This study investigated the buccal permeability properties of didanosine (ddI) and assessed the potential of *ALOE VERA* gel (AVgel) as a novel buccal permeation enhancer. Permeation studies were performed using Franz diffusion cells, and the drug was quantified by UV spectroscopy. Histomorphological evaluations were undertaken using light and transmission electron microscopy. The permeability of ddI was concentration-dependent, and it did not have any adverse effects on the buccal mucosae. A linear relationship ($R^2 = 0.9557$) between the concentrations and flux indicated passive diffusion as the mechanism of drug transport. AVgel at concentrations of 0.25 to 2%w/v enhanced ddI permeability with enhancement ratios from 5.09 (0.25%w/v) to 11.78 (2%w/v) but decreased permeability at 4 and 6%w/v. Ultrastructural analysis of the buccal mucosae treated with phosphate buffer saline pH 7.4 (PBS), ddI/PBS, and ddI/PBS/AVgel 0.5%w/v showed cells with normal plasmalemma, well-developed cristae, and nuclei with regular nuclear envelopes. However, cells from 1, 2, and 6%w/v AVgel-treated mucosae showed irregular nuclear outlines, increased intercellular spacing, and plasmalemma crenulations. This study demonstrates the potential of AVgel as a buccal permeation enhancer for ddI to improve anti-HIV and AIDS therapy.

Outpatient burns: prevention and care.

Abstract

Most burn injuries can be managed on an outpatient basis by primary care physicians. Prevention efforts can significantly lower the incidence of burns, especially in children. Burns should be managed in the same manner as any other trauma, including a primary and secondary survey. Superficial burns can be treated with topical application of lotions, honey, *aloe vera*, or antibiotic ointment. Partial-thickness burns should be treated with a topical antimicrobial agent or an absorptive occlusive dressing to help reduce pain, promote healing, and prevent wound desiccation. Topical silver sulfadiazine is the standard treatment; however, newer occlusive

dressings can provide faster healing and are often more cost-effective. Physicians must reevaluate patients frequently after a burn injury and be aware of the indications for referral to a burn specialist.

Safety evaluation of supercritical carbon dioxide extract of aloe vera gel.

Abstract

The gel of the *Aloe vera* plant has been used safely for oral and external applications. Previously, we found phytosterols derived from an extract of *Aloe vera* gel obtained with an organic solvent to have hypoglycemic and antiobesity effects. While developing of functional foods using *Aloe vera* gel, we produced an active *Aloe vera* gel extract (AVGE) using a supercritical carbon dioxide (CO₂) extraction procedure. In this study, we tested the safety of AVGE in vitro and in vivo. In an acute oral toxicological test in which AVGE was administered to rats at a dose of 150 mg/kg body weight, there were no deaths or apparent abnormalities at necropsy. In a 90-d toxicity test in which rats were continuously administered AVGE at 30 or 150 mg/kg, euthanized, and subjected to pathological examinations, no abnormalities attributable to the AVGE were found. AVGE was nonmutagenic in the Ames test and a chromosomal aberration test at concentrations of up to 5000 µg/plate and 1600 µg/plate, respectively, and in an in vivo bone marrow micronucleus test at up to 150 mg/kg/d. Practical Application: AVGE can be safely used as a functional food material.



Surviving in a Regulated Industry

By Anthony L. Young, Kleinfeld, Kaplan & Becker LLP, and AHPA General Counsel

Last year, the Food and Drug Administration (FDA) took a number of enforcement actions that prove what is so: the dietary supplement industry is regulated, and companies cannot simply ignore FDA inspectional observations or warning letters.

Why does FDA enforce? According to FDA's chief enforcement officer, Dara Corrigan, associate

commissioner for regulatory affairs, it does so because "dietary supplements have a significant role in the public's health." That is good news.

Enforcement Actions

The prime example of FDA enforcement action is its injunctive action against ATF Fitness Products Inc. (ATF), Manufacturing ATF Dedicated Excellence Inc., and James G. Vercellotti of Oakmont, Pa., owner and operator of both companies. The companies are alleged by FDA to have been "substituting ingredients and products without noting the changes on the final product labels," failure to comply with current good manufacturing practice (cGMP), and failure to report "serious adverse events associated with their products. In one case an individual who consumed one of the products reported experiencing a spike in blood pressure, hospitalization, and a subsequent mild heart attack."

Other examples include a California seizure of more than 4,000 pounds of raw material, *Cissus quadrangularis* and *Cassia angustifolia* extracts, that contained ephedrine alkaloids, alkaloids that nature does not put into these two botanicals; seizure of all products at Syntec Inc., a Wisconsin dietary supplement manufacturer with products making disease claims and with cGMP violations; a consent decree of permanent injunction with a Minnesota company making disease claims for amino acid products; a consent decree of permanent injunction with a New York company and an individual for making disease claims for ethylenediaminetetraacetic acid (EDTA) oral chelation products; seizure of probiotics from UAS Laboratories, a Minnesota-based manufacturer making disease claims for the products; and the seizure of elderberry juice products manufactured by Wyledwood Cellars, a Kansas company, for making drug claims. These actions signal clearly that FDA observations and warning letters cannot be ignored.

Warning Letters

The focus of FDA warning letters in 2011 has been on cGMP violations and on disease claims. Any manufacturer that does not have someone assigned to read these letters as they are issued and compare them to their own operations is missing an opportunity to prepare their company in advance of an FDA inspection. Make sure your quality control person

is reading the *AHPA Legal Alerts* that include FDA's warning letters. It may be the best way to keep current with respect to how FDA is enforcing the cGMPs.

National Advertising Division and Natural Products Foundation

What can be done about unfair competition? It is well known in the industry that the Federal Trade Commission (FTC) cannot police all the advertising in the dietary supplement industry. What some marketers are learning, however, is that the National Advertising Division of the Better Business Bureau opens many inquiries into dietary supplement claims and advertising. These actions are fueled in part by funding from the Council for Responsible Nutrition, but also by competitors anxious to assure a level playing field. In addition, the Natural Products Foundation accepts complaints from industry against competitors and pursues those advertisers that are not responsive by sending information to FTC for action. For now, FTC's resources are focused on POM Wonderful and the claims made for its POM Wonderful product, but even this massive case will come to an end at some time, and FTC can be expected to aggressively pursue unsubstantiated claims in the supplement industry.

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FTC Settles “Not Authentic” Hoodia Case; AHPA’s Botanical Authentication Program Provides Analytical ID Methods

The Federal Trade Commission (FTC) announced on Nov. 3 a settlement against two companies and three individuals for deceptively advertising products marketed as hoodia (*Hoodia gordonii*) as a weight-loss supplement ingredient. FTC's complaint, issued in April 2009, focused not only on the weight-loss claims for the companies' hoodia but also on the allegation

that “In truth and in fact, in one or more instances, the product sold ... as *Hoodia gordonii* was not authentic *Hoodia gordonii*.”

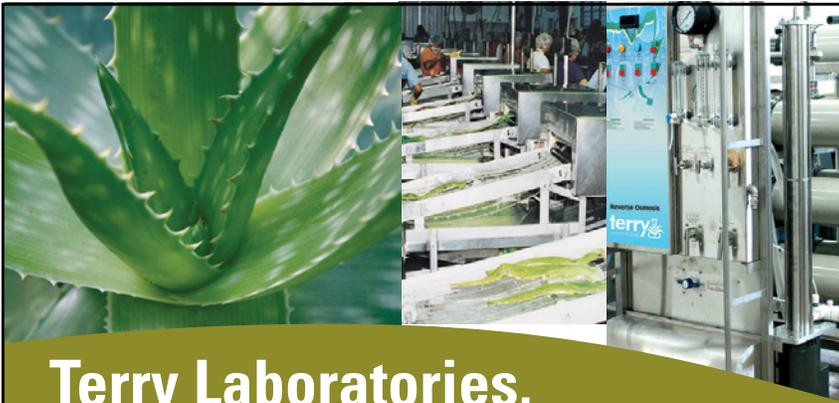
The American Herbal Products Association (AHPA) became aware of concerns about inauthentic hoodia in the market in 2006 and formed a Hoodia Committee to address the issue. AHPA had initiated its *Botanical Authentication Program* in 1997, consisting of two components: identification of botanicals known to be subject to adulteration in trade and determination of relevant analytical methods that can be used to prevent the specified potential adulteration.

AHPA was therefore able to use this decade of experience to solicit and evaluate analytical methods to assist companies marketing hoodia to make good purchasing decisions. Through the efforts of the AHPA Hoodia Committee and the Analytical Laboratories Committee, AHPA has made available on its [website](#) since 2007 microscopic, high-performance thin-layer chromatographic and high-performance liquid-chromatographic analytical techniques to differentiate between authentic and inauthentic hoodia. AHPA member companies Alkemists Pharmaceuticals, CAMAG Scientific Inc., and Flora Research Laboratories provided these methods. The methods are made available at no cost and can be accessed by members and nonmembers alike.

Promulgating these methods for quality assurance was thus part of AHPA's ongoing initiative—which continues to expand—to provide practical tools to the dietary supplement industry, and the AHPA Botanical Authentication Program is now entering its 15th year.

“AHPA has recognized since 1997 that its members and the entire herbal industry occasionally need to work together to create tools that can be used to address deliberate and accidental ingredient adulteration in the marketplace,” commented Michael McGuffin, AHPA president. “Hopefully, the work done on hoodia in our Botanical Authentication Program prevented others from being caught up in FTC's aggressive enforcement against companies accused of falsely claiming that their ingredient is one thing when it is not.”

The settlement announced was against Stella Labs LLC and Nutraceuticals International LLC, as well



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as the companies' principals, David J. Romeo, Craig Payton, and Deborah B. Vickery. All are prohibited from making any false or unsupported claims about foods, drugs, or dietary supplements, and Payton is also banned from marketing any foods, drugs, or dietary supplements. In addition, the settlement imposed a \$22.5 million claim against Romeo, which will be suspended when he forfeits a vacation home and \$635,000 in business loans owed to him. The settlement also requires Vickery to pay a \$4 million judgment, which has been suspended due to her inability to pay.

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AHPA Calls for Withdrawal of “Hugely Flawed” NDI Notification Guidance in Comments to FDA

The American Herbal Products Association (AHPA), in [comments](#) filed with the Food and Drug Administration (FDA) in early December, called for the agency to withdraw what it called the “hugely flawed” “[Draft Guidance for Industry: Dietary Supplements: New Dietary Ingredient Notifications and Related Issues](#).”

In submitting the comments, AHPA also called on the agency to issue new guidance, ensuring that it is consistent with the Dietary Supplement Health and Education Act (DSHEA or the Act) by incorporating revisions to conform to DSHEA and the intent of Congress with regard to new dietary ingredients (NDIs).

“Instead of providing guidance regarding DSHEA’s NDI notification provision, as directed by section 113(b) of the Food Safety Modernization Act (FSMA), the draft guidance seeks to erect extra-legal barriers to market entry, impose food additive- and pharmaceutical-type evaluative criteria, require multiple NDI notifications for dietary supplements beyond those required by law, and transform the legal requirements

for marketing of dietary supplements that contain NDIs from the notification process described under law to an FDA approval process,” AHPA wrote.

AHPA noted that instead of facilitating compliance with the NDI provision of the law, the draft guidance would, if implemented as written with the flaws identified, change the rules that have been in place for the last 17 years and significantly increase the burden on the supplement industry far beyond the intent of Congress with no concomitant benefit for consumers.

A key area of concern in the draft guidance is FDA’s call for multiple NDI filings of the same dietary ingredient, AHPA noted in its comments.

“AHPA believes that separate notifications are not required when the initial notification filed for the NDI provides a description of a dietary supplement or a range of dietary supplements that would include the NDI,” the association said.

“FDA’s actual practice has been to file without objection premarket notifications that describe the NDI specifically but that only generally describe dietary supplements that will contain the dietary ingredient.”

Also of concern in the guidance, “FDA proposes that manufacturers must establish the pedigrees of all old dietary ingredients they use and submit NDI notifications where required for each supplement containing new dietary ingredients,” the organization said. “The draft guidance would require these notifications to be supported by safety documentation meeting food additive petition requirements, the very requirements DSHEA struck out of the dietary supplement paradigm.”

Michael McGuffin, AHPA president, said that AHPA intends to submit subsequent comments to the draft guidance at a later date to offer extensive and specific comments on the section of the draft related to safety research. “AHPA’s view is that this section goes far beyond the intent of the law and is wholly unnecessary and inappropriate in many cases to establish a reasonable expectation of safety.

“One of the key features of AHPA’s comments is that it includes proposed solutions that specifically recommend revisions to the draft guidance,” McGuffin

added. “AHPA has provided FDA with a thoughtful, thorough—and most importantly, lawful—starting point for revised guidance.

“Let me be clear, AHPA has called for FDA to remove the guidance,” McGuffin continued. “Nonetheless, we believe there would be a benefit for FDA to offer guidance that doesn’t rewrite the law and that companies that do have NDIs would find useful.”

The full text of AHPA’s [comments](#) is available for downloading from the AHPA website.

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AHPA Submits Comments on FSMA Fees, Asks for Moratorium on Small Business Reinspection Fees

The American Herbal Products Association (AHPA) in late November submitted comments to the Food and Drug Administration (FDA) stating significant concerns about certain aspects of the agency’s fee structure relating to several provisions of the Food Safety Modernization Act (FSMA), which was enacted in January 2011.

Under FSMA, FDA is now required to assess fees for domestic and foreign facility reinspections, failure to comply with a recall order, and importer reinspections. FDA has now published fees for the current (2012) fiscal year of \$224/hour domestically and \$335/hour for foreign operations.

AHPA’s comments requested that no FSMA-associated fees be imposed on small businesses, with the possible exception of those related to failure to comply with a recall order, until guidance is published in consideration of the burden of fee amounts on small business. Such guidance is required under the law, and may include reduced fee amounts for small businesses.

“AHPA is concerned that FDA appears to already be

assessing FSMA reinspection fees on small business,” commented Michael McGuffin, AHPA president. “Even though FDA is not yet sending invoices, Congress clearly intended to make sure that the impact of this law on smaller companies was well understood in advance of creating any burden. FDA should delay its fee assessments until the mandated guidance is finalized.”

One area of relevance of the new FSMA fees to AHPA members and the dietary supplement trade is that FDA may now assess fees for any reinspection under the current good manufacturing practice rule, 21 CFR 111. If FDA conducts an inspection and records “inspectional observations” on a Form 483, it may start to assess these fees when it returns to a facility to determine whether its observations have been adequately addressed. Fees may also be assessed in relation to import-related activities, such as requests for reconditioning of an import initially subject to an import hold.

The full text of AHPA’s comments can be downloaded from the [AHPA website](#).

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This Is a Regulated Industry: the Evidence and the Response

By Anthony L. Young, Partner, Kleinfeld, Kaplan & Becker LLP, and AHPA General Counsel

Permanent injunction against ATF Fitness Products underscores need for industry compliance with DSHEA regulations

The Food and Drug Administration (FDA) announced November 23 that it is seeking a [permanent injunction](#) against ATF Fitness Products, a dietary supplement manufacturer and distributor in Oakmont, Pa. The injunction, if granted, will affect more than 400 products. FDA noted that the company had previously

received warning letters in May and November 2004 and that FDA had seized illegal ephedrine from the company in June 2006.

In its press release, FDA stated, “The FDA today took legal action against a dietary supplement maker and owner for substituting ingredients and products without noting the changes on the final product labels.” In addition, FDA’s permanent injunction “alleges that in addition to ‘adulterating’ and ‘misbranding’ their final products, the manufacturer and its owner failed to report serious adverse events associated with their products.”

Repeated warning letters and FDA-483 inspection observations need to be addressed to avoid this kind of enforcement action. FDA and the U.S. Department of Justice (DOJ) work together on cases like this because FDA must be represented by DOJ when it goes to court, since FDA has no independent litigation authority. The usual practice is to offer a company the opportunity to enter into a consent decree of permanent injunction. This allows a company to negotiate with the government and try to tailor the decree to its special circumstances. Recent examples of consent decrees entered with dietary supplement manufacturers and

distributors include [Artery Health Institute LLC](#) and [Beehive Botanicals](#).

In the food industry, such consent decrees are commonly used with respect to food manufacturing facilities that fail repeatedly to pass current good manufacturing process (cGMP) inspections. The decree entered into by [Sungwon Inc.](#) is an example of this.

Understanding that FDA has the will to enforce the Dietary Supplement Health and Education Act (DSHEA), as AHPA and the rest of the industry have called for over the last decade, companies are well advised to assure their products and their manufacturing and distribution operations are in compliance with the law. It may not be wise to assume that an FDA label review or cGMP-manufacturing review will result only in a FDA 483 with observations or an FDA warning letter with time to respond. This is especially the case if the company has already received an FDA 483 or a warning letter. It is a now a big risk to assume there will be two bites at the compliance apple.

FDA’s level of enforcement interest is often related to the particular FDA district where a company is located.

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Lawyers observing recent FDA activities have noted that FDA's Minneapolis District covering Minnesota, Wisconsin, North Dakota, and South Dakota is especially active with respect to enforcement actions. This district is followed by enforcement actions taken by the New England District and the New York District.

FDA respects companies that demonstrate compliance actions. Recalls are voluntary, and FDA works with companies that determine they must recall a product. In so doing, the agency learns how the company reacts in situations where the public interest is served by voluntary action. Similarly, in inspections, FDA has greater respect for companies that know how FDA conducts inspections and that provide cGMP and adverse event information, as required.

This does not mean that companies should supply documents and information not required under the regulations. FDA inspectors also respect the limits of their authority, but will use every possible device and artifice to try to extract such information from companies. Most importantly, always treat FDA inspectors and compliance officers with respect, even those who may be contentious.

Several pharmaceutical and medical device manufacturers are under FDA permanent injunctions, most negotiated by consent. They include Abbott Laboratories and KV Pharmaceutical. The dietary supplement industry should not be surprised if FDA uses injunctive relief, its biggest weapon after criminal prosecution, to reign in dietary supplement companies that fail to comply with the many regulations that now control the industry.

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USDA Launches Free Online Tool to Help Producers Achieve GAP

U.S. Department of Agriculture (USDA) Deputy Secretary Kathleen Merrigan announced in December a new online tool aimed at making it easier for U.S. producers to meet Good Agricultural Practices (GAP). The online tool will enable producers to maintain and reach harmonized standards and certification, which is expected to foster economic opportunities.

FamilyFarmed.org developed the online tool with funding from USDA's Risk Management Agency. Meeting USDA GAP standards and mitigating business risks are key components of the online tool, which may be accessed at the FamilyFarmed.org [website](http://FamilyFarmed.org).

"USDA believes that a strong farm safety net--including effective, market-based risk solutions for producers of all variety and size--is crucial to sustain the vitality of American agriculture," said Merrigan. "Effectively managing risk is important to all producers, and having an acceptable food safety program is in the best interest of consumers, buyers, and the farmers themselves. USDA is proud to have worked with private, public, and non-profit partners to introduce this free tool to farmers seeking to gain certification as a GAP producer."

For more information, visit the USDA [website](http://USDA).

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