



Exploring New Frontiers in the Nutraceutical and Dietary Supplement Markets

Deepali Mohindra
Food and Beverage Marketing Manager
Thermo Fisher Scientific
Sunnyvale, CA

Agenda

- Nutraceutical Market Trend
- Dietary Supplements
 - FDA Requirements
 - FDA Challenges
- Thermo Scientific Solutions
 - Portable Devices
 - Ion Chromatography
 - High Performance Liquid Chromatography
 - Gas Chromatography
 - GC-MS and LC-MS
 - ICP-MS



I want to live forever and be healthy

- Consumers looking for that
 - Miracle cure
 - Wonder drug
 - Fountain of youth
 - Best way to live a healthier life
- From this search we have:
 - Chinese Traditional Medicine
 - Homeopathic Medicine
 - Ayurvedic Medicine
 - **Dietary Supplements and Nutraceuticals**



Introduction: Nutraceutical

- Nutraceutical is combination of "nutrition" and "pharmaceutical"
- Are food products that provide medical or health benefits including prevention and treatment of a disease
- Nutraceutical market encompasses
 - Dietary Supplements
 - Vitamins, minerals, amino acids, herbs, botanicals
 - Functional Foods
 - Yogurts with probiotic cultures, fortified breakfast cereals
 - Functional Beverages
 - Vitamin water, sports drinks, energy drinks

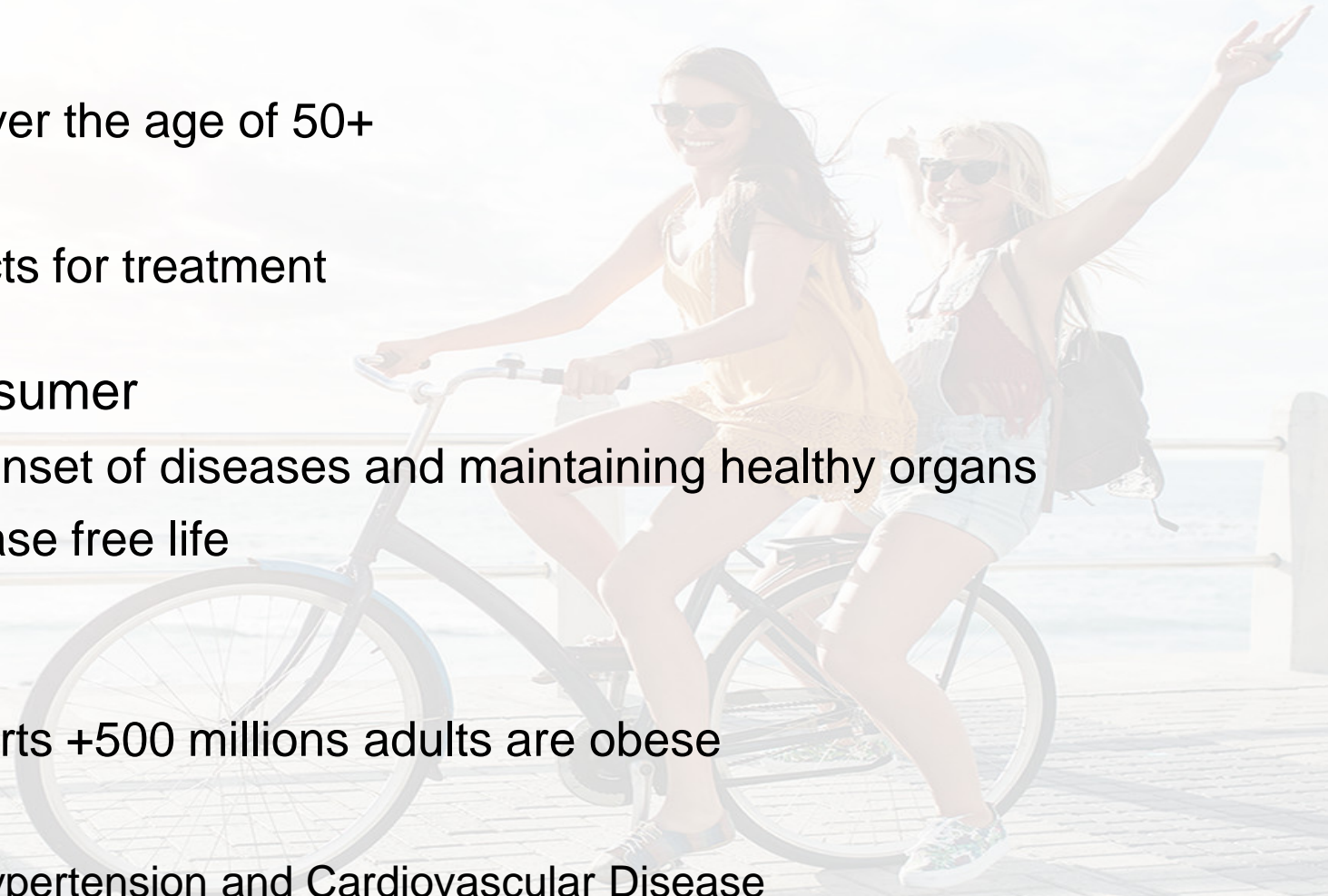
Nutraceutical Market

- The global Nutraceutical market was:
 - USD 183 Billion in 2015 and expected to reach USD 279 Billion by 2021
- North America is expected to dominate the global Nutraceutical market

Source: Transparency Market Research

Demand Drivers

- **Elderly Population**
 - Currently 1 Billion people are over the age of 50+
 - Chronic age related diseases
 - Looking to Nutraceutical products for treatment
- **Young Health Conscious Consumer**
 - Using supplements to prevent onset of diseases and maintaining healthy organs
 - Want to live a healthy and disease free life
- **Obese People**
 - World Health Organization reports +500 millions adults are obese
 - +1 Billion are overweight
 - Excess weight prime cause of Hypertension and Cardiovascular Disease



Demand Drivers (cont)

- Nutrient deficiencies are being supplemented with dietary supplements
- New research on vitamin deficiencies causing consumer to take note:
 - Iron, Vitamin D, Vitamin B12, etc
- Food manufacturers fortifying food and beverage products with vitamins
 - Vitamins waters, energy drinks, sports drinks, Omega III in foods, Iodine in salt, vitamins in cereals
- Pharmaceutical companies looking at herbal products for medicinal uses
 - Turmeric
- Cosmetic industry incorporating botanicals, fruits and vegetables in product
 - Turmeric, aloe vera, cucumber, Vitamin A and Vitamin C



Customer Interest in Nutraceuticals

- **Elderly**

- Arthritis, heart disease, high cholesterol, high BP, energy/fatigue, enhance memory

- **Women**

- Heart Disease, high cholesterol, cancers, energy/fatigue, weight control
- Menopause, arthritis, bone/joint problems

- **Men**

- Heart disease, high cholesterol, high BP, cancer, weight control, diabetes

- **Children/Teenager**

- Weight management, physical fitness, basic nutrition, reduced hyperactivity, enhanced performance

Nutraceuticals Market: Regulatory Agencies

Country	Given Label	Definition	Regulating Body
United States of America	Dietary Supplements	Any of the following which have a beneficial nutritional effect <ul style="list-style-type: none"> •Vitamins •Minerals •Botanicals and their extracts •Amino Acids •Concentrates and Extracts 	Food and Drug Authority(FDA)
European Union	Food Supplements	<ul style="list-style-type: none"> • Concentrated Sources of Nutrients • Other substances with a beneficial nutritional effect 	European Food Safety Authority
India	Food for Special Dietary Use	<ul style="list-style-type: none"> • Plants\Botanicals: Whole or extracts • Minerals, Vitamins, Amino Acids, Enzymes • Substances of Animal origin 	Food Safety and Standards Act
Japan	Food for Specific Health Use	Any food that can provide and/or supplement any of the following <ul style="list-style-type: none"> •Nutrition •Sensory Satisfaction •Beneficial Physiological Effects 	Japanese Health and Nutrition Food Association
China	Health Foods	Any food that <ul style="list-style-type: none"> •should be suitable for specific group(s) of people •should also be able to adjust body functions and •should not aim at curing diseases or cause acute, sub acute or chronic harm to the body 	State Food and Drug Administration

Nutraceutical Testing

Needed for:

- Research and Development
- New Product Development
- Quality Control of Raw Ingredients and Final Products
- Food Safety and Authenticity
- Food Labeling

Dietary Supplements



Dietary Supplement Health and Education Act of 1994 (DSHEA)

- Dietary supplement manufacturer is responsible for ensuring that a dietary supplement or ingredient is safe before it is marketed
- FDA is responsible for taking action against any unsafe dietary supplement product after it reaches the market
- FDA is responsible to ensure compliance of product information, such as labeling, claims, package inserts, and accompanying literature
- Manufacturer, packer, or distributor whose name appears on the label of a dietary supplement marketed in the United States is required to submit to FDA all serious adverse event reports associated with use of the dietary supplement in the United States

FDA Regulations on Dietary Supplements

- cGMP- current Good Manufacturing Practices
- As of June 2010 all companies need to adhere to cGMP guidelines set by FDA
 - Product needs to be tested (internal or external lab) for quality, identity and safety
 - Scientifically valid methods must be used
 - Standard reference material must be used in the quality test method
 - Certificate of Analysis from qualified vendor is acceptable
 - Detailed record of the test must be maintained
 - And More

Problems Seen by FDA with Dietary Supplements

- Inadequate identity testing
- Failure to establish specifications
- Failure to test products for specifications
- Inadequate records, laboratory testing, manufacturing record & batch record
- Failure to conduct material reviews
- Lack of adequate corrective action plans

Source: FDA

FDA Challenges with Dietary Supplements

- Illegal products claiming to be dietary supplements
- Pharmaceuticals disguised as dietary supplements
 - Weight loss products – containing sibutramine
 - Body-building products –containing steroids
 - Sexual enhancement products –containing drugs like Viagra, Cialis, and Levitra or an analog of the active ingredient
- Pharmaceuticals in mail order dietary supplements
- Counterfeits and Adulteration
- Toxic Metals
 - Pb, Se, Cr, Cd, Hg
- Deceitful labeling

Source: FDA

Tainted Products Confiscated by the FDA

FDA U.S. FOOD & DRUG ADMINISTRATION
SEARCH

Home Food Drugs Medical Devices Radiation-Emitting Products Vaccines, Blood & Biologics Animal & Veterinary Cosmetics Tobacco Products

Tainted Products Marketed as Dietary Supplements_CDER

[FDA Home](#) [Tainted Products Marketed as Dietary Supplements_CDER](#)

[FDA's Medication Health Fraud Page](#)

Disclaimer

This list only includes a small fraction of the potentially hazardous products with hidden ingredients marketed to consumers on the internet and in retail establishments. FDA is unable to test and identify all products marketed as dietary supplements on the market that have potentially harmful hidden ingredients. Even if a product is not included in this list, consumers should exercise caution before using certain products. To learn more about how to reduce your risk of encountering a product marketed as a dietary supplement with a hidden ingredient please visit FDA's Medication Health Fraud webpage linked above.

Click on this link to download all data from the selected searchable database in Excel format. If you need help accessing information in different file formats, see [Instructions for Downloading Viewers and Players](#).

Search Criteria

Sort by: No. of Records Found: 820

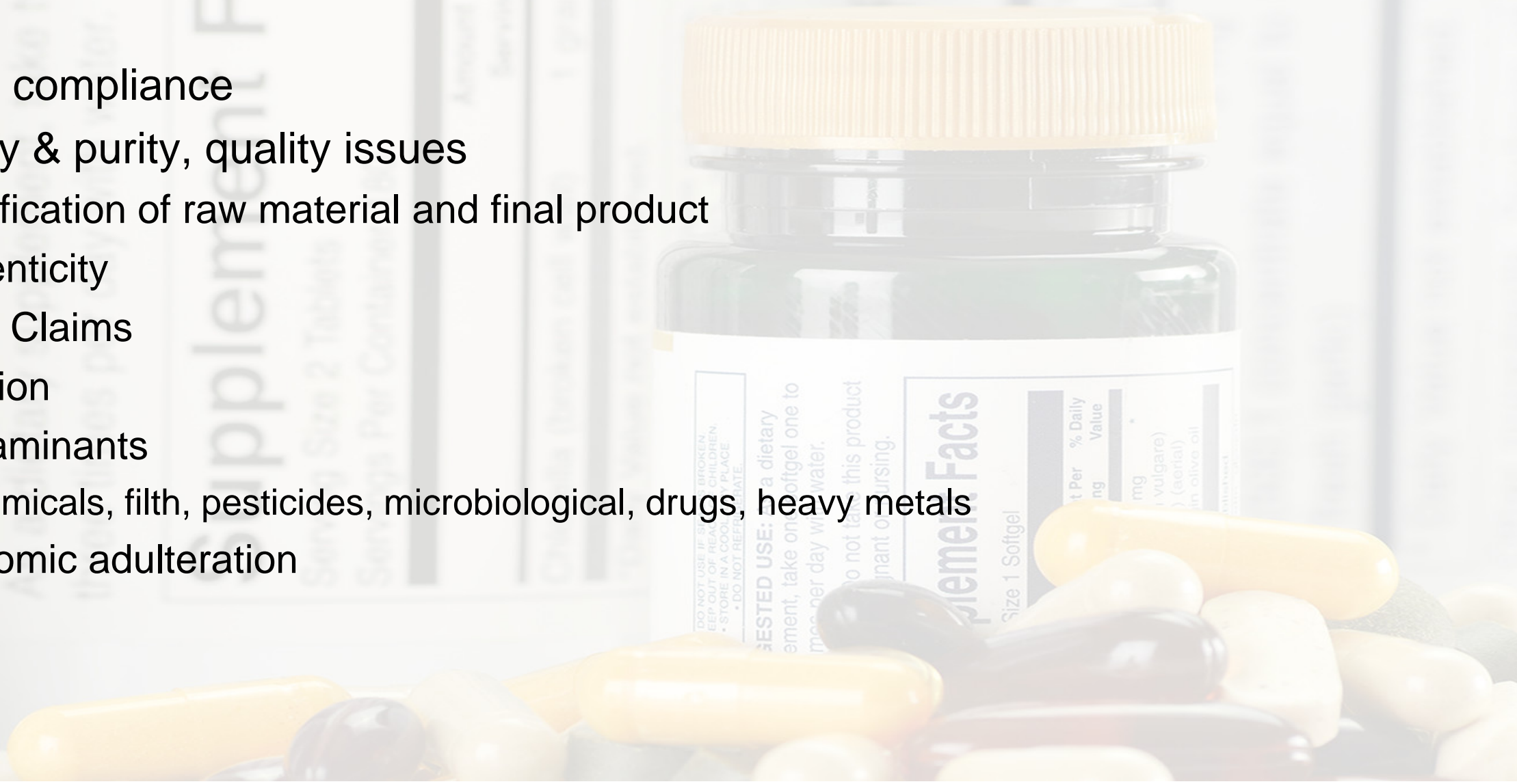
Date	Product Name	Company	Hidden Ingredient	Product Category	Lot
01/08/2013	MAXILOSS Weight Advanced	Various Distributors	sibutramine	Weight Loss	n/a
01/09/2014	"New" Extenze	Midwest Wholesale	sildenafil and/or tadalafil	Sexual Enhancement	Lot# 0512058, Exp 05/16
01/09/2014	Magic for Men	Midwest Wholesale	sildenafil and/or tadalafil	Sexual Enhancement	Lot# GP808, Exp 10/16; Lot#BN030613, Exp 2/6/15
01/09/2014	New XZen Platinum	Midwest Wholesale	sildenafil and/or tadalafil	Sexual Enhancement	Lot#130520PL, Exp 5/31/17
01/09/2014	Triple MiracleZen Platinum	Midwest Wholesale	sildenafil and/or tadalafil	Sexual Enhancement	Lot# OAWF1027, Exp 1/31/15; Lot# OAWF1003, Exp 1/31/15
01/09/2014	Boost Ultra	Midwest Wholesale	sildenafil and/or tadalafil	Sexual Enhancement	Lot#B70130, Exp 03/15; Lot#B70130, Exp 3/2015; Lot#06012011, Exp 6/2014
01/09/2014	XZone Gold	Midwest Wholesale	sildenafil and/or tadalafil	Sexual Enhancement	Lot#130710GL, Exp 7/31/18

Source: FDA Website

https://www.accessdata.fda.gov/scripts/sda/sdNavigation.cfm?sd=tainted_supplements_cder

Dietary Supplements Testing

- cGMP compliance
- Identity & purity, quality issues
 - Identification of raw material and final product
 - Authenticity
 - Label Claims
 - Nutrition
 - Contaminants
 - Chemicals, filth, pesticides, microbiological, drugs, heavy metals
- Economic adulteration



Thermo Fisher Scientific Solutions



- Portable Handheld Devices
- Ion Chromatography
- IC-ICP-MS
- Liquid Chromatography
- Gas Chromatography
- GC-MS and LC-MS
- ICP-MS

Portable Analytical Instruments

- Can sample and analyze in the receiving bay
- Good for early identification of incoming raw materials
- Can be used on the plan floor/ warehouse
- Traditionally this testing has been done with laboratory based instrumentation (FTIR or Near Infrared, NIR) or wet chemical assays
- Handheld solutions can replace (but not completely replace) benchtop instruments for Rapid Material Identification



Ion Chromatography

- Metal Speciation
- Carbohydrates
 - Total and added sugars
 - Profiling for adulteration
- Sugar Substitutes
- Sugar Alcohols
- Organic Acids
- Anions & Cations
- Glucosamine
- Amino Acids
- Sulfites
- Nitrates



Glucosamine in Dietary Supplement – HPAE-PAD

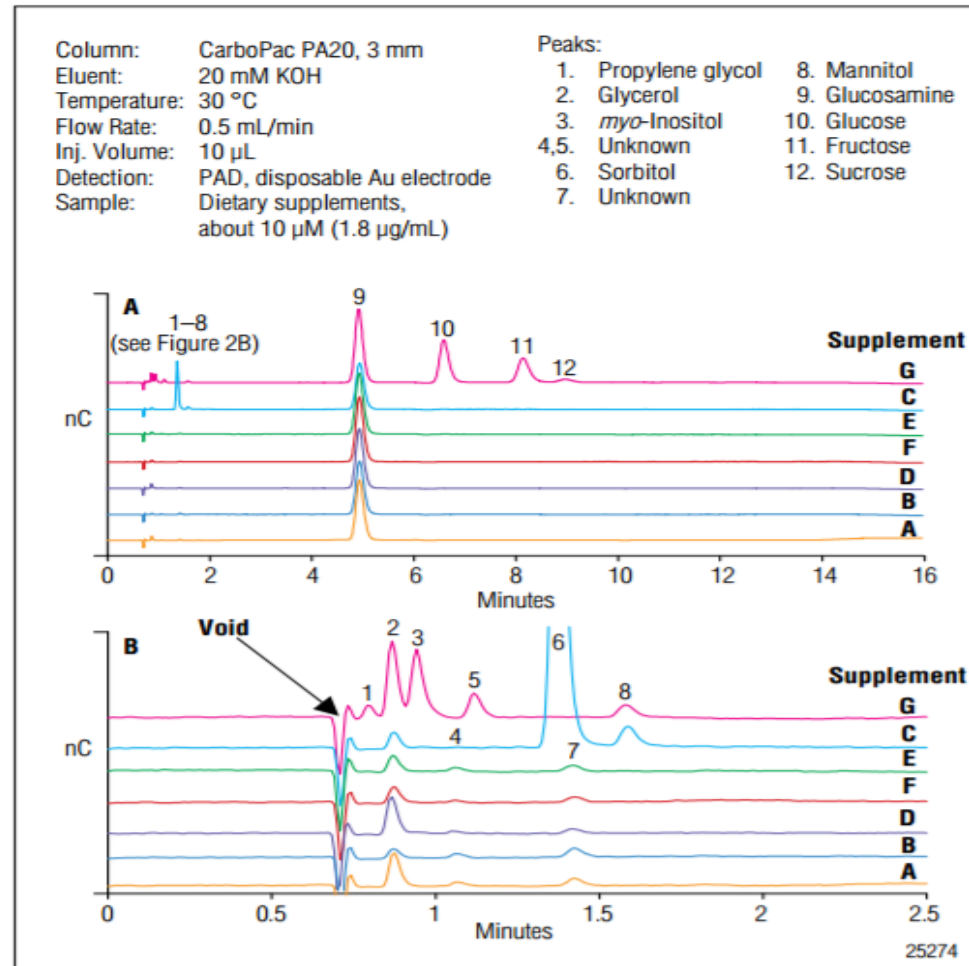


Figure 2. HPAE-PAD analysis of GlcN-containing dietary supplements. Seven dietary supplement samples diluted to approximately 10 µM (1.8 µg/mL) GlcN, 10-µL injection. A) Full chromatogram. B) Expanded early RT region of the chromatogram.

App Note 197 -
<https://tools.thermofisher.com/content/sfs/brochures/AN-LPN-3083-Beverages-Applications-Notebooks-Functional-Waters-LPN3083.pdf>

IC-ICP-MS- Speciation



Arsenic Speciation Results

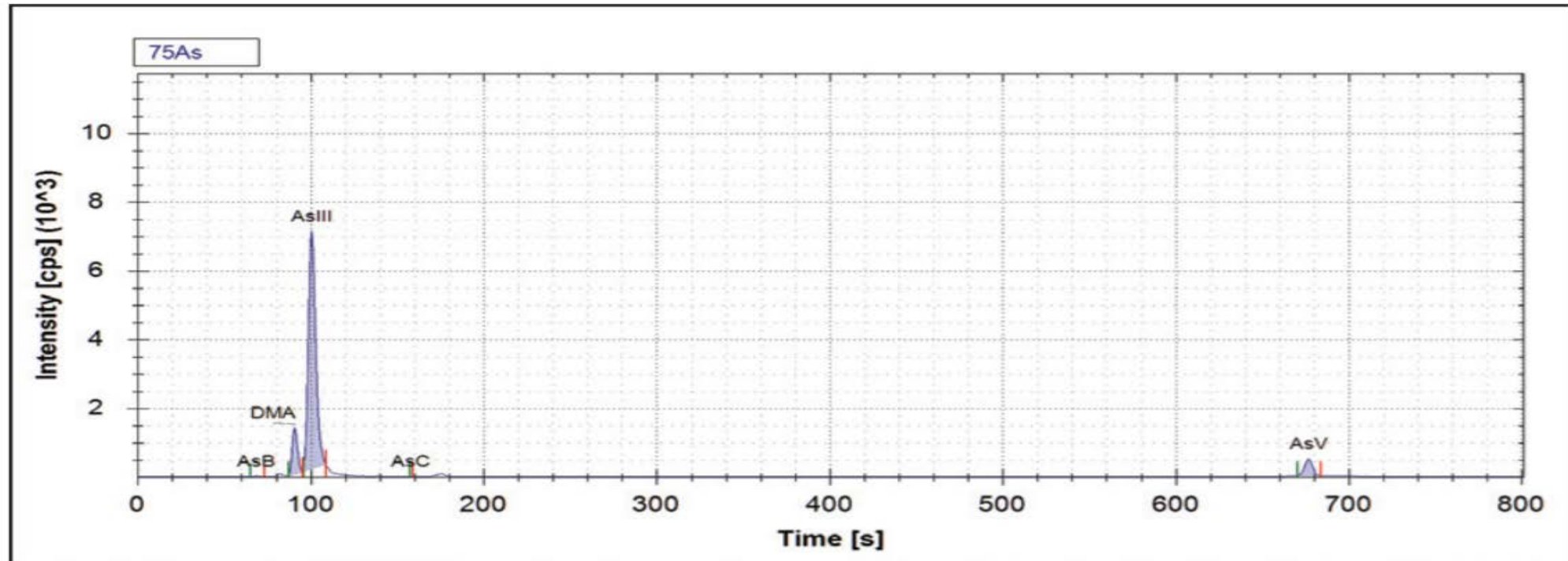
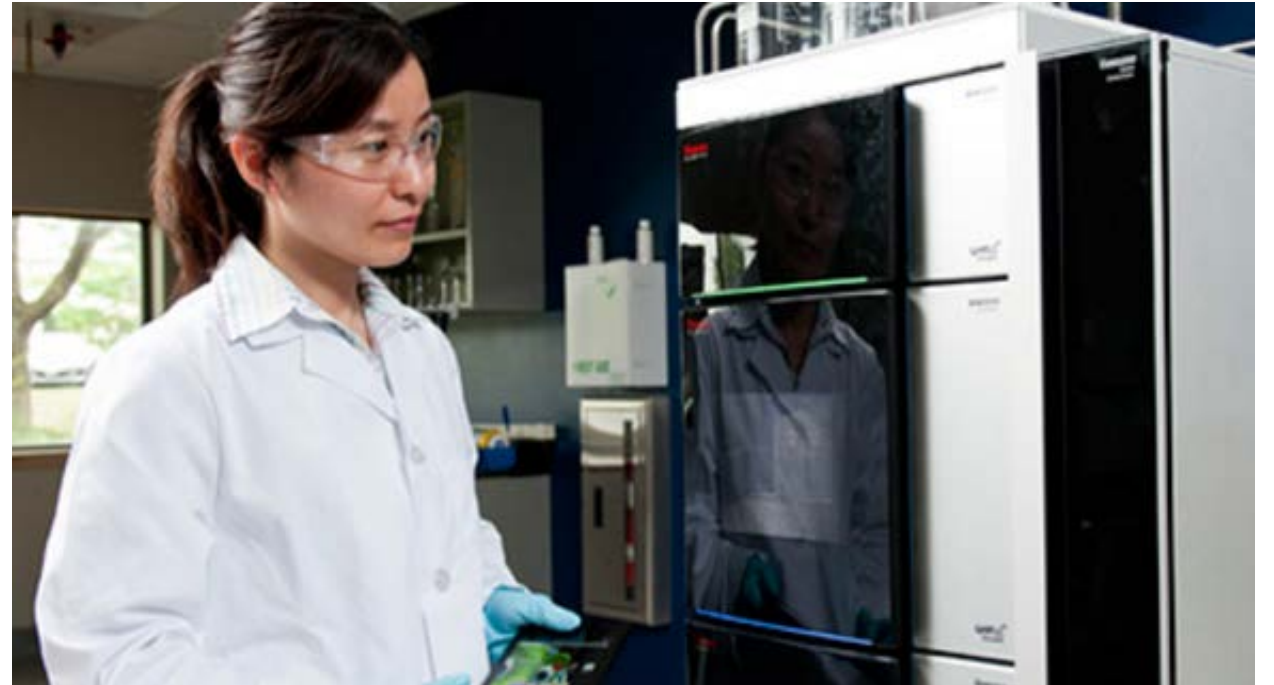


Figure 2. IC-ICP-MS chromatogram of Arsenic species found in a OBRS sample. As (III) was the most abundant species detected.

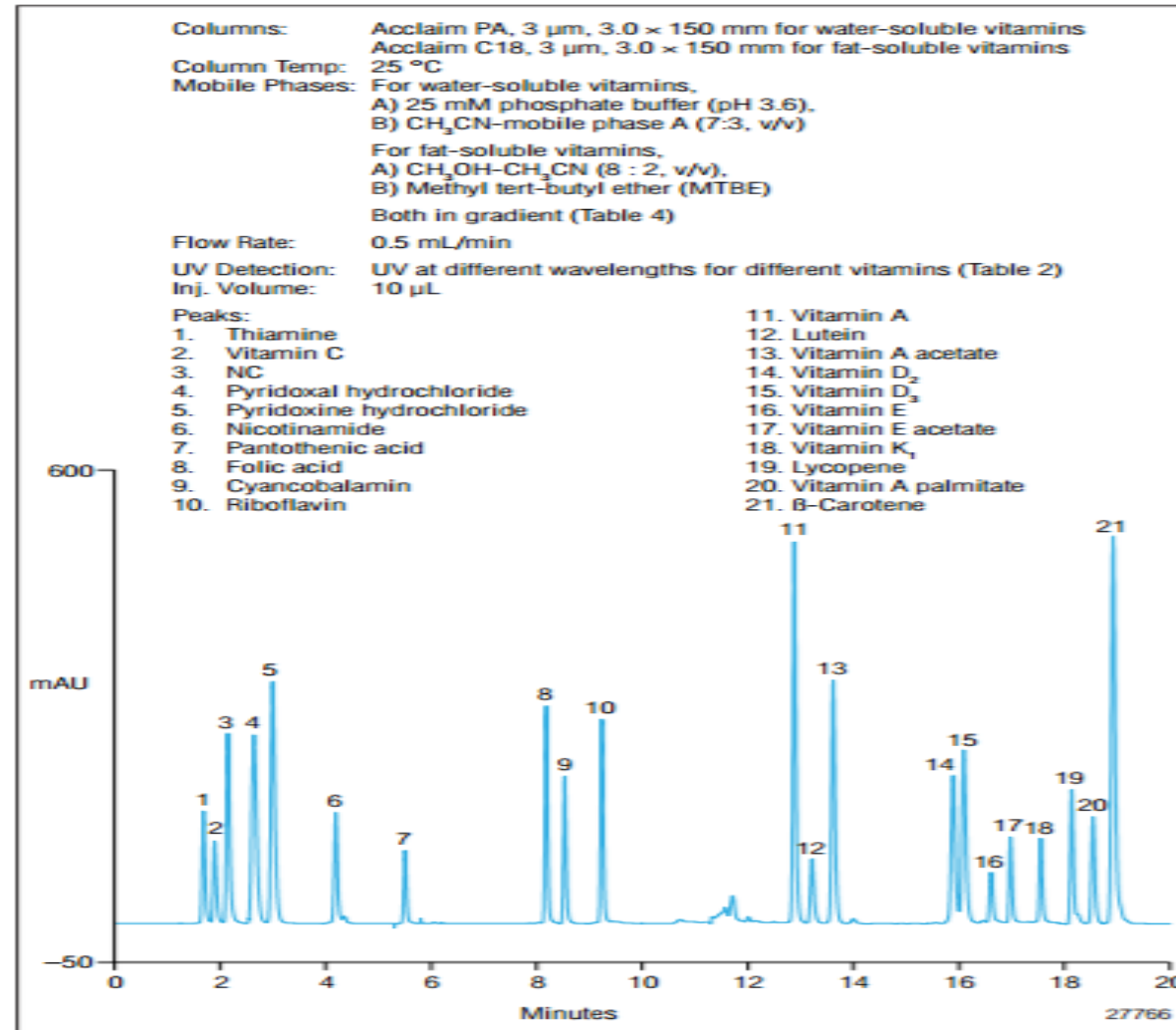
<https://static.thermoscientific.com/images/D03250~.pdf>

Liquid Chromatography

- Water and Fat Soluble Vitamins
- Carbohydrates
- Sugar substitutes
- Sugar alcohols
- Carotenoids
- Organic acids
- Amino acids
- Caffeine
- Additives
- Polyphenols
- Minerals
- Beta carotene
- Dietary Fiber
- Catechins in teas
- Herbal identification & potency verification
 - Adulteration/authenticity/counterfeit
- Traditional Chinese Medicine
- Raw material identification
- Speciation- LC-ICP-MS



Determination of 21 Water & Fat-Soluble Vitamins(HPLC)



Chromatograms of the simultaneous separation of 21 water- and fat-soluble vitamins.

TN 89

<http://tools.thermofisher.com/content/sfs/brochures/88784-TN89-HPLC-WaterFatSolubleVitamins-27Oct2010-LPN2598.pdf>

Gas Chromatography

- Herbal identification & potency verification
- Fish oil
 - Fatty acid profile
 - Omega III quantification
- Vitamin E
- Pesticides
- Carbohydrates



GCMS and LCMS

- Pesticides
- Veterinary drugs
- Pharmaceuticals
- Allergens
- Mycotoxins
- Gelatin species



**Application
Note: 51878**

Non-targeted Screening and Accurate Mass Confirmation of 510 Pesticides on the High Resolution Exactive Benchtop LC/MS Orbitrap Mass Spectrometer

Allen Zhang, James S. Chang, Christine Gu, Mark Sanders, Thermo Fisher Scientific, San Jose, CA, USA

Key Words

- Exactive
- High Mass Accuracy
- High Resolution
- Orbitrap Technology
- Pesticide Analysis

Overview

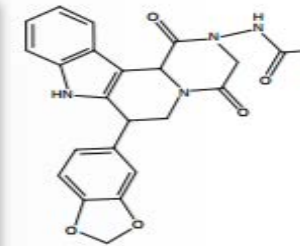
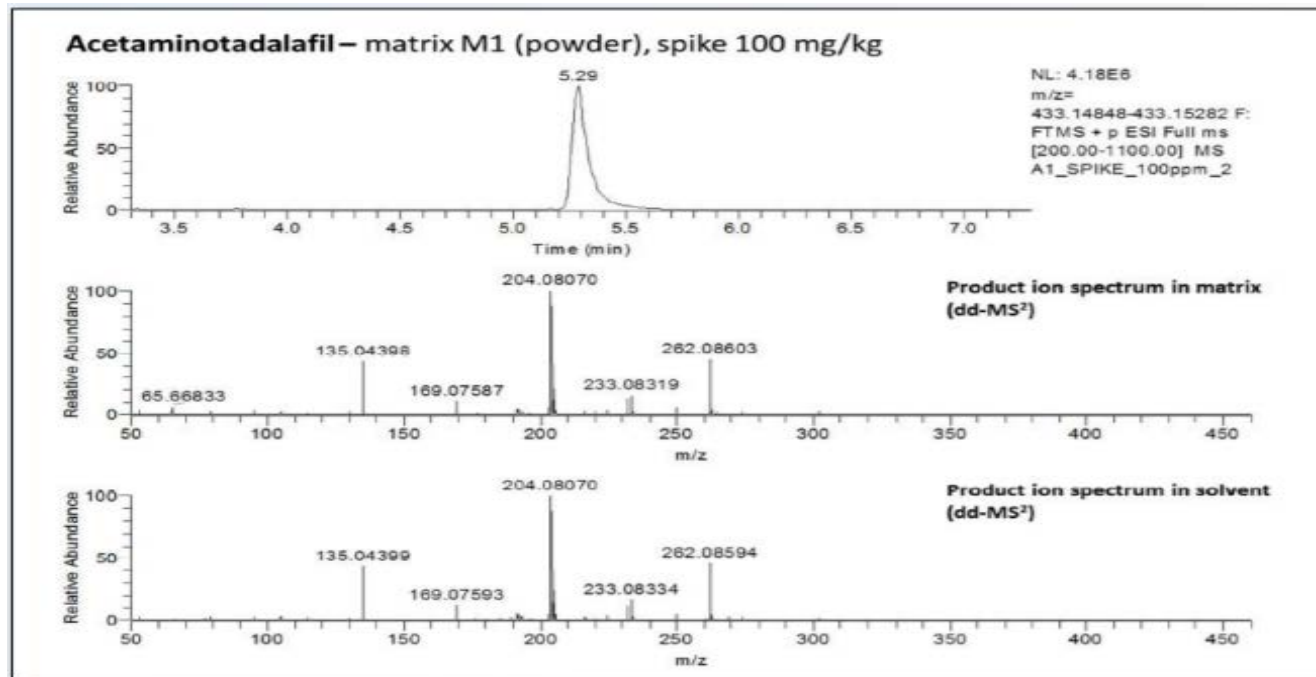
As agricultural trade grows and food safety concerns mount, stricter pesticide regulations are being enforced around the world. Increased pesticide testing and reductions in maximum permissible residue levels have driven demand for fast, sensitive and cost-effective analytical methods for high-throughput screening of multi-class pesticides in food. Detection of 510 pesticides at low ppb levels was achieved within 12 minutes using the Thermo Scientific Exactive benchtop LC/MS system powered by Orbitrap technology. The high resolving power of the Thermo Scientific Orbitrap platform enables accurate mass confirmation of all compounds, including isobaric pesticides. Accurate, robust, easy to use and cost-



Pesticides in food were traditionally monitored and

PDE5 Inhibitor Adulterants- Determination by Q Exactive Mass Spectrometer

- Sexual enhancement supplements are among the most adulterated.
- Adulterated with Phosphodiesterase type 5 (PDE5) inhibitors used in medicine to treat erectile dysfunction.
- Adulteration of dietary supplements is a serious problem because prescription PDE5 inhibitors have a long list of side effects.



◀ Example chromatogram and product ion spectra of Acetaminotadalafil in an extract of botanical powder and solvent demonstrating high selectivity of the method and reliable identification of the analyte. Acetaminotadalafil is an analogue of Tadalafil, the PDE5 inhibitor sold under the brand names Adcirca® and Cialis®.

- Heavy metals
- Calcium
- Iron
- Sodium
- Arsenic speciation when coupled with an IC system
- USP Chapter 2232
 - White paper:
<http://tools.thermofisher.com/content/sfs/brochures/WP-71654-ICP-MS-Trace-Elemental-Contaminants-Dietary-Supplements-WP71654-EN.pdf>





**Proposed USP General Chapter
Elemental Contaminants in
Dietary Supplements <2232>**

USP Chapter 2232 for Trace Elements in Dietary Supplements (in effect starting Jan 2018)

- Objective of USP chapter <2232>
 - Limit elemental contaminants in dietary supplements
 - This general chapter is not intended to set limits for dietary ingredients
 - Limits for dietary ingredients are set in the corresponding individual monographs.
- For Dietary Supplements
 - Dietary Ingredients
 - Excipients
- Does not apply to drug products
- Procedures in Elemental Impurities – listed under Procedures <233> are specified
- Speciation is critical for Dietary Supplements
 - Arsenic and Mercury procedures are addressed in this Chapter

USP 2232 for Trace Elements in Dietary Supplements

- The focus of <2232> is on the four major elements of toxicological concern:
 - **Arsenic**
 - **Cadmium**
 - **Lead**
 - **Mercury**
- Extent of testing can be determined using a risk-based approach considering the likelihood of contamination
- Manufacturers should consider the presence of unexpected elemental contaminants to determine compliance
- Permitted Daily Exposure (PDE) is derived from the Provisional Tolerable Weekly Intake (PTWI) that is recommended by the Food and Agriculture Organization of the United Nations and World Health Organization
- Other regulations may require different limits; manufacturers are responsible for compliance with applicable local requirements differing from these PDE values

LIMITS OF ELEMENTAL CONTAMINANTS

Element	PDE ($\mu\text{g}/\text{day}$) ^a
Arsenic (inorganic)	15
Cadmium	5
Lead	10
Mercury (total)	15
Methylmercury (as Hg)	2

^a Permitted Daily Exposure (PDE) is derived from the Provisional Tolerable Weekly Intake (PTWI) that is recommended by the Food and Agriculture Organization of the United Nations and World Health Organization (FAO/WHO) by subtracting the daily exposure ($\mu\text{g}/\text{day}$) to each elemental contaminant from air, food, and drinking water. A body weight of 50 kg and a safety factor are used to calculate the PDE.

Source: USP

http://www.usp.org/sites/default/files/usp_pdf/EN/USPNF/key-issues/2232_elemental_contaminants_in_dietary_supplements.pdf

Thank You

Resources:

Traditional Chinese Medicine-

<https://tools.thermofisher.com/content/sfs/brochures/AN-71120-HPLC-Chinese-Medicine-Notebook-AN71120-EN.pdf>

USP Chapter <2232>

<http://tools.thermofisher.com/content/sfs/brochures/WP-71654-ICP-MS-Trace-Elemental-Contaminants-Dietary-Supplements-WP71654-EN.pdf>

Dietary Supplement Webpage:

<http://www.thermofisher.com/us/en/home/industrial/food-beverage/food-beverage-learning-center/food-analytical-testing-information/dietary-supplements-testing-information.html>

Nutraceutical Webpage:

<http://www.thermofisher.com/us/en/home/industrial/food-beverage/food-beverage-learning-center/food-analytical-testing-information/nutraceutical-analysis-information.html>



THANK YOU

QUESTIONS