Finding New Pathways in Sports Nutrition

Underwritten by

Cluster Dextrin®
New Energy Source for Athletes

FUTURECEUTICALS

Lonza

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Sports nutrition surpasses $35B annually

U.S. sports nutrition industry grew 6.7% to $35.8B in 2018

Source: Nutrition Business Journal ($mil, consumer sales)
Sports Nutrition Categories

• **Bars and gels** settled on about mid-6% growth range (13.1% in 2014) = maturity
• **Functional sports beverages** growing about 14% (huge 23.5% jump in e-commerce sale)
• Mass market dominates **hydration and energy drinks** with a 93.3% share.
• **Sports drinks** facing sugar/sweetener challenges.
• **Protein supplements** (powders) facing challenge from foods/snacks/RTD beverages.
• What is the next big crossover ingredient? CBD? Creatine?
Pill fatigue?

- Sales of sports nutrition pills was $288 million in 2018.
- Growth is about even with the overall supplement market, about 6%.
- Safety a big issue.

Source: NBJ
NBJ data shows consistent annual growth around 7% from 2014 to 2018, with a resulting $5.4 billion in annual sales.
NEXT Concept Lab Trend Analysis: Which trends rose to the top in a conceptual marketplace?
We coded our database of 1500 product concepts to determine which trends garnered the highest cultural relevance and purchase intent.

For benchmarking purposes the bottom 5% of all concepts were treated as outliers and were removed from our analysis and averages.
Alt Delivery Formats Supplement Concepts Performance in Mainstream Consumer Concept Testing

Market Prediction vs. Purchase Intent

- **Highest Average Purchase Intent**
  - "I will buy it."

- **Average**
  - **Shots**
  - **Powder**
  - **Oils/Spray**

- **Highest Average Market Prediction**
  - "I believe others will buy more of it."

Product concepts analyzed include all supplements. Excluded from analysis: food and beverage, home, personal and pet care and select outliers.
Sports nutrition products are popular in the US

Consumers are using such products to replace “traditional” snacks and beverages

Everyday consumers are seeking out products that offer a convenient health boost and are a guilt-free options compared to traditional snack products

Proportion of consumers who have tried the following products in the US over the last six months, 2019

<table>
<thead>
<tr>
<th>Product</th>
<th>Proportion (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sports drinks</td>
<td>80%</td>
</tr>
<tr>
<td>Energy drinks</td>
<td>77%</td>
</tr>
<tr>
<td>Milk protein drinks</td>
<td>57%</td>
</tr>
<tr>
<td>Protein snack bars</td>
<td>52%</td>
</tr>
<tr>
<td>Sports snack bars</td>
<td>51%</td>
</tr>
<tr>
<td>Protein fortified foods</td>
<td>49%</td>
</tr>
<tr>
<td>Energy bars</td>
<td>49%</td>
</tr>
<tr>
<td>Protein powder to use in shakes/beverages</td>
<td>46%</td>
</tr>
<tr>
<td>High protein cookies</td>
<td>46%</td>
</tr>
<tr>
<td>Sports powder to use in shakes/beverages</td>
<td>46%</td>
</tr>
<tr>
<td>Protein ice cream</td>
<td>46%</td>
</tr>
<tr>
<td>RTD high protein drinks</td>
<td>46%</td>
</tr>
<tr>
<td>High protein yogurts</td>
<td>45%</td>
</tr>
<tr>
<td>Protein bar</td>
<td>40%</td>
</tr>
<tr>
<td>Protein fortified baked goods</td>
<td>36%</td>
</tr>
<tr>
<td>Protein shakes</td>
<td>27%</td>
</tr>
<tr>
<td>Protein water</td>
<td>23%</td>
</tr>
<tr>
<td>Weight management/meal replacement bar</td>
<td>22%</td>
</tr>
<tr>
<td>Nutritional supplements</td>
<td>18%</td>
</tr>
<tr>
<td>Sports gel</td>
<td>16%</td>
</tr>
<tr>
<td>Protein gel</td>
<td>10%</td>
</tr>
<tr>
<td>Energy powder</td>
<td>10%</td>
</tr>
<tr>
<td>Energy gels</td>
<td>7%</td>
</tr>
</tbody>
</table>
US consumers are looking to improve their health

Consumer are adopting a long-term holistic approach to health. As such, they are looking to make improvements to all aspects of their life.

Proportion of US consumers who have looked to do the following over the last two years, 2019

- Looked to reduce time being inactive: 81%
- Attempted to improve my diet: 59%
- Exercised more: 52%
- Looked to improve my overall health: 51%
- Adopted a more long-term approach to health: 48%
- Taken a greater interest in ingredients in food and drink that are known to boost health: 45%
- Looked to improve my mental sharpness and awareness: 44%
- Cut down on unhealthy snacks: 39%
- Educated myself more about my health: 39%
- Made active attempts to reduce sugar intake: 34%
- Started to take new vitamins, minerals, supplements: 33%
Physical, cognitive and emotive health is important to consumers

Consumers recognize that all elements of health are interlinked and want to address a variety of issues for overall wellbeing purposes.

Proportion of US consumers who want to improve the following over the next twelve months, 2019
Consumers are turning to sports nutrition products for many reasons

Instead, the market is being driven by health conscious, everyday consumers seeking out better-for-you product options. This behavioral change is being driven by both reactive and proactive reasons.

### Reactive reasons

- Concerns about the impact of “traditional” snacks such as chocolate and confectionery on health due to the link with high sugar intake
- Related to this, rising prices due to taxation and negative press on sugar is resulting in consumers examining their snacking habits
- Changing meal-time habits and meal skipping leading to consumers being concerned about missing vital nutritional intake
- Consumers regularly feeling tired and fatigued and seeking out products that offer an energy boost to get them through the day
- Consumers also feeling that their busy lifestyles means that they do not always have time to exercise and eat like they would want to
- Innovation in the sports nutrition/active nutrition market to make products more appealing to the mainstream through pushing indulgence

### Proactive reasons

- Consumers are adopting a long-term and holistic approach to health and want their diets to reflect this
- Consumers are taking a greater interest in certain ingredients – particularly protein – and their related benefits
- Consumers want to replace products that they deem to offer “empty calories” with products that offer genuine nutrition
- Consumers are taking a proactive approach to health and want to minimize the risk of illness, even if they are not suffering from symptoms
- Consumers wanting to challenge themselves when it comes to physical activity and wanting products to help facilitate this
- Self expression and consumers associating healthy living and eating as a reflection of their identity and good taste
Crossover Trends

- Natural and Organic
- Protein – grass-fed, native, plant/vegan
- Non-GMO
- Gluten-free
- Clean Label
- Transparency

Enjoy Maximum Taste and Quality

- 24 Grams Premium Grass-Fed Protein
- Certified Hormone (rBGH/rBST) Free
- Time-Released 4 Protein Blend
- Double Absorption Technology
- High-Quality Natural Ingredients
- No Artificial Sweeteners, Flavors or Colors
- Soy-Free
- Gluten-Free
- Non-GMO
Transparency

• Clear labeling and science-supported formulation

• Ingredient Sources – natural vs. synthetic

• Studies – many brands will tout “clinical” research, but do not include citations or other study info on labels, in marketing or on website.

• Proprietary blends:
  • Formulas have commonly listed mostly proprietary blends sometimes containing 10+ ingredients.
  • Only an overall dose for the blend is given.
  • Consumer has no way to know how individual ingredient doses compare to researched doses.
Female Sports Nutrition

“Females are greater than 50 percent of the participants in all sports activities.”

However...

“In studies that investigate injuries and performance, the two most important topics for athletes, only 2 to 3 percent of the subjects are female.”

- Susan Kleiner, Ph.D., R.D., owner of High Performance Nutrition LLC, co-founder of ISSN and nutritionist for many elite sports teams.

They found women were only 39 percent represented in 1,382 sports and exercise studies conducted between 2011 and 2013 and involving more than 6 million participants.
Female Challenges?

Menstrual cycle is the primary challenge:

• Women were perceived as more physiologically variable, and using only male participants would provide more meaningful results with fewer participants and less funding.

• “Estrogen is highly variable due to menstrual cycle, amenorrhea, pregnancy, nursing, menopause—all of which alters fuel utilization.” – Abbie Smith-Ryan, Ph.D., associate professor of exercise physiology and director of the Applied Physiology Lab at University of North Carolina, Chapel Hill

• 41.7 percent of exercising women believe their menstrual cycle has a negative impact on training and performance. (BJSM)

• Pregnancy and contraceptives can complicate results.
Gender Differences

• Estrogen v. testosterone
• Body size and composition - women are not small men.
• Fuel utilization and dietary habits (carbs vs. fats)
• Metabolism – caffeine, for example
• Micronutrient needs (calcium, iron, etc.)
• Bone health considerations
Active Women: Opportunity & Equality

The Global Wellness Summit predicted that by 2028, women will control close to 75 percent of discretionary world spending. (Hartman Group)

Share increase of 10.72 percent in product listings for women’s formula supplements between Natural Product Expos East and West 2016 and their 2018 editions. (New Hope Network’s NEXT Trend Database)
There are only a few female-specific sports/fitness brands.
• Don’t just “Pink it and Shrink it.”
• Messaging: Strong, not skinny
• “Wellness is a holistic pursuit for women, involving mind, body and spirit. Accordingly, women want products that speak to them at these points of connection.” (Hartman)
• Wellness must make sense to women; simplicity is the key.
• Solutions or retail experiences that are too complicated will create frustration and stress rather than calm and satisfaction.
• Avoid overly scientific formulations, long ingredient lists, busy packaging.
In 2014, for the first time, the majority of natural products sales were generated by Conventional Retailers. A great percentage of sales still occur in natural bricks-and-mortar stores. And Natural Product Retailers still drive a large share of sales.

Source: 2018 NFM Market Overview
E-commerce growth outpaces brick & mortar; 86% of sales still in N&S and mass market

U.S. N&O product industry: growth by channel

U.S. N&O product industry: market share by channel

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E-commerce has changed the sports nutrition retail landscape.

When all of Amazon’s sites (Direct, Marketplace and Subscription) are considered, Amazon comes out on top with 57 percent of all online protein powder purchases. (1010Data)
E-com becomes most popular channel for product launch

More than half of 0-3 year-old companies launch first product online

Q: Through which channel(s) did your company’s product(s) launch?
Thank You!

informa
Health & Nutrition
Supply Side West 2019

Workshop: Finding New Pathways in Sports Nutrition
September 16, 2019
Mandalay Bay,
Level 3, South Seas F
About the Speaker

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- Sports Nutrition – Olympic, Collegiate
- Co-founder – International Society of Sports Nutrition
- Co-editor, Journal of International Society of Sports Nutrition

Email – dkalman@nutrasource.ca
Sports nutrition is a broad interdisciplinary field that involves dietitians, biochemists, exercise physiologists, cell and molecular biologists, and occasionally psychotherapists. It has both a basic science aspect that includes such concerns as understanding the body's use of nutrients during athletic competition and the need for nutritional supplements among athletes; and an application aspect, which is concerned with the use of proper nutrition and dietary supplements to enhance an athlete's performance. The psychological or psychiatric dimension of sports nutrition is concerned with eating and other mental disorders related to nutrition among athletes.
An early ISSN assessment

“The field of sports nutrition is a dynamic one. Core competencies in exercise physiology, psychology, integrated metabolism and biochemistry are the initial parameters for a successful career in sports nutrition. In addition to the academic fundamentals, it is imperative that the sports nutritionist understand the sport in which our client participates. This sport specific understanding should manifest itself in fuel utilization, mechanics of movement, as well as psychological processes that motivate the participant to perform optimally. Sports nutrition as a field has grown substantially over the past 50 years, from glycogen loading to today's scientifically validated ergogenic aids.”

Defined as “Sports nutrition products include sports drinks, supplements, and food that include protein powders, Isotonic drink powder, capsule/tablets (creatine/branched chain amino acids and others), supplement powder, ready-to-drink protein drinks, carbohydrate drinks, protein bars, carbohydrate/energy bars and other supplements.”

Sports Nutrition

- The United States market
  - Total Supplement Industry Sales – Expected to be $219 Billion (NBJ)
  - Comprised of natural and organic supplements
  - Sports Nutrition (and Weight Loss) – comprises approximately $40 - $46 Billion (NBJ)
  - Sports Nutrition “year over year” growth estimated 6 to 8.5% (range, variety)
NBJ Sales Estimates/Data

U.S. Sports Nutrition vs. Total Supplement Sales Growth, 2007-2021e

Source: Nutrition Business Journal (Smil, consumer sales)
Amazon – Top 10 Sports Nutrition Products – Sales (10/16/19)

- Orgain Organic Protein Creamy Chocolate
- Blender Bottle Classic Loop
- Think High Protein Bars
- Optimum Gold Standard Whey
- Blender Bottle Classic Loop 20 oz.
- Liquid IV Hydration Multiplier
- Burn XT Thermogenic Fat Burner
- Orgain Organic Protein – vanilla
- Optimum Micronized Creatine
- CLIF Builders Protein Bars

https://www.amazon.com/Best-Sellers-Health-Personal-Care-Sports-Nutrition-Products/zgbs/hpc/6973663011
One take – using science as a judge for growth and innovation

ISSN exercise & sports nutrition review update: research & recommendations

Chad M. Kercise1, Colin D. Wilbom2, Michael D. Roberts3, Abbie Smith-Ryan4, Susan M. Kleiner5, Ralf Jäger6, Rick Collins7, Mathew Cooke8, Jodi N. Davis9, Elfego Galvan9, Mike Greenwood10, Lonnie M. Lowery11, Robert Wildman12, Jose Antonio13 and Richard B. Kreider14

Abstract

Background: Sports nutrition is a constantly evolving field with hundreds of research papers published annually. In the year 2017 alone, 2082 articles were published under the key words ‘sport nutrition’. Consequently, staying current with the relevant literature is often difficult.

Methods: This paper is an ongoing update of the sports nutrition review article originally published as the lead paper to launch the Journal of the International Society of Sports Nutrition in 2004 and updated in 2010. It presents a well-referenced overview of the current state of the science related to optimization of training and performance enhancement through exercise training and nutrition. Notably, due to the accelerated pace and size at which the literature base in this research area grows, the topics discussed will focus on muscle hypertrophy and performance enhancement. As such, this paper provides an overview of: 1) How ergogenic aids and dietary supplements are defined in terms of governmental regulation and oversight; 2) How dietary supplements are legally regulated in the United States; 3) How to evaluate the scientific merit of nutritional supplements; 4) General nutritional strategies to optimize performance and enhance recovery; and, 5) An overview of our current understanding of nutritional approaches to augment skeletal muscle hypertrophy and the potential ergogenic value of various dietary and supplemental approaches.

Conclusions: This updated review is to provide ISSN members and individuals interested in sports nutrition with information that can be implemented in educational, research or practical settings and serve as a foundational basis for determining the efficacy and safety of many common sport nutrition products and their ingredients.

Keywords: Sports nutrition, Performance nutrition, Position stand, Review, Recommendations, Efficacy, Double blind, Randomized, Placebo-controlled, Dietary supplements, Ergogenic aids, Weight gain, Hypertrophy, Strength, Capacity, Power

Evidence-Based – but is it representative of innovation?

Table 3 Summary of categorization of dietary supplements based on available literature

<table>
<thead>
<tr>
<th>Category</th>
<th>Muscle building supplements</th>
<th>Performance enhancement</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Strong Evidence to Support Efficacy and</td>
<td>HMB</td>
<td>β-alanine</td>
</tr>
<tr>
<td>Apparently Safe</td>
<td>Creatine monohydrate</td>
<td>Caffeine</td>
</tr>
<tr>
<td></td>
<td>Essential amino acids (EAA)</td>
<td>Carbohydrate</td>
</tr>
<tr>
<td></td>
<td>Protein</td>
<td>Creatine Monohydrate</td>
</tr>
<tr>
<td>II. Limited or Mixed Evidence to Support Efficacy</td>
<td>Adenosine-5′-Triphosphate (ATP)</td>
<td>Sodium Bicarbonate</td>
</tr>
<tr>
<td></td>
<td>Branched-chain amino acids (BCAA)</td>
<td>Sodium Phosphate</td>
</tr>
<tr>
<td></td>
<td>Phosphatidic acid</td>
<td>Water and Sports Drinks</td>
</tr>
</tbody>
</table>

Working or Operating for:

- Ideation

Defined as "Ideation" is the creative process of generating, developing, and communicating new ideas, where an idea is understood as a basic element of thought that can be either visual, concrete, or abstract.

[1] Ideation comprises all stages of a thought cycle, from innovation, to development, to actualization.

[2] Ideation can be conducted by individuals, organizations, or crowds. As such, it is an essential part of the design process, both in education and practice."

CRN Survey – Top Selling Supplements

Ten Most Popular Supplements Among U.S. Adults

- Multivitamin: 58%
- Vitamin D: 31%
- Vitamin C: 28%
- Protein: 21%
- Calcium: 20%
- Vitamin B/B Complex: 16%
- Omega 3/Fatty Acids: 15%
- Green Tea: 14%
- Magnesium: 13%
- Probiotics: 13%
- Iron: 12%
- Vitamin E: 12%
- Turmeric: 12%

% US Adults n=2,006

The "CBD Effect"

- Focus on Personalized Health & Wellness
- Pursue Data-Based Innovation in Product R&D
- Target Collaborative Partnerships and GMP
- CBD – Canopy Growth - acquisition of Canadian Co. BioSteel Sports Nutrition

“According to an October 2 Bloomberg report, Canopy CEO Mark Zekulin said, “This acquisition allows us to enter the sports nutrition space with a strong and growing brand as we continue towards a regulated market of food and beverage products that contain cannabis.”

METHODS FOR IMPROVING PHYSICAL PERFORMANCE AND CAPSICUM COMPOSITIONS USED THEREIN

METHODS FOR IMPROVING PHYSICAL PERFORMANCE AND CAPSICUM COMPOSITIONS USED THEREIN

ALGAL AND FUNGAL GENES AND THEIR USES FOR TAURINE BIOSYNTHESIS IN CELLS

TAURINE BIOSYNTHESIS IN CELLS

TREATMENT OF KERATIN-CONTAINING BIOLOGICAL MATERIALS

TREATMENT OF KERATIN-CONTAINING BIOLOGICAL MATERIALS

HOMOVAHILLIC ACID ESTER FOR REDUCING OR INHIBITING FATTY ACID ABSORPTION IN THE SMALL INTESTINE

HOMOVAHILLIC ACID ESTER FOR REDUCING OR INHIBITING FATTY ACID ABSORPTION IN THE SMALL INTESTINE

PROBIOTIC (BACILLUS SUBTILIS) SUPPLEMENTATION FOR IMPROVEMENT OF BODY COMPOSITION IN FEMALE ATHLETES

PROBIOTIC (BACILLUS SUBTILIS) SUPPLEMENTATION FOR IMPROVEMENT OF BODY COMPOSITION IN FEMALE ATHLETES

PEPTIDES FOR USE IN PROMOTING TRANSPORT OF GLUCOSE

PEPTIDES FOR USE IN PROMOTING TRANSPORT OF GLUCOSE

METHODS FOR HIGH TAURINE PRODUCTION IN UNICELLULAR ORGANISMS

METHODS FOR HIGH TAURINE PRODUCTION IN UNICELLULAR ORGANISMS

SPORTS SHAKER CUP

SPORTS SHAKER CUP

COMPOSITIONS AND METHODS FOR TREATING PRODUCE

COMPOSITIONS AND METHODS FOR TREATING PRODUCE

METHODS FOR THE BIOSYNTHESIS OF TAURINE OR HYPTAURINE IN CELLS

METHODS FOR THE BIOSYNTHESIS OF TAURINE OR HYPTAURINE IN CELLS

COMPOSITIONS AND METHODS FOR IMPROVING MITOCHONDRIAL FUNCTION

COMPOSITIONS AND METHODS FOR IMPROVING MITOCHONDRIAL FUNCTION

COMPOSITION FOR PRODUCING a Protein Hydrolysate

COMPOSITION FOR PRODUCING a Protein Hydrolysate

PROCEDURE FOR REDUCING CONTAMINANTS IN VEGETABLE PROTEIN MATTER

PROCEDURE FOR REDUCING CONTAMINANTS IN VEGETABLE PROTEIN MATTER

COMPOSITION FOR ENERGY SUPPLEMENTATION
Is this Innovation?

- Opening or creating a new market segment?
- Example, the Intra-workout category (Nutrex, ~2004)
- Example, nootropics crossing into sport or performance applications (Nitrosigine®, 2015/16)
- Remember - caffeine was first “nootropic” marketed and used by athletes
- Delivery format – RTM, RTD, Clear protein drink, bar
- Delivery format - Effervescent, Meltable
- Is the marketing the innovator (demand creation), but is it novel?
Sports Nutrition – Innovation & Game Changers

- Glycogen loading (E. Hultman, late 1960’s)
- Sport drinks (Gatorade, Stokely-Van Camp Co., 1967)
- Food science – advances aid growth in market, quality, popularity
- Thermogenics (category, ephedra… 1980’s)
- Creatine (1993)
- Vitargo® (1993/1994 patent)
- HMB (~MTI, EAS 1996)
Utilize Analytics available to you

Nutrasource (and other companies) have divisions that specialize in ideation clarification and assistance.
Scouting for Technology

➢ Technology Transfer (from University, government or private)

➢ Example - [https://www.pharmalicensing.com/sandbox/newhome/indexpl.html](https://www.pharmalicensing.com/sandbox/newhome/indexpl.html)

➢ USDA Technology Transfer (licenses, discovery and partnership - [https://www.ars.usda.gov/office-of-technology-transfer/](https://www.ars.usda.gov/office-of-technology-transfer/))

➢ FDA Technology Transfer ([https://www.fda.gov/science-research/fda-technology-transfer-program/fda-technology-transfer-program-contacts](https://www.fda.gov/science-research/fda-technology-transfer-program/fda-technology-transfer-program-contacts))

➢ University Technology Transfer – example UC Davis, Milk Fat Globules and Plant Oleosomes to deliver bioactive compounds [https://techtransfer.universityofcalifornia.edu/NCD/30561.html](https://techtransfer.universityofcalifornia.edu/NCD/30561.html)

Awareness and Due Diligence

Thank You!
Questions about:
Clinical, Regulatory, Substantiation
and more?
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Transparency

Industry Game Changer?

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About Me

• President/CEO, StrengthPro Inc.
• Co-Founder, Executive Chairman Transdermal Innovations and KAIO Cream
• COO, BYLT (Elite Beverages)
• Partner/Co-Founder Xology
• Partner, CarnoCo, LLC (BetaPrime)

• Advisor and Consultant for: Nutrition 21, Compound Solutions, Nura USA, DryBev Inc,
• Formerly: Chief Operating Officer, ProSupps USA
• Formerly: Director of Science for Metabolic Nutrition
• Formerly: Director of Science and Education for iSatori
• Formerly: NSCA, Chief Operating Officer

• Other Details:
  ◆ More than 27 Years Industry Experience
  ◆ University Assistant Professor
  ◆ Strength and Conditioning Coach
  ◆ Author, Columnist, Advisory Board Member
  ◆ Television Science Advisor
Today’s Goal

• Examine Transparency From Concept To Shelf Using The Product Development Process
• Understand How Transparency Affects The End User – The Consumer
• Understand How Transparency Affects The Supply Chain – The Ingredient Supplier, The Manufacturer, and The Brand
• Does Requesting Documents Ensure Transparency or Do We Need To Do More??
• Understand and Agree To a Definition of Transparency
• Next Steps As An Industry
Transparency Is The New Normal*

• Dictionary Definition: “The Condition of Being Transparent”

• A Better Definition May Be:
  • An Honest, Sincere Approach
  • Being Open About Who You Are And What You Do
  • Being Able to See The Entire Process
  • Understanding All The Nuances And Not Just Facts
  • Clear Definitions, Full Disclosure, Accurate and Complete Information Transfer

• “The Degree To Which A Company Or Person Shares Information About Processes, People, Practices, And Values”

* Forbes.com (May 2018) on its take-away from a business leader summit entitled: “The profile of the new consumer”
Why Has It Taken So Long For Transparency?

- Transparency is not a new concept
- There are no federal regulations requiring full transparency
- Many brands, manufacturers, patent holders and distributors are concerned about their IP being mishandled
- Some brands, manufacturers, and distributors don’t follow GMP, and don’t play by the rules although those groups are slowly falling to the wayside
- KNOWLEDGE – some groups simply don’t know any better, don’t know regulations, do not have compliance and/or regulatory advisors or employees, and don’t realize there are things they should be doing
- COST – the cost of doing business properly is greater than finding a solution that skips steps
- ACCESS – Consumers have more access to information than ever before so it is becoming increasingly more important to be transparent
Product Development

Project Managed, Stage-Gated Process
What Questions Should We Ask?

New Questions To Ask:

1) What do consumers want to know about this product?
2) How can we educate consumers?
3) What information is available to consumers?
4) What part(s) of our business are we willing to share in order to gain trust and confidence in our product and our brand?
Transparency Starts At The Beginning Of The Innovation Stage

• Unique:
  • How is the product different?
    • Idea, Science, Ingredients, Delivery System, Packaging

• Fit For Your Brand:
  • Does the idea "fit" with your Values, Strategic Direction, Target Market?

• Science:
  • Is there solid scientific efficacy behind the ingredient(s)?
Review Process and Risk Mitigation

Transparency Shares This Process With Customers

• SWOT Analysis
• Category and Channel Determination
• Financial Review
• Channel Pricing
• Risk Analysis
• Ingredient Review
• Legal, Trademark, Patent Clearance
The Product Look And Feel
Driven By Transparency

• Prototyping
• Consumer Research
• Claims, Market Strategy
  • Design, naming, etc.
• Market Testing
Can We Sell It??
Is It Desirable, Doable and Viable

Does Cash Flow And Brand Strength Have What It Takes To Launch The Product
Before You Launch

• Develop a Purpose Around The Product
• Develop The Guidelines You Will Follow
• Have a Defensible Rationale

THEN,
Try It, Have Others Try It, and Make Sure You Believe In It
Proper Planning Prevents Poor Execution

• Understand How The Product Will Fit In To Your Product Mix
• Understand How The Product Works
• Understand Why You Are Creating The Product

• Then Get Behind It, Believe In It, And Get It On Shelf
Consumer Transparency

• **Transparency** means being open and honest about what your brand is and does - for better and for worse. It also involves being proactive about sharing information and not just confessing when caught in the wrong. ([https://www.visioncritical.com/blog/be-transparent](https://www.visioncritical.com/blog/be-transparent), Apr 2019)

• **Transparency**, as used in science, engineering, **business**, the humanities and in other social contexts, is operating in such a way that it is easy for others to see what actions are performed. **Transparency** implies openness, communication, and accountability. ([https://en.wikipedia.org/wiki/Transparency_(behavior)](https://en.wikipedia.org/wiki/Transparency_(behavior))

• **Transparency** fosters trust, and trust is **important** for the health of every relationship under the sun. Building happiness and engagement through **transparency** means updating the entire company, regularly, on strategies and current events. ([https://www.forbes.com/sites/williamcraig/2018/10/16/10-things-transparency-can-do-for-your-company/](https://www.forbes.com/sites/williamcraig/2018/10/16/10-things-transparency-can-do-for-your-company/))

• **Transparent branding** is a concept that consumers are demanding from businesses, politicians and even public services. In a nutshell, having a **transparent brand** simply means being upfront and honest with customers. ([https://36creative.com/branding/1888/mean-transparent-brand](https://36creative.com/branding/1888/mean-transparent-brand))
Topics That Demonstrate A Brand's Transparency on Social Media

- Admitting mistakes: 61%
- Honest responses to customer questions: 58%
- Product/service pricing: 45%
- Manufacturing practices: 43%
- Marketing practices: 39%
- Employment diversity/demographics: 39%
- Financial performance: 37%
- Business performance: 35%
- Political/social issues: 31%

Published on MarketingCharts.com in August 2018 | Data Source: Sprout Social

Based on a survey of 1,000 US adults (18+)
Most Important Core Values for Brands to Embody

Based on a survey of 10,131 adults (18+) across 28 markets

January 2016

Quality: 57%
Reliability/durability: 56%
Honesty/transparency: 41%
Innovation: 33%
Authenticity: 32%
Fairness: 31%
Originality: 19%
Simplicity: 19%
Socially active: 17%
Vision: 14%
Passion: 13%
Generosity: 11%
Warmth: 9%
Fun: 5%
Playfulness: 3%
Politically active: 4%
None of these: 4%

"Looking at the following core values, please indicate which FIVE you think are most important for brands to embody."
Transparent Labelling

The Label And The Process

WITH GREAT DATA COMES GREAT RESPONSIBILITY
Transparent vs Clean Labelling

**Transparent**
- Having no proprietary blends of ingredients to form some kind of group/matrix
- Proper designation of ingredients, ingredient weights, and full disclosure of all ingredients
- Using label call-outs that can be verified, have substantiation, and/or have traceable ingredient pipelines

**Clean**
- Using as few ingredients as possible
- Using ingredients that are simple and recognizable by consumers
- Using ingredients that are considered “healthy”
- No artificial ingredients
- Could be Non-GMO, Gluten Free, etc.
## Supplement Facts

**Mr. Hyde Icon**

**Serving Size:** 1 Scoop (15.5g)  
**Servings Per Container:** 20

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Amount Per Serving</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Iconic Strength &amp; Power Matrix</strong></td>
<td>4.85g</td>
</tr>
<tr>
<td>Beta Alanine</td>
<td>3.2g*</td>
</tr>
<tr>
<td>Creatine HCL</td>
<td>1.5g*</td>
</tr>
<tr>
<td>Ancient Peat &amp; Apple Extract (as elevATP®)</td>
<td>150mg*</td>
</tr>
<tr>
<td><strong>Iconic mTOR Activation &amp; Recovery Matrix</strong></td>
<td>4.9g</td>
</tr>
<tr>
<td>L-Leucine</td>
<td>2g*</td>
</tr>
<tr>
<td>L-Isoleucine</td>
<td>200mg*</td>
</tr>
<tr>
<td>L-Valine</td>
<td>200mg*</td>
</tr>
<tr>
<td>Betaine Anhydrous</td>
<td>2.5g*</td>
</tr>
<tr>
<td><strong>Iconic Pump &amp; Performance Matrix</strong></td>
<td>2.795g</td>
</tr>
<tr>
<td>Arginine Silicate Inositol (as Nitrosigine®)</td>
<td>1.5g*</td>
</tr>
<tr>
<td>Cordyceps militaris (Cordyceps), Ganoderma lucidum (Reishi), Pleurotus eryngii (King Trumpet), Lentinula edodes (Shiitake), Hericium erinaceus (Lion’s Mane), and Trametes versicolor (Turkey Tail) (as PeakO2™)</td>
<td>1g*</td>
</tr>
<tr>
<td>Phyllanthus emblyca (fruit) extract (as CAPROS®)</td>
<td>250mg*</td>
</tr>
<tr>
<td>Nattokinase (as NSK-SD40®)</td>
<td>25mg*</td>
</tr>
<tr>
<td>1000 FU (Fibrinolytic Units) of enzyme activity</td>
<td>25mg*</td>
</tr>
<tr>
<td>Aframomum Melegueta (seed) (6-paradol 12%) (as CaloriBurn GP™)</td>
<td>20mg*</td>
</tr>
<tr>
<td><strong>Iconic Energy Matrix</strong></td>
<td>425mg</td>
</tr>
<tr>
<td>Caffeine Anhydrous</td>
<td>250mg*</td>
</tr>
<tr>
<td>Methyliberine (as Dynamine™ 40%)</td>
<td>125mg*</td>
</tr>
<tr>
<td>Theacrine (as TeaCrine® 40%)</td>
<td>50mg*</td>
</tr>
</tbody>
</table>

* Daily Value not established.

Other Ingredients: Citric Acid, Natural & Artificial Flavors, Malic Acid, Soluble Corn Fiber, Sucralose, Acesulfame Potassium, Calcium Silicate, Silicon Dioxide, Blue Lake #1
### Comparison Dr Jekyll FDM vs Specialty

<table>
<thead>
<tr>
<th>Specialty (mg)</th>
<th>Intgredient</th>
<th>FDM (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.9g</td>
<td>Performance Matrix</td>
<td>3.9g</td>
</tr>
<tr>
<td>1.6g</td>
<td>Beta Alanine</td>
<td>1.6g</td>
</tr>
<tr>
<td>1.5g</td>
<td>Creatine HCL</td>
<td>1.5g</td>
</tr>
<tr>
<td>800mg</td>
<td>nooLVL</td>
<td>800mg</td>
</tr>
<tr>
<td>750mg</td>
<td>Cognitive Matrix</td>
<td>750mg</td>
</tr>
<tr>
<td>0</td>
<td>Choline Bitartrate</td>
<td>450mg</td>
</tr>
<tr>
<td>250mg</td>
<td>L-Tyrosine</td>
<td>250mg</td>
</tr>
<tr>
<td>0</td>
<td>Ginseng Root</td>
<td>50mg</td>
</tr>
<tr>
<td>200mg</td>
<td>Lion's Mane</td>
<td>0</td>
</tr>
<tr>
<td>150mg</td>
<td>Alpinia Glanga</td>
<td>0</td>
</tr>
<tr>
<td>150mg</td>
<td>Celastrus Paniculatus</td>
<td>0</td>
</tr>
<tr>
<td>160mg</td>
<td>Adaptogenic Matrix</td>
<td>160mg</td>
</tr>
<tr>
<td>0</td>
<td>Ashwagandha (as KSM 66®)</td>
<td>125mg</td>
</tr>
<tr>
<td>125mg</td>
<td>Ashwagandha (as Swensoril®)</td>
<td>0</td>
</tr>
<tr>
<td>30mg</td>
<td>Aframomum Melegueta</td>
<td>30mg</td>
</tr>
<tr>
<td>5mg</td>
<td>Black Pepper Extract</td>
<td>5mg</td>
</tr>
</tbody>
</table>

Cognitive Matrixs total the same. Highlighted Ingredients show substitutes.

**Example:**

**How To Compete In Two Different Price Markets With Similar Products**
Brands Often Suggest That They Are Unapologetic

Perhaps They Should Add A Few Other Tenets

Be Proud
Be Honest
Be Transparent
Gaining Consumer Trust Through Transparent Practices

• Be Honest: Tell the truth, admit mistakes, and be open about your practices

• Ask For Help: You should be continually seeking help from not just experts and your employees/contractors, but from your consumers

• Ask For Permission: Let people know your intentions whether it is soliciting information or looking for ways to make the sale

• Provide Data: The more truthful you operate, the more information you share, and the more you back your information, the stronger consumer trust will be

• Keep Track Of Your Progress: When it comes to being transparent, try to measure your success against consumer satisfaction, not just sales
Supply Chain Transparency (Ingredients)

- Are all the ingredients accounted for?
- Are all the ingredients GRAS compliant?
- Is there adequate research/evidence on each ingredient?
- Does research of each ingredient indicate efficacy possibility in healthy/trained persons?
- Do all ingredients pass NDI requirements?
- Is there any history of ingredient issues? If so, has issues been resolved?
- Are there any ingredient/combinations that have patent or TM issues?
- Are ingredients reasonably available?
- Are there any international concerns and/or will we need multiple formulations or can we find a single ingredient solution?
- Are there any pending legal issues with regards to any ingredient or combination of?
- Identify possible structure/function claims
- Prioritize list of claims
- Validate claims with scientific support
Supply Chain Transparency (Ingredient Docs)

• Don’t Be Afraid To Ask For Documents
  • COAs/Specs
  • MSDS
  • Chain of Custody
  • Process/Flow Chart
  • Allergen
  • Halal
  • Kosher
  • Vegan
  • Gluten
  • (Non) GMO
Supply Chain Transparency (Manufacturing)

• Demand Master Manufacturing Records
• Work With Your Manufacturer To Source Ingredients
• Obtain Product Prototype Or Samples From Potential Manufacturer
• Don’t Be Afraid To Audit Practices
• Visit The Plant And Watch Your Product Being Produced
• Proper Label Analysis (Using Third Party Where Applicable)
  • Validate scoop size, desiccant packs, etc.
• Check With Ingredient Suppliers To See If Your Manufacturer Is Ordering Regularly From Them Against The Volumes Placed By Pos
• Use Third Party Testing Company To Verify Input Levels
• Verify Spec Sheets And Co-Analyze Formulas
Marketing Transparency

• People Want Transparency – Give It To Them
• How close do your ads and marketing reflect the true experiences your consumers will have with your brand?
• Will or Can your company exceed the expectations of your customers?
• What do your employees honestly think about your company and your advertising and marketing strategy?
• Does your company truly exhibit transparency and is that evident in your marketing efforts?
• Are you acting responsibly, fortuitously, purposefully, and meaningfully to be truthful and forthright with your customers?

• Do Your Marketing Efforts Match Your Label Claims?
• Do Your Batch Records And Test Results Match Your Claims?
A Potential Definition Of Transparency For The Supplement Industry As A Whole

If Transparency Is The “New Normal” And Consumers Are Seeking Brands That Live And Breath Transparency, Then We Need To Ask Permission, Seek Advice, And Demand Full Transparency From Our Partners. We Must Then Be Willing To Share The Truth, Expose Weakness, Continually And Openly Improve Processes, And Not Try To Seek Ways To Avoid, Circumvent, Or Artificially Inflate Those Transparent Actions.
Next Steps As An Industry

• Force Transparent Compliancy By Selecting Partners Along The Entire Supply Chain That Are Willing To Share, Be Open, And Encourage Transparency

• Spread The Gospel Of Transparency Throughout Your Organization And Practice Transparent Management

• Best Your Competition By “Owning It”. Rather Then Trying To Expose Your Competition’s Weakness Or Wrong-Doings, “Do It Right” And Earn Customer Trust And Confidence

• Share Transparent Practices And Educate Not Just Consumers, But Your Employees And Your Partners

• Collaborate On Best Practices And Encourage Your Competition To Join In Your Efforts
Thank You!!

Special Thanks To: Steve Myers, Alyssa Sanchez
Transparency

Industry Game Changer?

David Sandler
StrengthPro Inc.
david@strengthpro.com
LET’S GET INTRODUCED

JOSH
- ‘The CPG whisperer’
- Rust Belt Kid
- Process and Strategy Fanatic
- Focuses on ‘better for you’ category while averaging 1 half gallon of ice cream/week

DAN
- ‘Chief GHOST’
- Former Jet Pilot and supplement super User
- Industry Vet since 2009
- Sneaker and Cereal Addict
Quest Nutrition, maker of protein bars and other snacks, to be acquired for $1 billion in cash

PepsiCo Announces Acquisition of HaydenZ, Expansion of Plant-Based Presence in On-Trend Plant-Based Space

Canopy Growth Announces Purchase of Majority Stake in BioSteel Sports Nutrition Inc.
THE MARKETPLACE HAS CHANGED

-Where have all the gym-bros gone?
-Grandma LOVES SS Quest Bars
(maybe not denture-averse ones)
RETAIL IS CHANGING

- Where you buy your supplements is changing
- Alexa, find the nearest GNC location?
  “Sorry, I don’t know that one” (in Alexa voice)
THE WAL-MAZON MIGRATION

-Brands selling more or selling out?
-How is everyone coping?
(and the big winner is…)

[Logos of GNC and Walmart]
KEEP YOUR FRIENDS CLOSE
-Brands launching direct to consumer
-Retailers launching private label
-Amazon launching ‘look-alikes’
LAND BEFORE TIME or JURASSIC PARK

-The prehistoric era for legacy brands
-Low barriers to entry = daily launches
-MOQs/Retailers no longer provide buffer
BRAVE NEW WORLD

- The "If you aint Bangin’ You aint Hangin’" effect
- Convenience over everything
- "Newness"/The “Calendar of Excitement”
- In house science or in house marketing?
GOOD IDEA
BAD IDEA
USA USA
If it works here, it will work there

GLOBAL
The modern marketplace has no walls
SHOTGUN DISTRIBUTION
Stack it high and watch it fly

CONTROLLED DISTRIBUTION
Control your brand, control your future
PROPRIETARY BLENDS

A little bit of this,
A little bit of that

TRANSPARENT LABELS

Customers want all of this,
Customers want all of that
CHOCOLATE OR VANILLA

Or Sour batch / Skittles

NOSTALGIC AUTHENTIC DELICIOUS

Official or bust
HIGH MARGIN

"Fake" Original Prices and Contained Marketplaces

HIGH VALUE

Transparent Market Places
Fully Disclosed Formulas
Packaging, Flavors, Licensing, Tariffs

AND PRICE POINTS STAYED CONSTANT!
TRADITIONAL ADVERTISING

Centerfolds and faux science—
I hope they’ll see my really cool adventorial

DIGITAL MARKETING

A 24/7 data driven community—creating conversations on a limitless scale
ATHLETES
Mr. and Mrs. Olympia and the Spokesmodel mindset

SUPER USERS/
‘INFLUENCERS’

Big Networks, Small Calves
And EVERYTHING in between
GLOBAL BRAND
CONTROLLED
DISTRIBUTION
TRANSPARENT
LABELS
TRENDING
FLAVORS
HIGH VALUE
SOCIAL MEDIA
SUPER USERS
US FOCUSED
UNCONTROLLED
 DISTRIBUTION
PROP BLENDS
VANILLA
HIGH MARGIN
PRINT ADS
BODYBUILDERS
Finding New Pathways in Sports Nutrition: Emerging Ingredients

Steve Myers
Senior Editor
Informa Markets | Natural Products INSIDER
steve.myers@informa.com
CBD Market Size & Scope

• Published forecasts and projections vary wildly: US$2B to $20B
• NBJ: U.S. hemp CBD sales will reach $3.9B by 2023, with $2.8B in supplement sales alone.
• “Hemp CBD is attracting a diverse set of consumers, with knowledge strongest among Millennials, but interest still significant with Baby Boomers.”
• 2019 NBJ survey of 250+ brands: 29% selling CBD, 65% planning to launch CBD in 1-2 years.
• Sports hemp CBD launches: BodyChek Wellness; Floyd’s of Leadville; Mendi; Game Up Nutrition; Easy Day Hemp; Clean Remedies; NanoCraft
Macro Force

Consumer Characteristics & Drivers

• Almost 10 million U.S. adults use CBD/hemp oil, a fourfold increase over the previous year.
• Demographics skew Millennial, female, households w/children & Western U.S. residents.
• US leads; Germany has highest use rate (4%), followed closely by Argentina and China (France & Indonesia are the slowest.)

Source: NMI’s 2019 Global Supplements/OTC/Rx Database® (SORD)

Consumers’ use of hemp CBD

- Anxiety: 44%
- Pain: 36%
- Sleeplessness: 29%
- General well-being: 25%

Source: Nutrition Business Journal (NBJ)
Cognitive Connection

Performance/Nootropics

• Spearmint – reaction time
• Tyrosine – attn, memory, learning
• Taurine - memory, sleep
• Vinpocetine – attn, alertness
• Caffeine – reaction time, alert
• Methylcobalamin (B12) – focus, sleep
• Choline: Pre-Ach, muscle function
  • Alpha GPC & citocholine

Protection/Recovery

• Omega-3s – inflammation; TBIs
• CBD – inflammation, TBIs, anxiety, focus
• BDNF Boosters – brain-derived neurotrophic factor
  • Bacopa, ginkgo, rhodiola, AOX
• Curcumin – inflammation, BDNF
• Ketones – energy, BDNF
US consumers find a variety of protein sources appealing

Plant protein is the most appealing source of protein

Interest in a variety of protein sources is something that can help create genuine differentiation within the sports nutrition market

<table>
<thead>
<tr>
<th>Protein Source</th>
<th>Attractions 2019 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plant protein</td>
<td>76%</td>
</tr>
<tr>
<td>Native protein</td>
<td>74%</td>
</tr>
<tr>
<td>Collagen protein</td>
<td>72%</td>
</tr>
<tr>
<td>Whey protein concentrate</td>
<td>66%</td>
</tr>
<tr>
<td>Grass-fed protein</td>
<td>65%</td>
</tr>
<tr>
<td>Soy protein</td>
<td>65%</td>
</tr>
<tr>
<td>Wheat protein</td>
<td>64%</td>
</tr>
<tr>
<td>Whey protein isolates</td>
<td>64%</td>
</tr>
<tr>
<td>Rice protein</td>
<td>59%</td>
</tr>
<tr>
<td>Whey protein</td>
<td>59%</td>
</tr>
<tr>
<td>Chicken protein</td>
<td>58%</td>
</tr>
<tr>
<td>Whey protein hydrolysate</td>
<td>56%</td>
</tr>
<tr>
<td>Organic protein</td>
<td>55%</td>
</tr>
<tr>
<td>Pea protein</td>
<td>55%</td>
</tr>
<tr>
<td>Egg protein</td>
<td>51%</td>
</tr>
<tr>
<td>Hemp protein</td>
<td>49%</td>
</tr>
<tr>
<td>Casein protein</td>
<td>42%</td>
</tr>
<tr>
<td>Milk protein</td>
<td>36%</td>
</tr>
<tr>
<td>Potato protein</td>
<td>34%</td>
</tr>
<tr>
<td>Canola</td>
<td>30%</td>
</tr>
<tr>
<td>Insect protein</td>
<td>25%</td>
</tr>
<tr>
<td>Algae protein</td>
<td>22%</td>
</tr>
</tbody>
</table>

Proportion of US consumers who find the following protein sources appealing, 2019

FMCG Gurus sports nutrition survey, 1000 consumers, Q3 2019
Plant Power

Plant sources: beans, nuts, legumes, grains, fungi

Plant proteins in sports nutrition: soy, pea, rice, hemp, quinoa, sacha inchi

Most plant proteins are not “complete”

Blending multiple plant sources can make a “complete” protein product.
The proliferation of oats is undeniable and are newest to capture growth in the plant protein space, followed by flaxseed while major player, rice, is losing ground.

![Plant-Based Protein: Grains & Seeds](image)

Source: NEXT Trend Data

<table>
<thead>
<tr>
<th>Grain or Seed Type</th>
<th>Expo West 2017</th>
<th>Expo West 2019</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oats</td>
<td>384</td>
<td>421</td>
</tr>
<tr>
<td>Flaxseed</td>
<td>381</td>
<td>398</td>
</tr>
<tr>
<td>Sunflower Seed</td>
<td>329</td>
<td>328</td>
</tr>
<tr>
<td>Pumpkin Seed</td>
<td>216</td>
<td>212</td>
</tr>
<tr>
<td>Rice</td>
<td>798</td>
<td>881</td>
</tr>
<tr>
<td>Chia Seed</td>
<td>330</td>
<td>277</td>
</tr>
<tr>
<td>Hemp Seed</td>
<td>167</td>
<td>137</td>
</tr>
<tr>
<td>Quinoa</td>
<td>327</td>
<td>227</td>
</tr>
</tbody>
</table>

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Grain and seed-based proteins are a big part of the plant-protein market, but are losing share of product innovation at Expo West while legumes and nuts grow and algae emerges.

Plant-Based Proteins: Group Analysis

Source: NEXT Trend Data

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Plant-Based Protein: Nuts

Cashews are surging in their protein prowess, while almonds remain a steady protein alternative.
Plant-Based Protein: Legumes

Peanuts and beans have strength in market share and growth, while lentils continue to experience growth displacing soy and its tofu counterpart.

Expo West 2017 – Expo West 2019

<table>
<thead>
<tr>
<th>Legume Type</th>
<th>Product Volume 2017</th>
<th>Product Volume 2019</th>
<th>% Growth 2017-2019</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peanuts</td>
<td>247</td>
<td>320</td>
<td>26%</td>
</tr>
<tr>
<td>Lentils</td>
<td>93</td>
<td>113</td>
<td>18%</td>
</tr>
<tr>
<td>Beans</td>
<td>360</td>
<td>391</td>
<td>6%</td>
</tr>
<tr>
<td>Soy</td>
<td>92</td>
<td>89</td>
<td>-6%</td>
</tr>
<tr>
<td>Peas</td>
<td>199</td>
<td>181</td>
<td>-11%</td>
</tr>
<tr>
<td>Tofu</td>
<td>45</td>
<td>27</td>
<td>-42%</td>
</tr>
</tbody>
</table>

Source: NEXT Trend Data
Whey and egg are contracting, while collagen continues to gain innovation traction. Bee-derived ingredients have a commanding presence.
Plant-based and responsibly sourced animal proteins are poised for success

Protein Concepts Coded By Type
Performance in Mainstream Consumer Concept Testing

Product concepts analyzed include all food, beverage and supplements. Excluded from analysis: home, personal and pet care and outliers below 45 MP and 2 PI.

*Includes: generic references to plant based protein, or specific reference to soy, pea or bean proteins.
Innovation Activity: Animal vs. Plant Protein

Ingredients/Claims relating to Protein*
Volume at Expo West 2018

<table>
<thead>
<tr>
<th>Protein Type</th>
<th>Volume 2018</th>
<th>Growth 2016-2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>Animal Protein Total</td>
<td>499</td>
<td>5%</td>
</tr>
<tr>
<td>Plant Protein Total</td>
<td>680</td>
<td>38%</td>
</tr>
</tbody>
</table>

Share Growth within each Ingredient/Claim
Expo West 2016 – Expo West 2018

Source: New Hope’s NEXT Trend Database; *Ingredient analysis restricted to products making a protein claim
Innovation Activity: Animal Protein Sources

Ingredients/Claims relating to Protein* Volume at Expo West 2018

- WHEY: 241
- EGG PROTEIN: 151
- MILK PROTEIN: 75
- CASEIN: 32

Source: New Hope’s NEXT Trend Database; *Ingredient analysis restricted to products making a protein claim

Diet & Nutrition Share Growth Change Expo West 2016 – Expo West 2018

- -32%
- -62%
- -61%
- 88%

Food & Beverage Share Growth Change Expo West 2016 – Expo West 2018

- 26%
- 87%
- 182%
- 198%
Innovation Activity: Plant Protein Sources

Ingredients/Claims relating to Protein* Volume at Expo West 2018

<table>
<thead>
<tr>
<th>Protein</th>
<th>Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEA PROTEIN</td>
<td>323</td>
</tr>
<tr>
<td>RICE PROTEIN</td>
<td>150</td>
</tr>
<tr>
<td>HEMP PROTEIN</td>
<td>106</td>
</tr>
<tr>
<td>SOY PROTEIN</td>
<td>101</td>
</tr>
</tbody>
</table>

Diet & Nutrition Share Growth Change Expo West 2016 – Expo West 2018

<table>
<thead>
<tr>
<th>Protein</th>
<th>Growth Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEA PROTEIN</td>
<td>131%</td>
</tr>
<tr>
<td>RICE PROTEIN</td>
<td>7%</td>
</tr>
<tr>
<td>HEMP PROTEIN</td>
<td>-44%</td>
</tr>
<tr>
<td>SOY PROTEIN</td>
<td>-40%</td>
</tr>
</tbody>
</table>

Food & Beverage Share Growth Change Expo West 2016 – Expo West 2018

<table>
<thead>
<tr>
<th>Protein</th>
<th>Growth Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEA PROTEIN</td>
<td>486%</td>
</tr>
<tr>
<td>RICE PROTEIN</td>
<td>101%</td>
</tr>
<tr>
<td>HEMP PROTEIN</td>
<td>-25%</td>
</tr>
<tr>
<td>SOY PROTEIN</td>
<td>19%</td>
</tr>
</tbody>
</table>

Source: New Hope’s NEXT Trend Database; *Ingredient analysis restricted to products making a protein claim
Fermented Ingredients

The global fermented food and ingredient market is projected to reach US$689.34B by 2023. Major ingredient types include amino acids and organic acids. (BIS Research)
The global fermented ingredients market size was valued at U$22.0B in 2018 and is expected to expand at a CAGR of 8.5% from 2019 to 2025. (Grandview Research)
Joint Health growth continues to ramp up

Joint health and inflammation sales grew 5.2% in 2018 to $2.0B
# Innovation Activity: Recovery

<table>
<thead>
<tr>
<th>Ingredient*</th>
<th>Volume at Expo West 18</th>
<th>Share Growth within each Ingredient/Claim Expo West 2016 – Expo West 2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>PROBIOTICS</td>
<td>650</td>
<td>-1%</td>
</tr>
<tr>
<td>OMEGAS</td>
<td>644</td>
<td>15%</td>
</tr>
<tr>
<td>CURCUMIN/TUMERIC</td>
<td>524</td>
<td>170%</td>
</tr>
<tr>
<td>BEETS</td>
<td>398</td>
<td>18%</td>
</tr>
<tr>
<td>ELECTROLYTES</td>
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<td>90%</td>
</tr>
<tr>
<td>CHERRIES</td>
<td>209</td>
<td>-17%</td>
</tr>
<tr>
<td>ASHWAGHANDA</td>
<td>23</td>
<td>-13%</td>
</tr>
</tbody>
</table>

Source: New Hope’s NEXT Trend Database; *Ingredient analysis not specific to sports recovery context
# Innovation Activity: Recovery

## Ingredients
### Volume at Expo West 2018

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Volume</th>
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<tr>
<td>PROBIOTICS</td>
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<tr>
<td>OMEGAS</td>
<td>644</td>
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<tr>
<td>CURCUMIN/TURMERIC</td>
<td>524</td>
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<tr>
<td>BEETS</td>
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<tr>
<td>ELECTROLYTES</td>
<td>294</td>
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<tr>
<td>CHERRIES</td>
<td>209</td>
</tr>
<tr>
<td>ASHWAGHANDA</td>
<td>23</td>
</tr>
</tbody>
</table>

## Diet & Nutrition Share Growth Change
### Expo West 2016 – Expo West 2018

| Ingredient       | Change | Share |
|------------------|--------|
| PROBIOTICS       | 13%    |       |
| OMEGAS           | -20%   |       |
| CURCUMIN/TURMERIC| -35%   |       |
| BEETS            | -35%   |       |
| ELECTROLYTES     | -35%   |       |
| CHERRIES         | -64%   |       |

## Food & Beverage Share Growth Change
### Expo West 2016 – Expo West 2018

| Ingredient       | Change | Share |
|------------------|--------|
| PROBIOTICS       | 13%    |       |
| OMEGAS           | -11%   |       |
| CURCUMIN/TURMERIC| 33%    |       |
| BEETS            | 48%    |       |
| ELECTROLYTES     | 85%    |       |
| CHERRIES         | -9%    |       |
| ASHWAGHANDA      | 41%    |       |

Source: New Hope's NEXT Trend Database; *Ingredient analysis not specific to sports recovery context
Thank You!
CBD in Sports Nutrition:

Legal Q&A

SupplySide West 2019, Las Vegas, NV

Rick Collins, Esq.
foundling partner

DISCLAIMER: These materials are information, not legal advice. Laws, regulations and guidances are often open to interpretation. Materials represent the author’s personal views and opinions at the time of authorship. © Rick Collins 2019. All rights reserved.
“Can I speak with Rick?”
CBD 101

• Marijuana and Hemp come from same species of plant, *Cannabis sativa L.*
• Cannabidiol (CBD) is one of >100 naturally occurring cannabinoids found in both.
• Hemp typically has much less THC (delta-9 tetrahydrocannabinol), the psychoactive chemical that produces a “high” when consumed.
• The World Health Organization (WHO) Expert Committee on Drug Dependence discussed CBD during its meeting in November 2017, reporting that pure CBD does not exhibit effects in humans indicative of abuse, dependence potential, or any public health-related problems (600 mg daily).
• And yet … the legal status of CBD in the US is mired in an intricate web of regulatory and legal considerations.
Can the “Green Rush” take the Sports Nutrition market by storm?

• CBD oil and other “phytocannabinoids” may have benefits as a *pre-workout* supplement to improve focus or as a *recovery* supplement to help reduce inflammation, lower DOMS, support muscle and joint health, lower stress and anxiety, etc.
Q: Does the 2018 Farm Bill make CBD Dietary Supplements “Legal”?

• Agricultural Improvement Act of 2018 exempts “Hemp” from the definition of “marihuana”:
  • “Hemp” and Cannabinoids derived from hemp are no longer controlled substances.
  • THC limit for Hemp is “not more than 0.3 percent on a dry weight basis.”
• However … FDA (so far) says CBD is not a dietary ingredient, dietary supplement, or food additive!
Q: WHY?!!!!!!

• CBD was studied as a new drug and “substantial clinical investigations have been instituted” and “made public,” leading to the approval of the drug Epidiolex® (cannabidiol) on June 25, 2018.

• CBD would have had to have been legally marketed as a dietary supplement or food **prior** to GW Pharmaceuticals’ clinical investigations in 2007.

But it’s a little more complicated than that

- Department of Defense says CBD is completely forbidden, because of potential THC content.
Q: How much do state laws vary?

• In August, Washington became the latest state to ban CBD in food/beverages, joining numerous other states including Ohio and North Carolina.

• Some states (e.g., Maine and Massachusetts) loosened CBD laws.

• Even individual cities are enacting policies, such as New York City which banned CBD in food/beverages earlier this year.

• [https://hempsupporter.com/stateactioncenter/](https://hempsupporter.com/stateactioncenter/)

• The result is a hodgepodge!!! Laws are changing daily!
Q: How big a problem are DRUG CLAIMS?

• Putting aside those hurdles facing CBD as a dietary ingredient, no supplements can be marketed to diagnose, treat, cure, or prevent any disease state.

• Multiple companies that sell CBD products have received warning letters from the FDA for making “disease claims” related to their CBD supplements.

• And if FDA/FTC don’t catch you....
“New Dietary Ingredients”

• A dietary ingredient not marketed in the U.S. as a dietary supplement or as an article for use in food before October 15, 1994.

• Must show why the new dietary ingredient will *reasonably be expected to be safe under the conditions of use.*


• Sports nutrition market history of not filing NDIs... 😞

Q: Even if CBD were to be dietary ingredient (constituent of a botanical), was it on the market prior to 1994 (ODI...)?

– If it’s a new dietary ingredient, does it require a notification to FDA 75 days prior to marketing that it’s reasonably be expected to be safe under the conditions of use?

– Or was it “present in the food supply as an article used for food in a form in which the food has not been chemically altered”?

• CBD isolate ... NO (vs. crude extract or full spectrum hemp oil with CBD)
The Speeding Car Analogy

• How marketers see it:
  – 50 mph limit
  – Doing 70 (no claims)
  – Doing 90 (claims)
CBD in Sports Nutrition...
Q: Why has Sports Nutrition been Slow on CBD?

• Sports nutrition typically early adopters...
• But gradual expansion to on-the-go soccer dads (active lifestylers)
• Is CBD still too “soy”?
• Or is the “forbidden” sexy?
Rob Gronkowski says YES to CBD!

• Last month, Gronk announced his own CBD line to try to get the NFL to loosen its restrictions.

• He praised CBD for giving him a working body again.

• Note: he’s talking topicals so far, which FDA hasn’t said NO to…
Terrell Davis says YES to CBD!

- Two-time Denver Broncos Super Bowl champion Terrell Davis is advocating for the NFL to allow players to use CBD.
- “It’s a beautiful thing. It’s worked for me. It’s worked for a lot of players,” says the co-founder of the CBD-infused Defy sports drink brand.
Q: Are the risks lower in sports nutrition?

• Yes! Less of a problem with disease claims!

• Obviously, claims must be substantiated (to satisfy FTA, FTC, state attorneys general, and plaintiff class action lawyers).

• Can efficacy claims be substantiated at lower intakes?
Q: Are the risks *greater* in sports nutrition?

• Maybe! Active people may be more likely to be drug tested!

• Saying “THC Free” may be even riskier within this consumer base!

• Topical products face the same drug claim concerns, along with a higher risk due to drug testing.

• Plus…….
Q: Is CBD banned in sports?

• WADA (as of Sept. 2017), the PGA and pro tennis allow players to use CBD.
• But CBD remains prohibited in the NFL, NBA, MLB and NHL.
• Should you warn?
Q: Can CBD cause a positive drug test?

• Sports nutrition products are attractive to active people. Athletes aren’t the only ones who are subject to random urine screens. So are employees, police and firefighters, probationers, etc.

• Will a CBD sports nutrition product make a consumer (or athlete) test positive? How?!

• Too much THC!
CBD and THC

• THC is a Schedule 1 Drug and prohibited by WADA, NCAA and other testing organizations.

• Many CBD companies claim the product contains >0.3% THC but do not test them. What if the product, or a certain batch, contains more THC than listed on the label?

• What if the athlete/employee is taking multiple servings per day? Is this enough THC to cause a positive result in a drug tested athlete or employee?

• Can THC content increase over time in CBD products stored under certain conditions?

• Weight of the evidence says CBD does NOT convert to THC in vivo in humans (unlike in rats).
Q: What would Devin Logan say?

- Olympic silver medalist skier Devin Logan took CBD drops (with “trace amounts of THC”).
- CBD is allowed by WADA
- But she was suspended for three months after testing positive for a higher-than-permissible level of THC.
Q: What does USADA say?

• USADA said: “Athletes are advised that all natural and synthetic cannabinoids, except cannabidiol (CBD), are prohibited in-competition. Many products which claim to be pure CBD extract or oil from the cannabis plant have traces of THC or other cannabinoids. Thus, a consumer who buys a CBD oil, extract, or other CBD product should be aware that there is a high likelihood it is a mixture of CBD and other prohibited cannabinoids, such as THC” which could be more than claimed and trigger an anti-doping rule violation.
Q: Do all sports use the same THC detection levels?

- Per Oliver Catlin of the Banned Substances Control Group (www.bscg.org):
  - Current confirmation thresholds in sport and workplace drug testing:
  - NCAA, DOD, DOT, NBA: 15 ng/ml (NCAA increased from 5 to 15 in 2018-2019 season)
  - MLB: 18 ng/ml (note that many articles online state the level is 50 ng/ml, the confirmation level is 18 ng/ml according to page 76 of the joint drug agreement)
  - NFL: 35 ng/ml
  - WADA, UFC, PGA, LPGA, ITF: 150 ng/ml
  - NHL: Doesn’t test for THC
Q: How do I protect my CBD company?

• Don’t sell CBD as a dietary supplement 😊
• If you sell CBD, don’t make drug claims!
• Make sure your claims are substantiated!
• Consider adding substantiated ingredients to your product formulations that support health category (curcumin anti-inflammatory, melatonin sleep, etc.)
• Look for quality! CoA’s! Reputable suppliers!
• GMP compliance!
Protecting your CBD company

- Recognize that athletes are sometimes drug tested!
- Test! There are various programs that test products (www.bscg.org) or the supply chain from seed to shelf (every batch from harvest, extract, finished product) (www.USHempAuthority.org)
- Don’t make statements you may regret (“THC free”)
- Include appropriate warnings (children, pregnant women, athletes???) (THC free vs below LoD)
- Get knowledgeable consultants like Alan Roberts (www.nutritioninnovation.com) or Hector Lopez (cvsciences.com)
Q: What is the Future of CBD?

• On May 31, 2019, FDA held a public hearing on CBD with over one hundred (100) speakers and ten (10) hours of testimony. The purpose of the hearing was to obtain scientific data and information about the safety, manufacturing, marketing, labeling, quality and sale of products containing cannabis or cannabis-derived compounds.

• FDA began the hearing by expressing safety concerns over side effects, drug interactions, dosing, and adolescent use.

• Is there a regulatory pathway and what might it look like?

• Limits on CBD content?

• Additional GMPs?
Thank you!

Rick Collins

founding partner
516-294-0300
Just the Facts: Evidence on CBD and Leveraging the Endocannabinoid System for Sports Nutrition-Related Benefits

Hector Lopez, MD, CSCS, FAAPMR, FISSN
CMO/Partner: The Center for Applied Health Sciences (CAHS)
Co-Founder: NovaNutra (NN); Supplement Safety Solutions, LLC. (SSS) and THR Biosciences, LLC. (THR)

October 16, 2019
Finding New Pathways in Sports Nutrition
Relevant Financial Relationships in the Past Twelve Months by Presenter or Spouse/Partner:

**Supplement Safety Solutions-Nutravigilance/ Pharmacovigilance** consultant for companies that develop, market & distribute Cannabis-derived Phytocannabinoid /CBD products within CPG and Pharmaceutical Channels, and **The Center for Applied Health Sciences, LLC.** receives human clinical research grants for dietary ingredients, functional foods/ beverages, of which multiple are in the Cannabis-Hemp/ Phytocannabinoid/ CBD space;

Receive compensation from revenues generated by granted and pending patents/ IP within the greater dietary supplement, food and beverage industry.
Outline

• Broad Roles of Sports Nutrition
• Discovery of the Endocannabinoid System (ECS) & Origins
• The Major “Players” or components of the ECS
• Expanded ECS → “Endocannabinoidome”
• Mechanisms of action and physiologic roles of the ECS as a master regulator of homeostasis to physical, mental & emotional stressors
• Evidence Supporting a potential role in sports nutrition / human performance across multiple organ tissues
  – Limited/ Mixed LEVEL II & some borderline LEVEL I Evidence
• Prelimin data from 1st RCT on a Commercial Hemp-derived CBD product in healthy subjects
• CBD Science & Industry Myths & Misconceptions
• Salient Points, Future Directions and Considerations for product development
“Ergogenic Aids” in Sports, Active & Performance Nutrition

Catagories of Ergogenic aids

- **mechanical** — devices including heart rate monitors, weights, sports clothing and footwear, and equipment
- **nutritional** — food sources including caffeine, creatine and sports drinks
- **pharmacological** — synthetically produced drugs including anabolic steroids, beta blockers and amphetamines
- **psychological** — methods including imagery, meditation, music, relaxation
Broad Roles of Sports Nutrition—So many Options!

- Potential Mechanisms of Ergogenic Support:
  - Resistance to Fatigue
  - Structural substrates / Precursors / Energy Metabolism / Bioenergetics
  - Buffering metabolites / Work Capacity
  - CNS/Neurostimulation/HPA — Psycho-motor, Arousal / Perceived Skill — Task Performance / Perceived Challenge
  - Anti-inflammatory / Anti-fibrotic / Immunomodulators (Cytokines/Eicosanoids / SPMs) / Resolution
  - Anabolic / Anti-catabolic tissue remodeling
  - Red-Ox balance / Oxidative stress

- Categories of compounds:
  - Macronutrients (FOOD First)
  - Amino Acids (EAAs & NEAAs), Intact Proteins and Peptide Preparations
  - Nitrogenous Compounds & Alkaloids (Creatine, Caffeine, beta-alanine, Betaine/TMG, Citrulline, Taurine, HMB, Theacrine (TeaCrine®), Dopaminergic/Cholinergic donors, etc.)
  - EFAs - Bioactive Lipids (n-3 HUFA, AA, PA, GLA, Cetylated FAs, etc.)
  - Proteolytic enzymes
  - Organic & Inorganic Micronutrients (Bicarbonate, Phosphate, Vitamins, Minerals)
  - GAGs/PGs/MSM
  - Prebiotics / Probiotics
  - Botanical Ingredients (phenylpropanoids, polyphenolic/flavonoids, terpenes, tannins, saponins, catechins, etc.)

Adaptogen (classical reductionist def): a substance that increases an organism’s ability to adapt to environmental/external stress by modifying stress-response and normalizing disordered physiological function → Appears to be a MAJOR Node for CBD/ECS via Systems Biology

ECS Wide-Ranging Influence on Physiology Under Basal and Stressed Conditions
Concept of Recovery in Sports Nutrition

- Rehydration & Repletion of Volume & Electrolyte Losses
  - (Local & Systemic)

- Restoration of Key Substrates Oxidized During Physical Activity
  - Glucose/Glycogen
  - Amino Acid Pools
  - Intramyocellular Lipids (IMTG)
  - Neurotransmitter and Nucleotides Substrate Status (CNS)

- Remodel and Repair Ultra-Structural Damage
  - Myofibrillar proteins
  - Intra-muscular & Extra-muscular Connective Tissue Recovery

- Manage Oxidative Stress & Inflammation
  - ROS/RNS management
  - Modulate Immune Response
  - Neuro-endocrine support/ HPA axis
  - Sleep/ Circadian support

Potential Role For CBD/ ECS-based Ingredients
Robert Yerkes-John Dodson Law: ”Inverted U” model

• Perceived Stress/Anxiety/Arousal $\leftrightarrow$ Task Performance
• RAS of brain helps maintain levels of arousal from sensory inputs
• “Flow Experience/State” related to YD Model (M. Csíkszentmihályi & J. Nakamura); Alpha & Theta waves on EEG
• Opportunity for CBD/ECS Tone as more of: “Direct Ergogenic Aid” (e.g., Combat Athletes, Gymnast, Golf, Archery, eSports, Introverts or “Practice Superstar” $\rightarrow$ Underperform in front of audience or event day)
Historical Perspective (Discovery)

- **1940s** R.S. Adams, Wollner et al. isolated and synthesized CBN, CBD, CBDA and THC isomers
- R. Mechoulam et al: (-) Cannabidiol (CBD) enantiomer (1963)
- Gaoni and Mechoulam: Δ9-THC elucidated & characterized (1964)
- Dewey WL: CBD and >60 other phytocannabinoids (1988)
- Bonner T: CB1 cloning/characterization (1990)
- Vincenzo Di Marzo “Endocannabinoidome” (2011)
Sports, Active & Performance Nutrition Dietary Supplement Strategies Target:

- Acutely: supports exercise performance/capacity, metabolism or recovery
- Chronically: enhance recovery and adaptations (strength/power, speed, endurance, body composition, muscle hypertrophy)
Endocannabinoid System (ECS): An internal homeostatic regulatory system in chordates with three components (Triad):

- Endocannabinoid ligands: First known lipid-based neurotransmitters (now largest network; e.g., Anandamide, 2-AG)
- CB₁, CB₂ & TRPV1 (GPCRs-constitutive & inducible) receptors
- Their regulatory enzymes

Endocannabinoids are produced labile, on-demand, autocrine/paracrine, and quickly travel in retrograde fashion to inhibit neurotransmitter release within CNS.

“Entourage or Ensemble Effect” with major + minor ENDOCANNABINIDS or PHYTOcannabinoids + terpenes + phytochemical matrix (additive interactions) → likely influencing more than one component of this TRIAD
Phytocannabinoids = Cannabis (THC, CBD, etc.)

- Cannabidiol (CBD)
- Δ⁹-tetrahydrocannabinol (Δ⁹-THC)

Endocannabinoids = Lipid-PUFA based Cannabis-like Compounds *(made on-demand, para/ autocrine fashion & labile signaling vs. preformed, stored in vesicles like other NTs)*

- Arachidonoyl ethanolamide (anandamide)
  - AEA as a “stress-responsive” eCB
  - 5 pmol/g concentrations
  - Partial agonist; less adverse when overweighted” in ECS tone

- 2-arachidonoyl glycerol (2-AG)
  - 2-AG as a “workhorse” eCB
  - 10 nmol/g concentrations; plasma [ ] >200x
  - Full agonist; synaptic plasticity; more adverse when “overweighted”; psychobehavioral and metabolic;
Phytocannabinoids

THC  
THCA  
CBD  
CBDA  
CBN  
CBG  
CBC  
THCV

Endocannabinoids

AEA  
2-AG  
Met-F-AEA  
ACEA

Synthetic Cannabinoids and Cannabinoid Receptor Ligands

Nabilone (Cesamet®)  
Dronabinol (Marinol®)  
AM251  
JWH-133  
WIN 55,212-2  
HU-331, CBDHQ  
O-1663
CB1 Distribution: Brain, Peripheral Nerves, Liver, Lungs, Kidneys, Skeletal Muscle, Adipose and Most Tissues

CB2 Distribution:
Immune Cells – Monocytes, macrophages, B-cells, and T-cells
  ▪ Functions: Anti-inflammatory, Antioxidant, etc.
Peripheral Nerves
  ▪ Functions: Analgesic effects Peripheral Nervous System
GI Track
  ▪ Functions: Modulate Intestinal Inflammatory Response/ TLR/ mast & Macrophage
  ▪ Promotes Beneficial Microflora (Bacteroides: Firmicutes ratio)
  ▪ Decease Hypermobility; Reduce N/V (esp. CBDA, CBG)

Aizpurua-Olaizola, et al. Targeting the endocannabinoid system: future therapeutic strategies. Drug Discovery Today, 22(1); 2017
ECS Downstream Signaling

Functional Selectivity
- Biased signaling of different agonists of CB1/ CB2rs activates different "suites" of intracellular signaling molecules (ACTIVATION STATE & CELL TYPE)
  - Same receptor --> Different ligand --> Different conformational change

CBD acts here as a Negative Allosteric Modulator of CB1!

- Dimerization with other receptors to change the physiologic response

Partner Receptors & Conditions

- **Opioid Receptors**
  - CB1, δOR
  - Tolerance to pain-blocking effects of opiates
  - Anxiety and depression in chronic pain

- **Serotonin Receptors**
  - CB1, 5-HT2A
  - Memory impairments
  - Anxiety

- **Dopamine Receptors**
  - CB1, D2
  - Parkinson’s Disease

- **Adenosine Receptors**
  - CB1, A2A
  - Huntington’s Disease

- **Orexin Receptors**
  - CB1, OX1-2
  - Appetite, sleep, and pain

- **Chemokine Receptors**
  - CB2, CXCR4
  - Tumor metastasis

Mitigate the effects of and/or Adapt to Stress

- Based on Pharmacology (delta-9 THC)

- ECS activation of the system in a spatiotemporal manner leads to:
  - Increased reward, reduce pain, anxiety, body temperature and blood pressure
  - Stimulates appetite & feeding behavior/energy storage
  - Induce sleep, sedation and inhibit psychomotor behavior
  - Mediate extinction of aversive/trumatic/fearful processes & adaptive responses in CNS
  - Mediate neuroprotective and anti-inflammatory action

Like any regulatory system, when there is dysfunction → disease progression (e.g., obesity, metabolic syn/T2DM, neuro-inflammatory disorders, peripheral organ fibrosis) due to over- and/or misplaced activation

ECS → Pro-Homeostatic System for stress recovery & 

Sports, Active & Performance Nutrition 

Dietary Supplements Target:
- Acutely: support exercise performance/capacity or recovery
- Chronically: enhance recovery and adaptations (strength/power, speed, endurance, body composition, muscle hypertrophy)

AGAIN → These Wide-Ranging Systems Biology, Molecular & Physiologic Targets have Influence & Impact on SPORTS, ACTIVE & PERFORMANCE NUTRITION
Getting ready for and recovering from “The Hunt”

• GET READY
  – Seek/Obtain energy
  – Store energy
  – Expend less energy (thrifty)
  – Be mentally/emotionally resilient

• HUNT
  – Inflame & Fibrose
  – Endure painful events (fear/aversive memory extinction)

• RECOVER AFTER INJURY
  – Stay strong
  – Resolve infection, inflammation & fibrosis
  – Regenerate/Remodel tissue

• CB2 activates resolution of innate immune response in humans
  – Inflamm mediators
  – SPR lipid mediators, M-class switching, wound healing/repair
Expanded ECS $\rightarrow$ Endocannabinoidome

Complexity, Redundancy & Pleiotropy $\rightarrow$ >20 amino acids, >10 LC-PUFA/MUFAs... >200 eCBs characterized & more to come $\rightarrow$ THEME: Wide-ranging Influence & Impact on SPORTS, ACTIVE & PERFORMANCE NUTRITION
Potential to Leverage ECS, CBD and Hemp-Derived Phytocannabinoids in Sports/ Active/ Performance Nutrition?

- You’re already doing it! Pervasive & ubiquitous ECS is across all organ systems and how it is impacted by lifestyle factors [diet, activity/exercise, training load, sleep, psychological stress/management, medications (OTC and Rx) supplements]
- Endocannabinoid vs. Endorphin Hypothesis in endurance exercise-induced “blissful states”
- Neuroendocrine influence on recovery from exercise,
- Immunomodulatory impact on skeletal muscle adaptations and connective tissue remodeling
- Perceived Skill/ Challenge and Actual Mood State/ Mindset / Neuropsychological Arousal for Performance (anxiety and fear-extinction)
- Body composition, energy metabolism and feeding behavior/ appetite signaling
- Neuroplasticity and motor learning
- Rehabilitation from Injury (MSK or Neuro/ TBI)
Brief Primer for Phytocannabinoid (CBD)-Rich Cannabis/ Hemp-Derived Products Market

"Industrial Hemp" generally refers to variations of Cannabis Sativa bred specifically for non-psychoactive applications (<0.3% THC).

Some argue that the cultivars represent three species: Sativa, Indica, Ruderalis

1. Seeds (GRAS: hulled hemp seeds, hemp seed protein, and hemp seed oil)
2. Fiber, Shiv, and Hurd for food products, textiles, industrial products, and building materials
3. Extracts: cannabinoid yield (CBD, CBG, CBN, CBV)
1. **Cannabis Sativa**: Hemp and Marijuana are same genus and species

2. **Different Cultivars**: Genetics selected for desired attributes, Fiber (shiv & hurd), Seeds (seed oil, hemp hearts), flower (CBD, THC)

3. **Cannabinoids**: distinctive compounds in hemp (104-120 identified)

4. **CBD**: Celebrity cannabinoid – Cannabidiol

5. **Endo Cannabinoid Receptors**: two types found throughout human body

6. **Plant Bio-Mass**: Unrefined plant after harvest

7. **Extraction**: Separate bio-mass from crude oil (with Co2, ethanol, lipid, other)

8. **Winterization**: Separate waxes and lipids

9. **Distillation**: Refinement and isolation of specific compounds such as CBD

10. **Isolate**: Distilled and isolated cannabinoid (Rx territory)

11. **Terpenes and Flavonoids**: Polyphenolic molecules in hemp that influence sensory and nutritional attributes – as well as cell-signaling

12. **Full Spectrum Oil**: Refined oil as extracted from plant

13. **Broad Spectrum Oil**: Refined oil minus THC
There are over 100 Phytocannabinoids found in Cannabis with a Wide Variety of Actions

- Treasure Trove of nearly 1,000 identified chemical constituents (>200 Terpenes)
- Multi-molecular Library of Bioactives
- Therapeutic use over millenia not solely attributed to THC
Cannabidiol (CBD)

Pre-clinical and Clinical data supports the following mechanisms & applications (*immune, neuro/brain, stress response, pain, energy intake/storage/feeding, cell cycle-growth regulation*):

- Anti-inflammation – Decreased Cytokine and Chemokine actions
- Analgesic Effects
- Anti-nausea, Anti-emetic & GI Benefits
- Reduces neural excitability and pain
- Anxiolytic
- Anti-epileptic
- Neuroprotective
- Anti-cancer
- Anti-oxidant
- Apoptotic
Cannabidiol (CBD) + Other PhytoCBDs

<table>
<thead>
<tr>
<th>Effect</th>
<th>THC</th>
<th>CBD</th>
<th>CBG</th>
<th>CBN</th>
<th>CBD</th>
<th>THC+ CBG</th>
<th>CBG+ CBN</th>
<th>CBG+ THC</th>
<th>CBD+ THC</th>
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<td>Anti-diabetic</td>
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<td>Reduces vomiting and nausea</td>
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<td>Anti-emetic</td>
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<td>Reduces seizures and convulsion</td>
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<td>Anti-epileptic</td>
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<td>Treats fungal infection</td>
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<td>Antifungal</td>
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<td>Reduces inflammation</td>
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<td>Anti-inflammatory</td>
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<td>Reduces risk of artery blockade</td>
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<td>Anti-ischemic</td>
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<td>Inhibits cell growth in tumors/cancer cells</td>
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<td>Anti-proliferative</td>
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<td>Treats psoriasis</td>
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<td>Anti-psoriatic</td>
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<td>Tranquilizing, used to manage psychosis</td>
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<td>Anti-psychotic</td>
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<td>Suppresses muscle spasms</td>
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<td>Anti-spasmodic</td>
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<td>Relieves anxiety</td>
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<td>Anxiolytic</td>
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<td>Promotes bone growth</td>
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<td>Bone Stimulant</td>
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<td>Reduces function in the immune system</td>
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<td>Immunosuppressive</td>
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<td>Reduces contractions in the small intestines</td>
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<td>Intestinal Anti-prokinetic</td>
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<td>Protects nervous system degeneration</td>
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<td>Neuroprotective</td>
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</table>

Table 1. Overview of diseases for which CBD may have therapeutic benefits taken from Pisanti et al (2017) [69]

<table>
<thead>
<tr>
<th>Disease</th>
<th>Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alzheimer's disease</td>
<td>Antinflammatory, antioxidant, antiapoptotic in <em>in vitro</em> and <em>in vivo</em> models of Aβ-evoked neuroinflammatory and neurodegenerative responses.</td>
</tr>
<tr>
<td>Parkinson's disease</td>
<td>Improved signs of EAE in mice, antiinflammatory and immunomodulatory properties.</td>
</tr>
<tr>
<td>Huntington's disease</td>
<td>Neuroprotective and antioxidant in mice transgenic models; no significant clinically important differences in patients.</td>
</tr>
<tr>
<td>Hypoxia-ischemia injury</td>
<td>Short term neuroprotective effects; inhibition of excitotoxicity, oxidative stress and inflammation <em>in vitro</em> and in rodent models.</td>
</tr>
<tr>
<td>Pain</td>
<td>Analgesic effect in patients with neuropathic pain resistant to other treatments.</td>
</tr>
<tr>
<td>Psychosis</td>
<td>Attenuation of the behavioural and glial changes in animal models of schizophrenia; anti-psychotic properties on ketamine-induced symptoms</td>
</tr>
<tr>
<td>Anxiety</td>
<td>Reduction of muscular tension, restlessness, fatigue, problems in concentration, improvement of social interactions in rodent models of anxiety and stress; reduced social anxiety in patients.</td>
</tr>
<tr>
<td>Depression</td>
<td>Anti-depressant effect in genetic rodent model of depression.</td>
</tr>
<tr>
<td>Cancer</td>
<td>Antiproliferative and anti-inflammatory actions in a large range of cancer types; induction of autophagy-mediated cancer cell death; chemopreventive effects.</td>
</tr>
<tr>
<td>Nausea</td>
<td>Suppression of nausea and conditioned gaping in rats</td>
</tr>
<tr>
<td>Inflammatory diseases</td>
<td>Antinflammatory properties in several <em>in vitro</em> and <em>in vivo</em> models; inhibition of inflammatory cytokines and pathways.</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>Inhibition of TNF-α in an animal model</td>
</tr>
<tr>
<td>Infection</td>
<td>Activity against methicillin-resistant <em>Staphylococcus aureus</em></td>
</tr>
<tr>
<td>Inflammatory bowel and Crohn's diseases</td>
<td>Inhibition of macrophage recruitment and TNF-α secretion <em>in vivo</em> and <em>ex vivo</em>; reduction in disease activity index in Crohn's patients.</td>
</tr>
<tr>
<td>Cardiovascular diseases</td>
<td>Reduced infarct size through anti-oxidant and anti-inflammatory properties <em>in vitro</em> and <em>in vivo</em>.</td>
</tr>
<tr>
<td>Diabetic complications</td>
<td>Attenuation of fibrosis and myocardial dysfunction</td>
</tr>
</tbody>
</table>
CBD can act through ~65 discrete, specific molecular targets, including: **10 receptors**, **32 enzymes**, **10 ion channels**, and **13 transporters**!
CBD – Endocannabinoid + eCBome Signaling

CBD Biases toward CB2 Receptor Signaling due to: AEA amplification + CB1 Negative Allosteric Modulation + GPR55, 5HT1a, Gly, D2, A2A, CXR, ORX heterodimers (*also TRPV/A/M, PPARg, GABAr*):

CBD Also Enhances **Endogenous** Anandamide Levels from increased synthesis & decreased breakdown (*active at both CB1 & CB2*)
Potential Sources / Targets of EndoCBs

AGAIN ➔ These Wide-Ranging Systems Biology, Molecular & Physiologic Targets have Influence & Impact on SPORTS, ACTIVE & PERFORMANCE NUTRITION
CBD and CBDV on Markers of Muscle Differxn in Healthy and MDX models

- Histological analysis of mdx mice treated 32 days with CBD
- Also, rotarod and weight test vs. Veh

- Murine C2C12 myoblast transcript levels of canonical Myogenin/TroponinT after short and long duration exposure to CBD/ CBDV → Reduce Tissue Inflamm & Restore Fxn Autophagy
- Myotube Formation and Fusion Index via TRPV1 and TRPA1 in Healthy and MDX models

Iannotti FA, Di Marzo V, et al. Br J Pharm. 2018
Endocannabinoid Tone

- Critical physiologic system involved in establishing and maintaining human health by mitigating, responding to and adapting to stress → CLEAR IMPACT ON SPORTS/ ACTIVE/ PERFORMANCE NUTRITION

- Various **lifestyle factors** including background diet, sleep, psychosocial stress, relationships, body weight/composition and physical activity/exercise affect the overall ECS function or ‘endocannabinoid tone’

- Endocannabinoid tone is a function of:
  - Lifestyle & Epigenetic factors
  - Density of cannabinoid receptors
  - Their biosynthetic & metabolic enzymes (up/down-regulated)
  - Relative abundance or dearth of PUFA substrate
  - A host of other SNPs across CYP450, CB1, FAAH, MGL, AKT, COMT, DRD2, etc.
WHY SHOULD WE CARE ABOUT ECS TONE?

Mostly by Overactivation of CB1 Receptors
Re-visiting the Endocannabinoid System and Its Therapeutic Potential in Obesity and Associated Diseases

Dietary Linoleic Acid Elevates the Endocannabinoids 2-AG and Anandamide and Promotes Weight Gain in Mice Fed a Low Fat Diet

Peripheral cannabinoid 1 receptor blockade mitigates adipose tissue inflammation via NLRP3 inflammasome in mouse models of obesity
ECS interaction with HPA axis

- **Healthy Endocannabinoid (ECb) Signaling**
  - Lower baseline HPA axis activity, and constrains amygdalar inputs
  - Less stress response \([CRF/\text{ Cortisol}/\text{ Norepi}]\) with acute stress, and quick recovery to baseline (dampens CRF from PVN neurosec cells)

- **Disrupted ECb Signaling** (e.g., impaired CB1 signaling)
  - Higher baseline stress hormones [ ]
  - Exaggerated HPA response to acute stress

- **Chronic Stress**
  - Progressive and chronic stimulation of limbic CB1 signaling leads to desensitization and upregulation of CRF/ACTH and FAAH to dampen ECS reserve

Healthy human studies show baseline eCB tone regulates HPA axis reactivity to psychosocial stress; low baseline AEA leads to greater increase in cortisol after stress AND high baseline AEA seem to be protective against anxiety (i.e., Stress Resilience).
CBD and potential for Bone / MSK / Orthopedic resilience

• Kogan et al. demonstrated that CBD helps regulate the biomechanical properties and structure of bone in preclinical model

• CBD acted as ligand for receptors involved bone mineralization & protein content
  – Improvements in healing of a rat femoral fracture model & demonstrated increased load-bearing mechanical properties

• Numerous preclinical studies have demonstrated potent anti-inflammatory effects via activation of cannabinoid receptors (CB1, CB2, PPARs, GP18, and TRPV1) by both endocannabinoids as well as phytocannabinoids such as CBD (Gui et al., 2015)

• Overlap & Crosstalk with powerful family of lipids known as specialized pro-resolving lipid mediators (SPMs) → Active Resolution of Inflammation for remodeling of injured tissue

Kogan NM, et al. Cannabidiol, a Major Non-Psychotropic Cannabis Constituent Enhances Fracture Healing and Stimulates Lysyl Hydroxylase Activity in Osteoblasts. J Bone Miner Res. 2015

CBD and potential for Mitochondrial Support & Neuro-resilience / Neuroprotection

Molecular Medicine
2015; 21(1): 38–45

Cannabidiol Protects against Doxorubicin-Induced Cardiomyopathy by Modulating Mitochondrial Function and Biogenesis

Enkui Hao,1,2 Partha Mukhopadhyay,1 Zongxian Cao,1 Katalin Erdélyi,1 Eileen Holovac,1 Lucas Liaudet,3 Wen-Shin Lee,1,4 György Haskó,5 Raphael Mechoulam,6 and Pál Pacher1

Cannabidiol and (−)Δ9-tetrahydrocannabinol are neuroprotective antioxidants

A. J. Hampson‡, M. Grimaldi‡, J. Axelrod*, and D. Wink‡

*Laboratory of Cellular and Molecular Regulation, National Institutes of Mental Health, Bethesda, MD 20892; ‡Laboratory of Adaptive Systems, National Institute of Neurological Disorders and Stroke, Bethesda, MD 20892; and §Radiology and Biology Branch, National Cancer Institute, Bethesda, MD 20892

Contributed by Julius Axelrod, April 27, 1998
“Striking a Balance Within the System that Balances You”

While the ECS is a Major Pro-Homeostatic Signaling System, like any regulatory system, when disrupted, it Leads to Pathophysiology

“Holy Grail” appears to be Peripheral CB1r (-) and CB2r (+), with Central CB1r (sparing/ +)
There’s a SNP for that! Cannabinoid Pharmacogenetics

• CYP450: 2C9 (A/C LOF allele), 3A4, 2C19
• CNR1 (A/G allele LOF), FAAH (C/A allele LOF), COMT, DRD2, AKT, etc.
## Types of Cannabis sativa products/medications available

*Under prescription medications, nabiximols (Sativex) is not U.S. Food and Drug Administration-approved. It is available in Canada for cancer pain and multiple sclerosis.*

### Prescription Medications

<table>
<thead>
<tr>
<th>THC Dominant</th>
<th>Balanced THC/CBD</th>
<th>CBD Dominant</th>
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</thead>
<tbody>
<tr>
<td><strong>Dronabinol (Marinol): synthetic THC</strong></td>
<td><strong>Nabiximols (Sativex): 1:1 THC:CBD; refined extraction product</strong></td>
<td><strong>99% pure oil-based cannabidiol (Epidiolex): refined extraction product</strong></td>
</tr>
<tr>
<td>- Route: Oral</td>
<td>- Route: Oromucosal Spray</td>
<td>- Route: Oral solution (oil)</td>
</tr>
<tr>
<td>- Dose: 5mg THC/capsule</td>
<td>- Dose: 2.7mg THC/2.7mg CBD each spray</td>
<td>- Dose: 5mg/kg CBD per day</td>
</tr>
<tr>
<td>- Cost: $5 for 5mg dose</td>
<td>- Cost: $2-3/spray</td>
<td>- Cost: $32,500 for one year supply (~100mg CBD per day, assuming a 20kg child)</td>
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<tr>
<td><strong>Nabilone (Casamet): synthetic THC analog</strong></td>
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<tr>
<td>- Route: Oral</td>
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<tr>
<td>- Dose: 1mg/capsule</td>
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<td>- Cost: $235 for 5mg dose</td>
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### Extraction Products**

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<thead>
<tr>
<th>THC Dominant</th>
<th>Balanced THC/CBD</th>
<th>CBD Dominant</th>
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<tbody>
<tr>
<td><strong>Various Products—typically THC:CBD &gt;5:1</strong></td>
<td><strong>Various Products—typically THC:CBD ≈1:1</strong></td>
<td><strong>Various Products—typically CBD:THC &gt;10:1</strong></td>
</tr>
<tr>
<td>- Route: Oral (oils/pills), Inhalational (vaporizers/smoking), topical</td>
<td>- Route: Oral (oils/pills), Inhalational (vaporizers/smoking), topical</td>
<td>- Route: Oral (oils/pills), Inhalational (vaporized oil), topical</td>
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<tr>
<td>- Dose: varies</td>
<td>- Dose: varies</td>
<td>- Dose: varies</td>
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<tr>
<td>- Cost: $1 for 5mg THC dose</td>
<td>- Cost: $2.5 for 5mg THC/5mg CBD dose</td>
<td>- Cost: $10 for 100mg CBD only dose</td>
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</tbody>
</table>

### Whole Plant Products**

<table>
<thead>
<tr>
<th>THC Dominant</th>
<th>Balanced THC/CBD</th>
<th>CBD Dominant</th>
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</thead>
<tbody>
<tr>
<td><strong>Various whole plant products (e.g., joints (cannabis cigarettes), buds (dried cannabis flowers) for smoking or vaporization, and blunts (cannabis cigars)</strong></td>
<td><strong>Various whole plant products (e.g., joints (cannabis cigarettes), buds (dried cannabis flowers) for smoking or vaporization, and blunts (cannabis cigars)</strong></td>
<td><strong>Plant products with little THC</strong></td>
</tr>
<tr>
<td>- Route: Usually smoked or edibles</td>
<td>- Route: Usually smoked or edibles</td>
<td>- Route: CBD dominant flowers and buds for smoking or vaporization is not widely available. CBD dominant edibles widely available</td>
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<tr>
<td>- Dose: Ratio of THC/CBD often unknown, not reliable</td>
<td>- Dose: Ratio of THC/CBD often unknown, not reliable</td>
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<tr>
<td>- Cost: $3.5/joint (typically ~26mg THC)</td>
<td>- Cost: $3.5/joint (typically ~26mg THC)</td>
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**Extraction products are commonly produced through state programs. Whole plant products are available in state programs and on the open market ("street").**

**Hemp = Cannabis sativa with < 0.3% THC component.**

<table>
<thead>
<tr>
<th>Terpenoid</th>
<th>Structure</th>
<th>Commonly encountered in</th>
<th>Pharmacological activity (Reference)</th>
<th>Synergistic cannabinoid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Limonene</td>
<td><img src="image" alt="Structure" /></td>
<td>Lemon</td>
<td>Potent AD/immunostimulant via inhalation (Komori et al., 1995)</td>
<td>CBD</td>
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<td></td>
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<td></td>
<td>Anxiolytic (Carvalho-Freitas and Costa, 2002; Pultrini Ade et al., 2006) via 5-HT1A (Komiya et al., 2006)</td>
<td>CBD</td>
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<td></td>
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<td></td>
<td>Apoptosis of breast cancer cells (Vigushin et al., 1998)</td>
<td>CBD</td>
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<td></td>
<td>Active against acne bacteria (Kim et al., 2008)</td>
<td>CBD</td>
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<td></td>
<td>Dermatophytes (Sanguinetti et al., 2007; Singh et al., 2010)</td>
<td>CBD</td>
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<td>Gastro-oesophageal reflux (Harris, 2010)</td>
<td>THC</td>
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<tr>
<td>α-Pinene</td>
<td><img src="image" alt="Structure" /></td>
<td>Pine</td>
<td>Anti-inflammatory via PGE-1 (Gil et al., 1989)</td>
<td>CBD</td>
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<td></td>
<td>Bronchodilatory in humans (Falk et al., 1990)</td>
<td>THC</td>
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<td>Acetylcholinesterase inhibitor, aiding memory (Perry et al., 2000)</td>
<td>THC, CBD</td>
</tr>
<tr>
<td>β-Mycene</td>
<td><img src="image" alt="Structure" /></td>
<td>Hops</td>
<td>Blocks inflammation via PGE-2 (Lorenzetti et al., 1991)</td>
<td>CBD</td>
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<td></td>
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<td></td>
<td>Analgesic, antagonized by naloxone (Rao et al., 1990)</td>
<td>CBD, THC</td>
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<tr>
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<td></td>
<td>Sedating, muscle relaxant, hypnotic (do Vale et al., 2002)</td>
<td>THC</td>
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<td>Blocks hepatic carcinogenesis by aflatoxin (de Oliveira et al., 1997)</td>
<td>CBD, CBG</td>
</tr>
<tr>
<td>Linalool</td>
<td><img src="image" alt="Structure" /></td>
<td>Lavender</td>
<td>Anti-anxiety (Russo, 2001)</td>
<td>CBD, CBG?</td>
</tr>
<tr>
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<td>Sedative on inhalation in mice (Buchbauer et al., 1993)</td>
<td>THC</td>
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<td>Local anesthetic (Re et al., 2000)</td>
<td>THC</td>
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<td></td>
<td>Analgesic via adenosine A$_2$A (Pena et al., 2006)</td>
<td>CBD</td>
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<td></td>
<td>Anticonvulsant/anti-glutamate (Elisabetsky et al., 1995)</td>
<td>CBD, THCV, CBDV</td>
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<td>Potent anti-leishmanial (do Socorro et al., 2003)</td>
<td>?</td>
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<tr>
<td>β-Caryophyllene</td>
<td><img src="image" alt="Structure" /></td>
<td>Pepper</td>
<td>Al via PGE-1 comparable phenylbutazone (Basile et al., 1988)</td>
<td>CBD</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>Gastric cytoprotective (Tambe et al., 1996)</td>
<td>THC</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Anti-malarial (Campbell et al., 1997)</td>
<td>THC</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Selective CB$_2$ agonist (100 nM) (Gertsch et al., 2008)</td>
<td>THC</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Treatment of pruritus? (Karsak et al., 2007)</td>
<td>THC</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Treatment of addiction? (Xi et al., 2010)</td>
<td>CBD</td>
</tr>
<tr>
<td>Caryophyllene Oxide</td>
<td><img src="image" alt="Structure" /></td>
<td>Lemon balm</td>
<td>Decreases platelet aggregation (Lin et al., 2003)</td>
<td>THC</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Antifungal in onychomycosis comparable to ciclopiroxolamine and sulconazole (Yang et al., 1999)</td>
<td>CBC, CBG</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Insecticidal/anti-feedant (Bettarini et al., 1993)</td>
<td>THCA, CBGA</td>
</tr>
</tbody>
</table>
Cannabimimetics + Other PhytoCBs

Non-Cannabis Phytocannabinoids

• **Clove oil (concentrated for b-caryophyllene)** – Contains several analgesic ingredients, but the most researched for its effects on the ECS is b-caryophyllene. It is able to bind to CB2 receptors, one of its primary mechanisms in its ability to reduce pain.

• **Echinacea purpurea** – Alkylamides from the Echinacea species bind to CB2 with great affinity, helping CB2 receptors in modulating the immune system, and prolonging the effects of anandamide. Clinical studies with an alkamide-rich extract have shown positive effects in relieving stress and anxiety.

• **Zanthoxylum (Sichuan pepper)** – Contains alkylamides that show strong affinity to CB1 and CB2. These compounds also influence transient receptor potential channels that are involved in electrical control of cells, working closely with the ECS. The two systems overlap and are intricately interwoven in helping cells communicate with one another.

• **Peony** – Contains paeoniflorin, which exerts several benefits in close harmony with endocannabinoids’ influence on cellular function, including transient receptor channels involved in the electrical control of cells & feelings of pain.

• **Ginger** – Exerts a multitude of health benefits particularly related to pain, inflammation, and gastrointestinal effects, some of which are mediated by the ECS.

• **Magnolia** – Contains magnolol, which is a very potent CB1 and CB2 receptor agonist. Able to bind to both types of CB receptors. Magnolia extracts exert significant effects in promoting a relaxed mental state useful in reducing anxiety.
Brief Summary of Human RCTs with CBD

- 176 studies on CBD (67 completed)
- 46 different conditions: pain, anxiety, inflammation, autism, GI disorders, cancer, MS, epilepsy, tremors, PTSD, addictions
- Oral Doses range from 200mg to 1500mg CBD for isolate, and 15mg (HEMP POWER Trial at CAHS) to 25mg to 90mg CBD for complex/spectrum extracts
- Oral Bioavailability is variable between <10% to 13%-19%, affected by fed/fasted state, lipids, genetics, prior use, etc./
- t1/2 life: 1.4 to 10.9h after single OM dose, 2-5 days after chronic oral admin

HEMP POWER Trial: RCT to assess measures of stress tolerance, sleep, mood, appetite, body comp, metabolic/immune health

- RDBCT
- n=65 overweight, but otherwise healthy men (n = 32) and women (n = 33); (mean ± SD age, 35.2 ± 11.4 yr)
- Hemp Oil Extract [HEMP, 60 mg/d PlusCBD Oil™ (15 mg hemp-derived CBD)] or a placebo extra virgin olive oil vehicle (PLA) x 6 weeks
- No diet or exercise intervention
- Outcomes: A 14-item panel of various psychometric parameters, heart-rate variability, plasma chromogranin A, DEXA, as well as general markers of health (HR, SBP/DBP, and Metabolic Panel – Clinical Chemistry/Hematology)

Percent change from baseline (relative to week 6). All variables displayed observed statistically significant changes in the HEMP group only. See abstract for p-values.
HEMP POWER Trial: RCT to assess measures of stress tolerance, sleep, mood, appetite, body comp, metabolic/immune health

- These data represent the first RDBCT we are aware of regarding the safety and efficacy of a commercially available finished product (PlusCBD Oil™) containing a hemp-derived, CBD-rich extract in healthy humans.

- HEMP (PlusCBD Oil™) supplementation at **15mg active CBD**, containing a broad array of major/minor phytocannabinoids, terpenes, tocopherols/ tocotrienols, and fatty acids can improve self-reported psychometric measures of sleep, quality of life (life satisfaction) and reduce appetite within HEMP group, while demonstrating no adverse effects on standard biomarkers of safety.

- Future studies are warranted to fully characterize the complex phytochemical composition of the commercial HEMP extract (PlusCBD Oil™) finished product.

- Ongoing and future analyses will interrogate effects on inflammatory cytokines, HPA axis/stress hormones and targeted gene expression profiles, along with assessing PK with ascending doses to assess bioavailability, metabolism and elimination half-life of HEMP extract delivered as part of a complex spectrum of phytochemical constituents.

*Unpublished Data (Lopez HL, et al.)/ Scientific Proceedings ISSN- June 2019*
# CBD/ Endocannabinoid Applications in Sports, Active & Performance Nutrition

## Sports Performance Anxiety
- Perceived Stress, Anxiety, Fear, Psych distress impacts athletic performance
- Optimize “Arousal-Performance” Curve
- Combat sports, Golf, Archery, Marksmanship

## Metabolic Health/ Wellness
- Body Composition
- Nutrient Partitioning

## Recovery & Adaptation to Training
- Modulating Neuro-endocrine & HPA axis response to exercise (AKA \( \rightarrow \) ADPATOGEN)
- Stress Resilience & HPA Function for acute sessions/ events/ tournaments, and chronic periods/ blocks

## Injury Resilience
- Orthopedic / MSK/ Connective tissue support
- Neuroprotection & Neuro-recovery

CBD &/or Priming ECS Tone
Common Myths / Misconceptions (partial list 😊)

• CBD isolate vs. CBD-containing, Multi-Constituent Complex Hemp Extract
• 2018 Farm Bill (Ag Improvement Act) so all CBD products are fully lawful to sell in food/dietary supplements federally
• “CBD is completely safe with no adverse health risks!”
  – “Sola dosis facit venenum” -Paracelsus (Theophrastus von Hohenheim)
  – e.g., Sedation, Lightheadedness, Headache, Diarrhea, Dry Mouth, loss appetite
• “Since GW Pharma used 10mg to 20mg/ kg BWt. dose (400mg to 1.3 g CBD), then 25mg CBD from complex hemp-extract (FSHE/BSHE) can’t possibly work or have benefit”
• CBD acts directly on the classical Endocannabinoid System & CB receptors
• “Hemp & CBD-rich Cannabis extracts are not psychoactive”
Salient Points on Cannabis

- From Cannabis → lead to discovery of ECS expanded eCB System → Rx “SynCans” → Back to Cannabis for further botanical extracts for product dev
- Most phytocannabinoids (Cannabis/Hemp-derived) & cannabimimetics (other Botanicals) are pleiotropic, have multi-mechanistic targets, networks & pathways with Polypharmacy VS. Single Molecule-> Single Target-> Pharmacol agent

  **Complex multi-constituent CBD-rich Hemp extracts** ("full/broad-spectrum") appear to be more effective at lower CBD doses (15 mg to 90 mg) vs. Isolates (300 mg to 1500 mg; ~10-20 mg/ kg BWt)

- Hemp/ Cannabis-derived, CBD-rich Complex Extracts Low in THC have an Unusually Broad Therapeutic Index/ Margin Relative to other Botanical Extracts:
  - Lack of strong affinity to CB1r
  - Lack of Endocannabinoid Presence in Brainstem Driving Cardiorespiratory Centers
  - Pleiotropic to help mitigate over-activation of CB1r, while affecting other targets (TRPs, 5HT1a, PPARs, GPRs, etc.)
Psycho-neuro-endo-metabolic-immune axes (eCBs signal via localized, on-demand autocrine/paracrine vs. endocrine fashion or vs. exogenous phytocannabinoids)

- Various lifestyle factors including background diet, sleep, psychosocial stress, relationships, body weight/composition and physical activity/exercise affect the overall ECS function or ‘endocannabinoid tone’

Enormous overlap and crosstalk with other signaling & organ systems in humans

Take home on cannabinoid physiology

- More nuanced than simple, binary ON/OFF switch
- Great safety profile, large therapeutic index (particularly, non-THC predominant products)
BEYOND CBD and FUTURE DIRECTIONS

- Future hemp/cannabis-based products with unique “cannabinoid/terpene profiles” to strategically address various physiologic pathways

- Application of Pharmaco/Nutrigenetics/omics and “-Omics” technologies to major/minor cannabinoids found within Hemp Extracts → PERSONALIZED Nutrition/Wellness
  
  ✓ Various chemoprofiles to match CB-terpene-phytochem matrix with desired therapeutic/functional goal (i.e., pain, stress-resilience; obesity-met syn; circadian dysfunction; MSK-orthopedic)
  
  ✓ Different Cannabinoid + Terpene “fingerprints” (supply chain from genotype to chemotype of the raw material/ingredient/finished product)
  
  ✓ Targeting the Expanded ECS & Broader ‘Endocannabinoidome’

- SNPs within FAAH, CNR1/2, COMT, D2R and CYP2C9 have a large impact on pharmacodynamic response & efficacy (“responder vs. non-resp”) from ECS-targeting products (e.g., CBD-rich hemp extracts)
  
  ✓ Implications for clinical research in this area going forward & enormous variability → [inter-individual response heterogeneity]

- Another potential tool in the therapeutic or performance/ergogenic tool-box, but tread carefully with leading brands → start low/go slow
Salient Points on CBD/ECS in Sports, Active & Performance Nutrition

Therapeutic area/ applications/ categories (*Structure/Function-friendly*):

- **As a DIRECT Ergogenic Aid:** Limited/Scarce Evidence (Level III per ISSN) with one potential exception: in “Sports Performance Anxiety” /Arousal YD Inverted-U model
- **As an INDIRECT Ergogenic Aid:** More rationale & totality of evidence (Level II per ISSN) for Recovery & Adaptation in Sports Nutrition
- “Nervous System” health (mood/stress/arousal SNS response, restorative sleep & circadian rhythm optimization, neuroprotection- microglial activation, neuroinflamm, neurogenesis)
- “Stress Resilience” (HPA & Neuro-endocrine axis, CV/HRV, Cytokine/Hormone, Functional outcomes)

Preclinical / Lab data remains compelling:

- “Metabolic Health” (Body Composition, Adipose/BAT, insulin sensitivity, weight management, central obesity, adipokine profile; data demonstrating appetite/ hunger motivation/ satiety benefits)-- other CBs may be better suited here
- “Muscle Health” (via TRPV1, TRPA1 from CBD, CBDV and THCV
- “Supporting Immune health”/ Inflammatory response to stress, exercise & microtrauma of MSK-- muscle, tendon, bone, connective tissue recovery
- Gastrointestinal/ Digestive health
Salient Points on CBD/ECS in Sports, Active & Performance Nutrition

Rational Product Development/ Formulation & Synergistic Supplementation
(More Art at times, but must be anchored in Scientific Evidence)

• Stand-alone restorative/recovery bioactives
• Multi-ingredient with anti-inflammatory, "ECS-enhanced" Protein SKUs, Adaptogens such as Rhodiola, Ashwagandha, Panax Ginseng, Maca, Eleuthero, etc.
• Neuroactives for Neuro-resilience/ Neuroprotection
• Chondro/Fibro-centric/ Joint Health ingredients for Orthopedic resilience
• Metabolic Health/ Insulin Signaling/ AMPK / Incretin/ Beiging/Browning Bioactives
• Gut Health: Endocannabinoidome crosswalks with Microbiome; can co-formulate with Para/Synbiotics
• Omega-3 HUFAs/PUFAs/Other Fatty Acid Amides (EPA, DHA, PEA, OEA, etc.)
• Longevity/ Healthy Aging bioactives
CBD Athletes Panel

Alfredo Borrego  
MMA Fighter & Coach

Rachael Rapinoe  
Co-Founder & CEO, Head Coach  
Mendi

Ryan VandenBussche  
Retired Professional Ice Hockey Player, Founder & President of New Leaf Canada
INNOVATIONS IN PROTEIN IN SPORTS AND FITNESS

Robert Wildman PhD RD CISSN
SPORTS NUTRITION MARKET FORECAST
Based on sales and new product launches

The sports market is forecast to grow by 8% annually (+17 billion USD in 2021):
Protein powder and protein RTDs are the 2 fastest growing product categories.

Average annual growth of new product launches tracked (CAGR 12-17%):
- Protein powder +36.2%
- Sports Protein Based RTD +24.7%

Source: Sports Nutrition Mainstream: Active Nutrition - the new platform in the sports arena, August 2018.
Innova Market Insights
Protein Innovations

• Better Protein Understandings
• More Functional Protein Ingredients
• Protein Fortification
• Targeted Roles for Protein & Peptides
Protein Innovations

• Better Protein Understandings
• More Functional Protein Ingredients
• Protein Fortification
• Targeted Roles for Protein & Peptides
How much protein per meal?

Meal Thresholds are Important!

Whey Protein & Muscle Protein Production

0g Protein 10g Protein 20g Protein 40g Protein

No Exercise Post Exercise

The response of muscle protein synthesis following whole-body resistance exercise is greater following 40 g than 20 g of ingested whey protein.

Muscle Protein Building

*
Total Calories 2400

<table>
<thead>
<tr>
<th>% Diet</th>
<th>Calories</th>
<th>Cal/g</th>
<th>grams/d</th>
<th>Meals</th>
<th>g/meal</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHO</td>
<td>1200</td>
<td>4</td>
<td>300</td>
<td>4</td>
<td>75</td>
</tr>
<tr>
<td>Protein</td>
<td>480</td>
<td>4</td>
<td>120</td>
<td>4</td>
<td>30</td>
</tr>
<tr>
<td>Fat</td>
<td>720</td>
<td>9</td>
<td>80</td>
<td>4</td>
<td>20</td>
</tr>
</tbody>
</table>

Protein Throughout Day

Threshold

AM

Exercise

PM
Protein needs are more than doubled for people who exercise seriously to improve muscle strength & size and fitness.

Protein helps fight hunger better than calories derived from carbohydrate and fat.

Protein increases metabolism more than the same calorie level derived from either carbohydrate or fat.

Including more protein in a calorie intake aligned against weight management goals can support desirable changes.
<table>
<thead>
<tr>
<th>Category</th>
<th>Range (g/kg BW)</th>
<th>Additional Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>RDA</td>
<td>0.8-0.85</td>
<td>- Global minimum level to reduce risk of dietary deficiency</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Not applied to weight loss, exercise and sports, illness, etc.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Adequacy accuracy and methodology require reassessment</td>
</tr>
<tr>
<td>General Health</td>
<td>1.1-1.4</td>
<td>- Increase over global requirements which might be inadequate and lead to</td>
</tr>
<tr>
<td></td>
<td></td>
<td>overemphasis of dietary carb and fat</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Supports bodily systems for health and wellness</td>
</tr>
<tr>
<td>General Exercise &amp; Fitness</td>
<td>1.4-1.8</td>
<td>- Increase in muscle protein production and balance</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Supports increases in strength and exercise endurance</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Supports leaner body composition</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Reductions in body fat loss promoted by energy deficit created by exercise not</td>
</tr>
<tr>
<td></td>
<td></td>
<td>over-restriction</td>
</tr>
<tr>
<td>Healthier Weight Loss</td>
<td>1.4-1.6 g/kg BW</td>
<td>- Protein requirements increase as energy intake decreases</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Minimizes body protein losses during weight loss</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Supports hunger management</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Supports metabolism retention</td>
</tr>
<tr>
<td>Healthy Aging</td>
<td>1.4-1.75 g/kg BW</td>
<td>- Supports minimization in body protein loss</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Covers reduced efficiency of protein nutrition</td>
</tr>
<tr>
<td>Advanced Sport Performance &amp;</td>
<td>1.8 – 2.2 g/kg</td>
<td>- Muscle mass and strength development</td>
</tr>
<tr>
<td>Muscle Building</td>
<td>BW</td>
<td>- Endurance enhancement and increased use during performance</td>
</tr>
</tbody>
</table>

*Minimum intake levels for more desirable outcome

*Body Weight (BW) are short-term target weight based on goal

*Combination of applications can further enhance protein requirements further

**Best outcomes will involve resistance exercise
PROTEIN SAFETY

Proteins not allowed
PROTEIN SAFETY

Higher protein intakes cause:
• Renal Failure
• Overtaxed liver
• Early Osteoporosis

THE NONSENSE

PROVEN UNTRUE!!!
Protein Innovations

• Better Protein Understandings

• More Functional Protein Ingredients

• Protein Fortification

• Targeted Roles for Protein & Peptides
PROTEIN TYPES

- DAIRY
- WHEY & CASEIN
- MEAT
- EGG
- FISH
- CHICKEN
- TURKEY
- SOY
- PEA
- RICE
- POTATO
- HEMP
- SACHA INCHI
- INSECT
PROTEIN QUALITY INDICES: PDCAAS VS DIAAS

Maximum score of 1.0 for PDCAAS


FAO (1) recommends that the DIAAS method replaces PDCAAS as the preferred method to evaluate protein quality.
THE AMINO ACID PROFILE OF WHEY PROTEIN IS OPTIMAL TO SUPPORT MUSCLE SYNTHESIS

Leucine is a key amino acid in the stimulation of muscle protein synthesis
IOM Complete Protein
mg/g of protein

<table>
<thead>
<tr>
<th>Food</th>
<th>Limited Amino Acid</th>
<th>Complement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beans</td>
<td>Methionine</td>
<td>Grains, nuts, seeds</td>
</tr>
<tr>
<td>Grains</td>
<td>Lysine, threonine</td>
<td>Legumes</td>
</tr>
<tr>
<td>Nuts/seeds</td>
<td>Lysine</td>
<td>Legumes</td>
</tr>
<tr>
<td>Vegetables</td>
<td>Methionine</td>
<td>Grains, nuts, seeds</td>
</tr>
<tr>
<td>Corn</td>
<td>Tryptophan, lysine</td>
<td>Legumes</td>
</tr>
</tbody>
</table>

Keywords: vegetarian; vegan; plant-based; sustainability; health; nutrition; diet; athlete; exercise; protein

1. Introduction

Plant-based diets (including generally less animal-food intensive, vegetarian, or vegan diets) represent a growing area of interest in the promotion of physical and environmental health [1,2]. Reductions in risk for developing chronic diseases are linked to plant-based diets [3-5], and production of plant foods tends to be less resource-intensive and environmentally destructive for a number of reasons, especially due to lower levels of greenhouse gas emissions (GHG) compared to raising animals for human consumption [6-8]. However, in spite of well-documented human and environmental benefits of plant-based diets, among the general population, some continue to question the adequacy of plant-based diets in supporting exercise performance. This review addresses these issues by examining literature on differences between plant-based and meat-containing diets with respect to nutrient composition, health, human performance, and environmental impact. Particular focus is placed on differences between plant and animal proteins as well as discussion of literature comparing vegetarian, vegan, and omnivorous diets on exercise performance.
CHANGERS

IN SELECT CINEMAS SEPTEMBER 16

FUELED BY THE TRUTH

JAMES CAMERON

ARNOLD SCHWARZENEGGER

JACKIE CHAN

FROM EXECUTIVE PRODUCERS
Protein Innovations

• Better Protein Understandings

• More Functional Protein Ingredients

• Strategic Protein Fortification

• Targeted Roles for Protein & Peptides
Protein Food Fortification: Does TOTAL protein have to do ALL the heavy lifting?
Can we take the most potent protein and use less, but fortify with most potent Amino Acids?
LEU Fortification

- 6.25g WHEY + 3g ALA + 3g GLY
  - ΣLEU = 0.75g

- 6.25g WHEY + 2g LEU + 4g ALA/GLY
  - ΣLEU = 3.0g

- 25g WHEY
  - ΣLEU = 3.0g

- 6.25g WHEY + 4g LEU + 1g ISO + 1g VAL
  - ΣLEU = 5.0g

- 6.25g WHEY + 2g ALA/GLY
  - ΣLEU = 5.0g
Key Points

- Leucine fortification makes less whey better
- BCAAs with same level of LEU was not better!
- Complete WHEY protein was the benchmark
Protein Innovations

• Better Protein Understandings
• More Functional Protein Ingredients
• Strategic Protein Fortification
• Targeted Roles for Pre-Processed Proteins
Protein Hydrolysates
HYDROLYZING PROTEINS CREATES PEPTIDES & POLYPEPTIDES

= hydrolyzing ENZYME

tripeptide

polypeptide

dipeptide
Protein Hydrolysates

- Expansion of Protein Foods/Supplements
  - Functional Benefits (recipes)

- Targeted Roles for Peptides
  - Specific peptides yielding more potent or strategic outcomes
Hydrolyzed protein for functional advantages: More protein foods with more protein!
GETTING TOUGH ON HARD-TO-CHEW BARS
Texture deteriorates quickly on the shelf, impeding further category growth

- Protein bars experience rapid **texture deterioration** on the shelf (i.e. increased hardness and increased chewiness).
- The rapid texture deterioration of your protein bars makes it **more difficult for retailers to sell your products** at the end of their shelf life.
- Consumers are **less likely to make a repeat purchase** of your protein bars after a negative consumption experience.
Firmness (Hardness)

Numbers in percentage indicate reduction in firmness at the final day of measurement
Cohesiveness (Chewiness)

Numbers in percentage indicate reduction in cohesiveness at the final day of measurement
Hydrolyzed protein for physiological advantages: Faster Acting
FASTER ABSORPTION OF WHEY PROTEIN HYDROLYSATE VS INTACT WHEY PROTEIN

Plasma Total BCAA concentrations

- o - o - Whey hydrolysate
- — — Soy hydrolysate
- o - o - Whey
- — — Soy
- □ - □ - Intact protein
- ■ - ■ - Hydrolysed protein

Hydrolysis shortens time to peak
Hydrolysis increases BCAA levels in blood

#P < 0.05 significant difference between nonhydrolyzed protein and protein hydrolysates; *, P < 0.05 significant difference between dietary protein source.

Morifuji 2010 a
FASTER INITIAL ABSORPTION OF WPH VS WPC (INTACT WHEY PROTEIN)

Test subjects: 15 healthy males
Design: Acute meal RCT crossover
Groups:
- CHO: Maltodextrin 0.3 g CHO/kg LBM
- WPH: LactoProtein HYDRO365 0.3 g protein/kg LBM
- WPC: Whey protein concentrate 0.3 g protein/kg LBM

Similar total AUC (0-180 min)

Higher initial AUC (0-20 min)
- BCAA, val, leu, ile

May benefit regarding muscle repair and maintenance

Kerr 2018 (manuscript under submission)
Solutions:

- Casein
- Casein Hydrolysates:
  - 93% oligopeptides (avg 3.8 AAs)
  - 7% free AAs
Hydrolyzed Protein for Performance Advantages
ENDURANCE PERFORMANCE - LACPRODAN® HYDRO.365

Department of Public Health, Aarhus University, Denmark

Test subjects: 18 elite orienteers
Design: RCT parallel
Duration: 1 week
<table>
<thead>
<tr>
<th></th>
<th>Before</th>
<th>After</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHO</td>
<td>0.3 g CHO/kg</td>
<td>1.3 g CHO/kg</td>
</tr>
<tr>
<td>CHO-PRO</td>
<td>0.3 g PRO/kg</td>
<td>0.3 g PRO/kg &amp; 1.0 g CHO/kg</td>
</tr>
</tbody>
</table>

Time (minutes):
- <10 before
- 0
- <15 after
FASTER FINAL RUN AND LESS SIGN OF MUSCLE DAMAGE
LACPRODAN® HYDRO.365

* p < 0.05: Interaction between time and treatment
* p < 0.01: Improvement in performance in PRO-CHO at Day 7 compared with baseline.

~70% less muscle damage on day 7

### Graphs

- **4 km test run**
  - Baseline vs Day 7 comparison for CHO and PRO-CHO conditions.
  - 17±6 s improvement in PRO-CHO at Day 7.

- **Muscle damage**
  - Creatine kinase (U/L) levels over time for PRO-CHO and CHO.
  - * p < 0.01: Increased values during the week.
  - #: p < 0.01: Interaction between time and treatment.
  - $: p < 0.01: Increased after the last test run.
Collagen peptide supplementation in combination with resistance training improves body composition and increases muscle strength in elderly sarcopenic men: a randomised controlled trial

Denise Zdzięk1, Steffen Oesser2, Manfred W. Baumstark3, Albert Gollhofer1 and Daniel König1,3,*

1Department of Nutrition, Institute for Sports and Sports Science, University of Potsdam, Potsdam, 12489, Germany
2CIF, Collagen Research Institute GmbH, Kiel 24148, Germany
3Department of Rehabilitation, Prevention and Sports Medicine, Centre for Internal Medicine, University Hospital Potsdam, 15706 Potsdam, Germany

(Submitted 22 February 2015 – Final revision accepted 23 June 2015 – Accepted 29 June 2015)

Abstract
Protein supplementation in combination with resistance training may increase muscle mass and muscle strength in elderly subjects. The objective of this study was to assess the influence of post-exercise protein supplementation with collagen peptide on muscle mass and muscle function following resistance training in elderly subjects with sarcopenia. A total of fifty-three male subjects (72.1 ± 6.8 years) with sarcopenia (class I or II) completed this randomised double-blind placebo-controlled study. All the participants underwent a 12-week guided resistance training programme (three sessions per week) and were supplemented with either collagen peptides (Gelita group [GROUP]) (15g/day) or silica as placebo (silica group [PICO]). Fat-free mass (FFM), fat mass (FM) and bone mass (BM) were measured before and after the intervention using dual-energy X-ray absorptiometry. Isokinetic quadriceps strength (QAS) of the right leg was determined and sensory motor control (SMC) was investigated by a standardised one-leg stabilisation task. Following the training programme, all the subjects showed significantly higher (P<0.05) levels for FFM, BMI, IGS and SMC, with significantly lower (P<0.05) levels for FM. The effect was significantly more pronounced in subjects receiving collagen peptides: FFM (GROUP: +2.1 ± 0.3 kg; PICO: −0.4 ± 0.3 kg; P<0.05), BMI (GROUP: +0.5 ± 0.1 kg; PICO: −0.0 ± 0.1 kg; P<0.05). Our data demonstrate that collagen peptide supplementation in combination with resistance training further improved body composition by increasing FFM, muscle strength and the loss in FM.

Keywords: Sarcopenia; Collagen hydrolysate; Collagen peptides: Resistance exercise: Ageing: Protein supplementation

In general, ageing is associated with a decline in motor function, muscle mass and a decrease in muscular performance. Sarcopenia is associated with an increased risk for falls and an overall prevalence for frailty.7,23 Several investigations have shown that the onset of sarcopenia can be postponed and the progress decelerated by regular physical activity, mainly resistance exercise1,70,71,72,73. Furthermore, it has been demonstrated that additional dietary proteins enhance the rate of post-exercise net muscle protein synthesis and decrease muscle protein breakdown following resistance exercise1,7,23,74,75. Consequently, the combination of prolonged resistance exercise and post-exercise protein supplementation should increase fat-free mass (FFM) and/or muscle strength in randomised controlled trials (RCT). However, although several well-controlled studies have shown an increase in strength or FFM, a comparable number of investigations have yielded negative results.66,67,68 In a recent meta-analysis, Comalli and colleagues66,67 included twenty-two RCT that have investigated the effect of resistance exercise and protein supplementation on FFM and muscle strength in both young and older subjects. Their analysis showed that protein supplementation increases FFM and strength to a significantly higher level than placebo and that this effect of dietary protein was evident in both younger and older subjects. In most of these RCT, the proteins administered were whey, milk, soy or casein, in some studies, a mixture of different essential amino acids was administered. In the present study, we investigated the effect of post-exercise protein supplementation with collagen peptides on

Table 1. Amino acid composition of the collagen peptides

<table>
<thead>
<tr>
<th>Amino acid</th>
<th>Weight (%)</th>
<th>Mol (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydroxyproline</td>
<td>11.3</td>
<td>9.6</td>
</tr>
<tr>
<td>Arginine</td>
<td>5.8</td>
<td>4.8</td>
</tr>
<tr>
<td>Serine</td>
<td>4.2</td>
<td>3.5</td>
</tr>
<tr>
<td>Glutamic acid</td>
<td>10.1</td>
<td>7.5</td>
</tr>
<tr>
<td>Glycine</td>
<td>22.1</td>
<td>32.3</td>
</tr>
<tr>
<td>Histidine</td>
<td>1.2</td>
<td>0.8</td>
</tr>
<tr>
<td>Arginine</td>
<td>7.8</td>
<td>5.0</td>
</tr>
<tr>
<td>Threonine</td>
<td>1.8</td>
<td>1.7</td>
</tr>
<tr>
<td>Alanine</td>
<td>8.5</td>
<td>10.5</td>
</tr>
<tr>
<td>Proline</td>
<td>12.3</td>
<td>11.8</td>
</tr>
<tr>
<td>Tyrosine</td>
<td>0.9</td>
<td>0.9</td>
</tr>
<tr>
<td>Methionine</td>
<td>3.8</td>
<td>2.9</td>
</tr>
<tr>
<td>Lysine</td>
<td>3.8</td>
<td>2.9</td>
</tr>
<tr>
<td>Isoleucine</td>
<td>1.3</td>
<td>1.1</td>
</tr>
<tr>
<td>Leucine</td>
<td>2.3</td>
<td>2.3</td>
</tr>
<tr>
<td>Phenylalanine</td>
<td>2.1</td>
<td>1.4</td>
</tr>
</tbody>
</table>

*Corresponding author: Dr D. König, email: Daniel.Koenig@uni-potsdam.de

Abbreviations: FFM, fat-free mass; FM, fat mass; G, group; RT, randomised controlled trial; PICO, placebo group.

53 males (≈72 yoa)
- Sarcopenia (Class I or II)
- 12 week resistance training (3x/wk)
- Placebo (silica) or 15g collagen peptides postWO
  - Gelita BODYBALANCE™
- Body Composition& Strength
Outcomes
Nutritional Intake

% Calories

Protein: 0.91g/kg
Fat
Carbohydrate
Oral supplementation with specific bioactive collagen peptides improves nail growth and reduces symptoms of brittle nails

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3Collagen Research Institute (CRI), KIGA, Germany

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Summary

Background: Brittle nail syndrome is a common problem among women and refers to nails that exhibit surface roughness, raggedness, and peeling.

Aim: The goal of this study was to investigate whether daily oral supplementation with collagen peptides alleviates the symptoms of brittle nails and improves nail growth rate.

Methods: In this open-label, single-center trial, 25 participants took 2.5 g of specific bioactive collagen peptides (BCP, VERISOL®) once daily for 24 weeks followed by a 4-week off therapy period. Nail growth rate and the frequency of cracked and/or chipped nails as well as an evaluation of symptoms and global clinical improvement score of brittle nails were assessed by a physician during treatment and 4 weeks after discontinuation.

Results: Bioactive collagen peptides treatment promoted an increase of 12% nail growth rate and a decrease of 42% in the frequency of broken nails. Additionally, 64% of participants achieved a global clinical improvement in brittle nails, and 88% of participants experienced an improvement 4 weeks post-treatment. The majority of participants (80%) agreed that the use of BCP improved their nails' appearance, and were completely satisfied with the performance of the treatment.

Conclusions: This study demonstrated that the daily ingestion of BCP increased nail growth and improved brittle nails in conjunction with a notable decrease in the frequency of broken nails.

Keywords: bioactive collagen peptides, brittle nails, collagen hydrolysate, dietary supplements, fragile nails, nail growth

1 INTRODUCTION

Brittle nail syndrome is a disorder characterized by the increased fragility of the nail plate, exhibiting surface roughness, raggedness (fraying of the distal edge), and peeling. It affects about 30% of the population, and women are affected twice as often as men. Patients usually complain that their nails are soft, dry, weak, easily breakable, and incapable of growing long. The pathogenesis of brittle nails is usually related to an impaired water-binding capacity. This may reflect an abnormality in keratin, keratin-associated proteins, and/or lipid content. The treatment of brittle fingernails has been a big challenge for dermatologists.
Figure 1: Clinical improvement of brittle nail symptoms after 24 wk of oral supplementation with bioactive collagen peptides (BMP). A. Lamellar peeling. B. Flaking of the distal nail plate (edge irregularities). C. Longitudinal ridging/grooves (nail roughness).

Figure 2: Exemplary pictures of participants before (t0) and after 12 wk (t12) of oral supplementation with bioactive collagen peptides (BMP). A. The distal portion of the nail plate showed a lamellar configuration into fine horizontal layers, and triangular pieces could readily be torn from the free nail at baseline. B. No faults. C. The lamellar splitting improved noticeably, with isolated splits at the free edges, which sometimes extended proximally, visible at baseline and absent after 12 wk.

Figure 3: Frequency of cracked and/or chipped nails after daily treatment with bioactive collagen peptides for 24 wk, followed by 4-wk washout period. (mean ± SEM; n = 24; *p < .05).

SupplySide West
Thank You
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@thenutritiondoc
Internationalproteinboard.org
The potential for fermented ingredients in gut health and performance nutrition
5 Learning Objectives

- Fermentation technology as a tool for new product development
- Fermented foods and fermented ingredients
- Understanding the gut microbiome
- Performance nutrition and the gut microbiome
- Fermented products and their potential in gut health and performance
Fermentation – Back in Vogue Again

EVERYTHING OLD IS NEW AGAIN
Microbes as a tool for novel product development

- ‘Most of us think of microbes as germs to be feared and killed. In fact they hold the key to improving our health – and may be the key to tackling obesity’

- Microbes are powerful cellular factories which can transform key properties of ingredients and foodstuffs.

‘Microbial Terroir’

• Terroir concept has long been discussed in context of wine production... this is now a more widely used terminology....

• High quality taste compounds developed during fermentation

• Increased innovation e.g. Noma’s Fermentation Lab.

• Combining old and new knowledge, together with cultural exchanges and technology to discover new flavours and functionalities


Fermentation technology as a tool for new product development
Fermentation Science

- Louis Pasteur working with and applying yeast in fermentation in 1857.
- In ancient times fermentation of food was meant for food preservation and flavour improvement.
- It is one of the oldest and most economical methods of production and preservation of foods and various types of fermentations have been used by different civilizations since prehistoric times.

Fermented Foods and Fermented Ingredients

- Traditional food fermentation processes can be broadly classified into lactic acid fermentation, fungal fermentation, and alkaline fermentation.

- Examples of lactic acid fermented products: yoghurt, sausages, cheese, sauerkraut and kimchi.

- Most of the well-known soy-based fermented foods from Asia such as tempeh and soy sauce are produced by fungal fermentation, except natto, which is produced by alkaline fermentation.

Fermentation technology as a tool for new product development

• Besides preservation, fermentation imparts characteristic aroma, flavour, texture, and nutritional profile into food.

• Thus, although ancient civilizations developed fermentation primarily as a way of preserving perishable agricultural produce, the technology has evolved beyond preservation into a tool for creating desirable organoleptic profiles in foods and improving their palatability.

Fermentation as a production process is back in vogue.

The process is increasingly recognised for the delivery of health and taste benefits:

• Digestive health properties
• Unique tangy/acidic flavour profiles
• Younger consumers are starting to associate fermented foods with digestive health
Fermented foods and fermented ingredients
Fermented Foods: Consumer interest is on the rise...

- Searches for words like kefir and prebiotics are increasing globally
- Fermented foods are described as healthy, specially for digestive health
- Dairy is one of the most popularly discussed fermented foods
Fermented Launches continue to grow across the globe

Revived interest in gut health sparks innovation in dairy drinks
Digestive health is a key focus for dairy drink producers, especially those who offer fermented drinks.

Importance of Gut Health

68% of UK consumers agree that actively looking after gut health is essential for overall health.

Hefei Yili Dairy, China
Mango & Passion Fruit Flavour Greek Style Flavoured Yogurt is made with heat treated fermented milk.

Yangsen Dairy China
This product is made using quality milk sourced from the manufacturer’s farm and then fermented using imported strains and active lactobacillus.

Danone Mexico
Lemon Pie Flavored Drinking Yogurt fermented dairy product

Silva & Alves, Brazil
Dulce de Leche Flavored Skimmed Milk Drinking Yogurt with Whey Protein. contains 22g of protein with lactic ferments.
Fermented Launches in the Nutrition Space

**Nutramis – Italy**
The product is described as a food supplement of branched chain amino acids coming from vegetal fermentation indicated for adult athletes.

**Iron Vegan – Canada**
The glutamine has been derived entirely from non-GMO vegan sources (beets and/or corn), that have been fermented using bacterial cultures.

**Moldes – Italy**
Contains AMINO FE probiotic lactic ferments

**Biosteel – Canada**
Biosteel Sports Nutrition
Sport Greens Pomegranate Berry High Performance Superfood is a vegan-friendly sports drink mix which is claimed to be a high source of antioxidants, fermented amino acids and probiotics.
Fermented Launches in the Nutrition Space

STC Nutrition – France
This vegan product is made with a 100% vegetable triple complex protein from soya, pea and rice, and contains 17 g of protein per portion which contributes to building muscle. It is enriched with Aminolise®, an exclusive complex of natural substances including fibre, lactic ferments, digestive enzymes, and proteolytic enzymes.

Dr. Niedermaier – Germany
The unique Regulat ferment, which features lyophilised plant enzymes from fresh, sun-ripened fruit and vegetables, obtained by patented Cascade Fermentation.

New Chapter – USA
Proprietary ferment media (Molasses, Saccharomyces Cerevisiae, Maltodextrin, Gum Arabic, Soybean Flour, Lactic Acid Bacteria (Lactobacillus Acidophilus, Bifidobacterium Bifidum Lactobacillus Rhamnosus),

Awareness on the gut microbiome in China
67% of 20-49s have consumed beverages positioned at digestive health in the last six months.
Understanding the gut microbiome
The microbiome concept

• The human microbiome is the aggregate of all microbiota that reside on or within human tissues and biofluids along with the corresponding anatomical sites in which they reside.

• The gut microbiome, as defined by molecular biologist Joshua Lederberg, is the totality of microorganisms, bacteria, viruses, protozoa, and fungi, and their collective genetic material present in the gastrointestinal tract (GIT).

Source: Gail A.M. Cresci PhD, RDN, CNSC, Kristin Izzo MS, RDN, CNSC, in Adult Short Bowel Syndrome, 2019
Impacting factors on gut microbiome
The importance of the gut microbiome for our health

Microbes live on and within us, mostly in a mutually beneficial relationship. It has been estimated that 90-95% of these microbes are found in our gut, especially the colon. Although scientists do not yet know what constitutes the ideal gut microbiota, there is an agreement that these microbes and their activities are important for our health.
A healthy gut microbiome is key to healthy ageing

• In September 2017, The American Society for Microbiology published a study that highlighted a potential link between the gut microbiome and overall health and wellness.

• The key finding of this study, carried out in China and published in the journal mSphere, suggests that if a person lives to be 100 years old and in perfect health, their microbiome is likely to be relatively similar to a person in their mid-30s.

Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5615133/
https://www.sciencedaily.com/releases/2017/10/171011123728.htm
Communicating on the gut microbiome

• The gut microbiome is a hot topic in the media and in science. Using gut microbiome terminology in the digestive health space is very likely to interest consumers.

• Beyond 'immediate' digestive disorders such as irritable bowel syndrome or heartburn, scientific research continues to highlight links between the gut microbiome and many strands of health, from mental health to skin health, and even obesity.
Performance Nutrition and the gut microbiome
The importance of the Microbiome for Performance Nutrition

• Modifying the microbiota could be an important therapeutic tool to improve athletes' overall general health, performance, and energy availability while controlling inflammation and redox levels

• Changes to gut microbiome can positively alter body composition through a number of mechanisms

References:
• ‘Microbes in sport’ – The potential role of the gut microbiota in athlete health and performance’, 2017, Rankin et al. British Journal of Sports Medicine, DOI: 10.1136/bjsports-2016-097227
• ‘Endurance exercise and gut microbiota: A review’, 2016, Mach and Fuster. Journal of Sport and Health Science, DOI: 10.1016/j.js.hs.2016.05.001
Performance nutrition and the gut microbiome – key associated risks

• An undesirable gut microbiome (GM) composition has been associated with local inflammatory change leading to gut wall permeability.

• This in turn, may lead to systemic immune and metabolic dysfunctions. These processes are implicated in many chronic diseases.

• Allergic conditions are common in athletes whose airways are often exposed to environmental factors such as cold air or chlorine during aquatic sports.

• Gastrointestinal complaints are common in the spectrum of conditions associated with ‘relative energy deficiency in sport’ and the ‘female athlete triad’. In this low energy state, multiple body systems may experience compromise, including metabolic and hormonal functions.

References:
  • ‘Microbes in sport’ – The potential role of the gut microbiota in athlete health and performance’, 2017, Rankin et al. British Journal of Sports Medicine, DOI: 10.1136/bjsports-2016-097227
Performance Nutrition – impact on musculoskeletal conditions

• Multiple studies suggest a relationship between GM and inflammatory conditions such as rheumatoid arthritis, spondyloarthropathies and gout.

• Ensuring optimal bone health in athletes is important to reduce injury risk and to aid recovery. GM has a proposed regulatory effect on bone mass by altering the skeletal immune system, influencing hormonal regulation of bone metabolism and by production of bacterial metabolites that act as cellular messengers to the bone.

References:

• ‘Microbes in sport’ – The potential role of the gut microbiota in athlete health and performance’, 2017, Rankin et al. British Journal of Sports Medicine, DOI: 10.1136/bjsports-2016-097227

Performance Nutrition – general benefits to athlete health and performance

- Optimisation of GM for athlete health and injury treatment will produce indirect benefits to athletic performance.
- Changes to GM can positively alter body composition
- While research on the potential of GM in sports medicine is in its infancy, there is definite potential to positively impact athlete health, injury and ultimately performance

References:
Endurance and the Gut Microbiome

- Endurance athletes present a high prevalence of upper respiratory tract infections and gastrointestinal troubles e.g. ‘leaky gut’

- A recent observational study comparing the faecal bacterial profile of male elite rugby players with non-athlete healthy subjects showed that athletes had lower levels of *Bacteroidetes* and greater amounts of *firmicutes* than the control group.

- There is now a reasonable body of evidence that shows consuming fermentates regularly may positively modify the gut microbiota’s population and structure and may influence immune function

References:
- ‘Endurance exercise and gut microbiota: A review’, 2016, Mach and Fuster. Journal of Sport and Health Science, DOI: 10.1016/j.jshs.2016.05.001
Fermented products and their potential in gut health and performance
Potential for fermentates and fermented foods in gut health and performance

**Nutrient Metabolism**
- Breakdown of nutrients and key metabolites that feed critical metabolic pathways
- Supply of nutrient precursors and precursors to key metabolic targets

**Gut mobility /Gut Barrier**
- Modulation of gut microbiota to increase uptake
- Influence mucous thickness

**Inhibition & Immunity**
- Inhibit pathogenic growth
- Maintain balance across microbiome and promote key microbes like Bifidobacteria and others

**Synthesis**
- Synthesis of key vitamins and hormones
- Probiotic and prebiotic food types or food ingredients can stimulate key metabolic cascades

**References:**
Fermentates: The Future & Next Steps

• Research into prebiotic/probiotic and postbiotic products will continue to unearth the potential benefits for these products.

• Fermentation will continue to be a focal point for established foods as well as new cuisine development utilising the ‘microbial terroir’

• Increased consumer knowledge

• Targeted research into benefits for gut health and overall influence on human microbiome

• New launches in performance nutrition and general consumer products

• Move towards personalised nutrition/tailored solutions

• The industry needs to embrace the old world knowledge developed on fermented products and use new technology to build on these solid foundations...
To find out more on Fermented Dairy Ingredients Visit Carbery & Synergy at Stand #3021

Introducing Bifipro™ - Two mega trends in one ingredient

We’ve combined the nutritional goodness of Irish dairy from grass-fed cows with the ancient art of fermentation to create a range of nutritional ingredients that support digestive health.
Thank you, Questions?
References

- Gail A.M. Cresci PhD, RDN, CNSC, Kristin Izzo MS, RDN, CNSC, in Adult Short Bowel Syndrome, 2019
- ‘Endurance exercise and gut microbiota: A review’, 2016, Mach and Fuster. Journal of Sport and Health Science, DOI: 10.1016/j.jshs.2016.05.001
INFLAMMATORY STRESS IN SPORT, AND AFTER

Dr. Paul Clayton, IFFB

: THE SCIENCE BEHIND NATURE
SPORT / INFLAMMATION: THE GOOD

• Stress on muscle, ligaments and joints causes micro-damage = inflammation
  • autophagy: GLUT4 shift, mitochondrial neogenesis, tissue re-modelling & ESM regeneration
• Acute PE inflammation (2-48 hours) = ‘right’ amount of autophagy/remodeling, lessens with training, increases fitness
• Regular good training anti-inflammatory and adaptative
SPORT / INFLAMMATION: THE BAD

• Excessive PEI $\rightarrow$ slows recovery, limits fitness gains, degrades ECM and contributes to overuse injury
• Delayed-onset muscle soreness reduces performance, i.e. running economy up to 3%
• Excessive inflammation is maladaptive
DO ANDROIDS DREAM OF ELECTRIC SHEEP? (IT’S TELEOLOGICAL)

• Animals in the wild do not experience inflammatory muscle damage except in extremis
• Early man (before food security) did not experience chronic inflammatory stress
• Early man could not have been incapacitated by inflammatory stress: DOMS would have been lethal
INFLAMMO-MODULATION

• How to stay in the Goldilocks Zone?

• Modulated by ‘milieu interieur’ (diet)

• Anti: Omega 3, polyphenols, prebiotics, other

• Pro: Omega 6, AGE’s, ALE’s, LPS, other

• Modern diet highly pro-inflammatory
Supplemental EPA and/or DHA

Inflammatory Challenge

AA

Pro-inflammatory eicosanoids (PGE2, TXA2, LTA4)

↑ Pro-inflammatory cytokines; ↑ CRP

EPA + DHA

Anti-inflammatory eicosanoids (PGE3, TXA3, LTA5)

Pro-resolving lipid mediators (Resolvins, Protectins)

Resolution of Inflammation
Lipid mediators cause oedema ...

... shed exosomes
THE INFLAMMAZONE

Lipid mediators cause oedema ...

... shed exosomes

• ....which release MMP’s
• ... causing tissue destruction
THE INFLAMMAZONE

Lipid mediators cause oedema ...

... shed exosomes

• ...which release MMP’s
• ... causing tissue destruction
THE INFLAMMAZONE

Lipid mediators cause oedema ...

... shed exosomes

• which release MMP’s
• causing tissue destruction

\[ \frac{6}{3} \]

P-p
THE INFLAMMAZONE

Lipid mediators cause oedema ...

... shed exosomes

• ....which release MMP’s
• ... causing tissue destruction
Pathological Omega 6:3 ratio
Pathological lack of polyphenols
Pathological lack of prebiotics
Pathological lack of 1-3, 1-6 b-glucans
Pathological excess of AGE’s & ALE’s
Pathological glycemic index
Pathological Omega 6:3 ratio
Pathological lack of polyphenols
Pathological lack of prebiotics
Pathological lack of 1-3, 1-6 b-glucans
Pathological excess of AGE’s & ALE’s
Pathological glycemic index
CURCUMINOIDS PROMISE SO MUCH...

• Curcuminoids - require bioactivation (1)
• Metabolites down-regulate COX-2, LOX (various), MMP’s (various)
• Inhibit inflammatory cytokines TNF-a, IL’s 1, 2, 6, 8 12, MCP, other
• Down-regulate NF-κB signaling pathway
• Up-regulate AMP-K – so maybe → IL-6
...YET DELIVER SO LITTLE

• ‘.. should provide therapeutic benefits in inflammation *if the limitations in its oral bioavailability can be overcome.*’
  • (Ghosh et al ‘15)

• ‘.. anti-inflammatory effects, *but issues such as limited bioavailability currently limit its therapeutic outreach.*’
  • (Darvesh et al ‘12)
A PK STUDY ON A BRANDED CURCUMIN WITH DISPERSION TECHNOLOGY

- Single dose 800 mg “Branded Curcumin” containing 90% turmeric extract (95% curcuminoids) produces peak plasma levels 800 ng/ml / 2 uM.

- Pharmacological activity: 100nM - 5 uM.
A PK STUDY ON A BRANDED CURCUMIN WITH DISPERSION TECHNOLOGY

- 18 healthy male and female volunteers
- Single dose
- Randomised
- Double blind study
- Crossover - Seven volunteers

- Plasma concentrations determined at baseline and regular intervals over a 24-hour period following curcuminoid ingestion
Total Curcuminoids (parallel)

CWD90 with LipiSperse
Standard Curcumin

Time (hours)
DISPERSION TECHNOLOGY

Plasma levels per mg of curcuminoids ingested (based on published Cmax) (ng/ml)

Brand A                                   Brand B                          Brand C              Brand with Technology
BRANDED CURCUMIN WITH DISPERSION TECHNOLOGY DELIVERS 376MG CURCUMINOIDS/ CAPSULE
EXERCISE RECOVERY TRIAL

• 28 healthy exercising males; average 26.4 years
• 500mg Branded Curcumin with Dispersion Technology in 250ml drink
• Given pre/post induced local muscle fatigue (leg press), then daily for 3 days.

• Outcomes included
  • Blood markers – muscle damage, energy source, molecular pathway and inflammatory markers.
  • Recovery – Exhaustive exercise performance test, power & velocity
  • Delayed onset muscle soreness

• RDC Global / U. Queensland
SIGNIFICANT DECREASE IN LACTATE ACCUMULATION POST-EXERCISE, 30 MINUTES AFTER SINGLE DOSE ACTIVE VS PLACEBO
IL-10 SIGNIFICANTLY HIGHER 24 HOURS POST EXERCISE
IL-6 SIGNIFICANTLY ELEVATED AT 1, 24- AND 72-HOURS FOLLOWING EXERCISE
VAS SCORE FOR PAIN (DOMS): SIGNIFICANT REDUCTION AT 48 AND 72 HOURS
THIGH CIRCUMFERENCE: SIGNIFICANT REDUCTION AT 48 AND 72 HOURS
EXERCISE STUDY CONCLUSIONS

• Branded Curcumin with Dispersion Technology may allow a quicker return to exercise training or return to training at higher thresholds.

• May be due to this curcumin’s anti-inflammatory properties which reduce oedema and pain, and modulate energy metabolism.

• Branded Curcumin with Dispersion Technology combined with exercise stimulates PKB/mTOR pathway responsible for muscular hypertrophy / cellular survival.
PALMITOLETHANOLAMIDE (PEA)

• Endogenous fatty acid amide - autocoid
• Exercise-induced hypoalgesia
• PPAR-alpha, COX-2, down-regulation of Mast cells, GPR55, other

• Clinical anti-inflammatory effects – many clinical studies (neuropathic, arthritic, other)
• Sleep enhancement (CB1, TRPV1)
• May act at PPAR-d (anabolic)
## CBD vs PEA: Chemistry, Functionality Overlap

### Identical Anti-Inflammatory, Analgesic Benefits

<table>
<thead>
<tr>
<th>PEA</th>
<th>CBD</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Dietary supplement in EU, Canada, US</td>
<td>• Novel Food in EU / US FDA: not a supplement</td>
</tr>
<tr>
<td>• Well-documented alternative to CBD</td>
<td>• Negative perception by EFSA and MHRA</td>
</tr>
<tr>
<td>• No adverse effects</td>
<td>• Multiple side effects (anxiety, changes in appetite/mood etc.)</td>
</tr>
<tr>
<td>• Augments activity of AEA</td>
<td>• Anti-inflammatory and analgesic activity, demonstrating neuroprotective, anxiolytic and anticonvulsant properties</td>
</tr>
<tr>
<td>• Direct effect on CB1, CB2, GPR55, PPAR-a and TRPV1 receptors</td>
<td>• Acts at PPARy (with some activity at PPAR-a)</td>
</tr>
<tr>
<td>• Low affinity to CB2 receptors</td>
<td>• Low affinity to CB1 and CB2 receptors</td>
</tr>
<tr>
<td>• Antagonist of GPR55 (mediates non-psychotropic effects of cannabinoids)</td>
<td>• Negative allosteric modulator at CB1 receptor</td>
</tr>
<tr>
<td>• Reduces production of TNF-a and IL</td>
<td>• Inverse agonist of CB2</td>
</tr>
<tr>
<td>• Modulate mast cell degranulation (pain/allergy management)</td>
<td>• Antagonist of GPR55 &amp; TRPV1</td>
</tr>
<tr>
<td>• Microglial inhibition (analgesic action)</td>
<td></td>
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<tr>
<td>• Down-regulates COX-2 and iNOS</td>
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<tr>
<td>• Acts at GPR119 (hypoglycemic effects via upregulation of glucagon and insulin sensitivity)</td>
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</table>
## Exercise Recovery Study

### Design:
Double-blind, randomised, placebo-controlled study to evaluate effect of Branded PEA with Dispersion Technology on exercise recovery in recreationally trained healthy males.

### Participants:
- 28 healthy male volunteers (18-35 years)

### Treatment Regimen:
- Levagen+™ 150mg vs. Placebo
- Dosing: Pre- and Post-workout + daily after for 3 days
- Induce muscle fatigue (1RM and 70% of 1RM until failure using bench and leg press)

### Outcome Measures:
1. Muscle damage blood markers - Creatine Kinase, myoglobin, lactate dehydrogenase
2. Muscle Pain – DOMS; VAS pain score
3. Exercise recovery – Number of LP completed post supplementation; Maximum LP repetition as measured by a power meter.
4. Lactate, CRP, IL-6, IL-10, TFN-α, P38
5. MSFI Multidimensional Symptoms Fatigue Inventory; KOOS specific to leg pain and McGill; pain questionnaire; Muscle swelling (measurement of thigh circumference)
**EXERCISE STUDY RESULTS**

* Significant difference \( p < 0.05 \)

**Branded PEA with Dispersion Technology** group had lower blood concentration of myoglobin than placebo

*Reduced muscle damage*

**Significantly lower lactate levels post-exercise**

* Sparing of anaerobic energy substrates and increased lactate threshold
**EXERCISE RECOVERY: CONCLUSIONS**

- **Branded PEA with Dispersion Technology** may permit higher exercise intensities for longer time after an initial training session, allowing improved training / performance.

- Athletes who exercise/compete with quick succession may have improved performance when consuming **Branded PEA with Dispersion Technology**.

- Lower blood lactate concentration correlates with increased aerobic energy metabolism and decreased anaerobic energy metabolism.

- Sparing of anaerobic energy substrates by consuming **Branded PEA with Dispersion Technology** may allow participants to exercise at higher intensities for longer.

- PEA & exercise stimulates the PKB/mTOR pathway responsible for muscle synthesis and cellular survival.
TOP TIER RUGBY CLUB: PRELIMINARY REPORT (28 PLAYERS)

- 216 INJURIES RECORDED/TREATED DURING THE SEASON
  - 9 bone, 35 joint, 30 ligament, 88 muscle, 54 composite

- LIGAMENT / TENDON / JOINT: 1 CAP BRANDED CURCUMIN WITH DISPERSION TECHNOLOGY/DAY
  - If desired, 4 Branded PEA a.m. and 2 pm (before bed)

- RESPONSES OVERWHELMINGLY POSITIVE:
  - ‘Has become a critical part of my regime’
  - ‘Improved my sleep quality and patterns’
  - ‘I recovered so much faster from injury’
  - ‘Went from constant pain 4/10 to constant pain 1/10.’
THANK YOU

: THE SCIENCE BEHIND NATURE

DR. PAUL CLAYTON, IFFB