MB Clinical Research

SPRING 2017 NEWSLETTER

Improving health through research on chronic disease prevention and treatment

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Scientific Contributions

High-Amylose Maize Resistant Starch Health Claim Approved for Type 2 Diabetes

The U.S. Food and Drug Administration (FDA) recently approved a qualified health claim which will enable food companies to include messaging on the packaging of products which contain high-amylose maize resistant starch (HAM-RS). Type 2 diabetes (T2D) is characterized by insulin resistance which, over time, leads to exhaustion of the insulin-producing cells of the pancreas. Substantiation of the qualified health claim was supported by eight clinical trials, one of which was completed by members of the MB Clinical Research team. In this study, overweight and obese participants (11 men and 22 women) were randomly assigned to received either 0 (control), 15, or 30 g/d HAM-RS for four-week periods, separated by a three-week washout. In men, insulin sensitivity increased with daily intake of 15 and 30 g/d HAM-RS, relative to the control (48% and 56%, respectively, $p < 0.05$ for both vs. control). However, there were no significant differences in insulin sensitivity for women, relative to control. The FDA concluded that the totality of the evidence supports the following claims:

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MBCR Announcements

"High-amylose maize resistant starch may reduce the risk of Type 2 diabetes. FDA has concluded that there is limited scientific evidence for this claim."

"High-amylose maize resistant starch, a type of fiber, may reduce the risk of Type 2 diabetes. FDA has concluded that there is limited scientific evidence for this claim."

Comment: We are hopeful that the approval of this qualified health claim will stimulate more research evaluating the effects of fermentable dietary fibers on carbohydrate metabolism. There is consistent evidence from observational studies that indicate higher consumption of certain fibers, especially cereal fibers, is associated with lower risks for metabolic syndrome and T2D. Research is needed to more clearly define the characteristics of dietary fibers that are associated with these benefits and to elucidate the underlying mechanisms. Based on our work and that of others, we hypothesize the liberation of short-chain fatty acids during fermentation of HAM-RS is a mechanism for enhanced insulin sensitivity. Other mechanisms may be important as well, particularly alterations in the microbiome.

References:
U.S. Food and Drug Administration. RE: Petition for a Health Claim for High-Amylose Maize Starch (Containing Type-2 Resistant Starch) and Reduced Risk Type 2 Diabetes Mellitus (Docket Number FDA-2015-Q-2352-0023), December 12, 2016.

M**aki KC**, Pelkman CL, Finocchiaro ET, Kelley KM, Lawless AL, Schild AL, Rains TM. Resistant starch from high-amylose maize increases insulin sensitivity in overweight and obese men. J Nutr 2012;142:717-23.

An Omega-3 Fatty Acid Formulation With DPA Improves Lipoprotein-Related Variables

Approximately one-third of American adults have elevated triglyceride (TG) levels (≥150 mg/dL), which is associated with increased risk for cardiovascular disease (CVD). Prescription forms of long-chain omega-3 fatty acids containing eicosapentaenoic (EPA) or EPA and docosahexaenoic acid (DHA) have been shown to lower TG levels, and are approved for use in the U.S. for management of very high TG (≥500

Join us in welcoming the new additions to our team (in alphabetical order):

Veda Navsariwala, PhD; Nutrition Scientist

Lorrrie Neal, RN; Clinical Operations Manager

Ines Ramirez; Research Assistant

Katharine Shachar, LPN; Clinical Research Coordinator

Upcoming Presentations

mg/dL). A group of investigators, including members of the MB Clinical Research team, collaborated on a trial that evaluated the effects of MAT9001, an omega-3 fatty acid formulation containing EPA and docosapentaenoic acid (DPA). DPA is a fatty acid in the pathway for conversion of EPA to DHA, which appears to have substantial biologic activity.

Participants (31 men and 11 women with TG 200-499 mg/dL) were randomly assigned to receive either MAT9001 or EPA ethyl esters at 4 g/d during two 14-day treatment periods, separated by at least 35 days. Subjects were housed in a clinical research unit for the duration of each treatment period and consumed a low-fat diet. MAT9001 treatment resulted in significantly ($P < 0.05$) larger reductions in TG (-33% vs. -11%), total cholesterol (-9% vs. -6%), non-high-density lipoprotein cholesterol (-8.8% vs. -4.6%), very low-density lipoprotein cholesterol (-33% vs. -8%), apolipoprotein A1 (-15% vs. -10%), apolipoprotein C3 (-26% vs. -5%), and proprotein convertase subtilisin kexin type 9 (-12% vs. 9%), as compared to the EPA ethyl esters treatment. No significant differences were evident between MAT9001 and EPA ethyl esters treatments for high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and apolipoprotein B.

Comment: Different long-chain omega-3 fatty acids have varying biologic activities. DPA is found in small quantities in fish, but the results from our study suggest that it may be particularly powerful for lowering TG, in addition to other effects. Two large-scale clinical event trials are underway which are investigating the effects of omega-3 fatty acid concentrate drug therapies in men and women with elevated TG, who are at high risk for a CVD event. One trial is using EPA ethyl esters (REDUCE-IT, NCT01492361), and the other is using a carboxylic acid (free fatty acid) formulation that contains both EPA and DHA, as well as a very small amount of DPA (STRENGTH, NCT02104817). The REDUCE-IT trial is projected to be completed late in 2017, with results likely in 2018. The STRENGTH trial is projected to be completed in 2019. These trials should provide very useful evidence for judging the risks and benefits of prescription omega-3 fatty acid therapy in people with elevated TG who are at increased CVD risk.

Reference: **Maki KC**, Bobotas G, **Dicklin MR**, **Huebner M**, Keane WF. Effects of MAT9001 containing

NATIONAL LIPID ASSOCIATION SCIENTIFIC SESSIONS 2017 May 18–21 PHILADELPHIA

National Lipid Association Scientific Sessions, Philadelphia, PA, May 18-21, 2017.

Kevin Maki, PhD will present, "Key Clinical Lipidology Publications: 2016-17" on May 21st.

In addition, Kevin Maki, PhD will present "Evidence-Based Medicine, Cardiovascular Risk Assessment and Practice Guidelines" as part of the NLA Masters in Lipidology course.

IFT17 GO WITH PURPOSE

Institute of Food Technologists Annual Meeting & Food Expo, Las Vegas, NV, June 25-28, 2017.

Kevin Maki, PhD will moderate the session, "A Global Overview of Sugar Regulations: Implications for Consumers and Industry".

Special Features

Medscape

Statin Roundtable Series

eicosapentaenoic acid and docosahexaenoic acid, compared to eicosapentaenoic acid ethyl esters, on triglycerides, lipoprotein cholesterol, and related variables. J Clin Lipidol 2017; In Press.

Experimental Biology 2017

EB CHICAGO 2017
Experimental Biology
TRANSFORMING THE FUTURE THROUGH SCIENCE
APRIL 22-26

If you will be traveling to Chicago, please plan to attend our presentations:

April 25, 1:45 PM (poster) – Cranberry Beverage Consumption Reduces Antibiotic Use for Clinical Urinary Tract Infection in Women with a Recent History of Urinary Tract Infection (Abstract Number: 4157; Poster Board: C202)

April 25, 1:45 PM (poster) – Replacement of Refined Carbohydrates with a Combination of Egg Protein and Unsaturated Fatty Acids Improves Insulin Sensitivity in Adults with Elevated Triglycerides (Abstract Number: 4012; Poster Board: C253)

April 25, 1:45 PM (poster) – Replacement of Refined Carbohydrates with a Combination of Egg Protein and Unsaturated Fatty Acids Improves the Lipoprotein Lipid Profile in Adults with Elevated Triglycerides (Abstract Number: 4089; Poster Board: C254)

April 25, 1:45 PM (poster) – Replacement of Refined Carbohydrates with a Combination of Egg Protein and Unsaturated Fatty Acids: Effects on Lipoprotein Particle Concentrations and LDL Peak Size in Adults with Elevated Triglycerides (Abstract Number: 4113; Poster Board: C255)

April 26, 9:00 AM (poster) – Validation of a Macronutrient Mixed Challenge Beverage for Personalized Nutrition Applications Using a Reduced Sampling Period (Abstract Number: 9062; Poster Board: LB289)

April 26, 9:00 AM (poster) – Evaluation of a Reduced Sampling Schedule for Assessment of Pancreatic Beta-Cell Function with the Intravenous Glucose Tolerance Test During a Dietary Intervention (Abstract Number: 8691; Poster Board: LB284)

Kevin Maki, PhD recently presented: "Clinical Advances: Statin Selection in Patients at Risk – Installment 1 of a 16 part Medscape Roundtable Series," with Alan Brown, MD and moderated by Peter Toth, MD, PhD.

clinicallipid update FEBRUARY 24–26 2017 PHOENIX

National Lipid Association (NLA) Spring Clinical Update, Phoenix, AZ, February 24-26, 2017.

Kevin Maki, PhD recently presented "Challenges in Prescribing PCSK9 Inhibitors: Dinner Satellite Symposium" with Jerome Cohen, MD and Terry Jacobson, MD.

In addition, Kevin Maki, PhD presented, "Evidence-Based Medicine, Cardiovascular Risk Assessment and Practice Guidelines," as part of the NLA Masters in Lipidology course.

PTCE Pharmacy Times Continuing Education™

Omega-3 Fatty Acid Webinar Series

Kevin Maki, PhD presented a webinar series in collaboration with Pharmacy Times Continuing Education

April 26, 9:00 AM (poster) – A Randomized, Controlled, Crossover Trial to Assess the Acute Cognitive, Appetite, Glucose and Insulin Responses to Milk and Juice Beverages in Men and Premenopausal Women (Abstract Number: 8691; Poster Board: LB283)

Recent Publications

Maki KC, Johns C, Harris WS, Puder M, Freedman SD, Thorsteinsson T, Daak A, Rabinowicz AL, Sancilio FD. Bioequivalence demonstration for omega-3-acid ethyl ester formulations: Rationale for modification of current guidance. Clin Ther 2017;Feb 8 [Epub ahead of print].

Lopez-Toledano MA, Thorsteinsson T, Daak A, **Maki KC**, Johns C, Rabinowicz AL, Sancilio FD. A novel omega-3-acid ethyl ester formulation incorporating Advanced Lipid Technologies™ (ALT®) improves docosahexaenoic acid and eicosapentaenoic acid bioavailability compared with Lovaza®. Clin Ther 2017;Feb 8 [Epub ahead of print].

Lopez-Toledano MA, Thorsteinsson T, Daak AA, **Maki KC**, Johns C, Rabinowicz AL, Sancilio F. Minimal food effect for eicosapentaenoic acid and docosahexaenoic acid bioavailability from omega-3 acid ethyl esters with an Advanced Lipid Technologies™ (ALT®)-based formulation. J Clin Lipidol 2017;In Press.

Maki KC, Bobotas G, **Dicklin MR**, **Huebner M**, Keane WF. Effects of MAT9001 containing eicosapentaenoic acid and docosahexaenoic acid, compared to eicosapentaenoic acid ethyl esters, on triglycerides, lipoprotein cholesterol, and related variables. J Clin Lipidol 2017;In Press.

Maki K, Lawless AL, Kelley KM, Kaden VN, Geiger CJ, **Palacios OM**, **Dicklin MR**. Corn oil intake favorably impacts lipoprotein cholesterol, apolipoprotein, and lipoprotein particle levels compared with extra-virgin olive oil. Eur J Clin Nutr 2017;71:33-38.

entitled "Nothing Fishy About It: Increasing Appropriate Use of Omega-3 Fatty Acid Supplementation". Check out this link for more information.

American Heart Association. life is why™ | SCIENTIFIC SESSIONS

AHA Scientific Sessions Highlights

If you did not make it to the annual American Heart Association Meeting last November check out this link for highlights of the meeting including Kevin Maki's participation in a debate on statin-induced diabetes.

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