How C15:0 Does Under Pressure (Blood Pressure, That Is)

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Welcome to Issue 139 of Science Says! Our weekly newsletter where you'll learn the latest healthy aging and C15:0 research news that our team of doctors, scientists, and experts are most excited about—without having to go search for it.

Eric and Steph
Co-Founders, Doctors, Nerds

What Dr. Stephanie Venn-Watson, our co-founder and author of *The Longevity Nutrient* and over 80 peer-reviewed scientific publications, is reading.

HEALTHY AGING

The Building Case for C15:0 & Heart Health

A robust body of evidence continues to build around C15:0's role in supporting our whole-body health, including our heart health. Whether it's lowering LDL-cholesterol, decreasing proinflammatory cytokines in our vessels, or managing healthy iron metabolism, the gap between C15:0 being associated with versus causing optimal heart health is getting smaller. Along these lines, a recently published paper hypothesized that people with higher C15:0 serum levels would have healthier blood pressure. Let's dive in.

How was this most recent study done?

Since the 1960s, the U.S. has conducted a National Health and Nutrition Examination Survey (NHANES), which routinely collects individuals' data from health exams, laboratory tests, and dietary intake. This reliable health database has been used by research teams throughout the world to conduct and publish nearly 80,000 studies since its inception.

The latest study by Chen et al. used 2011-2014 NHANES data collected from 4,775 participants who were adults (mean age of 45 years) and had adequate data related to their C15:0 levels, blood pressure, and numerous potential confounding factors like age, gender, race, education, marital status, diabetes, smoking, alcohol frequency, BMI, economic status, total nutrient intake, and blood biomarkers of renal, lipid, and glucose health).

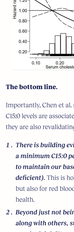
They then applied numerous statistical models, controlling for the confounding factors above, to evaluate associations between C15:0 levels and blood pressure.

Got it. What did they find?

Well, thanks to the myriad of statistical modelling applied by this team, Chen et al. had a healthy handful of really interesting results:

- **Most people had circulating C15:0 levels of around 20 uM, or about 0.2% of total fatty acids.** Chen et al. showed that people, on average, had C15:0 concentrations ranging from around 5 to 70 uM, while the C15:0 percentage range was around 0.08% to 0.45% (see below). These distributions are consistent with many other studies, which we summarized in our Metabolites publication.

- **The higher the serum C15:0 concentration, the lower the blood pressure.** When controlling for all potential confounding factors above, people with the highest C15:0 levels (the top 75th percentile, C15:0 around ~ 30 uM) were twice as likely to have healthy blood pressure compared to people with low C15:0 levels (the bottom 25th percentile, C15:0 around ~ 15 uM). This relationship was linear: the higher the C15:0 concentration, the healthier was one's blood pressure. This is also consistent with our Metabolites and Nutrients papers, where we provided evidence of optimal C15:0 levels between 20 and 50 uM.
- **Across all ages, folks with serum C15:0 % above 0.15% had significantly healthier blood pressure.** When it came to C15:0 %, the team demonstrated a threshold effect. Specifically, there is a clear inflection point for healthy blood pressure seen among people with C15:0 levels ~ 0.15%. While there were still improvements with increasing C15:0 % at blood pressure ~ 0.15%, the most remarkable change toward healthy blood pressure was to get C15:0 ~ 0.15%. Again, this finding is consistent with the proposed definition by Venn-Watson et al. of nutritional C15:0 deficiency, which is ~ 0.2% C15:0.



- **If you're over 65 years old, there is a strong linear association in healthy blood pressure as C15:0 increases from 0.15% to 0.4%.** Interestingly, the association between higher C15:0 % and healthy blood pressure gets even stronger among people who are older than 65. This linear improvement in blood pressure as C15:0% increases from 0.15% to 0.4% is consistent with Titles et al., which also showed this continued associated better heart health as C15:0 % increased from 0.2% to 0.55% (see below). Additionally, Manca et al. showed that people living in Sardinia's High Longevity Zone, who have strong long-term heart health, have C15:0 levels between 0.4 to 0.6%.

The bottom line.

Importantly, Chen et al. not only demonstrated that higher C15:0 levels are associated with healthy blood pressure, but they are also revaluating two key discoveries

1. *There is building evidence for a threshold effect, where a minimum C15:0 percentage (around ~ 0.2%) is needed to maintain our baseline health (aka not being C15:0 deficient).* This is holding not only for blood pressure, but also for red blood cell, immune, liver, and heart health.
2. *Beyond just not being deficient, this most recent study, along with others, support that optimal C15:0 levels may be 0.3-0.6%.*

Getting to the Heart of C15:0

Looking specifically at heart health, the evidence of C15:0's benefits are building:

- C15:0 activates PPARα/δ and AMPK and inhibits JAK-STAT. These activities support healthy, balanced metabolism, glucose control, cholesterol levels, and immune responses - all of which are critical to supporting heart health.
- C15:0 inhibits proinflammatory cytokines, including IL-6, TNFα, and MCP-1, in human vessel cell systems. Importantly, C15:0 has a dose-dependent effect that is optimal between 20 and 50 uM (similar to what was reported by Chen et al.).
- Pure C15:0 lowers cholesterol, IL-6, TNFα, and MCP-1 in rodent models within 12 weeks.
- Multiple meta-analyses of large prospective cohort studies have repeatedly shown that people with higher C15:0 levels have better long-term heart health.
- In a randomized, controlled human clinical trial, daily oral C15:0 lowered LDL cholesterol within 12 weeks.

These studies are getting to the heart of how C15:0 is not only associated with better health, but how it can positively and actively protect our long-term health.

- ☑ Step 1: Don't be C15:0 deficient.
- ☑ Step 2: Optimize your C15:0 levels.

Have a wonderful week, everyone!

Dive deeper into the science

READ THESE STUDIES

- Chen et al. Associations between serum pentadecanoic acid (C15:0) and blood pressure: a cross-sectional analysis of NHANES data.
- Venn-Watson et al. The Cellular Stability Hypothesis: Evidence of Pervasive and Accelerated Aging-Associated Diseases as Newly Identified Nutritional Pentadecanoic Acid (C15:0) Deficiency Syndrome.
- Venn-Watson et al. Pentadecanoic Acid (C15:0), an Essential Fatty Acid, Shares Clinically Relevant Cell-Based Activities with Leading Longevity-Enhancing Compounds.
- Trieu et al. Biomarkers of dairy fat intake, incident cardiovascular disease, and all-cause mortality: A cohort study, systematic review, and meta-analysis.
- Manca et al. Circulating fatty acids and endocannabinoidome-related mediator profiles associated to human longevity.
- Venn-Watson et al. Efficacy of dietary odd-chain saturated fatty acid pentadecanoic acid parallels broad associated health benefits in humans: could it be essential?
- Fu, W.C. et al. Pentadecanoic acid promotes basal and insulin-stimulated glucose uptake in C2C12 myotubes.
- To et al. Pentadecanoic acid, an odd-chain fatty acid, suppresses JAK2/STAT3 signaling.
- Li et al. Saturated Fatty Acid Biomarkers and Risk of Cardiometabolic Diseases: A Meta-Analysis of Prospective Studies.
- Chooi et al. Effect of An Asian-Adapted Mediterranean Diet and Pentadecanoic Acid on Fatty Liver Disease: The TANGO Randomized Controlled Trial.

- Nerd out on all the C15:0 science at DiscoverC15.com