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Strategies to Restore Mitochondrial Function and Support Healthy Aging: The Role of Urolithin A

A webinar featuring Dr. Anurag Singh, MD, PhD and Dr. Kara Fitzgerald, ND, IFMCP

A big thank you to everyone who joined us live and has already watched the webinar. What an amazing audience!

Unfortunately, due to the volume of attendees and time limitations, we were unable to answer all the questions posted during the live webinar. We've addressed some of these questions offline - you can find the responses below.

Reminder, you can access the recording, slides & other resources at drkarafitzgerald.com/webinars

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time—line

Give your patients access to the only clinically validated Urolithin A on the market. Join **[Timeline's provider network]** to unlock exclusive practitioner pricing, detailed clinical protocols, and resources designed to help you integrate Mitopure® into your practice.

Dosing & Administration

1. **What is the recommended dosage (500mg vs. 1000mg), and should it be taken as a single dose or divided? Can it be taken in a fed or fasted state?**
    a. Team Timeline Answer: Mitopure can be taken with or without food. It should be taken as a single dose, meaning all at once. (The portion regarding 500mg vs 1000mg was answered live during the Q&A).

2. **Is Urolithin A something that needs to be taken on an ongoing basis for life, or can it be used in intervals?**
    a. Team Timeline Answer: While our longest study is 4 months, we suspect that in order to maintain the benefits of optimizing mitophagy, you would need to continue taking this long term.

3. **What was the dosage given to mice compared to the best dose for humans? Is 500mg/daily sufficient for an active 68-year-old?**
    a. Team Timeline Answer: Adjusting for the size and weight of rodents and translating to humans, the effective dosages of Mitopure would be in the range of 250mg-1000mg that have been tested in RCTs. 500mg is found to consistently activate mitophagy, improve mitochondrial health, and significantly improve muscle strength after long-term use, and for an active person, it should be the correct maintenance dose.

4. **At what age should someone start taking this supplement? (e.g., late 30s vs. 50s and beyond)**
    a. Team Timeline Answer: Our clinical trials have shown benefits across a diverse range of ages. Keep in mind that mitochondrial function begins to decline in the 30's.

Muscle Health & Aging

5. **Are there long-term studies of Urolithin A in the elderly to specifically reduce muscle loss?**
    a. Team Timeline Answer: We conducted a 4-month study in older adults (age 65-90). After two months, those taking Mitopure experienced a significant improvement in

muscle endurance (hand and leg) compared to the placebo group. Publication located here.

6. **Have you evaluated the impact of Urolithin A on muscle capillary rarefaction?**
    a. Team Timeline Answer: While the impact on angiogenesis or blood flow has not been directly studied in humans, there are pre-clinical studies showing an impact of Urolithin A supplementation on muscle angiogenesis Urolithin A augments angiogenic pathways in skeletal muscle by bolstering NAD+ and SIRT1 | Scientific Reports

Safety, Side Effects & Interactions

7. **What is known about the long-term safety and adverse effects of chronic Urolithin A supplementation in both animal models and humans?**
    a. Team Timeline Answer: In all of our clinical trials, there were no differences in adverse events between Mitopure and the placebo group, demonstrating that it is safe and well-tolerated.

8. **Are there specific tolerance issues? Why might some patients with chronic illness feel "swollen and inflamed" after taking it?**
    a. Team Timeline Answer: Clinical studies and food safety reports confirm that no Mitopure-related adverse events have been reported when taking Mitopure at the recommended dosage for healthy adults over 18 years of age. Mitopure has only been investigated in clinical trials involving healthy participants and has not been clinically studied in different patients populations where chronic co-morbidity and co-medications can have an impact.

Scientific Mechanisms & Research

9. **How does Urolithin A differ from other mitochondrial supports like PQQ, CoQ10, or NAD+?**
    a. Team Timeline Answer: Mitopure has a unique mechanism of action that targets the mitochondrial recycling process called mitophagy. This foundational process removes damaged mitochondria and stimulates the creation of newer, healthier

mitochondria through a process called biogenesis. Urolithin A is the only molecule clinically proven to stimulate mitophagy.

10. **Why was it named Urolithin "A"—are there other versions like "B"?**
    a. Team Timeline Answer: Several other Urolithins have been identified, but Urolithin A has the most clinical research.

11. **What are the specifics of the gut-brain axis, the NAD+/NADH ratio, ROS quenching, and the specific genes responsible for processing UA in the stomach?**
    a. Team Timeline Answer: The gut–brain axis is the bidirectional communication network connecting the gut, immune system, and central nervous system through neural, endocrine, and metabolic signals. It's tightly linked to mitochondrial function and inflammation, both of which are impacted by Urolithin A . Urolithin A in pre-clinical models has been shown to augment NAD+ and dampen ROS production. Urolithin A augments angiogenic pathways in skeletal muscle by bolstering NAD+ and SIRT1 | Scientific Reports

       As for Urolithin A production genes, humans do not encode the enzymes that produce it; it is generated exclusively by specific gut microbes whose gene clusters encode the dehydroxylases and decarboxylases that convert ellagic acid to UA. This explains the wide variability in natural UA production across individuals

12. **How do muscle cells compare to other cells regarding the number of mitochondria?**
    a. Team Timeline Answer: Skeletal muscle has far more mitochondria than many other tissue types, due to the high energy demand of muscles. Other high energy demanding cells, like cardiac muscle or neurons will also have a high amount of mitochondria.

13. **To Dr. Singh: How actively do you use or depend on AI in your research?**
    a. Team Timeline Answer: Not very much currently, but can see the value of AI to mine through years of clinical biomarker data in the future.

14. **Did Dr. Singh say muscle cells have about 20,000 mitochondria? What do other cells have?**

a. Team Timeline Answer: skeletal muscle cells, cardiac cells, neuronal cells and kidney cells have the highest density of mitochondria in a cell (in thousands 10000-30000; neurons cells even higher) because these cells have a massive metabolic demand (they produce and consume the highest energy). Skin, hepatic, and immune cells typically have in the range of 500-2500 mitochondria/cell. Red blood cells have none. Oocytes also have a very high number (50000/cell).

Microbiome & Diagnostic Testing

15. **Are there commercial tests available to determine if a patient's microbiome can naturally produce Urolithin A? Where can we find the fingerprick/challenge test?**
    a. Team Timeline Answer: We have developed a test that is currently available as part of a clinical trial. You can sign up to take the test here: https://challenge.timeline.com/. You'll need to use the enrollment code **HCP**.

16. **Can you elaborate on the microbiome's role in Urolithin A production?**
    a. Team Timeline Answer: Because Urolithin A is a postbiotic, you need the right gut microbiome to make it. Urolithin A is not directly available in foods, instead your gut microbes will metabolize Urolithin A from dietary precursors. These precursors are the ellagitannins found in pomegranates, berries and nuts. However, only about 30-40% of the population has the right gut microbiome to make Urolithin A.

Lifestyle, Nutrition & Supplement Stacking

17. **Can Urolithin A be combined with or replace other supplements (Creatine, NAD+, Resveratrol, PQQ, CoQ10, etc.), and are there specific supplements that should be dropped if taking UA?**
    a. Team Timeline Answer: Urolithin A can be combined with other supplements, and some early lab data suggest that it may work synergistically with other supplements like CoQ10 or creatine. It may also replace the need for other supplements targeting biogenesis (like resveratrol or NAD+) as it helps to stimulate mitophagy and biogenesis.

18. **How about supplementing with pomegranate extract vs urolithin A? It's a lot less expensive, and contains 40-50% ellagic acid.**
    a. Team Timeline Answer: The concern here is that most people don't have the correct microbiome to convert ellagic acid into Urolithin A.

19. **What is the impact of coffee, protein intake (more vs. less), and exercise type (strength vs. cardio) on mitophagy and mitochondrial health?**
    a. Team Timeline Answer: Neither coffee nor protein will stimulate mitophagy, however all forms of exercise (strength, endurance, HIIT, etc) will benefit mitochondrial quality and efficiency.

20. **How should Urolithin A be used to help with post-exercise muscle soreness?**
    a. Team Timeline Answer: Many of our customers have noticed that Mitopure (at doses of both 500 and 1000mg) helps to reduce post-exercise muscle soreness.
    In a study of highly trained endurance runners, creatine kinase levels were significantly lower after a 3000 m time trial compared to placebo, suggesting less muscle strain after intense exercise. Study here.

Specific Health Conditions & Clinical Applications

21. **Is there research or data on Urolithin A regarding the following conditions: Diabetes, Chronic Fatigue Syndrome (ME/CFS), Fibromyalgia, Autoimmune diseases, IBD, Lyme infections, APOE4, Fluoroquinolone Toxicity, or Vision health?**
    a. Team Timeline Answer: The published clinical data currently available is in muscle, immune, and skin (topically) aging. There is promising preclinical data in several other areas, such as the brain and gut, however that science has not yet been translated into human data.

    Timeline's Urolithin A is commercially available in dietary supplements and cosmetics and is not intended to diagnose, treat, cure, or prevent any diseases.

22. **Can Urolithin A be used as an adjunct in stem cell regenerative therapy?**

a. Team Timeline Answer: Not yet trialled in humans, but there is a fascinating pre-clinical study from an independent group showing UA has a big impact on stem cells. https://www.nature.com/articles/s43587-023-00473-3

23. How does Urolithin A affect inflammation (CRP markers) and microglial activation in the brain?

a. Team Timeline Answer: Clinical studies have shown that Urolithin A helps reduce markers of inflammation, such as CRP in healthy adults as part of our muscle and immune aging studies. We have not yet clinically studied Urolithin A's impact on inflammatory markers associated with brain aging. Microglia are immune cells (like macrophages) in the brain and get inflamed. While not clinically studied so far, there are pre-clinical studies on UA showing benefit. https://pmc.ncbi.nlm.nih.gov/articles/PMC10993698/; https://www.frontiersin.org/journals/aging-neuroscience/articles/10.3389/fnagi.2024.1503336/full

24. Multiple myeloma (kind of cancer of old age, developes for long years) and its pre-states (CHIP, MGUS, SMM) could be treated with UA?

a. Team Timeline Answer: There is ongoing research to see how UA can augment cancer therapy. We have an ongoing trial with results expected in the first half of 2027. Stay tuned.
b. Timeline's Urolithin A is commercially available in dietary supplements and cosmetics and is not intended to diagnose, treat, cure, or prevent any diseases.

Product, Quality & Logistics

25. How does Mitopure compare to other Urolithin A products (e.g., AOR), and is it unique?

a. Team Timeline Answer: Mitopure stands out from other Urolithin A supplements based on:
    i. **Clinical studies:** Mitopure has been tested in 7+ clinical studies at the 1000 mg dose. The ingredient has been included in 12+ clinical studies, making it the most studied form. This report from SuppCo, a company that independently tests and rates the quality of supplements, states that

Mitopure is the most clinically studied form of Urolithin A to date. Without comparable clinical evidence, other Urolithin A products cannot assume or substantiate the same benefits.

ii. **Bioavailability:** Studies show that 1000 mg of Mitopure is bioavailable — it successfully raises plasma Urolithin A levels, stimulates mitophagy, renews mitochondria, and leads to measurable benefits in muscle strength, endurance, recovery and immunity.*

iii. **Patents:** This proprietary form of Urolithin A is protected under 80+ patents.

26. Why is the 1000mg dose only available through professionals? Is the skincare line or the test available in Europe?

a. Team Timeline Answer: Our consumer line (including skin) is available in the US, Canada, Switzerland and the UK. Currently our professional line is only available in the US. Many consumers choose to double their dose to get 1000mgs daily, however the 1000mg capsules are only available through healthcare providers.

27. Can Urolithin A be protective of the mitochondria in cancer cells just as NAD may do?

a. Team Timeline Answer: UA is an adaptogen- in all clinical and pre-clinical studies on cancer-related research, it has been safely shown to reduce the burden of disease and potentiate mitochondria in immune cells and selectively expand cancer-killing T-lymphocytes. Urolithin A inhibits breast cancer progression via activating TFEB-mediated mitophagy in tumor macrophages - ScienceDirect; https://www.cell.com/immunity/fulltext/S1074-7613(22)00508-8

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28. Where can I find Mitopure on Fullscript?

a. Team Timeline Answer: You can search Mitopure on Fullscript. You can also find it under "Cellular Longevity Pro." The 1000mg Pro line is available there now; professional skin care will be available in September.

29. Will there be a replay available?

a. Team DrKF Answer: You can access the recording, slides and other resources at drkarafitzgerald.com/webinars. All registrants will be notified when the replay is available.

Questions Answered Live During the Webinar:

- Are there specific contraindications for patients undergoing chemotherapy, radiation, or other oncology treatment?
- Can Urolithin A help those over 70 gain muscle mass, and is long-term use required?
- Potential side effects, specifically facial flushing/inflammation reactions in the first week.
- Is the recommended dose 500mg or 1000mg?
- Can it interact negatively with other supplements, and is it safe to take with HRT?
- Is the 17–22 hour half-life for UA and its metabolites accurate?
- Were genes associated with RAGE upregulated in sedentary/frail individuals?
- Can you combine Urolithin A with Creatine, NAD+, and others for a synergistic effect?
- Are there drug-nutrient interactions, and is it effective for those with a compromised gut?
- What impact if any does UrlothinA have on Lyme infections have?