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### MITOCHONDRIAL RENEWAL FEATURING MITOPURE<sup>™</sup> UROLITHIN A

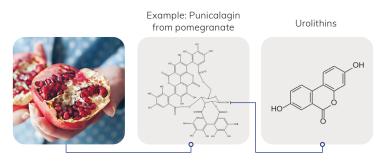
REN**UA**L offers a unique, novel combination of Mitopure<sup>™</sup> Urolithin A, resveratrol and coenzyme Q<sub>10</sub> to promote mitochondrial biogenesis and renewal for:





### What is Urolithin A?

Urolithin A is a major metabolite of ellagitannin-rich foods, such as pomegranates, black raspberries, raspberries, strawberries, walnuts and almonds. These ellagitannins are not absorbed intact into the bloodstream, but are hydrolyzed to ellagic acid in the gut, which is then metabolized by the gut microflora to form urolithins. Research indicates that the ability to synthesize urolithins declines with age and depends on the gut microflora, and there is a small percentage of the population that is unable to perform this conversion at all.<sup>1.2</sup>



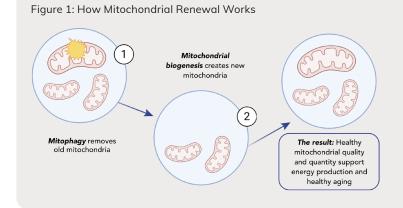
### **Functions of Urolithin A:**

Energy not only drives our daily activities—it ensures the health of our trillions of cells. Conversion of food molecules into usable energy occurs in organelles called mitochondria. But these energy powerhouses do more than simply recharge our bodies—they control cellular decisions that affect health and aging.

Recent research has deepened our definition of what optimal mitochondrial health looks like and how to achieve it. The life span of these organelles is limited, in part, by frequent exposure to oxidative stress that occurs during normal energy metabolism. As they age, mitochondria produce less energy, and may even disturb normal cellular functions as they accumulate. Therefore, a cell's energy output and overall health depends on mitochondrial removal and replacement. Supporting this recycling process is a newly recognized strategy for maintaining cellular health, particularly in muscles and other metabolically active tissues.<sup>3,4</sup> Optimal mitochondrial function, according to emerging scientific thought, is clinically achievable by supporting a well-established renewal process.

#### **Mitochondrial Renewal**

In the renewal process, old, dysfunctional mitochondria are destroyed through a process known as mitophagy, and new mitochondria are made through a process called mitochondrial biogenesis (Figure 1). Caloric restriction and exercise support healthy aging, in part by augmenting both processes.<sup>5,6</sup> This two-step system thrives in our youth, but grows sluggish with time, driving metabolic, bioenergetic and musculoskeletal hallmarks of advancing age. For example, diminished mitophagy is strongly implicated in the age-related decrease in muscle strength.<sup>7</sup>



\*This statement has not been evaluated by the Food & Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease. **in f** we be associated to a second s



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# Urolithin A

Urolithin A is unique as a dietary agent that has been specifically developed to target mitophagy. In a 2016 study published in Nature Medicine, Urolithin A (UA) stimulated mitophagy in preclinical models and improved muscle function and exercise capacity in two different rodent models. UA also improved muscle strength and longevity in *C. elegans*, a gold standard preclinical paradigm of human aging.<sup>8</sup>

This first-in-class phenolic "postbiotic" (a natural metabolite of intestinal bacteria) is produced by commensal microbiota after consuming foods rich in ellagitannins and ellagic acid — major health-promoting constituents of pomegranates, nuts and berries. These unique polyphenols undergo metabolism by intestinal bacteria to small, highly absorbable metabolites called urolithins, which mediate the widely acclaimed health benefits of pomegranates and other ellagitannin-rich foods.<sup>9,10</sup>

Owing to variations in gut microbiota, not everyone can generate UA after consuming these foods. Even with the right conversion "metabotype," intestinal extraction of UA from ellagitannins is incomplete, unpredictable and impeded by aging, making oral UA — a universally absorbed molecule — appropriate for precise dosing and evidence-based use. Not surprisingly, pure oral UA (as Mitopure<sup>™</sup>) outperforms pomegranate in its pharmacokinetic profile, as shown in a trial of healthy adults whose plasma UA levels were six times higher following a single dose of Mitopure<sup>™</sup> compared to an 8 oz. serving of pomegranate juice, one of the richest sources of ellagitannins.<sup>11</sup>

## Powers Healthy Muscle Function<sup>‡</sup>

In animal research, UA improved endurance and exercise capacity in both young and old models of age-related muscle decline. Compared to control mice, those supplemented with UA exhibited:<sup>84</sup>

- 9% stronger grip strength
- 57% more voluntary exercise
- 42% greater running endurance in elderly rats
- **65%** greater running capacity in young rats

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What is Autophagy? The natural process of cellular renewal in which the body degrades, clears and recycles cellular components.

What is Mitophagy? Mitochondrial clearance and recycling to prevent dysfunction and cellular degeneration.

### **Other Metabolic Benefits**

When mice were fed a high-fat diet for 12 weeks, supplementation with urolithin A promoted healthy insulin function and lipid metabolism, and decreased adipocyte size.<sup>12</sup> These results are believed to be the result of increased SIRT1 activity, a protein that mediates the healthy aging benefits of resveratrol, caloric restriction and exercise.<sup>13+</sup>

# **Supplement Facts**

### 2 capsules, 1-2 times daily, with or between meals.

| Two (size 0) Caplique <sup>®</sup> capsules contain:      |        |
|---|--------|
| Mitopure™ Urolithin A                                     | 250 mg |
| Trans-Resveratrol (from Japanese knotweed                 | 150 mg |
| (Polygonum cuspidatum) extract (root))                    |        |
| Coenzyme Q <sub>10</sub>                                  | 60 mg  |
| Other ingredients: vegetable glycerin, vegetarian capsule |        |
| (cellulose, water)  |        |

Kaneka Q<sub>10</sub><sup>®</sup> is a U.S. registered trademark of Kaneka Corporation. Mitopure<sup>™</sup> (proprietary Urolithin A) and the Mitopure<sup>™</sup> logo are trademarks of Amazentis SA. Patent www.amazentis.com/patents Caplique<sup>®</sup> is a registered trademark used with permission.

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| REN <b>UA</b> L®            | Quantity | Order<br>Code |
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