

Introduction

The lychee tree (*Litchi chinensis*) is a type of tropical fruit tree from Southeast Asia. Its fruit is sweet, translucent, and succulent after its red, bumpy skin is peeled off. As with all fruits, within the flesh of the lychee dwell bioactive phytochemicals (natural beneficial compounds from plants). One widely investigated class of plant-derived bioactive compounds is polyphenols, which are connected to the health benefits associated with increased consumption of fruits and vegetables (Pandey et al., 2009).

The most common sources of polyphenols are green tea, chocolate, berries, soy, and red wine, which are recognized for their healthful properties (Manach et al. 2004). Polyphenols are also the active compounds found in “superfruits” like mangosteen, pomegranate, etc. Lychee can be considered one of these superfruits, as it contains more polyphenols than any other edible plant on the planet besides strawberries. Lychee has also been associated with lasting beauty and longevity throughout Asia. Clinical research has already shown that polyphenols have many health benefits that include support for cardiovascular diseases, reduction in blood glucose levels, and improvements in the overall immune system (Pandey et al., 2009).

Bioavailability of Polyphenols

Polyphenols vary dramatically in their bioavailability. According to Dr. Robert Hackman, a researcher at University of California–Davis who has studied the bioavailability of polyphenols for many years, “It’s not a matter of what gets in your mouth, it’s a matter of what gets in your blood.” Flavonols have 10–30% bioavailability, which is higher than anthocyanins (< 0.1%) or quercetin (1–5%) and explains why this group of polyphenols has yielded the most promising human clinical results.

The reason the bioavailability of flavonols is higher can also be due to their size. Flavonols consist of short-chain and long-chain molecules. The short-chain molecules, including monomers, dimers, and

trimers, have low molecular weight and can be easily absorbed by the body. However, long-chain molecules (known as polymers) are high-molecular-weight molecules, which the human digestive tract cannot easily absorb, and often end up becoming waste.

Innovation of Oligonol®

The poor absorption of conventional long-chain polyphenols by the body was one of the main inspirations behind the development of Oligonol. Compared with conventional polyphenols, Oligonol is a functional ingredient containing catechin-type monomers and proanthocyanidin oligomers converted from polymers via a novel manufacturing process. To improve bioavailability, Amino Up Chemical Company (one of Japan’s leading bionutraceutical companies and the manufacturer of Oligonol) applied a proprietary technology that takes a pair of high-tech scissors to cut polyphenols into tiny pieces to improve their absorption rates. The final product, which contains high levels of low-molecular-weight flavonols, was tested in many human clinical trials. The results showed that the blood concentration of polyphenols in subjects who had taken a single dose of Oligonol was three times higher than that of those who had taken the regular lychee extract.

Oligonol, an optimized polyphenolic extract of lychee fruit and green tea, is a strong antioxidant that carries out redox reactions to neutralize reactive free radicals that could damage cells and cause aging and various diseases. Oligonol has also been shown to have superior anti-inflammatory capability, a protective effect on the endothelium, and the ability to downregulate body temperature under heat stress, which has interesting commercial implications in sports nutrition.

Health Benefits

Metabolic Syndrome

Mechanistic evidence suggests that Oligonol could have beneficial effects for those with visceral obesity and associated metabolic syndrome. In one recent

in vitro study, using Oligonol with human liver cell line HepG2 cells helped reverse palmitate-induced intracellular lipid accumulation, downregulated the expression of adipogenic genes, and upregulated genes for fatty acid degradation. In addition, Oligonol utilization restored insulin sensitivity, inhibited STAT3-SOCS3 signaling, and increased AMPK phosphorylation in HepG2 cells as well (Park J et al., 2015). Another study done by the same research group in 2014 demonstrated that Oligonol could inhibit 3T3-L1 preadipocyte differentiation by reducing adipogenic gene expression. The anti-adipogenic effect of Oligonol was found through its ability to inhibit the Akt and mammalian target of rapamycin (mTOR) signaling pathway by diminishing the phosphorylation of ribosomal protein S6 kinase (p70S6K), which is a downstream target of mTOR and forkhead box protein O1 (Foxo1) (Park J et al., 2014). All these results suggest Oligonol may potentially be an effective regulator of visceral fat accumulation by inhibition of adipogenesis and lipid accumulation, and by increasing fatty acid degradation.

As for human clinical trials, one study has been conducted thus far exploring this health benefit that was conducted by researchers at Hokkaido Information University in Japan, using 15 male and 4 female adult volunteers. These volunteers had to have an abdominal circumference greater than 85 cm (33.5 inches) to be enrolled in this randomized, double-blind, placebo-controlled trial. Half the subjects consumed 2 Oligonol capsules daily for 10 weeks, while the other half took placebo capsules. The results showed that the Oligonol group subjects experienced reductions in weight, body mass index, abdominal circumference, and waist circumference when compared with the placebo group. Abdominal CT scan analyses also revealed a dramatic 15% drop in visceral fat (Nishihira J et al., 2009).

To better understand the relevance of this data, we will explore the results of a study conducted by Duke University on 175 overweight men and women. This study found that participants who performed high-dose vigorous-intensity activities (equivalent

to 20 miles of jogging each week) saw visceral fat levels drop by only 7% in six months. In other words, Oligonol reduced visceral fat levels twice as much as a regimen of vigorous exercise was able to do in less than half the time. Although the exact mechanism of Oligonol's ability to help in visceral fat reduction remains unclear, blood tests show that the antioxidant ability of the Oligonol group trended higher than that of the placebo group, while their levels of triglycerides and lipid peroxides (fats that have been attacked by free radicals) were remarkably reduced. Other studies have shown that Oligonol may regulate the production of special hormones produced in the fat tissues that could work to facilitate fat metabolism. All the data presented here suggests that Oligonol may play an important role in managing metabolic syndrome symptoms, giving new hope to the 50 million Americans affected by this disorder.

Hyperglycemia is another major metabolic syndrome from which many people are suffering and which may cause serious cardiovascular problems. Postprandial hyperlipidemia has been recognized as a risk factor for atherosclerosis. A three-way, crossover clinical study conducted in 9 healthy male participants showed that when compared with the control group, administration of Oligonol lowered the serum postprandial triglyceride (TG) level, decreased chylomicron TG responses significantly, and delayed the time for reaching a maximum level of serum TG and chylomicron TG. The results suggested supplementation with Oligonol could inhibit fat absorption and improve postprandial hyperlipidemia in healthy subjects, which plays an important role in preventing atherosclerosis (Tani M et al., 2009).

Thermoregulation

Heat stress can be experienced by anyone in our everyday life, but it's especially an issue for professional athletes when performing strenuous physical exertion or being exposed to excessive environmental heat. Heat stress results in increased circulation of pro-inflammatory compounds in the

blood, contributing to fatigue, muscle soreness, and elevation of body temperature. Heat stress also induces various types of DNA damage (e.g., mispair, mutation) (Kantidze OL et al., 2016), which may lead to many severe health problems, including cancer. In addition, heat stress induces the body's sweat response, which results in a loss of fluids, reducing exercise performance.

Previous research suggests that Oligonol could reduce serum concentration of many inflammatory biomarkers, including cortisol, IL-1 β , and IL-6, after heat stress (Li S et al., 1999), and Oligonol supplementation could help improve exercise performance. One double-blind, crossover clinical study published in 2013 was performed on 17 healthy males from 21 to 22 years old using oral supplementation of 100 mg of Oligonol. Subjects ingested Oligonol or a placebo before half their body was submerged in hot water at 42°C for 30 minutes. Measurements were taken at rest, immediately after immersion, and 60 minutes after. The results showed that Oligonol intake significantly prevented elevation of tympanic temperature (difference of 0.17°C after heat stress, $p < 0.05$; 0.17°C at 60 minutes, $p < 0.05$) and mean body temperature (temperature difference: 0.18°C at post, $p < 0.05$; 0.15°C at re-60, $p < 0.05$) when compared with the placebo group. In addition, Oligonol ingestion lowered serum levels of prostaglandin E2 (PGE2) and cyclooxygenase-2 (COX-2) significantly when compared with the placebo group ($p < 0.05$) (Shin Y et al., 2013).

In one of the most recent placebo-controlled, crossover clinical trials, 19 healthy male subjects took 200 mg of Oligonol for 1 week before the test of half-body immersion in 42°C hot water. Supplementation with Oligonol resulted in a smaller increase in body temperature and reduced the amount of whole-body sweat loss, compared with the placebo group. In addition, the subjects in the Oligonol group maintained serum aldosterone at a relatively low level and serum sodium at a relatively higher level than the placebo group did (Jeong BL et al., 2015). These results indicated the important role Oligonol

plays in sweating, plasma volume, and osmolality in response to heat stress, suggesting its potential use in attenuating body temperature and excessive sweating under heat load in healthy humans, especially in professional athletes, who are under tremendous heat stress caused by intense training every day.

Sports Nutrition

Fatigue Prevention

As many know, when more blood is flowing to the muscle, more oxygen is delivered. In the meantime, more waste is being removed from the muscle. This combination prevents fatigue. That's one of the reasons why trained athletes do not tire easily when they exercise regularly. In one clinical study conducted in a total of 47 young male and female athletes (18–22 years old), half the participants consumed Oligonol, and the other half consumed regular lychee extract. At the end of the 52-day trial, not only did the Oligonol group report feeling improvements in recovery from fatigue, mental clarity, quality of sleep, eye fatigue, and stiff shoulders compared with the regular lychee group, but they also had lower urine levels of 8-OHdG, which is a marker for physical and mental fatigue (Ohno H et al., 2008).

Capsule vs. RTD Formulation

Oligonol is an ideal candidate for ready-to-drink products. Bioequivalence clinical studies showed that drinkable Oligonol has higher bioavailability than the hard-capsule formulation from two aspects: 1) The polyphenol concentration and antioxidant activity in blood of groups that consumed Oligonol as a hard capsule and Oligonol dissolved in a drink form both reached the maximum level 2 hours after intake. 2) The maximum value was doubled in the groups that took Oligonol dissolved in a drink compared with the groups that took Oligonol in hard capsule (Bioequivalence study of Oligonol, unpublished data, 2007).

Conclusion

In summary, accumulating animal and human clinical studies have shown that Oligonol can be an effective anti-oxidation and anti-inflammation natural ingredient, which our bodies can absorb quickly with high bioavailability. It can be used in attenuating exercise-induced inflammation, improving skin health and beauty, reducing visceral fat, and assisting with weight management, as well as many other health objectives. New evidence shows that it also helps increase blood flow, therefore downregulating body temperature and controlling fever-associated biomarkers. In addition, Oligonol in liquid form can be absorbed as fast as the conventional hard-capsule delivery form, with two times higher bioavailability. Scientific evidence indicates that Oligonol has robust anti-aging, sports nutrition, and anti-inflammatory effects, suggesting a very promising future for natural product formulation, especially in a liquid form and for an athletic consumer population.

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