

## OPITAC™ Glutathione Guide (L- Glutathione Reduced)

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- FULL US FDA GRAS Notified, USP Correspondent, GMP Approved, Kosher, HALAL

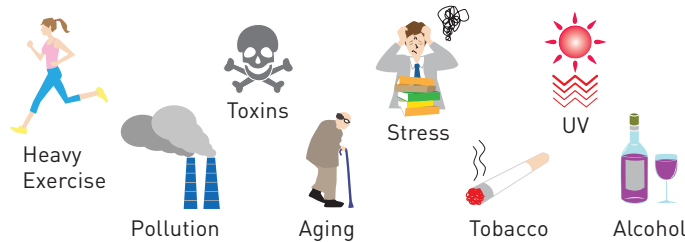
## What is OPITAC™ Glutathione?

L- Glutathione Reduced (GSH) is a tripeptide that exists in every cell of the human body. Its function is complex and remains the subject of ongoing research, but in sum we know that it detoxifies the body and activates liver function, serves as an antioxidant, and removes free radicals from the body. It's also shown to beautify the skin, and help relieve muscle fatigue. We know as well that as the body ages, as it is exposed to toxins and pollutants from inside and out, and

as it is subject to physical illness and immune system deficiency, the volume of Glutathione maintained in the body decreases dramatically.

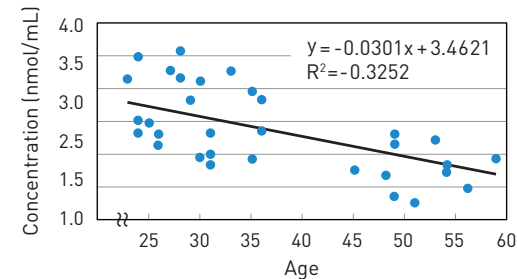
Effects of the exposure to free radicals and cell oxidation are regarded as leading signs of aging. In a very real sense, Glutathione works against aging throughout life, as it's been doing throughout human history.

### Glutathione Depleting Factors



Journal of Clinical Epidemiology 47: 1021-28 (1994)

### Total Glutathione Concentration in Plasma



KOHJIN Life Sciences, a GMP-approved factory, has been the largest provider of Glutathione in the world since 1968.

KOHJIN's high-quality Glutathione "OPITAC™" is the only ingredient of its kind to hold U.S. FDA-Notified FULL GRAS status (GRN #000293), is HALAL (MUI #00310028570304/JAKIM

#0100-01-147707) and KOSHER (KC #3721936-1) certified, and was the first to achieve JP & USP monograph designation.

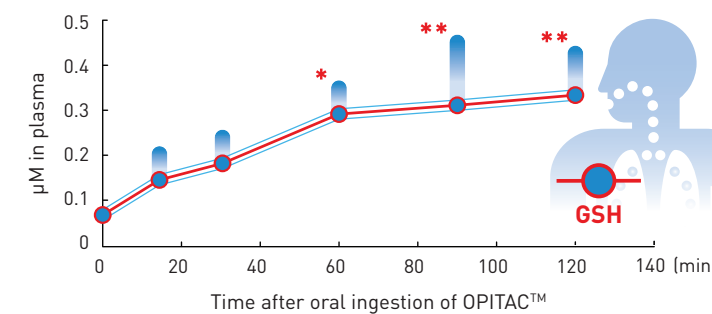


## Oral Supplementation: Clinically Proven Absorption

KOHJIN Life Sciences, a Mitsubishi Corporation Group Company, began its pioneering research on Glutathione nearly 50 years ago, first establishing it as an active pharmaceutical ingredient (API) for acute detoxification in Japan. Although users perceived clear benefits to other health aspects, scientists were unable to link the ingestion of OPITAC™ Glutathione to evidence that it could be increased in content and used by the body when taken orally, even with the analysis of the deproteinized fraction of blood plasma from human subjects.

Where prior research had failed to detect the Glutathione in blood serum, in 2013 KOHJIN researchers, in collaboration with a team from Kyoto Prefectural University and Kyoto University, found Glutathione in the protein-bound fraction of human plasma, and published their findings. In addition, animal models proved the presence of <sup>13</sup>C-labeled Glutathione in the liver at levels as high as 8~10% or more, in as little as two hours after oral administration.

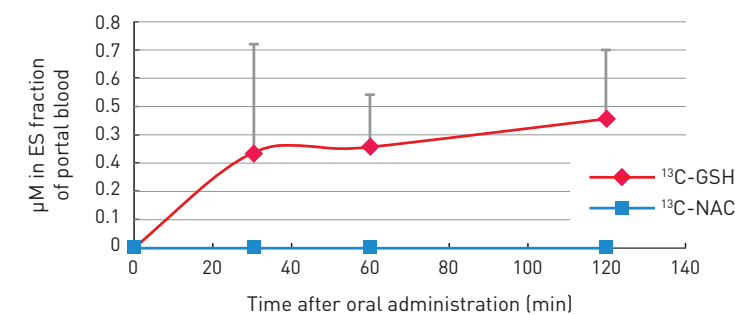
### OPITAC™ Oral Absorption



Contents of Glutathione (GSH) in the ethanol-precipitate fraction of plasma after oral ingestion of OPITAC™. "\*" and "\*\*\*" indicate significant difference from baseline, P < 5% and P < 1% respectively, as calculated using Scheffé's method post hoc.

Park et al, J. Agric. Food Chem (ACS). 62, 6183-6189 (2014)

### Glutathione (GSH) vs NAC Absorption



Glutathione concentration in portal and peripheral blood (rat) after oral administration of <sup>13</sup>C-Glutathione (<sup>13</sup>C-GSH) and <sup>13</sup>C-NAC, up to 120 minutes. In both samples <sup>13</sup>C-GSH was detected, but <sup>13</sup>C-NAC was not, suggesting that Glutathione was absorbed directly and intact, but NAC was converted by digestion to amino acids, etc.

K. Sato et al, ISNFF 2016. Session 14, O85 (2016)

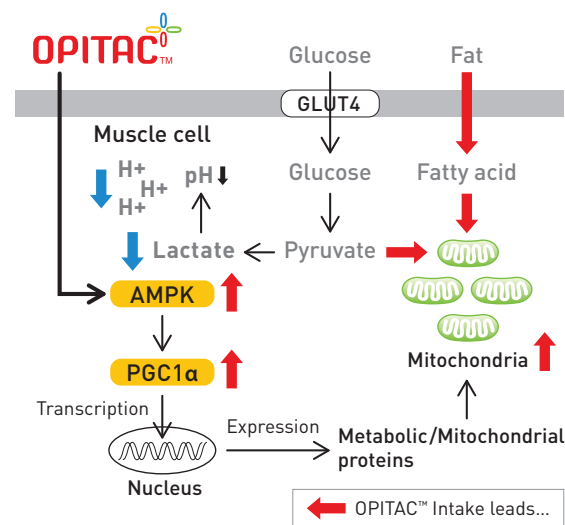
## Fitness and Lipid Metabolism (Mitochondria Biogenesis)

Because such popular sports as distance running and weight training are forms of self-induced stress, it became clear to KOHJIN's researchers that the same biochemical mechanisms that facilitate improved physical response to stressors would benefit athletes and all who aspire to athletic improvement.

KOHJIN, with assistance from Kyoto Prefectural University and Karolinska Institute, set out to map the mechanism by which OPITAC™ Glutathione led to improved conditioning against fatigue during vigorous physical activity. This

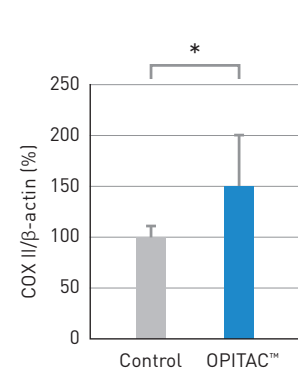
breakthrough came with a series of in vivo and human clinical studies that showed, for the first time, evidence of mitochondrial biogenesis resulting from the ingestion of OPITAC™. The study proved that daily oral administration of OPITAC™ resulted in enhancing aerobic metabolism, and Mitochondrial DNA expression in skeletal muscle, accelerating fatty acid utilization. The results made it clear that ingesting OPITAC™ improved lipid metabolism and acidification in muscle during exercise, which leads to increased lipid metabolism and decreased muscle fatigue (US Patent Pub. No. US2016/0158309 A1).

### OPITAC™ Increases Mitochondria Biogenesis



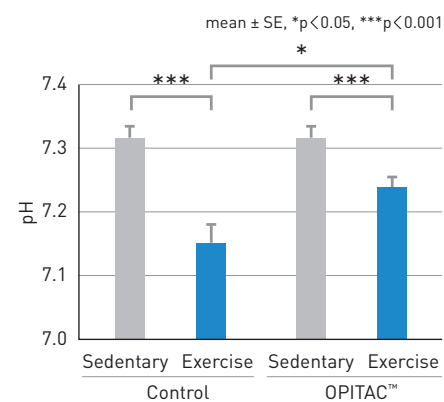
OPITAC™ supplementation improved lipid metabolism and acidification in skeletal muscles during exercise, leading to less muscle fatigue.

### Mitochondrial DNA



Daily oral administration of OPITAC™ resulted in AMP-activated kinase, PGC-1α gene, and Mitochondrial DNA expression, accelerating fatty acid utilization.

### Interstitial pH in Skeletal Muscle



OPITAC™ supplementation suppressed the steep decrease of pH level in skeletal muscle.

Aoi et al. Journal of the International Society of Sports Nutrition (2015)

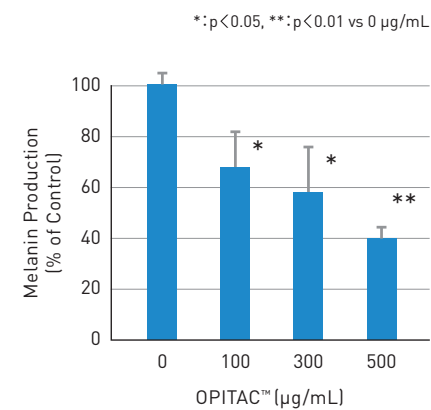
## Beauty from Within

The earliest known property of OPITAC™ Glutathione, the one that brought it to consumer attention, was its ability to make skin brighter, lighter, and generally improve its appearance. We now know that it achieves this by working in concert with the body's own natural functions. OPITAC™ inhibits the activity of tyrosinase, in turn, suppressing the development of eumelanin. At the same time, it disrupts the synthesis pathway of pheomelanin. This enhances protection against UV damage provided by topical skin care products (supplements and cosmetics) and reduces the appearance of dark areas. OPITAC™ makes skin appear healthier, suppler; achieved, in part, by accelerating the production of type I

collagen. The combination of OPITAC™ and collagen peptides results in a synergistic effect that even enhances the benefits of other antioxidants, such as vitamin C.

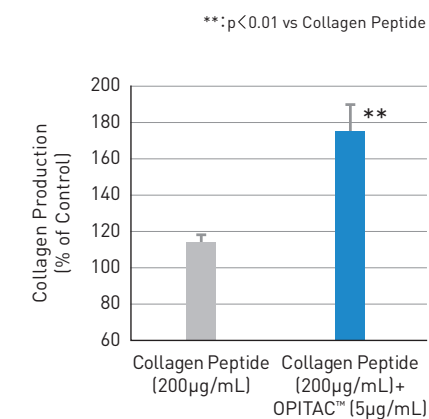
Unlike other, topical treatments, the mechanisms of those with OPITAC™ work at the molecular level, neutralizing free radicals in the system, scavenging heavy metals, and defending against environmental pollution. Today we have proof that daily intake of OPITAC™ renews this precious commodity throughout the system to infuse the skin's appearance with a youthful tone, helping maintain it as we age and our natural supply diminishes.

### Effect of Melanin Inhibition



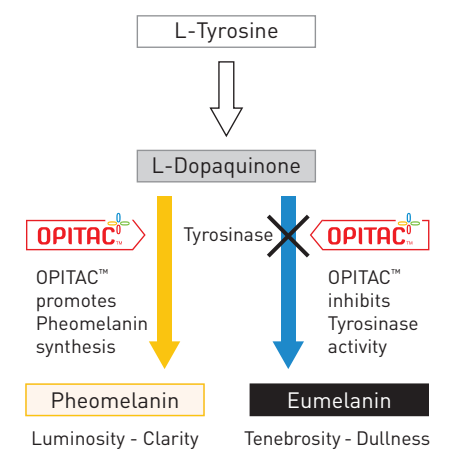
OPITAC™ can inhibit melanin production concentration-dependently (*in vitro*).

### Synergetic effect of OPITAC™ and Collagen



By adding a small portion of OPITAC™, collagen production by collagen peptide can be enhanced.

### The Biochemistry of Beautiful Skin



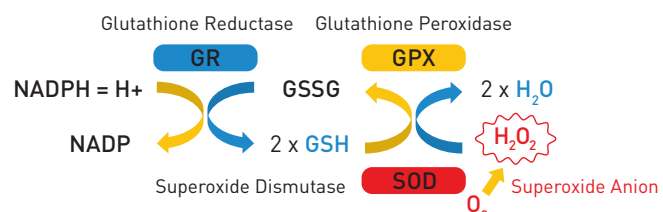
T. Nakagawa et al, New Food Indust. vol. 58 No. 10 (2016)

## Detoxification and Antioxidation

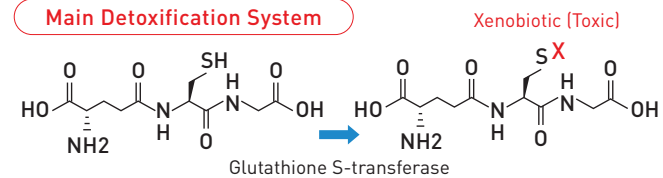
Glutathione has long been recognized and used worldwide as an antioxidant supplement. Through enzymatic reaction, OPITAC™ Glutathione scavenges the ROS (Reactive Oxygen Species). While research into its complex function continues, OPITAC™'s main role as an antioxidant has been corroborated, and decreasing Glutathione levels in cells has been shown to increase the risks of disease and toxicity.

It's known that every cell in the human body is subject to over 10,000 attacks by free radicals daily. Glutathione mediates the oxidation of cells at the mitochondrial level, and as measured using DPPH methodology, enhances the effects of other antioxidants synergistically. Oxidation can't be abated by dietary supplementation alone, but in studies, the antioxidant benefit of Vitamin C, for example, nearly doubles in combinatory effect with OPITAC™. So the addition of OPITAC™ improves the already antioxidant-rich diet that health-conscious consumers

### Glutathione's Antioxidant Capability



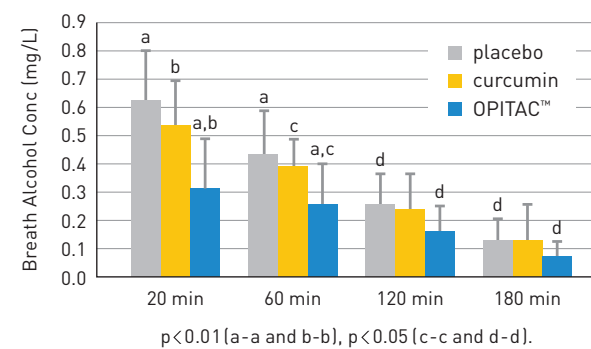
### Main Detoxification System



strive for, and the products they seek in that pursuit. The result is healthy, prolific cell life, resistance to aging, and protraction of the "glow of youth" that we experience early in our lives, before age takes its effect on Glutathione volumes in the body.

Early studies of whether oral ingestion of OPITAC™ helps improve liver condition and promote resistance to cell oxidation were subjectively-based. An in-house panel of male and female subjects imbibed a moderate, proportional amount of alcohol based on body weight. They were then administered either a placebo, curcumin (30 mg), or OPITAC™ (100 mg) and questioned at one-, two-, and three-hour intervals. Headache, heavy stomach, sleepiness, dizziness and other indications of lost sobriety appeared to diminish more rapidly and effectively in the OPITAC™ group. Clinical proof arrived in the concentration of alcohol in the subjects' exhalations — vastly lower than the control and curcumin in every measurement.

### Effects of Intake of Yeast Extract (100 mg as OPITAC™)



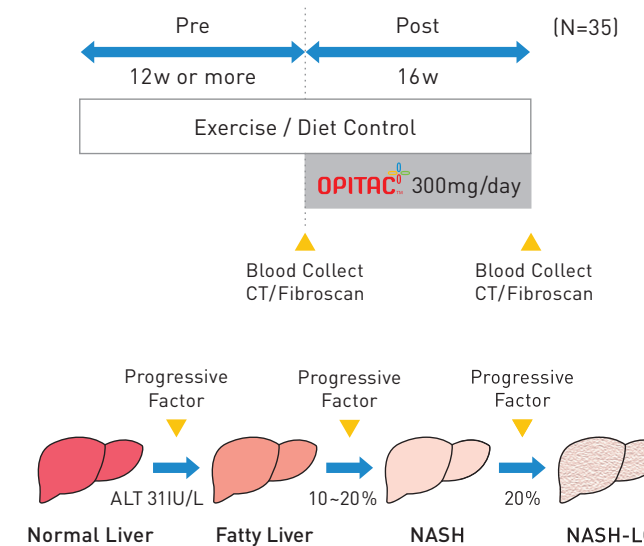
K. Nakano et al, Clinica Chimica Acta, vol. 19 (1968)  
 E. Ogawa et al, J. of Japan Accident Med Assoc, vol. 15-3 (1972)  
 N. Kudo, Japan Assoc of Rural Med, vol. 21-3 (1972)  
 Pharmaceutical Interview Form, Japan Standard Commodity No.873922 (2014)  
 N. Kaji et al, New Food Indust. vol. 58 No. 10 (2016)

## Liver Health (Fatty Liver)

It's an unfortunate fact that the morbidity rate due to fatty liver, especially nonalcoholic fatty liver (NAFL), is close to 25% in the Asia-Pacific region, and the number rises to nearly 30% in Europe and North America. NAFL can progress to nonalcoholic steatohepatitis (NASH), and is considered a hepatic manifestation of metabolic syndrome, which is related to obesity, hypertension, and oxidant stresses. No medication exists today to eradicate fatty liver, which makes monitoring liver parameters an especially significant gauge of personal health.

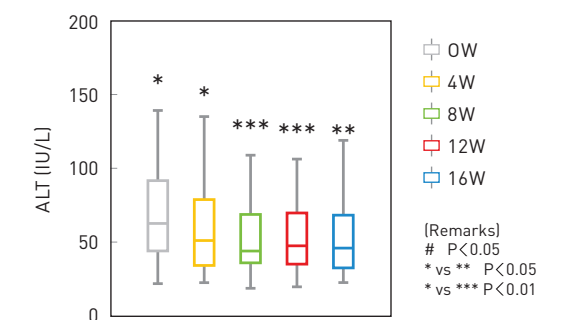
Adding to known proof that Glutathione serves to support the reduction of free radicals, clinical research undertaken by KOHJIN and Yokohama City University, a member of the Japan Study Group of Nonalcoholic Fatty Liver, proved – for the first time ever – that OPITAC™ Glutathione improved major clinical parameters of liver health (AST, ALT), lipid metabolism (FFA, VO2/VCO2), inflammation (Ferritin), and image-view observation (Fibroscan) significantly, after 16 weeks of OPITAC™ intake. (PCT Patent Pub. No. WO2016140237)

### Human Clinical Study (NAFL)



In our study, OPITAC™ Glutathione improved major clinical parameters and image-view observation significantly after 16 weeks OPITAC™ intake (WO2016140237, PCT/JP2016/056341).

### Results for Major Clinical Parameters and Image-View Observation



Variable	Pre (n=29)	Post (n=29)	P value
ALT (IU/L)	69.0 ± 36.1	58.0 ± 33.5	p<0.0455#
Ferritin (ng/mL)	219.8 ± 150.8	196.7 ± 141.2	p<0.0435#
Triglyceride (mg/dL)	195.2 ± 135.9	163.6 ± 122.0	p<0.0134#
Free fatty acid (μEq/L)	651.1 ± 242.5	533.5 ± 209.7	p<0.0231#
Fibroscan (based on CAP)	295.7 ± 44.9	285.4 ± 48.8	p<0.0240#

(After 16 weeks of OPITAC™ intake)

T. Kessoku et al. EASL LiverTree™, Apr 15, 2016; 125734