L-Ergo™

- **Product Description**
  - L-Ergo™ is synthetically derived l-ergothioneine, a ubiquitous, naturally occurring, sulfur-containing intracellular antioxidant found in most plants and animals.

- **Classification**
  - Natural Product
  - Chemical class: 2-thio-imidazole, amino acid.

- **Source**
  - Naturally biosynthesized by fungi and mycobacterium in the soil, subsequently assimilated by plant roots.
  - Cannot be synthesized by animal species, historically available only from dietary sources.
  - Commercial availability:
    - Microbiological route, (Miyoshi et al, 1968)[1]: low yield and purity.
    - OXIS' chemical route, (patent # 5,438,151)[2]: high yield and purity.

- **Properties**
  - 98 % pure, white crystalline solid.
  - Water soluble (Solubility limit of 0.9M at Room Temp.)
  - Does not auto-oxidize at physiological pH. Also very stable to strong alkali conditions.

- **Biochemical Activity**
  - Potent antioxidant[3,4]
    - Directly scavenges reactive oxygen species.
    - Activates key antioxidant enzymes.
    - Chelates metallic cations.

  - Metabolic regulation
    - Stimulates RBC energy production.
    - Stimulates normal respiratory energy production.

- **Potential Applications**
  - Dietary / Food supplement.
  - Dermal Protectant - Sunscreens/protective cosmetics.
  - Ophthalmic -Topical, replenish loss during cataract development.
  - Organ preservation - increase viability of organs used in transplants.

- **Safety/Toxicity Data**
  - Acute Toxicity (OXIS 1997)[5]:
    - Adult male rats single dosed at 62.5, 125, 250 and 500mg/kg. Followed 14 days.
  - Chronic Toxicity (OXIS,1997)[6]:
    - Dosed once a day at 50 and 200mg/kg for 14 days
  - Results:
    - No signs of toxicity as measured by mortality, clinical observation, variation in body weight or hematological and biochemical parameters. Further studies in progress.

- **Proprietary Position**
  - U.S. Patent #5,438,151 is a process patent for the synthesis of pure l-(+)-ergothioneine. Issued August, 1995. Patent Assignee, OXIS International, Inc.

Selected Research Findings Concerning Tissue Distribution

- ❖ Preferentially distributed to organ systems exposed to a high degree of oxidative stress.
- ❖ Aggressively conserved in RBCs, cataract-free lens, seminal fluid, kidney and liver.

Table I: Concentrations of l-ergothioneine in various animal tissues[7].

Tissue	Rat	Rabbit	Dog	Cat
Liver	13.3	0.3	0.9	2.7
RBC	10.4	10	6.6	2.9
Kidney	4.3	0.3	1.6	3.1
Heart	1.5	2.7	8.9	0.0
Lungs	1.5	0.3	0.6	0.8
Spleen	1.1	1.0	1.1	-
Testes	0.0	0.1	0.0	0.0

Values expressed as mgs/100g fresh tissue.

Table II: Blood concentration of l-ergothioneine in various animals.

Species	Ergothioneine Concentration
Man	1-4
Rat	1-6
Rabbit	1-10
Guinea Pig	1-4
Cat	0.5-2
Dog	3-6
Ox	0.5-2
Pig	3-27
Sheep	2-6
Fowl	2-10

Values expressed as mgs/100ml blood.

Table III: Human eye lens l-ergothioneine as a function of cataract development[8].

Stage of Cataract	L-ergothioneine concentration	Number of Samples
Normal	115.7 ± 6.3	10
Immature Nuclear	94.2 ± 7.3	20
Immature Cortical	79.4 ± 11.7	20
Mature	71.7 ± 13.7	50
Hypermature	60.8 ± 9.8	25

References:

[1] Miyoshi T, Sakai H. L-ergothioneine by microbial fermentation. IP patent 1968, number 450623 2

[2] Yadan JC, Xu I., US Patent 5,438,151, 1995. Assignee: Oxis International

[3] Hartrnan, PE. L-ergothioneine as antioxidant. Meth Enzy 1990; 186:310-318.

[4] Akanmu D. et al. The antioxidant action of 1-ergothioneine. Arch Biochem Biophys 1991; 288: 10-16.

[5] Oxis Final Report, Preliminary toxicity study of ergothioneine/single dose study, June, 1997

[6] Oxis Final Report, Preliminary toxicity study of ergothioneine/14 day study, June, 1997.

[7] Melville D.B. l-ergothioneine . Vitam. & Hormone., 17:155-204. 1958.

[8] Shukla Y., Kulshrestha, O.P., and Khuteta K.P., L-ergothioneine content in normal and senile human cataractous lenses. Ind. J. Med Res., 73:472-473, 1981.

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