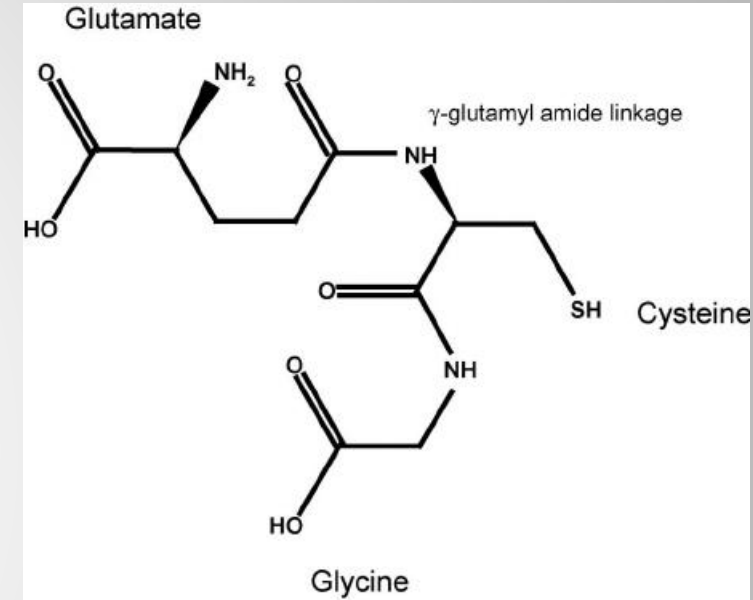
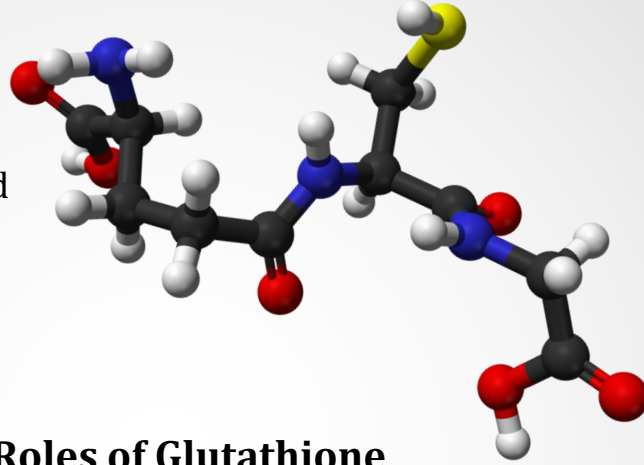


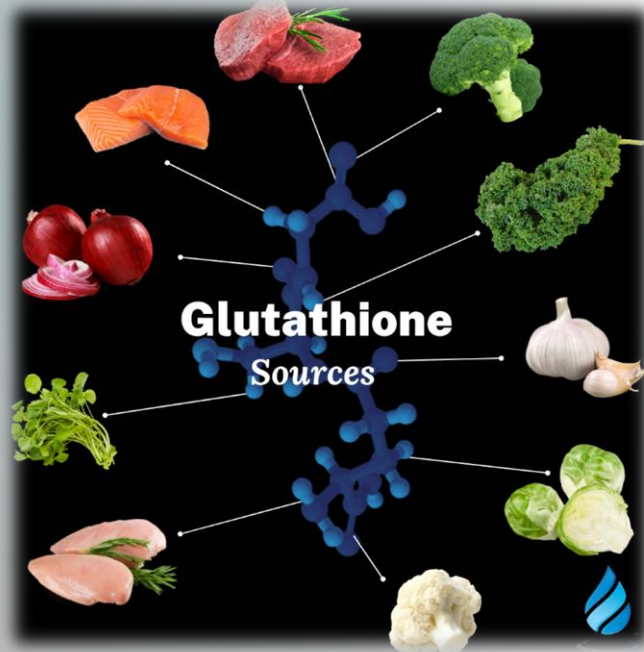
Lipokon™ glutathione (L- Glutathione)

- Glutathione is a powerful antioxidant naturally found in our cells. It's made up of three amino acids: glutamine, cysteine, and glycine.
- Its primary role is to protect cells from oxidative stress and damage by neutralizing free radicals.
- Helps in detoxification, supports immune function, and is crucial for various metabolic processes.



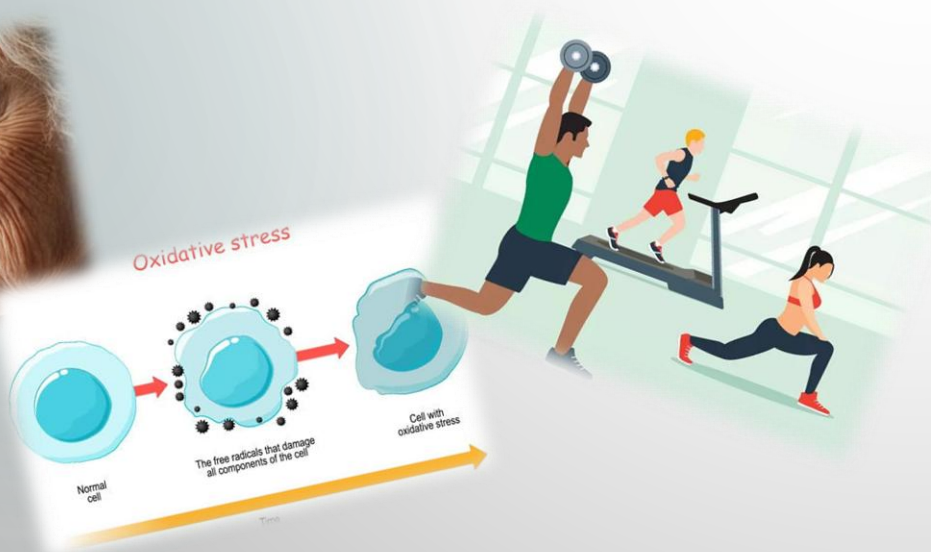
Critical Roles of Glutathione

- Cofactor for several antioxidant enzymes
- Regeneration of vitamins C and E
- Regulation of cellular proliferation and apoptosis (Useful in Anticancer treatment)
- Vital to mitochondrial function and maintenance of mitochondrial DNA (mt-dna)
- Acts as a detoxifying agent
- Helps with the metabolism of nutrients and keeps the immune system working properly



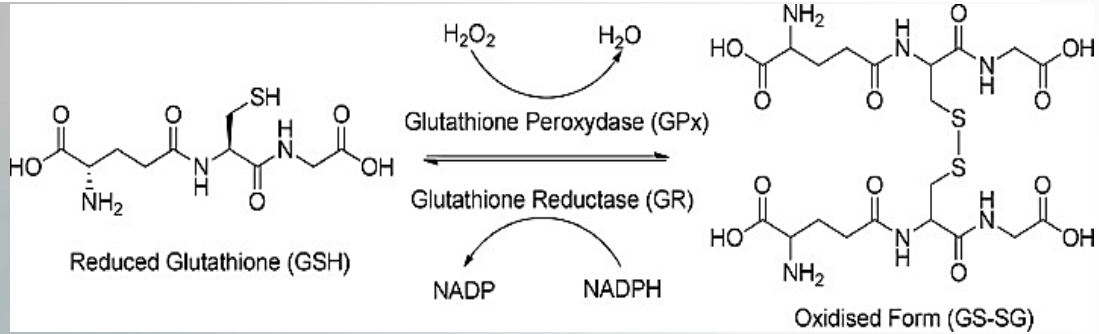
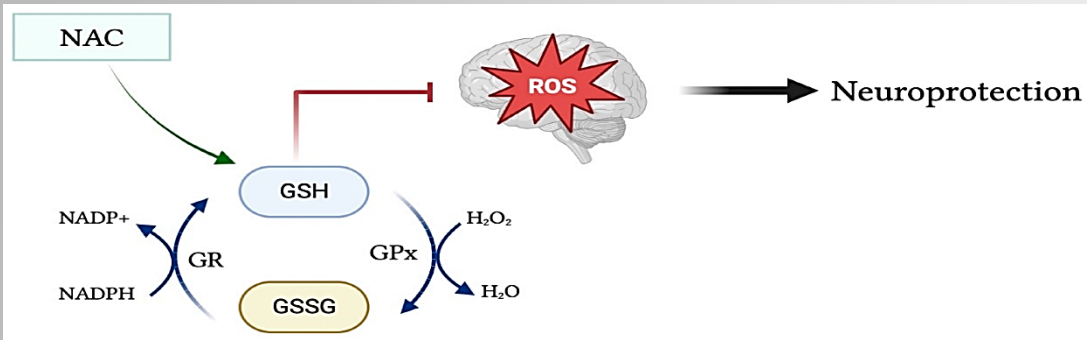
❖ **Factors that can affect glutathione levels:**

- **Aging:** As we age, glutathione levels tend to naturally decrease, which can contribute to oxidative damage and age-related diseases.
- **Oxidative Stress:** Chronic stress, exposure to toxins and certain illnesses can deplete glutathione levels.
- **Chronic Diseases:** Conditions like liver disease, diabetes, and autoimmune disorders can lower glutathione levels in the body.
- **Exercise:** Moderate physical activity can help increase glutathione levels, while intense or overexertion might lead to depletion.



❖ **How to boost glutathione levels:**

- **Diet:** Consuming foods rich in sulphur (like garlic, onions, and cruciferous vegetables) can help boost glutathione production.
- **Supplements:** Oral glutathione is debated in terms of absorption efficiency. Some people use precursor supplements like **N-acetyl cysteine (NAC)** or **alpha-lipoic acid**, which support the body's ability to produce glutathione naturally.
- **Lifestyle:** Reducing alcohol consumption, avoiding toxins, managing stress, and maintaining regular exercise can all support healthy glutathione levels.



- **Regeneration of Other Antioxidants:** Regenerate other antioxidants like vitamins C and E, enhancing the body's overall antioxidant defense.
- **Immune Support:** Supports immune function by maintaining the activity of white blood cells and modulating immune responses.
- **Enzyme Activation:** Activating enzymes, such as glutathione peroxidase, which further helps in neutralizing harmful compounds in the body.

❖ Mechanism of action (MOA)

A **strong antioxidant** and its involvement in various metabolic processes:

- **Antioxidant Defense:** Glutathione neutralizes free radicals and reactive oxygen species (ROS), preventing oxidative damage to cells, proteins, lipids, and DNA. This helps protect against inflammation and cellular aging.

Antioxidant support

Glutathione may help support the body's ability to manage the oxidative stress of cells. It may also improve the activity of other antioxidants such as vitamins C & E.

Heart health support

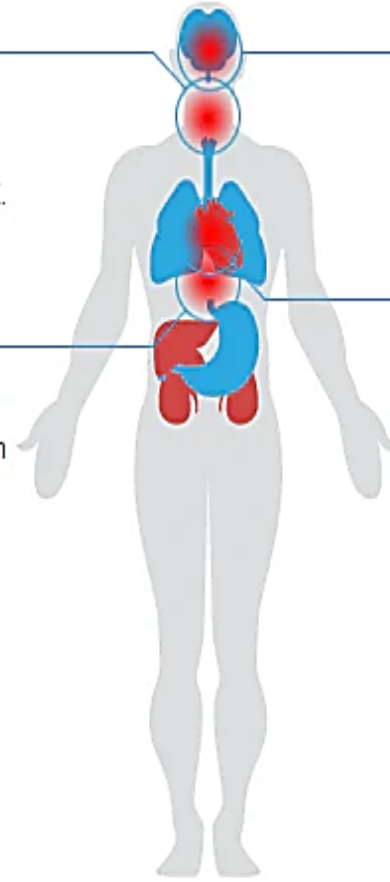
Glutathione may help support a healthy cardiovascular system, especially with respect to healthy circulation and maintain a healthy cholesterol profile.

Age support

Glutathione may also help maintain various systems as you age, including the eyes and skin.

Immune health support

Studies show that adequate glutathione levels in the lymphoid cells help support the immune system to function at its best. Lymphoid cells produce antibodies that destroy cellular invaders such as bacteria and viruses.



❖ Intake and Dosage:

- **Oral Supplements**

Standard Dosage: 250–500 mg per day.

Absorption Consideration: Oral glutathione may not be efficiently absorbed by the body. To enhance its effectiveness, many people take **N-acetyl cysteine (NAC)** alongside glutathione, as they help boost the body's natural production of glutathione.

- **Intravenous (IV) Glutathione**

Common Dosage: 600–1,000 mg per session.

Frequency: Typically administered 1–2 times per week, depending on individual health needs.

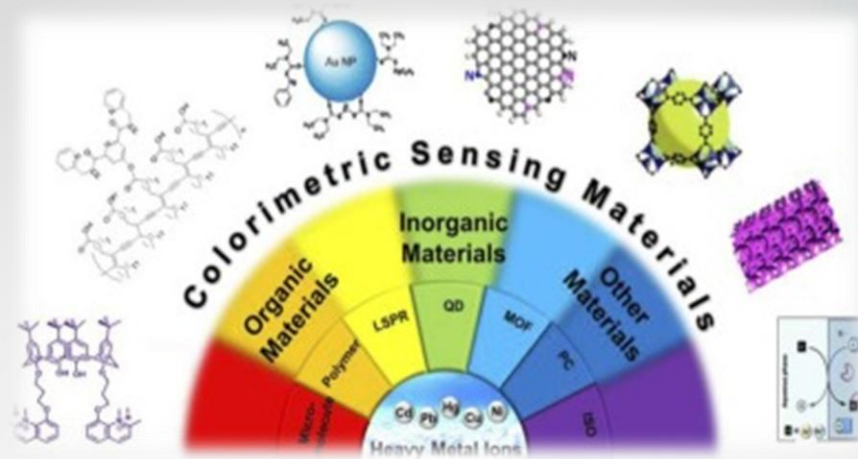
IV administration allows for higher bioavailability since it bypasses the digestive system.

- **Topical Glutathione**

Creams or serums containing glutathione can be applied directly to the skin.

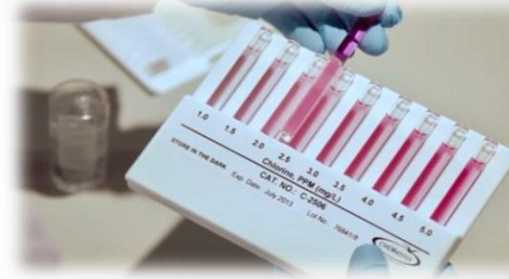
The effectiveness of topical applications, especially for skin lightening, may vary, but some formulations contain 1-2% glutathione.





❖ Lipokon™ Glutathione

- **Appearance:** Off-white powder.
- **Particle Size:** < 200 nm.
- **Glutathione Content:** At least 50% L-Glutathione.
- **Solubility:** Naturally hydrophilic (water-soluble).
- **Active Form:** The "L" isomer is the most biologically active form.
- **Study:** Comparative Cell Permeability Study of Lipokon Liposomal Reduced Glutathione (L – Reduced Glutathione) with Reduced Glutathione (GSH).
- In the context of cell permeability, we observed ability of glutathione pass through cell membranes. This was important for understanding its physiological functions and how alterations in cell permeability may impact cellular health.
- **Method:** Colorimetric Assay for Determination of Concentration of Glutathione in Cell.
- In colorimetric assays, **optical density (OD)** is used to measure the intensity of color produced by a chemical reaction. The higher the OD, the greater the concentration of the target substance. OD is directly related to the amount of light absorbed by the sample, which is influenced by the color intensity, indicating the presence and concentration of the analyte.



L-Glutathione Powder

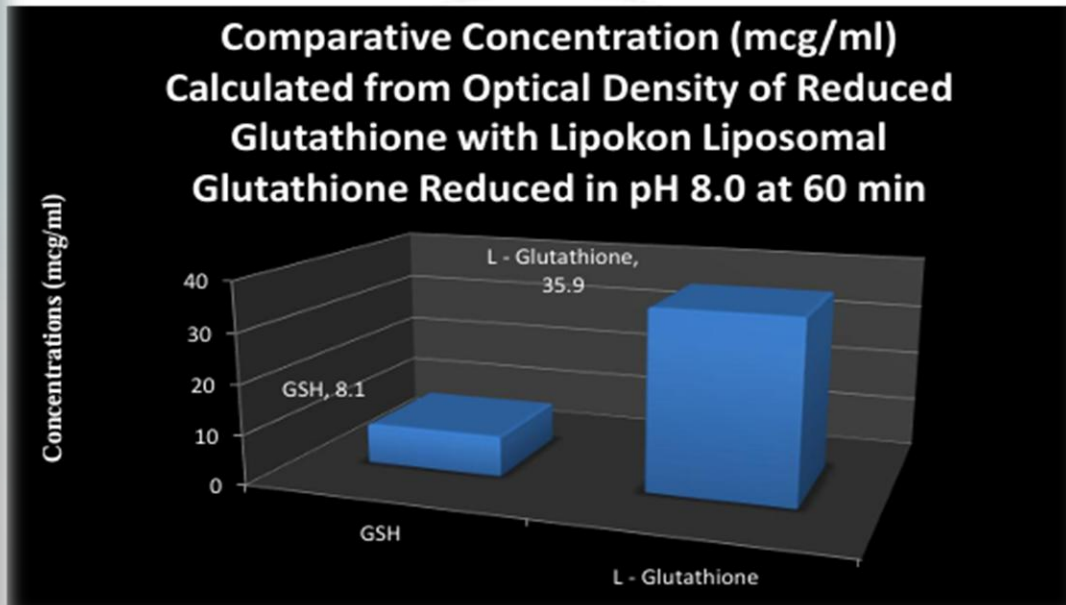


- **Measurement Using Colorimeter:** A colorimeter measured absorbance at 412 nm to determine glutathione concentration, with higher absorbance indicating greater levels of glutathione.
- **Cell Permeability Aspect:** The colorimetric assay on cells exposed to varying conditions (pH, concentrations, and sodium azide) showed how changes in cell membrane permeability impacted glutathione uptake and release.
- In a cell permeability study, the OD of a substance measured by a colorimeter reflects its concentration or the extent to which it absorbs light at a specific wavelength. The optical density of L-GSH was observed to be greater than that of reduced glutathione (GSH).
- Liposomal formulations enhance the permeability of bioactive substances, improving glutathione delivery and stability in cells. They may increase glutathione uptake, leading to higher OD due to greater accumulation. Additionally, liposomes protect glutathione from degradation or oxidation, ensuring a more stable form and contributing to higher OD readings.
- The lower OD of L-GSH and reduced glutathione (GSH) with sodium azide, compared to without, can be attributed to sodium azide's impact on cell metabolism and transport. By inhibiting mitochondrial respiration and blocking cytochrome c oxidase, sodium azide reduces ATP production, which in turn disrupts energy-dependent processes like active transport and endocytosis.
- Sodium azide may also affect cell membrane permeability and transporter function, crucial for glutathione uptake. By inhibiting ATP production, sodium azide reduces the activity of transporters like ABC transporters, limiting glutathione influx. This leads to less glutathione in the cells, resulting in lower optical density.

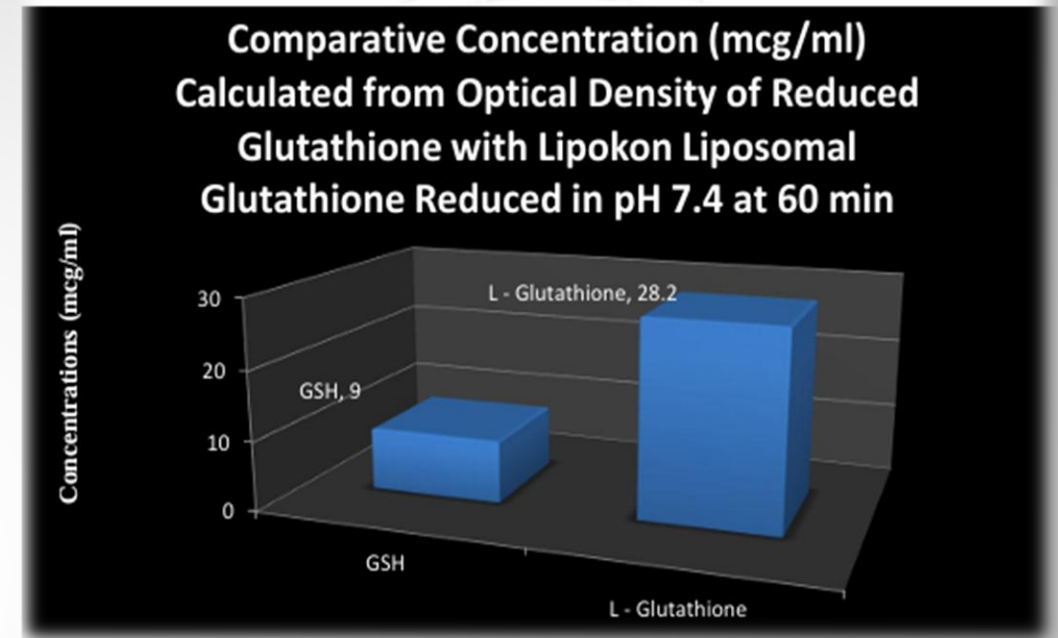
Concentrations (mcg/ml)	Optical Density
0	0
1	0.017
5	0.2
10	0.42
20	0.91
40	2

- At pH 7.4, which is near physiological pH, liposomal reduced glutathione shows significantly higher cell permeability than free reduced glutathione.
- Free GSH is hydrophilic and has limited ability to cross the lipid membrane, leading to a lower intracellular concentration.
- Liposomal GSH, being encapsulated in liposomes, benefits from the liposome's ability to fuse with the cell membrane or undergo endocytosis, allowing for enhanced delivery and uptake of GSH into the cell, resulting in a higher concentration.

Comparative Bar Graph of Reduced glutathione with Lipokon Glutathione Reduced



Comparative Bar Graph of Reduced glutathione with Lipokon Glutathione Reduced



- The significant difference in cell permeability between liposomal glutathione reduced (L-GSH) and reduced glutathione (GSH) at pH 8.0 after 60 minutes can be explained by a combination of factors related to the formulation of liposomal glutathione, physiological conditions, and the mechanisms of cellular uptake.
- **Conclusion:** Liposomal encapsulation significantly improves the cell permeability of reduced glutathione, especially at higher pH values (7.4 and 8.0). This suggests that liposomal glutathione may be a more effective delivery method, particularly in higher pH environments. These findings are important for therapeutic applications that require enhanced intracellular glutathione delivery, such as antioxidant treatments, detoxification, and cellular health support.

