### What is glutathione and why is it important?

**Glutathione** is an important **antioxidant** in our body and acts to **detoxify** metabolic products including pollutants, heavy metals, and **drugs**. It is a water-soluble tripeptide made up of the amino acids' glutamine, cysteine, and glycine, acting as a storage and transport form of cysteine. Sulphur amino acids, i.e., cysteine and methionine (which can be converted to cysteine via the cystathionine pathway in the liver), are essential components for glutathione synthesis as cysteine availability is recognised as the rate limiting step in glutathione production. A shortage of cysteine appears to limit the absolute synthesis rate of glutathione.

In the absence of glutathione, numerous oxidative and nitrosative **free radicals** (ROS) persist, which can lead to **damage** to mitochondrial function, the lipid membranes of **cells** (lipid peroxidation) and **DNA**. As damaging processes continue, cellular changes can alter messaging and physiological function, increasing the risk of **metabolic disease**, **environmental toxicity**, and physiological **aging**. There are no research data to date demonstrating prevention of disease, but observational studies suggest **increased dietary glutathione may reduce risk of acute and chronic disease**.

**Glutathione** thus forms an important **line of defence**, **protecting** the body as part of the biotransformation and elimination system, by **conjugating** a toxic molecule so the body can expel it. This means the **liver** attaches another molecule to the toxin, **modulating** it to make it **less harmful**. The body is then able to eliminate the toxin either from the liver via **bile** as a **faecal metabolite**, or to the **kidney** where it is excreted in **urine**.

Paracetamol detoxification may deplete stores of glutathione by 90%.

Doi: 10.1046/j.13652710.2003.00493.x.

The mechanism of glutathione conjugation is **catalysed** by an **enzyme** which activates the sulfhydryl group, the part of the molecule which can bind to another. The glutathione catalysts are ubiquitous and seem to fulfil very important functions. They are different in every tissue and cell type, such as in the brain, testes, lung, liver, and kidneys.

Glutathione therefore is a substrate, used by specific enzymes to exert antioxidant effects. In response to oxidative and nitrosative stress, within the reversible S-glutathionylation cycle, it can regulate protein structure/ function and elicit adaptive responses or trigger cellular death.

Glutathione isn't lost from the body as it gets **recycled**, but it can get **depleted** and run down. We replace components of glutathione such as **cysteine** in the **diet**, by consuming whey protein for example, but **supplementing glutathione with bioavailable GlutathioneMax means we always have adequate stores**.



Choline Bitartrate 4000mg
Setria® Glutathione 200mg
S-Acetyl Glutathione 200mg

# The role of glutathione in detoxification, inflammation, and so much more!

Along with the suggested **detoxifying**, **mitochondrial functioning** and **healthy aging** benefits of **glutathione** are the more specific uses. The role of glutathione in **health** cannot be taken lightly and depletion has been indicated in hepatocyte stress pathways leading to **inflammation** and **non-alcoholic fatty liver disease**.

Glutathione and Non-alcoholic fatty liver disease (NAFLD)

**NAFLD** is a term given to a group of conditions in which a build-up of excess liver fat is not caused by heavy alcohol consumption. It may also be termed metabolic associated fatty liver disease (MAFLD) (as it is common among obese individuals or those with metabolic syndrome (obesity and high blood pressure). Left untreated it can exacerbate to non-alcoholic steatohepatitis (NASH). There is a strong association with elevated alanine transaminase (ALT) and NAFLD. In the nationwide 2012 AusDiab Study researching obesity and lifestyle, 4,747 Australian's aged 34-97 years, elevated ALT was highly correlated with MAFLD and a risk for advanced fibrosis.

Doi: 10.1038/s41598-022-05168-0.

High levels of fat in the liver increase the risk of further health problems, such as **diabetes**, **high blood pressure** and **kidney disease**.

**Oral glutathione** has been shown to **reduce triglyceride** and non-esterified fatty acids (**NEFA**), inducers of inflammatory responses and liver fat accumulation. Thirty-four NAFLD patients received 300 mg/ day oral glutathione for 4 months. Along with improvements in lifestyle habits, ALT significantly reduced.

Doi: 10.1186/s12876-017-0652-3.

Increases in **ferratin** and body iron stores are common in NAFLD. Ferratin and iron can lead to the development of **NAFLD** through **oxidative stress** and oral glutathione has reduced ferratin in this condition. Other than suggestions of reducing oxidative stress, the mechanism remains unclear.

Research looking at the use of bioavailable oral glutathione for the treatment of non-alcoholic fatty liver disease (**NAFLD**), showed the amount of glutathione bound to red blood cells increased **1-2 hours** after ingestion, suggesting its' rapid **absorption into the blood** and increased protein-bound glutathione levels in the **liver**.

You are at increased risk of NAFLD if you:

- are obese or overweight
- have type 2 diabetes
- are insulin resistant
- have an underactive thyroid
- have high blood pressure
- have high cholesterol
- have metabolic disease (high blood pressure and insulin resistance)
- have binge eating disorder
- smoke

Doi: <u>10.1016/s0009-2797(00)00214-3</u>.

Doi: <u>10.1186/s12876-107-0652-3</u>.

Doi: 10.1021/jf501338z.

Doi: 10.1080/15216540701196944.

Doi: 10.20524/aog.2017.0200.

Accumulation of liver fat can result from **choline deficiency**. The build-up of lipid may cause oxidative stress and inflammatory processes leading to NAFLD and NASH.

# Glutathione and the cardiovascular system

Glutathione plays an important role in the prevention of cardiovascular disease. In the vasculature, cellular redox is maintained by antioxidants and antioxidant enzymes to prevent the build-up of excess and damaging ROS. ROS decrease the amount of nitric oxide and cause the loss of endothelial function. Accumulation of ROS can cause polymorphism, an alteration, in the antioxidant enzymes, making them unable to perform their task. Vessel wall oxidant stress can lead to dysfunction, hypertension, and atherosclerosis (coronary artery disease). The glutathione peroxidase polymorphisms increase the risk of stroke. Polymorphisms to glutathione S-transferase increase the risk of coronary heart disease. The damages are due to the oxidising effects on proteins, lipids, and DNA.

Doi: 10.1161/01.ATV0000163846.51473.09.

Doi: 10.3390/antiox10081220.

#### Glutathione in high blood sugar and uncontrolled diabetes

Just as high oxidative stress and cellular damage may lead to metabolic diseases, long-term high blood sugar can lower levels of glutathione. The outcome being increased oxidative stress and cellular damage. Yup, it's one of those vicious circles. It was found increasing glutathione levels reduced oxidative stress and tissue damage in people with high blood sugar and uncontrolled diabetes.

Doi: 10.2337/dc10-1006.

#### Glutathione and autoimmune disease

**Glutathione** may potentiate **nitric oxide signalling, improving circulation**. A study assessed the reduction of pain in patients with peripheral artery disease. Glutathione increased the distance the participants were able to walk pain-free.

It has also been suggested glutathione may help reduce chronic inflammation caused by autoimmune diseases such as rheumatoid arthritis, celiac disease, and lupus. The reduction of oxidative stress and interaction with the **immune system** controlling **inflammation**.

Doi: 10.1016/j.autrev.2009.02.020.

### Glutathione and autism

Autism spectrum disorders is associated with higher levels of oxidative damage and lower levels of glutathione. An 8-week trial using oral and transdermal glutathione

supplements in children 3-13 years, improved al metabolites of the transsulfuration pathway, taurine, sulfate, and cysteine. Cysteine being the limiting substrate for glutathione production. The group receiving **oral glutathione increased plasma glutathione**.

Doi: 10.12659/MSM.882125.

# Glutathione and acne vulgaris

**Reduced levels of glutathione** have been found in the stratum corneum, the outermost layer of the epidermis (skin) of people with **acne vulgaris**. Research has reported oxidative stress components (ROS) or lipid peroxide (reduced cell membrane fluidity as a result of ROS) are involved in the process. It is thought the role of glutathione as an **antioxidant** and **anti-microbial** in combination with nitric oxide, increasing **microcirculatory function**, may be beneficial in the treatment of skin disorders.

Doi: <u>10.1111/j.1473-2165.2011.00570x</u>.

### What does GlutathioneMax contain?

### Choline Bitartrate 4000 mg

Choline bitartrate is the simplest form of choline and reliably increases liver concentrations and systemic trimethylglycine levels (TMG). TMG is known as a betaine molecule which acts as a methyl donor, necessary to accelerate or preserve body reactions for metabolic 'maintenance'. It reduces blood homocysteine concentration, which may be increased in metabolic syndrome. Choline is necessary for cell-membrane structure and signalling and lipid transport. Choline deficiency can result in NAFLD. Researchers fed choline to mice with altered cholesterol metabolism and high-fat diet. Cholesterol transport was increased, NAFLD was prevented, and liver function was improved.

Choline is important for canaliculus membrane integrity and biliary processes. Due to progressive inflammatory and fibrosing processes in the liver, cells can become damaged around the bile ducts, tubes which move bile from the liver to the small intestine. This bile excretion failure or bile transport failure is termed cholestasis. Researchers supplemented choline in mice on a high-fat diet. Choline prevented and reversed the development of high-fat diet induced cholestasis.

Doi: <u>10.3945/jn.113.185389</u>. Doi: <u>10.1002/hep4.1302</u>.

# Setria® Glutathione 200 mg

A 6-month randomised trial of Setria® glutathione was evaluated in 54 non-smoking participants. Blood glutathione levels were found to increase after 1, 3 and 6 months for doses of 250 or 1,000 mg/ day compared to placebo.

Doi: 10.1007/s00394-014-0706-z.

Setria® glutathione was found to prevent the oxidative reduction of nitric oxide in a study supplementing L-citrulline and/ or Setria® glutathione in humans and in mice.

Doi: <u>10.1186/s12970-015-0086-7.ecollection2015</u>.

### S-Acetyl Glutathione 200 mg

Oral administration of glutathione has low bioavailability. S-Acetyl-glutathione (SAG) is a glutathione precursor which is more stable in plasma and is taken up directly by cells and later converted to glutathione. In 18 healthy individuals, a study compared plasma levels of glutathione 24 hours after oral supplementation with SAG or glutathione. Rate and extent of SAG in plasma was higher than glutathione after a single dose.

Doi: 10.15344/2456-8171/2018/134.

Research has found SAG more lipophilic than plain glutathione, it's more stable in blood plasma and it enters the cells directly, increasing uptake rate.

In a study comparing 7 days/ 200 mg SAG with IV 1400 mg single dose, oral SAG compared favourably to IV administered glutathione.

#### **GlutathioneMax** best use tips:

Strom's GlutathioneMax is a well dosed formulation, and we suggest trying the product with 1 full serving once a day. It has a potent antioxidant effect so may be best taken before or away from exercise to maximise the adaptative responses to training.

It works well on its own, The Blood Lab can give testimonials, but it also stacks well with NAC, GlycoMax and ZMax, and SupportMaxNeuro.

Considering glutathione is involved in the elimination of harmful substances that induce a state of oxidative stress, it is highly relevant glutathione homeostasis is maintained.

One strategy to reduce glutathione depletion is to reduce oxidative stress by reducing toxic load. For most people, this isn't a realistic option! Another is to directly supplement bioavailable glutathione.

The use of performance enhancing drugs induces high levels of oxidative stress.

Prevention is better than cure so don't wait for raised ALT to begin. Daily supplementation with <u>orally bioavailable GlutathioneMax</u> can help to ensure your adequate glutathione stores.

To LEARN more about STROM or for more information on their products visit their YOUTUBE or STROMUCATION.COM education site.

If you have any further questions, please don't hesitate to ask!