

# Ovothiols for the treatment of chronic low-grade systemic inflammation (CLGSI) and related diseases



## Abstract

The patent concerns the use of histidine amino acid derivatives, referred to as ovothiols, for the treatment of Chronic Low Grade Systemic Inflammation (CLGSI) and related diseases, such as, i.e., cardiovascular diseases, auto-immune diseases, chronic degenerative diseases, obesity, diabetes, hypertension, osteoporosis, respiratory diseases and polycystic ovary syndrome.

## State of the art

Diseases associated with oxidative stress linked to cardio- and cerebrovascular diseases are currently receiving particular attention. Among these, the most widespread is diabetes mellitus, which is associated with the establishment of plasma oxidative stress and chronic vascular inflammation, which are the main alterations underlying the development of diabetes-associated cardiovascular diseases. In particular, endothelial dysfunction is the main cause of the development of cardiovascular diseases and is linked to increased expression of endothelial adhesion molecules and monocyte infiltration in the intima, two events that are crucial in promoting atherosclerosis. The search for new active ingredients of natural origin that can be used as food supplements to prevent the onset of inflammatory diseases and as medicines to treat the same diseases is particularly innovative.

## Invention Description

It is shown that ovothiol is assimilated by endothelial cells and acts on the endogenous mechanism of inflammation, which is regulated mainly by inflammatory cytokines. In particular, we show that the pathway triggered by the inflammatory cytokine  $TNF\alpha$  is inhibited by incubation with ovothiol in endothelial cultures derived from the umbilical cord of women with gestational diabetes.

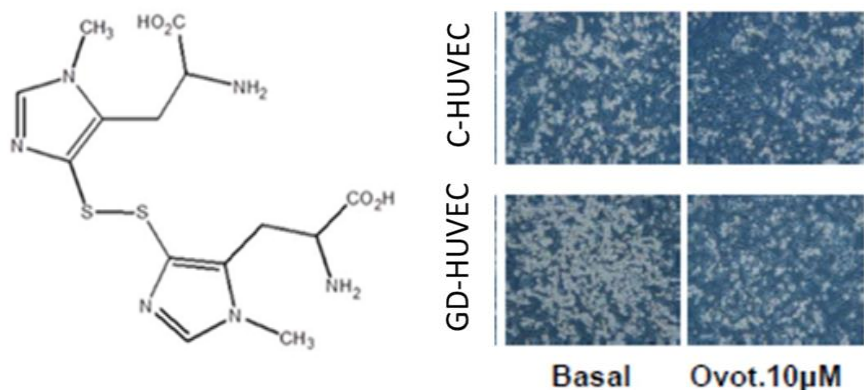


Figure 1 - The adhesion of monocytes to endothelial cells

As an example, the figure shows the adhesion of monocytes to endothelial cells in healthy pregnant women (C-HUVEC) and pregnant women with gestational diabetes (GD-HUVEC). The adhesion of monocytes to vessel endothelium is a process that occurs during the formation of atherosclerotic plaques, which can cause heart attacks and strokes. Treatment with ovothiols reduces the adhesion of monocytes to vessel endothelium, thus having a protective and anti-atherosclerotic effect.

## Industrial Property

Entry into national phases of PCT/IB2018/057098:

- European Patent application filing No. 18782202.8
- Patent application filing in China no. 2018800606770

Italian patent granted with no. 02017000104529 filed on 19/09/2017

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## Advantages

The advantages of this patent are the following:

- ovothiols are a class of natural products currently extracted and purified from sea urchin eggs (fig. 2);
- no toxic side-effects – the use of ovothiols allows for the reduction of inflammation associated with several conditions for which market drugs often prove to be damaging over time.
- High antioxidant and anti-inflammatory effect at low dosages - the concentrations of ovothiol (10-50  $\mu\text{M}$ ) are lower than those of other drugs used for diabetes, such as lipoic acid (100-200  $\mu\text{M}$ ) and comparable to those of carotenoids often used as supplements in the diet.

## Applications

This patent finds application in the following areas:

- scientific research;
- pharmaceutical sector - for the use of these compounds as medicaments for the treatment of diseases associated with CLGSI ;
- nutraceutical sector - as food supplements in the prevention of the onset of inflammatory diseases.

The importance of the invention is due to the fact that the pharmaceutical and nutraceutical sectors are pushing for more effective and side-effect-free active ingredients of natural origin.

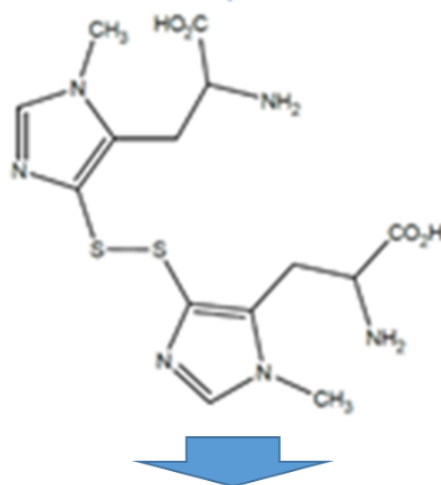
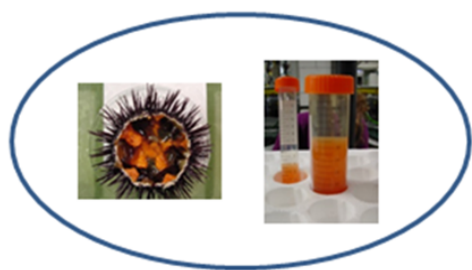
## Development stage

### Current TRL: 3

*In vitro* and *ex vivo* experiments were carried out to evaluate the effectiveness of the invention.

### Perspective TRL: 4

Animal models will be used in preclinical studies to identify and assess the potential safety and toxicity problems, adverse events and side effects.



Reduction of chronic low-grade systemic inflammation (CLGSI)  
chronic inflammatory, cardiovascular, degenerative diseases, diabetes

Figure 2 - Graphical representation of sea urchin ovothiols extraction.