# Effects of cardiovascular disruption of UV-B filter octylmethoxycinnamate in pregnant women with hypothyroidism


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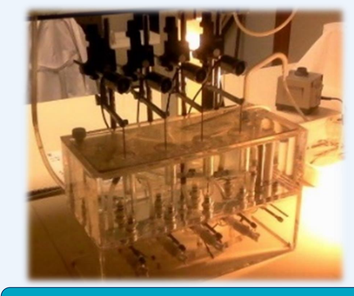
## Introduction

Increasing evidence relating the exposure and/or bioaccumulation of endocrine-disrupting compounds (EDCs) in the cardiovascular system are arising. Octylmethoxycinnamate (OMC) is the most widely used UV-B filter and as EDC interacts with thyroid hormone receptors. However, their effects on thyroid diseases during pregnancy remain unknown. The purpose of this work was to assess the short- and long-term effects of OMC on arterial tonus of pregnant women with hypothyroidism.

## Methods

### HUA smooth muscle cells

- Human umbilical arteries (HUA) from pregnant women with and without hypothyroidism were used to explore the vascular effects of OMC.
- Primary cultures of HUA smooth muscle cells (HUASMC) were obtained through explants of the umbilical arteries to perform the cellular experiments.



### Contractility Experiments

- Short- and long-term effects of OMC on vascular contractility patterns were investigated by arterial and cellular experiments. Serotonin (5-HT; 1 µmol/L) and histamine (His; 10 µmol/L) were used to contract the HUA rings or HUASMC, which were pre-incubated 24 hours with OMC (0 and 50 µmol/L).

### Computational Simulations

- Molecular Docking simulations were used to analyze the binding energy and the modes of interaction of the OMC into the active center of the TSHR and THRα.

## Results

**1**

OMC in the short-term experiments induced a contraction effect in the hypothyroidism group contracted with 5-HT **(Fig. 1 A1)** and a relaxation in the hypothyroidism group when contracted with His **(Fig. 1 B1).**

- In general, the exposure of 24 h to 50 µmol/L of OMC induced a small relaxation in both groups after contracted with 5-HT **(Fig. 1 A2)** and in HUA contracted with His, effects could not be assessed since stable contractions were not obtained **(Fig. 1 B2).**

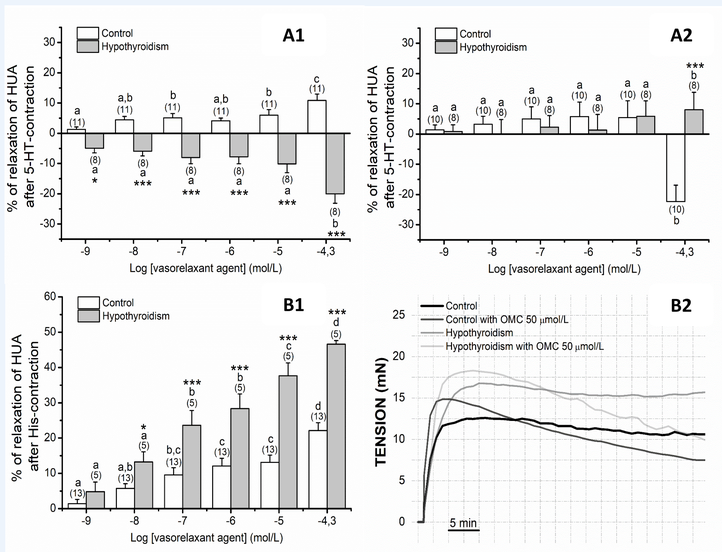



**Figure 1.** Percentage of relaxation of human umbilical artery (HUA) rings without (control) and with hypothyroidism incubated with **(1)** 0 µmol/L and **(2)** 50 µmol/L of octylmethoxycinnamate (OMC) and contracted by **(A)** serotonin (5-HT; 1 µmol/L) and **(B)** histamine (His; 10 µmol/L). Each bar represents the mean, vertical lines the S.E.M. and the number within brackets the n. Asterisk * represents a significant difference hypothyroidism versus control: * p<0.05 and *** p<0.001; and, different letters represents significant differences between OMC concentrations (p<0.05); two-way ANOVA method followed by Holm–Sidak post-hoc tests. **(B2)** represent the real tension (mN) of the HUA rings control and rings with hypothyroidism, both incubated with OMC (0 and 50 µmol/L).

**2**

The exposure to OMC induced a vasoconstriction effect in HUASMC contracted with 5-HT of the hypothyroidism group **(Fig. 2A)**.

- The exposure to OMC induced a vasorelaxant effect in the hypothyroidism HUASMC group contracted with His, similarly to the observed in control group **(Fig. 2B)**.

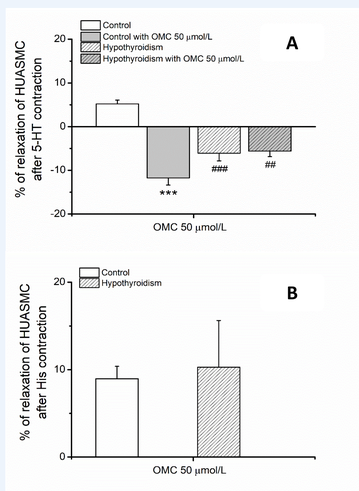



**Figure 2.** Percentage of relaxation of human umbilical artery smooth muscle cells (HUASMC) after **(A)** serotonin (5-HT; 1 µmol/L) and **(B)** histamine (His; 10 µmol/L) contraction. Each bar represents the mean, vertical lines the S.E.M. and the number within brackets the n. Asterisk * represents a significant difference incubation versus no incubation: *** p<0.001, and Hashtag # represents a significant difference hypothyroidism versus control: ## p<0.01 and ### p<0.001; two-way ANOVA method followed by Holm–Sidak post-hoc tests.

**3**

OMC bound to the active center of THRα and TSHR with a binding energy of −7.69 kcal/mol and 0.68 kcal/mol, respectively.

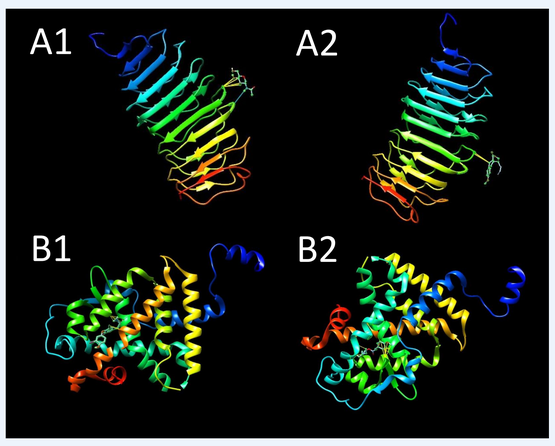



**Figure 3.** Docking views of the complex between the natural ligands **(1)** and OMC **(2)** within TSHR **(A)** and TRHα **(B)** using Quimera 1.15 software. **(A1 and A2)** show the 3D representation of the interactions and preferred conformation between natural ligand 2-acetamido-2-deoxy-beta-D-glucopyranose (NAG) and octylmethoxycinnamate (OMC), respectively, within TSHR active center. **(B1 and B2)** show the 3D representation of the interactions and preferred conformation between natural 3,5,3'Triiodothyronine (T3) and octylmethoxycinnamate (OMC), respectively, within THRα active center.

## Conclusions

- The long-term exposure to the UV-filter OMC altered the contractility patterns of HUA contracted with serotonin and histamine possibly due to an interference with serotonin and histamine receptors;
- The molecular docking analysis showed that OMC compete with T3 for the binding center of THRα;
- The alterations obtained in the reactivity of HUA as result of OMC-exposure may be involved in the development and increased risk of cardiovascular diseases.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