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CV: A Powerful Plant-Based extract to Combat Cellulite Inside and Out

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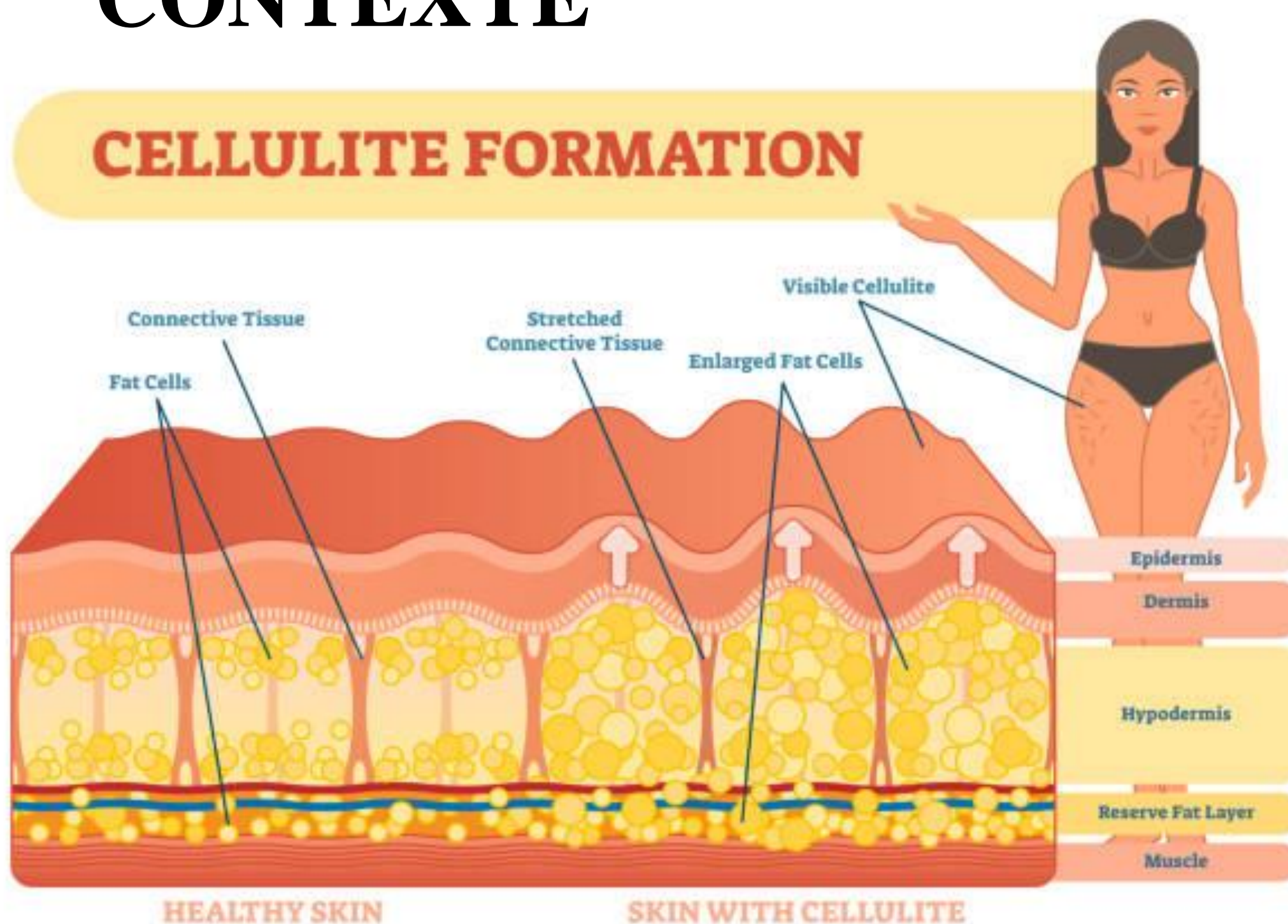
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CONTEXTE

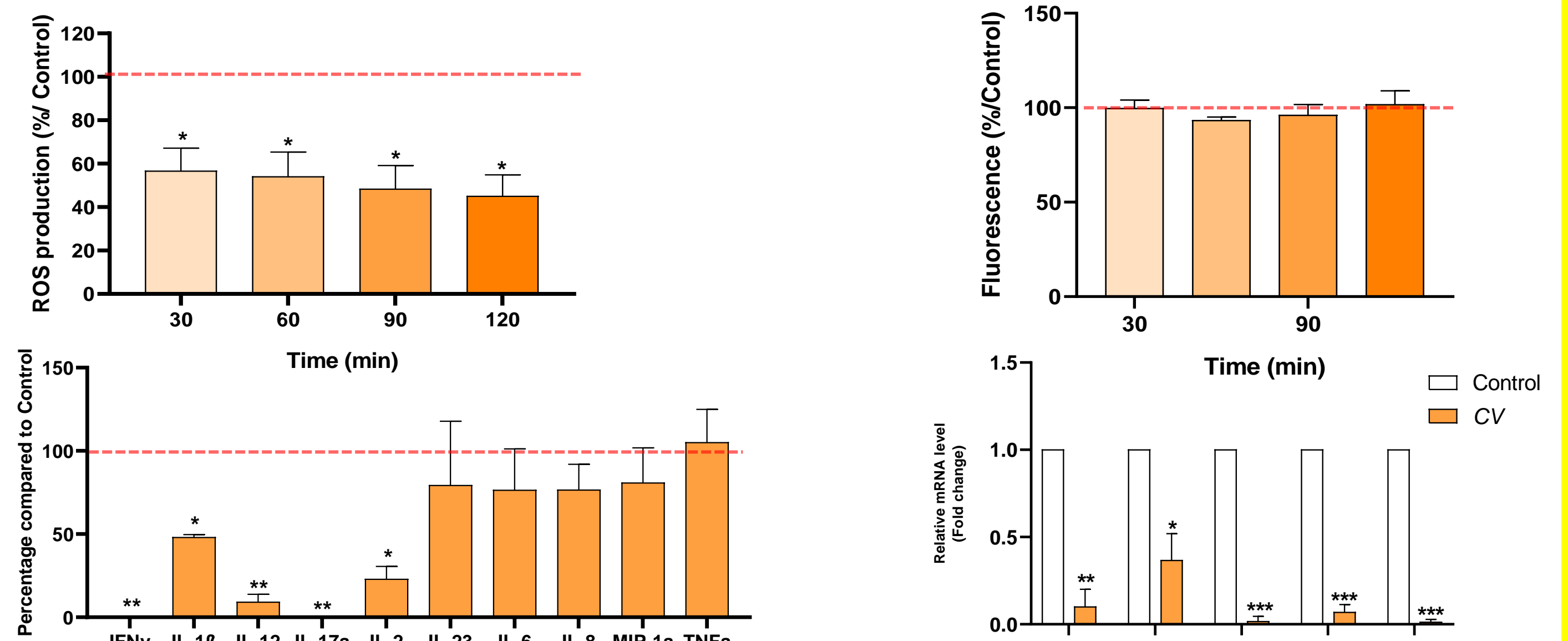
CELLULITE FORMATION

Cellulite is a common condition characterized by dimpled skin, primarily affecting the thighs, buttocks, and abdomen. It occurs when fat deposits push through connective tissue, leading to an uneven surface. Overweight significantly contributes to the development of cellulite, as excess fat exacerbates its appearance.

Additionally, a lack of collagen production and chronic inflammation can further compromise the structural integrity of connective tissue, making cellulite more pronounced. Factors such as enhanced circulation, which increases blood flow to the skin and underlying tissues while delivering essential nutrients and oxygen, can stimulate fibroblast activity for collagen production, thereby strengthening connective tissue and potentially reducing the visibility of cellulite. Medicinal plants are vital in pharmaceutical development for preventing and treating overweight, which is associated with chronic low-grade inflammation, cellulite, and other serious diseases.



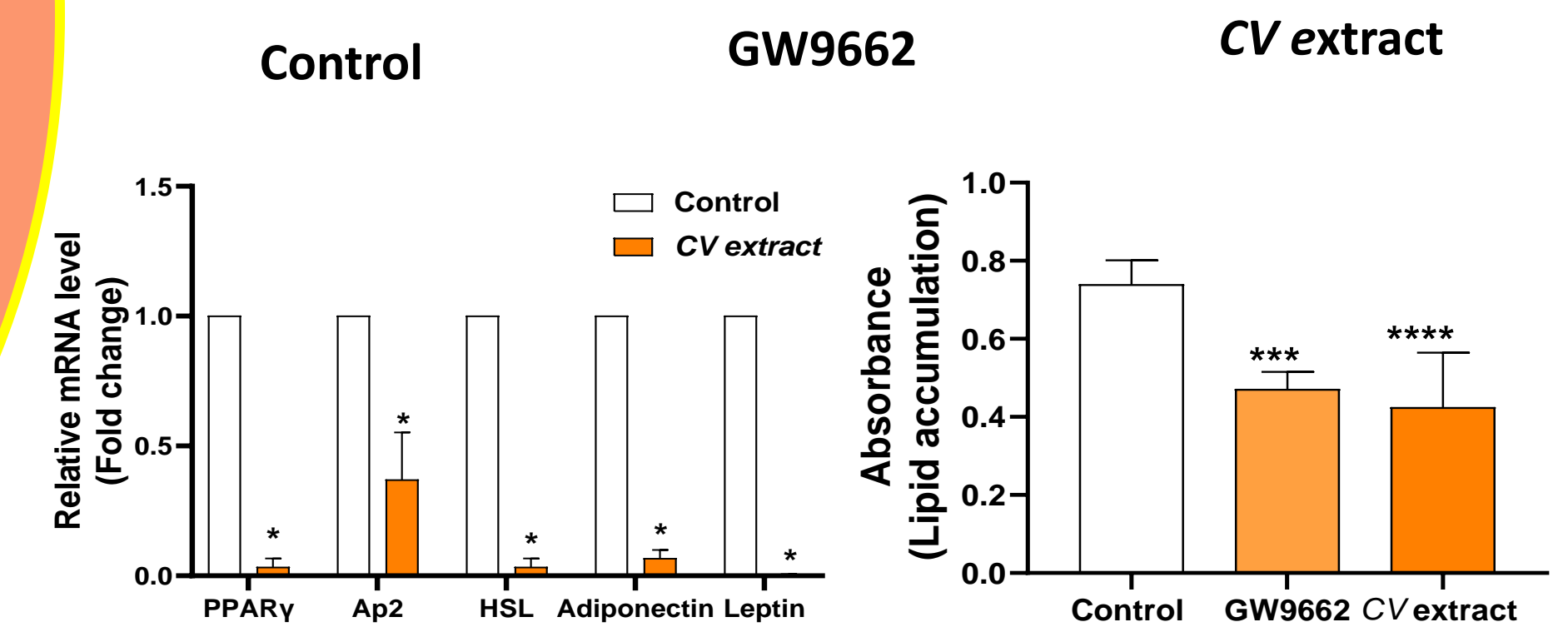
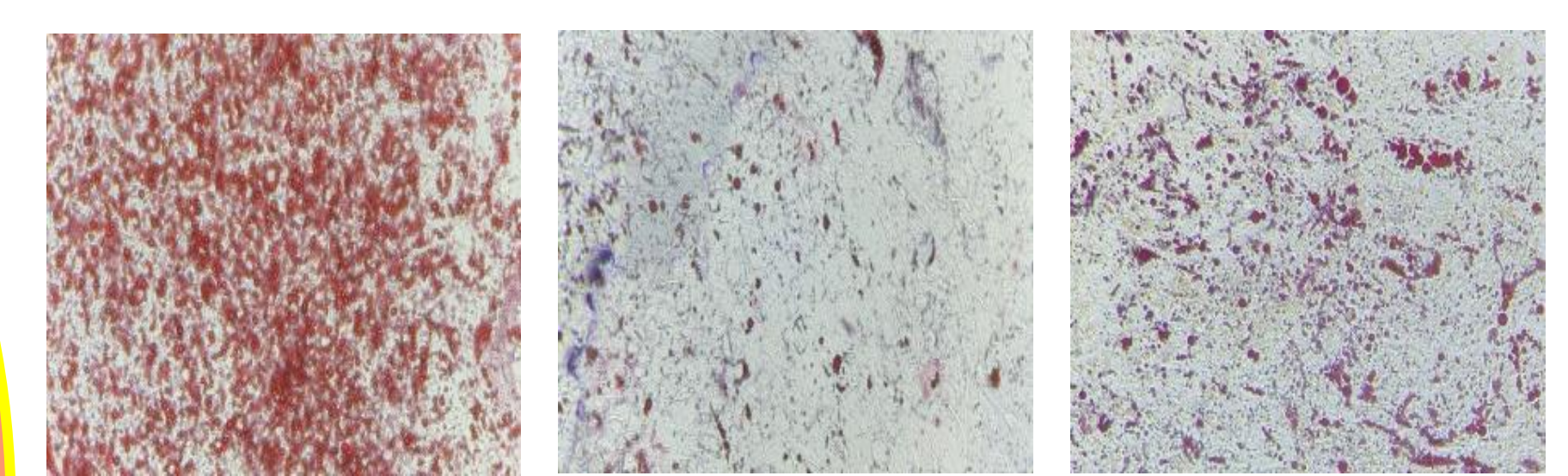
RESULTS - PBMCs



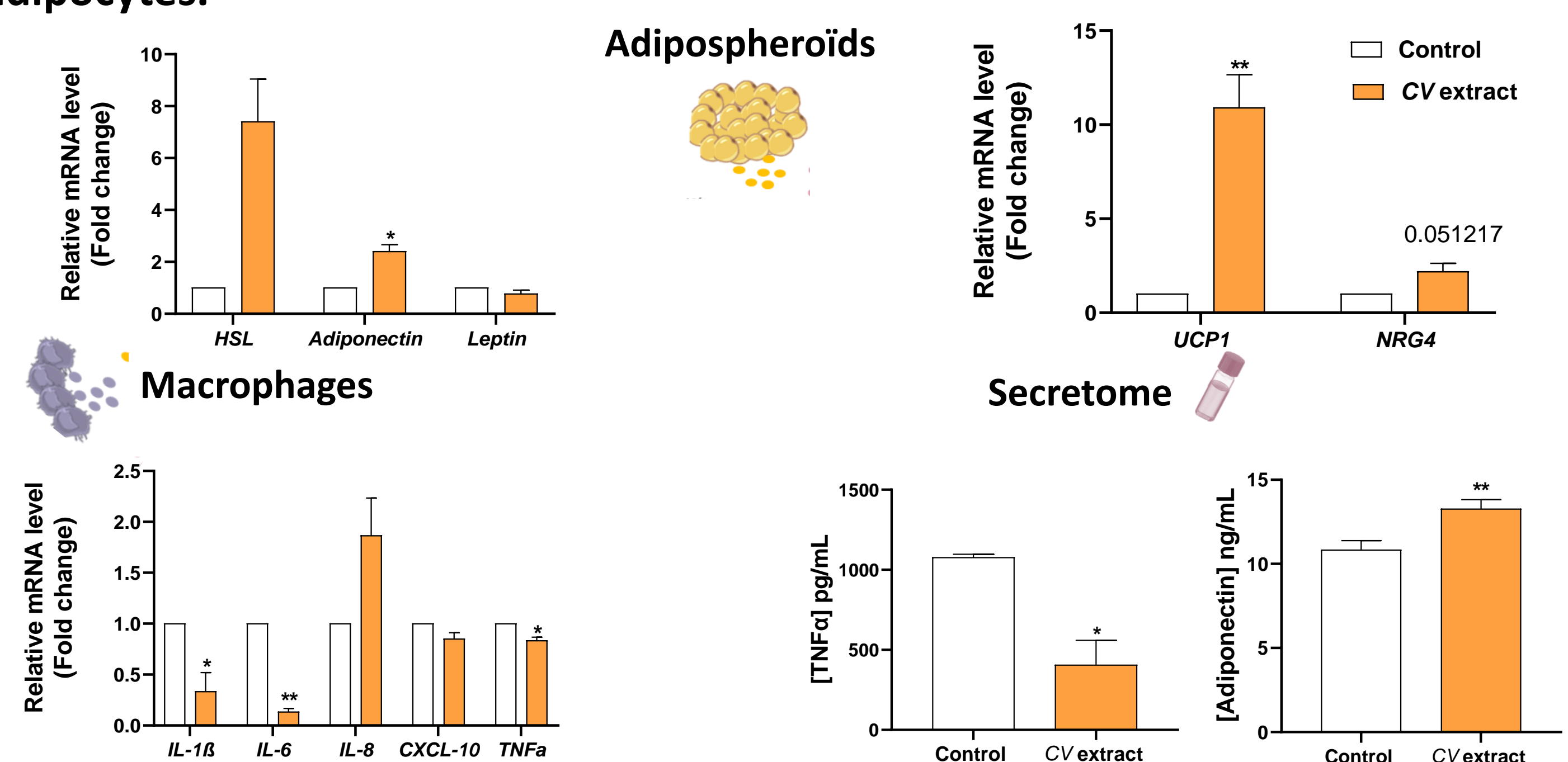
A strong antioxidant and non-cytotoxic activity of the plant extract were observed, with a significant decrease of over 60% ($p < 0.01$ vs untreated cells) in the production of ROS at a concentration of 50 $\mu\text{g/mL}$. A strong anti-inflammatory effect of the extract was observed, with a significant reduction in the production of IFN- γ , IL-1 β , IL-12, IL-2, and IL-17 α by PBMCs, as well as a decrease in the expression of *TNF α* , *IL-6*, *IL-8*, *IL-1 β* , and *CXCL10* by M1-like macrophages.

RESULTS - Adipocytes

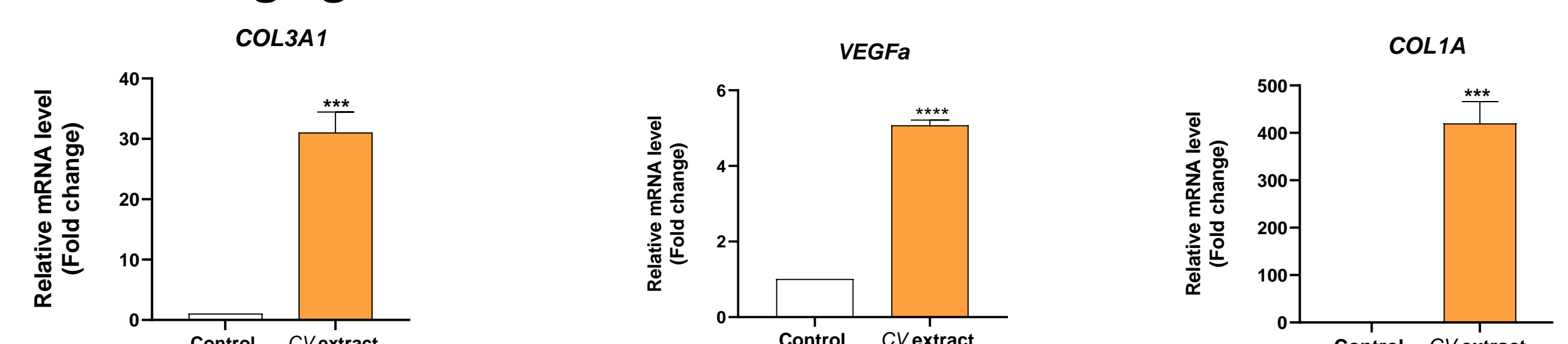
The extract significantly inhibited intracellular lipid accumulation by 45% ($p < 0.01$ vs control) in mature adipocytes (MA), with a significant decrease in the mRNA expression of *PPAR γ* and *AP2*.



In the co-culture model between adipospheroids and M1-like macrophages, the extract altered the functionality of MA resulting in decreased secretion of leptin and *TNF α* ($p < 0.05$ vs control), increased secretion of adiponectin ($p < 0.05$ vs control), and decreased expression of the cytokines *IL-6*, *TNF α* , and *IL-1 β* in M1 macrophages. Surprisingly, we observed a significant increase in the expression of the genes *UCP1* and *NRG4* in adipospheroids, which are involved in the browning of adipocytes.

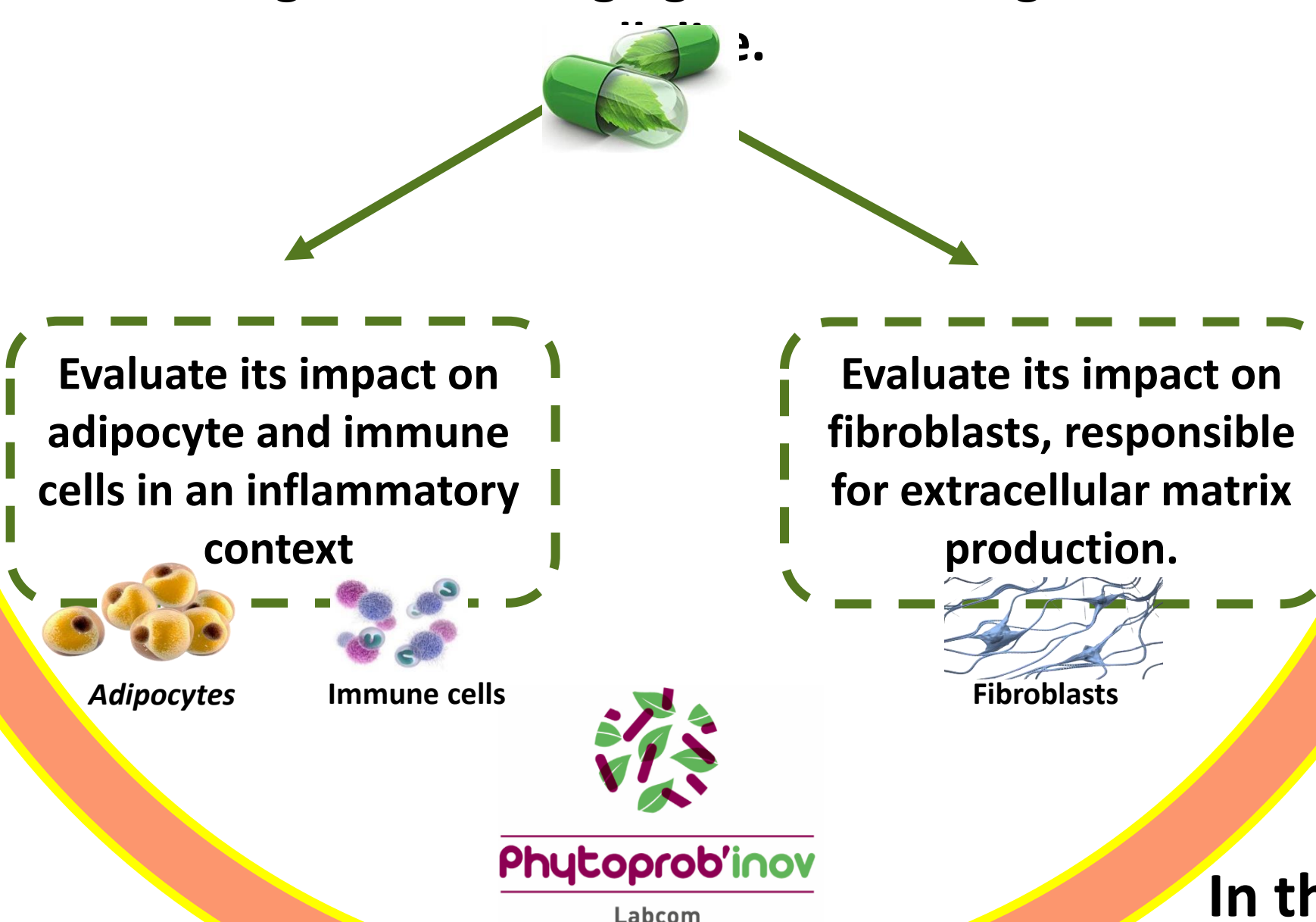


Finally, at the fibroblast level, we found that treatment with our extract significantly increased the expression of *COL3A1* and *COL1A*, which are genes associated with collagen production, as well as that of *VEGF α* , a gene involved in angiogenesis.



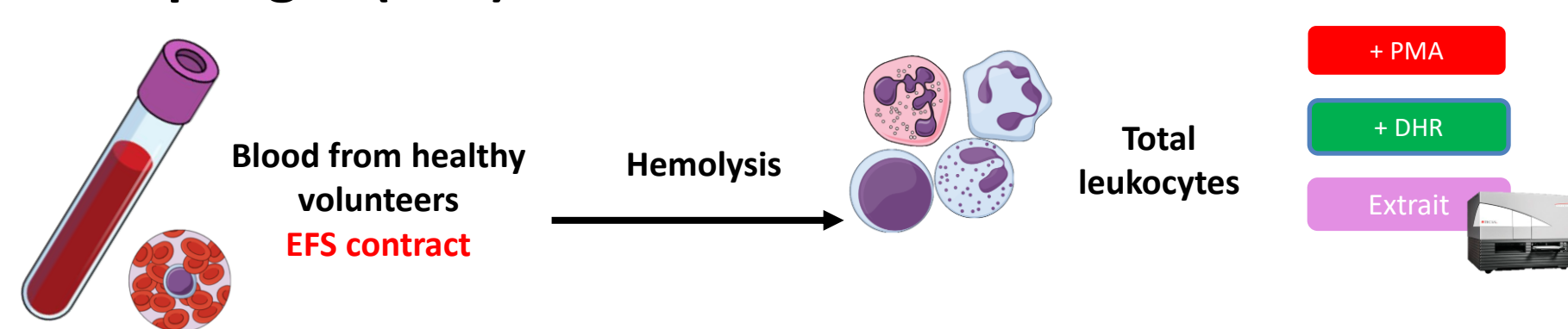
OBJECTIVES

Our study aims to examine the effects of an innovative plant extract on inflammation, adipose tissue, and fibroblast functionality in the context of overweight, offering potential strategies for managing both overweight and



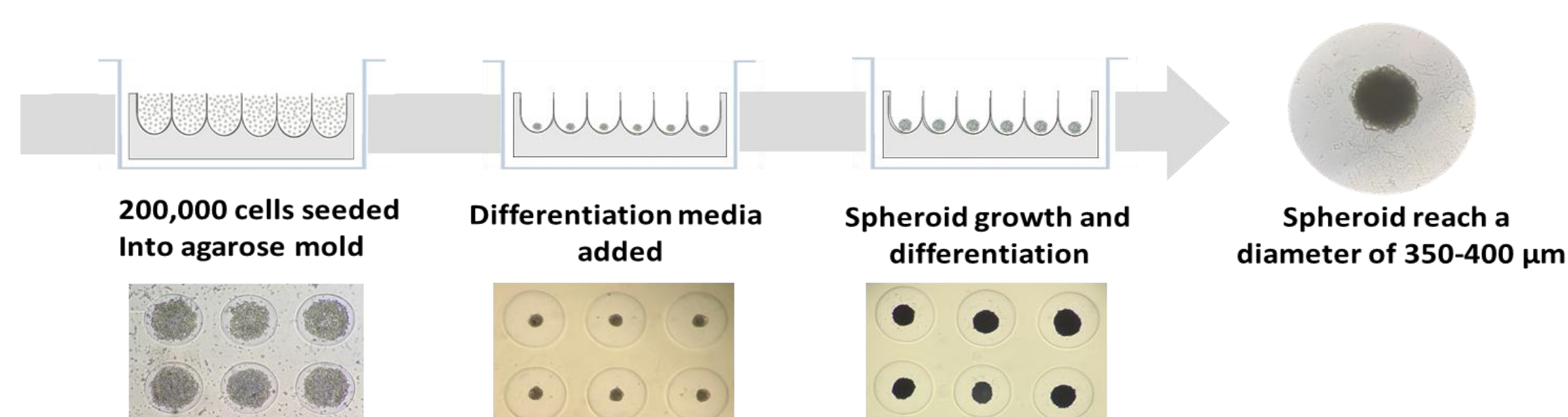
Experimental Methods

Total leukocytes and peripheral blood mononuclear cells (PBMCs) isolated from blood of healthy volunteers ($n=9$) were cultured with the CV extract following stimulation with PMA or PHA to evaluate the production of reactive oxygen species (ROS) and the protein expression of 10 pro-inflammatory cytokines (ProcartaPlex Immunoassay[®] kit). The effect of the extract was also assessed on the polarization of monocytes (THP1 cell line) into activated M0 macrophages and M1-like pro-inflammatory macrophages ($n=6$).

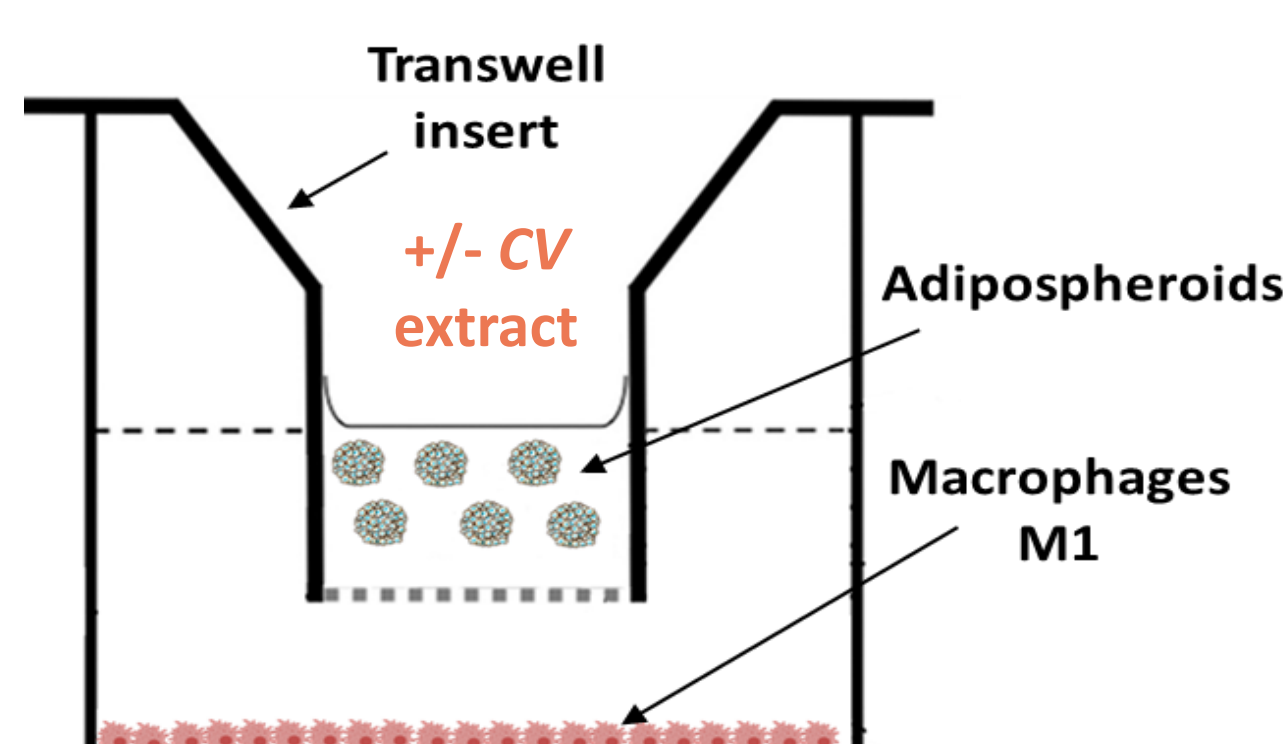


The impact of CV extract was also evaluated directly on the subcutaneous adipose tissue. To reproduce an overweight/obesity situation, adipocyte stem cells were extracted from subcutaneous adipose tissue samples of obese women, and their differentiation capacity into mature adipocytes (MA) was evaluated in the presence of the extract by visualizing lipids (Oil Red O) and measuring the expression of genes involved in this differentiation ($n=6$). Finally, the impact of the extracts was evaluated in 3D co-culture model between spheroids of MA (*i.e.*, "adipospheroids") and polarized M1-like macrophages ($n=3$) to determine the effect on the inflammatory state generated by this cellular interaction.

Formation of spheroids



Co-culture model



The final target was fibroblasts, the main cell type in the skin, which are responsible for extracellular matrix production. For this, primary dermal human fibroblasts (HDFa) were cultured in the presence or absence of our extract to determine their effect on the production of several extracellular components.

CONCLUSION

By reducing ROS production and pro-inflammatory cytokines, the innovative extract may attenuate the chronic inflammation associated with overweight, a key factor in the development of cellulite. Additionally, the ability to inhibit lipid accumulation in mature adipocytes and enhance collagen production in fibroblasts indicates a dual benefit of improving adipose tissue health and strengthening skin structure. Overall, these findings highlight the promising role of CV extract in developing effective natural treatment targeting both obesity and cellulite.