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Capacity of curcumin, a polyphenol presenting vasculo-protective properties, to modulate secretion and miRNA and protein profiles of endothelial microparticles

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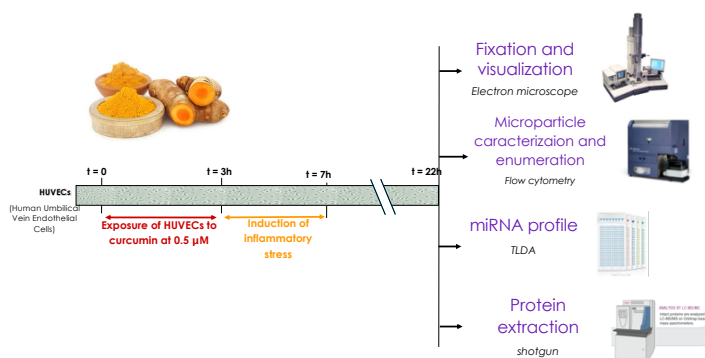
INTRODUCTION

High levels of endothelial microparticles (EMP) have been observed in patients with cardiovascular diseases and other diseases with endothelial dysfunction. In addition, cardiovascular risk factors, such as diabetes, high blood pressure or dyslipidaemia, are accompanied by elevated plasma levels of EMP.

Polyphenols are plant bioactive compounds present in large quantities in most fruits and drinks of plant origin, such as tea, wine or coffee. The work from our group and that of others have shown that polyphenols play an important role in protection of vascular endothelium integrity and functionality.

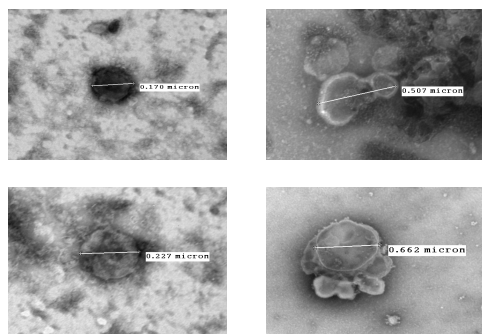
The aim of this study was to evaluate the ability of a polyphenol, curcumin, to modulate the release of EMPs following an inflammatory stress and modify their protein and miRNA profiles.

STUDY DESIGN



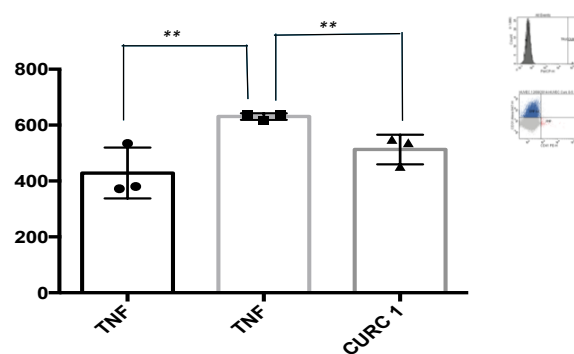
RESULTS

1) Visualization of the microparticles isolated from the culture medium



Electron microscopy revealed microparticles with size ranging from 0.1 to 0.6 micrometer

2) Enumeration of microparticles in culture medium using flow cytometry



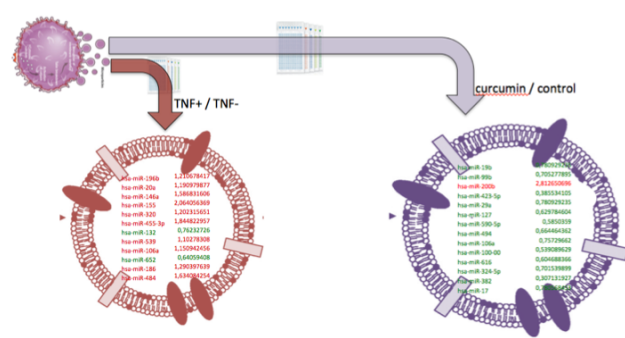
Curcumin decrease the number of microparticles liberated by EC in inflammatory condition

3) Global protein profile of microparticles released by endothelial cells

Accession	Peptides	Score	Accession	Score	Accession	Score	Description	Average normalized abundance
ALBU_HUMAN	4	346.35	0.95	1.01	Serum albumin	0.15e+005	2.13e+007	2.13e+007
ACTB_HUMAN	5	268.36	0.93	1.41	Actin, cytoplasmic 1	0.15e+005	1.68e+005	1.68e+005
IBA1_HUMAN	2	140.13	0.45	1.22	Membrane inducible alpha 1	0.15e+005	3.75e+005	3.75e+005
ITGA1_HUMAN	3	156.37	0.42	1.30	Alpha 1 integrin	0.15e+005	4.15e+005	4.15e+005
ITGB1_HUMAN	2	121.64	0.44	1.36	Integrin beta 1	0.15e+005	1.87e+004	1.87e+004
ALDH3_HUMAN	2	79.03	0.36	1.36	Aldehyde dehydrogenase 3	0.15e+005	9.29e+004	9.29e+004
PAI1_HUMAN	1	42.75	0.39	1.42	Plasminogen activator inhibitor 1	0.15e+005	7226.49	7226.49
ITGB2_HUMAN	1	42.32	0.31	1.30	Integrin beta 2	0.15e+005	4.43e+004	4.43e+004
ITGB3_HUMAN	1	50.62	0.30	1.34	Integrin beta 3	0.15e+005	4.56e+004	4.56e+004
ITGB4_HUMAN	1	57.27	0.30	1.34	Integrin beta 4	0.15e+005	4.56e+004	4.56e+004
ITGB5_HUMAN	1	56.94	0.32	1.32	Integrin beta 5	0.15e+005	5.15e+004	5.15e+004
ITGB6_HUMAN	1	51.14	0.30	1.34	Integrin beta 6	0.15e+005	2.42e+004	2.42e+004
ITGB7_HUMAN	1	46.37	0.30	1.40	Integrin beta 7	0.15e+005	3.19e+005	3.19e+005
ITGB8_HUMAN	1	45.22	0.30	1.37	Integrin beta 8	0.15e+005	7.72e+004	7.72e+004
ITGB9_HUMAN	1	40.44	0.30	1.36	Integrin beta 9	0.15e+005	3.15e+004	3.15e+004
ITGB10_HUMAN	1	39.54	0.30	1.36	Integrin beta 10	0.15e+005	3.15e+004	3.15e+004
ITGB11_HUMAN	1	39.34	0.30	1.36	Integrin beta 11	0.15e+005	2.86e+005	2.86e+005
ITGB12_HUMAN	1	38.91	0.30	1.37	Integrin beta 12	0.15e+005	1.46e+005	1.46e+005
ITGB13_HUMAN	1	38.92	0.31	1.36	Integrin beta 13	0.15e+005	4.87e+005	4.87e+005
ITGB14_HUMAN	1	38.98	0.30	1.36	Integrin beta 14	0.15e+005	4.87e+005	4.87e+005
ITGB15_HUMAN	1	37.56	0.31	1.15	Integrin beta 15	0.15e+005	7.35e+004	7.35e+004
ITGB16_HUMAN	1	37.17	0.30	1.36	Integrin beta 16	0.15e+005	7.87e+004	7.87e+004
ITGB17_HUMAN	1	37.12	0.30	1.46	Integrin beta 17	0.15e+005	1.75e+004	1.75e+004
ITGB18_HUMAN	1	36.58	0.30	1.13	Integrin beta 18	0.15e+005	1.35e+005	1.35e+005
ITGB19_HUMAN	1	36.18	0.30	1.42	Integrin beta 19	0.15e+005	3.35e+004	3.35e+004
ITGB20_HUMAN	1	34.05	0.30	1.01	Integrin beta 20	0.15e+005	1.32e+004	1.32e+004
ITGB21_HUMAN	1	31.30	0.30	1.20	Integrin beta 21	0.15e+005	1.01e+005	1.01e+005

Both TNF and pre-exposure to curcumin modify the protein profile in the microparticles released by endothelial cells

4) Global miRNA profile of microparticles released by endothelial cells



TNF modulate miRNA profile of microparticles. Pre-exposure of HUVECs to curcumin counteract the effect of TNF at the miRNA profile of microparticles

CONCLUSION

In conclusion, curcumin can counteract the inflammatory effect of TNF α on the EMPs profile by decreasing their release and modifying their miRNA and protein contents. The proteins, as well as the identified miRNA target genes are involved in the regulation of endothelial cell integrity, particularly the processes regulating monocyte adhesion and their transendothelial migration. We therefore assume that their bioactivity could also be modulated, hypothesis that is currently under evaluation.