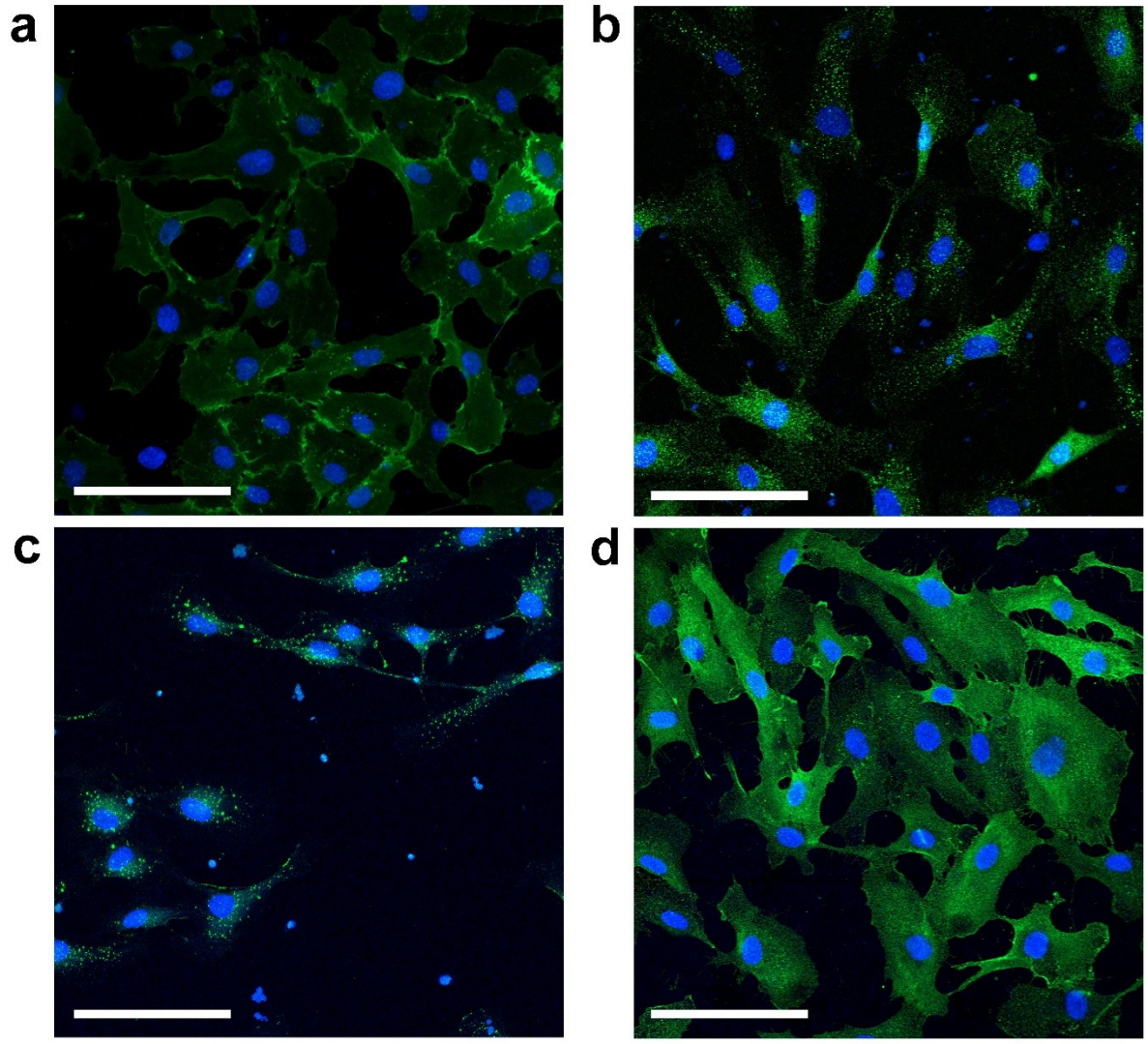
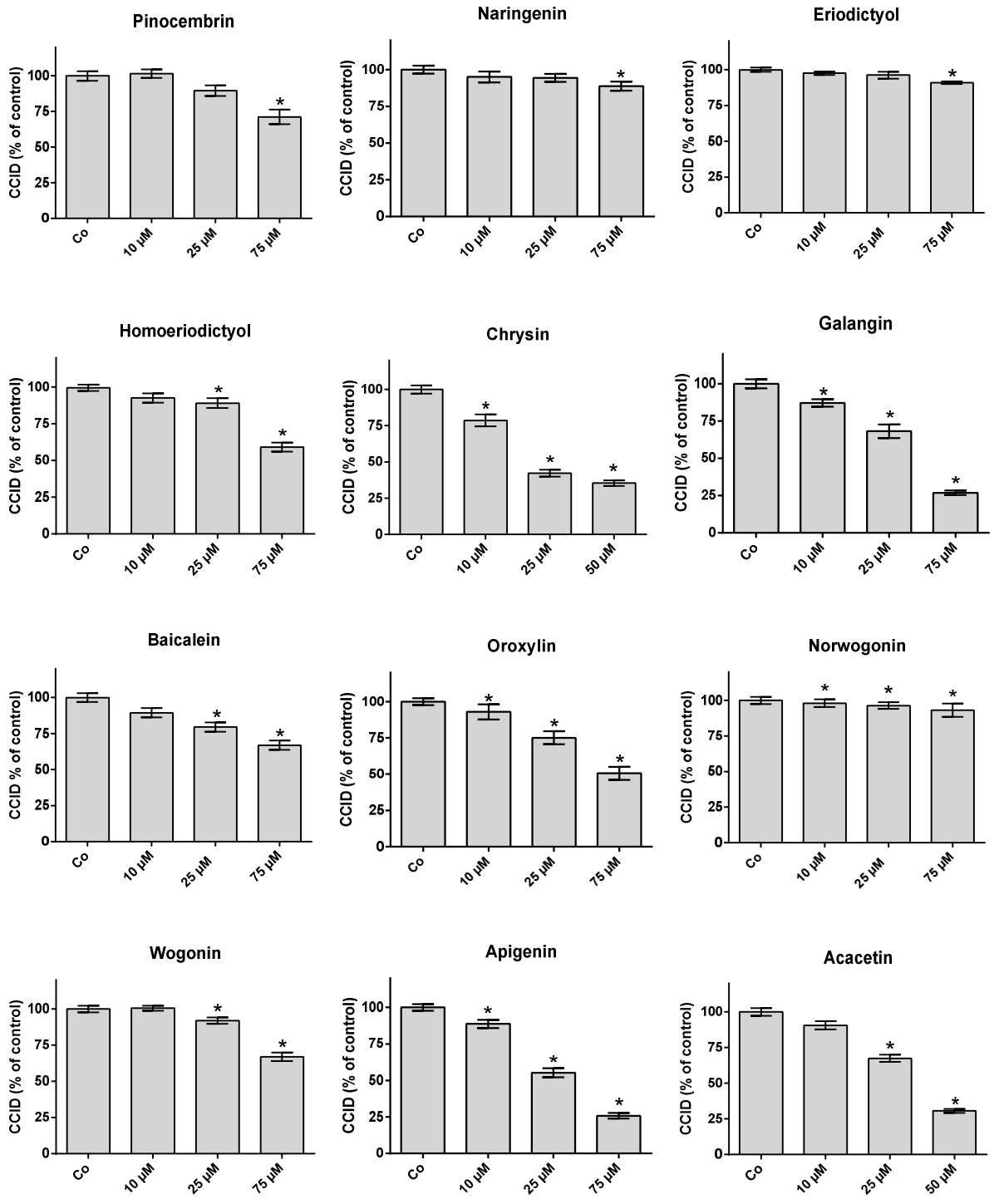
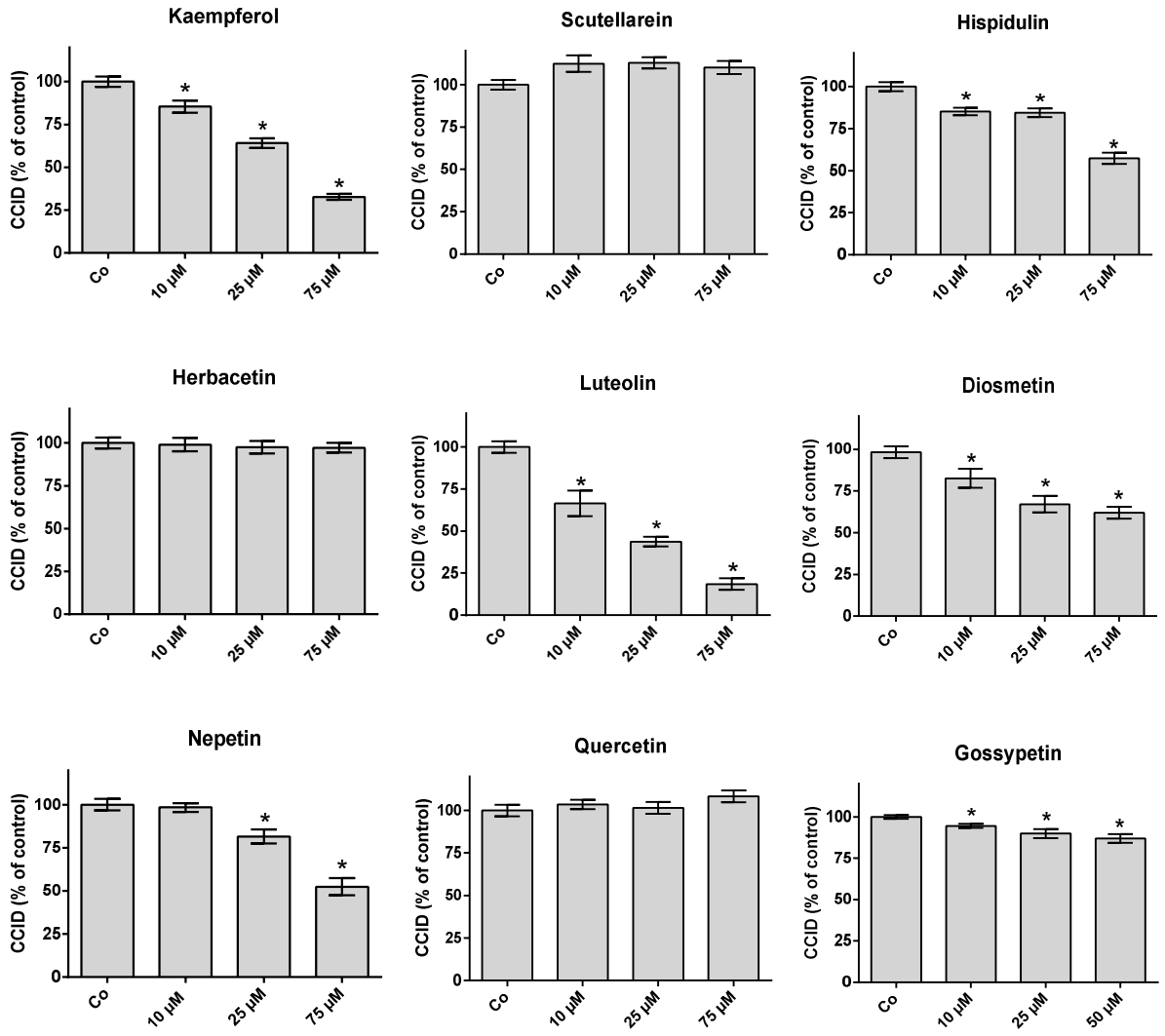
Supplemental figure 1: Lymph-endothelial marker expression in LEC



Immunofluorescence: Cells were grown on glass chamberslides and fixed with 2% paraformaldehyde for 20 min at 20°C. After rinsing in phosphate-buffered saline and blocking with 5% goat serum the cells were stained with primary antibody against (a) CD31 to verify endothelial cell type, and (b) LYVE-1, (c) PROX1 and (d) podoplanin to demonstrate the lymphendothelial origin. Scale bar 100 μM

Supplemental figure 2a: Treatment of the MCF-7/LEC model with flavonoids

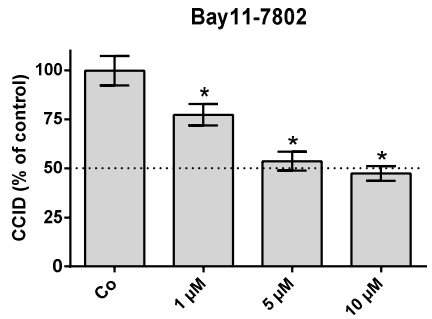




Analysis of flavonoids on CCID formation

MCF-7 spheroids were placed on LEC monolayers and treated with solvent (DMSO, Co) or with the indicated flavonoid concentrations for 4 h when CCID areas were measured using an Axiovert microscope and Zen little 2012 software. At least 12 replicates were analyzed. Error bars indicate means +/- SEM and asterisks and rhomboids significance ($p<0.05$; ANOVA and Tukey´s post hoc test).

Supplemental figure 2b: Treatment of the MCF-7/LEC model with Bay11-7802



Analysis of NF-kB inhibitor Bay11-7802 on CCID formation

MCF-7 spheroids were placed on LEC monolayers and treated with solvent (DMSO, Co) or with the indicated concentrations Bay11-7802 for 4 h when CCID areas were measured using an Axiovert microscope and Zen little 2012 software. At least 12 replicates were analyzed. Error bars indicate means +/- SEM and asterisks and rhomboids significance ($p<0.05$; ANOVA and Tukey´s post hoc test).

Supplemental Figure 3: Correlation of logP values (o/w) and pIC50 values of 13 flavonoids which showed activity in the CCID assay