Reduced heart exposure of diclofenac by its polymeric micellar formulation, normalizes CYP- mediated metabolism of arachidonic acid imbalance in adjuvant arthritis rat model: Implications in reduced cardiovascular side effects of diclofenac by nano-drug delivery

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Supporting Information

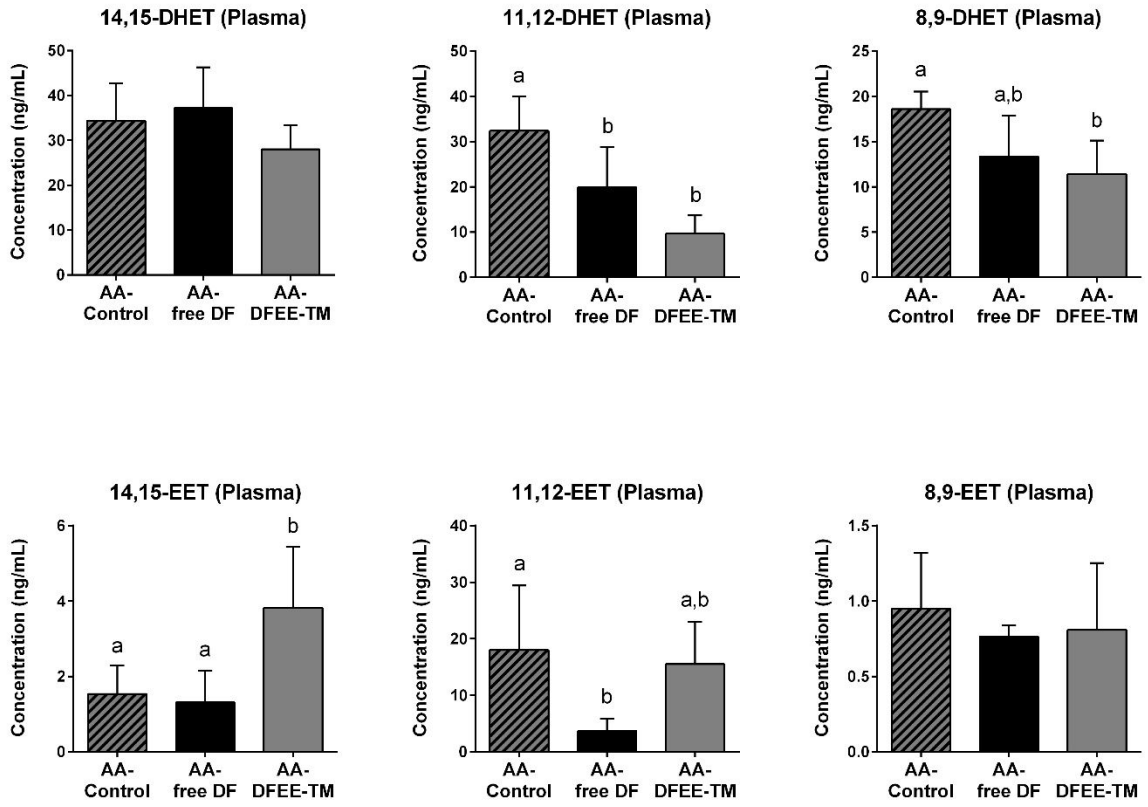

Figure S1. Concentrations of CYP metabolites of arachidonic acid (14,15-, 11,12- and 8,9-DHET, 14,15-, 11,12-, and 8,9-EET) in the plasma of adjuvant arthritis inflamed rats receiving no treatment (AA-Control), or treated with free diclofenac (AA-free DF), or with the diclofenac ethyl ester traceable micelles (AA-DFEE-TM) (n=6/group). Bars sharing the same letter are not significantly different based on one-way ANOVA (α=0.05) with post-hoc Tukey HSD.

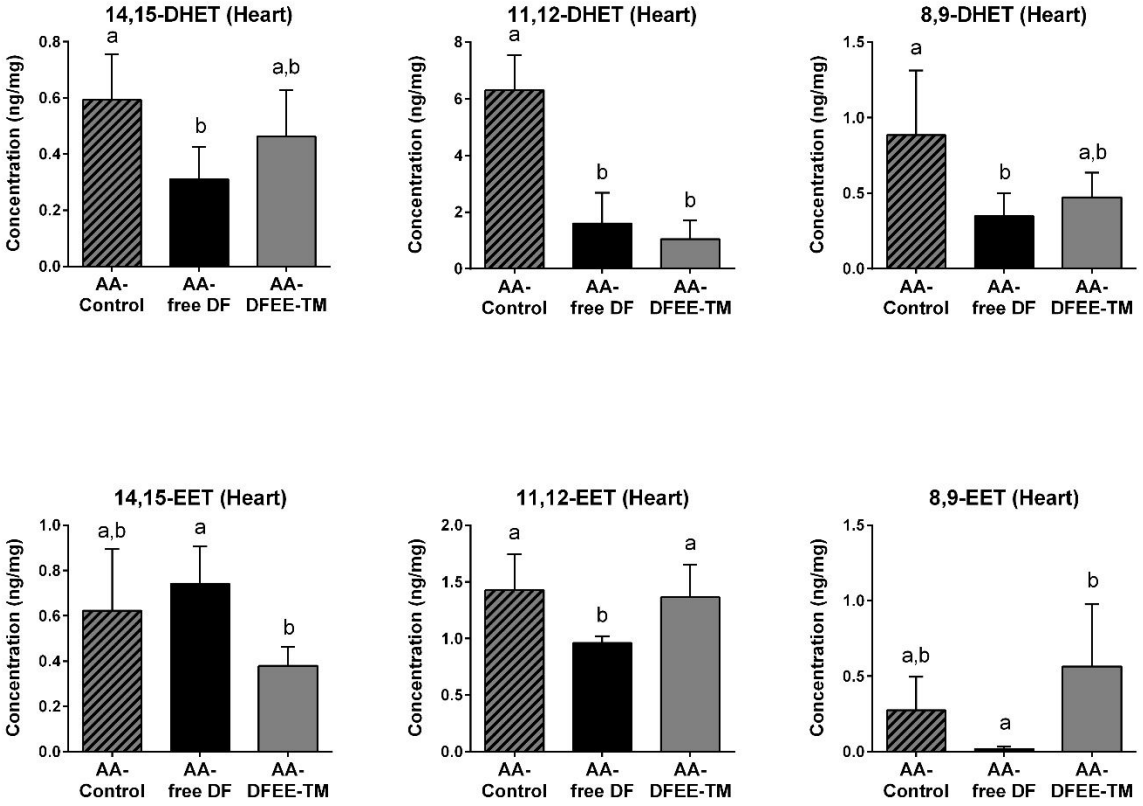

Figure S2. Concentrations of CYP metabolites of arachidonic acid (14,15-, 11,12- and 8,9-DHET, 14,15-, 11,12-, and 8,9-EET) in the cardiac tissues of adjuvant arthritis inflamed rats receiving no treatment (AA-Control), or treated with free diclofenac (AA-free DF), or with the diclofenac ethyl ester traceable micelles (AA-DFEE-TM) (n=6/group). Bars sharing the same letter are not significantly different based on one-way ANOVA (α=0.05) with post-hoc Tukey HSD.

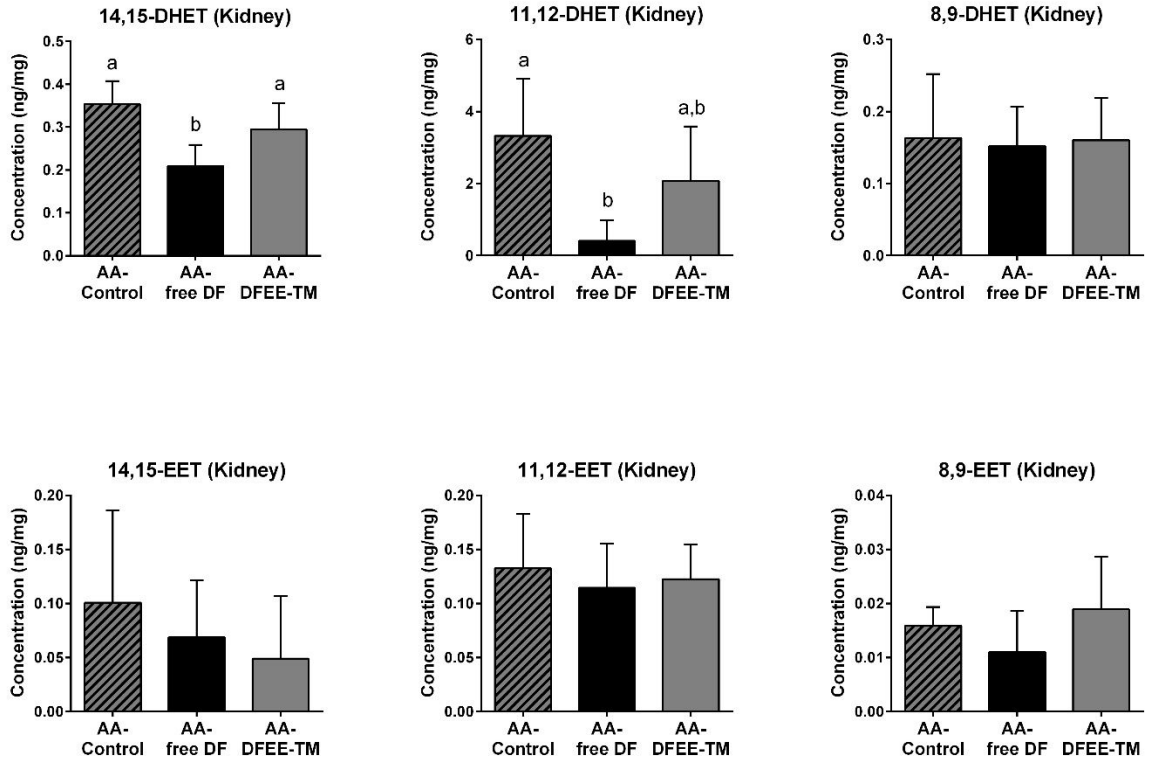

Figure S3. Concentrations of CYP metabolites of arachidonic acid (14,15- , 11,12- and 8,9-DHET, 14,15-, 11,12-, and 8,9-EET) in the kidney tissues of adjuvant arthritis inflamed rats receiving no treatment (AA-Control), or treated with free diclofenac (AA-free DF), or with the diclofenac ethyl ester traceable micelles (AA-DFEE-TM) (n=6/group). Bars sharing the same letter are not significantly different based on one-way ANOVA (α=0.05) with post-hoc Tukey HSD.

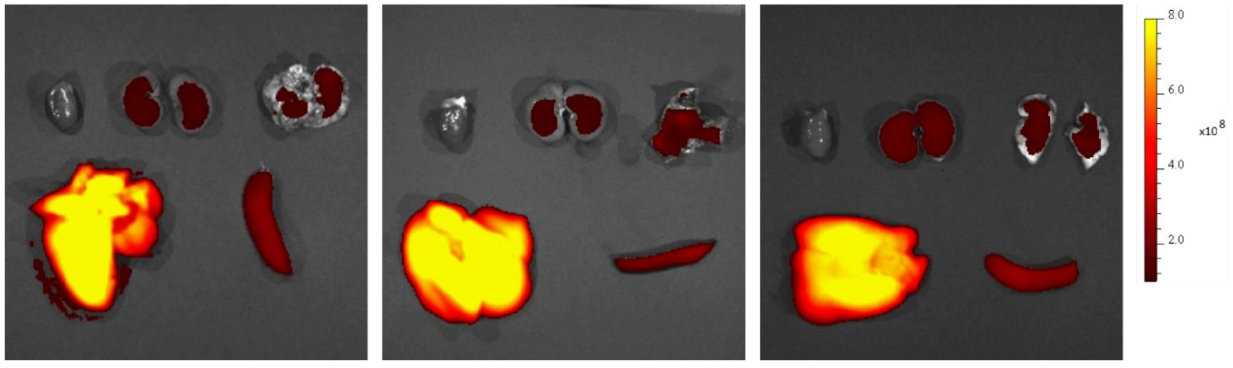

Figure S4. *ex vivo* near-infrared optical images of major organs (heart, kidneys, lungs, spleen, and liver in clockwise ordering) of adjuvant arthritic rats (n=3) at 6 h following a single iv dose of the DFEE-TM.