**Supplementary Material for:**

**Nanosized silver, but not titanium dioxide or zinc oxide, enhances oxidative stress and inflammatory response by inducing 5-HETE activation in THP-1 cells**

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| --- | --- | --- | --- | --- | --- | --- | --- |
| **6h** | **Ctrl** | **n-TiO2** | **b-TiO2** | **n-ZnO** | **b-ZnO** | **n-Ag** | **i-Ag** |
| **Polyunsaturated fatty acids (PUFAs)** |
| **AA** (ng/mg protein) | 189.86 ± 34.52 | 208.71 ± 21.12 | 221.46 ± 64.80 | 177.36 ± 38.23 | 230.08 ± 27.47 | 165.94 ± 42.48 | 185.86 ± 55.11 |
| **AdA** (ng/mg protein) | 29.73 ± 11.00 | 30.79 ± 11.97 | 33.70 ± 7.85 | 30.77 ± 13.50 | 32.11 ± 10.17 | 24.80 ± 11.09 | 26.07 ± 14.89 |
| **DHA** (ng/mg protein) | 0.196 ± 0.062 | 0.251 ± 0.061 | 0.187 ± 0.025 | 0.186 ± 0.039 | 0.205 ± 0.042 | 0.137 ± 0.040 | 0.141 ± 0.058 |
| **DPA** (ng/mg protein) | 616.31 ± 240.48 | 827.23 ± 364.45 | 658.72 ± 133.66 | 660.76 ± 218.60 | 654.77 ± 112.22 | 494.41 ± 130.41 | 597.43 ± 399.39 |
| **EPA** (ng/mg protein) | 12160.13 ± 5208.53 | 14607.68 ± 7794.39 | 16070.10 ± 10408.98 | 14123.28 ± 7246.06 | 18642.42 ± 9716.05 | 11116.70 ± 4237.84 | 10043.44 ± 3859.69 |
| **Enzymatically oxidized lipid metabolites** |
| **5-HETE : AA** | 0.00469 ± 0.00168 | 0.00567 ± 0.00195 | 0.00487 ± 0.00118 | 0.00397 ± 0.00129 | 0.00465 ± 0.00082 | 0.00495 ± 0.00193 | 0.00416 ± 0.00131 |
| **8-HETE : AA** | 0.00298 ± 0.00127 | 0.00300 ± 0.00055 | 0.00254 ± 0.00129 | 0.00258 ± 0.00083 | 0.00277 ± 0.00047 | 0.00278 ± 0.00129 | 0.00225 ± 0.00051 |
| **9-HETE : AA** | 0.01772 ± 0.00485 | 0.01698 ± 0.00545 | 0.01064 ± 0.00857 | 0.02065 ± 0.00954 | 0.01947 ± 0.00725 | 0.02257 ± 0.01478 | 0.01062 ± 0.00286 |
| **11-HETE : AA** | 0.00279 ± 0.00122 | 0.00296 ± 0.00117 | 0.00280 ± 0.00158 | 0.00247 ± 0.00178 | 0.00312 ± 0.00122 | 0.00259 ± 0.00180 | 0.00195 ± 0.00075 |
| **12-HETE : AA** | 0.00699 ± 0.00200 | 0.00601 ± 0.00191 | 0.00665 ± 0.00292 | 0.00805 ± 0.00258 | 0.00711 ± 0.00281 | 0.00843 ± 0.00486 | 0.00648 ± 0.00213 |
| **15-HETE : AA** | 0.00714 ± 0.00243 | 0.00885 ± 0.00417 | 0.00713 ± 0.00315 | 0.00823 ± 0.00229 | 0.00926 ± 0.00363 | 0.00944 ± 0.00389 | 0.00747 ± 0.00188 |
| **4-HDoHE : DHA** | 11.54 ± 4.21 | 14.44 ± 7.10 | 14.30 ± 4.28 | 9.04 ± 1.47  | 9.91 ± 1.88 | 13.20 ± 5.41 | 17.67 ± 8.55 |
| **7-HDoHE : DHA** | 2.41 ± 1.01 | 2.67 ± 1.16 | 3.51 ± 0.48 | 1.98 ± 0.77 | 2.45 ± 0.74 | 2.88 ± 0.90 | 4.27 ± 2.47 |
| **8-HDoHE : DHA** | 17.23 ± 6.47 | 20.76 ± 9.33 | 22.13 ± 13.10 | 18.85 ± 7.89 | 23.50 ± 8.68 | 25.43 ± 11.32 | 25.71 ± 4.94 |
| **11-HDoHE : DHA** | 8.72 ± 2.19 | 9.24 ± 3.41 | 8.31 ± 4.50 | 7.99 ± 2.69 | 9.35 ± 2.64 | 10.90 ± 4.19 | 11.41 ± 1.48 |
| **14-HDoHE : DHA** | 20.27 ± 5.62 | 26.70 ± 13.20 | 32.88 ± 21.15 | 29.62 ± 10.04 | 31.78 ± 15.72 | 25.96 ± 15.37 | 42.15 ± 15.67 |
| **17-HDoHE : DHA** | 9.80 ± 4.62 | 9.28 ± 2.44 | 11.00 ± 5.57 | 9.83 ± 5.36 | 12.48 ± 4.56 | 12.91 ± 8.17 | 17.28 ± 7.01 |
| **Non-enzymatically oxidized lipid metabolites**  |
| **F2-IsoPs : AA** | 0.00842 ± 0.00182 | 0.01113 ± 0.00389 | 0.00901 ± 0.00146 | 0.00780 ± 0.00139 | 0.00811 ± 0.00109 | 0.01120 ± 0.00423 | 0.01118 ± 0.00488 |

**Table S1(A). Levels of PUFAs and other detectable PUFA metabolites at 6h.** Levels of PUFAs were expressed as absolute quantity normalized with the protein content. Levels of PUFA metabolites were expressed as ratio of metabolite to precursor PUFA. All results are shown as mean ± SD (n = 5). Significance tested by one-way ANOVA.

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| **24h** | **Ctrl** | **n-TiO2** | **b-TiO2** | **n-ZnO** | **b-ZnO** | **n-Ag** | **i-Ag** |
| **Polyunsaturated fatty acids (PUFAs)** |
| **AA (ng/mg protein)** | 190.73 ± 39.39 | 196.90 ± 45.08 | 225.58 ± 73.56 | 239.93 ± 57.54 | 191.43 ± 51.26 | 192.40 ± 17.45 | 189.78 ± 34.21 |
| **AdA (ng/mg protein)** | 39.23 ± 13.17 | 39.94 ± 6.15 | 38.81 ± 8.83 | 39.78 ± 3.50  | 34.08 ± 6.86 | 33.67 ± 7.56 | 37.31 ± 10.50 |
| **DHA (ng/mg protein)** | 0.187 ± 0.072 | 0.128 ± 0.032 | 0.191 ± 0.096 | 0.234 ± 0.151 | 0.244 ± 0.076 | 0.204 ± 0.059 | 0.232 ± 0.033 |
| **DPA (ng/mg protein)** | 668.48 ± 320.89 | 637.38 ± 311.20 | 701.29 ± 364.75 | 756.41 ± 268.12 | 743.60 ± 364.28 | 829.23 ± 362.44 | 838.60 ± 211.32 |
| **EPA (ng/mg protein)** | 11361.80 ± 4585.70 | 14229.71 ± 10682.56 | 16718.44 ± 10464.01 | 17637.94 ± 13744.15 | 14637.73 ± 8091.32 | 15271.89 ± 8221.45 | 17264.63 ± 12535.77 |
| **Enzymatically oxidized lipid metabolites** |
| **5-HETE : AA** | 0.00372 ± 0.00088 | 0.00447 ± 0.00091 | 0.00461 ± 0.00077 | 0.00446 ± 0.00165 | 0.00427 ± 0.00077 | 0.00660 ± 0.00135\*\*  | 0.00438 ± 0.00126 |
| **8-HETE : AA** | 0.00319 ± 0.00222 | 0.00335 ± 0.00167 | 0.00354 ± 0.00189 | 0.00315 ± 0.00092 | 0.00273 ± 0.00095 | 0.00343 ± 0.00157 | 0.00291 ± 0.00112 |
| **9-HETE : AA** | 0.00964 ± 0.00671 | 0.01459 ± 0.00935 | 0.01957 ± 0.01605 | 0.01742 ± 0.00632 | 0.01325 ± 0.00702 | 0.02175 ± 0.01162 | 0.01701 ± 0.00590 |
| **11-HETE : AA** | 0.00219 ± 0.00110 | 0.00251 ± 0.00040 | 0.00229 ± 0.00157 | 0.00366 ± 0.00124  | 0.00266 ± 0.00100 | 0.00331 ± 0.00093 | 0.00303 ± 0.00181 |
| **12-HETE : AA** | 0.00365 ± 0.00195 | 0.00424 ± 0.00258 | 0.00478 ± 0.00284 | 0.00601 ± 0.00435 | 0.00474 ± 0.00299 | 0.00561 ± 0.00312  | 0.00485 ± 0.00295 |
| **15-HETE : AA** | 0.00424 ± 0.00273 | 0.00512 ± 0.00332 | 0.00537 ± 0.00375 | 0.00638 ± 0.00416 | 0.00582 ± 0.00334 | 0.00712 ± 0.00373 | 0.00609 ± 0.00326 |
| **4-HDoHE : DHA** | 8.77 ± 2.80 | 15.07 ± 7.27 | 12.17 ± 9.03 | 9.97 ± 4.16 | 7.74 ± 2.69 | 10.74 ± 3.57 | 9.96 ± 4.31 |
| **7- HDoHE : DHA** | 2.46 ± 2.03 | 4.60 ± 1.91 | 2.31 ± 0.78 | 2.48 ± 1.96 | 2.03 ± 0.76 | 2.72 ± 0.82 | 2.43 ± 1.49 |
| **8- HDoHE : DHA** | 12.26 ± 6.85 | 19.20 ± 14.19 | 13.34 ± 5.51 | 18.29 ± 9.22 | 11.04 ± 7.61 | 17.75 ± 9.65 | 14.36 ± 7.44 |
| **11- HDoHE : DHA** | 4.52 ± 2.94 | 6.03 ± 2.53 | 5.29 ± 0.77 | 5.97 ± 2.58 | 4.77 ± 2.45 | 7.47 ± 4.22 | 4.72 ± 2.86 |
| **14- HDoHE : DHA** | 19.30 ± 5.67 | 29.34 ± 4.97 | 23.12 ± 6.95 | 23.18 ± 6.06 | 12.47 ± 7.73 | 20.61 ± 9.06 | 24.15 ± 10.70 |
| **17- HDoHE : DHA** | 6.54 ± 2.90 | 6.69 ± 0.66 | 6.98 ± 2.77 | 10.28 ± 7.02 | 6.87 ± 6.66 | 9.88 ± 6.85 | 8.01 ± 8.45 |
| **Non-enzymatically oxidized lipid metabolites**  |
| **F2-IsoPs : AA** | 0.00897 ± 0.00318 | 0.01003 ± 0.00364 | 0.01075 ± 0.00310 | 0.01279 ± 0.00963 | 0.01177 ± 0.00441 | 0.01262 ± 0.00332 | 0.01134 ± 0.00309 |

**Table S1(B). Levels of PUFAs and other detectable PUFA metabolites at 24h.** Levels of PUFAs were expressed as absolute quantity normalized with the protein content. Levels of PUFA metabolites were expressed as ratio of metabolite to precursor PUFA. All results are shown as mean ± SD (n = 5). Significance level \*\*p < 0.01 determined by one-way ANOVA. F2-Isoprostanes (F2-IsoPs)



**Figure S1. Levels of HETEs at 6h.** No significant changes on the AA-to-HETE conversions were observed at 6h across all exposures. Results are expressed as mean ± SD (n = 5).