Supplementary Information

Insights into the Protective Effect of Pycnogenol Against Methotrexate-Induced Toxicity: *in silico* and *in vivo* study

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Supplement for regression analysis

1- Biochemical analysis:

a) Serum biomarkers:

i. Liver function: activities of ALT, AST enzymes

ii. Kidney function: level of urea and creatinine

iii. Heart function: level of troponin and activities of CK and CK-MB enzymes

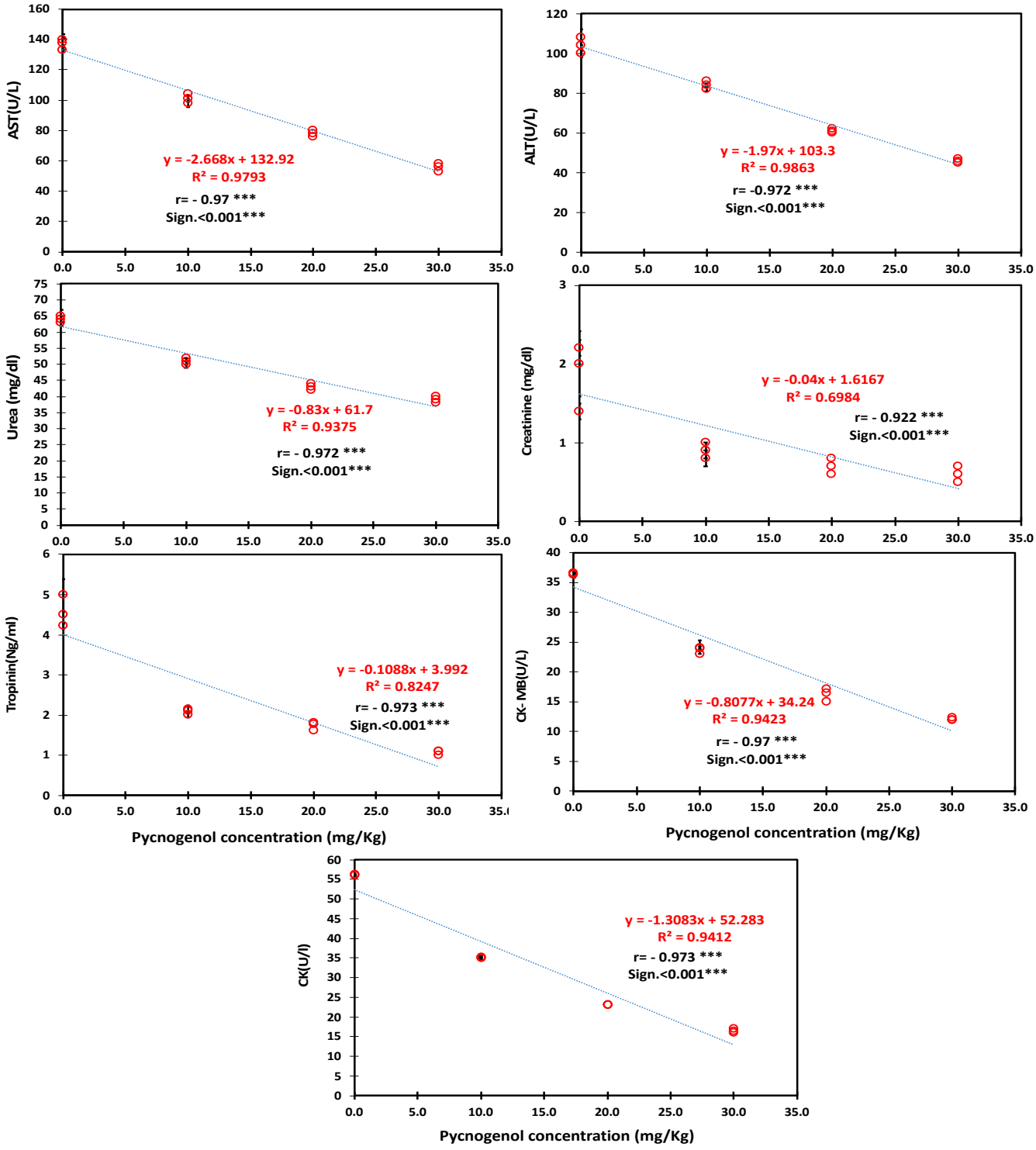

Figure S1. Regression trendline showing the relationship between increasing Pycnogenol levels (10, 20, and 30 mg Kg^{-1}) with various serum biomarkers.

B) Tissue markers: (heart, liver and kidney)

i. Inflammatory biomarkers: NF-κB and TNF-α level

ii. Oxidative stress markers: MDA, ATP and GSH levels, activities of SOD and CAT enzymes

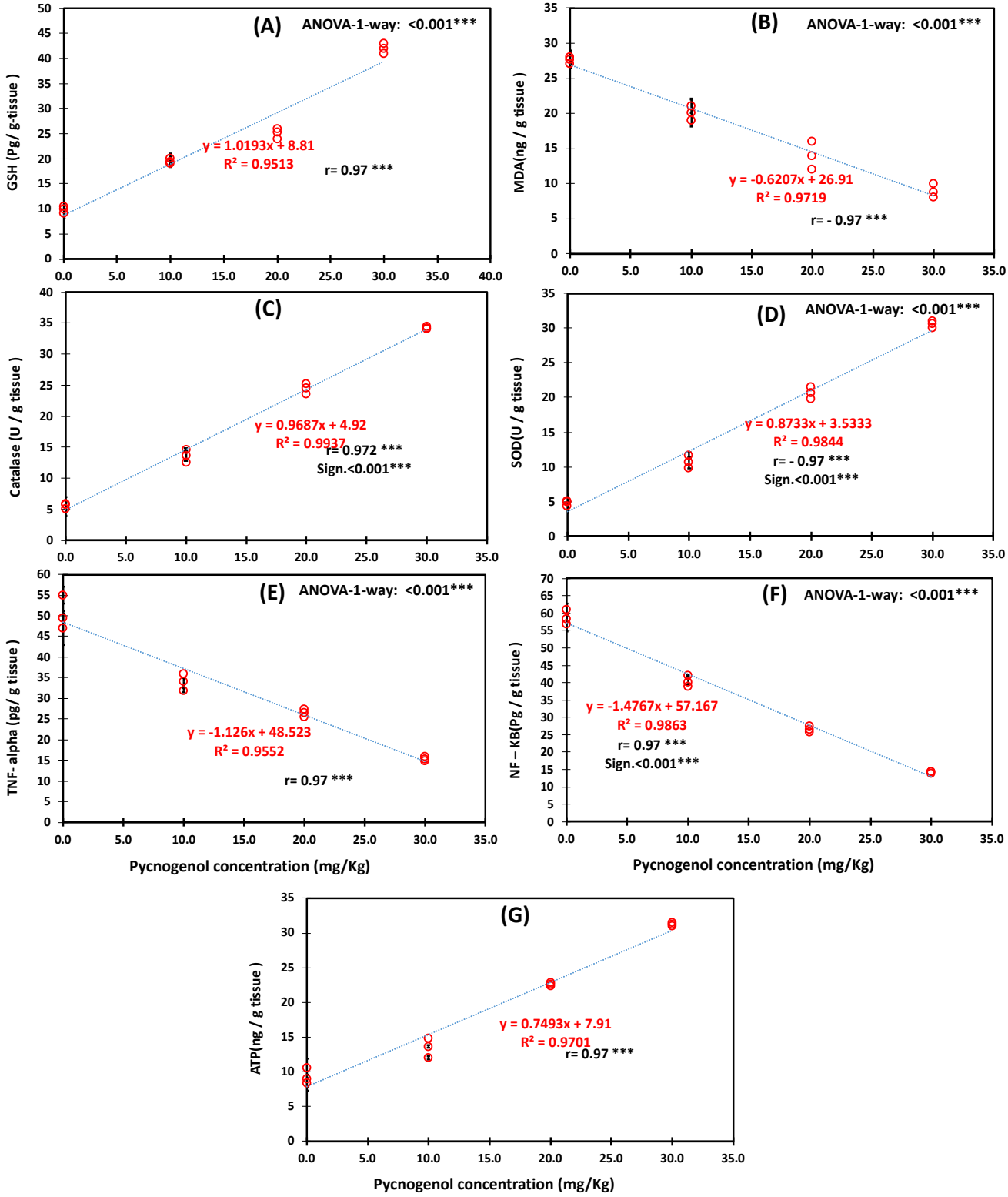

Figure S2. Regression trendline showing the relationship between increasing Pycnogenol levels (10, 20, and 30 mg Kg-1) and various heart biomarkers.

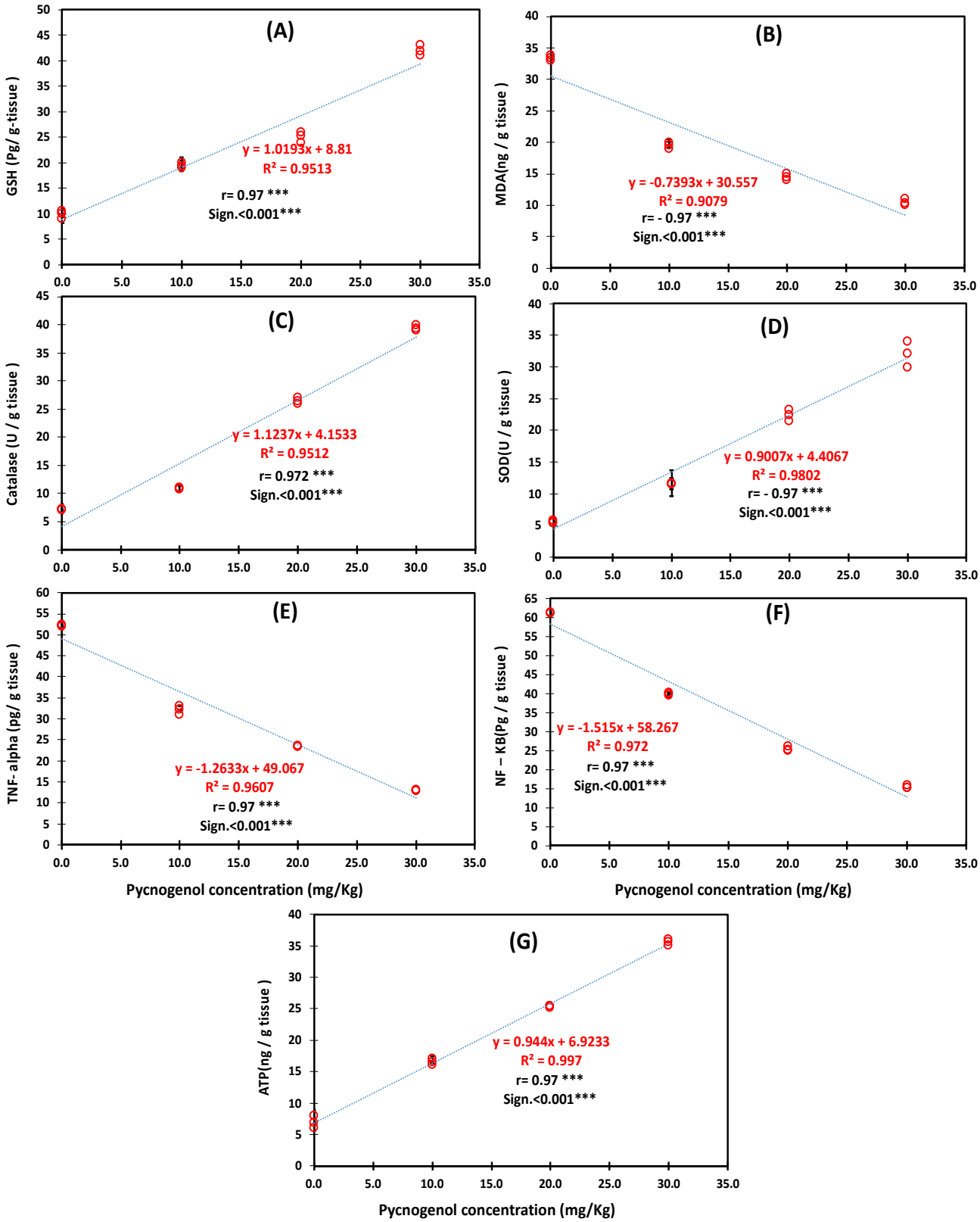

Figure S3. Regression trendline showing the relationship between increasing Pycnogenol levels (10, 20, and 30 mg Kg-1) and various liver biomarkers.

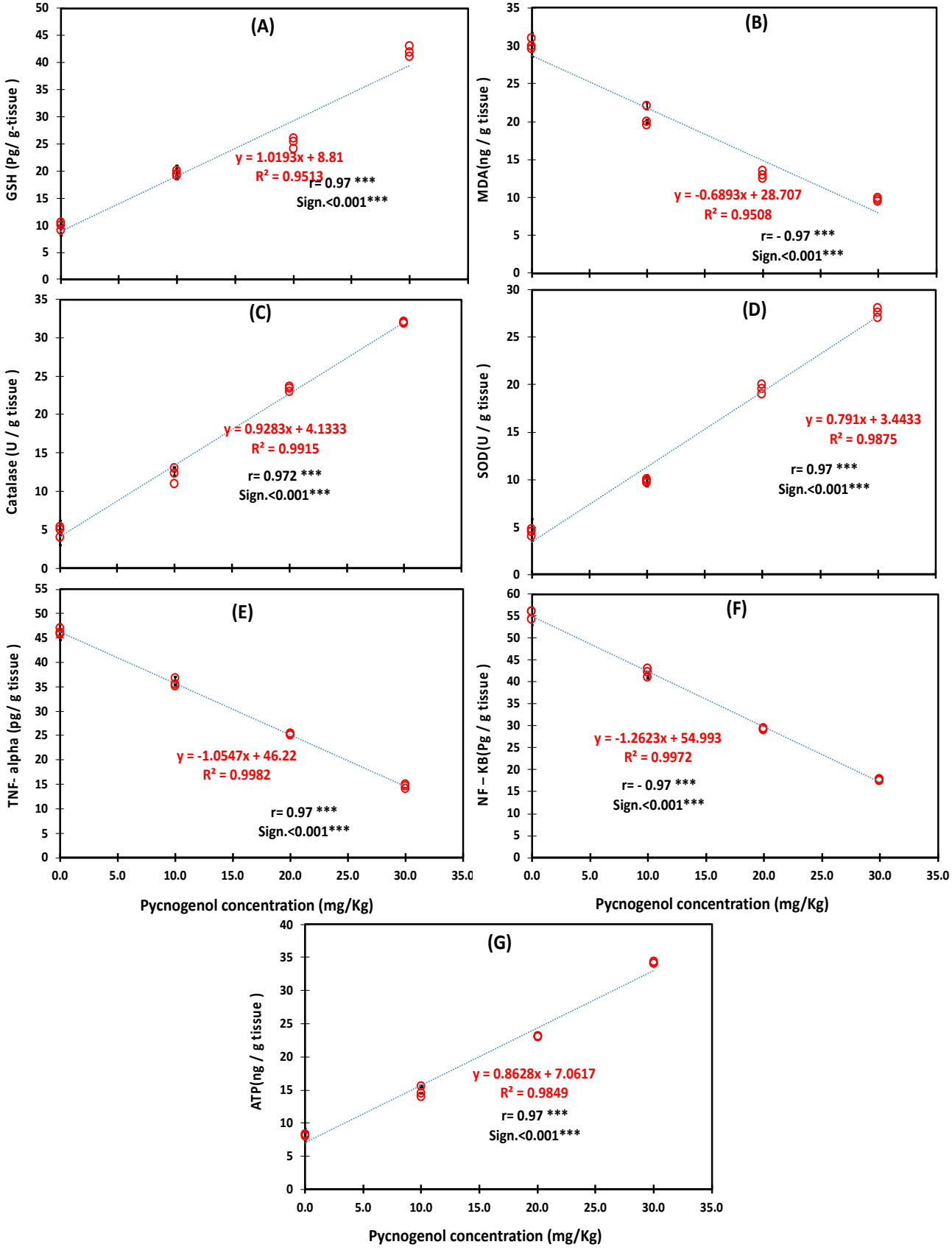

Figure S4. Regression trendline showing the relationship between increasing Pycnogenol levels (10, 20, and 30 mg Kg-1) and various kidney biomarkers.