Supporting Information

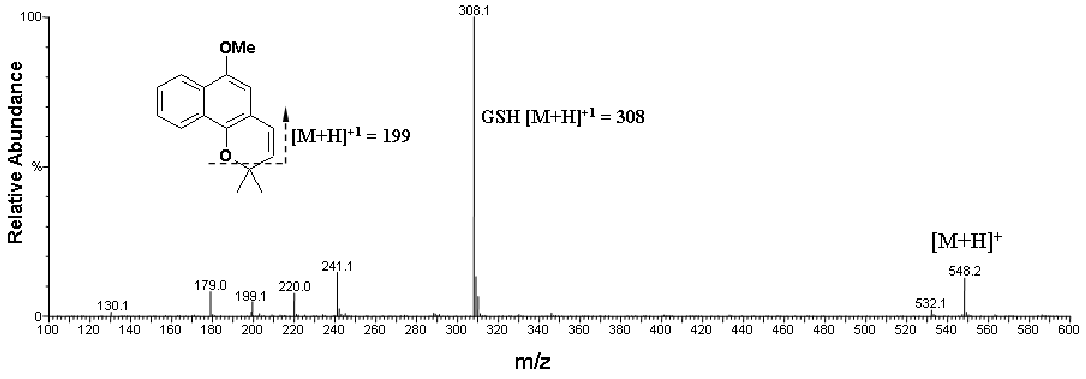

Figure S1- ESI-mass spectrum of the lapachenole-glutathione conjugate. The base peak at 308 amu is derived from the glutathione nucleus, while the peak at 199 amu is the lapachenole nucleus after loss of a propyl group from its dimethylated carbon center.

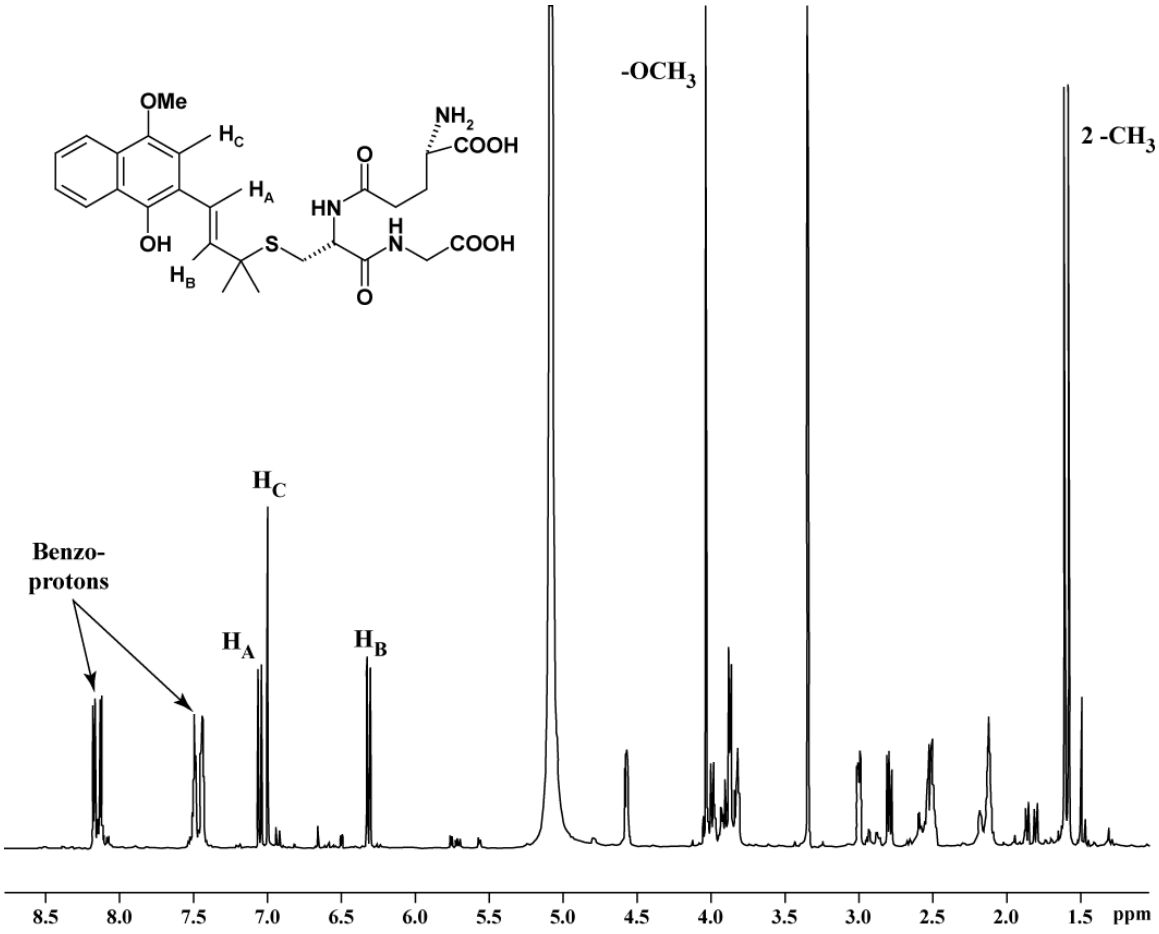

Figure S2- ^{1}H NMR spectrum of the lapachenole-glutathione conjugate obtained at 750 MHz in deuterated methanol.

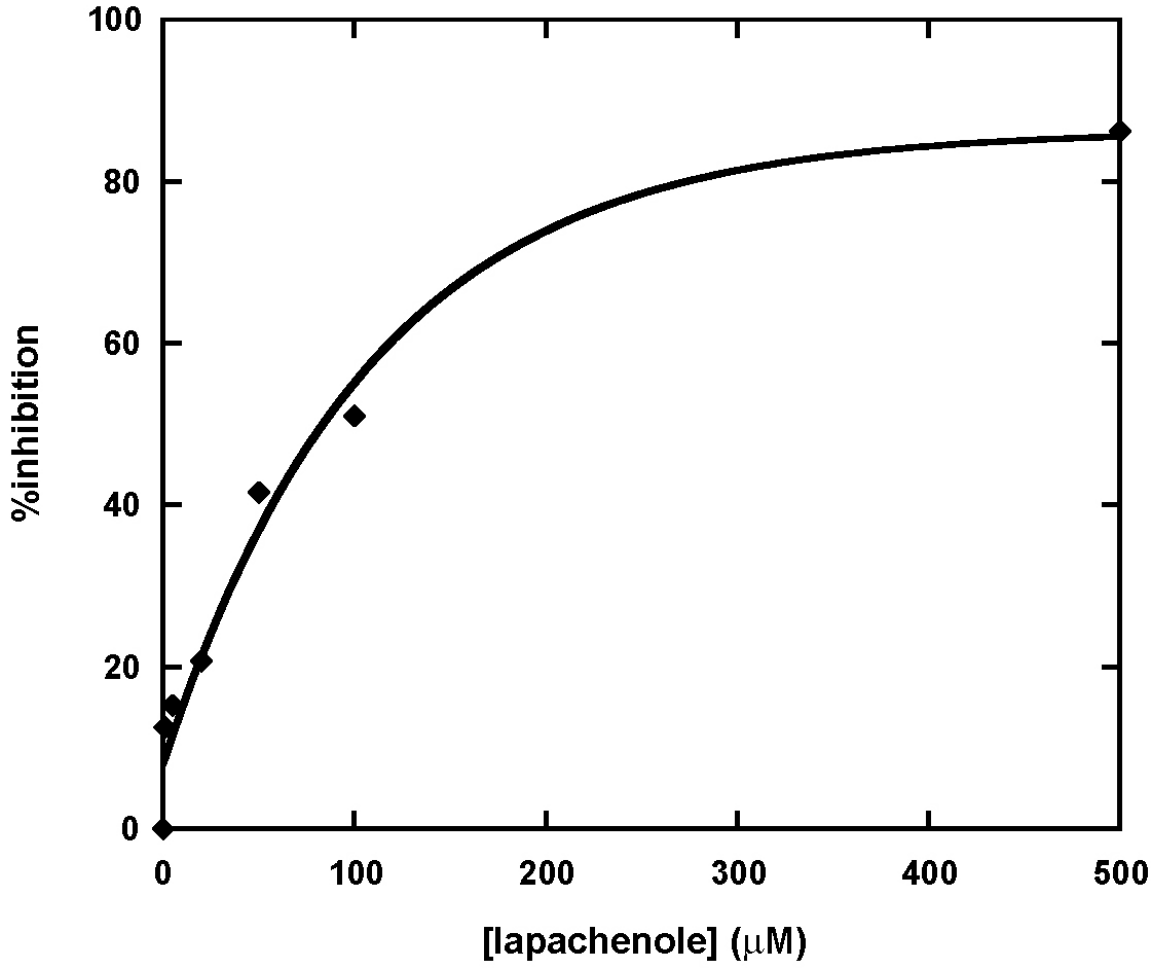

Figure S3- Inhibition of P450 3A4-mediated oxidation of midazolam by lapachenole.

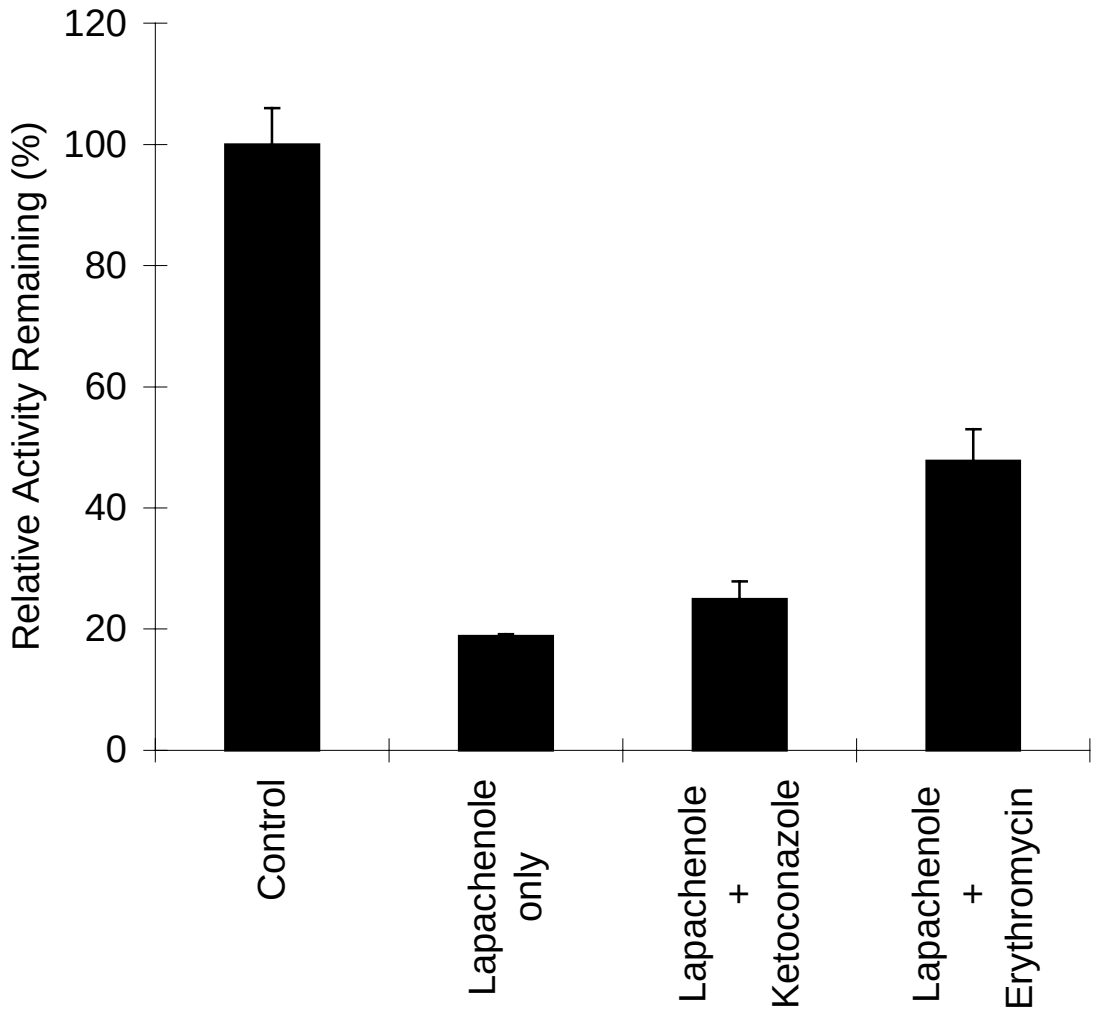

Figure S4- Photolabeling inhibition of CYP3A4-HT activity by lapachenole as measured by CYP3A4 midazolam 1'-hydroxylation activity. Ketoconazole-treated preparations were exposed to 50 μM ketoconazole prior to irradiation. Erythromycin-treated samples were exposed to 60 μM erythromycin prior to irradiation.

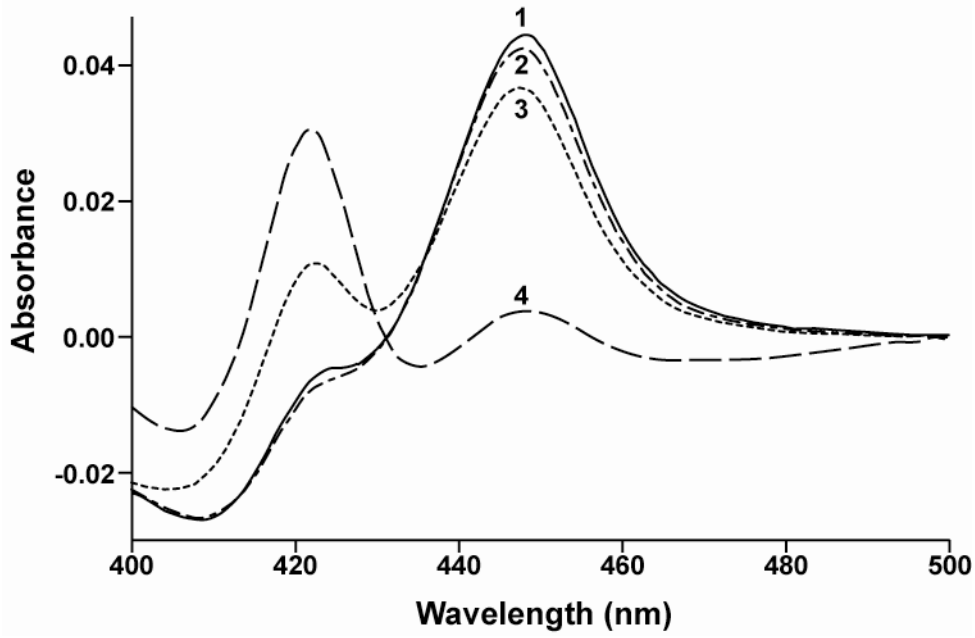

Figure S5- Influence of lapachenole binding to P450 3A4 on CO-reduced difference spectra. Trace 1: P450 3A4-HT. Trace 2: Enzyme preparation subjected to photolysis conditions. Trace 3: Enzyme preparation treated with 200 μM lapachenole in the dark. Trace 4: Enzyme preparation treated with lapachenole and irradiated for one minute.