Appendix 1: Ordinary differential equations of the model

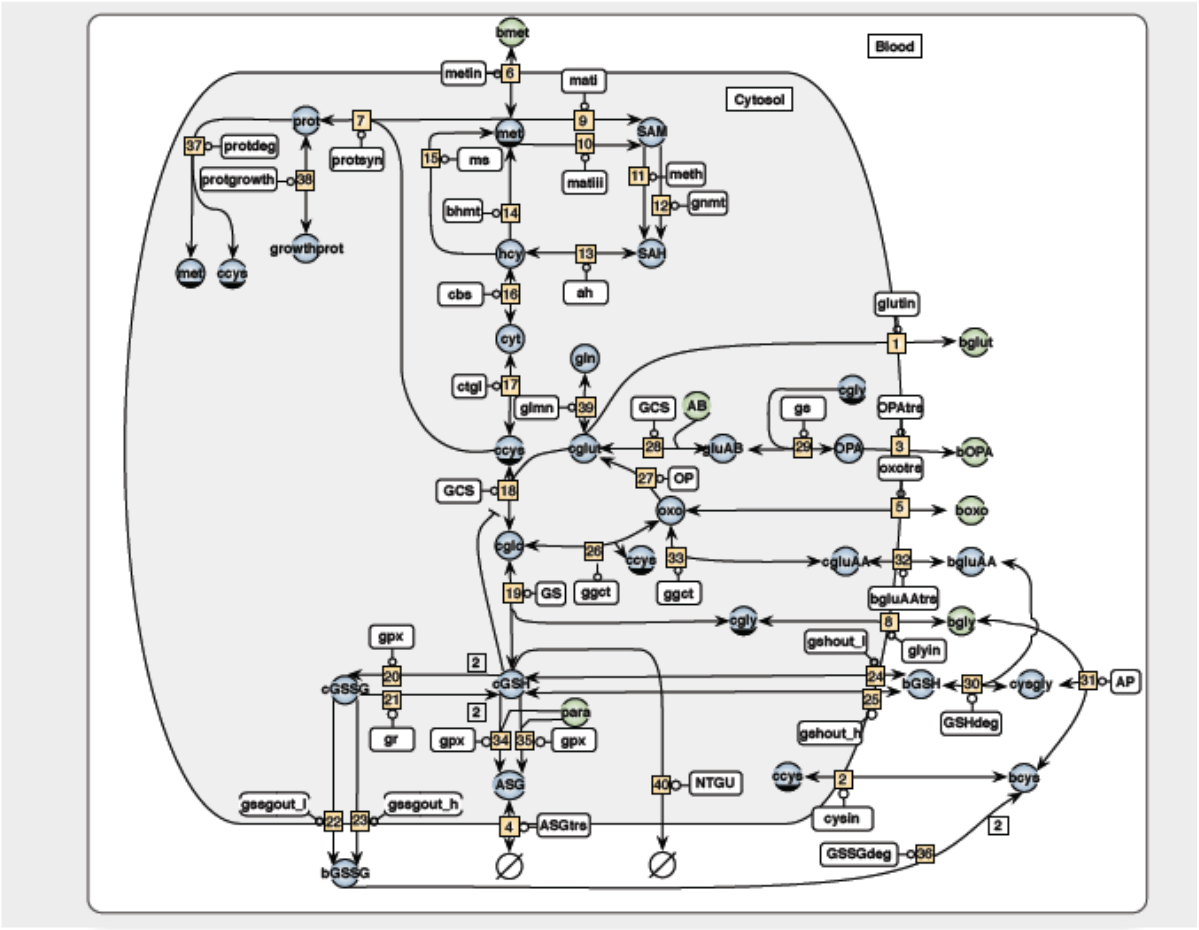

Figure A1.1: Schematic of glutathione systems model

Appendix 2: Initial concentrations and quantities of the model. Values are rounded to three significant digits.

	Units	Initial concentration human model	Initial concentration rat model
cglut	µM	1000	993
bcys	µM	29.6	29.5
ccys	µM	278	278
OPA	µM	0.05	0
bOPA	µM	0.45	0
ASG	µM	0	0
bASG	µM	0	0
oxo	µM	1100	651
boxo	µM	9450	12
bmet	µM	13	13
met	µM	316	316
cgly	µM	1050	1050
SAM	µM	4.54	4.64
SAH	µM	148	152
hcy	µM	1.77	1.78
cyt	µM	274	274
cglc	µM	72.3	43.8
cGSH	µM	10000	6100
cGSSG	µM	69.8	57.6
bGSSG	µM	3.71	3.08
bGSH	µM	3.49	3.45
gluAB	µM	0.11	0.08
bgluAA	µM	9.53	9.33
cysgly	µM	0.97	0.97
cgluAA	µM	36.4	34.8
growthprot	µM	3290	3290
gln	µM	1020	1020
prot	µM	3090	3090
Spara	µM	1.00	1.00
para	µM	0.00	0.00
Gpara	µM	1.00	1.00
pArt	µmoles	0.00	0.00
pLung	µmoles	0.00	0.00
pVen	µmoles	0.00	0.00
pTiss	µmoles	0.00	0.00
pKid	µmoles	0.00	0.00
pUri	µmoles	0.00	0.00
pExt	µmoles	0.00	0.00
opArt	µmoles	0.14	0.00
opLung	µmoles	0.05	0.00

opTiss	µmoles	3.12	0.01
opKid	µmoles	0.02	0.00
opDEG	µmoles	0.00	0.00
oxArt	µmoles	3020	8.09
oxLung	µmoles	1130	0.88
oxTiss	µmoles	65700	161
oxKid	µmoles	371	1.60
oxUri	µmoles	0.00	0.00
ivpara	µmoles	13200	43.9

Appendix 3: The rat model predictions of the hepatic paracetamol and metabolite concentrations changes with varying paracetamol and methionione

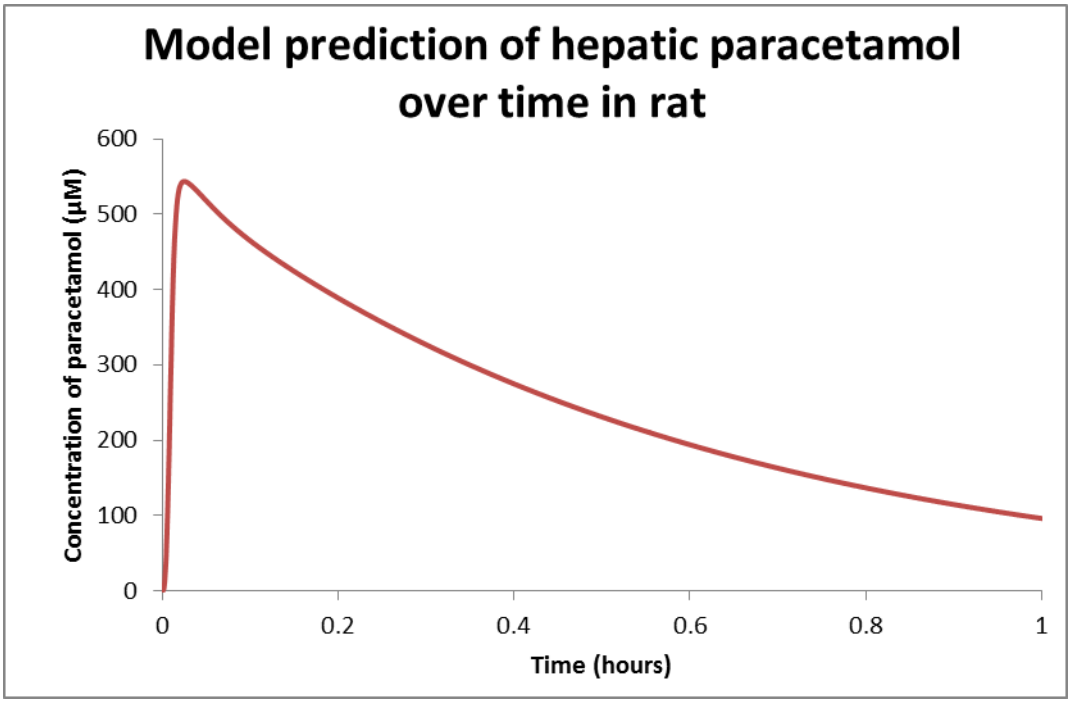

Figure A3.1: Model predicted time course of paracetamol concentration in the rat liver compartment following a 15 mg/kg paracetamol IV infusion.

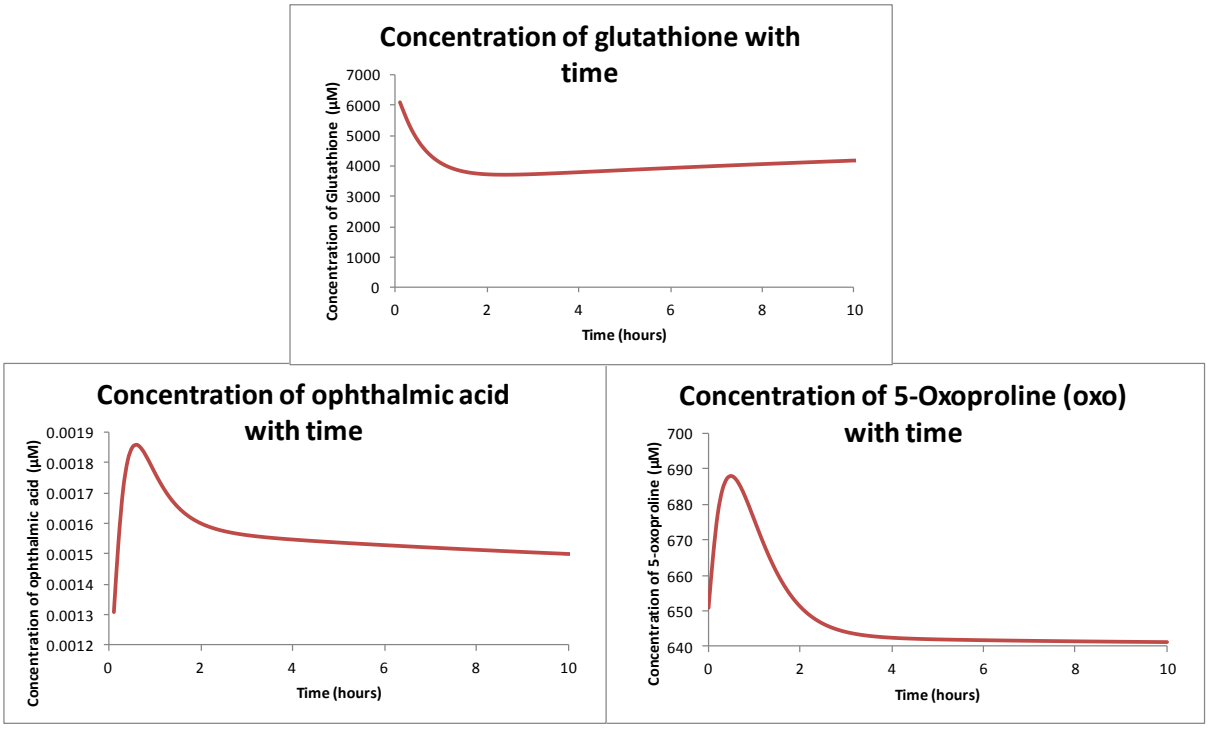

Figure A3.2: Predicted changes to the rat model concentration of glutathione, ophthalmic acid and 5-oxoproline in the liver compartment following a 15 mg/kg paracetamol IV infusion.

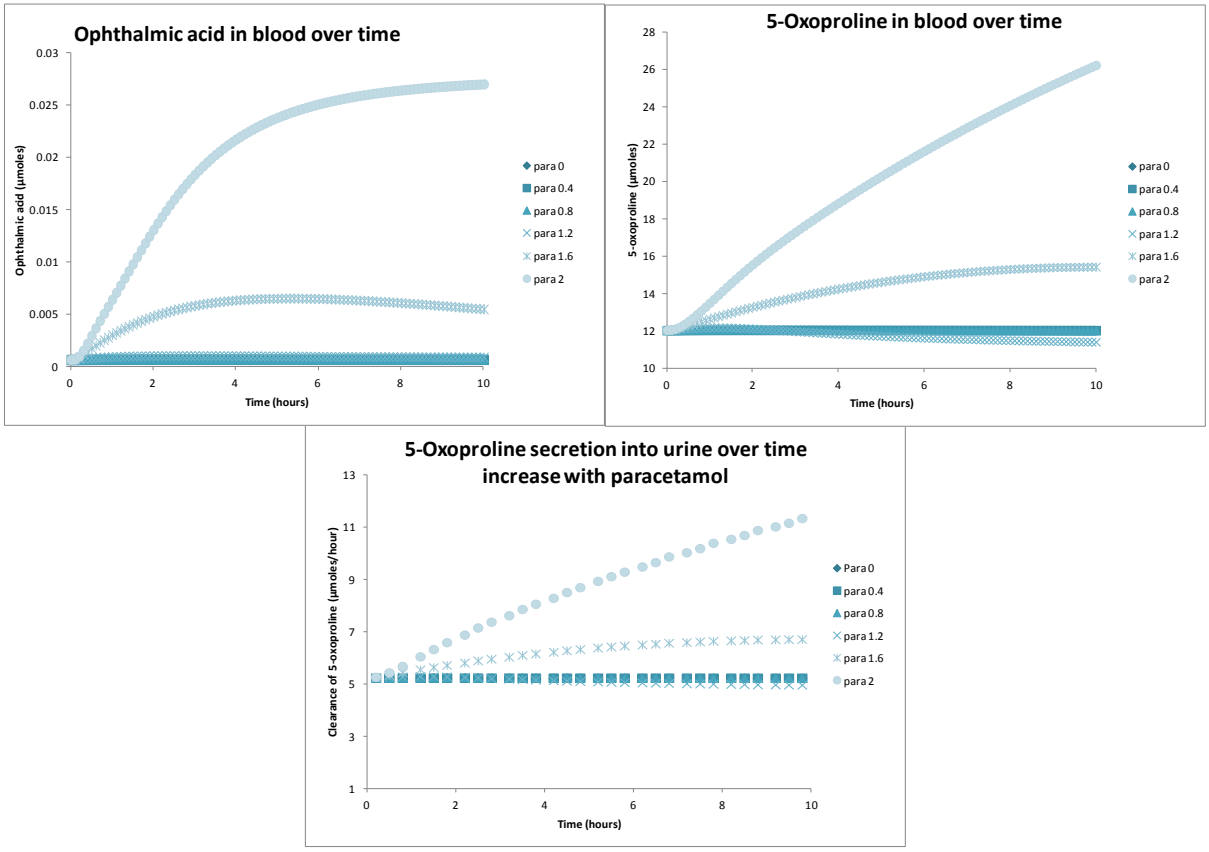

Figure A3.3: Model predictions of the concentration of biomarkers in the blood (top) and the rate of secretion into the urine (bottom) when varying paracetamol from 0 to 2 mmoles