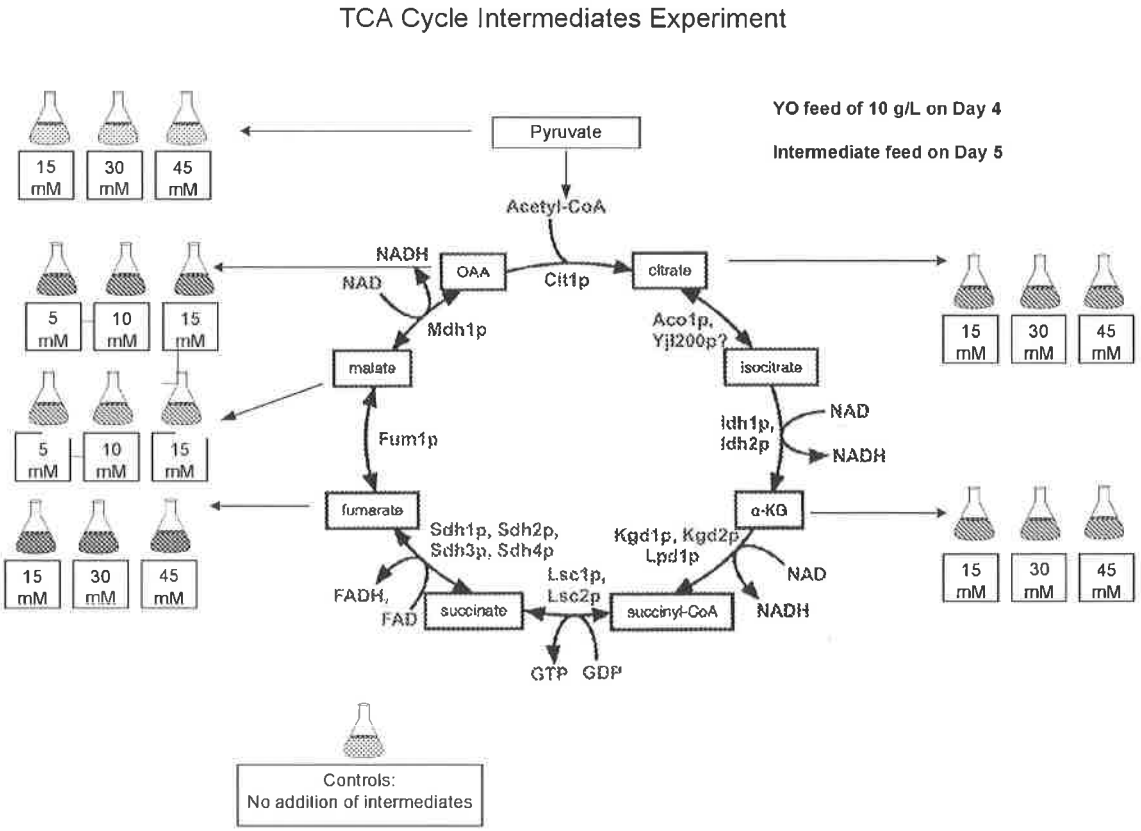


Figure 1 Experimental design for dose response study of the TCA cycle intermediates

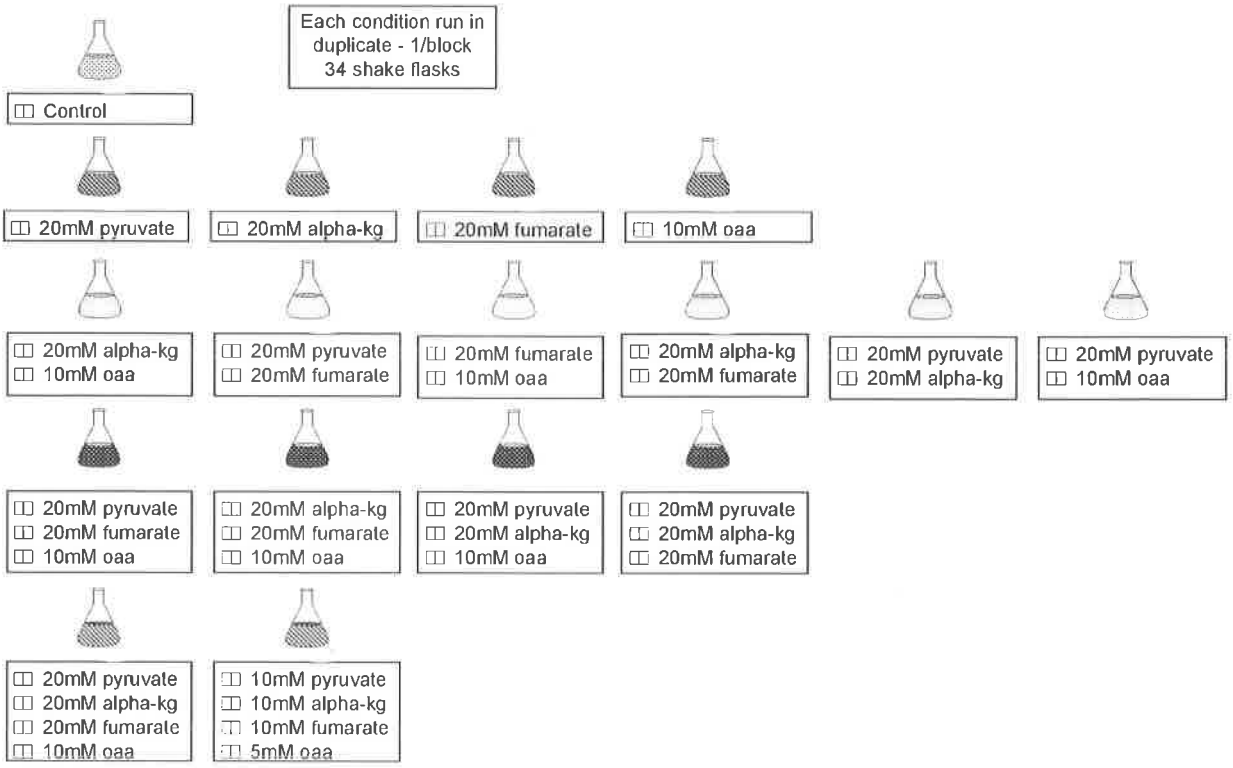


Figure 2 Experimental design for block # 1 of the TCA cycle intermediates interaction study

Malate Intermediates Interaction Experiment
Block 2

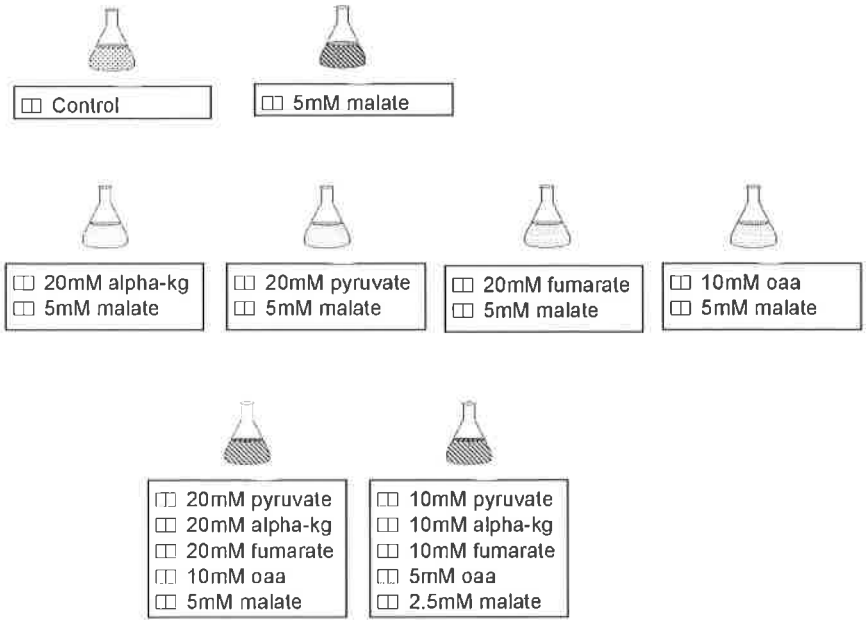


Figure 3 Experimental design for block # 2 of the TCA cycle intermediates interaction study

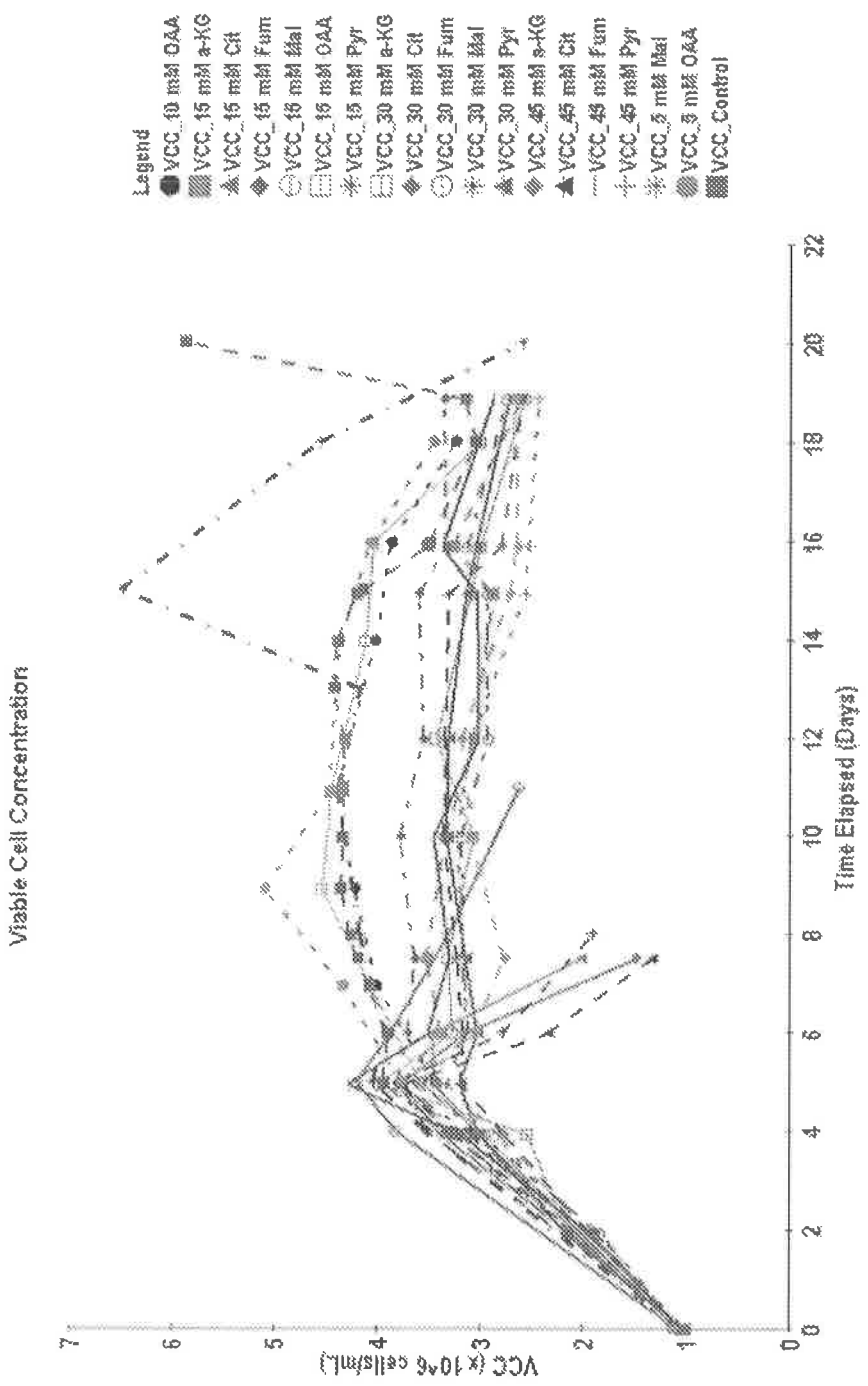


Figure 4 Viable Cell Concentration for conditions, lines show average of duplicate shake flasks

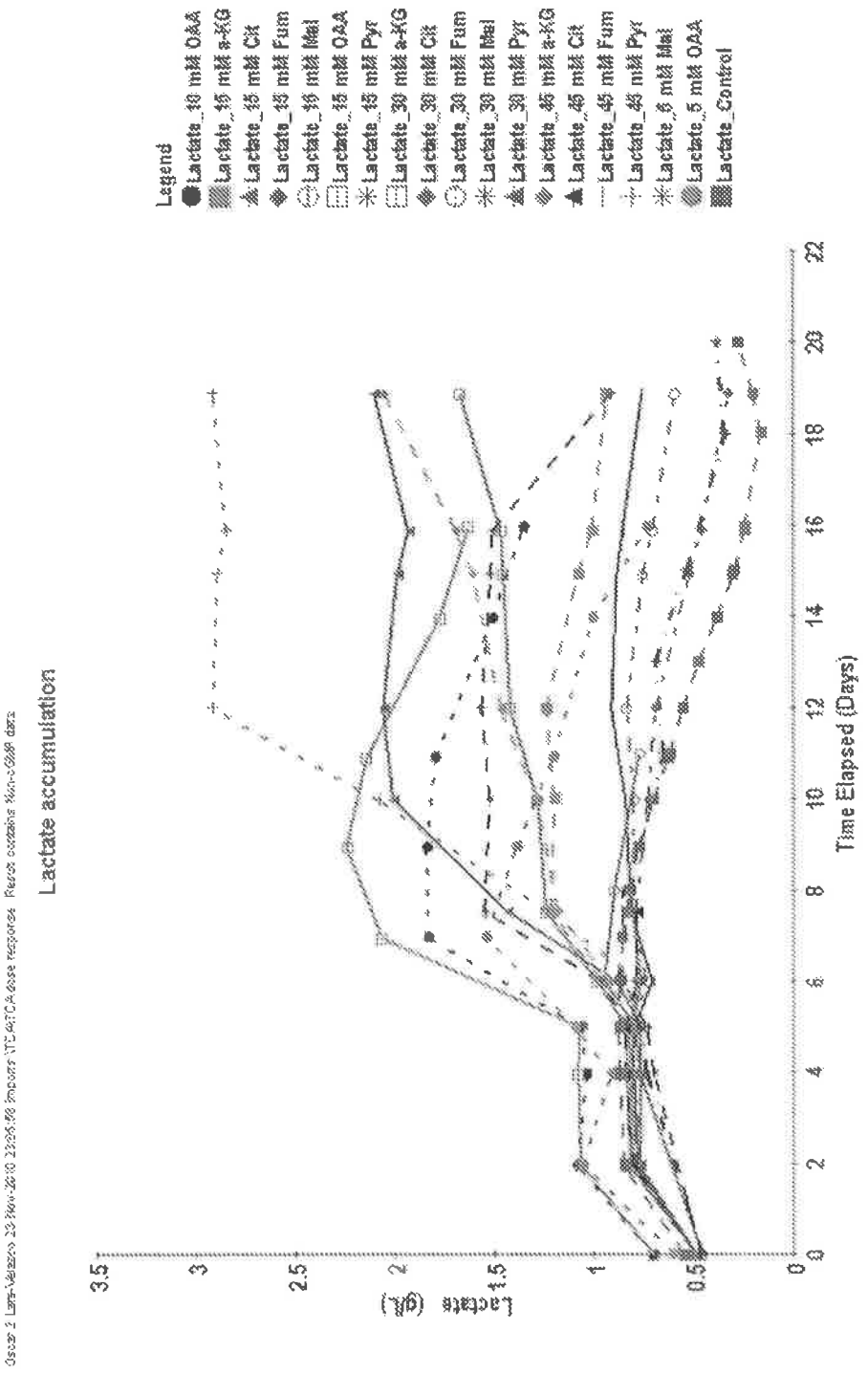


Figure 5 Lactate accumulation in shake flask studies. Lines show average of duplicate conditions

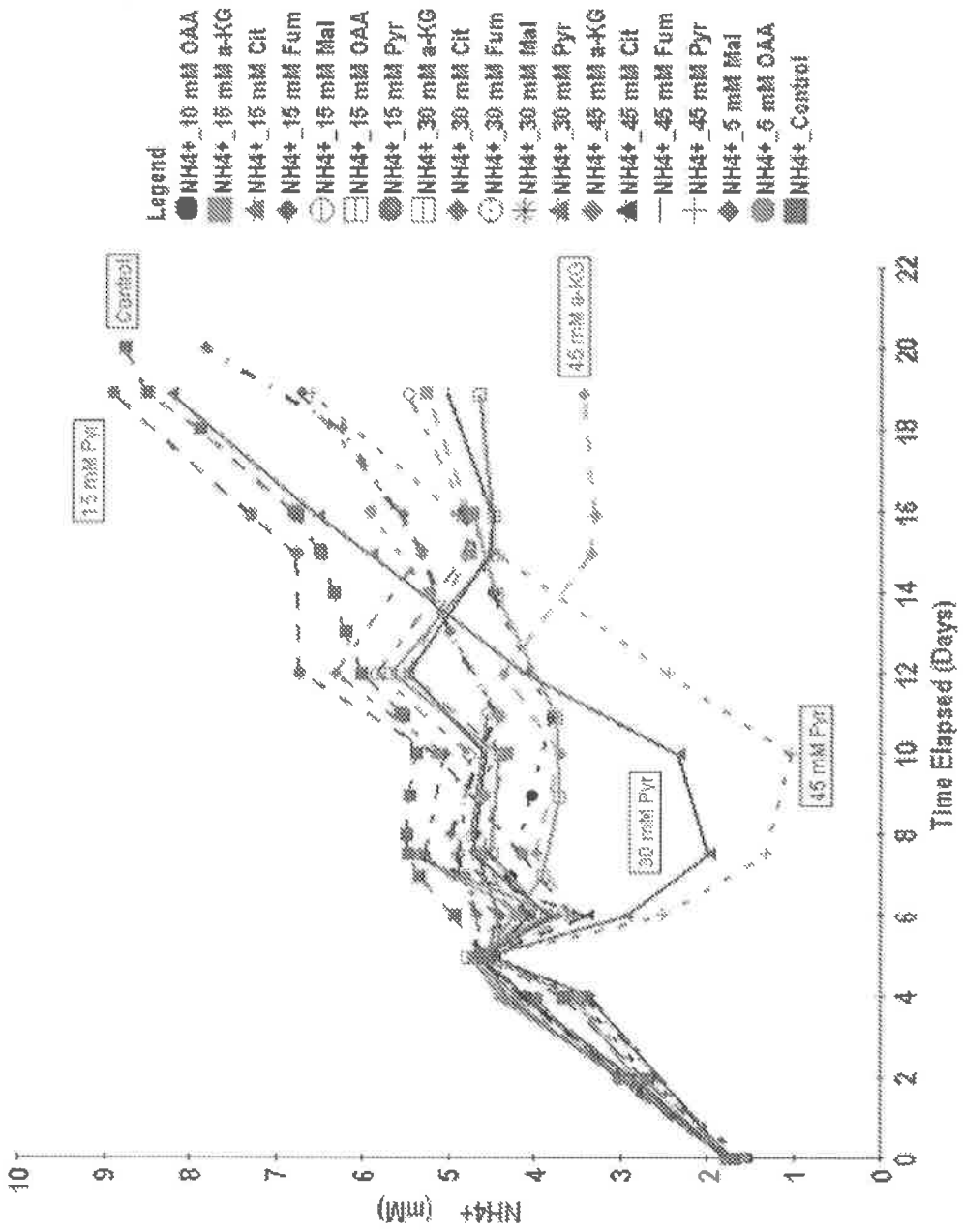


Figure 6 Ammonium accumulation for all conditions tested. Lines show average of duplicate shake flasks for each condition tested

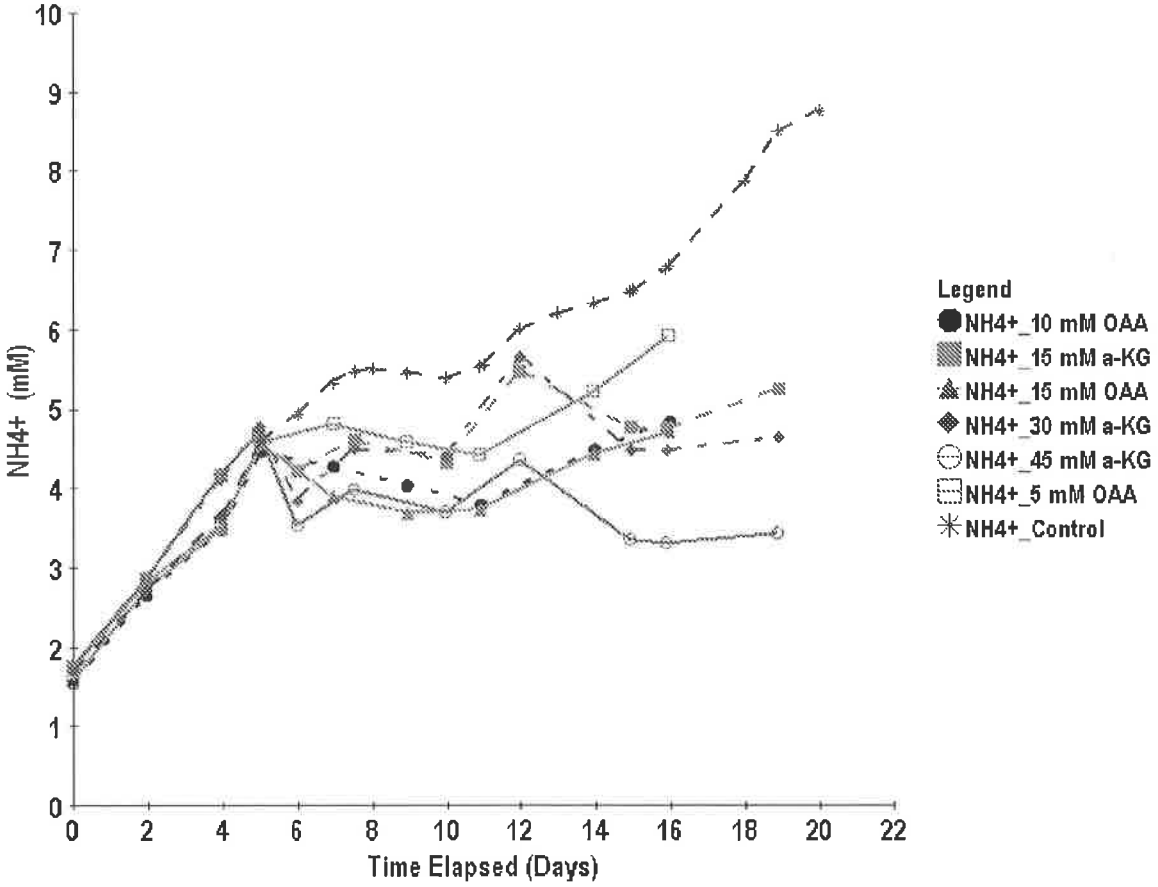


Figure 7 Ammonium accumulation for α-KG and oxaloacetic acid addition to culture. Lines show average of duplicate shake flasks for each condition tested

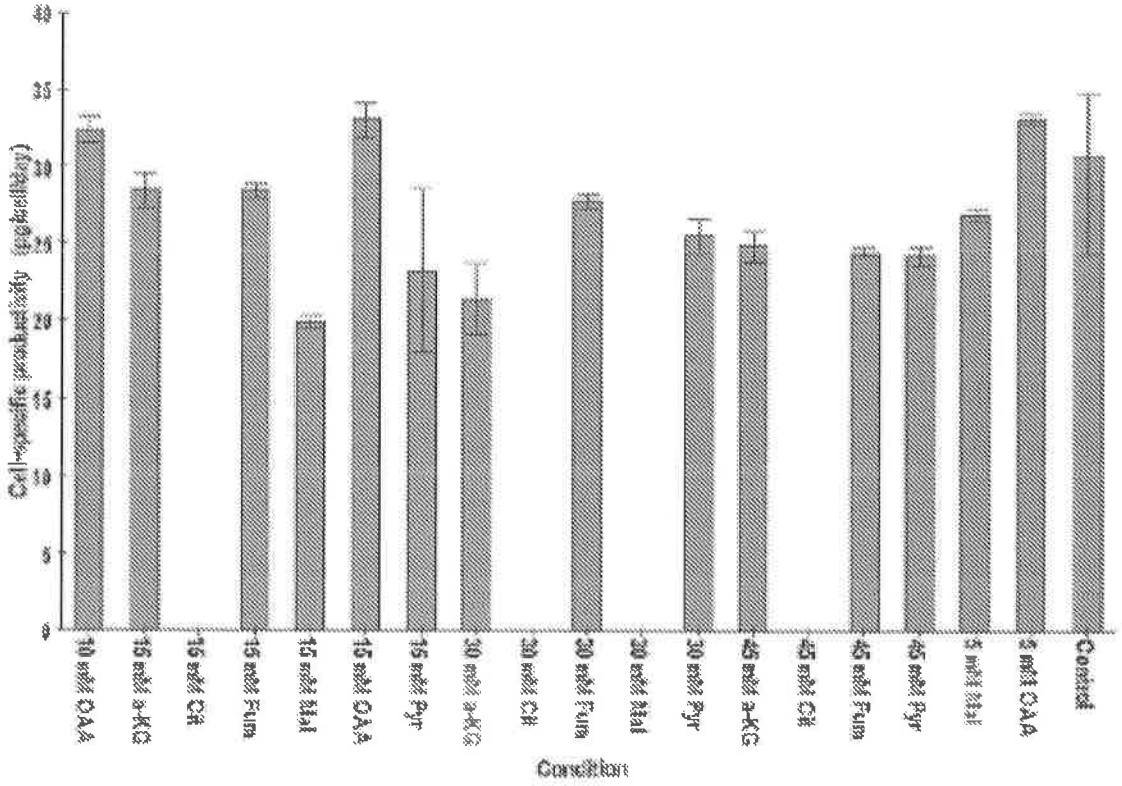


Figure 8 Cell-specific productivity of cultures treated with different levels of TCA intermediates. Error bars show value ranges

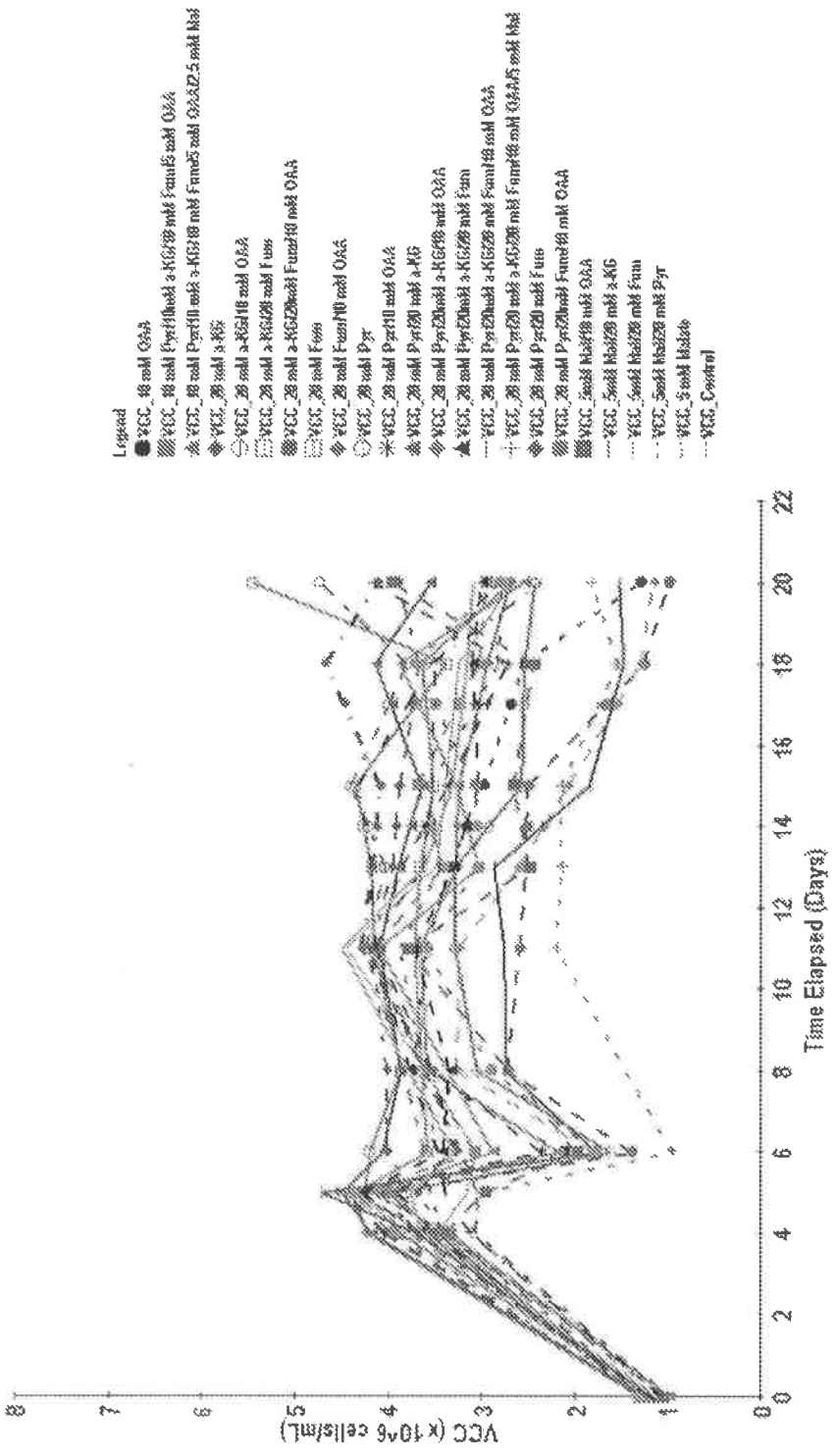


Figure 9 Viable cell concentration for all conditions tested in Block 1 and Block 2 of the DOE

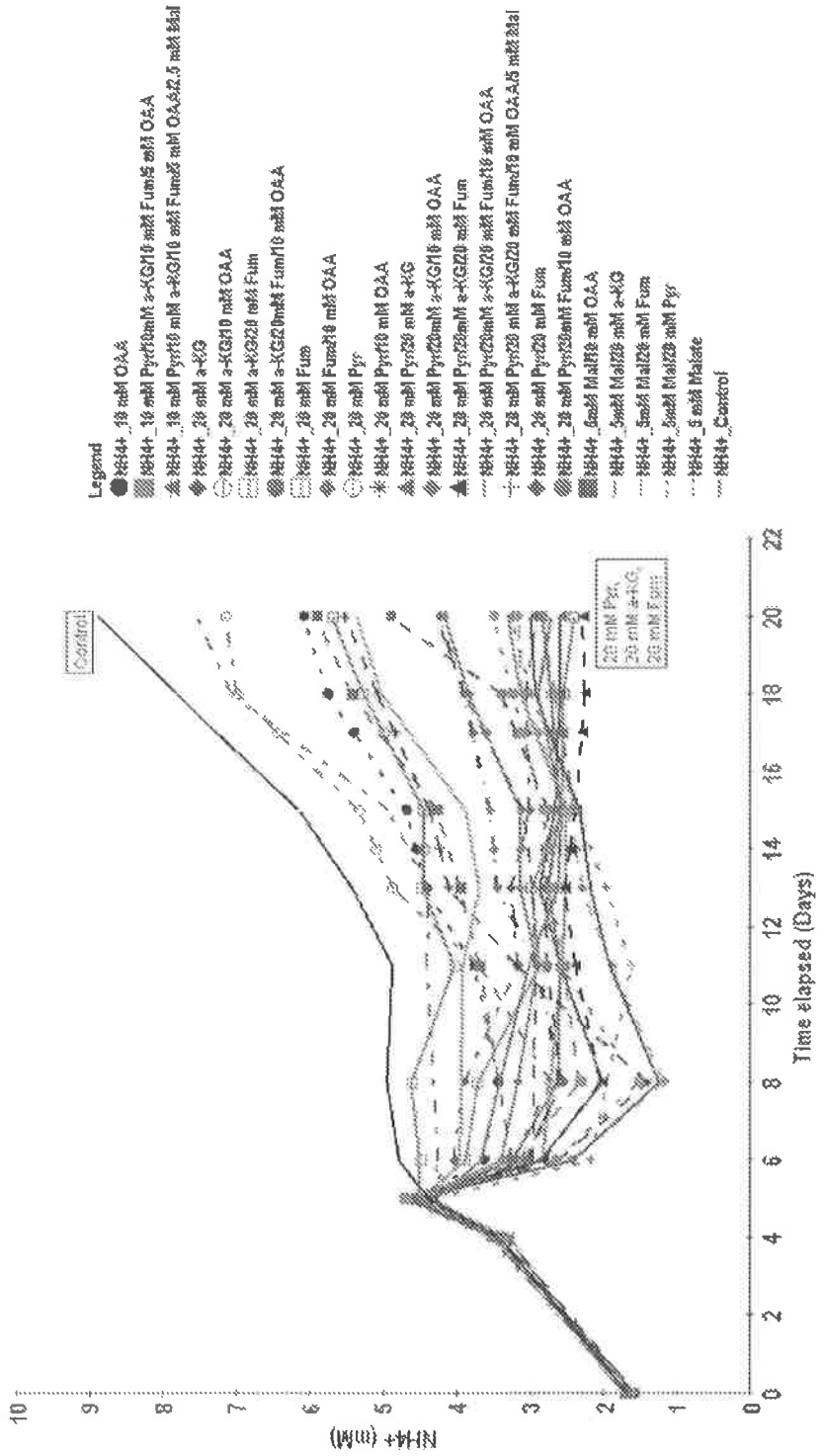


Figure 10 Ammonia accumulation profiles for all conditions tested in Block 1 and Block 2 of the DOE.

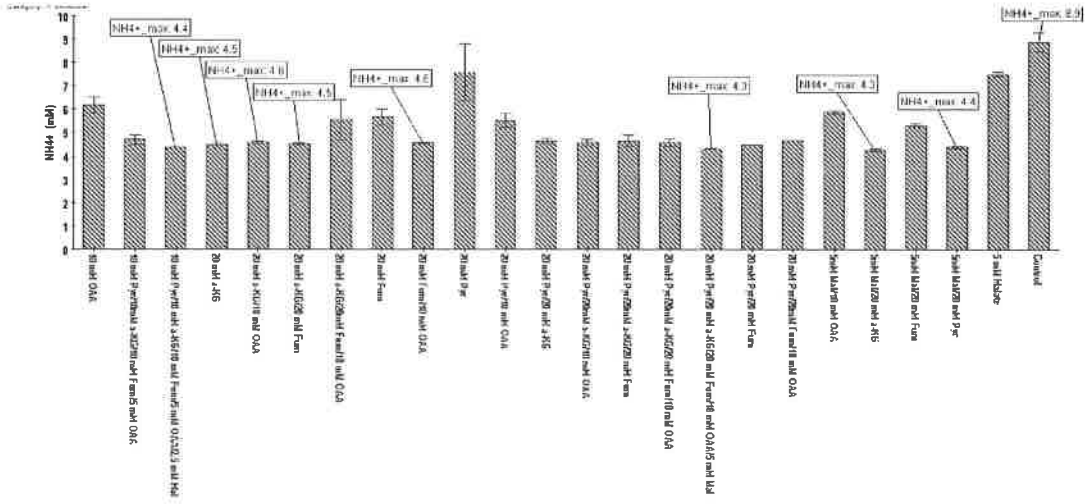


Figure 11 Maximum ammonia accumulation for all conditions tested in Block 1 and Block 2 of the DOE

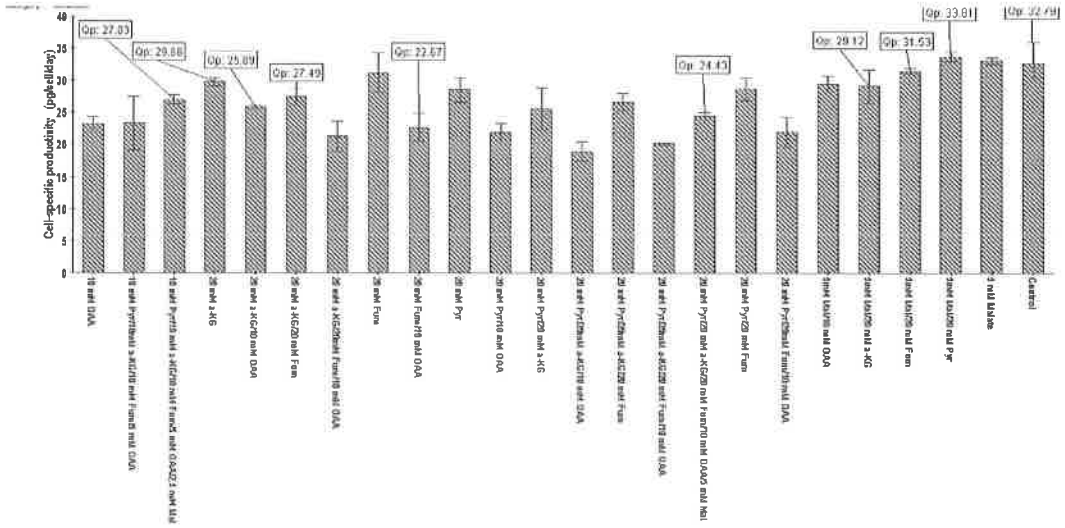


Figure 12 Final cell-specific productivity for all conditions tested in Block 1 and Block 2 of the DOE

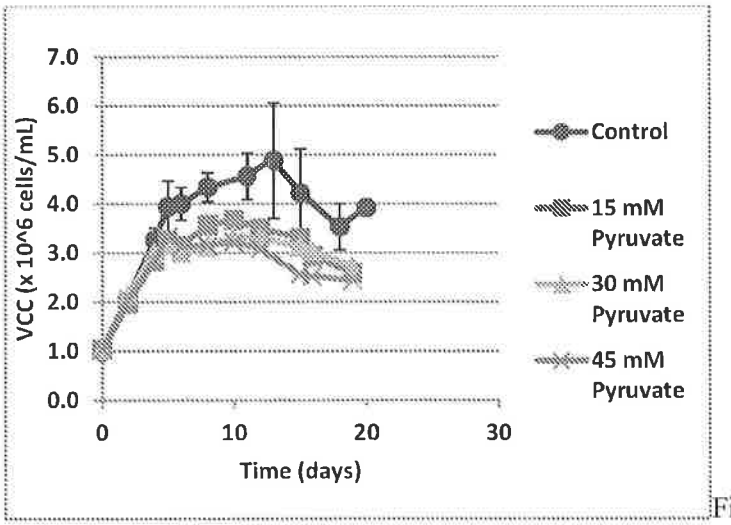


Figure 12a

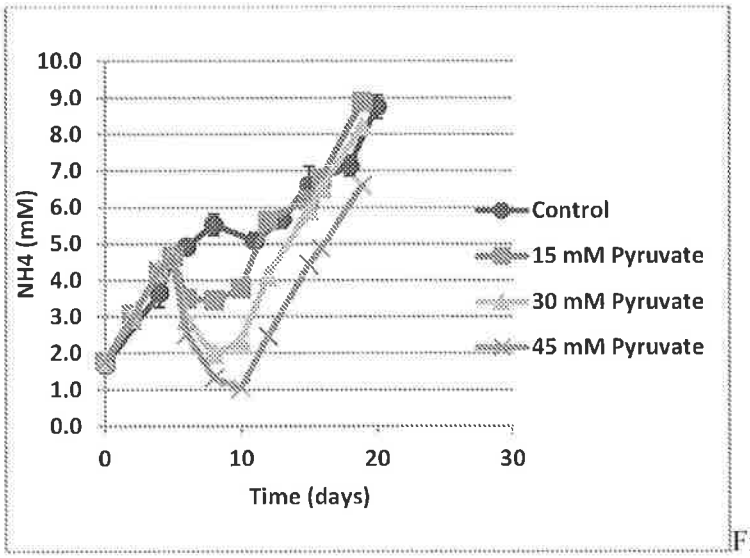


Figure 12b

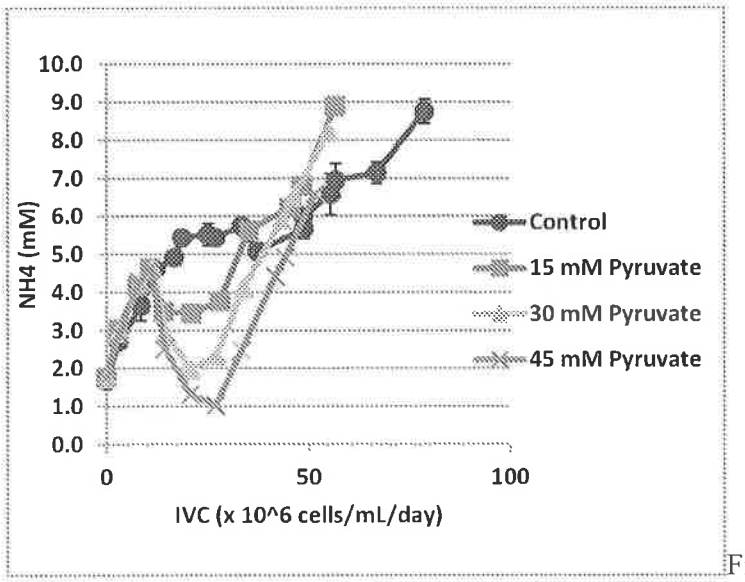


Figure 12c

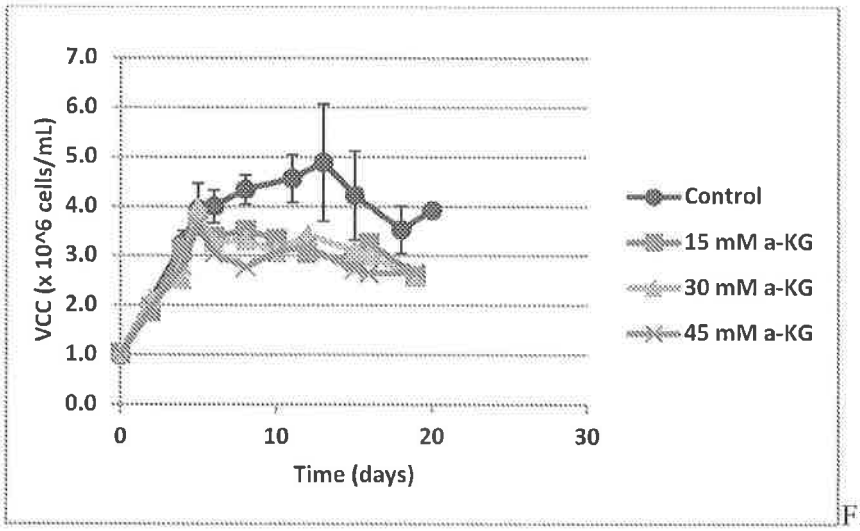


Figure 13a

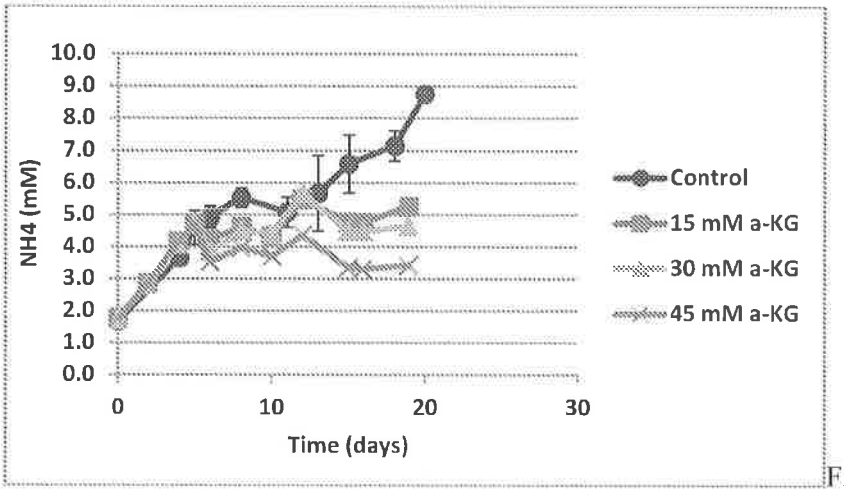


Figure 13b

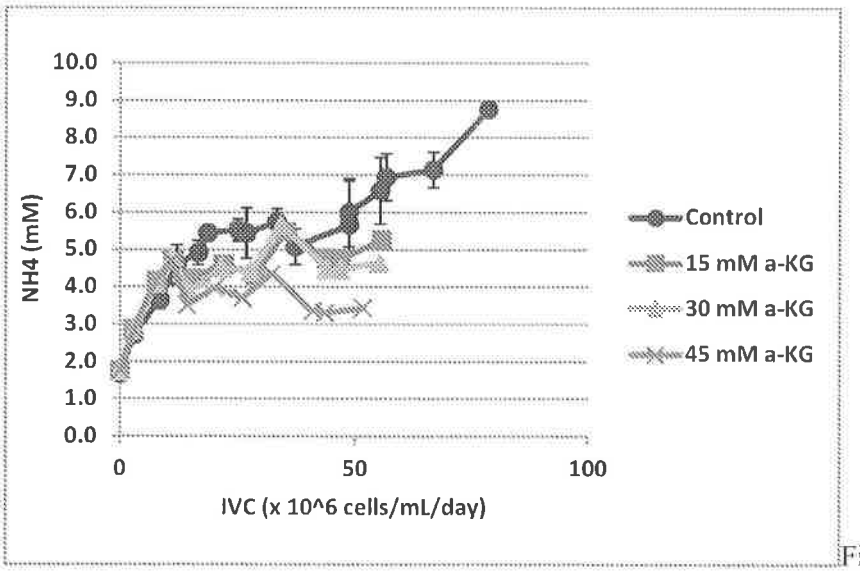


Figure 13c

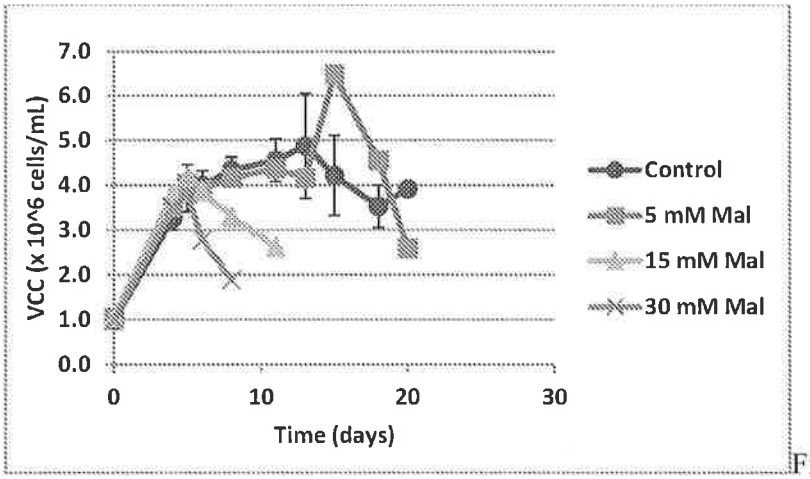


Figure 14a

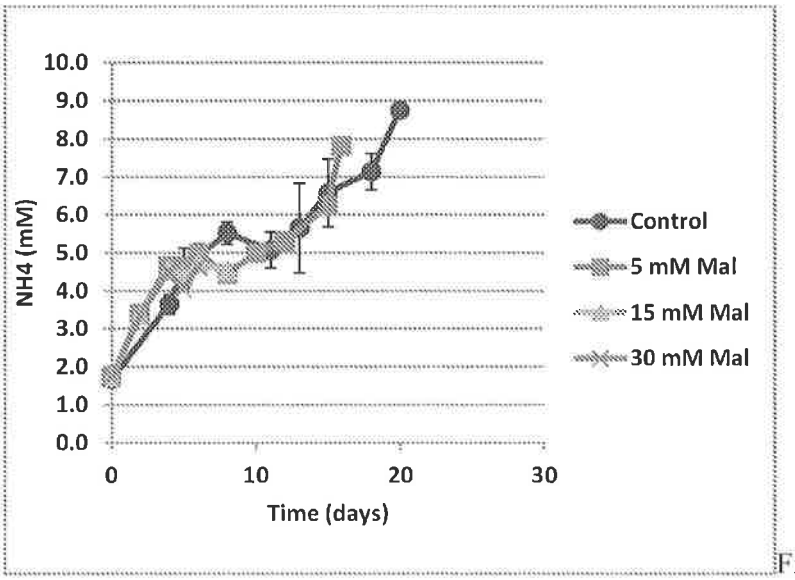


Figure 14b

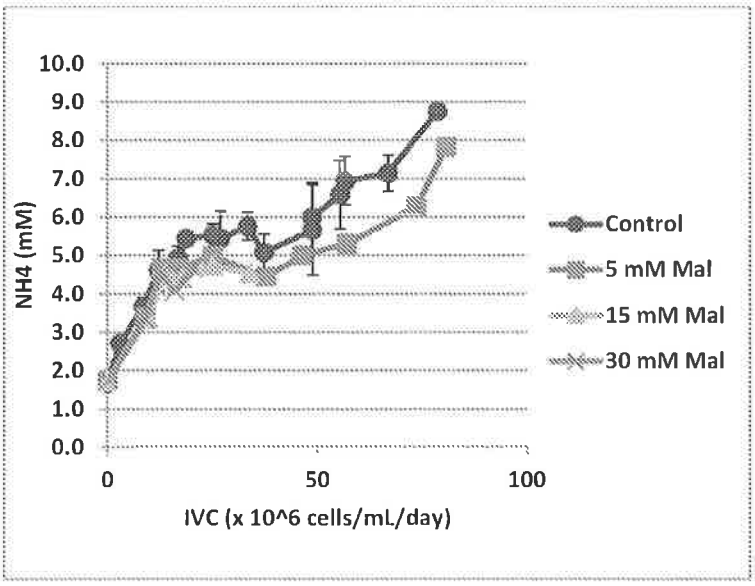


Figure 14c

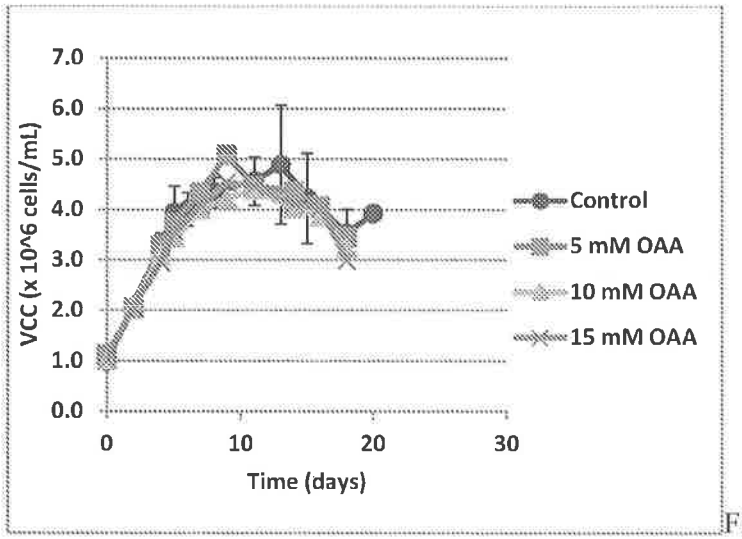


Figure 15a

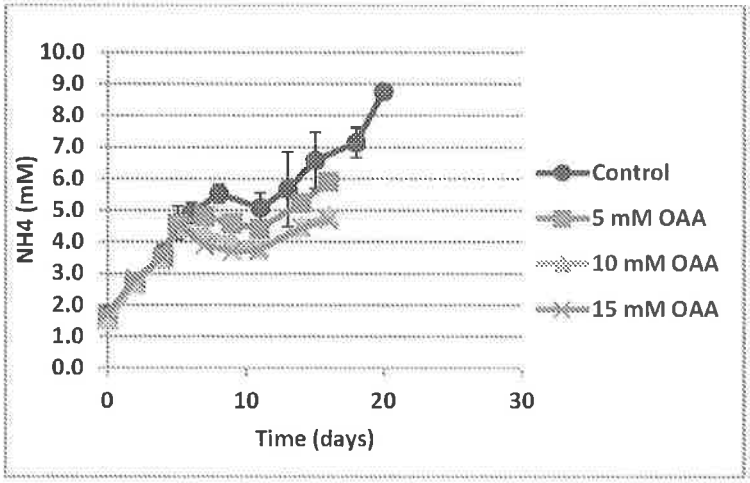


Figure 15b

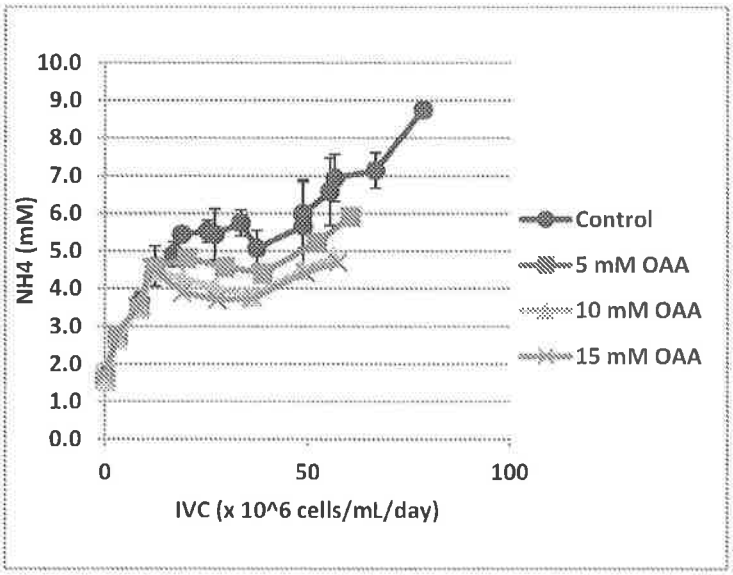


Figure 15c

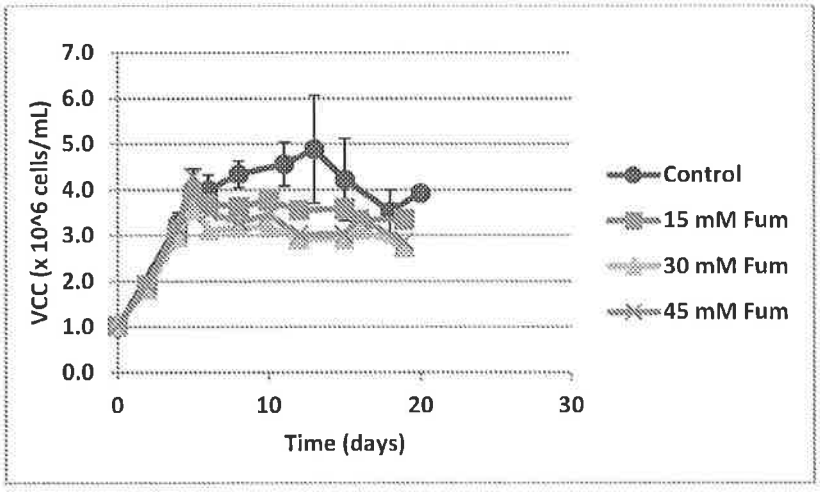


Figure 16a

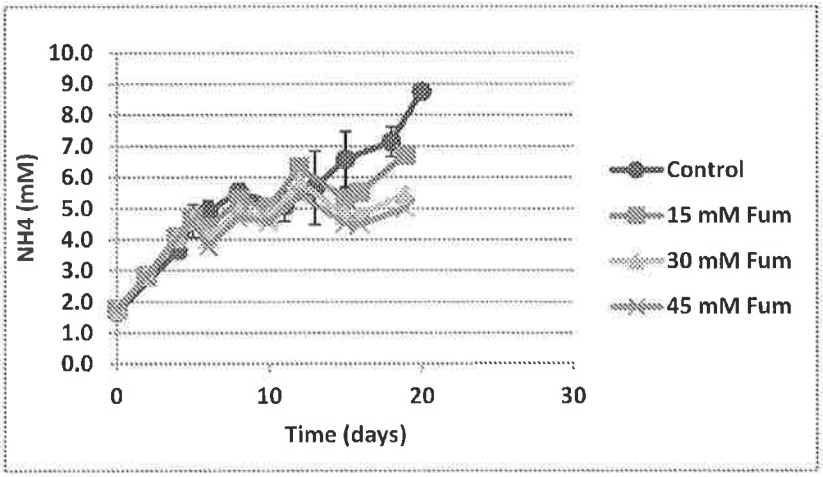


Figure 16b

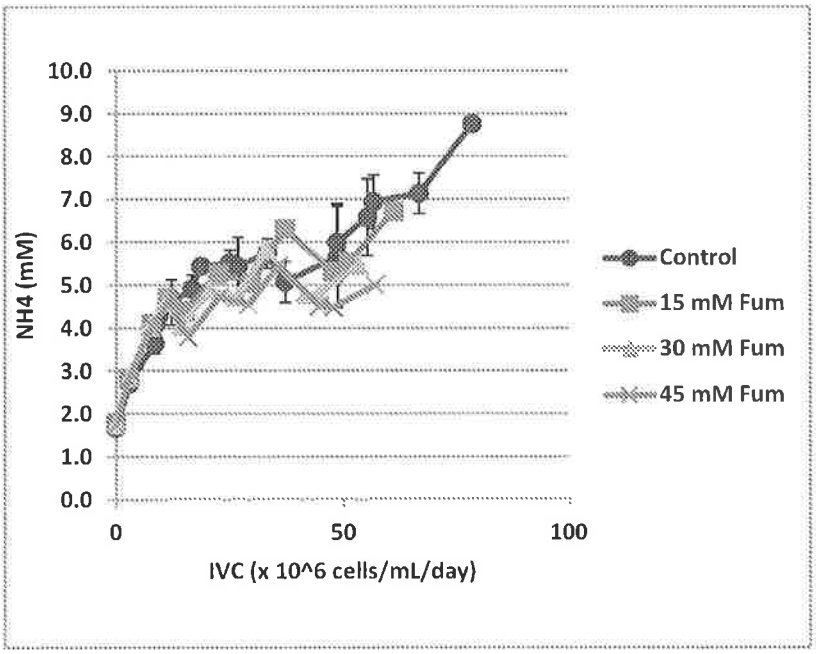


Figure 16c

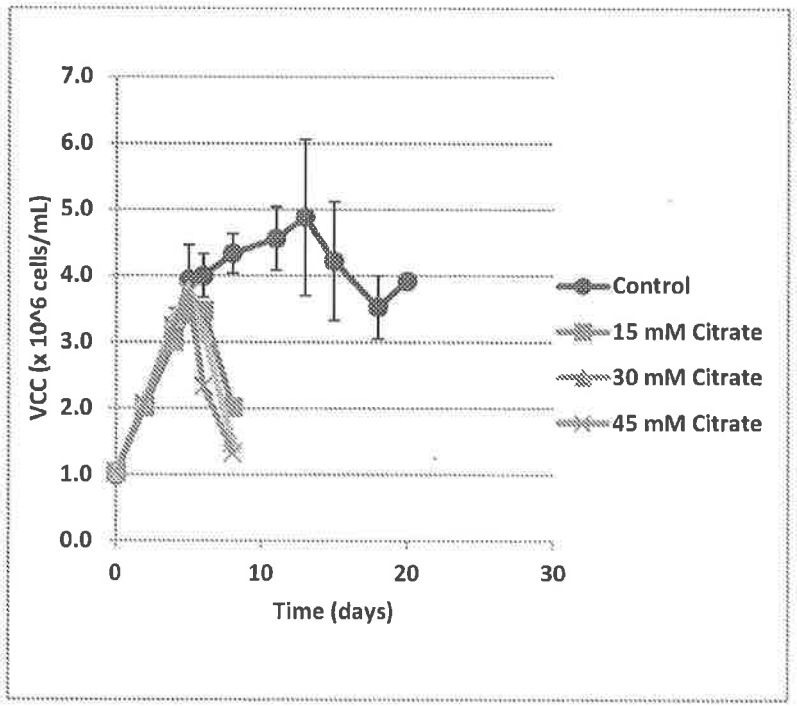

7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
VCC (x 10^6 cells/mL)
0
10
20
30
Time (days)
Control
15 mM Citrate
30 mM Citrate
45 mM Citrate

Figure 17

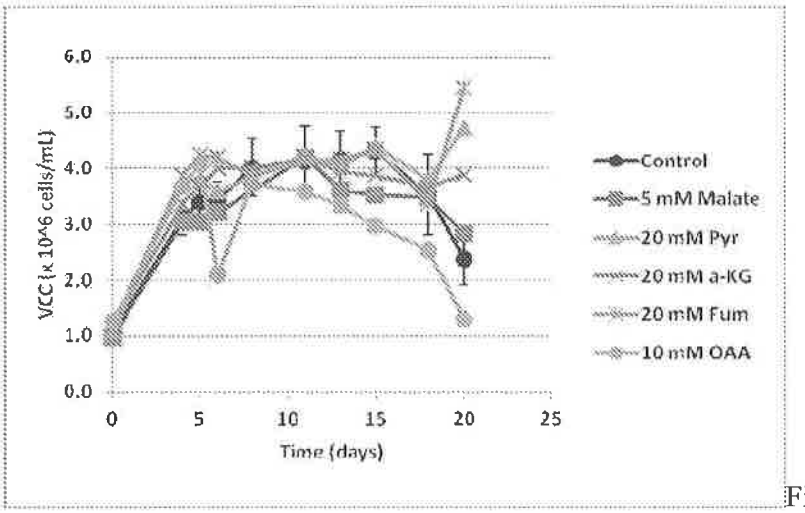


Figure 18a

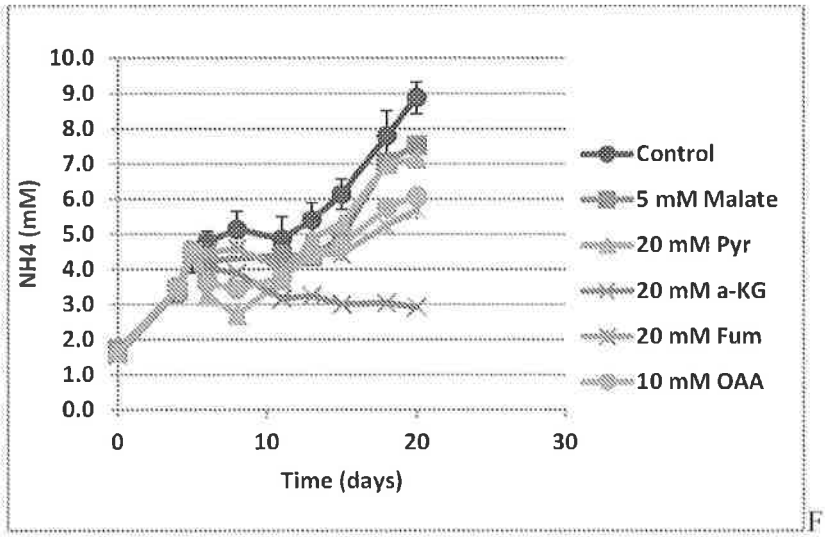


Figure 18b

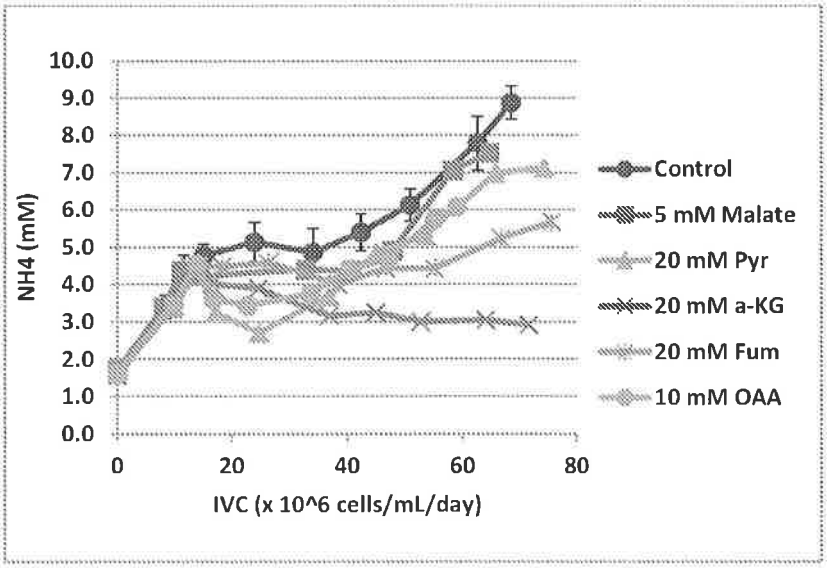


Figure 18c

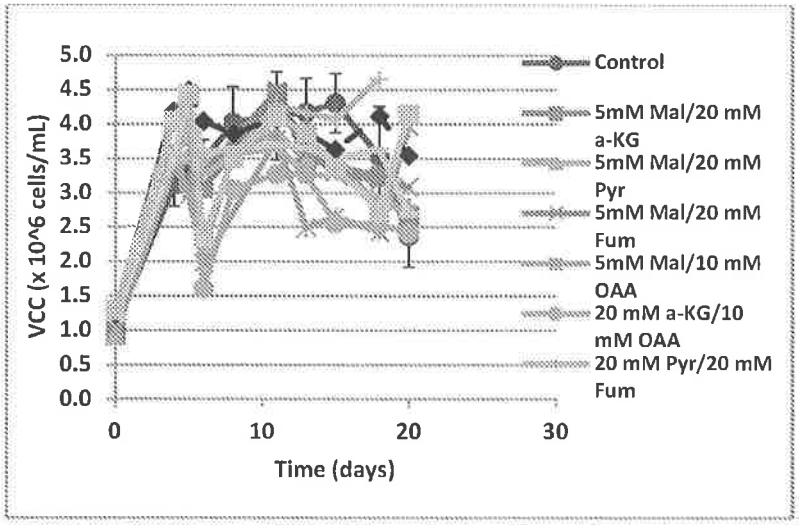


Figure 19a

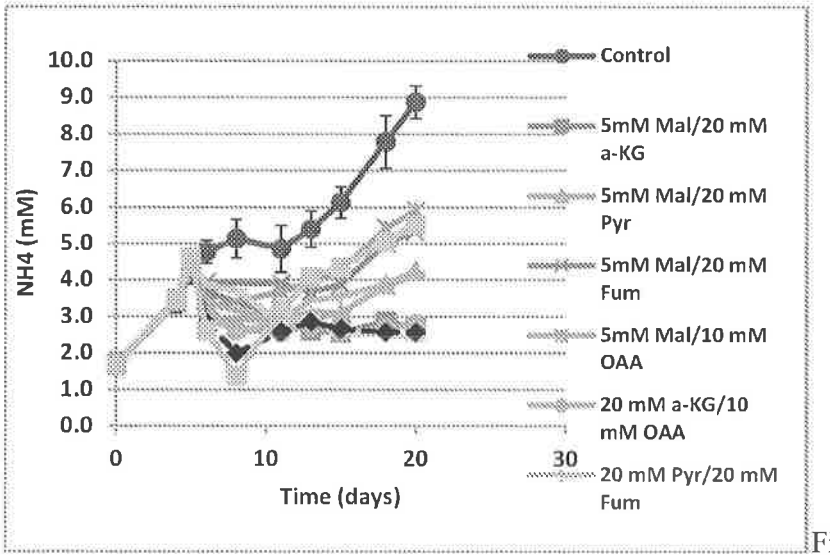


Figure 19b

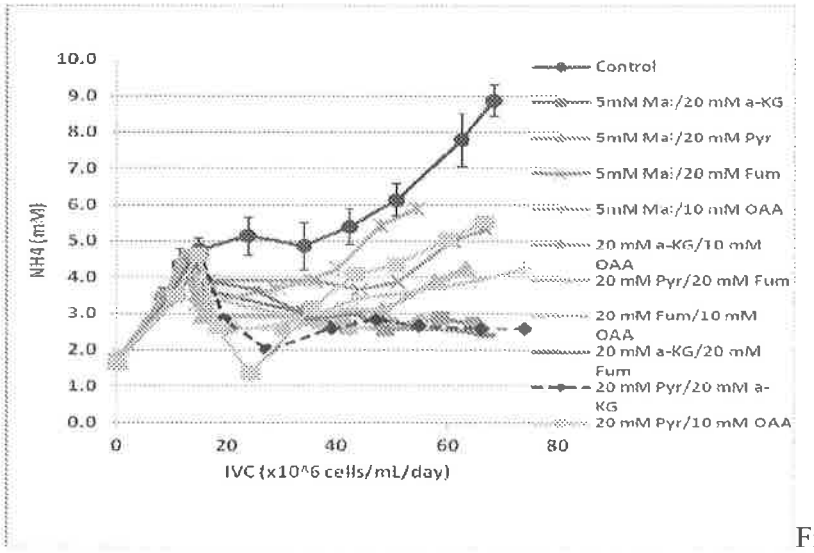


Figure 19c

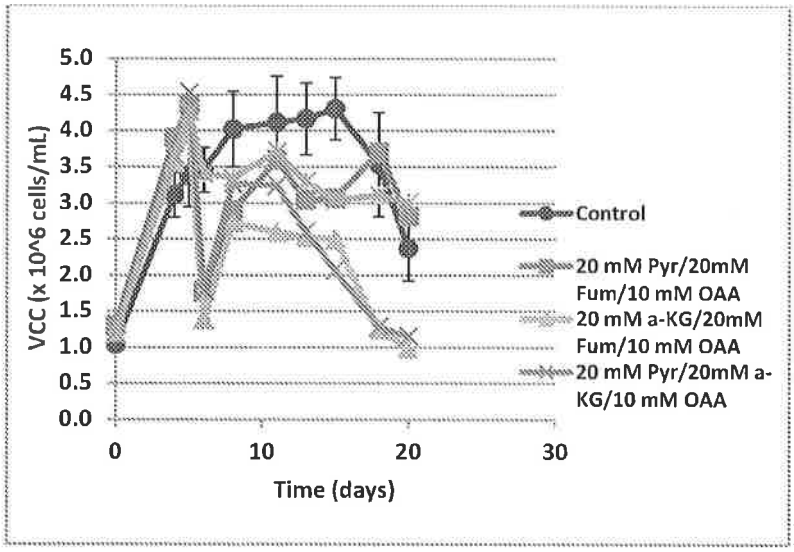


Figure 20a

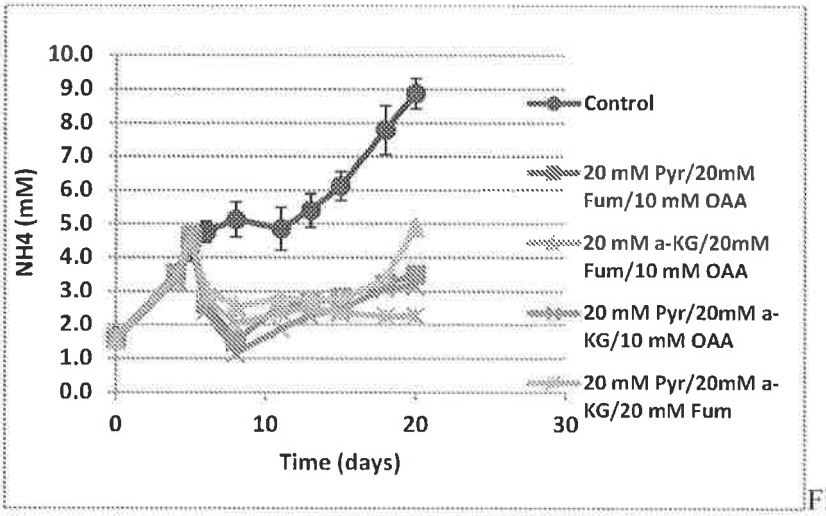


Figure 20b

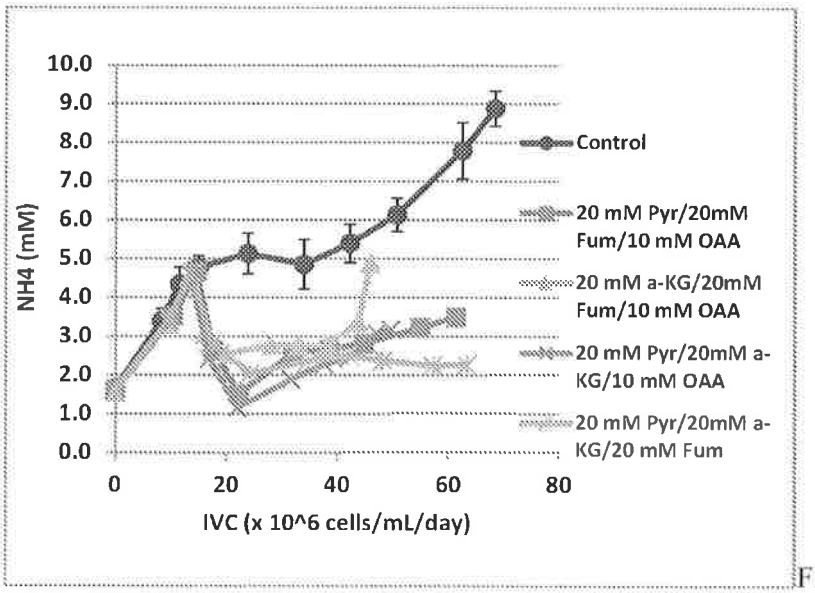


Figure 20c

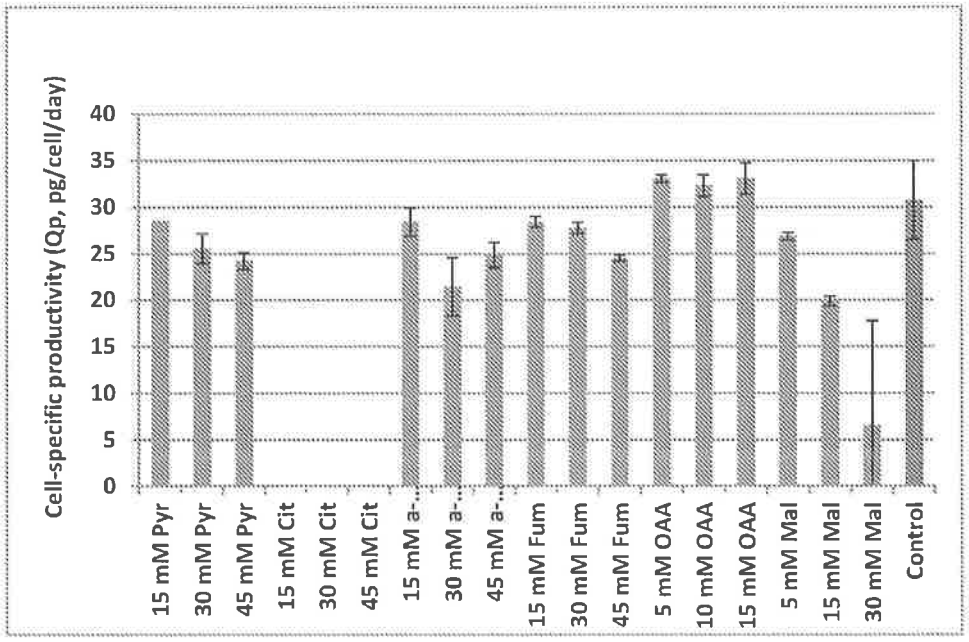

Cell-specific productivity (Qp, pg/cell/day)
40
35
30
25
20
15
10
5
0
15 mM Pyr
30 mM Pyr
45 mM Pyr
15 mM Cit
30 mM Cit
45 mM Cit
15 mM a-...
30 mM a-...
45 mM a-...
15 mM Fum
30 mM Fum
45 mM Fum
5 mM OAA
10 mM OAA
15 mM OAA
5 mM Mal
15 mM Mal
30 mM Mal
Control

Figure 21

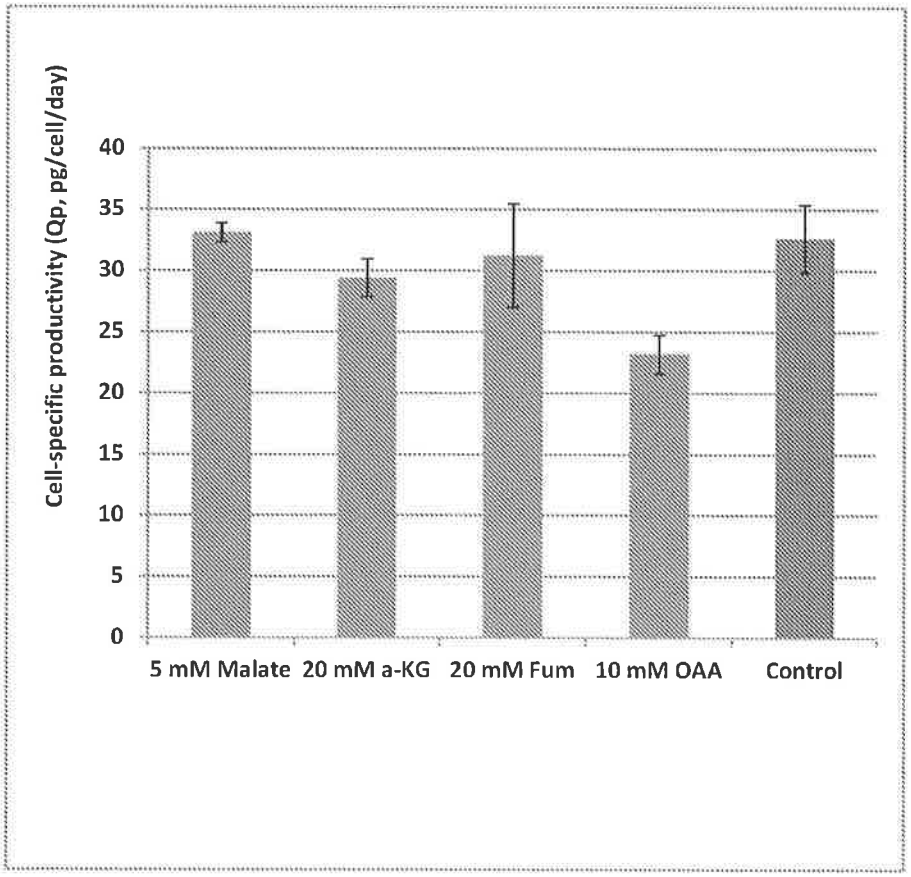

Cell-specific productivity (Qp, pg/cell/day)
40
35
30
25
20
15
10
5
0
5 mM Malate
20 mM a-KG
20 mM Fum
10 mM OAA
Control

Figure 22

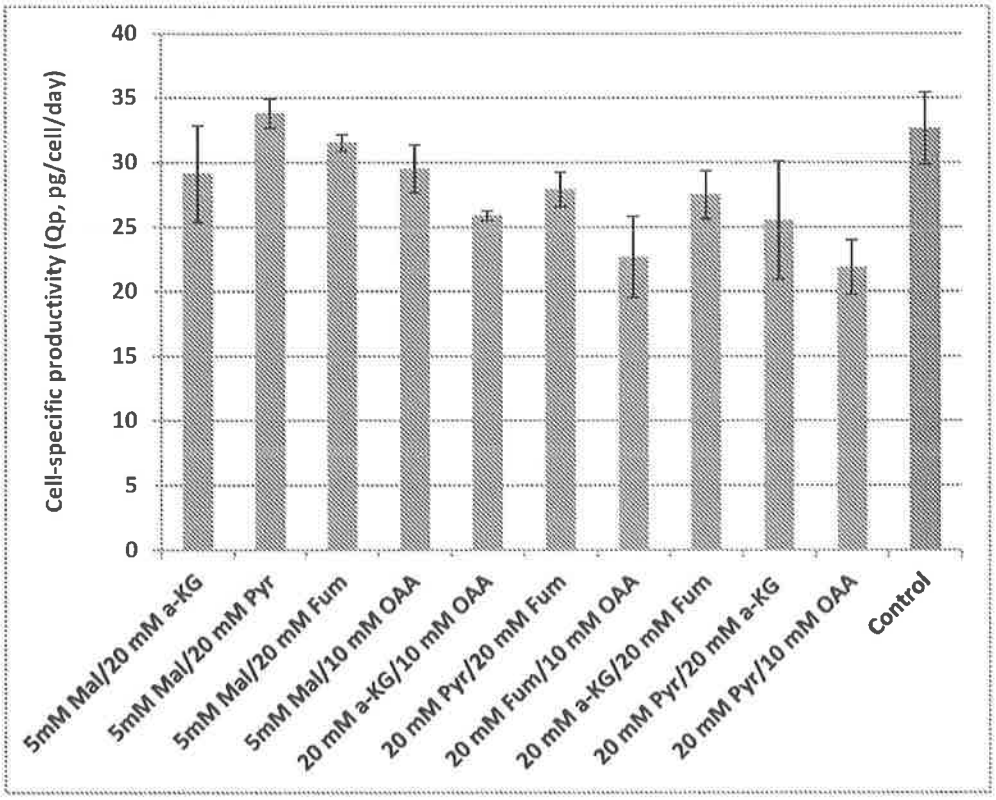

Cell-specific productivity (Qp, pg/cell/day)
40
35
30
25
20
15
10
5
0
5mM Mal/20 mM a-KG
5mM Mal/20 mM Pyr
5mM Mal/20 mM Fum
5mM Mal/10 mM OAA
20 mM a-KG/10 mM OAA
20 mM Pyr/20 mM Fum
20 mM Fum/10 mM OAA
20 mM a-KG/20 mM Fum
20 mM Pyr/20 mM a-KG
20 mM Pyr/10 mM OAA
Control

Figure 23

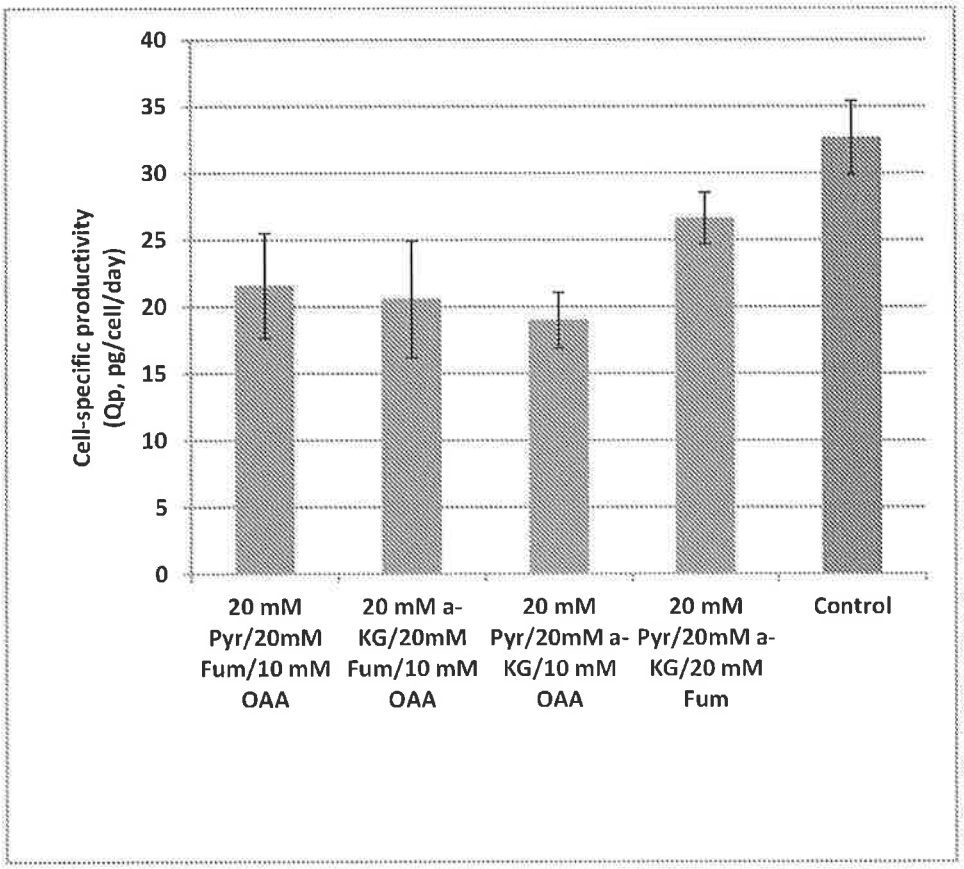

Cell-specific productivity (Qp, pg/cell/day)
40
35
30
25
20
15
10
5
0
20 mM Pyr/20mM Fum/10 mM OAA
20 mM a-KG/20mM Fum/10 mM OAA
20 mM Pyr/20mM a-KG/10 mM OAA
20 mM Pyr/20mM a-KG/20 mM Fum
Control

Figure 24