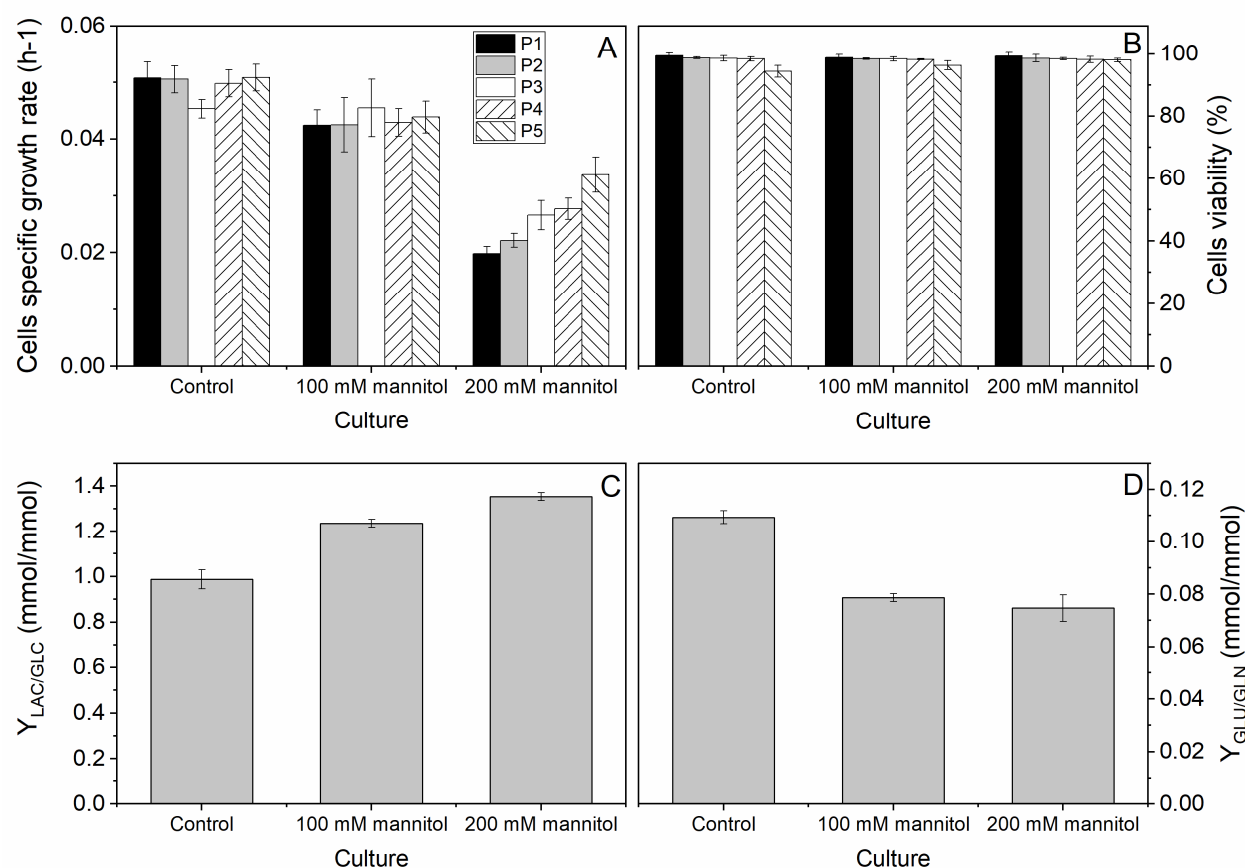
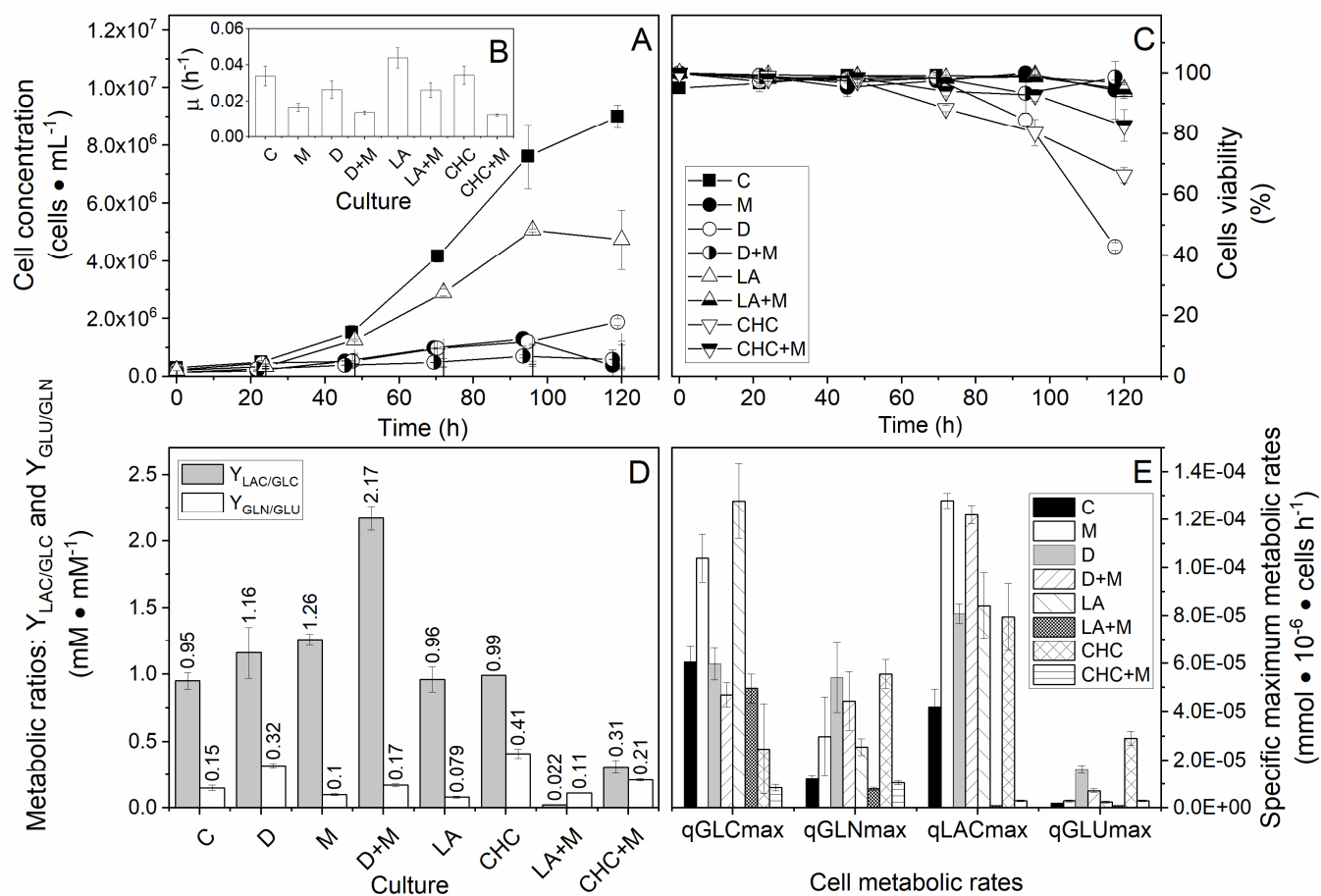


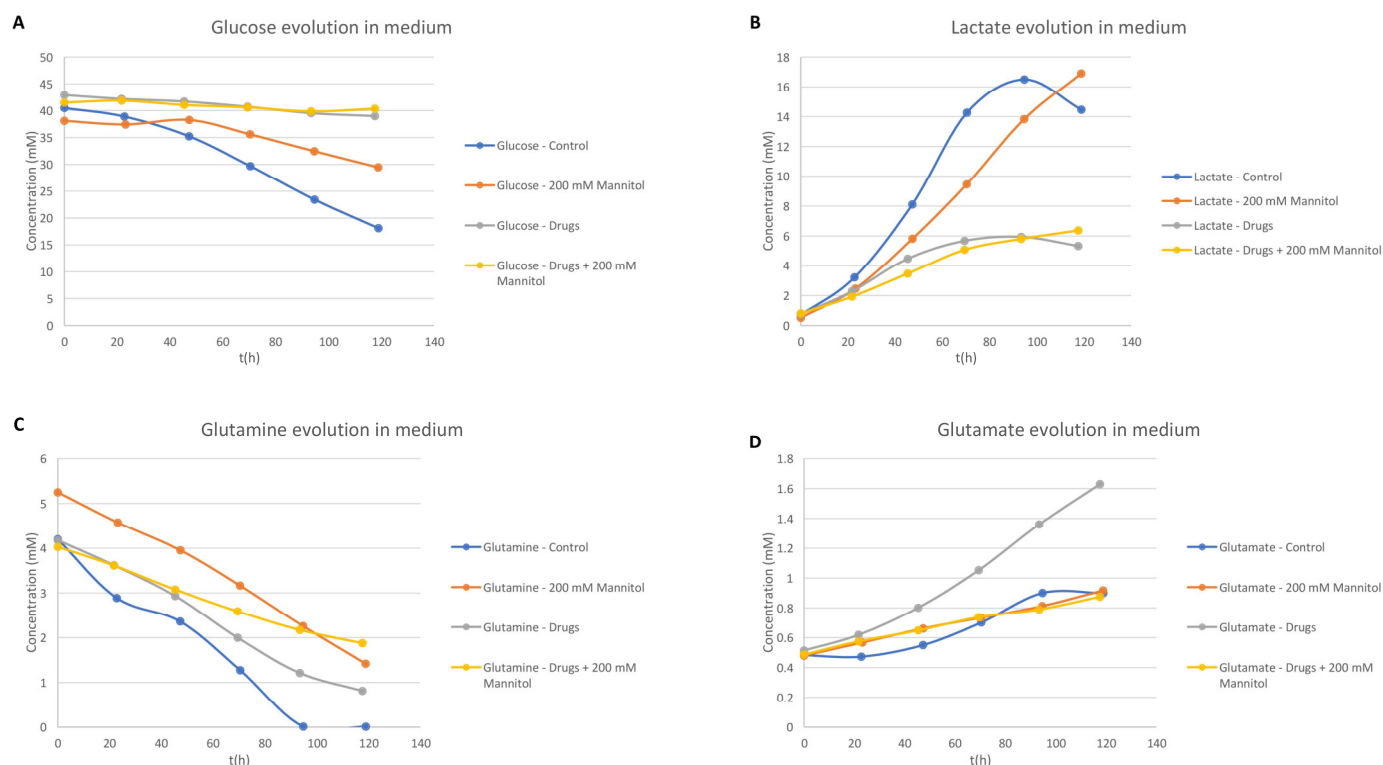
## Supplementary Materials



**Figure S1.** CHO cells behavior along successive passages under high osmolarity conditions. **(A)** Cells specific growth rates in control and high osmolarity (100 mM and 200 mM mannitol) conditions along successive passages (P1-5). Growth rates were more affected under 200 mM mannitol compared to other conditions. **(B)** Cell viability remained flat for all conditions along P1-5. **(C)** Mean lactate yields of the five passages per mole of consumed glucose ( $Y_{LAC/GLC}$ ) were reported better in high osmolarity conditions. **(D)** Conversely, mean glutamate yield per mole of consumed glutamine were lower in high osmolarity conditions.



**Figure S2.** Effects of hyperosmotic culture conditions combined with lipoic acid and hydroxycitrate drugs. C = control, M = mannitol, D = drugs combination, D+M = drugs and M culture. LA = alpha-lipoic acid, LA+M = alpha-lipoic acid and mannitol, HCA = hydroxycitrate, HCA+M = hydroxycitrate and mannitol.



**Figure S3.** Metabolites variation in different batch cultures. **(A)** Glucose consumption is highly inhibited under drug conditions (D and D+Mannitol) compared to the control condition or under mannitol alone. **(B)** Lactate production is correlated with glucose consumption for each condition. **(C)** Glutamine is globally less consumed under disturbed conditions. It is noted that it is more consumed in drug conditions compared to Mannitol. **(D)** Glutamate, which is mainly derived from the consumption of glutamine, is significantly more important in drug conditions. This is a marker of saturation of the glutaminolysis pathway in drug conditions.