

# Hyperosmolality in CHO Culture: Effects on cellular behavior and morphology

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## Abstract

Exposure of Chinese hamster ovary cells (CHO) to highly concentrated feed solution during fed-batch cultivation is known to result in an unphysiological osmolality increase ( $>300$  mOsm/kg), affecting cell physiology and morphology. Extending previous observation on osmotic adaptation, the present study investigates for the first time potential effects of hyperosmolality on CHO cells on both population and single-cell level. We intentionally exposed CHO cells to hyperosmolality of up to 545 mOsm/kg during fed-batch cultivation. Contrarily to an expected osmosis effect promoting cell shrinkage, hyperosmolality-exposed CHO cells showed a nearly triplicated volume accompanied by ablation of proliferation. On the molecular level, we observed a strong hyperosmolality-dependent increase in mitochondrial activity in CHO cells compared to control. The companion article “Hyperosmolality in CHO Culture: Effects on Proteome” provides a proteome-based insight into the effects of hyperosmolality on mitochondria. In contrast to mitochondrial activity, hyperosmolality-dependent proliferation arrest of CHO cells was not accompanied by DNA accumulation or caspase-3/7-mediated apoptosis. Notably, we demonstrate for the first time a formation of up to eight multiple, small nuclei in single hyperosmolality-stressed CHO cells. The here presented observations reveal unknown hyperosmolality-dependent morphological changes and support existing data on the osmotic response in mammalian cells.

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