INTRODUCTION: Mutations in the galactose-1-phosphate uridyltransferase gene (GAL7 in yeast) cause the human disease classic galactosemia. This disease affects 1:20,000 newborns in Brazil, has no cure and its main symptoms are cataract formation, dementia and developmental problems. Cells of these patients accumulate galactose-1-phosphate leading to cytotoxicity, but the precise mechanism of toxicity of this compound is still unknown. Yeast metabolizes galactose similarly to human cells, and mutations in GAL7 induce galactose toxicity. Yeast treated with galactose and lithium – an inhibitor of phosphoglucomutase – also accumulates galactose-1-phosphate and have a similar galactose-induced toxicity phenotype. We and others have discovered that mutants deleted on genes related with calcium metabolism have altered sensitivity to lithium and galactose. The main goal of this project is to investigate the influence of calcium metabolism on the context of classic galactosemia.

MATERIAL AND METHODS: We used Saccharomyces cerevisiae mutant strains derived from the wildtype strain BY4741 in all experiments. Growth tests were performed in YPD, YPGal or YPGly+0.007% galactose agar plates to test the effects of mutations, or of the supplementation with lithium, calcium, EGTA or inositol. Plates were incubated for 2 to 4 days at 30°C and results were photographed. RESULTS AND DISCUSSION: Deletion of calcium metabolism-related genes (CNB1, PMC1 and PMR1) altered sensitivity to lithium. Interestingly, deletion of PMC1 or PMR1 suppressed the toxicity of lithium in galactose. Calcium supplementation enhanced the sensitivity to galactose of the gal7Δ strain; but increased lithium tolerance in the presence of galactose in a calcineurin-dependent manner. Inositol supplementation had no effect on galactose sensitivity of gal7Δ strain. CONCLUSIONS: These results indicate that proteins related to calcium metabolism may affect galactose toxicity during galactosemia. Our perspective is to understand the connection of calcium metabolism with complications already described on classic galactosemia.

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KEYWORDS: calcium, classic galactosemia, galactose, lithium, yeast