Zinc enhances intestinal epithelial barrier function through the PI3K/AKT/mTOR signaling pathway in Caco-2 cells.

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BACKGROUND: Zinc plays an important role in maintaining intestinal barrier function as well as modulating cellular signaling recognition and protein kinase activities. The phosphatidylinositol 3-kinase (PI3K) cascade has been demonstrated to affect intercellular integrity and tight junction (TJ) proteins.

OBJECTIVE: The current study investigated the hypothesis that zinc regulates intestinal intercellular junction integrity through the PI3K/protein kinase B (AKT)/mammalian target of rapamycin (mTOR) pathway.

METHODS: A transwell model of Caco-2 cell was incubated with 0, 50 and 100 μM of zinc at various time points. Transepithelial electrical resistance (TEER), paracellular permeability, TJ proteins, cell proliferation, differentiation and cell damage were measured.

RESULTS: Compared with controls, 50 and 100 μM of zinc increased cell growth at 6, 12 and 24 h and the expression of proliferating cell nuclear antigen at 24 h. Zinc (100 μM) significantly elevated TEER at 6-24 h and reduced TJ permeability at 24 h, accompanied by the up-regulation of alkaline phosphatase (AP) activity and zonula occludens (ZO)-1 expression. In addition, zinc (100 μM) affected the PI3K/AKT/mTOR pathway by stimulating phosphorylation of AKT and the downstream target mTOR. Inhibition of PI3K signaling by LY294002 counteracted zinc promotion, as shown by a decrease in AP activity, TEER, the abundance of ZO-1 and phosphorylation of AKT and mTOR. Additionally, TJ permeability and the expression of caspase-3 and LC3II (markers of cell damage) were increased by addition of PI3K inhibitor.

CONCLUSION: In conclusion, the activation of PI3K/AKT/mTOR signaling by zinc is involved in improving intestinal barrier function by enhancing cell differentiation and expression of TJ protein ZO-1.

PMID: 28193579