Dose-dependent cellular damage caused by indomethacin in nucleated cells

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Abstract

Indomethacin is a widely used NSAID with strong anti-inflammatory and pain-relieving effects, but its clinical use is limited by serious side effects such as gastrointestinal ulcers, liver and kidney damage, blood disorders, and increased risk of stroke. While these effects are mainly linked to its inhibition of cyclooxygenase and reduction in prostaglandins, oxidative stress also plays a key role. Oxidative stress, caused by an imbalance between reactive oxygen species (ROS) and antioxidants, can lead to DNA damage and genotoxicity. Indomethacin increases ROS, stimulates neutrophil adhesion (contributing to gastric ulcers), and elevates lipid peroxidation markers like malondialdehyde (MDA), further exacerbating tissue damage and toxicity in organs like the liver and bone marrow. Indomethacin treatment led to cell shrinkage, elongation, dissociation, and loss of stress fibers—indicating cytoskeletal disruption. Other studies have demonstrated that indomethacin causes significant, time- and dose-dependent morphological changes in A549 lung cancer cells, including loss of stress fibers by uniquely reducing E-cadherin and collagen IV levels, increases MMP-9 activity, and enhances cell motility through PPARγ regulation. These effects—reduced growth but increased migration—may explain why indomethacin is challenging to use for lung cancer treatment. Indomethacin alters cell membrane properties by selectively enhancing cholesterol-dependent nanoclustering, potentially impacting plasma membrane–associated cell signaling pathways.
In this study, we investigate the effects of indomethacin on the morphology of nucleated blood cells using different doses in attempt to assess a dose-dependant relation between the concentration used and the induced level of damage.

References

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