Ginkgo Biloba Flavonoids Damage Lateral Line Hair Cells via Oxidative Stress Mechanisms

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Several drugs, including aminoglycosides and platinum-based chemotherapy agents, are well known for their ototoxic properties. However, the ototoxic potential of most therapeutic compounds is unknown. FDA-approved drugs are not routinely tested for ototoxicity, so their potential to affect hearing often goes unrecognized. This issue is further compounded for natural products, where there is a lack of FDA oversight and the manufacturer is responsible for ensuring the safety of their products. Using the zebrafish lateral line a natural products library was screened to identify new potential ototoxins. Three flavonoids quercetin, kaempferol, and isorhamentin, all from the Gingko Biloba plant, demonstrated significant ototoxicity, killing up to 30% of lateral line hair cells. I then assessed the health of the surviving hair cells using the vital dye FM 1-43FX. Mean intensity of FM 1-43FX fluorescence was lower in hair cells treated with quercetin, kaempferol, or isorhamnetin than in the hair cells from untreated fish, suggesting that the health of the remaining hair cells was compromised. Since known ototoxins often activate cellular stress responses, we asked if reactive oxygen species were necessary for flavonol ototoxicity. Co-treatment with the antixodant D-methionine significantly protected hair cells from each flavonoid, suggesting that antioxidant therapy could prevent hair cell loss. This research demonstrates the potential for ototoxic damage caused by unregulated herbal supplements and suggests that further supplement characterization is warranted.

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