

ABSTRAK

Gangguan pendengaran akibat penggunaan obat kemoterapi cisplatin bersifat irreversible dengan angka kejadian ototoksisitas yang bervariasi antara 0% hingga 100%. Kerusakan ini berkaitan dengan proses inflamasi dan stres oksidatif yang memicu aktivasi jalur molekuler seperti Nuclear Factor kappa beta (NF- κ B) dan apoptosis pada sel-sel koklea. Curcuminoid dan madu diketahui memiliki sifat antioksidan dan antiinflamasi yang berpotensi mencegah atau memperbaiki kerusakan ototoksik akibat cisplatin. Penelitian ini bertujuan menilai efek pemberian curcuminoid dan madu terhadap ekspresi NF- κ B, apoptosis, serta fungsi pendengaran yang dinilai melalui nilai Signal to Noise Ratio (SNR).

Penelitian ini merupakan penelitian eksperimental menggunakan 25 ekor *Rattus norvegicus* yang dibagi menjadi lima kelompok. Kelompok kontrol negatif (K1) diberikan suspensi CMC (Carboxymethyl cellulose). Kelompok kontrol positif (K2) diberikan injeksi intraperitoneal cisplatin dosis tunggal 8 mg/kgBB. Kelompok K3 diberikan cisplatin 8 mg/kgBB diikuti curcuminoid 200 mg/kgBB per oral selama 7 hari. Kelompok K4 diberikan cisplatin 8 mg/kgBB diikuti madu 2 g/kgBB per oral selama 7 hari. Kelompok K5 diberikan cisplatin 8 mg/kgBB diikuti kombinasi curcuminoid 200 mg/kgBB dan madu 2 g/kgBB per oral selama 7 hari. Pemeriksaan pendengaran dilakukan menggunakan Distortion Product Otoacoustic Emissions (DPOAE) pada hari ke-0, ke-3, ke-4, dan ke-7. Pada hari ke-7 hewan coba diterminasi untuk pemeriksaan ELISA (NF- κ B dan apoptosis) dari plasma serta imunohistokimia NF- κ B dan TUNEL assay pada jaringan koklea.

Hasil penelitian menunjukkan bahwa curcuminoid, madu, maupun kombinasi keduanya mampu menurunkan rerata ekspresi NF- κ B pada jaringan organ Corti koklea, dengan nilai terendah pada kelompok madu. Pada pemeriksaan plasma, rerata NF- κ B terendah ditemukan pada kelompok curcuminoid. Indeks apoptosis jaringan koklea terendah dijumpai pada kelompok kombinasi curcuminoid dan madu, sedangkan penurunan signifikan apoptosis plasma hanya terjadi pada kelompok curcuminoid. Pemeriksaan SNR menunjukkan nilai tertinggi pada kelompok kombinasi curcuminoid dan madu. Meskipun terjadi penurunan SNR pada hari ke-3 dan ke-4, peningkatan pada hari ke-7 menunjukkan bahwa pemberian curcuminoid dan madu dapat memperlambat kerusakan akibat ototoksisitas cisplatin. Analisis korelasi menunjukkan hubungan kuat antara ekspresi NF- κ B dengan nilai SNR serta hubungan sedang antara indeks apoptosis dan nilai SNR. Semakin rendah ekspresi NF- κ B dan apoptosis, semakin tinggi nilai SNR yang mencerminkan fungsi pendengaran yang lebih baik.

Kata Kunci: curcuminoid, cisplatin, NF- κ B, apoptosis, SNR

ABSTRACT

Cisplatin-induced hearing loss is characterized as irreversible, with the incidence of ototoxicity varying widely from 0% to 100%. This damage is associated with inflammatory processes and oxidative stress that activate molecular pathways such as Nuclear Factor kappa beta (NF- κ B) and apoptosis in cochlear cells. Curcuminoid and honey are known to possess antioxidant and anti-inflammatory properties that may help prevent or reduce ototoxic damage caused by cisplatin. This study aimed to evaluate the effects of curcuminoid and honey administration on NF- κ B expression, apoptosis, and auditory function as assessed by Signal-to-Noise Ratio (SNR).

*This experimental study used 25 *Rattus norvegicus* which were randomly divided into five groups. The negative control group (K1) received CMC (Carboxymethyl cellulose) suspension. The positive control group (K2) received a single intraperitoneal injection of cisplatin at a dose of 8 mg/kg body weight. Group K3 received cisplatin followed by oral administration of curcuminoid at 200 mg/kg body weight for 7 days. Group K4 received cisplatin followed by oral administration of honey at 2 g/kg body weight for 7 days. Group K5 received cisplatin followed by a combination of curcuminoid (200 mg/kg body weight) and honey (2 g/kg body weight) orally for 7 days. Hearing function was assessed using Distortion Product Otoacoustic Emissions (DPOAE) on day 0, day 3, day 4, and day 7. On day 7, all animals were terminated for plasma examination using ELISA (NF- κ B and apoptosis), while cochlear tissues were collected for NF- κ B immunohistochemistry and apoptosis assessment using the TUNEL assay.*

The results showed that curcuminoid, honey, and their combination were able to reduce the mean expression of NF- κ B in the organ of Corti within the cochlea, with the lowest level observed in the honey-treated group. In plasma examination, the lowest NF- κ B level was found in the curcuminoid group. The lowest apoptosis index in cochlear tissue was observed in the group receiving the combination of curcuminoid and honey, whereas a statistically significant reduction in plasma apoptosis expression was found only in the curcuminoid group. The SNR measurement showed the highest value in the combination group. Although a decrease in SNR occurred on day 3 and day 4, an increase on day 7 indicated that curcuminoid, honey, and their combination could slow the progression of cisplatin-induced ototoxic damage. Correlation analysis demonstrated a strong relationship between NF- κ B expression and SNR values, as well as a moderate correlation between the apoptosis index and SNR. Lower NF- κ B expression and apoptosis levels were associated with higher SNR values, indicating better hearing function.

Keywords: *curcuminoid, cisplatin, NF- κ B, apoptosis, SNR*