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The Effect of Carvacrol on 5-Fluorouracil-Induced Optic Neuropathy in Rats. Histopathological and Biochemical Analysis

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SUMMARY. **5-Fluorouracil (5-FU) is also known to cause ocular toxicity. The purpose of this study was to investigate the effects of Carvacrol upon possible 5-FU-induced optic nerve damage in rats biochemically and histopathologically. In this study totally, eighteen albino Wistar male rats were used. The rats were grouped under three categories as the healthy (HG) (n=6), 100 mg/kg 5-FU treated alone (FUG) (n=6) and 50 mg/kg Carvacrol+100 mg/kg 5-FU (CFU) groups (n=6). Carvacrol at 50 mg/kg was injected intraperitoneally (ip) to the CFU group. The same volume of 0.9% NaCl was administered as the solvent ip to HG and FUG groups. One hour after administrating Carvacrol and solvent, 100 mg/kg 5-FU was ip injected to CFU and FUG groups. Carvacrol was administered once daily for 10 days. Three-dose 5-FU was administered on the 1st, 3rd, and 5th days as one dose each. On the 10th day, the animals were euthanised with high-dose anesthesia and optic nerve tissues were removed. Malondialdehyde (MDA), reduced glutathione (GSH), superoxide dismutase (SOD), catalase (CAT), and Interleukin (IL-6) levels were measured in optic nerve tissues. The tissues were also examined histopathologically. The results obtained from HG and CFU groups were compared with the FUG group. Significantly higher MDA and IL-6 levels ($p < 0.001$) and significantly lower ($p < 0.001$) tGSH, SOD, and CAT levels were determined in optic nerve samples of the FUG group rather than HG and CFU groups. In histopathological analyses, determined that astrocyte and oligodendrocyte nuclei were mostly darkly stained, the majority of astrocytes were hypertrophied and degenerated, and some oligodendrocytes were degenerated in the FUG group unlike HG and CFU groups. Moreover, the optic nerve tissue was determined to be vacuolized and intensely edematous, and blood capillaries were intensely dilated and congested. In conclusion, 5-FU caused optic neuropathy due to oxidative and inflammatory damage, and Carvacrol reduced this oxidative and inflammatory damage and histopathological changes in tissues. This revealed that Carvacrol was possibly to be efficient upon 5-FU-induced optic nerve toxicity.**

RESUMEN. Se sabe que el 5-fluorouracilo (5-FU) causa toxicidad ocular. El propósito de este estudio fue investigar los efectos bioquímicos e histopatológicos de Carvacrol sobre el posible daño del nervio óptico inducido por 5-FU en ratas. En este estudio se utilizaron en total dieciocho ratas macho Wistar albinas. Las ratas se agruparon en tres categorías como sanas (HG) (n=6), 100 mg/kg de 5-FU tratadas solas (FUG) (n=6) y 50 mg/kg de carvacrol + 100 mg/kg de 5-FU. (UFC) grupos (n=6). Se inyectó carvacrol a 50 mg/kg por vía intraperitoneal (ip) al grupo de CFU. Se administró el mismo volumen de NaCl al 0,9% como disolvente ip a los grupos HG y FUG. Una hora después de administrar Carvacrol y el disolvente, se inyectaron ip 100 mg/kg de 5-FU a los grupos CFU y FUG. Carvacrol se administró una vez al día durante 10 días. Se administraron tres dosis de 5-FU los días 1, 3 y 5 como una dosis cada uno. El día 10, los animales fueron sacrificados con anestesia de alta dosis y se extirparon los tejidos del nervio óptico. Se midieron los niveles de malondialdehído (MDA), glutatión reducido (GSH), superóxido dismutasa (SOD), catalasa (CAT) e interleucina (IL-6) en los tejidos del nervio óptico. Los tejidos también se examinaron histopato-

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lógicamente. Los resultados obtenidos de los grupos HG y CFU se compararon con el grupo FUG. Se determinaron niveles significativamente más altos de MDA e IL-6 ($p < 0,001$) y niveles significativamente más bajos ($p < 0,001$) de tGSH, SOD y CAT en muestras de nervio óptico del grupo FUG en lugar de los grupos HG y CFU. En los análisis histopatológicos, se determinó que los núcleos de astrocitos y oligodendrocitos estaban en su mayoría teñidos de oscuro, la mayoría de los astrocitos estaban hipertrofiados y degenerados, y algunos oligodendrocitos estaban degenerados en el grupo FUG a diferencia de los grupos HG y CFU. Además, se determinó que el tejido del nervio óptico estaba vacuolizado e intensamente edematoso, y los capilares sanguíneos estaban intensamente dilatados y congestionados. En conclusión, el 5-FU provocó neuropatía óptica por daño oxidativo e inflamatorio, y el Carvacrol redujo este daño oxidativo e inflamatorio y los cambios histopatológicos en los tejidos. Esto reveló que Carvacrol posiblemente sería eficaz en la toxicidad del nervio óptico inducida por 5-FU.