

# Efek mangiferin terhadap kerusakan otak akibat stres oksidatif dan inflamasi yang ditimbulkan oleh pemberian doxorubisin = The effect of mangiferin against brain damage caused by oxidative stress and inflammation induced by doxorubicin / Soni Siswanto

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## Abstrak

[<b>ABSTRAK</b><br>

Latar belakang. Doxorubisin (DOK), suatu antibiotika antrasiklin, digunakan secara luas untuk terapi antikanker, namun penggunaan DOK dapat menimbulkan efek samping, salah satunya gangguan kognitif. Penggunaan kemoterapi berbasis DOK menunjukkan hingga 76% pasien mengalami penurunan kognitif.

Kerusakan otak akibat penggunaan DOK disebabkan oleh peningkatan TNF- $\alpha$ ; di otak melalui uptake reseptor di sawar darah otak dan peningkatan produksi melalui aktivasi NF- $\kappa$ B. Peningkatan TNF- $\alpha$ ; lebih lanjut dapat menyebabkan inflamasi kronis yang dapat menimbulkan kematian sel saraf atau penyakit degenerasi saraf. Mangiferin (MAG) merupakan salah satu senyawa neuroprotektif, akan tetapi efek terhadap kerusakan otak akibat pemberian DOK belum diketahui. Penelitian ini bertujuan untuk mengetahui efek MAG terhadap kerusakan otak yang ditimbulkan oleh pemberian DOK.

Metode. Penelitian dilakukan terhadap tikus Sprague-Dawley yang diinduksi menggunakan DOK dengan dosis total 15 mg/kgBB secara i.p mulai minggu kedua. Pemberian MAG dilakukan secara p.o dengan dosis 30 dan 60 mg/kgBB selama 7 minggu. Parameter yang diamati adalah fungsi kognitif, inflamasi (TNF- $\alpha$ ;, NF- $\kappa$ B dan iNOS), stres oksidatif (SOD dan MDA) dan histopatologi dengan pewarnaan HE.

Hasil. Pemberian DOK menyebabkan gangguan kognitif yang ditandai dengan penurunan penggiliran labirin Y dan penurunan indeks diskriminasi pada pengenalan obyek baru, disertai peningkatan parameter inflamasi yaitu ekspresi TNF- $\alpha$ ;, NF- $\kappa$ B dan iNOS. Pemberian MAG bersama DOK menyebabkan peningkatan fungsi kognitif, penurunan inflamasi dan penurunan stres oksidatif serta histopatologi dengan pewarna HE.

Kesimpulan. Berdasarkan hasil pemeriksaan parameter pada penelitian mengindikasikan bahwa mangiferin memiliki efek neuroproteksi terhadap pemberian DOK.

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<b>ABSTRACT</b><br>

Introduction. Doxorubicin (DOK), an anthracycline antibiotic, is widely used for anticancer therapy, but the use of DOK causing side effects, one of them is cognitive impairment. Up to 76% of patients experienced cognitive decline caused

by DOK-based chemotherapy. Brain damage due to the use of DOK lead by an increase in TNF- $\alpha$ ; in the brain through the receptors uptake in the blood brain barrier and increasing production through activation of NF- $\kappa$ B. Increased TNF- $\alpha$ ; can further lead to chronic inflammation which can lead nerve cells death or nerve degeneration diseases. Mangiferin (MAG) is one of the neuroprotective compound, but the effect on brain damage induced by DOK is still unknown. This study aims to determine the effect of MAG on brain damage induced by DOK.

**Methods.** Research carried out on Sprague-Dawley rats induced by DOK i.p with total dose 15 mg/kg that divided into 6 dose and given within 2 weeks, started from 2nd week. The rats was administrated by MAG p.o with dose 30 and 60 mg/kg daily for 7 weeks. Parameters measured were cognitive function, inflammatory parameters (TNF- $\alpha$ ;, NF- $\kappa$ B and iNOS), oxidative stress parameters (SOD and MDA) and histopatology using HE staining.

**Results.** DOK cause cognitive disorders that characterized by decreased Y maze alteration and discrimination index in new object recognition, and accompanied by increasing inflammatory parameters that showed in increasing TNF- $\alpha$ ;, NF- $\kappa$ B and iNOS expressions. Coadministration MAG with DOK led an increasing on cognitive function, reducing the inflammation and oxidative stress.

**Conclusion.** Based on the results of the study, MAG indicated has a neuroprotective effect on brain damage induced by DOK;

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