

**POTENSI DELIMA (*Punica granatum*) SEBAGAI HEPATOPROTEKTOR TERHADAP PERBAIKAN HISTOPATOLOGI HEPAR PADA KEADAAN HEPATOTOKSISITAS IMBAS OBAT SECARA IN VIVO
SYSTEMATIC LITERATURE REVIEW**

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Abstrak

Latar Belakang: Konsumsi senyawa asing (xenobiotik) dapat mengakibatkan terjadinya hepatotoksitas imbas obat (*drug-induced liver injury*, DILI). Hepatotoksitas imbas obat adalah penyebab utama gagal hati akut dan dapat berkembang menjadi cedera hepar kronis serta dapat progresif menjadi gagal hati. Tingkat ROS dan stres oksidatif yang tinggi pada DILI dapat menginduksi kematian sel serta peningkatan inflamasi. Delima (*Punica granatum*) sebagai antioksidan dan anti-inflamasi berpotensi menjadi pilihan alternatif pengobatan DILI. Tujuan penelitian ini diharapkan dapat menilai potensi delima sebagai hepatoprotektor terhadap perbaikan histopatologi hepar pada keadaan hepatotoksitas imbas obat secara *in vivo*. **Metode:** *Systematic Literature Review* dilakukan berdasarkan *the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols* (PRISMA-P) 2015. *Database* yang digunakan adalah PubMed dan Google Scholar yang membahas tentang delima, hepatotoksitas, dan histopatologi. **Hasil:** 2 dari 10 jurnal meneliti dan menunjukkan adanya reduksi apoptosis akibat pemberian delima. 9 dari 10 jurnal meneliti reduksi nekrosis dimana 7 di antaranya menunjukkan adanya reduksi nekrosis. Di samping itu, dari 10 jurnal yang dikaji, 8 di antaranya menunjukkan adanya reduksi infiltrasi sel inflamasi. **Kesimpulan:** Delima dengan kandungan senyawa antioksidan dan dapat berfungsi sebagai anti-inflamasi serta mampu memodulasi ekspresi protein terkait apoptosis berpotensi menjadi hepatoprotektor yang mampu memperbaiki gambaran histopatologi hepar pada keadaan hepatotoksitas imbas obat secara *in vivo* berupa reduksi apoptosis, nekrosis, dan infiltrasi sel inflamasi bila dosis dan waktu pemberian yang digunakan dengan metode yang tepat.

Kata kunci: Delima, obat, hepatotoksitas, hepatoprotektif, histopatologi

**POMEGRANATE (*Punica granatum*) POTENTIAL AS A
HEPATOPROTECTOR ON LIVER HISTOPATOLOGICAL
IMPROVEMENT TOWARDS IN VIVO DRUG INDUCED
HEPATOTOXICITY
SYSTEMATIC LITERATURE REVIEW**

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Abstract

Background: Consumption of foreign compounds (xenobiotics) can cause drug-induced hepatotoxicity (drug-induced liver injury, DILI). Drug-induced hepatotoxicity is a major cause of acute liver failure and can develop to chronic liver injury and able to become a liver failure. High level of ROS and oxidative stress on DILI can induce cell death as well as increased inflammation. Pomegranate (*Punica granatum*) as an antioxidant and anti-inflammatory can be an alternative option for DILI treatment. The aim of this study is to assess the potential of pomegranate as a hepatoprotector to improve histopathology of the liver in the state of drug-induced hepatotoxicity *in vivo*. **Methods:** A systematic review was done according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) 2015. Database used was PubMed and Google Scholar which discusses about pomegranate, hepatotoxicity, and histopathology. **Results:** 2 out of 10 journals researched and demonstrated a reduction in apoptosis due to pomegranate administration. 9 out of 10 journals investigated the reduction of necrosis of which 7 of them showed a reduction of necrosis. In addition, of the 10 journals reviewed, 8 of them showed a reduction in inflammatory cell infiltration. **Conclusion:** Pomegranate contain antioxidant compounds and can function as anti-inflammatory as well as being able to modulate the expression of apoptosis-related proteins potential as hepatoprotector that can improve the histopathological image of the liver in the state of drug-induced hepatotoxicity *in vivo* in the form of reduction of apoptosis, necrosis, and inflammatory cell infiltration if the dose and time of administration used with the right method.

Key words: Pomegranate, drug, hepatotoxicity, hepatoprotective, histopathology