INTISARI

Latar Belakang

Hepatic ischemia-reperfusion injury (IRI) adalah penyebab utama morbiditas dan mortalitas setelah transplantasi hepar. *Hepatic* IRI adalah pemulihan aliran darah ke jaringan yang sebelumnya iskemia yang menyebabkan cedera berkepanjangan. Ekstrak *Piper betle* telah diketahui dapat menghambat *reactive oxygen species* dan sekresi sitokin pro-inflamasi. Meskipun demikian, belum ada penelitian tentang aktivitas ekstrak *P. betle* pada model *hepatic* IRI. Oleh karena itu, penelitian ini bertujuan untuk mengetahui aktivitas ekstrak *P. betle* terhadap fungsi hepar, enzim antioksidan, dan apoptosis model *hepatic* IRI.

Metode

Ekstrak *P. betle* diekstrasi dengan metode *ultrasonic-assisted extraction* menggunakan etanol 80%. *Hepatic* IRI diinduksi pada tikus Wistar jantan (2 bulan, 130-200 g) dengan menjepit trias porta selama 60 menit, diikuti reperfusi selama 3 hari. Selama reperfusi, ekstrak *P. betle* dosis 100, 200, dan 400 mg/kg diberikan secara oral sekali sehari. Fungsi hepar dinilai berdasarkan kadar serum *alanine aminotransferase* (ALT). Histologi jaringan hepar diamati dengan pewarnaan hematoksilin-eosin (HE). Ekspresi Bax, *superoxide dismutase*-1 (SOD-1), dan *catalase* diukur dengan *reverse transcription-polymerase chain reaction* (RT-PCR).

Hasil

Tikus yang diberi ekstrak *P. betle* menunjukkan kadar serum ALT yang lebih rendah ($p<0,05$) dibandingkan kontrol *hepatic* IRI. Pemberian ekstrak *P. betle* menghasilkan perbaikan histologi hepatosit. Ekspresi mRNA Bax sebagai penanda apoptosis pada kelompok ekstrak *P. betle* juga lebih rendah ($p<0,01$) dibandingkan kontrol *hepatic* IRI. Ekstrak *P. betle* menunjukkan ekspresi mRNA enzim antioksidan yang lebih tinggi dibandingkan kontrol *hepatic* IRI, yaitu SOD-1 ($p<0,05$) dan *catalase* ($p<0,01$). Kelompok SR-400 menunjukkan efek ameliorasi tertinggi di antara kelompok perlakuan ekstrak *P. betle* lainnya.

Kesimpulan

Dengan demikian, ekstrak *P. betle* mempunyai aktivitas hepatoprotektif terhadap *hepatic* IRI dengan menginduksi ekspresi enzim antioksidan dan menghambat peningkatan mediator apoptosis.

Kata kunci: *Piper betle*, *hepatic ischemia-reperfusion injury*, enzim antioksidan, dan apoptosis

ABSTRACT

Background

Hepatic ischemia-reperfusion injury (IRI) is the leading cause of morbidity and mortality following liver transplantation. Hepatic IRI is defined as the restoration of blood flow to previously ischemic tissues which leads to prolonged injury. *Piper betle* extract has been studied to inhibit reactive oxygen species and pro-inflammatory cytokines production. However, the effect of *P. betle* extract in hepatic IRI has not been elucidated yet. This study aimed to determine the activity of *P. betle* extract in attenuating liver function, antioxidant enzyme, and apoptosis in hepatic IRI.

Method

P. betle extract was prepared by ultrasonic-assisted extraction using 80% ethanol. Hepatic IRI was performed in male Wistar rats (2 months, 130-200 g) by clamping the portal triad for 60 minutes, followed by 3 days of reperfusion. During reperfusion, *P. betle* extract doses of 100, 200, and 400 mg/kg were orally administered once daily. Liver function was assessed by serum level of alanine aminotransferase (ALT). The histology of the liver tissue was observed by hematoxylin-eosin (HE) staining. The expression of Bax, superoxide dismutase-1 (SOD-1), and catalase were measured by reverse transcription-polymerase chain reaction (RT-PCR).

Results

The rats given *P. betle* extract showed significantly lower serum ALT levels ($p<0.05$) compared to the hepatic IRI control group. Administration of *P. betle* extract led to improvements in hepatocyte histology. The expression of mRNA Bax, a marker of apoptosis, was also lower ($p<0.01$) in the *P. betle* extract group compared to the hepatic IRI control group. *P. betle* extract demonstrated higher expression of antioxidant enzyme mRNA compared to the hepatic IRI control group, specifically SOD-1 ($p<0.05$) and catalase ($p<0.01$). Among the different *P. betle* extract treatment groups, the SR-400 group exhibited the highest ameliorative effect.

Conclusion

In conclusion, *P. betle* extract has hepatoprotective activity for hepatic IRI by inducing expression of antioxidant enzymes and inhibiting elevation of apoptosis mediator.

Keywords: *Piper betle,* hepatic ischemia-reperfusion injury, antioxidant enzyme, and apoptosis