

Mekanisme Kerja H. sabdariffa. terhadap Steatosis Akibat Restriksi Vitamin B12: Kajian Molekular Persinyalan Stres Retikulum Endoplasma dan Lipogenesis = Mechanism of Action of H. sabdariffa. Against Steatosis due to Vitamin B12 Restriction: Molecular Study of Endoplasmic Reticulum Stress Signaling and Lipogenesis

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Abstrak

Belum banyak studi mempelajari keterkaitan antara defisiensi vitamin B12 dan toksisitas homosistein. Hiperhomosisteinemia dikaitkan dengan penyakit selular terkait NAFLD. Toksisitas homosistein dapat berupa steatosis atau inflamasi sel hati. H. sabdariffa. dan konstituen aktifnya memiliki efek pencegahan terhadap cedera seluler. Ekstrak H. sabdariffa. diuji pada tikus Sprague-Dawley (SD) dalam penelitian ini. Penelitian ini untuk melihat efek H. sabdariffa terhadap peningkatan homosistein pada hati tikus SD yang diberikan diet restriksi vitamin B12.

Penelitian ini merupakan penelitian in vivo yang dilakukan di Fakultas Kedokteran Universitas Indonesia. Sebanyak 30 ekor tikus SD dibagi menjadi enam kelompok sesuai waktu perlakuan di 8 dan 16 minggu sebagai berikut: Kelompok kontrol diberikan diet standar AIN-93M, kelompok restriksi vitamin B12 diberi diet AIN-93M dengan modifikasi pengurangan komponen vitamin B12 dan kelompok restriksi vitamin B12 diberi AIN-93M dengan modifikasi pengurangan komponen vitamin B12 ditambah ekstrak etanol H. sabdariffa (HSE). Setelah 8 dan 16 minggu, kadar vitamin B12 dan homosistein diukur. Peningkatan aktivitas toksisitas homosistein dilihat dari ekspresi protein GRP78, SREBP1c dan NF-kB. Aktivitas hepatoprotektif HSE dinilai menggunakan AST, ALT, GGT, dan NAFLD Activity Score (NAS).

Kadar vitamin B12 pada 8 minggu (233 ± 10.8 vs 176 ± 5.4 pg/L; $p < 0.001$) dan 16 minggu (226 ± 13 vs 190.6 pg/L; $p < 0,001$), lebih tinggi secara bermakna pada kelompok restriksi vitamin B12 dengan diet HSE dibandingkan kelompok diet restriksi vitamin B12 tanpa HSE. Kadar plasma homosistein plasma lebih rendah secara bermakna pada kelompok restriksi vitamin B12 dengan HSE dibandingkan kelompok restriksi vitamin B12 tanpa HSE di usia perlakuan 8 minggu ($2,25 \pm 0,07$ vs $2,63 \pm 0,1$ mol/L; $p < 0,001$) dan 16 minggu ($2,18 \pm 0,07$ vs $2,64 \pm 0,09$ mol/L; $p < 0,001$). Aktivitas GGT plasma di usia 16 minggu perlakuan menurun secara bermakna pada kelompok restriksi vitamin B12 dengan HSE dibandingkan kelompok restriksi vitamin B12 tanpa HSE ($14,5 \pm 1,1$ vs $22,9 \pm 2,4$ IU; $p < 0,05$). Ekspresi protein GRP78, SREBP1c, dan NfKB diukur menggunakan protein GAPDH sebagai kontrol internal. Pada minggu ke-8 dan 16, ekspresi protein NF-kB lebih rendah pada kelompok restriksi vitamin B12 dengan HSE dibandingkan dengan grup restriksi vitamin B12 tanpa HSE ($0,78 \pm 0,08$ vs $1,08 \pm 0,06$; $p < 0,05$). Ekspresi protein SREBP1c lebih rendah pada kelompok restriksi vitamin B12 dengan HSE dibandingkan dengan grup restriksi vitamin B12 tanpa HSE pada usia perlakuan 16 minggu ($0,55 \pm 0,03$ vs $1,00 \pm 0,02$; $p < 0,05$). Kelompok restriksi vitamin B12 dengan HSE memiliki gambaran histopatologis steatosis, inflamasi, dan fibrosis lebih baik dibandingkan kelompok yang restriksi vitamin B12 tanpa HSE setelah 16 minggu perlakuan.

Disimpulkan peningkatan homosistein akibat diet restriksi vitamin B12 pada tikus SD menyebabkan steatosis hati, inflamasi, dan fibrosis. Ekstrak etanol H.Sabdariffa memiliki efek pencegahan terhadap kondisi steatosis, inflamasi dan fibrosis akibat peningkatan homosistein pada tikus SD yang diberi diet restriksi vitamin B12.

.....There haven't been many studies on the link between vitamin B12 deficiency and homocysteine toxicity. Homocysteine is linked to NAFLD-related cellular disease, and toxicity can manifest as steatosis or inflammation of the liver cells. H. sabdariffa. and its active constituents have a preventive effect against cellular injury. H. sabdariffa extract was tested on Sprague-Dawley (SD) rats with NAFLD in this study. This study aimed to examine the effect of H. sabdariffa on increasing homocysteine in the liver of SD rats fed a vitamin B12 restriction diet.

This research is an in vivo study conducted at the Faculty of Medicine, University of Indonesia. 30 SD rats were divided into six groups based on treatment time at 8 and 16 weeks, with the following treatments: the control group received the standard AIN-93M diet, the vitamin B12 restriction group received the AIN-93M diet with a modified reduction of the vitamin B12 component, and the vitamin B12 restriction + HSE group received the AIN-93M diet with a modified reduction of the vitamin B12 component and an ethanol extract of H. sabdariffa (HSE). After 8 and 16 weeks, vitamin B12 and homocysteine levels were measured. The increase in homocysteine toxicity activity was seen from the expression of GRP78, SREBP1c, and NF-kB proteins. The hepatoprotective activity of HSE was assessed using the AST, ALT, GGT, and NAFLD Activity Score (NAS).

Vitamin B12 levels at 8 weeks (233 ± 10.8 vs 176 ± 5.4 pg/L; $p < 0.001$) and 16 weeks (226 ± 13 vs 190.6 pg/L; $p < 0.001$), significantly higher in the HSE group with a vitamin restriction diet. B12. Plasma homocysteine levels were significantly lower in the vitamin B12 restriction group with HSE than in the vitamin B12 restriction group without extract at 8 weeks of age (2.25 ± 0.07 vs. 2.63 ± 0.1 mol/L; $p < 0.001$) and 16 weeks (2.18 ± 0.07 vs. 2.64 ± 0.09 mol/L; $p < 0.001$). Plasma GGT activity at 16 weeks of treatment decreased significantly in the vitamin B12-restricted group with HSE compared to the vitamin B12-restricted group without HSE (14.5 ± 1.1 vs. 22.9 ± 2.4 IU; $p < 0.05$). GRP78, SREBP1c, and NfKB protein expressions were measured using GAPDH protein as an internal control. At weeks 8 and 16, NF-kB protein expression was lower in the vitamin B12 restriction group with HSE compared to the vitamin B12 restriction group without HSE (0.78 ± 0.08 vs. 1.08 ± 0.06 ; $p < 0.05$). SREBP1c protein expression was lower in the vitamin B12 restriction group with HSE compared to the vitamin B12 restriction group without HSE at 16 weeks of treatment (0.55 ± 0.03 vs. 1.00 ± 0.02 ; $p < 0.05$). The vitamin B12 restriction group with HSE had better histopathological features of steatosis, inflammation, and fibrosis than the vitamin B12 restriction group without HSE after 16 weeks of treatment.

It was concluded that the increase in homocysteine due to dietary restriction of vitamin B12 in SD rats caused liver steatosis, inflammation, and fibrosis. The ethanolic extract of H. Sabdariffa had a preventive effect on steatosis, inflammation, and fibrosis due to increased homocysteine in SD rats fed a vitamin B12 restriction diet.