HEPATOPROTECTIVE EFFECTS OF *NIGELLA SATIVA* SEEDS EXTRACT AGAINST ETHANOL INDUCED HEPATIC TISSUE CHANGES.  
( EXPERIMENTAL STUDY IN WISTAR RATS )

Thesis
Submitted as partial fulfilling of the requirement for
Master of Biomedical Science

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POST GRADUATE PROGRAM
DIPONEGORO UNIVERSITY
SEMARANG
2012
DECLARATION

“I am here declare that in this thesis is my own work and that, to the best of my knowledge and belief, it contains no material previously published or written by another person nor material which to a substantial extent has been accepted for the award of any other degree or diploma of the university or other institute of higher learning, except where due acknowledge is made in the text”

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ABBREVIATIONS AND THEIR INTERPRETATION

ADH  Alcohol dehydrogenase
AH   Alcoholic hepatitis
ALDH Aldehyde dehydrogenase
ALD  Alcoholic liver disease
AMPK 5-Adenosine monophosphate-activated protein kinase
CAT  Catalase
CD14 Cluster of differentiation 14
CYP2E1 Cytochrome P-450 isoenzyme-1
DHTQ Dihydrothymoquinone
EGR-1 Early growth response protein 1
ERK Extracellular-signal-regulated kinase
GSH Glutathione
GSH-PX Glutathione peroxidase
Hhcy Hyperhomocysteinemia
MAA Malondialdehyde-acetaldehyde-protein adducts
MAPK Mitogen-activated protein kinase
MCP-1 Monocyte chemotactic protein-1
MEOS Microsomal ethanol oxidizing system
NAD Nicotinamide adenine dinucleotide
NADH Nicotinamide adenine dinucleotide
NADPH Nicotinamide adenine dinucleotide phosphate
NASH None-alcoholic steatohepatitis activity score
PMNs Polymorphonuclear neutrophilic leukocytes
PPAR-α Peroxisome proliferator-activated receptor –α
<table>
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<tr>
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<tr>
<td>ROS</td>
<td>Reactive oxygen species</td>
</tr>
<tr>
<td>SAH</td>
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</tr>
<tr>
<td>SAMe</td>
<td>S-Adenosyl methionine</td>
</tr>
<tr>
<td>SOD</td>
<td>Superoxide dismutase</td>
</tr>
<tr>
<td>SREBP-1c</td>
<td>Sterol Regulatory Element Binding Protein-1c</td>
</tr>
<tr>
<td>TCA Cycle</td>
<td>Tricarboxylic acid cycle or citric acid cycle or krebs cycle</td>
</tr>
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<td>T helper 2</td>
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<td>TLR4</td>
<td>Toll-like receptor 4</td>
</tr>
<tr>
<td>TQ</td>
<td>Thymoquinone</td>
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<tr>
<td>TRIF</td>
<td>Toll–interleukin-1–receptor domain-containing adapter-inducing interferon-beta</td>
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ABSTRACT

**Background:** It has been reported that *Nigella sativa* seeds extract posses a hepatoprotective effects in liver toxicity models, additionally has been used in the treatment of liver disease in traditional medicine.

**Goal:** The aim of the study was to investigate the hepatoprotective effects of *Nigella sativa* seeds extract towards ethanol-induced hepatic tissue changes.

**Method:** The design of the study was a post test control group design. Twenty four Wistar rats were randomly allocated into four groups; the first group treated with ethanol only, group 2, 3, and 4 were given extracts of *Nigella sativa* seeds intragastrically with the dose of 0.5, 1 and 1.5 g/kg b.w/day respectively followed by ethanol 12 g/kg b.w/day for 8 weeks. Hepatic tissue changes were stained by HE and analyzed by Kruskal-Wallis test and Mann-Whitney test. Meanwhile, Mallory bodies were analyzed by Kendall's tau-b test.

**Result:** The liver tissue in the control group showed a remarkable hepatic steatosis, hepatic inflammation and the present of Mallory bodies. There were significantly lower difference between all groups, with p=0.000, for both of hepatic steatosis and hepatic inflammation respectively. However there was no significant difference of hepatic steatosis between group 1 and control group (P=0.241). There was also a significant association (p=0.001) between *Nigella sativa* seeds extract and none presence Mallory bodies in treatment groups.

**Conclusion:** *Nigella sativa* seeds extract has a hepatoprotective effect towards ethanol induced hepatic tissue changes. The optimal dose of extract was 1.5g/kg b.w.

**Keywords:** *Nigella sativa* seeds extract; Hepatoprotective; Hepatic steatosis; Hepatic inflammation; Mallory bodies.
ABSTRAK

Latar Belakang: Ekstrak biji Nigella sativa telah diketahui memiliki efek hepatoprotektif dalam beberapa penelitian mengenai toksisitas hepar. Pada pengobatan tradisional, ekstrak ini juga digunakan dalam pengobatan penyakit-penyakit hepar kronik.

Tujuan: Menganalisis efek pemberian ekstrak biji terhadap perubahan histopatologi hepar pada tikus yang diinduksi ethanol.

Metode: Design penelitian ini adalah post test control group. Duapuluh empat ekor tikus Wistar dibagi secara random menjadi 4 kelompok. Kelompok pertama hanya diberi perlakuan dengan etanol saja, sedangkan kelompok 2, 3, 4 diberi perlakuan ekstrak biji secara intragastrikal dengan 3 dosis bertingkat 0.5, 1, dan 1.5 g/kgBB, dilanjutkan dengan pemberian ethanol dosis 12 gr/kgBb/hari secara intragastrikal selama 8 minggu. Kelompok kontrol hanya mendapat perlakuan pemberian ethanol. Perubahan pada histopatologi hepar dievaluasi secara statistik menggunakan tes Kruskal–Wallis, dilanjutkan tes Mann–Whitney. Sedangkan tes Kendall’s tau–b digunakan untuk menganalisa pemeriksaan “Mallory bodies”.

Hasil: Jaringan hati pada kelompok kontrol, menunjukkan steatosis hati, peradangan sel hati dan presentasi “Mallory bodies”. Terdapat penurunan bermakna steatosis dan inflamasi sel hati pada semua kelompok perlakuan dengan p=0.000, untuk kedua variabel steatosis dan peradangan hati, kecuali pada kelompok 1 didapatkan hasil tidak signifikan (p=0.241). Diperoleh hasil yang bermakna juga pada hubungan antara dosis pemberian ekstrak dan mallory bodies, pada semua kelompok perlakuan.

Kesimpulan: Ekstrak biji Nigella sativa memiliki potensi efek hepatoprotektif terhadap perubahan jaringan hepar yang diinduksi ethanol. Dosis yang paling baik adalah dosis 1.5 gr/ kg BB.

Kata kunci: Ekstrak biji Nigella sativa; Hepatoprotektif; steatosis hepar; inflamasi hepar; Mallory bodies.