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Methanol extract of *Muntingia calabura* leaves attenuates CCl₄-induced liver injury: possible synergistic action of flavonoids and volatile bioactive compounds on endogenous defence system

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PHARMACEUTICAL BIOLOGY

Volume: 57 Issue: 1 Pages: 335-344

DOI: 10.1080/13880209.2019.1606836

Published: JAN 1 2019

Document Type: Article

[View Journal Impact](#)

Abstract

Context: *Muntingia calabura* L. (Muntingiaceae) exerts antioxidant and anti-inflammatory activities, thus, it might be a good hepatoprotective agent. **Objective:** This study investigates the effect of methanol extract of *M. calabura* leaves (MMCL) on hepatic antioxidant and anti-inflammatory activities in CCl₄-induced hepatotoxic rat. **Materials and methods:** Sprague Dawley rats (n = 6) were treated (p.o.) with 10% DMSO (Groups 1 and 2), 50 mg/kg N-acetylcysteine (Group 3) or, 50, 250, or 500 mg/kg MMCL (Groups 4-6) for 7 consecutive days followed by pretreatment (i.p.) with vehicle (Group 1) or 50% CCl₄ in olive oil (v/v) (Groups 2-6) on day 7th. Plasma liver enzymes and hepatic antioxidant enzymes and pro-inflammatory cytokines concentrations were measured while liver histopathology was examined. **Results:** MMCL, at 500 mg/kg, significantly (p < 0.05) ameliorated CCl₄-induced hepatotoxicity by decreasing the plasma level of alanine transaminase (429.1 versus 168.7 U/L) and aspartate transaminase (513.8 versus 438.1 U/L) as well as the tissue level of nitric oxide (62.7 versus 24.1 nmol/g tissue). At 50, 250, or 500 mg/kg, MMCL significantly (p < 0.05) reduced the tumour necrosis factor alpha (87.8 versus 32.7 pg/mg tissue), interleukin-1 beta (1474.4 versus 618.3 pg/mg tissue), and interleukin-6 (136.7 versus 30.8 pg/mg tissue) while increased the liver catalase (92.1 versus 114.4 U/g tissue) and superoxide dismutase (3.4 versus 5.5 U/g tissue). Additionally, qualitative phytochemicals analysis showed that MMCL contained gallic acid, ferulic acid, quercetin, and genistein. **Discussion and conclusions:** MMCL ability to attenuate CCl₄-induced hepatotoxicity could be helpful in the development of hepatoprotective agents with fewer side effects.

Keywords

Author Keywords: Muntingiaceae; hepatoprotective activity; antioxidant activity; oxidative stress markers; pro-inflammatory mediators; phytoconstituents; UHPLC-ESI; GCMS

KeyWords Plus: TETRACHLORIDE-INDUCED HEPATOTOXICITY; CARBON-TETRACHLORIDE; NITRIC-OXIDE; DOSING VEHICLES; DAMAGE; MECHANISM; RATS

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Funding

Funding Agency	Grant Number
Research Acculturation Collaborative Effort grant (RACE) - Universiti Putra Malaysia (UPM), Malaysia	R/RACE/A07.00/00290A/002/2015/000234

[View funding text](#)

Publisher

TAYLOR & FRANCIS LTD, 2-4 PARK SQUARE, MILTON PARK, ABINGDON OX14 4RN, OXON, ENGLAND

Journal Information

Impact Factor: [Journal Citation Reports](#)

Categories / Classification

Research Areas: Plant Sciences; Medical Laboratory Technology; Pharmacology & Pharmacy

Web of Science Categories: Plant Sciences; Medical Laboratory Technology; Pharmacology & Pharmacy

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Sanad, Fatma Abdel-Azim; Ahmed, Samah Fathy; El-Tantawy, Walid Hamdy. Antidiabetic and hypolipidemic potentials of *Solidago virgaurea* extract in alloxan-induced diabetes type 1. ARCHIVES OF PHYSIOLOGY AND BIOCHEMISTRY (2020)

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1. **Antioxidant and anti-inflammatory activities contribute to the prophylactic effect of semi-purified fractions obtained from the crude methanol extract of *Muntingia calabura* leaves against gastric ulceration in rats** Times Cited: 24
By: Balan, Tavamani; Sani, Mohd. Hijaz Mohd.; Ahmad, Salahuddin Haji Mumtaz; et al.
JOURNAL OF ETHNOPHARMACOLOGY Volume: 164 Pages: 1-15 Published: APR 22 2015
2. **Antiulcer activity of *Muntingia calabura* leaves involves the modulation of endogenous nitric oxide and nonprotein sulfhydryl compounds** Times Cited: 11
By: Balan, Tavamani; Sani, Mohd. Hijaz Mohd.; Suppaiah, Velan; et al.
PHARMACEUTICAL BIOLOGY Volume: 52 Issue: 4 Pages: 410-418 Published: APR 2014
3. **Hepatoprotective Effect of *Otostegia persica* Boiss. Shoot Extract on Carbon Tetrachloride-Induced Acute Liver Damage in Rats** Times Cited: 14
By: Bezenjani, Sedighe Nasiri; Pouraboli, Iran; Afshar, Reza Malekpour; et al.
IRANIAN JOURNAL OF PHARMACEUTICAL RESEARCH Volume: 11 Issue: 4 Pages: 1235-1241 Published: FAL 2012
4. **Mechanism of carbon tetrachloride-induced hepatotoxicity. Hepatocellular damage by reactive carbon tetrachloride metabolites** Times Cited: 114
By: Boll, M; Weber, LWD; Becker, E; et al.
ZEITSCHRIFT FUR NATURFORSCHUNG C-A JOURNAL OF BIOSCIENCES Volume: 56 Issue: 7-8 Pages: 649-659 Published: JUL-AUG 2001
5. **Liver enzyme alteration: a guide for clinicians** Times Cited: 564
By: Giannini, EG; Testa, R; Savarino, V
CANADIAN MEDICAL ASSOCIATION JOURNAL Volume: 172 Issue: 3 Pages: 367-379 Published: FEB 1 2005
6. **The ameliorating effects of green tea extract against cyromazine and chlorpyrifos induced liver toxicity in male rats** Times Cited: 17
By: Heikal, T.M.; Mossa, A.H.; Rasoul, M.A.A.; et al.
Asian J. Pharm. Clin. Res. Volume: 6 Issue: 1 Pages: 48-55 Published: 2013
[\[Show additional data\]](#)
7. **Effect of methanol extract of *Dicranopteris linearis* against carbon tetrachloride-induced acute liver injury in rats** Times Cited: 17
By: Kamisan, Farah Hidayah; Yahya, Farhana; Mamat, Siti Syariah; et al.
BMC COMPLEMENTARY AND ALTERNATIVE MEDICINE Volume: 14 Article Number: 123 Published: APR 4 2014
8. **Resveratrol pretreatment reduces circulating inflammatory interleukins in CCl₄-induced hepatotoxicity rats.** Times Cited: 2
By: Kandil, Y. I.; Maraqa, A. D.; Oriquat, G. A.; et al.
Bulletin of the Faculty of Pharmacy, Cairo University Volume: 55 Issue: 2 Pages: 319-323 Published: 2017
9. **EFFECT OF ORAL DOSING VEHICLES ON THE ACUTE HEPATOTOXICITY OF CARBON-TETRACHLORIDE IN RATS** Times Cited: 40
By: KIM, HJ; ODENDHAL, S; BRUCKNER, JV
TOXICOLOGY AND APPLIED PHARMACOLOGY Volume: 102 Issue: 1 Pages: 34-49 Published: JAN 1990
10. **EFFECT OF DOSING VEHICLES ON THE PHARMACOKINETICS OF ORALLY-ADMINISTERED CARBON-TETRACHLORIDE IN RATS** Times Cited: 65
By: KIM, HJ; BRUCKNER, JV; DALLAS, CE; et al.
TOXICOLOGY AND APPLIED PHARMACOLOGY Volume: 102 Issue: 1 Pages: 50-60 Published: JAN 1990
11. **Ferulic acid protects against carbon tetrachloride-induced liver injury in mice** Times Cited: 84
By: Kim, Hyo-Yeon; Park, Juhyun; Lee, Kwan-Hoo; et al.
TOXICOLOGY Volume: 282 Issue: 3 Pages: 104-111 Published: APR 11 2011
12. **Protective role of genistein in acute liver damage induced by carbon tetrachloride** Times Cited: 31
By: Kuzu, Nalan; Metin, Kerem; Ferda Dagli, Adile; et al.
MEDIATORS OF INFLAMMATION Article Number: 36381 Published: 2007
13. **The hepatoprotective effects of baicalein against CCl₄-induced acute liver injury in mice** Times Cited: 7
By: Liu, Jianhui; Jia, Min; Yao, Lu; et al.
INTERNATIONAL JOURNAL OF CLINICAL AND EXPERIMENTAL MEDICINE Volume: 9 Issue: 12 Pages: 23206-23213 Published: 2016
14. **Amelioration of paracetamol-induced hepatotoxicity in rat by the administration of methanol extract of *Muntingia calabura* L** Times Cited: 1
By: Mahmood, D; Mamat, SS; Kamisan, FH; et al.
leaves. Biomed Res Int Volume: 2014 Article Number: 695678 Published: 2014
[\[Show additional data\]](#)

15. **Muntingia calabura: A review of its traditional uses, chemical properties, and pharmacological observations** Times Cited: 12
 By: Mahmood, N. D.; Nasir, N. L. M.; Rofiee, M. S.; et al.
 PHARMACEUTICAL BIOLOGY Volume: 52 Issue: 12 Pages: 1598-1623 Published: DEC 2014
16. **Controlled modulation of inflammatory, stress and apoptotic responses in macrophages.** Times Cited: 29
 By: Malyshev, I. Yu.; Shnyra, A.
 Current Drug Targets - Immune Endocrine and Metabolic Disorders Volume: 3 Issue: 1 Pages: 1-22 Published: March 2003
17. **Postulated carbon tetrachloride mode of action: A review** Times Cited: 244
 By: Manibusan, Mary K.; Odin, Marc; Eastmond, David A.
 JOURNAL OF ENVIRONMENTAL SCIENCE AND HEALTH PART C-ENVIRONMENTAL CARCINOGENESIS & ECOTOXICOLOGY REVIEWS Volume: 25 Issue: 3 Pages: 185-209
 Published: 2007
18. **Distinct roles of tumor necrosis factor-alpha and nitric oxide in acute liver injury induced by carbon tetrachloride in mice** Times Cited: 128
 By: Morio, LA; Chiu, H; Sprowles, KA; et al.
 TOXICOLOGY AND APPLIED PHARMACOLOGY Volume: 172 Issue: 1 Pages: 44-51 Published: APR 1 2001
19. **Cytokines and fatty liver diseases** Times Cited: 7
 By: Niederreiter, L; Tilg, H.
 Liver Res Volume: 2 Pages: 14-20 Published: 2018
20. **Octacosanol attenuates disrupted hepatic reactive oxygen species metabolism associated with acute liver injury progression in rats intoxicated with carbon tetrachloride** Times Cited: 26
 By: Ohta, Yoshiji; Ohashi, Koji; Matsura, Tatsuya; et al.
 JOURNAL OF CLINICAL BIOCHEMISTRY AND NUTRITION Volume: 42 Issue: 2 Pages: 118-125 Published: MAR 2008
21. **Effects of quercetin on liver damage in rats with carbon tetrachloride-induced cirrhosis** Times Cited: 83
 By: Pavanato, A; Tunon, MJ; Sanchez-Campos, S; et al.
 DIGESTIVE DISEASES AND SCIENCES Volume: 48 Issue: 4 Pages: 824-829 Published: APR 2003
22. **Methanolic Extract of Clinacanthus nutans Exerts Antinociceptive Activity via the Opioid/Nitric Oxide-Mediated, but cGMP-Independent, Pathways** Times Cited: 10
 By: Rahim, Mohammad Hafiz Abdul; Zakaria, Zainul Amiruddin; Sani, Mohd Hijaz Mohd; et al.
 EVIDENCE-BASED COMPLEMENTARY AND ALTERNATIVE MEDICINE Article Number: 1494981 Published: 2016
23. **Role of nitric oxide in inflammatory diseases** Times Cited: 365
 By: Sharma, J. N.; Al-Omran, A.; Parvathy, S. S.
 Inflammopharmacology Volume: 15 Issue: 6 Pages: 252-259 Published: DEC 2007
24. **Occupational and Environmental Hepatotoxicity** Times Cited: 4
 By: Tolman, Keith G.; Dalpiaz, Anthony S.
 DRUG-INDUCED LIVER DISEASE, 3RD EDITION Pages: 659-675 Published: 2013
25. **Cytotoxicity and hepatoprotective attributes of methanolic extract of Rumex vesicarius L.** Times Cited: 8
 By: Tukappa, Asha N. K.; Londonkar, Ramesh L.; Nayaka, Hanumantappa B.; et al.
 BIOLOGICAL RESEARCH Volume: 48 Article Number: 19 Published: MAR 25 2015
26. **Protective effect of Acacia confusa bark extract and its active compound gallic acid against carbon tetrachloride-induced chronic liver injury in rats** Times Cited: 65
 By: Tung, Yu-Tang; Wu, Jyh-Horng; Huang, Chi-Chang; et al.
 FOOD AND CHEMICAL TOXICOLOGY Volume: 47 Issue: 6 Pages: 1385-1392 Published: JUN 2009
27. **EVALUATION OF LIVER WEIGHT CHANGES FOLLOWING A SINGLE ORAL-ADMINISTRATION OF CARBON-TETRACHLORIDE IN RATS** Times Cited: 9
 By: UEMITSU, N; NAKAYOSHI, H
 TOXICOLOGY AND APPLIED PHARMACOLOGY Volume: 75 Issue: 1 Pages: 1-7 Published: 1984
28. **Hepatotoxicity and mechanism of action of haloalkanes: Carbon tetrachloride as a toxicological model** Times Cited: 929
 By: Weber, LWD; Boll, M; Stampfl, A
 CRITICAL REVIEWS IN TOXICOLOGY Volume: 33 Issue: 2 Pages: 105-136 Published: 2003
29. **Antinociceptive, anti-inflammatory and antipyretic effects of Muntingia calabura aqueous extract in animal models** Times Cited: 29
 By: Zakaria, Z. A.; Hazalin, N. A. Mohd Nor; Zaid, S. N. H. Mohd; et al.
 JOURNAL OF NATURAL MEDICINES Volume: 61 Issue: 4 Pages: 443-448 Published: OCT 2007
30. **Mechanism(s) of action underlying the gastroprotective effect of ethyl acetate fraction obtained from the crude methanolic leaves extract of Muntingia calabura** Times Cited: 12
 By: Zakaria, Zainul Amiruddin; Balan, Tavamani; Azemi, Ahmad Khusairi; et al.
 BMC COMPLEMENTARY AND ALTERNATIVE MEDICINE Volume: 16 Article Number: 78 Published: FEB 24 2016

