SKRIPSI

PENGARUH FRAKSI NONPOLAR KAYU MANIS (*CINNAMOMUM BURMANNII)* TERHADAP KADAR KORTISOL TIKUS PUTIH MODEL INSOMNIA

Oleh:

Barian Muchtar Pratama

04011181924006

FAKULTAS KEDOKTERAN

UNIVERSITAS SRIWIJAYA

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Diajukan untuk memenuhi salah satu syarat memperoleh gelar Sarjana Kedokteran (S.Ked)

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HALAMAN PENGESAHAN

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Karya tulis ilmiah berupa Laporan Akhir Skripsi ini dengan judul "Pengaruh Fraksi Nonpolar Kayu Manis (*Cinnamomum burmannii*) terhadap Kadar Kortisol Tikus Putih Model Insomnia" telah dipertahankan di hadapan Tim Penguji Karya Tulis Ilmiah Program Studi Pendidikan Dokter Fakultas Kedokteran Universitas Sriwijaya pada tanggal 9 Desember 2022

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Menyatakan bahwa skripsi saya merupakan hasil karya sendiri didampingin tim pembimbing dan bukan hasil penjiplakan/*plagiat*. Apabila ditemukan unsri penjilplakan/*plagiat* dalam skripsi ini, maka saya bersedia menerima sanksi akademik dari Universitas Sriwijaya sesuai aturan yang berlaku.

Demikian pernyataan ini saya buat dalam keadaan sadar dan tanpa ada penekanan dari siapapun

Palembang, 28 November 2022

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ABSTRAK

PENGARUH FRAKSI NONPOLAR KAYU MANIS (*Cinnamomum burmannii*) TERHADAP KADAR KORTISOL TIKUS PUTIH MODEL INSOMNIA

(Barian Muchtar Pratama, Desember 2022, 140 halaman)

Fakultas Kedokteran, Universitas Sriwijaya

Latar belakang: Insomnia merupakan gangguan tidur yang menurunkan kualitas hidup. Insomnia mempengaruhi aksis HPA sehingga meningkatkan kadar kortisol. *Cinnamomum burmannii* memiliki kemampuan antiinflamasi dan antioksidan. Penelitian ini bertujuan untuk mengetahui pengaruh fraksi nonpolar kayu manis terhadap kadar kortisol.

Metode: Penelitian ini merupakan studi eksperimental *in vivo* dengan rancangan *post test only* dan kelompok kontrol di Eureka Research Laboratory. Tiga puluh ekor tikus putih jantan galur Wistar dibagi ke dalam enam kelompok perlakuan, yaitu kontrol normal (Na-CMC 0,5%), kontrol negatif (PCPA), kontrol positif (estazolam 0,1 mg/KgBB), dan Fraksi Nonpolar Kayu Manis (FNKM) 5 mg/KgBB, 10 mg/KgBB, dan 20 mg/KgBB. FNKM didapatkan melalui metode corong pisah dengan pelarut n-heksana dari simplisia kayu manis yang dimaserasi dengan etanol 96%. Tikus dalam setiap kelompok diinduksi insomnia, kecuali kontrol normal dengan pemberian intraperitoneal 300 mg/KgBB *p-chlorophenylalanine* (PCPA) selama dua hari. Pemberian FNKM dan Na-CMC 0,5% dilakukan dengan sonde intragastrik selama 14 hari. Tikus dieuthanasia dan darah diambil dari aorta abdominalis untuk diukur kadar kortisol pada serum dengan metode ELISA. Data dianalisis dengan bantuan *software* SPSS dengan kemaknaan statistik $p < 0,05$.

Hasil: Rerata kadar kortisol setiap kelompok dalam ng/mL secara berurutan adalah 30,340 ± 0,11402; 46,720 ± 0,13038; 38,340 ± 0,11402; 41,620 ± 0,13038; 33,560 ± 0,20736.; 32,640 ± 0,11402. Penurunan rerata kadar kortisol pada kelompok yang mendapatkan FNKM bermakna secara statistik ($p < 0,05$) dengan dosis FNKM 10 mg/KgBB dan 20 mg/KgBB memberikan efikasi yang lebih baik dibandingkan dosis estazolam 0,1 mg/KgBB.

Kesimpulan: FNKM memiliki efikasi dalam menurunkan kadar kortisol pada serum darah tikus putih model insomnia.

Kata kunci: *Cinnamomum burmannii*, Fraksi nonpolar, Insomnia, kortisol

ABSTRACT

THE EFFECT OF NONPOLAR FRACTION OF CINNAMON (*Cinnamomum burmannii*) ON KORTISOL LEVELS IN INSOMNIA-INDUCED ALBINO RAT

Barian Muchtar Pratama, Desember 2022, 140 pages

Medical Faculty of Sriwijaya University

Background: Insomnia is a sleep disorder that reduces the quality of life. Insomnia affects the HPA Axis by increasing cortisol levels. *Cinnamomum burmannii* is a plant that has antiinflammatory and antioxidant activity. This study aims to determine effect of nonpolar fraction of cinnamon on cortisol levels.

Methods: This study was an in vivo experimental study using a post-test only design and a control group at the Eureka Research Laboratory. Thirty male Wistar Rats were divided into six groups: normal control (Na-CMC 0,5%), negative control (PCPA), positive control (0.1 mg/KgBW estazolam), and Cinnamon Nonpolar Fraction group (CNF) 5 mg/KgBW, 10 mg/KgBW, and 20 mg/KgBW. CNF is obtained through the separating funnel method with n-hexane solvent from cinnamon simplicia macerated with 96% ethanol. Insomnia was induced in each group, except for the normal group, by intraperitoneal administration of 300 mg/KgBB p-chlorophenylalanine (PCPA) for two days. Administration of CNF and 0,5% Na-CMC was carried out with an intragastric tube for 14 days. The rats were euthanized and blood was taken from the abdominal aorta to measure cortisol levels in serum by the ELISA method. The data were analyzed using SPSS software with a statistical significance of $p < 0.05$.

Results: The mean cortisol levels for each group in ng/mL respectively were 30.340 ± 0.11402; 46.720 ± 0.13038; 38.340 ± 0.11402; 41.620 ± 0.13038; 33.560 ± 0.20736.; 32.640 ± 0.11402. The reduction in mean cortisol levels in the group receiving CNF was statistically significant ($p < 0.05$) with a dose of 10 mg/KgBW and 20 mg/KgBW of CNF providing better efficacy than a dose of 0.1 mg/KgBB of estazolam.

Conclusion: CNF has efficacy in reducing cortisol serum levels in the insomnia model of white rats

Keywords: *Cinnamomum burmannii*, Nonpolar fraction, Insomnia, kortisol

RINGKASAN

PENGARUH FRAKSI NONPOLAR KAYU MANIS (*Cinnamomum burmannii*) TERHADAP KADAR KORTISOL TIKUS PUTIH MODEL INSOMNIA
Karya Tulis Ilmiah berupa Skripsi, 5 Desember 2022

Barian Muchtar Pratama, dibimbing oleh Septi Purnamasari, S.ST. M.Bmd dan dr. Rachmat Hidayat, M.Sc.

Program Studi Pendidikan Dokter, Fakultas Kedokteran, Universitas Sriwijaya

xviii + 122 halaman, 10 tabel, 17 gambar, 5 lampiran

Insomnia merupakan gangguan tidur yang menurunkan kualitas hidup. Insomnia mempengaruhi aksis HPA sehingga meningkatkan kadar kortisol. *Cinnamomum burmannii* memiliki kemampuan aktivitas antiinflamasi dan antioksidan. Penelitian ini bertujuan untuk mengetahui pengaruh fraksi nonpolar kayu manis terhadap kadar kortisol.
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Sciencetific Paper in the form of Skripsi, 5 Desember 2022

Barian Muchtar Pratama: supervised by Septi Purnamasari, S.ST. M.Bmd and dr. Rachmat Hidayat, M.Sc.

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xviii + 122 pages, 10 tables, 17 pictures, 5 attachments

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The mean cortisol levels for each group in ng/mL respectively were 30.340 ± 0.11402; 46.720 ± 0.13038; 38.340 ± 0.11402; 41.620 ± 0.13038; 33.560 ± 0.20736.; 32.640 ± 0.11402. The reduction in mean cortisol levels in the group receiving CNF was statistically significant ($p <0.05$) with a dose of 10 mg/KgBW and 20 mg/KgBW of CNF providing better efficacy than a dose of 0.1 mg/KgBB of estazolam.
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Keywords: *Cinnamomum burmannii*, Nonpolar fraction, Insomnia, kortisol

KATA PENGANTAR

Penulis menyampaikan puji dan syukur kepada Allah SWT karena atas segala karunia-Nya, penulis dapat menyelesaikan penelitian skripsi berjudul "Pengaruh Fraksi Nonpolar Kayu Manis (*Cinnamomum burmanii*) terhadap Kadar Kortisol Tikus Putih Model Insomnia" dengan baik dan tepat waktu. Skripsi ini dibuat sebagai salah satu syarat untuk memperoleh gelar sarjana kedokteran (S.Ked) Kemudian, Penulis juga menyadari mendapatkan banyak bantuan dan dukungan dalam penulisan penelitian skripsi ini. Maka dari itu, Penulis ingin menyampaikan terimakasih kepada:

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Palembang, 5 Desember 2022

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Memberikan izin kepada Pembimbing dan Universitas Sriwijaya, untuk mempublikasikan hasil penelitian saya untuk kepentingan akademik apabila dalam waktu 1 (satu) tahun tidak mempublikasikan karya penelitian saya. Dalam kasus ini saya setuju untuk menempatkan Pembimbing sebagai penulis korespodensi (*Corresponding author*).

Demikian, pernyataan ini saya buat dalam keadaan sadar dan tanpa ada paksaan dari siapapun.

Palembang, 5 Desember 2022

Barian Muchtar Pratama

DAFTAR ISI

DAFTAR TABEL

DAFTAR GAMBAR

DAFTAR SINGKATAN

5-HT : 5-hidroksitriptamin/Serotonin

ACTH : *Adrenocorticoptropic Hormone*

ANS : *Autonomic Nervous System*

ADHD: *Attention Deficit Hyperactivity Disorder*

ARAS : *Ascending Reticular Activating System*

BDNF : *Brain-Derived Neurotrophic Factor*

BZ : Benzodiazepin

BZRA : *Benzodiazepine Receptor Agonists*

cAMP : *Cyclic Adenosine Monophosphate*

CBT : *Cognitive behavioral therapy*

COX-2 : *Cyclooxygenase*-2

CRH : *Corticotropin-Releasing Hormone*

DA : Dopamin

EEG : Elektroensefalogram

ELISA : *Enzyme-linked immunosorbent assay*

GABA : Asam γ-aminobutirat

GC : *Gas Chromatography*

GHT : *Geniculohypothalamic Tract*

GPCR : *G-protein-Coupled Receptors*

GR: *Glucocorticoid Receptor*

GRE: *Glucocorticoid Receptor Element*

HPA : Hipotalamus-pituitari-adrenal

HPLC: *High Performance Liquid Chromatography*

IGL : *Intergeniculate leaflet*

IML: *Intermediolateral Nucleus*

iNOS : *Inducible Nitric Oxide Synthase*

ipRGC : *intrinsically photosensitive Retinal Ganglion Cells*

LC : *Locus Coeruleus*

MnPO : *Median Preoptic Nucleus*

MAE : *Microwave Assisted Extraction*

NE : Norepinefrin

NF-κB : *Nuclear Factor Kappa-B*

NPY : Neuropeptida Y

NREM : *Non-rapid eye movement*

PACAP : *Pituitary Adenylate Cyclase-Activating Polypeptide*

PCPA : *p-chlorophenylalanine*

PLE *: Pressurized Liquid Extraction*

PVN : *Paraventricular Nucleus*

PNS: *Parasympathetic Nervous System*

REM : *Rapid Eye Movement*

SCN : *Suprachiasmatic Nucleus*

SFC : *Supercritical Fluid Extraction*

SLE : *Solid-Liquid Extraction*

SNS: *Sympathic Nervous System*

SNP: *Single Nucleotide polymorphism*

SOL : *Sleep Onset Latency*

SWS : *Slow Wave Sleep*

TLC: *Thin Layer Chromatography*

TMN : *Tuberomammillary Nucleus*

TNF- α : *Tumor Necrosis Factor-alpha*

VLPO : *Ventrolateral Preoptic Nucleus*

VLC : *Vacuum Liquid Chromatography*

BAB 1
PENDAHULUAN

1.1 Latar Belakang

Tidur memiliki banyak fungsi, seperti perbaikan organ, pengaturan kekebalan tubuh, peningkatan kerja memori (konsolidasi memori), pengaturan nafsu makan, dan mengurangi stres serta meregulasi metabolisme tubuh.[1–5] Beberapa penelitian studi telah dilakukan untuk mengetahui efek dari kurang tidur.[6–8] Gangguan tidur diketahui dapat bermanifestasi dalam berbagai efek pada kehidupan, seperti mengurangi kualitas hidup dan menjadi faktor risiko terjadinya penyakit lain.[9]

Pada masa pandemi COVID-19, banyak masyarakat di dunia, termasuk di Indonesia memiliki kualitas tidur yang kurang baik. Penelitian studi yang dilakukan oleh Philips Asean Pacific menyatakan bahwa 62% masyarakat Asia Pasifik mengalami penurunan kualitas tidur.[10] Masalah tidur dapat juga disebabkan karena kondisi tertentu yang dialami oleh individu tersebut. Salah satu penyebab masalah tidur tersebut adalah insomnia.[11] Gangguan insomnia (*Insomnia Disorder*) didefinisikan sebagai kesulitan untuk tidur, mempertahankan kondisi tidur, dan bangun dari tidur yang terlalu cepat yang menyebabkan gangguan aktivitas pada siang hari.[12] Secara umum penyebab insomnia dikarenakan berbagai faktor, seperti stres sosial, pengaruh lingkungan (misalnya, suasana lingkungan tidur), zat-zat tertentu (misalnya, alkohol dan kafein), penyakit tertentu yang mengganggu tidur (penyakit hiperplasia prostat dan asma), faktor gaya hidup (misalnya, lebih sering beraktivitas di malam hari), dan faktor psikis (misalnya, skizofrenia dan penyakit kecemasan).[13–17]

Berbagai penelitian di seluruh dunia telah menunjukkan prevalensi insomnia pada 10-30% dari populasi, bahkan mencapai 50-60% pada tahun 2016.[17] Hal tersebut umum terjadi pada orang dewasa yang lebih tua, wanita, dan orang-orang dengan kesehatan medis dan mental yang buruk.[17] Di Indonesia, pada tahun 2018 terdapat 10% atau 28 juta orang yang mengalami insomnia.[18] Salah satu penelitian

di Palembang, yaitu di Panti Werdha Dharma Bakti dan Tresna Werdha Teratai pada periode November hingga Desember 2014 didapatkan prevalensi hingga sebesar 43,3%. Hal tersebut menunjukkan insomnia juga memiliki kasus yang tinggi bagi para lansia.[19]

Insomnia diketahui berkaitan dengan peningkatan produksi kortisol karena kortisol memiliki pengaruh dalam siklus bangun tidur.[20] Aksis Hipotalamus-Hipofisis-Adrenal (HPA) memodulasi siklus bangun tidur sementara disfungsinya dapat mengganggu tidur. Kemudian, kurang tidur diketahui dapat mempengaruhi aksis HPA yang menyebabkan hiperaktivasi dari aksis tersebut. Kortisol disekresikan dari aksis Hipotalamus-Hipofisis-Adrenal (HPA) dalam pola sirkadian. Kortisol mulai meningkat secara bertahap di paruh kedua tidur malam. Kortisol mulai meningkat sebelum mencapai puncaknya pada sekitar jam 9 pagi. Setelah itu, kortisol akan mengalami penurunan secara bertahap sepanjang hari dan mencapai tingkat terendah sekitar tengah malam. Aktivitas sumbu kortisol akan berkurang ke tingkat terendah di malam hari, tepat di sekitar waktu tidur. Dengan cara ini, kortisol memainkan peran penting dalam siklus bangun tidur. Penelitian studi mendapatkan bahwa membatasi tidur secara eksperimental pada orang dewasa memberikan gambaran tingkat kortisol pagi yang lebih tinggi.[20] Kortisol akan mengalami penurunan secara bertahap sepanjang hari dan mencapai tingkat terendah sekitar tengah malam. Aktivitas sumbu kortisol akan berkurang ke tingkat terendah di malam hari, tepat di sekitar waktu tidur.[21]

Terapi yang diutamakan untuk mengatasi insomnia saat ini adalah CBT-I *(Cognitive Behavioural Therapy for Insomnia*).[22–24] Farmakoterapi yang dapat digunakan adalah Benzodiazepin, BZRA (*Benzodiazepine Receptor Agonist*), antidepresan, antipsikotik, antihistamin, zat fitoterapi, dan melatonin. [23,25] Namun, efek dari penggunaan benzodiazepin akan hilang atau menurun dalam beberapa minggu. Benzodiazepin juga dapat menyebabkan ketergantungan apabila pemakaian jangka lama. Kemudian, benzodiazepin juga dapat menyebabkan amnesia anterograde dan penurunan kognitif serta fraktur tulang pinggul.[26] Oleh karena itu, peneliti mengusulkan ide penggunaan obat alternatif, yaitu obat herbal dalam mengobati insomnia.

Kayu manis adalah tanaman perdu atau pohon kecil yang berasal dari famili *lauraceae* dan tersebar di Asia Tenggara serta dibudidayakan di sebagian wilayah Indonesia dan Filipina. Jenis kayu manis yang tumbuh dan di Indonesia dan terkenal di pasar dunia adalah *Cinnamomum burmanii* atau dikenal juga dengan nama *cassiavera*/*cinnamon/*padang *cassia*.[27] Senyawa nonpolar yang terdapat pada kayu manis, seperti benzena, *trans-cinnamaldehyde*, dan n-heksana.[28] Senyawa nonpolar utama yang terkandung dalam tanaman ini adalah *trans-cinnamaldehyde* yang merupakan gugus fenol dan memiliki peluang terhadap pengobatan insomnia.[29–31] Tanaman kayu manis memiliki banyak manfaat, seperti tanaman obat, kebutuhan industri, dan wewangian.[27,30,32] Akhir-akhir ini tumbuhan sebagai sumber obat semakin populer.[33] Berbagai tahap persiapan tanaman obat, meliputi pembuatan simplisia, ekstraksi, fraksinasi, dan isolasi senyawa bioaktif jika ada.[34] Pembuatan simplisia, maserasi, dan fraksinasi sangat penting dalam proses pembuatan tanaman obat.[35]

Salah satu jenis tikus yang sering digunakan pada penelitian adalah tikus putih (*Rattus norvegicus*).[36,37] Terdapat tiga galur tikus putih yang memiliki kekhususan untuk digunakan sebagai hewan percobaan antara lain Wistar, Long Evans, dan Sprague dawley. Kelebihan dari tikus putih (*Rattus norvegicus*) sebagai binatang percobaan, antara lain bersifat omnnivora (pemakan segala), mempunyai struktur fisiologi, anatomi, dan jaringan serta gizi yang dibutuhkan hampir sama dengan manusia.[38,39]

Senyawa aktif yang terkandung di kayu manis, yaitu *cinnamaldehyde* dapat menekan terjadinya proses inflamasi di otak. Penelitian ini dilakukan untuk meneliti pengaruh fraksi nonpolar (*cinnamaldehyde*) dari kayu manis (*Cinnamomum burmann*ii) dalam mengatasi gangguan insomnia dan bisa mengetahui jenis obat alternatif yang berbahan dasar alami.

1.2 Rumusan masalah

Bagaimana pengaruh fraksi nonpolar kayu manis (*Cinnamomum burmannii*) terhadap kadar kortisol pada tikus putih model insomnia?

1.3 Tujuan Penelitian

1.3.1 Tujuan Umum

Mengidentifikasi pengaruh fraksi nonpolar kayu manis (*Cinnamomum burmannii*) terhadap kadar kortisol pada serum tikus putih model insomnia.

1.3.2 Tujuan Khusus

1. Mengidentifikasi rata-rata kadar kortisol serum pada setiap kelompok tikus putih yang diberikan perlakuan dengan metode ELISA (*Enzyme-Linked Immunosorbent Assay*).
2. Menganalisis beda hasil rata-rata kadar kortisol serum pada setiap kelompok tikus putih yang diberikan perlakuan.

1.4 Hipotesis Penelitian

Terdapat pengaruh pemberian Fraksi nonpolar kayu manis (*Cinnamomum burmannii*) terhadap kadar kortisol serum tikus putih model insomnia.

1.5 Manfaat Penelitian

1.5.1 Manfaat Teoritis

1. Memicu lebih lanjut terkait eksplorasi fraksi nonpolar dari tanaman kayu manis dalam bidang kesehatan.
2. Menjadi landasan teori dan referensi untuk penelitian selanjutnya terkait penemuan pengobatan baru untuk insomnia menggunakan tanaman kayu manis.

1.5.2 Manfaat Tatalaksana

Penelitian ini dapat dijadikan sebagai pertimbangan untuk menjadikan fraksi nonpolar kayu manis sebagai bahan alternatif untuk terapi insomnia.

1.5.3 Manfaat Masyarakat

Masyarakat dapat lebih mengenal manfaat kayu manis (*Cinnamomum burmannii*) tidak hanya sebagai bahan masakan, melainkan dapat digunakan dalam kesehatan, terutama dalam pengobatan insomnia.

DAFTAR PUSTAKA

1. Eugene AR, Masiak J. The Neuroprotective Aspects of Sleep. 2015
2. Herculano-Houzel S. Sleep It Out. Science. Science (1979). 2013;
3. Karna B, Gupta V. Sleep Disorder. https://www.ncbi.nlm.nih.gov/books/NBK560720/. 2021.
4. Pradeep C. B, Kaur H. Sleep Medicine: Insomnia and Sleep. Sleep Med. 2019 Feb;
5. Underwood E. Sleep: the brain's housekeeper? . Science (1979). 2013;
6. Sunni E, Callender E. What Happens When You Sleep? Sleep Foundation. 2022 Jul 8;
7. Whitney P, Hinson JM, Chee MWL, Honn KA, van Dongen HPA. Sleep Deprivation and Cognition. 2019.
8. Spira AP, Gamaldo AA, An Y, Wu MN, Simonsick EM, Bilgel M, et al. Self-reported sleep and β-amyloid deposition in community-dwelling older adults. JAMA Neurol. 2013;70(12):1537–43.
9. Rémi J, Pollmächer T, Spiegelhalder K, Trenkwalder C, Young P. Sleep-Related Disorders in Neurology and Psychiatry. Vol. 116, Deutsches Arzteblatt international. NLM (Medline); 2019. p. 681–8.
10. Rai SS. COVID-19's Effect on Sleep Revealed in New Philips Sleep Study. https://www.philips.com.my/a-w/about/news/archive/standard/news/press/2021/20211703-covid-19-effect-sleep-revealed-new-philips-sleep-study.html. 2021.
11. Hanson JA, Huecker MR. Sleep Deprivation. Statpearl. 2022 Mar 7;
12. Gebara MA, Siripong N, DiNapoli EA, Maree RD, Germain A, Reynolds CF, et al. Effect of insomnia treatments on depression: A systematic review and meta-analysis. Vol. 35, Depression and Anxiety. Blackwell Publishing Inc.; 2018. p. 717–31.
13. al Karaki G, Hallit S, Malaeb D, Kheir N, Sacre H, Salameh P, et al. Prevalence and factors associated with insomnia among a representative sample of the lebanese population: Results of a cross-sectional study. J Epidemiol Glob Health. 2020 Jun 1;10(2):124–30.
14. Pachecho D, Vyas N. Caffeine and Sleep. https://www.sleepfoundation.org/nutrition/caffeine-and-sleep. 2022.
15. Zhang C, Yang L, Liu S, Ma S, Wang Y, Cai Z, et al. Survey of Insomnia and Related Social Psychological Factors Among Medical Staff Involved in

the 2019 Novel Coronavirus Disease Outbreak. Front Psychiatry. 2020 Apr 14;11.

16. Chakravorty S, Chaudhary NS, Brower KJ. Alcohol Dependence and Its Relationship With Insomnia and Other Sleep Disorders. Vol. 40, Alcoholism: Clinical and Experimental Research. Blackwell Publishing Ltd; 2016. p. 2271–82.

17. Bhaskar S, Hemavathy D, Prasad S. Prevalence of chronic insomnia in adult patients and its correlation with medical comorbidities. J Family Med Prim Care. 2016;5(4):780.

18. Nashori F, Dwi Wulandari E, Nugraha PS. Insomnia-Cognitive Behaviour Therapy to Improve the Subjective Well-Being of University Students. Researchgate. 2019;

19. Rarasta M, Nita S. Prevalensi Insomnia pada usia lanjut Prevalensi Insomnia pada Usia Lanjut Warga Panti Werdha Dharma Bakti dan Tresna Werdha Teratai Palembang. Biomedical Journal of Indonesia: Jurnal Biomedik Fakultas Kedokteran Universitas Sriwijaya [Internet]. 2018;4(2). Available from: https://doi.org/10.32539/BJI.V4I2.7961

20. Bublitz MH, Bourjeily G, D'Angelo C, Stroud LR. Maternal Sleep Quality and Diurnal Cortisol Regulation Over Pregnancy. Behavioral Sleep Medicine. 2018 May 4;16(3):282–93.

21. Hirotsu C, Tufik S, Andersen ML. Interactions between sleep, stress, and metabolism: From physiological to pathological conditions. Sleep Science. 2015;

22. A. Dopheide J. Insomnia Overview. AJMC. 2020 Apr 13;

23. D. Krystal A, A. Prather A, H. Ashbrook L. The assessment and management of insomnia: an update. Pubmed. 2019 Sep 9;

24. Koffel EA, Koffel JB, Gehrman PR. A meta-analysis of group cognitive behavioral therapy for insomnia. Vol. 19, Sleep Medicine Reviews. W.B. Saunders Ltd; 2015. p. 6–16.

25. Riemann dieter, Baglioni C, Basetti C, Ellis JG. European guideline for the diagnosis and treatment of insomnia. Jorunal of Sleep Research. 2013 Sep 5;

26. Johnson B, Streltzer J. Risks Associated with Long-Term Benzodiazepine Use [Internet]. Vol. 88. 2013. Available from: www.aafp.org/afp.

27. Cardoso-Ugarte GA, López-Malo A, Sosa-Morales ME. Cinnamon (Cinnamomum zeylanicum) Essential Oils. In: Essential Oils in Food Preservation, Flavor and Safety. Elsevier; 2015. p. 339–47.

28. Abubakar AR, Haque M. Preparation of Medicinal Plants: Basic Extraction and Fractionation Procedures for Experimental Purposes. Journal of Pharmacy. 2020;12(1).

29. Silva M, Caro V, Guzmán C, Perry G, Areche C, Cornejo A. α-Synuclein and tau, two targets for dementia. In: Studies in Natural Products Chemistry. Elsevier B.V.; 2021. p. 1–25.

30. Rao PV, Gan SH. Cinnamon: A multifaceted medicinal plant. Vol. 2014, Evidence-based Complementary and Alternative Medicine. Oxford University Press; 2014.

31. Doyle A, Stephensen JC. A review of cinnamaldehyde and its derivatives as antibacterial agents . Fitoterapia. 2019 Nov;

32. Abdallah EM, Rauf A, Sadeek AMM. Cinnamon bark as antibacterial agent: A mini-review. Traditional Medicine. 2020 Jan;

33. Pandey A, Tripathi S. Concept of standardization, extraction and pre phytochemical screening strategies for herbal drug. ~ 115 ~ Journal of Pharmacognosy and Phytochemistry. 2014;2(5):115–9.

34. Azwanida NN. A Review on the Extraction Methods Use in Medicinal Plants, Principle, Strength and Limitation. Med Aromat Plants (Los Angel). 2015;04(03).

35. Gupta A, Kothari V. Modern extraction methods for preparation of bioactive plant extracts. Anal Chem. 2012;

36. Howe K. The genome sequence of the Norway rat, Rattus norvegicus Berkenhout 1769. 2021;

37. Snyder JS, Grigereit L, Russo A, Seib DR, Brewer M, Pickel J, et al. A transgenic rat for specifically inhibiting adult neurogenesis. eNeuro. 2016;3(3):464–6.

38. Suckow M, Hackenson FC. The Laboratory Rat. 2019.

39. L MR, Downes N. Anatomy and Histology of the Laboratory Rat in Toxicology and Biomedical Research. Academic Press; 2019.

40. Connolly AJ, Finkbeiner WE, Ursell PC, Davis RL. Fasciulata Layer. Autopsy Pathology: A Manual and Atlas. 2016;108–31.

41. Angelousi A, Margioris AN, Tsatsanis C. ACTH Action on the Adrenals. NCBI. 2020;

42. Thau L, Gandhi J, Sharma S. Physiology Cortisol. StatPearls Publishing. 2021 Sep 6;

43. J. Allen M, Sharma S. Physiology, Adrenocorticotropic Hormone (ACTH). Statpearl (Internet). 2021 Aug 17;

44. Rhodes ME. Adrenocorticotropic Hormone. Stress: Neuroendocrinology and Neurobiology. 2017 Jan 1;2:109–16.

45. Ando H, Kazuyoshi U, Nagata S. Handbook of Hormones Comparative Endocrinology for Basic and Clinical Research. 2nd ed. New York : Elsevier; 2021.

46. Klimes-Dougan B, Papke V, Carosella KA, Wiglesworth A, Mirza SA, Espensen-Sturges TD, et al. Basal and reactive cortisol: A systematic literature review of offspring of parents with depressive and bipolar disorders. Neurosci Biobehav Rev. 2022 Apr 1;135:104528.

47. Breuner CW, Beyl HE, Malisch JL. Corticosteroid-binding globulins: Lessons from biomedical research. Mol Cell Endocrinol. 2020 Aug 20;514:110857.

48. Scherholz ML, Schlesinger N, Androulakis IP. Chronopharmacology of glucocorticoids. Adv Drug Deliv Rev. 2019 Nov 1;151–152:245–61.

49. Fuh J, Urban F, Quals C, Dorin RI. SAT-738 Sources of Error in Estimation of Cortisol Half-Life Using Conventional, Single-Compartment Model: Bias Due to Variation in CBG Concentration. J Endocr Soc. 2020 Mar;

50. Chergui N, Mormede P, Foury A, Khammar F, Amirat Z. Seasonal effects on plasma cortisol concentrations in the Bedouin buck: circadian studies and response to ACTH. Animal. 2017 Jan 1;11(3):445–51.

51. Louwies T, Meerveld BGV. Cortisol Receptors. Comprehensive Pharmacology [Internet]. 2022 [cited 2022 Jul 21];132–63. Available from: https://linkinghub.elsevier.com/retrieve/pii/B9780128204726000372

52. Amasi-Hartoonian N, Sforzini L, Cattaneo A, Pariante CM. Cause or consequence? Understanding the role of cortisol in the increased inflammation observed in depression. Curr Opin Endocr Metab Res. 2022 Jun 1;24:100356.

53. Pariante CM. Why are depressed patients inflamed? A reflection on 20 years of research on depression, glucocorticoid resistance and

inflammation. European Neuropsychopharmacology. 2017 Jun 1;27(6):554–9.

54. Schiffer L, Bernard L, Baranowski ES, C. Gilligan L, Taylor AE, Arit W, et al. Human steroid biosynthesis, metabolism and excretion are differentially reflected by serum and urine steroid metabolomes: A comprehensive review. Journal Steroid Biochemistry Mollecular Biology. 2019 Nov;

55. El-Farhan N, Rees D. A, Carol E. Measuring cortisol in serum, urine and saliva – are our assays good enough? . 2017 Mar 16;

56. Katsu Y, Baker ME. Cortisol. Handbook of Hormones: Comparative Endocrinology for Basic and Clinical Research. 2021 Jan 1;947–9.

57. Yaribeygi H, Panahi Y, Sahraei H, Johnston TP, Sahebkar A. The impact of stress on body function: A review. Vol. 16, EXCLI Journal. Leibniz Research Centre for Working Environment and Human Factors; 2017. p. 1057–72.

58. Rotenberg S, McGrath JJ. Inter-relation between autonomic and HPA axis activity in children and adolescents. Biol Psychol. 2016 May 1;117:16–25.

59. Barel E, Abu-Shkara R, Colodner R, Masalha R, Mahagna L, Cohen A. Gonadal hormones modulate the HPA-axis and the SNS in response to psychosocial stress . Journal of Neuorscience Research. 2018;

60. Zhang X, Ge TT, Yin G, Cui R, Zhao G, Yang W. Stress-induced functional alterations in amygdala: Implications for neuropsychiatric diseases. Vol. 12, Frontiers in Neuroscience. Frontiers Media S.A.; 2018.

61. K. Adam E, E. Quinn M, Tavernier R, McQuillan T M, A. Dahlke K, E. Gilbert K. Diurnal cortisol slopes and mental and physical health outcomes: A systematic review and meta-analysis . Psychoneuroendocrinology [Internet]. 2017 [cited 2022 Jul 20]; Available from: https://www.ncbi.nlm.nih.gov/books/NBK539805/

62. Maduka IC, Neboh EE, Ufelle SA. The relationship between serum cortisol, adrenaline, blood glucose and lipid profile of undergraduate students under examination stress. Afr Health Sci. 2015;15(1):131–6.

63. Shah N, Ruiz HH, Zafar U, Post KD, Buettner C, Geer EB. Proinflammatory cytokines remain elevated despite long-term remission in Cushing's disease: a prospective study . Clin Endocrinol (Oxf). 2017 Jan;

64. Nicolas C. C, N. Vgontzas A, Kritikou I. HPA Axis and Sleep. 2020 Nov 24;

65. Ramamoorthy S, Cidlowski JA. Corticosteroids. Mechanisms of Action in Health and Disease. Vol. 42, Rheumatic Disease Clinics of North America. W.B. Saunders; 2016. p. 15–31.

66. Trachitella T. The Role of Cortisol and Melatonin in the Synchronization of the Circadian Rhythm. 2022;

67. H. Jawabri K, Raja A. Physiology, Sleep Patterns. Statpearls. 2022;

68. Troynikov O, Watson C, Nazia N. Sleep environments and sleep physiology: A review. J Therm Biol. 2018;

69. v Vyazovskiy V, Delogu A. NREM and REM Sleep: Complementary Roles in Recovery after Wakefulness . Neuroscientist [Internet]. 2014 [cited 2022 Jul 20]; Available from: https://www.ncbi.nlm.nih.gov/books/NBK539805/

70. Abhang PA, Gawali BW, Mehrotra SC. Technological Basics of EEG Recording and Operation of Apparatus. Introduction to EEG- and Speech-Based Emotion Recognition. Elsevier. 2016;

71. S. Nayak C, C. Anilkumar A. EEG Normal Waveforms. 2022;

72. K. Patel A, Reddy V, F. Araujo J. Physiology, Sleep Stages. 2022;

73. Nava Zisapel C, Zisapel N. New perspectives on the role of melatonin in human sleep, circadian rhythms and their regulation. 2018; Available from: http://onlinelibrary.wiley.com/doi/10.1111/bph.v175.16/issuetoc

74. American Medical Association. What is Insomnia. JAMA. 2021 Dec 21;

75. C. Levenson J, B. Kay D, J. Buysse D. The Pathophysiology of Insomnia. Pubmed. 2015 Apr;

76. Brewster GS, Riegel B, Gehrman PR. Insomnia in the Older Adult. Sleep Med Clin. 2022 Jun 1;17(2):233–9.

77. A. Schlarb A, Jaeger S, Schneider S, In-Albon T. Sleep Problems and Separation Anxiety in Preschool-Aged Children: A Path Analysis. J Child Fam Stud. 2015;

78. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 5th ed. New York: American Psychiatric Publishing; 2013.

79. A. Kalmbach D, R. Anderson J, L. Drake C. The impact of stress on sleep: Pathogenic sleep reactivity as a vulnerability to insomnia and circadian disorders . J Sleep Res. 2018;

80. Bragg S, Benich JJ, Christian N, Visserman J, Freedy J. Updates in insomnia diagnosis and treatment . International Journal of Psychiatry In Medicine9. 2019 Sep;

81. The NCBI taxonomy database. Taxonomy Rattus Norvegicus. https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=10116. 2020.

82. Linley SB, Vertes RP. Serotonergic Systems in Sleep and Waking. In: Handbook of Behavioral Neuroscience. Elsevier B.V.; 2019. p. 101–23.

83. Shen CY, Li XY, Ma PY, Li HL, Xiao B, Cai WF, et al. Nicotinamide mononucleotide (NMN) and NMN-rich product supplementation alleviate p-chlorophenylalanine-induced sleep disorders. J Funct Foods. 2022 Apr 1;91:105031.

84. Si Y, Wang L, Lan J, Li H, Guo T, Chen X, et al. Lilium davidii extract alleviates p-chlorophenylalanine-induced insomnia in rats through modification of the hypothalamic-related neurotransmitters, melatonin and homeostasis of the hypothalamic-pituitary-adrenal axis. Pharm Biol. 2020 Jan 1;58(1):915–24.

85. Waly NE, Hallworth R. Circadian pattern of melatonin MT1 and MT2 receptor localization in the rat suprachiasmatic nucleus. J Circadian Rhythms. 2015;13(1):1–7.

86. Duan DD., Wang KX., Zhou YZ., Qin XM, Gao L., du GH. Baicalein exerts beneficial effects in d-galactose-induced aging rats through attenuation of inflammation and metabolic dysfunction. Rejuvenation Res. 2017;

87. Ren X, Wang Q, Zhang X, Wang G, Liu T, Deng N, et al. Establishment of a rat model with ageing insomnia induced by D-galactosef and para-chlorophenylalanine. Exp Ther Med. 2020 Jul 29;

88. Zhao Q, Peng C, Wu X, Chen Y, Wang C, You Z. Maternal sleep deprivation inhibits hippocampal neurogenesis associated with inflammatory response in young offspring rats. Neurobiol Dis. 2014 Aug 1;68:57–65.

89. Xiang B, Liu K, Yu M, Liang X, Huang C, Zhang J, et al. Systematic genetic analyses of GWAS data reveal an association between the immune system and insomnia. Mol Genet Genomic Med. 2019 Jul 1;7(7).

90. Hu Y, Wang YN, Zhang GQ, Dong ZZ, Liu- Wan-wan, Liu P. Gan-Dan-Liang-Yi-Tang alleviates p-chlorophenylalanine-induced

insomnia through modification of the serotonergic and immune system. Clinical Pharmacology and Pharmacy,. 2016;

91. L. Perlman R. Mouse models of human disease. Pubmed Medicine. 2016 May 21;

92. B. Deryabina I. Effects of Thryptophan Hydroxylase Blockade by P-Chlorophenylalanine on Contextual Memory Reconsolidation after Training of Different Intensity . Mollecular Sciences. 2020 Jan 28;

93. Zeng X, Huang J, Zhou C, Wang X, Zhang Y, Zhang Y. Effect of Songyu Anshen Fang on expression of hypothalamic GABA and GABA(B) receptor proteins in insomniac rats induced by para-chlorophenylalanine. Tropical Journal of Pharmaceutical Research. 2018 Jan 1;17(1):17–22.

94. Chen P, Sun J, Ford P. Differentiation of the four major species of cinnamons (C. burmannii, C. verum, C. cassia, and C. loureiroi) using a flow injection mass spectrometric (FIMS) fingerprinting method. J Agric Food Chem. 2014 Mar 26;62(12):2516–21.

95. Nunes C, de J. Raposo MF, Petronilho S, Machado F, Fulgêncio R, Gomes MH, et al. Cinnamomum burmannii decoction: A thickening and flavouring ingredient. LWT. 2022 Jan 1;153.

96. Susilowati R, Abdul Malik S. Cinnamomum burmannii (Nees & T. Nees) Blume and Eleutherine palmifolia (L.) Merr. extract combination ameliorate lipid profile and heart oxidative stress in hyperlipidemic mice. Vet World. 2020 Jul 2;

97. Fajar A, Abdillah Ammar G, Hamzah M, Manurung R, Yusuf Abduh M. Effect of tree age on the yield, productivity, and chemical composition of essential oil from Cinnamomum burmannii. 2019;

98. The NCBI taxonomy database. Taxonomy of Cinnamomum burmanni. https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?mode=Info&id=119261. 2020.

99. Jalbayu. Types Of Species In Indonesia #10 Kayu Manis (Cinnamomum burmannii). https://steemit.com/natural/@jalbayu/types-of-species-in-indonesia-10-kayu-manis-cinnamomum-burmannii. 2018.

100. Al-Dhubiab BE. Pharmaceutical applications and phytochemical profile of Cinnamomum burmannii. Vol. 6, Pharmacognosy Reviews. 2012. p. 125–31.

101. Moh SQ. TESTING THE EFFECTIVENESS OF VARIOUS CONCENTRATIONS OF Cinnamon (Cinnamomum burmannii) LEAF EXTRACT CONCENTRATIONS AGAINST THE DIAMETER OF THE

GROWTH INHIBITED ZONE OF THE BACTERIA Staphylococcus epidermidis AS A BIOLOGICAL LEARNING SOURCE. UMM. 2017;

102. CABI. Cinnamomum burmanni (padang cassia). https://www.cabi.org/isc/datasheet/13516. 2019.

103. Tjokroprawiro A, Murtiwi S, R. Tjandrawinata R. DLBS3233, a combined bioactive fraction of Cinnamomum burmanii and Lagerstroemia speciosa, in type-2 diabetes mellitus patients inadequately controlled by metformin and other oral antidiabetic agents . J Complement Integr Med. 2016;

104. Othman ZS, Yusof Maskat M, Hassan HN. Optimization of Cinnamaldehyde Extraction and Antioxidant Activity of Ceylon Cinnamon Extract. Sains Malays. 2020;

105. Ribeiro-Santos R, Mariana AA, Nathalia R de M, Santos frances. Biological activities and major components determination in essential oils intended for a biodegradable food packaging. Industrial Cropsand Products. 2017;

106. Rahadian Aji Muhammad D, Lemarcq V, Alderweireldt E, Vanoverberghe P. Antioxidant activity and quality attributes of white chocolate incorporated with Cinnamomum burmannii Blume essential oil. J Food Sci Technol. 2019 Dec;

107. Muhammad DRA, Tuenter E, Patria GD, Foubert K, Pieters L, Dewettinck K. Phytochemical composition and antioxidant activity of Cinnamomum burmannii Blume extracts and their potential application in white chocolate. Food Chem. 2021;

108. Plumeriastuti H, Helmi M, Budiastuti. Identification of bioactive compound of the essential oils of Cinnamomum burmannii from several areas in Indonesia by gas chromatography-mass spectrometry method for antidiabetic Patient. National Journal of Physiology Pharmacy and Pharmacology ·. 2019;

109. Liang Y, Yi Li, Sun A. Chemical compound identification and antibacterial activity evaluation of cinnamon extracts obtained by subcritical n-butane and ethanol extraction . Pubmed. 2019 May 16;

110. Azura S. EXTRACTION OF ESSENTIAL OIL FROM CINNAMOMUM ZEYLANICUM BY VARIOUS METHODS AS A PERFUME OIL. Universiti Malaysia Pahang. 2013 Feb;

111. Yeh HF, Luo CY, Lin CY, Cheng SS, Hsu YR, Chang ST. Methods for thermal stability enhancement of leaf essential oils and their main

constituents from indigenous cinnamon (Cinnamomum osmophloeum). J Agric Food Chem. 2013 Jul 3;61(26):6293–8.

112. Wen-Yi Qiu, Cai WD, Wang M, Yan JK. Effect of ultrasonic intensity on the conformational changes in citrus pectin under ultrasonic processing. Food Chem. 2019;

113. Pulungan A, Pane Sari Y. The benefit of cinnamon (Cinnamomum burmannii) in lowering total cholesterol levels after consumption of high-fat containing foods in white mice (Mus musculus) models . 2020 Mar 6;

114. Sari I. THE CHARACTERIZATION OF SIMPLISIA, ISOLATION AND IDENTIFICATION OF CHEMICAL CONSTITUENS FROM THALLUS Turbinaria decurrens Bory. Jurnal Natural. 2015;15(2).

115. School G, Negeri Malang U, Sri Sulasmi E, Endah Indriwati S, Suarsini E. Responding to Current Issues Preparation of Various Type of Medicinal Plants Simplicia as Material of Jamu Herbal. 2016.

116. Altemimi A, Lakhssassi N, Baharlouei A, Watson DG, Lightfoot DA. Phytochemicals: Extraction, isolation, and identification of bioactive compounds from plant extracts. Vol. 6, Plants. MDPI AG; 2017.

117. Hidayat R, Wulandari P. Methods of Extraction: Maceration, Percolation and Decoction. Eureka Herba Indonesia. 2021;2(1).

118. Wen-Zhang Q, Lin LG, Ye WC. Techniques for extraction and isolation of natural products: a comprehensive review. Chin Med. 2018 Apr 17;13(20).

119. Gopi S, Balakrishnan P. Handbook of Nutraceuticals and Natural Products. 1st ed. John Wiley & Sons; 2022.

120. Deng Y, Wang W, Zhao S, Yang X, Xu W, Guo M, et al. Ultrasound-assisted extraction of lipids as food components: Mechanism, solvent, feedstock, quality evaluation and coupled technologies – A review. Trends Food Sci Technol. 2022 Apr 1;122:83–96.

121. Oliveira Chaves J, Correa de Souza M, da Silva LC, Lachos-Perez D, Torres-Mayanga PC, da Fonseca AP. Extraction of Flavonoids From Natural Sources Using Modern Techniques. Green and Sustainable Chemistry . 2020;

122. Chan CH, Rozita Y, Ngoh GC. Modeling and kinetics study of conventional and assisted batch solvent extraction. University of Malaya. 2014;

123. Elboughdiri N. Effect of Time, Solvent-Solid Ratio, Ethanol Concentration and Temperature on Extraction Yield of Phenolic Compounds From Olive

Leaves. Engineering, Technology, and Applied Science Research. 2018;8(2).

124. Majekodunmi SO. Review of extraction of medicinal plants for pharmaceutical research. MRJMMS. 2015;1:98–106.

125. Patel K, Panchal N, Ingle P. Review of Extraction Techniques Extraction Methods: Microwave, Ultrasonic, Pressurized Fluid, Soxhlet Extraction, Etc. International Journal of Advanced Research in Chemical Science (IJARCS). 2019;

126. Chairunnisa S, Wartini NM, Suhendra L. Effect of Temperature and Maseration Time on Characteristics of Bidara Leaf Extract (Ziziphus mauritiana L.) as Saponin Source. Journal of Agroindustrial Engineering and Management. 2019 Dec;

127. Bintoro A, Ibrahim AM, Situmeang B. Analysis and Identification of Saponin Compound from Bidara Leaves (Zhizipus mauritania L. Jurnal ITEKIMA. 2017;

128. Wahyuni, Wijnadarko. Effect of Solvent Type and Extraction Time on Pumpkin Carotenoid Extract with Ultrasonic Wave Method. Journal of Food and Agroindustry. 2015;

129. Ćujić N, Šavikin K, Janković T, Pljevljakušić D, Zdunić G, Ibrić S. Optimization of polyphenols extraction from dried chokeberry using maceration as traditional technique. Food Chem. 2016 Aug 18;194:135–42.

130. Albuquerque BR, Prieto MA, Barreiro MF, Rodrigues AE, Curran TP, Barros L, et al. Catechin-based extract optimization obtained from Arbutus unedo L. fruits using maceration/microwave/ultrasound extraction techniques. Ind Crops Prod. 2017 Jan 1;95:404–15.

131. Jovanović AA, Đorđević VB, Zdunić GM, Pljevljakušić DS, Šavikin KP, Gođevac DM, et al. Optimization of the extraction process of polyphenols from Thymus serpyllum L. herb using maceration, heat- and ultrasound-assisted techniques. Sep Purif Technol. 2017 May 31;179:369–80.

132. Wang H, Yang L, Zu Y, Zhao X. Microwave-assisted simultaneous extraction of luteolin and apigenin from tree peony pod and evaluation of its antioxidant activity. Scientific World Journal. 2014;2014.

133. Ramadan MF, Ayoub TEM, Rohn S. Opuntia spp.: Chemistry, Bioactivity and Industrial Applications. Google books; 2021.

134. Zhang H, Wang W., Fu Zm., Han CC., Song Y. Study on comparison of extracting fucoxanthin from Undaria pinnatifid with percolation extraction and refluxing methods. Zhongguo Shipin Tianjiaji. 2014;

135. Napagoda M, Jayasinghe L. Chemistry of Natural Products: Phytochemistry and Pharmacognosy of Medicinal Plants. Google Books; 2022.

136. Conde-Hernández LA, Espinosa-Victoria JR, Trejo A, Guerrero-Beltrán J. CO2-supercritical extraction, hydrodistillation and steam distillation of essential oil of rosemary (Rosmarinus officinalis). J Food Eng. 2017 May 1;200:81–6.

137. Falcão MA, Scopel R, Almeida RN, do Espirito Santo AT, Franceschini G, Garcez JJ, et al. Supercritical fluid extraction of vinblastine from Catharanthus roseus. Journal of Supercritical Fluids. 2017 Nov 1;129:9–15.

138. Suna S, Tamer CE, Özcan-Sinir G. Trends and Possibilities of the Usage of Medicinal Herbal Extracts in Beverage Production. In: Natural Beverages. Elsevier; 2019. p. 361–98.

139. Zt Guo, Xq Luo, Jp Liang, Yang Z, Ai X. Comparativ e study on extraction of febrifugine from traditional Chinese medicine Dichroa febrifuga by refux method and ultrasonic method. . Shizhen Guoyi Guoyao. 2015;

140. Wu QS, Wang C, Lu JJ, Lin LG. Simultaneous Determination of Six Saponins in Panacis Japonici Rhizoma Using Quantitative Analysis of Multi-Components with Single-Marker Method. 2017 Mar;

141. Chemat F, Rombaut N, Sicaire AG, Meullemiestre A, Fabiano-Tixier AS, Abert-Vian M. Ultrasound assisted extraction of food and natural products. Mechanisms, techniques, combinations, protocols and applications. A review. Vol. 34, Ultrasonics Sonochemistry. Elsevier B.V.; 2017. p. 540–60.

142. Barba FJ, Zhu Z, Koubaa M, Sant'Ana AS, Orlien V. Green alternative methods for the extraction of antioxidant bioactive compounds from winery wastes and by-products: A review. Vol. 49, Trends in Food Science and Technology. Elsevier Ltd; 2016. p. 96–109.

143. Zhang WL, Chen JP, Lam KYC, Zhan JYX, Yao P, Dong TTX, et al. Hydrolysis of glycosidic flavonoids during the preparation of Danggui Buxue Tang: an outcome of moderate boiling of Chinese herbal mixture. Evid Based Complement Altern Med. 2014;

144. Zhang Q, Wang CH, Ma YM, Zhu EY, Wang Z tao. UPLC-ESI/MS determination of 17 active constituents in two categorized formulas of traditional Chinese medicine, Sanhuang Xiexin Tang and Fuzi Xiexin Tang: application in comparing the differences in decoctions and macerations . Biomedical chromatography . 2013 Mar 30;

145. Vinatoru M, Mason TJ, Calinescu I. Ultrasonically assisted extraction (UAE) and microwave assisted extraction (MAE) of functional compounds from plant materials. Vol. 97, TrAC - Trends in Analytical Chemistry. Elsevier B.V.; 2017. p. 159–78.

146. Chen H. Optimization of microwave-assisted extraction of resveratrol from Polygonum cuspidatum . Nat Prod Indian J. 2013;9(4):138–42.

147. Bernoussa H., Farhat A., Romdhane M., Bouajila J. Enhanced solvent-free microwave extraction of Foeniculum vulgare Mill. Essential oil seeds using d double walled reacto. Arabian J Chemistry. 2016;

148. Xiong W, Chen X, Lv G, Hu D, Zhao J, Li S. Optimization of microwave-assisted extraction of bioactive alkaloids from lotus plumule using response surface methodology. J Pharm Anal. 2016 Dec 1;6(6):382–8.

149. Bouras M, Grimi N, Bals O, Vorobiev E. Impact of pulsed electric fields on polyphenols extraction from Norway spruce bark. Ind Crops Prod. 2016 Feb 1;80:50–8.

150. Chen H, Zhou X, Zhang J. Optimization of enzyme assisted extraction of polysaccharides from Astragalus membranaceus. Carbohydr Polym. 2014 Oct 13;111:567–75.

151. Liu T, Sui X, Li L, Zhang J, Liang X, Li W, et al. Application of ionic liquids based enzyme-assisted extraction of chlorogenic acid from Eucommia ulmoides leaves. Anal Chim Acta. 2016 Jan 15;903:91–9.

152. Enzyme and high pressure assisted extraction of carotenoids from tomato waste. Food and Bioproducts Processing. 2015 Apr 1;94:668–74.

153. Verma SK, Goswami P, Verma RS, Padalia RC, Chauhan A, Singh VR, et al. Chemical composition and antimicrobial activity of bergamot-mint (Mentha citrata Ehrh.) essential oils isolated from the herbage and aqueous distillate using different methods. Ind Crops Prod. 2016 Nov 30;91:152–60.

154. Chemat F., Cravotto G. Microwave - assisted extraction for bioactive compounds. Microwave assisted extraction for bioactive compounds. 2013;

155. Peral C. Biomass Pretreatment Strategies (Technologies, Environmental Performance, Economic Considerations, Industrial Implementation). Biotransformation of Agricultural Waste and By-Products: The Food, Feed, Fibre, Fuel (4F) Economy. 2016 Mar 1;125–60.

156. Kumar S, Bhandari C, Sharma P, Agnihotri N. Soxhlet Extraction. Role of Nutraceuticals in Chemoresistance to Cancer. 2018;259–86.

157. NurAtiqah Mohd Shamsuddin, Yusup Suzana, Wan Asma Ibrahim, Awais Bohkari. Oil Extraction from Calophyllum inophyllum L. via Soxhlet Extraction Optimization using Response surface technology (RSM). 2015;

158. Sanjeet. Soxhlet extractor : An Important apparatus for isolation of bioactive compounds from medicinal plants . 2013 Mar 16;

159. Pharmacognosy. Soxhlet Extraction – Principle, Working, Uses With Diagrams. 2021 Dec 24;

160. Alvarez-Rivera G, Bueno M, Ballesteros-Vivas D, Mendiola JA, Ibañez E. Pressurized Liquid Extraction. Liquid-Phase Extraction. 2020 Jan 1;375–98.

161. Duarte K, C. Duarte A. Analysis of Marine Samples in search of Bioactive Compounds. Comprehensive Analytical Chemistry. 2014;

162. Usenko S, Subedi B, Aguilar L, Robinson E. High-Throughput Analysis of PPCPs, PCDD/Fs, and PCBs in Biological Matrices Using GC–MS/MS. Comprehensive Analytical Chemistry. 2013 Jan 1;61:143–58.

163. Ho TC, Kiddane AT, Khan F, Cho YJ, Park JS, Lee HJ, et al. Pressurized liquid extraction of phenolics from Pseuderanthemum palatiferum (Nees) Radlk. leaves: Optimization, characterization, and biofunctional properties. Journal of Industrial and Engineering Chemistry. 2022 Apr 25;108:418–28.

164. Cao Y, Liu W, Gong X, Yu J, Tu P, Li J, et al. Online pressurized liquid extraction enables directly chemical analysis of herbal medicines: A mini review. J Pharm Biomed Anal. 2021 Oct 25;205:114332.

165. Fraterrigo Garofalo S, Demichelis F, Mancini G, Tommasi T, Fino D. Conventional and ultrasound-assisted extraction of rice bran oil with isopropanol as solvent. Sustain Chem Pharm. 2022 Oct 1;29:100741.

166. Yusoff IM, Mat Taher Z, Rahmat Z, Chua LS. A review of ultrasound-assisted extraction for plant bioactive compounds: Phenolics, flavonoids, thymols, saponins and proteins. Food Research International. 2022 Jul 1;157:111268.

167. Watrelot AA, Bouska L. Optimization of the ultrasound-assisted extraction of polyphenols from Aronia and grapes. Food Chem. 2022 Aug 30;386:132703.

168. Cîntă Pînzaru S, Fălămaș A, Dehelean CA. Raman Spectroscopy: A Key Analytical Tool for New Drugs Research and Development. Studies in Natural Products Chemistry. 2018 Jan 1;61:211–50.

169. Priego-Capote F. Solid–liquid extraction techniques. Analytical Sample Preparation With Nano- and Other High-Performance Materials. 2021 Jan 1;111–30.

170. Mandal SC, Mandal V, Das AK. Essentials of Botanical Extraction. Academic Press.; 2015.

171. Canencia OP, Angelo Mark P., Walag. Oal Combustion from Power Plant Industry Inmisamis Oriental, Philippines: a Potential Groundwater Contamination and Heavy Metal Detection. Asian Journal of Microbiology, Biotechnology & Environmental Sciences. 2016;1(18).

172. Pin C, Rodriguez J. Separation Methods Based on Liquid–Liquid Extraction, Extraction Chromatography, and Other Miscellaneous Solid Phase Extraction Processes. Treatise on Geochemistry: Second Edition. 2014 Jan 1;15:147–70.

173. Banu KS., Catherine L. General techniques involved in phytochemical analysis. Int J Adv Res Chem Sci . 2015;2:25–32.

174. Parisa N, Hidayat R, Maritska Z, Prananjaya BA. Antidepressant effect of cinnamon (Cinnamomum burmannii) bark extract in chronic stress-induced rats. Open Access Maced J Med Sci. 2020;8(A):273–7.

175. Partan RU, Hidayat R, Saleh MI, Parisa N, Tanzil NS. Effect of supplementation kayu manis (Cinnamomum burmannii) extract in neuronal cell death protection in wistar rats lir-psychotic on haloperidol therapy. Asian Journal of Pharmaceutical and Clinical Research. 2018;11(2):363–5.

176. Hidayat R, Adelia Safitri RA, Umar TP, Maretzka A. The Efficacy of Sauropus androgynus Leaves Extract To Improve Cognitive Function in Wistar Rats Induced Alzheimerâ€™s. Bioscientia Medicina : Journal of Biomedicine and Translational Research. 2018 Dec 6;2(3):35–44.

177. Amin M, Saleh I, Hidayat R. The Anticancer Activity of Srikaya Leaves Fraction (Annona squamosa L.): An In Vitro Study. Bioscientia Medicina : Journal of Biomedicine and Translational Research. 2019;3(4):39–44.

178. Hu Y, Wang YN, Zhang GQ, Dong XZ, Liu WW, Liu P. Gan-Dan-Liang-Yi-Tang alleviates p-chlorophenylalanine-induced insomnia through modification of the serotonergic and immune system. Exp Ther Med. 2016;12(5):3087–92.

179. Si Y, Wang L, Lan J, Li H, Guo T, Chen X, et al. Lilium davidii extract alleviates p-chlorophenylalanine-induced insomnia in rats through modification of the hypothalamic-related neurotransmitters, melatonin and

homeostasis of the hypothalamic-pituitary-adrenal axis. Pharm Biol. 2020;58(1):915–24.

180. Sun Y, Zhang N, Qu Y, Cao Y, Li J, Yang Y, et al. Shuangxia decoction alleviates p-chlorophenylalanine induced insomnia through the modification of serotonergic and immune system. Metab Brain Dis. 2020;35(2):315–25.

181. Zhao Q, Luo L, Qiao Y, Zhang J. Effects of Evodia rutaecarpa Acupoint Sticking Therapy on Rats with Insomnia Induced by Para-Chlorophenylalanine in 5-HT1Aand 5-HT2A Gene Expressions. Brazilian Archives of Biology and Technology. 2022;65.

182. Nair A, Jacob S. A simple practice guide for dose conversion between animals and human. J Basic Clin Pharm. 2016;7(2):27.

183. Tang N na, Wu C wen, Chen M qi, Zeng X ai, Wang X feng, Zhang Y, et al. Therapeutic effects of Jiaotai pill on rat insomnia via regulation of GABA signal pathway. Tropical Journal of Pharmaceutical Research. 2017 Oct 4;16(9):2135.

184. Xiao-juan R, Guan-ying W, Xing-ping Z, Qing-quan W, Zhi-peng P. Sedative and Hypnotic Effects and Transcriptome Analysis of Polygala tenuifolia in Aged Insomnia Rats. Chinese Jounral of Integrative Medicine. 2020;26(6):434–41.

185. Hidayat R, Wulandari P, Reagan M. The Potential of Cinnamon Extract (Cinnamomum burmanii) as Anti-insomnia Medication through Hypothalamus Pituitary Adrenal Axis Improvement in Rats. Acta Med Acad. 2022 Oct 25;51(2):79.

186. Li J, Hong J, Zhou F, Tang S, Wu X. Regulatory mechanism of melatonin on the retinal ganglion cell photoreaction in mice. Exp Ther Med. 2017 Aug;14(2):1491–5.

187. Pal MM. Glutamate: The Master Neurotransmitter and Its Implications in Chronic Stress and Mood Disorders. Front Hum Neurosci [Internet]. 2021 Oct 29 [cited 2022 Dec 12];15:592. Available from: https://www.frontiersin.org/articles/10.3389/fnhum.2021.722323/full

188. Hidayat R, Wulandari P, Reagan M. The Potential of Cinnamon Extract (Cinnamomum burmanii) as Anti-insomnia Medication through Hypothalamus Pituitary Adrenal Axis Improvement in Rats. Acta Med Acad. 2022 Oct 25;51(2):79.

189. Ataie Z, Mehrani H, Ghasemi A, Farrokhfall K. Cinnamaldehyde has beneficial effects against oxidative stress and nitric oxide metabolites in the

brain of aged rats fed with long-term, high-fat diet. J Funct Foods. 2019 Jan 1;52:545–51.

190. Hu Y, Wang YN, Zhang GQ, Dong XZ, Liu WW, Liu P. Gan-Dan-Liang-Yi-Tang alleviates p-chlorophenylalanine-induced insomnia through modification of the serotonergic and immune system. Exp Ther Med. 2016 Nov 1;12(5):3087–92.

191. Song HT, Sun XY, Yang TS, Zhang LY, Yang JL, Bai J. Effects of sleep deprivation on serum cortisol level and mental health in servicemen. International Journal of Psychophysiology. 2015 Jun 1;96(3):169–75.

192. Parisa N, Hidayat R, Maritska Z. Antidepressant effect of cinnamon (Cinnamomum burmannii) bark extract in chronic stress-induced rats. . Journal Medical Science. 2020;

193. HelmyAbdou KA, Rashad Amed R, Ibrahim MA, Gawad A. The anti-inflammatory influence of Cinnamomum burmannii against multi-walled carbon nanotube-induced liver injury in rats. Environmental Science and Pollution Research . 2019;36063–72.

194. Momtaz S, Hassani S, Khan F, Ziaee M, Abdollahi M. Cinnamon, a promising prospect towards Alzheimer's disease. Vol. 130, Pharmacological Research. Academic Press; 2018. p. 241–58.

195. Karunaweera N, Raju R, Gyengesi E, Munch G. Plant polyphenols as inhibitors of nf-Kb induced cytokine production—A potential anti-inflammatory treatment for alzheimer's disease? Front Mol Neurosci. 2015 Jun 16;8(June).

196. Chen YF, Wang YW, Huang WS, Lee MM, Wood WG, Leung YM, et al. Trans-Cinnamaldehyde, An Essential Oil in Cinnamon Powder, Ameliorates Cerebral Ischemia-Induced Brain Injury via Inhibition of Neuroinflammation Through Attenuation of iNOS, COX-2 Expression and NFκ-B Signaling Pathway. Neuromolecular Med. 2016 Sep 1;18(3):322–33.

197. Flik G, Folgering JHA, Cremers TIHF, Westerink BHC, Dremencov E. Interaction Between Brain Histamine and Serotonin, Norepinephrine, and Dopamine Systems: In Vivo Microdialysis and Electrophysiology Study. Journal of Molecular Neuroscience. 2015 Jun 8;56(2):320–8.

198. Bloomfield MA, McCutcheon RA, Kempton M, Freeman TP, Howes O. The effects of psychosocial stress on dopaminergic function and the acute stress response. Elife. 2019 Nov 1;8.

199. Koch CE, Leinweber B, Drengberg BC, Blaum C, Oster H. Interaction between circadian rhythms and stress. Vol. 6, Neurobiology of Stress. Elsevier Inc; 2017. p. 57–67.

200. Herman JP, McKlveen JM, Ghosal S, Kopp B, Wulsin A, Makinson R, et al. Regulation of the hypothalamic-pituitary- adrenocortical stress response. Compr Physiol. 2016 Apr 1;6(2):603–21.

201. Kim ME, Na JY, Lee JS. Anti-inflammatory effects of trans-cinnamaldehyde on lipopolysaccharide-stimulated macrophage activation via MAPKs pathway regulation. Immunopharmacol Immunotoxicol. 2018 May 4;40(3):219–24.

202. Kalsum U, Khotimah H, Titisari Sulihah N, Firdaus T, Aulia Lisabilla F, Fukata E, et al. NEUROPROTECTIVE EFFECT OF CINNAMON ACTIVE COMPOUNDS VIA ACTIVATION OF SIRT1: A MOLECULAR DOCKING APPROACH. MNJ (Malang Neurology Journal). 2022 Jul 1;8(2):117–21.

203. Mustarichie R, Saptrini NM, Megantara S. Molecule Attachment and Prediction of ADMET Compounds in Cinnamomum burmannii on Orexin Receptor as Anti-insomnia. Pharmacognosy Journal. 2022;

204. Sci-Hub | Neuroprotective Effect of trans-Cinnamaldehyde on the 6-Hydroxydopamine-Induced Dopaminergic Injury. Biological and Pharmaceutical Bulletin, 36(12), 1928–1935 | 10.1248/bpb.b13-00537 [Internet]. [cited 2022 Nov 25]. Available from: https://sci-hub.se/https://doi.org/10.1248/bpb.b13-00537

205. Pyo JH, Jeong YK, Yeo S, Lee JH, Jeong MY, Kim SH, et al. Neuroprotective effect of trans-cinnamaldehyde on the 6-hydroxydopamine- induced dopaminergic injury. Biol Pharm Bull. 2013 Dec;36(12):1928–35.

206. Huo M, Cui X, Xue J, Chi G, Gao R, Deng X, et al. Anti-inflammatory effects of linalool in RAW 264.7 macrophages and lipopolysaccharide-induced lung injury model. Journal of Surgical Research. 2013 Mar;180(1).