

**KAJIAN PUSTAKA PROSES ISOLASI, ANALISIS DAN
AKTIVITAS FARMAKOLOGI SENYAWA SKOPOLETIN**

NASKAH TUGAS AKHIR

**JESICHA DIAN YENBYEEBE MANOBI
A 161 066**



**SEKOLAH TINGGI FARMASI INDONESIA
YAYASAN HAZANAH
BANDUNG
2020**

**KAJIAN PUSTAKA PROSES ISOLASI, ANALISIS DAN
AKTIVITAS FARMAKOLOGI SENYAWA SKOPOLETIN**

NASKAH TUGAS AKHIR

Sebagai salah satu syarat untuk memperoleh gelar sarjana farmasi

**JESICHA DIAN YENBYEEBE MANOBI
A 161 066**



**SEKOLAH TINGGI FARMASI INDONESIA
YAYASAN HAZANAH
BANDUNG
2020**

**KAJIAN PUSTAKA PROSES ISOLASI, ANALISIS DAN AKTIVITAS
FARMAKOLOGI SENYAWA SKOPOLETIN**

**JESICHA DIAN YENBYEEBE MANOBI
A161066**

Oktober 2020

Disetujui oleh:

Pembimbing

Pembimbing

Dr. apt. Adang Firmansyah, M.Si.

apt. Wiwin Winingsih, M.Si.

Kutipan atau saduran baik sebagian ataupun seluruh naskah, harus menyebut nama pengarang dan sumber aslinya, yaitu Sekolah Tinggi Farmasi Indonesia

Skripsi ini dipersembahkan khusus untuk ayah (alm), ibu, kakak grice, apfia, adik carlo dan kevin, bangtan sonyoendan, serta keluarga yang selalu mendoakan dan memberikan dukungan hingga dapat menyelesaikan studi S1 Farmasi.

ABSTRAK

KAJIAN PUSTAKA PROSES ISOLASI, ANALISIS DAN AKTIVITAS FARMAKOLOGI SENYAWA SKOPOLETIN

Oleh

Jesicha Dian Yenbyeebe Manobi

NIM: A 161 066

Skopoletin (*7-hydroxy-6-methoxy coumarin*) merupakan senyawa fenolik kumarin yang banyak ditemukan pada tumbuhan dan termasuk turunan kumarin yang merupakan unggulan pada beberapa jenis tumbuhan. Artikel ini dibuat untuk memberikan informasi mengenai proses isolasi, analisis, dan aktivitas farmakologis. Metode yang digunakan adalah mempelajari dan menganalisis artikel skopoletin dari jurnal nasional dan internasional. Dari sumber data yang ditelaah, didapat rendemen ekstrak skopoletin dalam *Morinda citrifolia* L yaitu 0,93%, *Helichrysum italicum* yaitu 1,933mg/100g. Kandungan skopoletin dalam *Convolvulus pluricaulis* yaitu 0,17%, *Artemisia annua* yaitu 0,3%, *Lasianthus lucidus* yaitu 54 mg, dan *Morus alba* L. (Po-sa) yaitu 0,0009%. Rendemen ekstrak skopoletin terbanyak yaitu 0,93% yang terdapat dalam buah mengkudu (*Morinda citrifolia* L) dengan menggunakan metode Soxhlet. Kandungan skopoletin tertinggi yaitu 0,3% dalam *Artemisia annua* dengan menggunakan kolom kromatografi dan direkristalisasi. Identifikasi skopoletin dapat dilakukan dengan menggunakan Kromatografi Lapis Tipis (KLT), Kromatografi Cair Kinerja Tinggi (KCKT), Spektrofotometer *Fourier Transform Infra Red* (FTIR), Resonansi Magnetik Nuklir, dan Spektrometri Massa. Berdasarkan studi *in vitro*, skopoletin mempunyai aktivitas farmakologis, antara lain sebagai antihepatotoksitas, antibakteri, antijamur, antituberkular, dan antioksidan. Aktivitas farmakologi yang sudah dibuktikan secara *in vivo* yaitu aktivitas antitiroid, antihipertensi, antiproliferatif, antiinflamasi, neurologis, antidopaminergik dan antiadrenergik, antidiabetes, serta antihiperurikemik. Dari berbagai aktivitas farmakologi skopoletin tersebut, dapat berpotensi untuk dikembangkan lebih lanjut.

Kata kunci: skopoletin, isolasi, analisis, aktivitas farmakologi

ABSTRACT

Literature Review Isolation Process, Analysis And Pharmacological Activities Of Scopoletin Compounds

Written by:

Jesicha Dian Yenbyeebe Manobi

NIM: A 161 066

*Scopoletin (7-hydroxy-6-methoxy coumarin) is a coumarin phenolic compound that is widely found in plants and includes coumarin derivatives which are superior in several types of plants. This article was created to provide information regarding the isolation process, analysis and pharmacological activity. The method used is to study and analyze scopoletin articles from national and international journals. From the data sources studied, the yield of scopoletin extract in *Morinda citrifolia* L was 0.93%, *Helichrysum italicum* was 1.933mg / 100g. The scopoletin content in *Convolvulus pluricaulis* is 0.17%, *Artemisia annua* is 0.3%, *Lasianthus lucidus* is 54 mg, and *Morus alba* L. (Po-sa) is 0.0009%. The highest yield of scopoletin extract was 0.93% found in noni (*Morinda citrifolia* L) using the Soxhlet method. The highest scopoletin content was 0.3% in *Artemisia annua* using column chromatography and recrystallization. Scopoletin identification can be done using Thin Layer Chromatography (TLC), High Performance Liquid Chromatography (HPLC), Fourier Transform Infrared Spectrophotometer (FTIR), Nuclear Magnetic Resonance, and Mass Spectrometry. Based on in vitro studies, scopoletin has pharmacological activities, including as an antihepatotoxicity, antibacterial, antifungal, antitubercular, and antioxidant. Pharmacological activities that have been proven in vivo are antithyroid, antihypertensive, antiproliferative, anti-inflammatory, neurological, antidopaminergic and antiadrenergic, antidiabetic, and antihyperuricemic activities. From the various pharmacological activities of scopoletin, it has the potential to be further developed.*

Keywords: *scopoletin, isolation, analysis, pharmacological activity*

KATA PENGANTAR

Pertama-tama penulis panjatkan segala puji syukur kepada Tuhan Yang Maha Esa atas rahmat dan karunia-Nya sehingga penulis dapat menyelesaikan tugas akhir yang berjudul **“Proses Isolasi, Analisis Dan Aktivitas Farmakologi Senyawa Skopoletin”**.

Penelitian dan penulisan kajian pustaka naskah tugas akhir ini dilakukan untuk memenuhi salah satu syarat untuk mendapatkan gelar sarjana pada jurusan Farmasi Sekolah Tinggi Farmasi Indonesia.

Penulis mengucapkan terima kasih kepada dosen pembimbing Dr. apt. Adang Firmansyah, M.Si. dan apt. Wiwin Winingsih, M.Si. atas bimbingan, nasihat, dukungan serta pengorbanan yang diberikan. Pada kesempatan ini, tidak lupa penulis mengucapkan terima kasih yang sebesar – besarnya kepada :

1. Dr. apt. Adang Firmansyah, M.Si. selaku Ketua Sekolah Tinggi Farmasi Indonesia,
2. Apt. Revika Rachmaniar, M.Farm. selaku Ketua Program Studi Sarjana Farmasi Sekolah Tinggi Farmasi Indonesia,
3. Nur Asni Setiani, M.Si. selaku Dosen wali yang telah banyak memberikan bimbingan dan arahan kepada penulis,
4. Seluruh staf dosen, staf administrasi serta karyawan Sekolah Tinggi Farmasi Indonesia,
5. Sahabat-sahabat angkatan 2016 yang telah memberikan inspirasi dan kegembiraan selama penulis kuliah di Sekolah Tinggi Farmasi Indonesia,
6. Sahabat terdekat apfia, dea, nurul, iken, namjooie, soekjinie, min suga, hobissi, jiminie, taetae, jungkookie, yang selalu memberikan semangat kepada saya untuk meraih mimpi saya, yaitu salah satunya adalah menyelesaikan skripsi ini.

Dalam penyusunan naskah tugas akhir ini masih banyak kesalahan dan kekurangan karena pengetahuan yang masih sangat terbatas. Oleh karena itu, dengan segala kerendahan hati diharapkan masukan berupa kritik dan saran yang

bersifat membangun untuk perbaikan di masa yang akan datang. Penulis berharap semoga tugas akhir ini akan memberikan manfaat bagi penulis sendiri dan juga bagi pihak lain yang berkepentingan.

Bandung, Oktober 2020

Penulis

DAFTAR ISI

LEMBAR PENGESAHAN	i
KUTIPAN	ii
PERSEMBAHAN	iii
ABSTRAK	iv
ABSTRACT	v
KATA PENGANTAR	vi
DAFTAR ISI	viii
DAFTAR TABEL	x
DAFTAR GAMBAR	xi
DAFTAR LAMPIRAN	xii
BAB I PENDAHULUAN	1
1.1 Latar Belakang	1
1.2 Tujuan Naskah Tugas Akhir	2
1.3 Luaran Naskah Tugas Akhir	2
BAB II METODOLOGI	3
2.1 Desain Penelitian	3
2.2 Populasi Dan Sampel.....	3
2.2.1 Populasi	3
2.2.2 Sampel	3
2.3 Variabel Penelitian	4
2.3.1 Variabel Dependen	4
2.3.2 Variabel Independen.....	4
2.4 Metode Pengumpulan Data	4
2.4.1 Data Sekunder	4
2.4.2 Metode Kajian Pustaka	5
2.5 Metode Analisi Data	5
2.6 Publikasi	5
BAB III ULASAN PUSTAKA YANG TELAH DITERBITKAN	7
3.1 Skopoletin	7
3.1.1 Sumber Skopoletin	7

3.1.2	Aktivitas Farmakologis Skopoletin	7
3.1.3	Sifat Fisikokimia Skopoletin	8
3.2	Proses Isolasi Skopoletin	9
3.2.1	Ekstraksi	9
3.2.2	Fraksinasi Dan Pemurnian.....	13
3.3	Proses Analisis Skopoletin	13
3.3.1	Kromatografi Lapis Tipis	13
3.3.2	Spektrofotometer Uv-Vis	14
3.3.3	Kromatografi Cair Kinerja Tinggi.....	15
BAB IV	PROSPEK DAN REKOMENDASI	19
4.1	Isolasi Skopoletin	19
4.2	Analisis Skopoletin	21
4.3	Aktivitas Farmakologi Skopoletin	30
BAB V	KESIMPULAN.....	37
5.1	Kesimpulan	37
DAFTAR PUSTAKA		38
LAMPIRAN.....		48

DAFTAR TABEL

Tabel	Halaman
4.1 Proses Isolasi Skopoletin	20
4.2 Metode Identifikasi Skopoletin Dengan KLT.....	23
4.3 Metode Analisis Skopoletin Oleh KCKT	24
4.4 Data Spektrum FTIR Dari Standar Skopoletin	25
4.5 Data Spektrum NMR Dari Standar Skopoletin.....	28
4.6 Aktivitas Farmakologis Skopoletin.....	33

DAFTAR GAMBAR

Gambar	Halaman
3.1 Struktur Kimia Skopoletin	9
4.1 Kromatogram HPLC Skopoletin	25
4.2 Kromatogram HPLC Standar Skopoletin	25
4.3 Spektrum IR dari Skopoletin standar	26
4.4 Spektrum IR Senyawa Terisolasi	27
4.5 Spektrum IR Senyawa Terisolasi	27
4.6 Spektrum IR Senyawa Terisolasi	27
4.7 Spektrum IR Senyawa Terisolasi	28
4.8 NMR Skopoletin standar	29
4.9 Spektrum NMR Senyawa Terisolasi	30
4.10 Spektrum NMR Senyawa Terisolasi	30

DAFTAR LAMPIRAN

Lampiran	Halaman
1. Bukti submit jurnal <i>publisher</i> BRIAC	48

DAFTAR PUSTAKA

- Ahmed, O. H., Hamad, M. N, Jaafar, N. S., 2017. *Phytochemical Investigation Of Chenopodium Murale (Family: Chenopodiaceae) Cultivated In Iraq, Isolation And Identification Of Scopoletin And Gallic Acid*. Vol 10, Issue 11
- Ahn, M. J., Hur, S. J., Kim, E. H., Lee, S. H., Shin, J. S., Kim, M. K., Uchizono, J. A., Whang, W. K., & Kim, D. S. 2014. "Scopoletin from *Cirsium setidens* increases melanin synthesis via CREB phosphorylation in B16F10 cells". *Korean Journal of Physiology and Pharmacology*, 18(4), 307–311.
- Aldi, Y., Yuliandra, Y., Nasrul, E., Yanwirasti, Handayani, D., & Bakhtiar, A. 2015. "Decreased interleukin-4 level of type i hypersensitive mice using scopoloetin isolated from noni fruit (*Morinda citrifolia* L.)". *Research Journal of Pharmaceutical, Biological and Chemical Sciences*, 6(4), 1823–1829.
- Arcos Barreiro, M. L., Cremaschi, G., Werner, S., Coussio, J., Ferraro, G., & Anesini, C. 2006. "Tilia cordata Mill. Extracts and scopoletin (isolated compound): Differential cell growth effects on lymphocytes". *Phytotherapy Research*, 20(1), 34–40.
- Arunachalam, K. D., Kuruva, J. K., Hari, S., Annamalai, S. K., & Baskaran, K. V. 2015. "HPTLC finger print analysis and phytochemical investigation of morinda tinctoria roxb leaf extracts by hplc and gs ms". *International Journal of Pharmacy and Pharmaceutical Sciences*, 7(2), 360–366.
- Bayoumi, S. A. L., Rowan, M. G., Blagbrough, I. S., & Beeching, J. R. 2008. "Biosynthesis of scopoletin and scopolin in cassava roots during post-harvest physiological deterioration: The E-Z-isomerisation stage". *Phytochemistry*, 69(17), 2928–2936.
- Buschmann, H., Rodriguez, M. X., Tohme, J., & Beeching, J. R. 2000. "Accumulation of hydroxycoumarins during post-harvest deterioration of tuberous roots of Cassava (*Manihot esculenta* Crantz)". *Annals of Botany*, 86(6), 1153–1160.
- Capra, J. C., Cunha, M. P., Machado, D. G., Zomkowski, A. D. E., Mendes, B. G., Roberto, A., Santos, S., Pizzolatti, M. G., Lúcia, A., & Rodrigues, S. 2010. *Antidepressant-like effect of scopoletin , a coumarin isolated from Polygala sabulosa (Polygalaceae) in mice: Evidence for the involvement of monoaminergic systems*. 643, 232–238.
- Carpinella, M. C., Ferrayoli, C. G., & Palacios, S. M. 2005. "Antifungal synergistic effect of scopoletin, a hydroxycoumarin isolated from *Melia azedarach* L. fruits". *Journal of Agricultural and Food Chemistry*, 53(8), 2922–2927.

- Darmawan, A., Kosela, S., Kardono, L. B. S., And Syah, Y. M. 2012. "Scopoletin, A Coumarin Derivative Compound Isolated From Macaranga Gigantifolia Merr". *Journal Of Applied Pharmaceutical Science*. Vol. 2 (12), Pp. 175-177.
- Das, S., Czuni, L., Báló, V., Papp, G., Gazdag, Z., Papp, N., & Koszegi, T. 2020. "Cytotoxic action of artemisinin and scopoletin on planktonic forms and on biofilms of Candida species". *Molecules*, 25(3), 1–18.
- Ding, Z., Dai, Y., Hao, H., Pan, R., Yao, X., & Wang, Z. 2008. "Anti-inflammatory effects of scopoletin and underlying mechanisms". *Pharmaceutical Biology*, 46(12), 854–860.
- Dirjen POM. 2014. *Farmakope Indonesia Edisi V*. Jakarta: Depkes RI
- Effendy. 2004. *Kromatografi Cair Kinerja Tinggi dalam Bidang Farmasi*. Sumatera Utara: FMIPA USU.
- Ferdinal, N., Alfajri, R., & Arifin, B. 2015. "Isolation and characterization of scopoletin from the bark of fagraea ceilanica thumb and antioxidants tests". *International Journal on Advanced Science, Engineering and Information Technology*, 5(2), 126–130.
- Gandjar, I.G. 2007. *Kimia Farmasi Analisis*. Yogyakarta: Pustaka Pelajar.
- Gandjar, I. G. dan Abdul Rohman. 2007. *Kimia Farmasi Analisis*. Yogyakarta: Pustaka Pelajar.
- Gay, N. H., Suwanjang, W., Ruankham, W., Songtawee, N., Wongchitrat, P., Prachayasittikul, V., Prachayasittikul, S., & Phopin, K. 2020. "Butein, isoliquiritigenin, and scopoletin attenuate neurodegeneration via antioxidant enzymes and SIRT1/ADAM10 signaling pathway". *RSC Advances*, 10(28), 16593–16606.
- Gnonlonfin, G. J. B., Sanni, A., & Brimer, L. 2012. "Review Scopoletin - A Coumarin Phytoalexin with Medicinal Properties". *Critical Reviews in Plant Sciences*, 31(1), 47–56.
- Guetchueng, S. T., Nahar, L., Ritchie, K. J., Daud Ismail, F. M., Dempster, N. M., Nnanga, E. N., & Sarker, S. D. 2020. "Phenolic compounds from the leaves and stem bark of Pseudospondias microcarpa (A. Rich.) Engl. (Anacardiaceae)". *Biochemical Systematics and Ecology*, 91(May), 104078.
- Gwak, M.-K., Choi, H.-S., Manochai, B., & Hong, J.-H. 2011. "Extraction Procedures for Free Radical Scavenging Activity from Noni Fruit (Morinda citrifolia)". *Korean Journal of Medicinal Crop Science*, 19(1), 38–4

- Harborne, J.B.1987. Metode Fitokimia: Cara Modern Menganalisa Tumbuhan Edisi I. Terjemahan oleh K. Padmawinata dan I. Soediro. Bandung: ITB.
- Harmita. 2006. Buku Ajar Analisis Fisikokimia. Departemen Farmasi FMIPA Universitas Indonesia. Depok.
- Hornick, A., Lieb, A., Vo, N. P., Rollinger, J. M., Stuppner, H., & Prast, H. 2011. "The coumarin scopoletin potentiates acetylcholine release from synaptosomes, amplifies hippocampal long-term potentiation and ameliorates anticholinergic- and age-impaired memory". *Neuroscience*, 197, 280–292.
- Jain, D.C., Neerja, P., Madan, M.G., Rajendra, S.B., Ram, K.V., Sudeep, T., Shiv, K.Gu., Amit, T.Wa., Atul, P.K., Sushu, Kumar. 2002. Process For The Isolation Of Compound Scopoletin Useful As Nitric Oxide Synthesis Inhibitor. *United States Patent*. Us 6,337,095 B1.
- Jamaludin, R., Kim, D. S., Md Salleh, L., & Lim, S. Bin. 2020. "Optimization of high hydrostatic pressure extraction of bioactive compounds from noni fruits". *Journal of Food Measurement and Characterization*, 14(5), 2810–2818.
- Jamuna, S., Karthika, K., Paulsamy, S., Thenmozhi, K., Kathiravan, S., & Venkatesh, R. 2015. "Confertin and scopoletin from leaf and root extracts of *Hypochaeris radicata* have anti-inflammatory and antioxidant activities". *Industrial Crops and Products*, 70, 221–230.
- Jang, J. H., Park, J. E., & Han, J. S. 2020. "Scopoletin increases glucose uptake through activation of PI3K and AMPK signaling pathway and improves insulin sensitivity in 3T3-L1 cells". *Nutrition Research*, 74, 52–61.
- Jokić, S., Rajić, M., Bilić, B., & Molnar, M. 2016. Supercritical Extraction of "Scopoletin from *Helichrysum italicum* (Roth) G. Don Flowers". *Phytochemical Analysis*, January, 290–295.
- Kang, H. R., Kim, H. J., Kim, B., Kim, S., So, J., Cho, S. J., & Kwon, H. S. 2020. *Inhibitory Effect of Scopoletin Isolated from Sorbus commixta on TNF- α - Induced Inflammation in Human Vascular Endothelial EA . hy926 Cells through NF- κ B Signaling Pathway Suppression*. 30(4), 343–351.
- Kang, H. R., Kim, H. J., Kim, B., Kim, S., So, J., Cho, S. J., & Kwon, H. S. 2020. *Inhibitory Effect of Scopoletin Isolated from Sorbus commixta on TNF- α - Induced Inflammation in Human Vascular Endothelial EA . hy926 Cells through NF- κ B Signaling Pathway Suppression*. 30(4), 343–351.
- Kang, S. Y., Sung, S. H., Park, J. H., & Kim, Y. C. 1998. "Hepatoprotective activity of scopoletin, a constituent of *Solanum lyratum*". *Archives of Pharmacal Research*, 21(6), 718–722.

- Kang, T. H., Pae, H. O., Jeong, S. J., Yoo, J. C., Choi, B. M., Jun, C. D., Chung, H. T., Miyamoto, T., Higuchi, R., & Kim, Y. C. 1999. "Scopoletin: An inducible nitric oxide synthesis inhibitory active constituent from *Artemisia feddei*". *Planta Medica*, 65(5), 400–403.
- Kashyap, P., Ram, H., Shukla, S. D., & Kumar, S. 2020. "Scopoletin: Anti-amyloidogenic, Anticholinesterase, and Neuroprotective Potential of a Natural Compound Present in *Argyrea speciosa* Roots by In Vitro and In Silico Study". *Neuroscience Insights*, 15.
- Khan, N. M. M. U., And Hossain, M. S. 2015. "Scopoletin And B-Sitosterol Glucoside From Roots Of *Ipomoea Digitata*". *Journal Of Pharmacognosy And Phytochemistry*. 4(2): 05-07.
- Kresnanugraha. 2012. "Uji Penghambatan Aktivitas Enzim Xantin Oksidase dari Ekstrak Daun Belimbing Wuluh (*Averrhoa bilimbi* L.) dan Identifikasi Golongan Senyawa dari Fraksi Aktif". Depok : Farmasi UI.
- Kurdekar, R. R., Hegde, G. R., Kulkarni, M. V., And Mulgund, G. S. 2014. "Isolation And Characterization Of Scopoletin - An Anticancer Compound From The Bark Of *Hymenodictyon Obovatum* Wall". *Int. J. Pharm. Phytopharmacol.* 3 (6): 469-471.
- Lee, B. Z., Kim, K. M., Chae, S., Jeong, S. K., Lee, S., Hong, K. W., & Lee, I. S. 2020. "New coumarins isolated from the stem bark of *Fraxinus rhynchophylla* inhibit human neutrophil elastase and LPS-induced inflammation in RAW 264.7 cells". *Phytochemistry Letters*, 35, 78–83.
- Lee, J., & Cho, H.-J. 2020. "Neuroprotective Effects of Scopoletin on Neuro-damage caused by Alcohol in Primary Hippocampal Neurons". *Biomedical Science Letters*, 26(2), 57–65.
- Lee, J., Kim, N. H., Nam, J. W., Lee, Y. M., Jang, D. S., Kim, Y. S., Nam, S. H., Seo, E. K., Yang, M. S., & Kim, J. S. 2010. "Scopoletin from the flower buds of *Magnolia fargesii* inhibits protein glycation, aldose reductase, and cataractogenesis Ex Vivo". *Archives of Pharmacal Research*, 33(9), 1317–1323.
- Lee, S. H., Ding, Y., Yan, X. T., Kim, Y. H., & Jang, H. D. 2013. "Scopoletin and scopolin isolated from *Artemisia iwayomogi* suppress differentiation of osteoclastic macrophage RAW 264.7 cells by scavenging reactive oxygen species". *Journal of Natural Products*, 76(4), 615–620.
- Li, J., and Wu, J. 2016. "Scopolin, a glycoside form of the phytoalexin scopoletin, is likely involved in the resistance of *Nicotiana attenuata* against *Alternaria alternata*". *Journal of Plant Pathology*, 98(3), 641–644.

- Luo, L., Sun, T., Yang, L., Liu, A., Liu, Q. Q., Tian, Q. Q., Wang, Y., Zhao, M. G., & Yang, Q. 2020. "Scopoletin ameliorates anxiety-like behaviors in complete Freund's adjuvant-induced mouse model". *Molecular Brain*, 13(1), 1–13.
- Mahattanadul, S., Ridditid, W., Nima, S., Phdoongsombut, N., Ratanasuwon, P., & Kasiwong, S. 2011. "Effects of *Morinda citrifolia* aqueous fruit extract and its biomarker scopoletin on reflux esophagitis and gastric ulcer in rats". *Journal of Ethnopharmacology*, 134(2), 243–250.
- Mardiningsih A. Tri. 2017. Penghambatan Aktivitas Enzim *Xantin Oksidase* Oleh Ekstrak Etanol Daun Kacang Tanah (*Arachis hypogaea* L.) Secara *In Vitro*". Malang : Universitas Islam Negeri Maulana Malik Ibrahim.
- Masturoh, I., dan N. Anggita. 2018. Metodologi Penelitian Kesehatan. Jakarta: Kementerian Kesehatan RI.
- Mauliku, N. E., W., H., Saputro, S. H., & Kristina, T. N. 2017. "Anti-Tubercular Activity of Extract and Coumpounds of Noni (*Morinda Citrifolia* Linn)". *International Journal of Pharmacy and Pharmaceutical Sciences*, 9(12), 105.
- Mauliyanti R. 2017. "Uji Aktivitas Gel Ekstrak Etanol Daun Cempedak (*Arthocarpus champeden*) Terhadap Bakteri Penyebab Jerawat". Makassar: Universitas Islam Negeri Alauddin.
- Mehul, B. K, Kishor, D. K And Ajay, S. K. 2011. "Isolation And Structure Elucidation Of Scopoletin From *Ipomoea Reniformis* (Convolvulaceae)". *Journal Of Applied Pharmaceutical Science*. 01 (05): 138-144.
- Miller, D., Sutcliffe, R., & Thauvette, J. 1990. "Sticker stain formation in hardwoods: Isolation of scopoletin from sugar maple (*Acer saccharum* Marsh.)". *Wood Science and Technology*, 24(4), 339–344.
- Mishra Nibha, Awadesh Oraona, Abhimanyu Deva, Venkatesan Jayaprakasha, Arijit Basua, Ashok K. Pattnaika, Satya N. Tripathi A, Mustari Akhtar A, Sadab Ahmada, Shreyshri Swaroopa, Mahua Basub. 2010. "Anticonvulsant Activity Of *Benkara Malabarica* (Linn.) Root Extract: In Vitro And In Vivo Investigation". *Journal Of Ethnopharmacology*.
- Moon, P. D., Lee, B. H., Jeong, H. J., An, H. J., Park, S. J., Kim, H. R., Ko, S. G., Um, J. Y., Hong, S. H., & Kim, H. M. 2007. "Use of scopoletin to inhibit the production of inflammatory cytokines through inhibition of the I κ B/NF- κ B signal cascade in the human mast cell line HMC-1". *European Journal of Pharmacology*, 555(2–3), 218–225.

- Muenmuang, C., Narasingha, M., Phusantisampan, T., & Sriariyanun, M. 2017. "Chemical profiling of morinda citrifolia extract from solvent and soxhlet extraction method". *ACM International Conference Proceeding Series, Part F1309*, 119–123.
- Nahata, A., Sethiya, N. K., Jain, N., & Dixit, V. K. 2018. "Analysis of scopoletin and mangiferin in botanicals and formulations of Shankhpushpi by HPLC". *Herba Polonica*, 64(4), 54–62.
- Nandhasri, P., Pawa, K. K., Kaewtubtim, J., Jeamchanya, C., Jansom, C., & Sattaponpun, C. 2005. "Nutraceutical properties of thai "yor", morinda citrifolia and "noni" juice extract". *Songklanakar J. Sci. Technol*, 27(2), 579–586.
- Napiroon, T., Bacher, M., Balslev, H., Tawaitakham, K., Santimaleworagun, W., & Vajrodaya, S. 2018. "Scopoletin from *Lasianthus lucidus* Blume (Rubiaceae): A potential antimicrobial against multidrug-resistant *Pseudomonas aeruginosa*". *Journal of Applied Pharmaceutical Science*, 8(9), 1–6.
- Narasimhan, K. K. S., Jayakumar, D., Velusamy, P., Srinivasan, A., Mohan, T., Ravi, D. B., Uthamaraman, S., Sathyamoorthy, Y. K., Rajasekaran, N. S., & Periandavan, K. 2019. "Morinda citrifolia and Its Active Principle Scopoletin Mitigate Protein Aggregation and Neuronal Apoptosis through Augmenting the DJ-1/Nrf2/ARE Signaling Pathway". *Oxidative Medicine and Cellular Longevity*, 2019.
- National center for Biotechnology Information. Scopoletin. PubChem Compound Database. <https://pubchem.ncbi.nlm.nih.gov/compound/5280460> diakses September 2020
- Nitteranon, V., Zhang, G., Darien, B. J., & Parkin, K. 2011. "Isolation and synergism of in vitro anti-inflammatory and quinone reductase (QR) inducing agents from the fruits of *Morinda citrifolia* (noni)". *Food Research International*, 44(7), 2271–2277.
- Njankouo Ndam, Y., Nyegue, M. A., Mounjouenpou, P., Kansci, G., Kenfack, M. J., & Eugène, E. E. 2020. "LC-MS quantification of scopoletin in cassava (*Manihot Esculenta* Crantz) varieties, local derived foods, and activity on some food spoilage fungi". *Journal of Food Processing and Preservation*, 44(4), 1–8.
- Notoatmodjo, S. 2012. *Promosi Kesehatan dan Perilaku Kesehatan*. Jakarta: Rineka Cipta.
- Nu, T. T. (2012). *Investigation of Antimicrobial Activity and Isolation of Phytoconstituents from Leaves of *Clausena excavata* Burm f.* 3(5), 1893–1901.

- Ojewole, J. A. O. (1984). "Effects of scopoletin on autonomic transmissions". *Pharmaceutical Biology*, 22(2), 81–93.
- Oliveira, E.J., Romero, M.A., Silva, M.S., Silva, B.A., Medeiros, I.A. 2001. "Intracellular Calcium Mobilization As A Target For The Spasmolytic Action Of Scopoletin". *Planta Medica*. 67, 605 – 608.
- Pachauri, S. D., Khandelwal, K., Bhaisora, M., Pandey, R. R., Srivastava, A., Tripathi, P., Verma, P. R. P., & Dwivedi, A. K. 2014. "The preparation of morinda citrifolia (Noni)-phospholipid complex and its pharmacokinetics study in rats". *Journal of Biomaterials and Tissue Engineering*, 4(3), 221–226.
- Pan, R., Gao, X., Lu, D., Xu, X., Xia, Y., & Dai, Y. 2011. "Prevention of FGF-2-induced angiogenesis by scopoletin, a coumarin compound isolated from *Erycibe obtusifolia* Benth, and its mechanism of action". *International Immunopharmacology*, 11(12), 2007–2016.
- Panda, S And Kar, A. 2006. "Evaluation Of The Antithyroid, Antioxidative And Antihyperglycemic Activity Of Scopoletin From *Aegle Marmelos* Leaves In Hyperthyroid Rats". *Phytotherapy Research Phytother. Res.* 20, 1103–1105.
- Pandy, V., Narasingam, M., Kunasegaran, T., Murugan, D. D., & Mohamed, Z. 2014. "Effect of noni (*Morinda citrifolia* Linn.) Fruit and its bioactive principles scopoletin and rutin on rat vas deferens contractility: An Ex vivo study". *Scientific World Journal*, 2014.
- Potterat, O., Von Felten, R., Dalsgaard, P. W., & Hamburger, M. 2007. "Identification of TLC markers and quantification by HPLC-MS of various constituents in noni fruit powder and commercial noni-derived products". *Journal of Agricultural and Food Chemistry*, 55(18), 7489–7494.
- Prabowo, W. C., Wirasutisna, K. R., Insanu, M., 2013. "Isolation And Characterization Of 3-Acetyl Aleuritolic Acid And Scopoletin From Stem Bark Of *Aleurites Moluccana* (L.) Willd". *International Journal Of Pharmacy And Pharmaceutical Sciences*. Vol 5, Issue 3.
- Puzi, Wina. 2015. *Isolasi dan Identifikasi Senyawa Flavonoid dari Daun Tumbuhan Sirih Merah (*Piper crocatium* Ruiz)*. Bandung: Prosiding Penelitian Unisba.
- Reigh, D. L., Wender, S. H., And Smith, E. C., 1973. "Scopoletin: A Substrate For An Isoperoxidase From *Nicotiana Tabacum* Tissue Culture W-38". *Phytochemistry*. Vol. 12, Pp. 1265 To 1268.

- Rinawati., Gesa, G. P., Ni, L. G. R. J. 2020. Review: Green Analytical Chemistry: Pemanfaatan *Supercritical Fluid Extraction* (Sfe) Dan *Microwave-Assisted Extraction* (Mae) Sebagai Metode Ekstraksi Senyawa Diterpena Pada Minyak Biji Kopi Shangrai. *Analit: Analytical and Environmental Chemistry*. Volume 5, No.01.
- Salmiwanti. 2016. Isolasi Senyawa Metabolit Sekunder Fraksi N-Heksana Daun Pegagan (*Centella asiatica* L. Urban) Dan Uji Antibakteri Terhadap *Mycobacterium Tuberculosis*. Makassar: Fakultas Sains Dan Teknologi Uin Alauddin.
- Sann, E. E., Soe, M. M., & Khine, M. M. 2020. *Isolation And Identification Of Some Phytoconstituents From Leaves Of Morus Alba L . And Screening Of Antioxidant Activity*. *Xviii*.(1).
- Sari Jayanti Fonda. 2011. “Penerapan Metode Kromatografi Lapisan Tipis (KLT) untuk membedakan *Curcuma domestica* Val., *Curcuma xanthorrhiza* Roxb., *Curcuma zedoaria* Rosc., *Curcuma mangga* Val. & van Zijp., *Curcuma aeruginosa* Roxb. dalam campuran”. Surabaya: Universitas Airlangga.
- Sekhara, I., Benaissa, O., Amrani, A., Giangiacomo, B., Benabderrahmane, W., Chaouch, M. A., Zama, D., Benayache, S., & Benayache, F. 2020. “Antioxidant activity and chemical constituents of *Anthriscus vulgaris* Bernh. (Apiaceae) from Algeria”. *Acta Scientifica Naturalis*, 7(1), 59–70.
- Sethiya, N. K., Trivedi, A., & Mishra, S. H. 2015. “Rapid validated high performance thin layer chromatography method for simultaneous estimation of mangiferin and scopoletin in *Canscora Decussata* (South Indian Shankhpushpi) extract”. *Revista Brasileira de Farmacognosia*, 25(3), 193–198.
- Shaw, C. Y., Chen, C. H., Hsu, C. C., Chen, C. C., & Tsai, Y. C. 2003. “Antioxidant properties of scopoletin isolated from *Sinomonium acutum*”. *Phytotherapy Research*, 17(7), 823–825.
- Shinde, P. B., Katekhaye, S. D., Mulik, M. B., & Laddha, K. S. 2014. “Rapid simultaneous determination of marmelosin, umbelliferone and scopoletin from *Aegle marmelos* fruit by RP-HPLC”. *Journal of Food Science and Technology*, 51(9), 2251–2255.
- Sichaem, J., Inthanon, K., Funnimid, N., Phontree, K., Phan, H. V. T., Tran, T. M. D., Niamnont, N., Srikittiwanna, K., Sedlak, S., & Duong, T. H. 2020. “Chemical Constituents of the Stem Bark of *Bombax ceiba*”. *Chemistry of Natural Compounds*, 56(5), 779–780.

- Silva, W. P. K., Deraniyagala, S. A., Wijesundera, R. L. C., Karunanayake, E. H., & Priyanka, U. M. S. 2002. "Isolation of scopoletin from leaves of *Hevea brasiliensis* and the effect of scopoletin on pathogens of *H. brasiliensis*". *Mycopathologia*, 153(4), 199–202.
- Sugiyono (2015). *Metode Penelitian Kombinasi (Mix Methods)*. Bandung: Alfabeta.
- Sugiyono. 2007. *Metode Penelitian Kuantitatif Kualitatif dan R&D*. Bandung: Alfabeta.
- Tabatabaei, S. M., Farimani, M. M., Nejad-Ebrahimi, S., & Salehi, P. 2020. "Phytochemical study of *tanacetum sonbolii* aerial parts and the antiprotozoal activity of its components". *Iranian Journal of Pharmaceutical Research*, 19(1), 77–83.
- Thani, W., Vallisuta, O., Siripong, P., & Ruangwises, N. 2010. "Anti-proliferative and antioxidative activities of Thai noni/Yor (*Morinda citrifolia* Linn.) leaf extract". *Southeast Asian Journal of Tropical Medicine and Public Health*, 41(2), 482–489.
- Thengyai, S., Thiantongin, P., Sontimuang, C., Ovatlarnporn, C., & Puttarak, P. 2020. " α -Glucosidase and α -amylase inhibitory activities of medicinal plants in Thai antidiabetic recipes and bioactive compounds from *Vitex glabrata* R. Br. stem bark". *Journal of Herbal Medicine*, 19, 100302.
- Thomaz, D. V., Couto, R. O., Roberth, A. de O., Oliveira, L. A. R., Leite, K. C. de S., Bara, M. T. de F., Ghedini, P. C., Bozini, M. C. V., Lobón, G. S., Gil, E. de S., & Machado, F. B. 2018. "Assessment of Noni (*Morinda citrifolia* L.) product authenticity by solid state voltammetry". *International Journal of Electrochemical Science*, 13(9), 8983–8994.
- Thuc, D. N., Thuy, V. T., Mai, V. T. H., Thanh, L. N., & Van Quan, V. 2020. "Chemical constituents from ethyl acetate extract of the stems of *Rourea oligophlebia* Merr". *Vietnam Journal of Chemistry*, 58(3), 298–301.
- Tobo, F., Mufidah, Taebe, B., Mahmud, A.I. 2011. *Buku Pegangan Laboratorium Fitokimia 1*. Makassar: Universitas Hasanuddin.
- Tripathi, A. K., Bhakuni, R. S., Upadhyay, S., & Gaur, R. 2011. "Insect feeding deterrent and growth inhibitory activities of scopoletin isolated from *Artemisia annua* against *Spilarctia obliqua* (Lepidoptera: Noctuidae)". *Insect Science*, 18(2), 189–194.
- Tzeng, T. C., Lin, Y. L., Jong, T. T., & Chang, C. M. J. 2007. "Ethanol modified supercritical fluids extraction of scopoletin and artemisinin from *Artemisia annua* L". *Separation and Purification Technology*, 56(1), 18–24.

- Vidya K. S., Raghavendra, A. Muthusamy, S. B. Vidhu, J. Subramani, P. M. Gopinath, K. Satyamoorthy. 2012. "Cytotoxic efficacy of Noni (*Morinda citrifolia* L.) fruit extracts and scopoletin on a preponderant panel of human tumor cell lines". *International Journal of noni Research*. Vol. 7 No. 1.
- Vipul, U., Neeru, S., Amit, T. K., M, J. H., Amreesh, M., Brijpal, S., & Singh, B. kalakot. 2013. "Standardization of HPLC Method of Scopoletin in Different Extracts of *Convolvulus pluricaulis*". *International Journal of Pharmaceutical Sciences and Drug Research*, 5(1), 28–31.
- Vyas, N., Raval, M., & Patel, N. 2020. "Quantitative estimation of scopoletin from *Argyrea speciosa* (L. f.) sweet by a validated high performance thin layer chromatographic method". *Separation Science Plus*, 3(8), 362–368.
- West Brett J. And Shixin Deng. 2010. "Thin Layer Chromatography Methods For Rapid Identity Testing Of *Morinda Citrifolia* L. (Noni) Fruit And Leaf". *Advance Journal Of Food Science And Technology*. 2(5): 298-302.
- Wheatley, C. C., & Schwabe, W. W. 1985. "Scopoletin involvement in post-harvest physiological deterioration of cassava root (*Manihot esculenta* crantz)". *Journal of Experimental Botany*, 36(5), 783–791.
- Wigati, D., Anwar, K., Sudarsono, & Nugroho, A. E. 2017. "Hypotensive Activity of Ethanolic Extracts of *Morinda citrifolia* L. Leaves and Fruit in Dexamethasone-Induced Hypertensive Rat". *Journal of Evidence-Based Complementary and Alternative Medicine*, 22(1), 107–113.
- Xia, Y., Dai, Y., Wang, Q., & Liang, H. 2007. "Determination of scopoletin in rat plasma by high performance liquid chromatographic method with UV detection and its application to a pharmacokinetic study". *Journal of Chromatography B: Analytical Technologies in the Biomedical and Life Sciences*, 857(2), 332–336.
- Yogita Nancy Bansal And Gulshan Bansal. 2015. "Hplc-Uv/Fd Methods For Scopoletin And Asiatic Acid: Development, Validation And Application In Who Recommended Stability Testing Of Herbal Drug Products". *Biochem Anal Biochem*. 4:4.
- Zeng, Y., Ma, Y., Yang, Z., Mao, J., & Zheng, Y. 2020. "Antihyperuricemic efficacy of Scopoletin-loaded Soluplus micelles in yeast extract/potassium oxonate-induced hyperuricemic mice". *Drug Development and Industrial Pharmacy*, 46(9), 1550–1557.
- Zhou, R., Kan, S., Cai, S., Sun, R., Yuan, H., & Yu, B. 2020. "Scopoletin Activates Adenosine Monophosphate-Activated Protein Kinase/Mammalian Target of Rapamycin Signaling Pathway and Improves Functional Recovery after Spinal Cord Injury in Rats". *Pharmacology*, 105(5–6), 349–359.