



Source details

Pharmacognosy Journal

Scopus coverage years: from 2009 to Present

Publisher: Pharmacognosy Network Worldwide

ISSN: 0975-3575

Subject area: [Pharmacology, Toxicology and Pharmaceutics: Pharmacology](#)

[Pharmacology, Toxicology and Pharmaceutics: Drug Discovery](#)

Source type: Journal

CiteScore 2022

1.9



SJR 2022

0.229



SNIP 2022

0.484



[View all documents >](#)

[Set document alert](#)

[Save to source list](#)

[CiteScore](#) [CiteScore rank & trend](#) [Scopus content coverage](#)

i Improved CiteScore methodology

CiteScore 2022 counts the citations received in 2019-2022 to articles, reviews, conference papers, book chapters and data papers published in 2019-2022, and divides this by the number of publications published in 2019-2022. [Learn more >](#)



CiteScore 2022

$$1.9 = \frac{1,691 \text{ Citations 2019 - 2022}}{878 \text{ Documents 2019 - 2022}}$$

Calculated on 05 May, 2023

CiteScoreTracker 2023

$$1.6 = \frac{1,220 \text{ Citations to date}}{741 \text{ Documents to date}}$$

Last updated on 07 June, 2023 • Updated monthly

CiteScore rank 2022

Category	Rank	Percentile
Pharmacology, Toxicology and Pharmaceutics	#219/301	27th
└ Pharmacology		
Pharmacology, Toxicology and Pharmaceutics	#121/156	22nd
└ Drug Discovery		

[View CiteScore methodology >](#) [CiteScore FAQ >](#) [Add CiteScore to your site](#)

SJR Scimago Journal & Country Rank


Home Journal Rankings Country Rankings Viz Tools Help About Us

Pharmacognosy Journal

<p>COUNTRY</p> <p>India</p> <p>Universities and research institutions in India</p> <p>Media Ranking in India</p>	<p>SUBJECT AREA AND CATEGORY</p> <p>Pharmacology, Toxicology and Pharmaceutics</p> <ul style="list-style-type: none"> Drug Discovery Pharmacology 	<p>PUBLISHER</p> <p>EManuscript Technologies</p>	<p>H-INDEX</p> <p>30</p>
<p>PUBLICATION TYPE</p> <p>Journals</p>	<p>ISSN</p> <p>09753575</p>	<p>COVERAGE</p> <p>2009-2022</p>	<p>INFORMATION</p> <p>Homepage</p> <p>How to publish in this journal</p> <p>editor@phcogj.com</p>

SCOPE

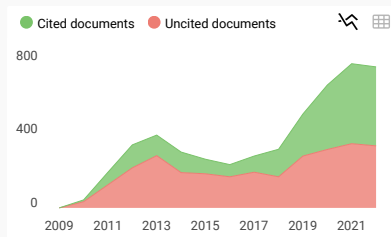
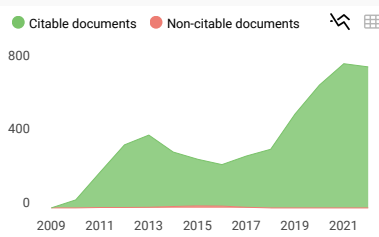
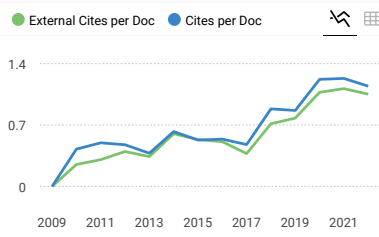
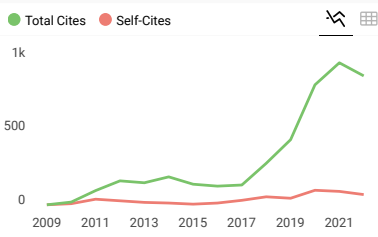
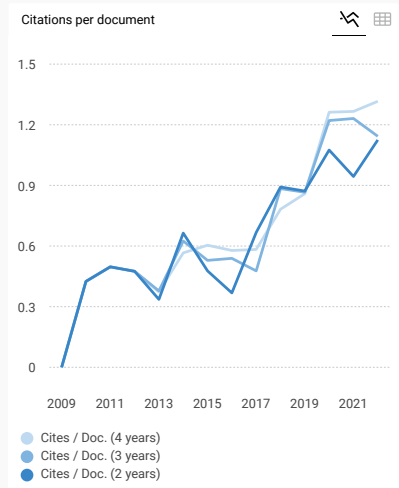
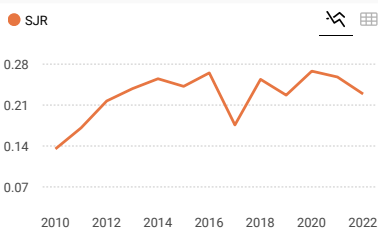
Pharmacognosy Journal (Phcog J.) covers different topics in natural product drug discovery, and also publishes manuscripts that describe pharmacognostic investigations, evaluation reports, methods, techniques and applications of all forms of medicinal plant research

 Join the conversation about this journal

FIND SIMILAR JOURNALS ?

options ⋮

<p>1 Oriental Pharmacy and Experimental Medicine USA</p> <p>82% similarity</p>	<p>2 Pharmacognosy Research IND</p> <p>81% similarity</p>	<p>3 Indian Journal of Natural Products and Resources IND</p> <p>77% similarity</p>	<p>4 Journal of Herbs, Spices and Medicinal Plants USA</p> <p>76% similarity</p>	<p>5 Pharmacognosy Magazine IND</p> <p>76% similarity</p>
--	---	---	--	---



Pharmacognosy Journal

← Show this widget in your own website

Q3 Pharmacology
best quartile

SJR 2022
0.23

powered by scimagojr.com

Just copy the code below and paste within your html code:
<https://www.scimagojr.com>

SCImago Graphica

Explore, visually communicate and make sense of data with our **new data visualization tool**.

[Home \(/\)](#)[About Journal ▾](#)[Editorial Board \(/editorial-board-2020-21\)](/editorial-board-2020-21)[For Authors ▾](#)[Contact Us \(/contact-us\)](/contact-us)

Pharmacognosy Journal (/)

An Open Access, Peer Reviewed Journal in the field of
Pharmacognosy

Enter terms then hit Search...

[Articles In Press \(/inpress\)](/inpress)[Current Issue \(/v15/i2\)](/v15/i2)[Archives \(/archives\)](/archives)[RSS Feeds \(/rss.xml\)](/rss.xml)[Submit Article \(https://www.phcogj.info\)](https://www.phcogj.info)

[HOME \(/\)](#) / [PHARMACOGN J. VOL 14, ISSUE 2, MAR-APR, 2022](#)

Pharmacogn J. Vol 14, Issue 2, Mar-Apr, 2022

[View \(/pharmacogn-j-vol-14-issue-2-mar-apr-2022\)](/pharmacogn-j-vol-14-issue-2-mar-apr-2022)[What links here \(/node/1759/backlinks\)](/node/1759/backlinks)

Submitted by sys1 (/users/sys1) on Sat, 04/30/2022 - 10:59

The Activities of Pegagan Embun (*Hydrocotyle sibthorpioides* Lam.) on TNF- α , Macrophages and Leukocytes Male White Mice Exposed by H5N1 Virus Antigens (/article/1760)

GC-MS Profiling, Antioxidants and Antimicrobial Activity of Prickly Pear (*Opuntia ficus-indica*) Pulp Extract (/article/1761)

The Potential Effect of Nigericin from *Streptomyces hygrosopicus* subsp. *Hygrosopicus* Against the Syndemic of Malaria and COVID-19 through Molecular Docking Perspective (/article/1762)

Anti-Ulcer Activity of Spray-dried Powders Prepared from Aerial Parts Extracts of *Ampelopsis cantoniensis* (/article/1763)

Molecular Docking, Physicochemical and Drug-likeness Properties of Isolated



- Compounds from *Garcinia latissima* Miq. on Elastase Enzyme: In Silico Analysis (/article/1764)
- Antibacterial and Cytotoxic Activity of Selected Raw-Consumed Vegetables in West Java, Indonesia (/article/1765)
- Potential of Stem Cells in Overcoming Infertility Problems in Women (/article/1766)
- Screening of Secondary Metabolites and Antioxidant Activity of Wild Edible Termite Mushroom (/article/1767)
- Optimization of Ultrasound-Assisted Extraction of *Tinospora crispa* Stem, Phytochemical Screening, Total Phenolic Content and Anti Gout Potential Activity (/article/1768)
- Pasuchaca (*Geranium ruizii* Hieron.): A Medicinal Plant of the Geraniaceae Family with Hypoglycemic Effect on Alloxan-Induced Hyperglycemia in Mice (/article/1769)
- The Effect of Antioxidant activity, Total Phenols and Total Flavonoids on Arginase Inhibitory Activity on Plants of Genus *Sterculia* (/article/1770)
- Evaluation of Antibacterial and Antioxidant Activity of Endophytic Fungi Isolated from *CAPSICUM ANNUUM* L. and *ALLIUM CEPA* L. (/article/1771)
- Determination Antioxidant Activity of *Coffea Arabica*, *Coffea Canephora*, *Coffea Liberica* and Sunscreens Cream Formulation for Sun Protection Factor (SPF) (/article/1772)
- An In Silico Study of Examining Bioactive Compounds from *Azadirachta indica* Juss. (Neem) as Potential Death Receptor 5 Inductor in Hepatoma Cells (/article/1773)
- Preliminary Identification and Quantification of Four Secondary Metabolites, Total Tannin and Total Flavonoid Contents in Guava Fruit Ethanol Extract (/article/1774)
- Clinical Studies of Silymarin as a Protective Agent Against Liver Damage Caused by Anti-TB Drugs, Methotrexate, and in Cases of Chronic Hepatitis C and Diabetes Mellitus (/article/1775)
- Formulation and Characterization of Meniran (*Phyllanthus Niruri* Linn) Extract Nanoparticle on Antibacterial Activity Against *Salmonella Pullorum* (/article/1776)
- Cytotoxic Effects of Kirinyuh Herb (*Austroeupatorium inulaefolium* (Kunth) R. d. King & H. Robinson) Extracts and Fractions on BSLT, MCF-7 Cells and T-47D Cells (/article/1777)
- The Potential of Moringa (*Moringa oleifera* Lamk) Seed Oil as Anti- Alopecia (/article/1778)



Mechanism of the Bioactive Sargassum cristaefolium in Inhibiting Inflammatory Mediators in a Nitroglycerin-Induced Migraine Model in Rats (/article/1779)

Optimization of the Ultrasound Assisted Extraction of Phaleria macrocarpa (Scheff.) Boerl. Fruit Peel and its Antioxidant and Anti-Gout Potential (/article/1780)

Potency of Antidiabetic Effects of the Combination of Syzygium cumini and Andrographis paniculata in Rats with High-Fat Diet and Streptozotocin-Induced Diabetes (/article/1781)

Preliminary Data on the Antibacterial Activity of Coffea Arabica, Coffea Canephora and Coffea Liberica (/article/1782)

Anxiolytic and Antidepressant-like Effects of Foeniculum vulgare Essential Oil (/article/1783)

Optimization of Ultrasound-Assisted Extraction of Andrographis paniculata Nees Leaves, Phytochemical Screening, Total Phenolic Content and Anti-Gout Potential Activity (/article/1784)

Coleus atropurpureus (L) Benth. Leaves as a New Promising Drug for Abscesses Caused by Methicillin-resistant Staphylococcus aureus and Staphylococcus aureus (/article/1785)

Ten Commonly Available Medicinal Plants in Malaysia with Potential Sun Protection Factor and Antioxidant Properties – A Review (/article/1786)

A Review of an Important Plants: Annona squamosa Leaf (/article/1787)

Virgin coconut oil and tuberculosis: A mini-review (/article/1788)

Inhibitory Capacity of Xanthine Oxidase in Antigout Therapy by Indonesian Medicinal Plants (/article/1789)

The Activities of Pegagan Embun (Hydrocotyle sibthorpioides Lam.) on TNF- α , Macrophages and Leukocytes Male White Mice Exposed by H5N1 Virus Antigens > (/article/1760)

776 reads

SHARE THIS ARTICLE

[EMAIL](#) (MAILTO:?SUBJECT=%20PHARMACOGNOSY%20JOURNAL%20ISSUE%202%20MAR-APR%2022) /SHARER.PHP?U=HTTPS://WWW.PHARMACOGNOSY.COM/ISSUE/2022/MAR-APR/1760/PIN/CREATE?url=https://www.phcogj.com/pharmacogn-j-vol-14-issue-2-mar-apr-2022/article/1760/&title=The+Activities+of+Pegagan+Embun+(Hydrocotyle+sibthorpioides+Lam.)+on+TNF- α ,+Macrophages+and+Leukocytes+Male+White+Mice+Exposed+by+H5N1+Virus+Antigens+>+(/article/1760)

[FACEBOOK](#) /SHAREARTICLE?MINI=TRUE&URL=HTTPS://WWW.PHARMACOGNOSY.COM/ISSUE/2022/MAR-APR/1760/PIN/CREATE?url=https://www.phcogj.com/pharmacogn-j-vol-14-issue-2-mar-apr-2022/article/1760/&title=The+Activities+of+Pegagan+Embun+(Hydrocotyle+sibthorpioides+Lam.)+on+TNF- α ,+Macrophages+and+Leukocytes+Male+White+Mice+Exposed+by+H5N1+Virus+Antigens+>+(/article/1760)

[LINKEDIN](#) /SHAREARTICLE?MINI=TRUE&URL=HTTPS://WWW.PHARMACOGNOSY.COM/ISSUE/2022/MAR-APR/1760/PIN/CREATE?url=https://www.phcogj.com/pharmacogn-j-vol-14-issue-2-mar-apr-2022/article/1760/&title=The+Activities+of+Pegagan+Embun+(Hydrocotyle+sibthorpioides+Lam.)+on+TNF- α ,+Macrophages+and+Leukocytes+Male+White+Mice+Exposed+by+H5N1+Virus+Antigens+>+(/article/1760)

[TWITTER](#) /TWEET?TEXT=%20PHARMACOGNOSY%20JOURNAL%20ISSUE%202%20MAR-APR%2022%20ARTICLE%201760%20-%20THE+ACTIVITIES+OF+PEGAGAN+EMBUN+(HYDROCOTYLE+SIBTHORPIOIDES+LAM.)+ON+TNF- α ,+MACROPHAGES+AND+LEUKOCYTES+MALE+WHITE+MICE+EXPOSED+BY+H5N1+VIRUS+ANTIGENS+%26gt%3B+(/article/1760)

[GOOGLE+](#) /SHARE?URL=HTTPS://WWW.PHARMACOGNOSY.COM/ISSUE/2022/MAR-APR/1760/PIN/CREATE?url=https://www.phcogj.com/pharmacogn-j-vol-14-issue-2-mar-apr-2022/article/1760/&title=The+Activities+of+Pegagan+Embun+(Hydrocotyle+sibthorpioides+Lam.)+on+TNF- α ,+Macrophages+and+Leukocytes+Male+White+Mice+Exposed+by+H5N1+Virus+Antigens+>+(/article/1760)

Home (/) About Journal v Editorial Board (/editorial-board-2020-21) For Authors v

Contact Us (/contact-us)

Pharmacognosy Journal (/)

An Open Access, Peer Reviewed Journal in the field of Pharmacognosy

Enter terms then hit Search...



Articles In Press (/inpress) Current Issue (/v15/i2) Archives (/archives)

RSS Feeds (/rss.xml) Submit Article (https://www.phcogj.info)



(http://www.phcogj.com/#/)

HOME (/) / EDITORIAL BOARD (2020-21)

View (/editorial-board-2020-21)

What links here (/node/25/backlinks)

Time to read
1 minute

Editorial Board (2020-21)

Editors & Editorial Board Members (2021)

Share



Dr. Djemli Samir

Department of Biology , Applied Neuroendocrinology Laboratory
Bach Mokrhar Annaba University

(https://www.facebook.com/

/sharer Algeria

/sharer.php?u=https

%3A%2F

Dr. Raghava Naidu, Ph.D

Department of Human Oncology,
University of Wisconsin,

%2Fwww.phcogj.com%2Feditorial-

board- 1111, Highland Ave, Madison,

2020-21& Wisconsin 53705, USA

t=Editorial+Board+%282020-21%29)

Dr. Karim Raafat

Associate Professor of Pharmacognosy and Phytochemistry,

(https://plus.google.com/



Pharmaceutical Sciences Department,



/share?url=https://www.phcogj.com/editorial-board-2020-21)
 Faculty of Pharmacy,
 Beirut Arab University (BAU),
 Beirut 115020, Lebanon

Orlad Alzeus Tantengco, MD-PhD Molecular Medicine
 2020-21)
 College of Medicine, University of the Philippines Manila
 Pedro Gil Street, Ermita, Manila, Philippines, 1000
 (http://twitter.com

Janib Achmad
 Editorial Board+2020-21%29&
 url=https://www.phcogj.com/editorial-board-2020-21)
 Lecturer of Faculty of Fisheries and Marine Science,
 University of Khairun Ternate
 Kampus 2 Jalan Pertamina, Kelurahan Gambesi,
 Ternate Selatan

Muammar Fawwaz, Ph.D
 2020-21)
 Department of Pharmaceutical Chemistry
 Faculty of Pharmacy
 Universitas Muslim Indonesia
 Makassar 90231, South Sulawesi, Indonesia



Print

a- a+

Hany Ezzat Khalil

Associate Professor,
 College of Clinical Pharmacy,
 King Faisal University,
 KSA

Emad Yousif

Department of Chemistry
 College of Science
 Al-Nahrain University
 Baghdad, Iraq

Sughosh Upasani

R.C Patel Institute of pharmacy,
 Shirpur, Dist-Dhule, Maharashtra,
 India.

Gurusiddaiah suresh kumar

Scientist
 Dept of biochemistry
 CSIR-CFTRI
 Mysore, Karnataka, INDIA

Arjun Patra

Assistant Professor
 School of Pharmaceutical Sciences
 Guru Ghasidas Central University



Koni, Bilaspur - 495 009
Chattisgarh, India

Francis O. Atanu, Ph.D

Department of Biochemistry
Faculty of Natural Sciences
Kogi State University
Anyigba, Nigeria.

Vijay Kumar Chattu

Faculty of Medical Sciences
University of the West Indies
St. Augustine, Trinidad & Tobago.

Dr.Kunle Okaiyeto, PhD

Applied and Environmental Microbiology Research Group (AEMREG)
Department of Biochemistry and Microbiology
University of Fort Hare
Alice campus
5700, Alice
South Africa.

Dr. Srisailam Keshetti, Ph.D

Principal, University College of Pharmaceutical Sciences, Satavahana University
Karimnagar 505001
Telangana
INDIA

Dr. Gayathri M Rao

Associate Professor
Department of Biochemistry
Kasturba Medical Collge, Mangaluru.

Shuge Tian

Experimental Teaching Demonstration Center of TCM in Xinjiang Medical University
Department of traditional medicine ,TCM
Xinjiang Medical University
Xinjiang CHINA 830054

Dr. Ramachandra Setty Siddamsetty,

Professor, Govt College of Pharmacy,
Mission Road, Bengaluru, INDIA

Dr. (Mrs.) Sayyada Khatoon

HOD, Pharmacognosy Division
CSIR-National Botanical Research Institute,
Rana Pratap Marg, Post Box 436,



Lucknow-226001 (U.P.) India

Dr. A. Sajeli Begum

Department of Pharmacy
Birla Institute of Technology & Science
Hyderabad, India

Olga Silva

Department of Pharmacological Sciences,
Faculdade de Farmácia,
Universidade de Lisboa, Portugal

Xinwen Wang

Department of Clinical Pharmacy
University of Michigan
USA

Roman Lysiuk

Department of Pharmacognosy and Botany,
Danylo Halytsky Lviv National Medical University,
Pekarska,69., Lviv 79010, Ukraine

Arif Nur Muhammad Ansori

Universitas Airlangga
Indonesia

103115 reads

SHARE THIS ARTICLE

EMAIL (MAILTO:?SUBJECT=EDITORIAL BOARD-2020-21%29&BODY=HTTPS%3A%2F%2FWWW.PHCOGJ.COM%2FEDITORIAL-BOARD-2020-21)	FACEBOOK HTTPS://WWW.FACEBOOK.COM/SHARER.PHP?U=HTTPS%3A%2F%2FWWW.PHCOGJ.COM%2FEDITORIAL-BOARD-2020-21	LINKEDIN HTTPS://WWW.LINKEDIN.COM/SHAREARTICLE?MINI=TRUE&URL=HTTPS%3A%2F%2FWWW.PHCOGJ.COM%2FEDITORIAL-BOARD-2020-21	TWITTER HTTPS://TWITTER.COM/INTENT/TWEET?TEXT=EDITORIAL-BOARD-2020-21&URL=HTTPS%3A%2F%2FWWW.PHCOGJ.COM%2FEDITORIAL-BOARD-2020-21	GOOGLE+ HTTPS://PLUS.GOOGLE.COM/SHARE?URL=EDITORIAL-BOARD-2020-21&PIN/CREATEURL=HTTPS%3A%2F%2FWWW.PHCOGJ.COM%2FEDITORIAL-BOARD-2020-21
--	---	---	--	--

About

Pharmacognosy Journal (Phcog J.) covers different topics in natural product drug discovery, and also publishes manuscripts that describe pharmacognostic investigations, evaluation reports, methods, techniques and applications of all forms of medicinal plant research

Distinctions: The most widely read, cited, and known Pharmacognosy journal and website is well browsed with all the articles published. More than 50,000 readers in nearly every country in the world each month

ISSN : 0975-3575 ; **Frequency :** Rapid at a time publication (6 issues/year)

Indexed and Abstracted in : SCOPUS, Scimago Journal Ranking, Chemical Abstracts, Excerpta Medica /



Mechanism of the Bioactive *Sargassum cristaefolium* in Inhibiting Inflammatory Mediators in a Nitroglycerin-Induced Migraine Model in Rats

Olivia Mahardani Adam^{1,2}, Jusak Nugraha^{3,*}, Muhammad Hamdan⁴, Agus Turchan⁵

Olivia Mahardani Adam^{1,2}, Jusak Nugraha^{3,*}, Muhammad Hamdan⁴, Agus Turchan⁵

¹Doctoral Program, Faculty of Medicine, Universitas Airlangga, Surabaya, INDONESIA.

²Department of Neurology, Faculty of Medicine, Universitas Hang Tuah, Surabaya, INDONESIA.

³Department of Clinical Pathology, Faculty of Medicine, Universitas Airlangga, Surabaya, INDONESIA.

⁴Department of Neurology, Faculty of Medicine, Universitas Airlangga, Surabaya, INDONESIA.

⁵Department of Neurosurgery, Faculty of Medicine, Universitas Airlangga, Surabaya, INDONESIA.

Correspondence

Jusak Nugraha

Department of Clinical Pathology, Faculty of Medicine, Universitas Airlangga, Surabaya, INDONESIA.

Email: jusak-n@fk.unair.ac.id

History

- Submission Date: 07-02-2022;
- Review completed: 22-02-2022;
- Accepted Date: 01-03-2022.

DOI : 10.5530/pj.2022.14.

Article Available online

<http://www.phcogj.com/v14/i2>

Copyright

© 2022 Phcogj.Com. This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International license.

ABSTRACT

Background: Migraine headaches are a form of sterile neurogenic inflammation. The sterile inflammatory process of the trigeminal nerve releases the vasoactive neuropeptide CGRP which stimulates the release of inflammatory mediators. In the incidence of migraine there is an increase in TNF- α and IL-10. *Sargassum cristaefolium* ethanol extract contains flavonoids, alkaloids, triterpenoids, steroids, and tannins, which has analgesic and anti-inflammatory function. **Method:** *Sargassum cristaefolium* was extracted using maceration method with 70% ethanol as solvent. Animal models were divided into 5 groups and given NTG induction 5 times with 1 day intervals, treated for 3 weeks. All data were analyzed using IBM SPSS version 26.0. **Results:** *Sargassum cristaefolium* ethanol extract - CGRP levels β : -0.26, p: 0.17; *Sargassum cristaefolium* ethanol extract - CGRP expression β : -0.04, p: 0.85; *Sargassum cristaefolium* ethanol extract - TNF- α levels β : -0.63, p: 0.01; *Sargassum cristaefolium* ethanol extract - TNF- α expression β : -0.40, p: 0.04; *Sargassum cristaefolium* ethanol extract - IL-10 levels β : 0.77, p: 0.00; *Sargassum cristaefolium* ethanol extract - IL-10 expression β : 0.45, p: 0.01. **Conclusions:** A significant path between the administration of *Sargassum cristaefolium* ethanol extract and a decrease in TNF- α and an increase in IL-10. But the effect of giving *Sargassum cristaefolium* ethanol extract on CGRP levels did not have a significant relationship.

Key words: Inflammatory mediator, Migraine, Nitroglycerin, *Sargassum cristaefolium*.

INTRODUCTION

Migraine is a headache with pain attacks lasting 4-72 hours, unilateral, throbbing, with moderate to severe pain intensity, aggravated by activity, and may be accompanied by nausea and vomiting, and/or photophobia phonophobia.¹ Genetically susceptible and influenced by population area, climate change, socioeconomic status and lifestyle.

Many studies state that migraine headaches are a sterile form of neurogenic inflammation of the trigeminal nerve that releases vasoactive neuropeptides such as Calcitonin Gene Related Peptide (CGRP) which causes vasodilation of blood vessels and activates endothelial cells, mast cells and platelets to release vasoactive substances. CGRP will bind to its receptors on meningeal mast cells and stimulate the release of inflammatory mediators, causing sterile inflammation of neurons.

The pathophysiology of migraine is multifactorial, with most studies showing increased peripheral circulating concentrations of the pro-inflammatory cytokines IL-1 β , IL-6, TNF- α and IL-8 and the anti-inflammatory cytokine IL-10. During the ictal period IL-1 β , IL-6, IL-8 and TNF- α were increased, while the anti-inflammatory cytokines IL-4 and IL-5 decreased and IL-10 increased compared to during the interictal period.²

As many as 80% of patients use analgesics to treat headaches. NSAIDs are drugs that are widely used in migraine sufferers because they can provide anti-inflammatory, analgesic, and antipyretic effects. Analgesic therapy is the most widely

prescribed drug in the world, although these drugs often cause serious side effects. Therefore, it is necessary to look for new alternative drugs derived from natural ingredients that are relatively easy to obtain and come from plants that have analgesic and anti-inflammatory functions.

Indonesia is a country that has a very wide sea area, about two-thirds of the country's territory is ocean. Seaweed or better known as seaweed or algae is one of the most abundant biological resources in Indonesian waters, which is about 8.6% of the total marine biota. The bioactive substances contained in the *Sargassum cristaefolium* algae include flavonoids, alkaloids, tannins, terpenoids and steroids. Flavonoids act as anti-inflammatory by inhibiting the secretion of pro-inflammatory mediators. Alkaloids have a function as analgesics, while tannins, terpenoids and steroids function as anti-inflammatory.

MATERIALS AND METHODS

Ethics, consent and permissions

Ethics and experimental procedures were approved by the Faculty of Veterinary Medicine, Universitas Airlangga Surabaya Indonesia and the testing service unit of the Faculty of Pharmacy, Universitas Widya Mandala Surabaya Indonesia.

Characteristics of research subjects

Method Cohort using male *Rattus norvegicus* wistar strain, animals were randomized to treatment conditions. The treatment group involved the induction of NTG 10 mg/kg. It was administered intraperitoneally 5 times.

Cite this article: Adam OM, Nugraha J, Hamdan M, Turchan A. Mechanism of the Bioactive *Sargassum cristaefolium* in Inhibiting Inflammatory Mediators in a Nitroglycerin-Induced Migraine Model in Rats. *Pharmacogn J.* 2022;14(2):.

Extracts obtained from the leaves and stems of brown algae originating from the waters of Ra'as Island, Sumenep Regency, were extracted using the maceration method with 70% ethanol solvent and thickened with a rotary evaporator at 40°C and 1% Na CMC solvent was given to rats orally using probe. The bioactive components contained in brown seaweed *Sargassum cristaefolium* use a test method based on which includes:³

Flavonoid test

2 mL of *Sargassum cristaefolium* extract was added with 1 mL of 2N NaOH. The presence of flavonoid content was indicated by the formation of a yellow color in the extract.

Alkaloid test

2 mL of *Sargassum cristaefolium* extract was added with 2N HCl, and a few drops of Dragendorff's test were added to the Meyer and Wagner tubes. The presence of alkaloids was indicated by the formation of a yellowish white precipitate in the Meyer tube, a brown precipitate in the Wagner tube and an orange-red precipitate with Dragendorph's reagent.

Triterpenoids/Steroid test

Dissolve 4 g of *Sargassum cristaefolium* extract in 25 mL of ethanol and then filtered. Then 0.5 mL of *Sargassum cristaefolium* extract added 2 ml of chloroform and aquades (1:1). The layer formed was dried on a hot plate and 1 drop of Lieberman-Burchard reagent was added. The presence of triterpenoids is indicated by the formation of a red color and a blue-green color for steroid content.

Tannin test

1 mL of *Sargassum cristaefolium* extract was added with 1 mL of 5% FeCl₃. The presence of tannin content is indicated by the formation of a dark blue or blackish green color.

Saponin test

2 mL of *Sargassum cristaefolium* extract added 2 ml of distilled water and shaken in a test tube for 15 minutes. The presence of saponins was indicated by the formation of a 1 cm foam layer.

Statistical analysis

All data were analyzed using IBM SPSS version 26.0. The significance level for statistical analyzes $p < 0.05$ was considered statistically significant.

Procedure

The experiment was started after adaptation for 7 days, given NTG induction 5 times, 1 day apart, treatment for 3 weeks. Experimental animals were divided into 5 groups, namely:

K- = Negative control group + placebo

K+ = Positive control group + NTG + placebo

KP1 = Treatment group (1) + NTG + *Sargassum cristaefolium* ethanol extract dose 250 mg/kg body weight

KP2 = Treatment group (2) + NTG + *Sargassum cristaefolium* ethanol extract dose 500 mg/kg body weight

KP3 = Treatment group (3) + NTG + *Sargassum cristaefolium* ethanol extract dose 750 mg/kg body weight

RESULTS

The test results for the content of Flavonoids, Alkaloids, Terpenoids, Steroids, Tannins and Saponins in the ethanolic extract of *Sargassum*

cristaefolium were carried out using the spectrophotometric method. Phytochemical test results on brown algae *Sargassum cristaefolium* showed positive results for the presence of flavonoid compounds, steroids/triterpenoids, alkaloids, and tannins (Table 1).

The results of the description test for levels and expressions of CGRP, TNF- α and IL-10 in the form of average and standard deviation can be seen in Table 2.

NTG induction increased the mean plasma CGRP levels by comparing the K- and K+ groups. The administration of *Sargassum cristaefolium* ethanol extract reduced CGRP levels by comparing the K+ group to the P1, P2 and P3 groups. The average comparison between groups of CGRP levels can be seen in Figure 1 and Figure 2.

NTG induction increased the mean plasma TNF- α levels by comparing the K- and K+ groups. The administration of *Sargassum cristaefolium* ethanol extract reduced TNF- α levels by comparing the K+ group to the P1, P2 and P3 groups. The average comparison between groups of TNF- α levels can be seen in Figure 3 and Figure 4.

NTG induction increased the mean plasma IL-10 levels by comparing the K- and K+ groups. The administration of *Sargassum cristaefolium* ethanol extract reduced IL-10 levels by comparing the K+ group to the P1 group. The administration of *Sargassum cristaefolium* ethanol extract increased IL-10 levels by comparing the K+ group to the P2 and P3 groups. The average comparison between groups of IL-10 levels can be seen in Figure 5 and Figure 6.

The results of the regression and significance values between *Sargassum cristaefolium* ethanol extract on levels and expression of CGRP, TNF- α and IL-10 can be seen in Table 3.

DISCUSSION

The ethanolic extract of *sargassum* contains bioactive flavonoids, alkaloids, triterpenoids, steroids, tannins and saponins. Flavonoid compounds are thought to have antioxidant, antitumor, antiviral, anti-inflammatory and antibiotic activities.⁴ Flavonoids have strong antioxidant abilities because their chemical structure contains more than one phenol group and has a conjugated double bond. The ability to bind and prevent the formation of free radicals indicates that flavonoids apart from being analgesics, antioxidants also have anti-inflammatory functions.⁵ Alkaloids function as antibiotics, analgesics, anti-inflammatory and blood circulation.⁶ Tannins are active secondary metabolites which are known to have several properties, namely as astringent, antidiarrheal, antibacterial, anti-inflammatory and antioxidant. Terpenoids and steroids function as anti-inflammatory.^{5,7}

A study showed that the extraction method and the type of solvent did not affect the flavonoid content. This is presumably because in its structure, flavonoids have polar and nonpolar parts with almost the same parts.⁸ In this study, 70% ethanol was used because the selection of ethanol as a solvent has the ability to find compounds in a wide polar range, from polar to non-polar compounds, is non-toxic and effective in finding active ingredients.

The dose of *Sargassum cristaefolium* commonly used by humans is 18 grams/50kg BW, with an average human weight of 50 kg. The conversion factor from 70 kg adult human to 200 gram rat is 0.08.⁹ Therefore, in this study, the optimal dose of *Sargassum cristaefolium* ethanol extract for rats was 500 mg/kg BW, minimum dose 250 mg/kg BW, maximum dose 750 mg /kg body weight and given by oral procedure.

In this study, the results of the phytochemical test of *Sargassum cristaefolium* were positive for flavonoids, alkaloids, triterpenoids, steroids, and tannins but did not show the presence of saponins. The highest levels are found in terpenoids and steroids that function as

Table 1: Phytochemical test results of *Sargassum cristaefolium*.

Phytochemical test results			
Parameters	Fresh	Dry	Powder
Alkaloid	++	+	+
Flavonoid	++	+	+
Triterpenoid/ Steroid	++	++	++
Tanin	+	+	+
Saponin	-	-	-

Table 2: Descriptive test results mean and standard deviation of CGRP, TNF- α and IL-10 levels in experimental animal plasma.

Group	Mean \pm SD					
	CGRP		TNF- α		IL-10	
	level	expression	level	expression	level	expression
K-	80.30 \pm 7.47	6.28 \pm 1.93	228.79 \pm 104.51	5.25 \pm 1.99	55.41 \pm 3.30	2.35 \pm 1.10
K+	115.38 \pm 8.36	7.98 \pm 2.52	395.68 \pm 156.99	6.48 \pm 2.05	57.41 \pm 4.08	3.97 \pm 1.69
P1	102.57 \pm 8.92	5.73 \pm 3.11	186.88 \pm 94.92	4.25 \pm 0.91	56.74 \pm 3.65	3.27 \pm 1.03
P2	70.26 \pm 9.35	4.87 \pm 3.45	130.20 \pm 79.12	4.08 \pm 1.75	65.52 \pm 5.32	3.47 \pm 1.48
P3	84.92 \pm 20.78	7.48 \pm 3.09	138.70 \pm 22.80	4.07 \pm 1.10	69.90 \pm 3.70	5.98 \pm 3.41

Description:

K- = Negative control group + placebo

K+ = Positive control group + NTG + placebo

KP1 = Treatment group (1) + NTG + *Sargassum cristaefolium* ethanol extract dose 250 mg/kg body weight

KP2 = Treatment group (2) + NTG + *Sargassum cristaefolium* ethanol extract dose 500 mg/kg body weight

KP3 = Treatment group (3) + NTG + *Sargassum cristaefolium* ethanol extract dose 750 mg/kg body weight

Table 3: Regression and significance values between *Sargassum cristaefolium* ethanol extract on levels and expression of CGRP, TNF- α and IL-10.

No.	Variable	Beta (β)	R ²	Nilai P
1.	<i>Sargassum cristaefolium</i> ethanol extract -> CGRP levels	-0.26**	0.07	0.17
2.	<i>Sargassum cristaefolium</i> ethanol extract -> CGRP expression	-0.04**	0.00	0.85
3.	<i>Sargassum cristaefolium</i> ethanol extract -> TNF- levels	-0.63**	0.55	0.01*
4.	<i>Sargassum cristaefolium</i> ethanol extract -> TNF- α expression	-0.40**	0.37	0.04*
5.	<i>Sargassum cristaefolium</i> ethanol extract -> IL-10 levels	0.77	0.60	0.00*
6.	<i>Sargassum cristaefolium</i> ethanol extract -> IL-10 expression	0.45	0.20	0.01*

Description:

Beta (β) : Regression coefficient, shows the relationship of the independent variable to the variable dependent (increase or decrease)

R² : The coefficient of determination, the contribution of the independent variable to the variation (up and decrease) dependent variable

P value : The value of the probability of significance, declared significant/significant if the p value <0.05

Sign* : Significant or meaningful

Sign** : Negative relationship

anti-inflammatory. This is in line with research conducted by Riwanti which stated that *Sargassum polycystum* obtained from Madura was positive for alkaloids, steroids/triterpenoids, flavonoids, polyphenols, and tannins.¹⁰ Lailiyah's research showed that the phytochemical test results of *Sargassum cristaefolium* methanol extract obtained from Madura allegedly contained steroids that had antioxidant and anti-inflammatory activities.³ Another study by Gazali found that the ethanol extract of *Sargassum sp* obtained in the Aceh area contained higher levels of terpenoids and alkaloids.⁶

Flavonoids are efficacious as analgesics whose mechanism of action is to inhibit the work of the cyclooxygenase enzyme which reduces the

production of prostaglandins, thereby reducing pain.¹¹ CGRP is widely distributed in the body, central and peripheral nervous system, as a very potent and long-lasting vasodilator at all levels of the vascular system and has a major role in sensory nerve transmission.^{12,13} Cerebral vascular dysfunction caused by abnormal levels of neuropeptides such as CGRP, plays an important role in migraine. After the vascular active substances are not balanced, there is vasomotor dysfunction, vasodilation and pain in migraine.¹⁴

In this study, *Sargassum cristaefolium* has not been able to reduce plasma CGRP levels and CGRP expression in the brain tissue of experimental animals. The above findings indicate that the analgesic

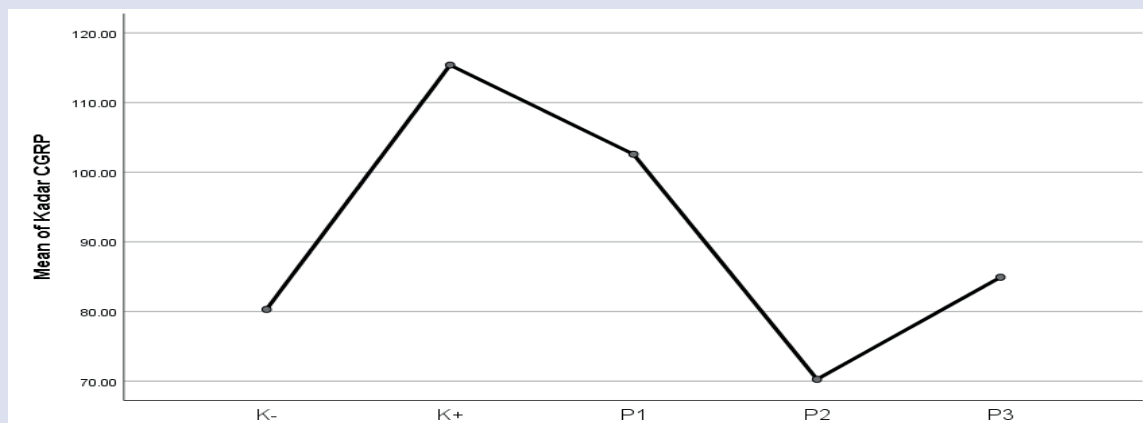


Figure 1: The average comparison between groups of CGRP levels.

Description:

K- = Negative control group + placebo

K+ = Positive control group + NTG + placebo

KP1 = Treatment group (1) + NTG + *Sargassum cristaefolium* ethanol extract dose 250 mg/kg body weight

KP2 = Treatment group (2) + NTG + *Sargassum cristaefolium* ethanol extract dose 500 mg/kg body weight

KP3 = Treatment group (3) + NTG + *Sargassum cristaefolium* ethanol extract dose 750 mg/kg body weight

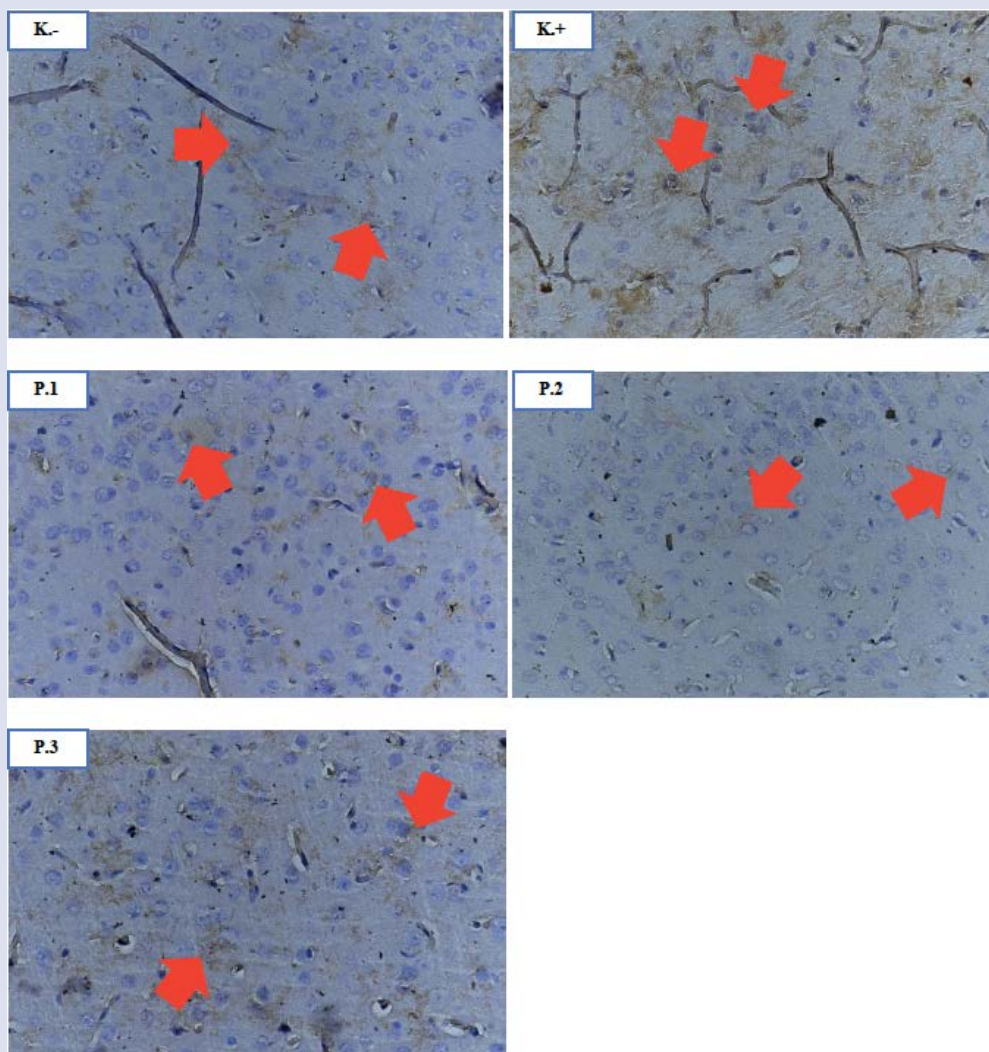


Figure 2: Comparison of CGRP expression in brain tissue groups (K-, K+, P.1, P.2, P.3). Red arrows indicate the presence of serotonin expression in the cerebrum which is indicated by the presence of a brown chromogen color. IHC. 400x.

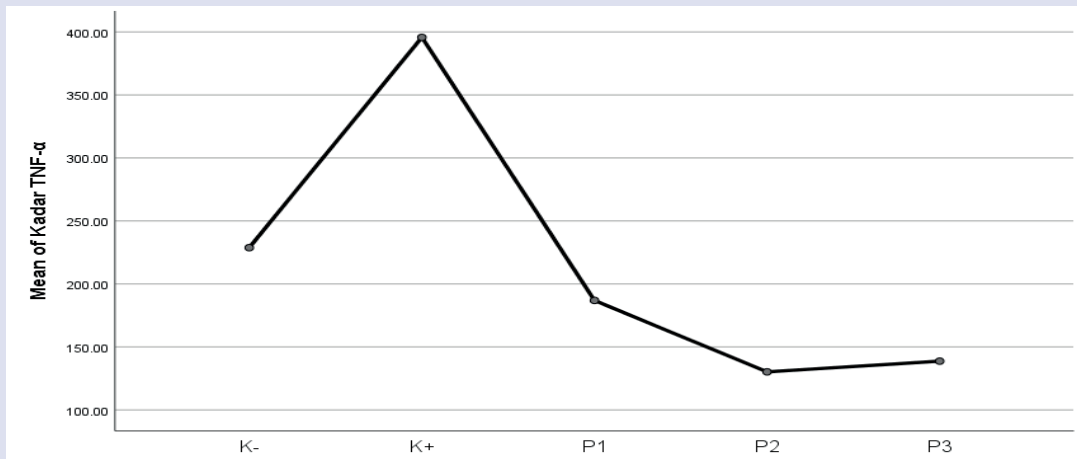


Figure 3: The average comparison between groups of TNF-α levels.

Description:

K- = Negative control group + placebo

K+ = Positive control group + NTG + placebo

KP1 = Treatment group (1) + NTG + *Sargassum cristaefolium* ethanol extract dose 250 mg/kg body weight

KP2 = Treatment group (2) + NTG + *Sargassum cristaefolium* ethanol extract dose 500 mg/kg body weight

KP3 = Treatment group (3) + NTG + *Sargassum cristaefolium* ethanol extract dose 750 mg/kg body weight

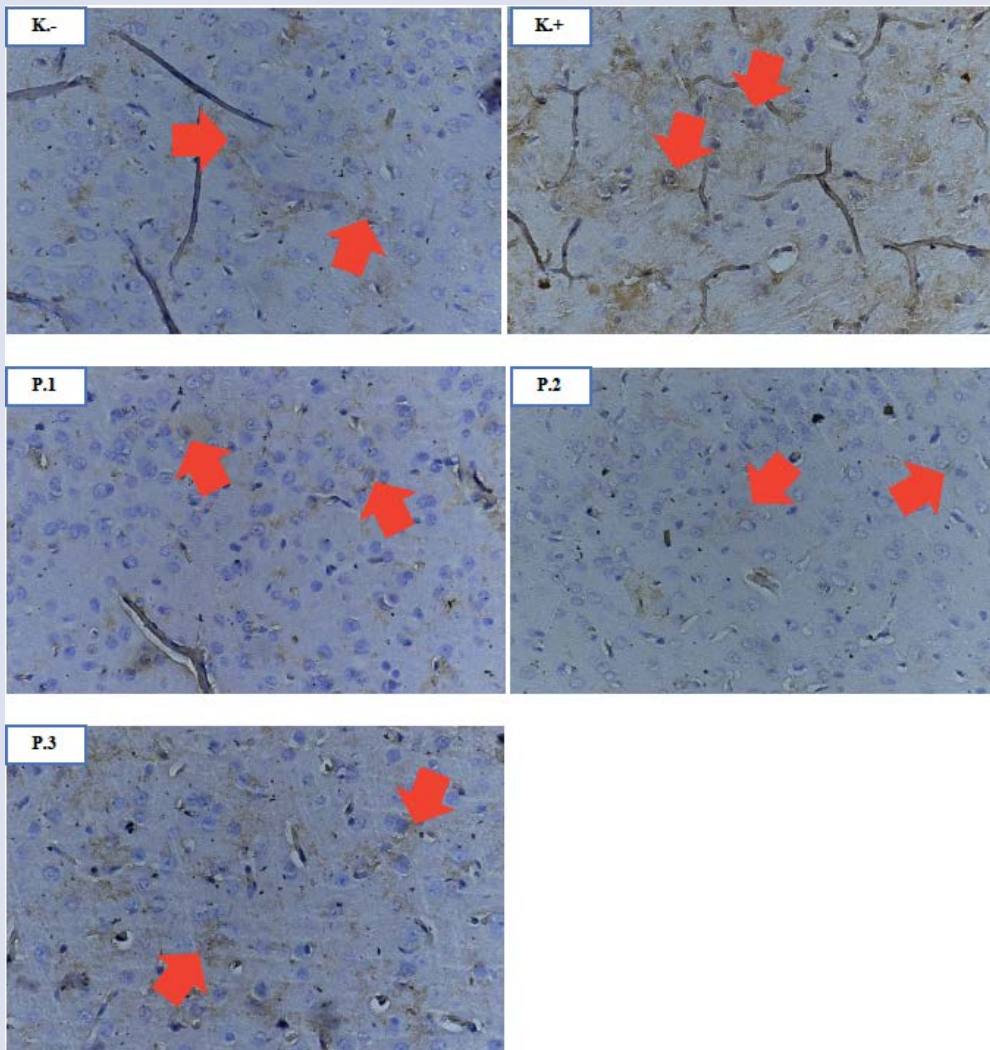


Figure 4: Comparison of TNF-α expression in brain tissue groups (K-, K+, P.1, P.2, P.3). Red arrows indicate the presence of serotonin expression in the cerebrum which is indicated by the presence of a brown chromogen color. IHC. 400X.

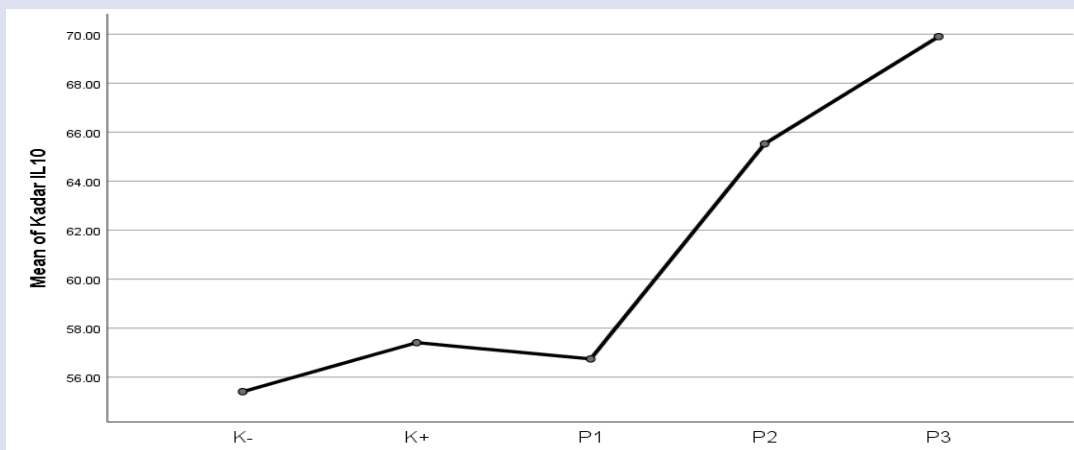


Figure 5: The average comparison between groups of IL-10 levels.

Description:

K- = Negative control group + placebo

K+ = Positive control group + NTG + placebo

KP1 = Treatment group (1) + NTG + *Sargassum cristaefolium* ethanol extract dose 250 mg/kg body weight

KP2 = Treatment group (2) + NTG + *Sargassum cristaefolium* ethanol extract dose 500 mg/kg body weight

KP3 = Treatment group (3) + NTG + *Sargassum cristaefolium* ethanol extract dose 750 mg/kg body weight

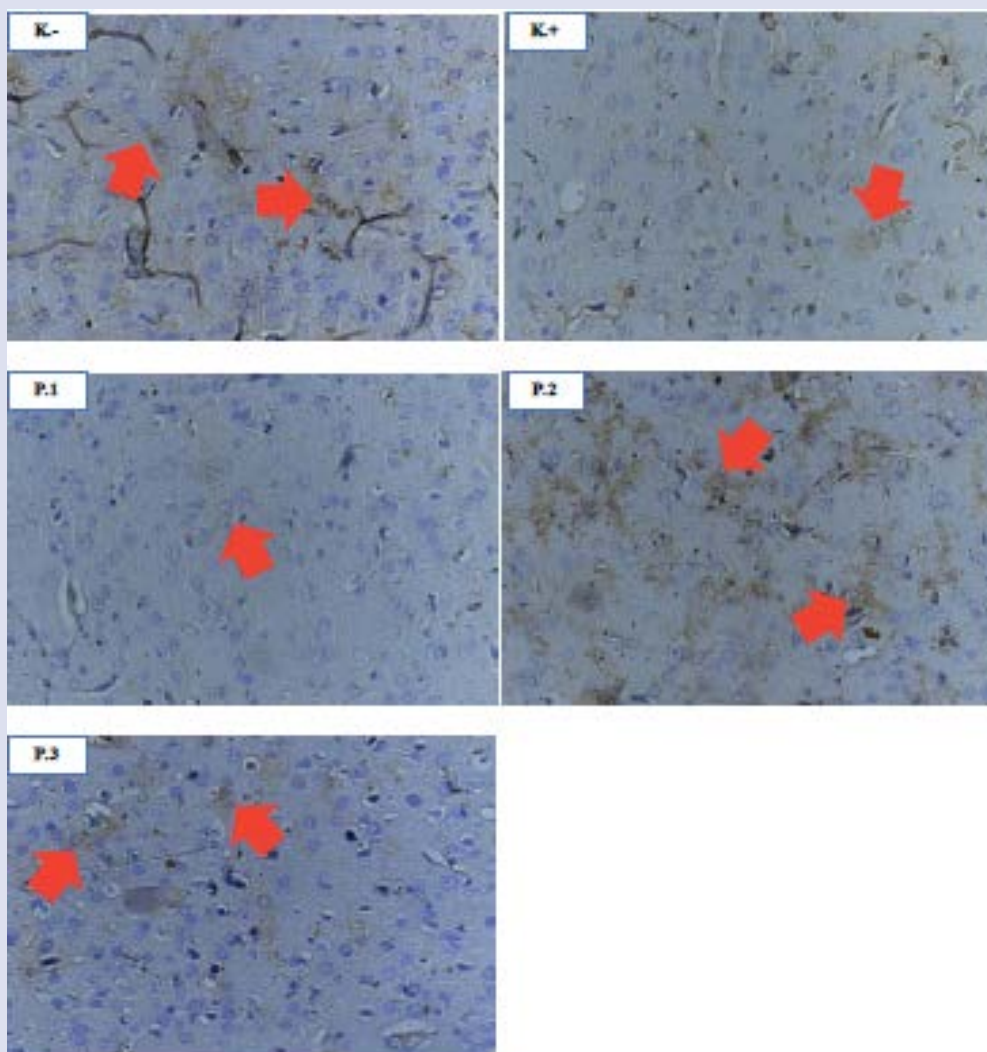


Figure 6: Comparison of IL-10 expression in brain tissue groups (K-, K+, P.1, P.2, P.3). Red arrows indicate the presence of serotonin expression in the cerebrum which is indicated by the presence of a brown chromogen color. IHC. 400x.

effect of flavonoids on *Sargassum cristaefolium* is lacking, possibly related to the adjustment of vasoactive substances, neurotransmitters and doses of *Sargassum cristaefolium* extract, although there is a decrease in CGRP levels in migraine experimental animals after administration of *Sargassum cristaefolium* extract.

Study by Abbey showed that the secretion of CGRP by trigeminal nerve stimulation can be inhibited directly by the flavonoid-containing methanol extract of *Theobroma cacao* bean. In the TMJ inflammation model, CGRP release from trigeminal neurons can be inhibited by flavonoids. It was stated that the flavonoids in *Theobroma cacao* only suppressed the release of stimulated CGRP but did not inhibit basal CGRP secretion.¹⁵

IL-10 downregulates proinflammatory cytokines such as TNF- α , IL-6 and IL-1. One study suggested the anti-inflammatory activity of flavonoids through their potential downregulation of transcriptional downregulation of cyclooxygenase-2, prostaglandin E2, and TNF- α .¹⁶ Another study showed the lowest TNF- α expression level in wound skin given *Sargassum illicifolium* extract containing alkaloid compounds compared to the control group during the healing process through RT-PCR analysis.¹⁷

Another study showed that the ethanolic extract of *Sargassum cristaefolium* could inhibit the proinflammatory cytokines TNF- α and IL-6 in skin lesions of rats treated with UVR by reducing epidermal thickness. Anti-inflammatory cytokine IL-10 levels were higher in mice treated with UVR with *Sargassum cristaefolium* ethanol extract due to its faster regenerative healing properties.¹⁸

IL-10 is produced by monocytes and astrocytes in brain tissue and is found in plasma in migraine sufferers, IL-10 functions as a macrophage inhibitor, reduces antigen presentation, and inhibits the production of IFN- γ , IL-6 and TNF- α . IL-10 plays a role in neutralizing macrophage pathology in migraine by inhibiting the secretion of IFN- γ and TNF- α .² In the serum of migraine sufferers, there was an increase in the level of TNF- α and an increase in the level of IL-10. Elevated levels of IL-10 during migraine attacks in response balance the increased plasma proinflammatory cytokine levels during attacks.¹⁸ However, excessive increases in IL-10 can suppress the immune response and worsen disease outcome. The IL-10/TNF- α ratio in the range of 1.3-1.9 has an anti-inflammatory effect.¹⁹

CONCLUSION

The results showed that the ethanol extract of *Sargassum cristaefolium* could reduce levels and expression of CGRP compared to the positive control in the treatment group at a dose of 500 mg/kgBW. decreased levels and expression of TNF- compared to the positive control in the treatment group at a dose of 500 mg/kgBW. The levels and expression of IL-10 increased compared to the positive control in the treatment group at a dose of 750 mg/kgBW. The relationship that has a positive direction is the administration of *Sargassum cristaefolium* ethanol extract and IL-10 levels. While the relationship that has a negative direction is the administration of *Sargassum cristaefolium* ethanol extract and CGRP levels; administration of *Sargassum cristaefolium* ethanol extract and levels of TNF- α . From the path analysis carried out, it was found that there was a significant path between the administration of *Sargassum cristaefolium* ethanol extract and a decrease in TNF- α ; administration of *Sargassum cristaefolium* ethanol extract with an increase in IL-10. The effect of giving *Sargassum cristaefolium* ethanol extract on CGRP levels did not have a significant relationship.

ACKNOWLEDGMENT

We thank the EJA Team, Indonesia (<https://ejatranslation.wixsite.com/home>) for editing the manuscript. This study was supported by the Medical Faculty, Universitas Hang Tuah, Surabaya, Indonesia.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

ABBREVIATIONS

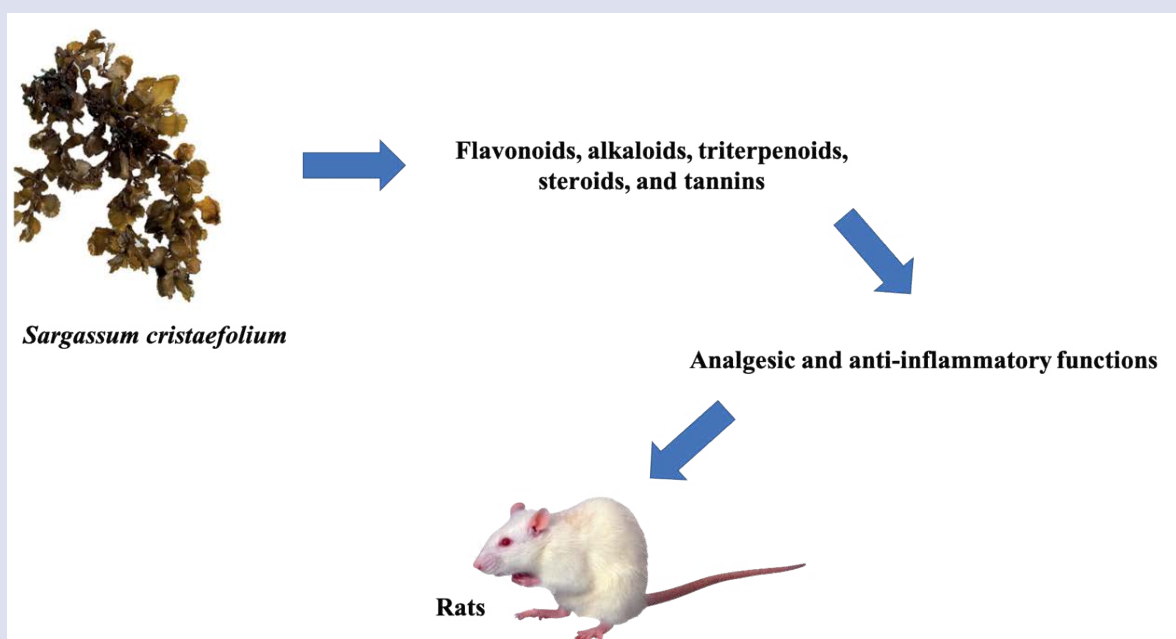
BW: body weight; FeCl: Ferric Chloride; HCl: Hydrogen Chloride; IFN: Interferon; IL: Interleukin; LPS: Lipopolysaccharide; ml : mililiter; NaOH: Natrium Hidroksida; NA: Neurokinin A; NO: Nitric Oxide; NOS: Nitrous Oxide Systems; NSAID: Non-steroidal anti-inflammatory drugs; NTG: Nitroglycerin; RT-PCR: Real time polymerase chain reaction; SD: Standart Deviation; SP: Substance P; SPSS: Statistical Package for the Social Sciences; TNF: Tumor Necrosis Factor; UVR: Ultraviolet radiation.

REFERENCES

- Gasparini CF, Smith RA, Griffiths LR. Genetic and biochemical changes of the serotonergic system in migraine pathobiology. *J Headache Pain*. 2017;18(1):20.
- Oliveira AB, Bachi ALL, Ribeiro RT, Mello MT, Tufik S, Peres MFP. Unbalanced plasma TNF- α and IL-12/IL-10 profile in women with migraine is associated with psychological and physiological outcomes. *J Neuroimmunol*. 2017;313:138-44.
- Lailiyah A, Adi TK, Yusnawan E. Antioxidant Capacity and Total Phenolic Compound Content of Coarse Extract of Brown Algae *Sargassum cristaefolium* from Sumenep Beach, Madura. *Alchemy*. 2014.
- Husen SA, Setyawan MF, Syadzha MF, Susilo RJK, Hayaza S, Ansori ANM, et al. A novel therapeutic effects of *Sargassum illicifolium* alginate and okra (*Abelmoschus esculentus*) pods extracts on open wound healing process in diabetic mice. *Res J Pharm Technol*. 2020;13(6):2764-2770.
- Husen SA, Syadzha MF, Setyawan MF, Pudjiastuti P, Ansori ANM, Susilo RJK, et al. Evaluation of the combination of *Sargassum duplicatum*, *Sargassum illicifolium*, *Abelmoschus esculentus* and *Garcinia mangostana* extracts for open wound healing in diabetic mice. *Sys Rev Pharm*. 2020;11(9):888-892.
- Gazali M, Nurjanah N, Zamani NP. Exploration of Bioactive Compounds of Brown Algae *Sargassum* sp. Agardh as an Antioxidant from the West Coast of Aceh. *J Processing of Indonesian Fishery Products*. 2018;21(1):167.
- Kartikaningsih H. Antibacterial Ethanol Extract Dry Powder *Sargassum cristaefolium* Against *Escherichia coli* and *Salmonella thyposa* bacteria. *JFMR-Journal Fish Mar Res*. 2020;4(1):53-60.
- Septiana AT, Asnani A. Study of Physicochemical Properties of *Sargassum Duplicatum* Brown Seaweed Extract using Various Solvents and Extraction Methods. *Agrointek J Teknol Ind Pertan*. 2012;6(1):22-8.
- Pangestuti BME. Anti-Inflammatory Test of *Eurycoma Longifolia* Jack Root Methanol Extract in Carrageenin Induced Swiss Strain Male Mice. 2016.
- Riwanti P, Izazih F. Phytochemical Screening of 96% *Sargassum polycystum* Ethanol Extract and Profile with Infrared Spectrophotometry. *Acta Holistica Pharm*. 2019;2(1):34-41.
- Syamsul ES, Andayani F, Soemarie YB. Test of Analgetic Activity of Ethanolic Extract of Kerehau Leaves (*Callicarpa longifolia* Lamk.) on White Mice. *Tradit Med J*. 2016;21(2):99-103.
- Goadsby PJ. Pathophysiology of migraine. *Ann Indian Acad Neurol*. 2012;15(1):15-22.
- Edvinsson L, Haanes KA, Warfvinge K, Krause DiN. CGRP as the target of new migraine therapies - Successful translation from bench to clinic. *Nat Rev Neurol*. 2018;14(6):338-350.
- Hou M, Tang Q, Xue Q, Zhang X, Liu Y, Yang S, et al. Pharmacodynamic action and mechanism of Du Liang soft capsule, a traditional Chinese medicine capsule, on treating nitroglycerin-induced migraine. *J Ethnopharmacol*. 2017;195:231-237.

- Abbey MJ, Patil VV, Vause CV, Durham PL. Repression of calcitonin gene-related peptide expression in trigeminal neurons by a *Theobroma cacao* extract. *J Ethnopharmacol.* 2008;115(2):238-248.
- Prasedya ES, Martyasari NWR, Abidin AS, Pebriani SA, Ilhami BTK, Frediansyah A, *et al.* Macroalgae *Sargassum cristaefolium* extract inhibits proinflammatory cytokine expression in BALB/C Mice. *Scientifica.* 2020;2020:9769454.
- Premarathna AD, Ranahewa TH, Wijesekera SK, Harishchandra DL, Karunathilake KJK, Waduge RN, *et al.* Preliminary screening of the aqueous extracts of twenty-three different seaweed species in Sri Lanka with *in-vitro* and *in-vivo* assays. *Heliyon.* 2020;6(6):e03918.
- Barbagallo M, Vitaliti G, Greco F, Pavone P, Matin N, Panta G, *et al.* Idiopathic intracranial hypertension in a paediatric population: A retrospective observational study on epidemiology, symptoms and treatment. *J Biol Regul Homeost Agents.* 2017;31(1):195-200.
- Junita D, Prasetyo AA, Muniroh M, Kristina TN, Mahati E. The effect of glutathione as adjuvant therapy on levels of TNF- α and IL-10 in wistar rat peritonitis model. *Ann Med Surg.* 2021;66:102406.
- Malone Rubright SL, Pearce LL, Peterson J. Environmental toxicology of hydrogen sulfide. *Nitric Oxide - Biol Chem.* 2017;71(412):1-13.
- Aman NR. The Relationship between Smoking and Migraine Severity Based on MIDAS (Migraine Disability Assessment). Muhammadiyah University of Yogyakarta. 2018.
- Winarni D, Husna FN, Syadzha MF, Susilo RJK, Hayaza S, Ansori ANM, *et al.* Topical administration effect of *Sargassum duplicatum* and *Garcinia mangostana* extracts combination on open wound healing process in diabetic mice. *Scientifica.* 2022;2022:9700794.
- Arie Afriansyah. The Authority of the Coastal State in Managing the Sea Area. *J Huk Developer.* 2015;45(4):608-635.

GRAPHICAL ABSTRACT



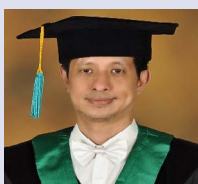
ABOUT AUTHORS



Dr. Agus Turchan, dr., SpBS(K) is a lecturer in Department of Neurosurgery Dr. Soetomo General Hospital, Faculty of Medicine Airlangga University, Surabaya.



Dr. Muhammad Hamdan, dr., Sp.S(K) is a lecturer in Department of of Neurology, Faculty of Medicine, Universitas Airlangga, Surabaya.



Prof. Dr. Jusak Nugraha, dr, MS., SpPK(K) is a professor in Department of Clinical Pathology, Dr. Soetomo General Hospital, Faculty of Medicine Airlangga University, Surabaya.



Olivia Mahardani Adam, dr., Sp.S is a lecturer in the Departement of Neurology Faculty of Medicine Hang Tuah University, Surabaya.

Cite this article: Adam OM, Nugraha J, Hamdan M, Turchan A. Mechanism of the Bioactive *Sargassum cristaefolium* in Inhibiting Inflammatory Mediators in a Nitroglycerin-Induced Migraine Model in Rats. *Pharmacogn J.* 2022;14(2):.