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#### ABSTRACT

The societies of the Central Kalimantan have a traditional treatment for skin allergies derived from charcoal. The charcoal was obtained from the fin waste of *Channa pleurophthalma* fish. The present study aimed to analyze the bioactive compounds of *Channa pleurophthalma* fin waste charcoal (CFWC) and determine the biological potential using bioinformatics methods and visual empirical evidence approach. Bioactive substances were screened using LC-HRMS. The 2D structure and 3D structure of bioactive compounds were obtained from PubChem. PASSOnline was applied to analyze the prediction of hydrolyzed compounds biological activity. There were 10 highest compounds in CSWC: octyl decyl phthalate, hexadecanamide, oleamide, cetrimonium, dibutyl phthalate, pyroquilon, stearamide, 6-methoxyquinoline, 8hydroxyquinoline and tridemorph. CSWC has potential effect as anti-allergies, anti-inflammation, anti-pruritic, anti-fungi, and anti-microbe. CFWC cauld be an effective treatment to heal skin wounds due to the allergy of *Channa pleurophthalma*.

#### **INTRODUCTION**

The potential of natural resources in the form of natural and traditional medicinal ingredients hereditary has been used as a traditional treatment. The traditional medicine that used animal or plant source is expected can be used in the development of health in societies. The advance of modern knowledge and technology are unable to shift the role of traditional medicines, even nowadays, the government is encouraging the use of traditional medicines (back to nature) [1]. The advantages of natural medicine are constructive and have a low side effect. So. the use of natural medicine is relatively safer than chemical or synthetical drug on the market [2]. The animal sources, as traditional medicine are usually dead animals [3]. The parts of the animal body that commonly used include meat, horn, bone, tail, hair, nail, fat, bile, and shell. Usually, the potential animal source as traditional medicine is widely available in nature, able to cure severe disease and also has economic value.

Kerandang fish (Channa pleurophthalma Blkr) is phenomenal in Central Kalimantan due to the charcoal made from several parts of the body that is not consumed can be utilized as traditional medicine for allergies in human. Channa pleurophthalma contains 19.5% protein, 8.26 % albumin, a high amount of aspartate and glutamate [4]. The fish that lives in peatlands function as a guardian of biodiversity and ecology of peatlands. Besides that, it contains bioactive compounds that worthwhile for treatment [5]. In some cases, people that consume Channa pleurophthalma provoke allergy such as itching and onset of red spots to resemble small dots on the skin. Allergy is a condition caused by specific immunological reactions produce by the allergen [6]. The emersion of allergy due to the alteration of body reaction becomes vulnerable against daily material in the environment [7]. The allergy reaction

Keywords: Allergy, Channa pleurophthalma Blkr, charcoal, finfish

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associate with the crosslinked of allergen and IgE against the high-affinity receptors in mast cells surface [8].

Based on the evidence of people who have experience on skin allergy caused by *Channa pleurophthalma*, the use of charcoal made from body parts of *Channa pleurophthalma* was believed and approved hereditary to cure skin allergy. The body parts of *Channa pleurophthalma* were burned to charcoal which was then smeared in the allergic skin. This treatment effectively cures the allergy due to the charcoal effect as an anti-allergic agent. The charcoal can be made from scalps, scales, and fins of parrotfish *(Oreochromis niloticus)* as *fishbone hydroxyapatite*, [9] bone of tuna fish *(Thunnus sp.)*, gourami *(Osphronemidae)*, and mackerel tuna *(Euthynnus affinis)* [10]. The chemical composition of the fishbone is hydroxyapatite, collagen, glycosaminoglycan, proteoglycan, and glycoprotein [11,12].

Therefore, the study aimed to analyze the bioactive substances in *Channa pleurophthalma* fin waste charcoal (CFWC) and its biological potential through bioinformatics and visual empirical evidence approach.

#### MATERIALS AND METHODS Materials

The raw materials used in the study were parts of *Channa pleurophthalma* body which were not eaten including dorsal fins, pectoral, pelvic, anal, and caudal fins that were obtained from collecting fisherman in Sebangau Kereng Bengkirai Lake in Central Kalimantan, Indonesia. The tools used in the study were sample bottles, porcelain cups, oven, desiccator, analytical scales, and LC-HRMS *Thermo Scientific Dionex Ultimate* 3000 RSLCnano.

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#### Sample preparation

The dorsal, pectoral, pelvic, anal, and caudal fin of *Channa pleurophthalma* fish were collected, cleaned, and dried for 2-3 days. The dried fins were burned to charcoal by using an oven with maximum temperature 200°C. Charcoal obtained from fins burning were then weighed for 500g each sample.

#### **LC-HRMS** analysis

The extracted sample was diluted with a solvent (polar) and done by reaching the final volume of 1300 µl with a concentration of the extract that was not too thick or runny. After dilution, the sample was then mixed with vortex for 1 min and spindown for 2 min. The supernatant was collected and filtered by using a 0.22 µm syringe filter and put in a vial. Sample in the vial was then placed in autosampler and injected to LC-HRMS following the injection method, which was desired. The data obtained was later converted to the format of NetCDF to make it easier to be processed with mzCloud. The data processing of mzCloud consists of some steps such as the construction based on molecular weight, and arrangement of data.

#### **Bioinformatics analysis**

Bioinformatics analysis is done by accessing the PubChem server (https://pubchem.ncbi.nlm. nih.gov/) to obtain 2D structure and 3D structure information from bioactive compounds. Prediction of biological activity of hydrolyzed compounds was analyzed by online prediction of activity specifications for substances (PASS) (http://www.way2drug.com/ PASSOnline/index.php).

#### **RESULTS AND DISCUSSION**

Kerandang fish (Channa pleurophthalma Blkr) is a type of freshwater fish from the Channidae family. The size of the fish is from medium to large with a total length up to 40 cm (15.7 inches). Dorsal fin base consists of 17-20 scales from the tip of the snout. The dorsal fin starts from above the bottom of the pectoral fin, and the tip is found in behind the anal fin. There were approximately 10-12 rows of scales located in the behind of eye up to the rear boundary of pre-operculum. Furthermore, 5-6 rows of scales located in its operculum [13]. The back colour of its fish is brown, and the bottom side is yellowish-white. Two dark bands that are parallel from behind the eyes and slightly tilted in the direction of inter-operculum. Four or five circles like an eye (ocellus) are circled by the yellow colour that found along the side of the body: the first circle is in the above gill cover, and the fifth is in around the base of the tail. The dorsal fin, anal, and tail are faintly striped [13]. Channa pleurophthalma used in the study was shown in Figure 1A. Figure 1B showed that the color of Channa pleurophthalma fin waste charcoal (CFWC) was deep black. Charcoal is a porous black residue from hightemperature combustion of materials contained carbon through the pyrolysis process. Pyrolysis process generates charcoal, steam, gas, H2O, CO, CO2, hydrocarbon [14]. Indeed, some of the industry products have been developed charcoal as energy, pharmacy, and cosmetic [15].



(A)

**(B)** 

Figure 1. (A) The morphology of Channa pleurophthalma; (B) Channa pleurophthalma fin waste charcoal (CFWC)

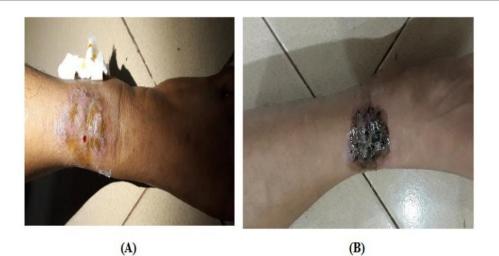
Figure 2A showed the condition of skin allergy caused by the consumption of the meat of Channa pleurophthalma. Allergy can be defined as hypersensitivity; the high immune system responds or excessive for some stimulus or external stimuli. It also described as the manifestation of hypersensitivity reaction that occurs due to the presence of antigen that enters the body and forms Immunoglobulin E (IgE). IgE bound to mast cells and basophils through the Fc receptor. The binding of antigen and IgE cause degranulation from mast cells and basophils so that it released chemical mediators such as histamine, prostaglandin, bradykinin, and arachidonic acid [16]. Histamine has a vital role in pathogenesis through the regelation of lymphocyte CD4+ Th cell differentiation. Histamine inhibition mechanism by antihistamine (AH) was blocking and driving away from its receptor [17]. Due to the inhibition of mast cell degranulation, so the secretion of vasoactive, lipid mediator and cytokine would be decreased. Antihistamine was long prescribed for

atopic dermatitis as an additional therapy with a topical agent that can inhibit the action of histamine in the skin [18].

The allergic reaction that occurs will form part of a board spectrum of adverse reaction to food, including microbe and chemical toxicity and the pharmacological effect caused by the metabolic error [19]. The primary allergen that responsible for the crosslink reactivation in between fish species was parvalbumin [20]. Figure 2A showed clinical symptoms of allergic contact dermatifis. The clinical signs related to the fish allergic such as urticaria, allergic contact of dermatifis, rhinoconjunctivitis, asthma, oral allergic syndrome, diarrhoea, or anaphylaxis [7].

Figure 2B showed the way of CFWC treatment in the wound of the skin caused by an allergy. CFWC treatment used coconut oil media so that charcoal could stick to the skin. The coconut oil function as moisturizer and cream in CSWC so it can be used as a cleaning or scrab [21].

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Figures 3A and 3B showed the treatment progression of CFWC in skin allergy. It showed that a satisfactory result because in 7 days of treatment has significantly improved in skin sores and texture. The additional of 0.01 M CaCl<sub>2</sub> and 200 mg NaNO<sub>3</sub> in 25 g charcoal could inhibit the

biodegradation by incidental bacteria. Charcoal was a new ingredient in the cosmetics world, which was currently popular in various parts of the world. It also claimed to bind sebum in the face to the pores due to the high adsorption power of charcoal [22]



Figure 3. (A) Skin after 3 days of treatment; (B) Skin after 7 days of CFWC treatment

Table 1 showed the highest ten compounds contained in CFWC such as octyl decyl phthalate, hexadecanamide, oleamide, cetrimonium, dibutyl phthalate, pyroquilon, stearamide, 6-methoxyquinoline, 8-hydroxyquinoline, and tridemorph. Hexadecanamide has the activity of anti-fungi *Fusarium moniliforme* in Ampupu (*Eucalyptus alba Reinw. Ex. Blume*) bark [23]. Oleamide has anti-

inflammation activity through the inhibition of NF-kappaB [24]. Dibutyl phthalate exhibited strong activity against gram-positive and negative bacteria, and also against unicellular and filaments fungi with no acute toxicity [25]. From some CFWC compounds showed the anti-fungi, antiinflammation, and anti-microbe activity.

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No	Name/Formula	2D	No	Name/Formula	2D
1.	Octyl decyl phthalate C <sub>26</sub> H <sub>42</sub> O <sub>4</sub>		6.	Pyroquilon C <sub>11</sub> H <sub>11</sub> NO	
2.	Hexadecanamide C <sub>16</sub> H <sub>33</sub> NO	<b>4</b>	7.	Stearamide C <sub>18</sub> H <sub>37</sub> NO	<b>4</b> 7
3.	Oleamide C18H35NO	• <b>~</b> ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	8.	6- Methoxyquinoline C10H9NO	<b>^</b> ©Ç
4.	Cetrimonium C <sub>19</sub> H <sub>42</sub> N+	·%	9.	8- Hydroxyquinoline C9H7NO	<u>ş</u> ç
5.	Dibutyl phthalate C <sub>16</sub> H <sub>22</sub> O4	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	10.	Tridemorph C <sub>19</sub> H <sub>39</sub> NO	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~

Table 1. Ten highest compounds contained in CFWC

Table 2 showed compounds contained in CFWC showed biological activity potential as anti-inflammatory, anti-pruritic, anti-allergic, and antiseptic. PASS Online predict

the probable profile of biological activity from organic compounds of drugs (with a range of molecular weight 50-1250 Da) based on the structural formula [26].

Table 2. Biological potential of 10 compounds in CFWC through PASS Online

No		Prediction of potential biological activities				
	Compounds	Antiinflammatory	Antipruritic	Antiallergic	Antiseptic	
1	Octyl decyl phthalate	0.481	0.584	0.584	0.566	
2	Hexadecanamide	0.472	0.505	0.505	-	
3	Oleamide	0.440	0.518	-	0.206	
4	Cetrimonium	-	-	-	-	
5	Dibutyl phthalate	0.461	0.574	0.238	0.522	
6	Pyroquilon	0.330	0.327	-	-	
7	Stearamide	0.472	0.505	-	0.264	
8	6-Methoxyquinoline	0.388	0.399	0.435	0.308	
9	8-Hydroxyquinoline	0.379	0.481	0.494	0.626	
10	Tridemorph	0.310	0.287	-	-	

The estimation was based on the analysis of the structureactivity correlation for a broad training set that involved the substances of the drug, drug-candidates in various stages of clinical and preclinical investigations, pharmaceutical agents, chemical probe, and compound for which specific toxicity information was known. Table 2 showed the compounds contained in CFWC have the potential effect as anti-allergy, anti-inflammation, antipruritic, anti-fungi, and anti-microbe. Therefore, the skin wound caused by the allergy can be healed after 7 days of CFWC (Figure 3A and 3B).

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#### CONCLUSION

CFWC can heal skin wounds due to the allergy of *Channa pleurophthalma* meat consumption. CFWC contains several bioactive compounds that potential as anti-allergy, anti-inflammation, anti-pruritic, anti-fungi, and anti-microbe.

#### CONFLICT OF INTEREST

All authors declared no conflict of interest.

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#### REFERENCES

- Wijayakusuma HMH. Tanaman berkhasiat obat di Indonesia. 1st ed. Jakarta: Prestasi Insan Indonesia; 1999. p. 174.
- Semiawan, F., Ahmad, I., & Masruhim, M. A. (2015). Aktivitas antiinflamasi ekstrak daun kerehau (Callicarpa Longifolia L.). *Jurnal Sains dan Kesehatan*, 1(1), 1-4. https://doi.org/10.25026/jsk.v1i1.7
- Costa-Neto, E. M. (2005). Animal-based medicines: biological prospection and the sustainable use of zootherapeutic resources. *Anais da Academia Brasileira de ciências*, 77(1), 33-43. https://doi.org/10.1590/S00013765200500010000
- Suprayitno, E., Nursyam, H., & Mustafa, A. (2013). Chemical Composition and Amino Acid Profile of Channidae Collected From Central Kalimantan, Indonesia. *IEESE International Journal of Science and Technology*, 2(4), 25.
- Liu, W., Li, G., Miao, Y., & Wu, X. (2009). Preparation and characterization of pepsin-solubilized type I collagen from the scales of snakehead (Ophiocephalus Argus). *Journal of food biochemistry*, *33*(1), 20-37. https://doi.org/10.1111/j.17454514.2008.00207.x
- Abbas, A. K., Lichtman, A. H., & Pillai, S. (2014). Basic immunology: functions and disorders of the immune system. Elsevier Health Sciences.
- Van Do, T., Elsayed, S., Florvaag, E., Hordvik, I., & Endresen, C. (2005). Allergy to fish parvalbumins: studies on the cross-reactivity of allergens from 9 commonly consumed fish. *Journal of Allergy and Clinical Immunology*, *116*(6), 1314-1320. https://doi.org/10.1016/j.jaci.2005.07.033
- Segerstrom, S. C., & Miller, G. E. (2004). Psychological stress and the human immune system: a metaanalytic study of 30 years of inquiry. *Psychological bulletin*, 130(4), 601.
- Lokapuspita, G., Hayati, M., & Purwanto, P. (2012). Pemanfaatan Limbah Ikan Nila Sebagai Fishbone Hydroxyapatite Pada Proses Adsorpsi Logam Berat Krom Pada Limbah Cair. *Jurnal Teknologi Kimia Dan Industri, 1*(1), 379-388.
- Amalia, V., Hadisantoso, E. P., Hidayat, D., Diba, R. F., Dermawan, M. F., & Tsaniyah, S. W. (2018). Isolasi dan Karakterisasi Hidroksiapatit dari Limbah Tulang Hewan. *ALCHEMY*, 5(4), 114-119. https://doi.org/10.18860/al.v5i4.4705
- Zhao, F., Yin, Y., Lu, W. W., Leong, J. C., Zhang, W., Zhang, J., ... & Yao, K. (2002). Preparation and histological evaluation of biomimetic three-

dimensional hydroxyapatite/chitosan-gelatin network composite scaffolds. *Biomaterials, 23*(15), 3227-3234.

- https://doi.org/10.1016/S01429612(02)00077-7
- Kim, S. K., & Mendis, E. (2006). Bioactive compounds from marine processing byproducts-a review. *Food Research International*, 39(4), 383-393. https://doi.org/10.1016/j.foodres.2005.10010
- Kottelat, M., Whitten, A. J., Kartikasari, S. N., & Wirjoatmodjo, S. (1993). Freshwater fishes of western Indonesia and Sulawesi.
- Alvarez, M. E., Pennell, R. I., Meijer, P. J., Ishikawa, A., Dixon, R. A., & Lamb, C. (1998). Reactive oxygen intermediates mediate a systemic signal network in the establishment of plant immunity. *Cell*, 92(6), 773-784.

https://doi.org/10.1016/S00928674(00)81405-1

- Loppies, J. E. (2016). Karakteristik arang kulit buah kakao yang dihasilkan dari berbagai kondisi pirolisis. Jurnal Industri Hasil Perkebunan, 11(2), 105-111.
- Roitt I, Brostoff J, Male D. Immunology. 2<sup>nd</sup> ed. London: Gower Medical Publ; 1990. p. 176-177.
- Molderings, G. J., Brettner, S., Homann, J., & Afrin, L. B. (2011). Mast cell activation disease: a concise practical guide for diagnostic workup and therapeutic options. *Journal of hematology & oncology*, 4(1), 10. https://doi.org/10.1186/1756-8722-4-10
- Tamura, T., Matsubara, M., Takada, C., Hasegawa, K., Suzuki, K., Ohmori, K., & Karasawa, A. (2004). Effects of olopatadine hydrochloride, an antihistamine drug, on skin inflammation induced by repeated topical application of oxazolone in mice. *British Journal of Dermatology*, 151(6), 1133-1142. https://doi.org/10.1111/j.13652133.2004.06172.x
- Bruijnzeel-Koomen, C. A. F. M., Ortolani, C., Aas, K., Bindslev-Jensen, C., Björkstén, B., Moneret-Vautrin, D., & Wüthrich, B. (1995). Adverse reactions to food. *Allergy*, *50*(8), 623-635.
- Hamada, Y., Tanaka, H., Ishizaki, S., Ishida, M., Nagashima, Y., & Shiomi, K. (2003). Purification, reactivity with IgE and cDNA cloning of parvalbumin as the major allergen of mackerels. *Food and chemical toxicology*, *41*(8), 1149-1156. https://doi.org/10.1016/S02786915(03)00074-7
- Widiyati, E. PEMBUATAN DAN KARAKTERISASI KRIM KOSMETIK DENGAN BAHAN BAKU MINYAK KELAPA DAN ARANG TEMPURUNG KELAPA (Doctoral dissertation, Universitas Gadjah Mada).
- Erdawati, E., & Suhartono, S. (2019). Pengaruh Massa Bio-char Kayu Akasia (Acacia mangium) Dan Waktu Perendaman Bio-char Terhadap Adsorpsi Sebum Buatan. Jurnal Riset Sains dan Kimia Terapan, 8(1), 37-44. https://doi.org/10.21009/JRSKT.081.05
- Metboki, B. (2018). Identifikasi Senyawa Aktif Kulit Batang Ampupu (Eucalyptus alba Reinw. Ex. Blume) dalam Menghambat Pertumbuhan Jamur Fusariummoniliforme. *Savana Cendana*, 3(01), 11-13. https://doi.org/10.32938/sc.v3i01.251
- 24. Oh, Y. T., Lee, J. Y., Lee, J., Lee, J. H., Kim, J. E., Ha, J., & Kang, I. (2010). Oleamide suppresses lipopolysaccharide-induced expression of iNOS and COX-2 through inhibition of NF-κB activation in BV2 murine microglial cells. *Neuroscience letters*, 474(3), 148-153.

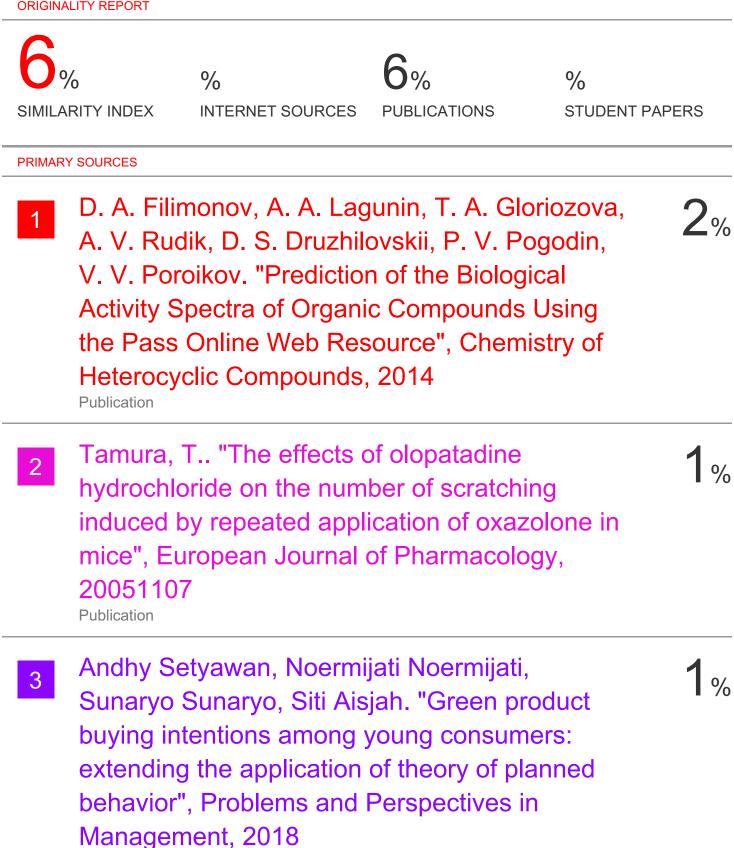
https://doi.org/10.1016/j.neulet.2010.03.026

Systematic Reviews in Pharmacy

- Roy, R. N., Laskar, S., & Sen, S. K. (2006). Dibutyl phthalate, the bioactive compound produced by Streptomyces albidoflavus 321.2. *Microbiological* research, 161(2), 121-126.
- https://doi.org/10.1016/j.micres.2005.06.007
  26. Filimonov, D. A. (2006). Forecast range of biologically active organic compounds/Filimonov DA, Poroikov VV. *Rus. Chem. journal, 50*(2), 66-75.

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- R.N. Roy, S. Laskar, S.K. Sen. "Dibutyl phthalate, the bioactive compound produced by Streptomyces albidoflavus 321.2",
   Microbiological Research, 2006 Publication
- 5 Van Do, T.. "Allergy to fish parvalbumins: Studies on the cross-reactivity of allergens from 9 commonly consumed fish", The Journal of Allergy and Clinical Immunology, 200512 Publication
- 6 Cong Thanh Nguyen, Min Yuan, Jing Song Yu, Tai Ye, Hui Cao, Fei Xu. "Isolation of ice structuring collagen peptide by ice affinity adsorption, its ice-binding mechanism and breadmaking performance in frozen dough", Journal of Food Biochemistry, 2018 Publication
  - Divyani Gandhi, Dinesh Kr. Agarwal, Priyanka Kalal, Amit Bhargava, Dinesh Jangid, Shikha Agarwal. "Synthesis, characterization and evaluation of novel benzothiazole clubbed chromene derivatives for their anti-inflammatory potential", Phosphorus, Sulfur, and Silicon and the Related Elements, 2018 Publication

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