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HASIL PENILAIAN SEJAWAT SEBIDANG ATAU PEER REVIEW
KARYA ILMIAH : JURNAL ILMIAH

Judul Karya Ilmiah (Artikel) : Morpological And Histological Effects Of Bruceina a On The Larvae Of Aedes Aegypti Linnaeus (Diptera : Culicidae)

Jumlah Penulis : 4 Orang (**Dwi Sutiningsih**, Mustofa, Tri Baskoro Tunggul Satoto, Edhi Martono)

Status Pengusul : Pertama dan Korespondensi

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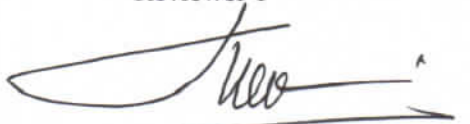
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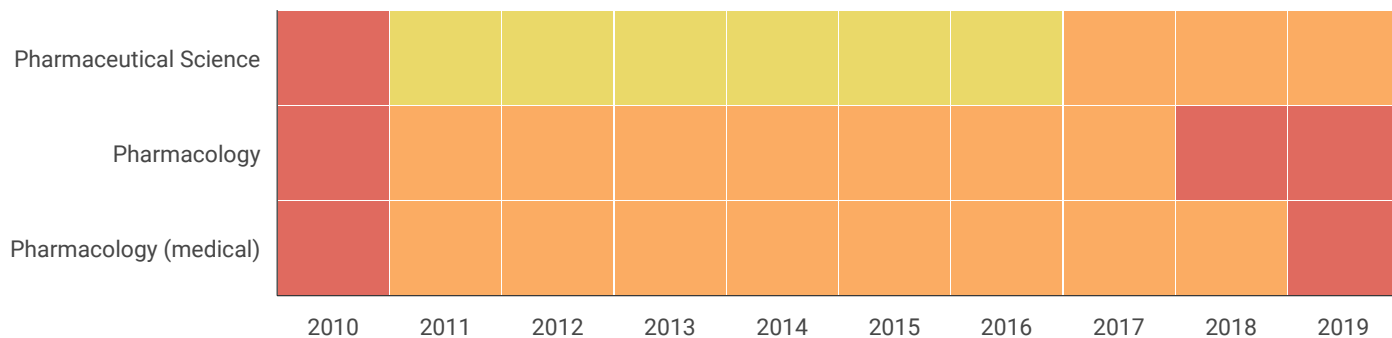
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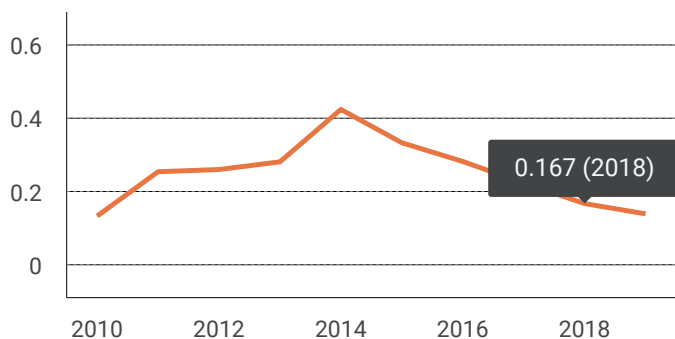
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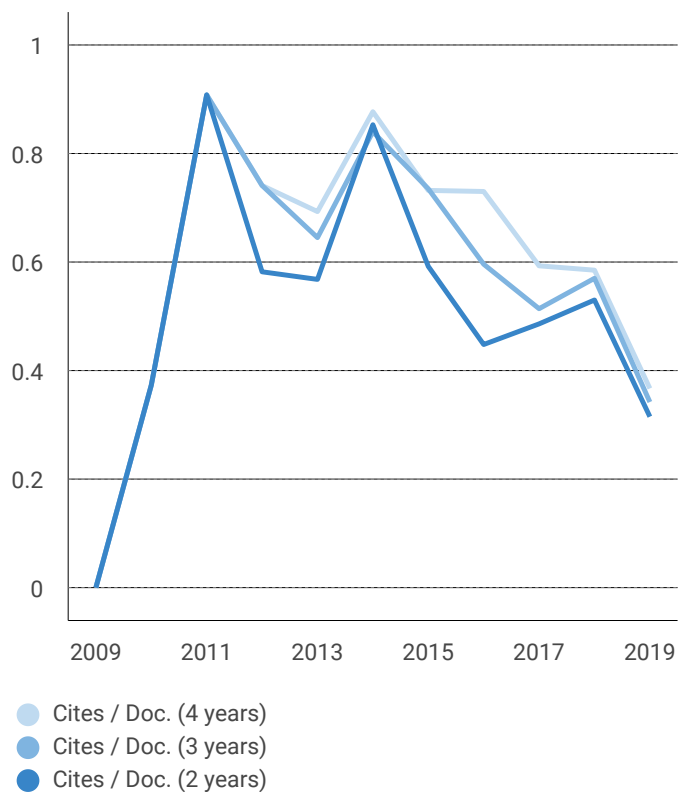
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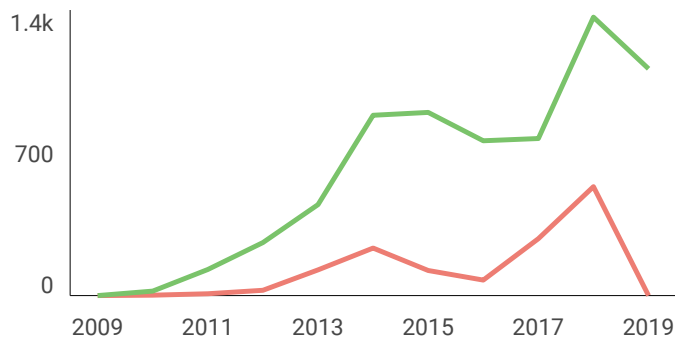
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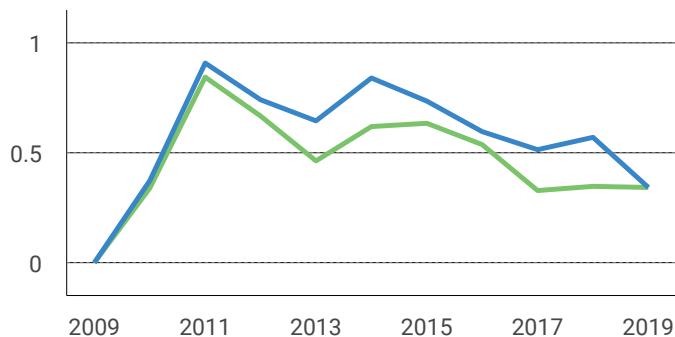
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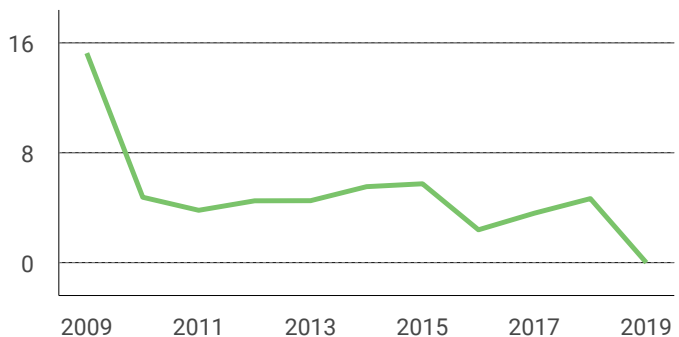
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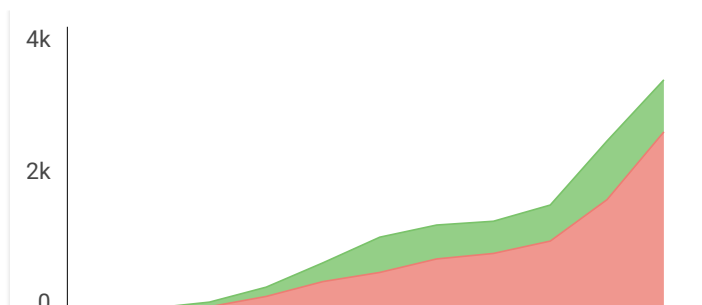


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MORPHOLOGICAL AND HISTOLOGICAL EFFECTS OF BRUCEINE A ON THE LARVAE OF AEDES AEGYPTI LINNAEUS (DIPTERA: CULICIDAE)

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ABSTRACT

Objective: This study aimed to determine a target of action of bruceine A on the basis of its morphological and histological effects on the larvae of *Aedes aegypti* Linnaeus.

Methods: Bruceine A was isolated from *Brucea javanica* (L.) Merr. seeds in accordance with the Mangungsong method. Larvae of *A. Aegypti* (L.) in instar III to the beginning of instar IV were treated with various concentrations of bruceine A. The negative control group did not receive any treatment, whereas the positive control group received 1 ppm temefos. Dead larvae were collected after 24 h of treatment for the examination of morphological and histological changes.

Results: The negative control group did not exhibit any morphological and histological changes. Larvae treated with bruceine A, however, had visible damaged heads, cuticles, digestive and respiration tracts,

EUCLEA CRISPA: REVIEW OF ITS BOTANY, ETHNOMEDICINAL USES, AND PHARMACOLOGICAL PROPERTIES**ALFRED MAROYI***Department of Botany, Medicinal Plants and Economic Development Research Centre, University of Fort Hare, Private Bag X1314, Alice 5700, **South Africa**. Email: amaroyi@ufh.ac.za

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ABSTRACT

Euclea crispa is widely used as herbal medicine in southern Africa. This study was aimed at reviewing the botany, ethnomedicinal uses, and validated pharmacological properties of *E. crispa*. The literature search for information on ethnomedicinal uses and pharmacological activities of *E. crispa* was undertaken using databases such as web of science, BMC, science direct, elsevier, scopus, PubMed, and scielo. Other relevant literature sources included books, book chapters, websites, theses, conference papers, and other scientific publications. The extensive literature survey revealed that the bark, fruits, leaves, and roots of *E. crispa* are commonly used as herbal medicines for wounds, constipation, cough, stomach disorders, epilepsy, rheumatism, and diabetes. Pharmacological studies on *E. crispa* indicate that the species has amyloid β -peptide lowering effects, antibacterial, antidiarrheal, antifungal, and cell membrane disruption activities. *E. crispa* should be subjected to further scientific evaluations aimed at elucidating its chemical, pharmacological, and toxicological properties. Such detailed research should also include experimental animal studies, randomized clinical trials, and target-organ toxicity studies involving *E. crispa* extracts and its derivatives.

Keywords: *Euclea crispa*, Ethnopharmacology, Indigenous knowledge, Southern Africa, Traditional medicine.

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INTRODUCTION

Euclea crispa (Thunb.) Gürke is a member of the Ebenaceae or ebony family, which is pantropical in distribution with 600 species [1]. Phylogenetic studies carried out by Duangjai *et al.* [2] showed that family Ebenaceae consists of two subfamilies, Lissocarpoideae and Ebenoideae, and four genera, *Diospyros* L., *Euclea* Murr., *Lissocarpa* Benth. and *Royena* L. The family Ebenaceae is a conspicuous forest component of tropical and subtropical areas of Africa and Asia, and a major source of several economically important products including timber (ebony) and edible fruits (persimmons) [2]. Ebenaceae is recognized by its fruits which appear such as little persimmons, often brownish, and seated on a persistent calyx [3]. A variety of constituents have been isolated and characterized from the family including naphthoquinones, terpenoids (especially lupanes, ursanes, oleananes, and taraxeranes), benzopyrones, polyphenols, and tannins [1]. The Ebenaceae family is characterized by the occurrence of 1, 4-naphthoquinonoid compounds, usually in dimeric forms, and often considered as taxonomic markers of the plant species belonging to this family [4,5]. At least 20 species of the Ebenaceae family are used as herbal medicines to expel intestinal worms and to treat and manage viral infections in the Asia Pacific region alone [3]. Some members of the Ebenaceae family are characterized by nutritious and delicious fruits which contain several bioactive phytochemicals such as tannins, proanthocyanidins, and flavonoids which impart a diverse array of pharmacological properties such as antioxidant activity, anticancer, antihypercholesterolemic, antidiabetic, cardioprotective, neuroprotective, antihypertensive, anti-skin whitening, and antiaging activities [6]. Some naphthoquinones are marketed as pharmaceutical drugs and health products, such as atovaquone which is used as an alternative agent for malaria and *Pneumocystis jirovecii* pneumonia infection [6].

E. crispa and five other *Euclea* species, namely *Euclea coriacea* A. DC., *Euclea divinorum* Hiern, *Euclea natalensis* A. DC., *Euclea racemosa* L., and *Euclea undulate* Thunb. are widely used as herbal medicines in southern Africa [7-9]. Research by several authors [10-15] showed that *E. crispa* is an important medicinal plant used by both rural and

urban communities throughout its native distributional range in southern Africa. According to Dlamini and Geldenhuys [16], *E. crispa* is regarded as a multipurpose plant species in Swaziland, popular for its edible fruits, different plant parts used as herbal medicines, fuelwood, charcoal, building material, and fences. *E. crispa* is used for dyeing mats and tanning leather in Malawi and South Africa [16,17], weaving baskets and as construction timber in South Africa [17,19]. According to Moteetee [20], *E. crispa* is mixed with *Alepidea cordifolia* L., *Brunsvigia radulosa* Herb., *E. coriacea* DC., and *Lobelia dregeana* and the mixture used for washing the divining bones to make them accurate. The fleshy part of the fruit is eaten by humans, birds, and animals, and the leaves and bark are eaten by game and livestock [11,17-30]. Leaves of *E. crispa* are used to brew an astringent medicinal tea often consumed as a tisane or herbal tea by the Khoi and San people of South Africa [31]. Bark, root, and stems of *E. crispa* are sold as herbal medicine in informal medicinal plant markets in the Gauteng province, South Africa [32]. It is within this context that the ethnomedicinal uses pharmacological activities of *E. crispa* were evaluated [33]. Therefore, this review is aimed at assessing if there is a correlation between the ethnomedicinal uses of *E. crispa* and documented phytochemical and pharmacological properties of the species. It is hoped that this ethnomedicinal and pharmacological information will highlight the value and importance of *E. crispa* as a potential source of a wide range of pharmaceutical products in southern Africa and will provide useful information to other researchers interested in the plant species.

BOTANICAL PROFILE AND TAXONOMY OF *E. UNDULATA*

E. crispa belongs to the Ebenaceae or Ebony family confined to Africa and Arabia, and in southern Africa, the family is represented by two genera, namely *Euclea* and *Diospyros* [17,34-40]. *Euclea* is a small genus of about 20 species, mostly trees, shrubs, or suffrutes with 16 of them recorded in southern Africa [39,41]. The genus name "*Euclea*" is derived from the Greek word "*eukleia*," which is derived from "*eu*" meaning "good," and "*kleios*" meaning report [42]. This is possibly in reference to the good quality wood of some *Euclea* species, particularly that of *Euclea pseudebenus* E. Mey. ex A. DC. [42]. The specific name is

PROTECTIVE EFFECT OF *CHLORELLA VULGARIS* ON DNA DAMAGE, OXIDATIVE STRESS, AND LUNG MORPHOLOGICAL CHANGES IN CIGARETTE SMOKE-EXPOSED RATS**ZAMRI KS¹, NORRIPIN MKN¹, DARUS FI¹, EKAMBARAM DG¹, ABDUL RAOF ND¹, ROSLAN NH¹, AHMAD F²,
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ABSTRACT**Objective:** The aim of this study was to determine the protective effect of *Chlorella vulgaris* (ChV), antioxidant-rich unicellular green alga, and in cigarette smoke-exposed rats.**Methods:** Male Sprague Dawley rats were divided into 4 groups: Control Group (C), ChV group (300 mg/kg body weight), cigarette smoke-exposed (S) group, and S group treated with ChV (S+ChV). Blood samples were drawn from the orbital sinus on days 0, 15, and 30 for the determination of DNA damage by Comet assay and plasma malondialdehyde (MDA) using high-performance liquid chromatography. Rats were killed on day 30, and lung tissue samples were taken for the evaluation of airspace enlargement and number of inflammatory cells.**Results:** Increased DNA damage (1004.8 au + 329.2, day 15; 1102.7 + 197.8, day 30) and high MDA levels (10.66 + 0.27, day 15; 10.29 + 0.9 day 30) were found in cigarette smoke-exposed rats on days 15 and 30 but were reduced significantly ($p < 0.05$) when treated with ChV (DNA: 482.6 + 223.3, day 15; 423.5 + 74.6, day 30 and MDA: 6.1 + 0.6, day 15; 6.6 + 2.5, day 30) for both days. Hematoxylin and eosin staining showed that cigarette smoke-exposed rats had high frequency of airspace enlargement and number of inflammatory cells which were reduced when treated with ChV.**Conclusion:** ChV has a protective role in cigarette smoke-exposed rats by reducing oxidative DNA damage, MDA levels, lung cells inflammation, and airspace enlargement.**Keywords:** *Chlorella vulgaris*, DNA damage, Malondialdehyde, Inflammatory cells, Airspace enlargement.© 2018 The Authors. Published by Innovare Academic Sciences Pvt Ltd. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>) DOI: <http://dx.doi.org/10.22159/ajpcr.2018.v11i10.26352>**INTRODUCTION**

Cigarette smoke consists of a complex and reactive mixture of harmful chemicals. Majority of these chemicals are hazardous to health and can cause chronic inflammatory lung diseases including chronic obstructive pulmonary disease (COPD) and respiratory related diseases including lung cancer [1]. The generation and accumulation of free radicals as a result of smoking and the imbalance between oxidants and antioxidants in our body may play a central role in the pathogenesis of smoking-induced airways diseases such as COPD and emphysema [2,3]. Cigarette smoke was shown to induce oxidative stress and apoptosis in human lung fibroblasts [4]. Polycyclic aromatic hydrocarbons, a carcinogenic agent found in cigarette smoke, intercalate between bases in DNA causing damage and initiate the carcinogenic process in lung cells [5]. Smoking was also found to increase the number of the goblet and inflammatory cells within the epithelium of peripheral airways causing chronic bronchitis and airflow limitation [6]. In addition, smoking can also cause airspace enlargement in a smoke-induced rat model [7]. Airspace enlargement is one of the pathogenesis of emphysema in COPD due to chronic lung inflammation that caused an imbalance between proteases and anti-proteases causing disruption of extracellular matrix, enhanced apoptosis and loss of alveolar units [8].

Alternative medicines have been the focus of recent research in ameliorating complications caused by cigarette smoking. Administration of Chinese green tea followed by cigarette smoke exposure ameliorated lung injury which was associated with decreased oxidative stress marker serum 8-isoprostane level, and an increase in lung antioxidant enzymes [9]. Banerjee *et al.* [10] have shown that cigarette smoke exposure to guinea pigs resulted in progressive protein damage,

inflammation, apoptosis, and lung injury. However, administration of Vitamin C (15 mg of Vitamin C/guinea pig/day) prevented the pathophysiological changes significantly. Koike *et al.* [11] showed that Vitamin C treatment on SMP30-KO mice after cessation of cigarette smoke exposure prevents emphysema as indicated by the pulmonary restoration. In addition, Vitamin C diminished oxidative stress, increased collagen synthesis, and improved vascular endothelial growth factor levels in the lungs. Tualang honey supplementation to smokers reduced plasma F2-isoprostane and increased total antioxidant status level as well as glutathione peroxidase and catalase activity, suggesting that honey reduced oxidative stress in smokers [12]. Broccoli intake was associated with increased protection against H₂O₂-induced DNA strand breaks and lower levels of oxidized DNA bases in peripheral blood mononuclear cells from smokers [13]. Muda *et al.* [14] have demonstrated that honey supplementation to cigarette smoke-induced rats reduced the number of macrophages in the interalveolar septa of lungs compared to smoke-induced rats. Carob aqueous extract given to rats exposed to water pipe smoke for 8 weeks showed protective effects in the liver and kidney functions as well as decreased malondialdehyde (MDA) and glutathione levels [15]. Nithya *et al.* [16] demonstrated that thymoquinone restored the damage caused by benzo[a]pyrene (found in cigarette smoke) in lung cancer induced Swiss albino mice.

Chlorella vulgaris (ChV) is a unicellular microalga which contains a wide variety of antioxidant compounds including beta-carotene, chlorophyll, alfa-tocopherol, ascorbic acid, lycopene, lutein, zeaxanthin, Vitamin C, and Vitamin E [17,18]. In streptozocin-induced diabetic rats, ChV was shown to reduce oxidative stress [19]. Patients with obstructive pulmonary disorders supplemented with 2.7 g/day of ChV had a low frequency of coughing, shortness of breath, wheezing, and coughed-out sputum. [20]