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

Judul Jurnal Ilmiah (Artikel) : Synthesis and antibacterial activity of epoxide from hyptolide (Hyptis pectinata (L.) Poit) against Gram-positive and Gram-negative bacteria

Jumlah Penulis : 5 orang (**Bambang Cahyono**, Meiny Suzery, Nur Dina Amalina, Wahyudi, Damar Nurwahyu Bima)

Status Pengusul : penulis ke-1

Identitas Jurnal Ilmiah :

- a. Nama Jurnal : Journal of Applied Pharmaceutical Science
- b. Nomor ISSN : 2231-3354
- c. Vol, No., Bln Thn : Volume: 10, Issue: 12, December, 2020, Pages: 013-022
- d. Penerbit : MediPoeia
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- g. Terindex : Scopus, Q2

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 Unit Kerja : Teknik Kimia FT UNDIP

Reviewer 1

Prof. Dr. Widayat, S.T., M.T.  
 NIP. 197206091998031001  
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12-04-2022

Jurnal termasuk dalam list predator merupakan alasan mengapa nilai diturunkan menjadi 30.

Penilaian sudah sesuai

DocuSigned by:

5D535F69BD8D411...

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Artikel ditulis lengkap dan sesuai template yang terdiri dari pendahuluan, metode hasil dan pembahasan serta referensi. Artikel berisi tentang ekstraksi senyawa aktif hypoteloida dari tanaman *Hyptis pectinata*. Bahan aktif dilakukan uji bakteri dan disampaikan dalam bentuk dokumen /foto uji anti bakterinya. Uji ANOVA yang disampaikan di method tidak ada sama sekali sebatas standar deviasi.

**2. Ruang lingkup dan kedalaman pembahasan:**

Ruang lingkup bahan alam. Pembahasan berisi tentang tentang senyawa aktif yang berperan dan disertai dengan literature pembanding dan control dari senyawa aktif

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Abstrak dan kesimpulan singkat, jumlah referensi cukup dan 90% referensi terkini

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**2. Ruang lingkup dan kedalaman pembahasan:**

Artikel sudah cukup mendalam kajiannya dari aspek molekular. Hipotesis kajian sudah dituliskan dengan jelas di pendahuluan. Metode sudah cukup jelas dituliskan termasuk merk dan tipe peralatan analisisnya. Pembahasan juga disupport oleh data-data penelitian yang mencukupi dari hasil karakterisasi dan analisis. Keterkaitan antar hasil karakterisasi dan dengan performance juga dikaji dengan baik. Simpulan juga cukup ringkas dan fokus.

**3. Kecukupan dan kemutakhiran data/informasi dan metodologi:**

Data-data yang menunjang hipotesis penelitian mencukupi dan mutakhir. Referensi artikel juga mencukupi dan mutakhir, dan sebagian besar dari literatur jurnal ilmiah

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Kualitas terbitan cukup bagus (level Q2 dg SJR: 0.25) dan CiteScore Scopus cukup tinggi: 1.4

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## Synthesis and antibacterial activity of epoxide from hyptolide (Hyptis pectinata (L.) Poit) against Gram-positive and Gram-negative bacteria [\(Article\)](#) [\(Open Access\)](#)

Cahyono, B.<sup>a</sup> [✉](#), Suzery, M.<sup>a</sup>, Amalina, N.D.<sup>b</sup>, Wahyudi<sup>a</sup>, Bima, D.N.<sup>a</sup> [👤](#)<sup>a</sup>Chemistry Department, Faculty of Sciences and Mathematics, Diponegoro University, Semarang, Indonesia<sup>b</sup>Pharmacy Study Program, Chemistry Department, Faculty of Mathematics and Natural Sciences, Universitas Negeri Semarang, Semarang, Indonesia

### Abstract

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Recently, drug resistance due to excessive use of antibiotics has become a severe problem, and alternative antibiotics' development has become an urgent problem. Epoxy hyptolide is a compound of the synthesis of hyptolide through the reaction using meta-chloroperoxybenzoic acid (mCPBA) oxidizer, potentially developed as a natural antibiotic. This study aimed to investigate the relationship between hyptolide and its epoxide structure on the antibacterial activity against Gram-positive and Gram-negative bacteria. The results indicated that epoxy hyptolide was a successful synthesis of hyptolide from the isolation of the leaves of Hyptis pectinata (L.) Poit using the mCPBA. The chemical characterization of hyptolide and its epoxidation revealed a melting point of 86.9°C–87.8°C and 79°C–80°C, respectively. The Fourier-transform infrared spectrum of epoxy hyptolide showed the presence of a lactone ring on wavenumbers 1,250 cm<sup>-1</sup> and 814 cm<sup>-1</sup>. On the other hand, a detailed 1H nuclear magnetic resonance spectrum of a chemical shift of 3.5 ppm indicated the presence of an oxygen ring due to the transformation of C=C olefin double bond into an epoxide form. Furthermore, the test of the antibacterial activity of hyptolide and epoxy hyptolide was carried out by disk diffusion method. The results revealed that hyptolide and epoxy hyptolide have a border antimicrobial spectrum in a dose-dependent manner. The maximum inhibition zone (IZ) of hyptolide was observed in Bacillus subtilis and the IZ was found to be 28.00 mm in comparison with amoxicillin as the control had 7.58 mm IZ. Interestingly, the most effective antibacterial activity in Salmonella typhi caused by the presence of epoxy hyptolide with the maximum IZ was 21.80 mm, compared to amoxicillin that had 6.320 mm IZ. It can be concluded that Gram-negative bacteria was more susceptible to epoxy hyptolide in comparison to hyptolide. The cell wall structure of the Gram-positive and Gram-negative bacteria could be the main reason for the bacteria's susceptibility. © 2020 Bambang Cahyono et al. This is an open access article distributed under the terms of the Creative Commons Attribution 4.0 International License

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Topic: Mesosphaerum Pectinatum | Hyptis | Caryophyllene

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(2019) *IOP Conference Series:  
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Antiproliferative and apoptosis  
effect of hyptolide from hyptis  
pectinata (L.) poit on human  
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Suzery, M. , Cahyono, B. ,  
Amalina, N.D.  
(2020) *Journal of Applied  
Pharmaceutical Science*

α-Pyrone and a 2(5H)-furanone  
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- **Prof. Srinivas Mutalik**, has joined as new Editor-in-chief from Dec, 20 onwards.

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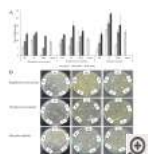


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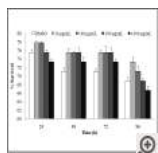


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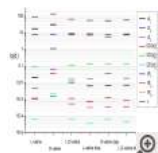


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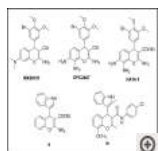


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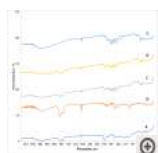


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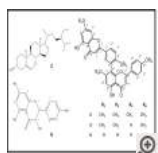


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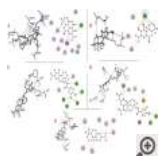


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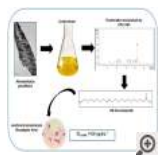


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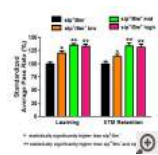


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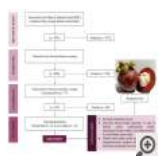
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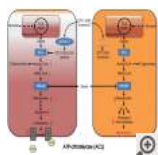


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DOI: [10.7324/JAPS.2020.101217](https://doi.org/10.7324/JAPS.2020.101217) Pages: 130–139[\[Abstract\]](#) [\[Full Text PDF\]](#) [\[XML: Abstract + References\]](#)**Review Article: Pharmacology activities and extraction of  $\alpha$ -chitin prepared from crustaceans: A review**

Renny Amelia, Nyi Mekar Saptarini, Eli Halimah, Yuli Andriani, Aliya Nurhasanah, Jutti Levita, Sri Adi Sumiwi

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# Synthesis and antibacterial activity of epoxide from hyptolide (*Hyptis pectinata* (L.) Poit) against Gram-positive and Gram-negative bacteria

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## ARTICLE INFO

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### Key words:

*Hyptis pectinata* (L.) Poit, mCPBA epoxidation, hyptolide, Gram-positive and Gram-negative bacteria.

## ABSTRACT

Recently, drug resistance due to excessive use of antibiotics has become a severe problem, and alternative antibiotics' development has become an urgent problem. Epoxy hyptolide is a compound of the synthesis of hyptolide through the reaction using meta-chloroperoxybenzoic acid (mCPBA) oxidizer, potentially developed as a natural antibiotic. This study aimed to investigate the relationship between hyptolide and its epoxide structure on the antibacterial activity against Gram-positive and Gram-negative bacteria. The results indicated that epoxy hyptolide was a successful synthesis of hyptolide from the isolation of the leaves of *Hyptis pectinata* (L.) Poit using the mCPBA. The chemical characterization of hyptolide and its epoxidation revealed a melting point of 86.9°C–87.8°C and 79°C–80°C, respectively. The Fourier-transform infrared spectrum of epoxy hyptolide showed the presence of a lactone ring on wavenumbers 1,250 cm<sup>-1</sup> and 814 cm<sup>-1</sup>. On the other hand, a detailed <sup>1</sup>H nuclear magnetic resonance spectrum of a chemical shift of 3.5 ppm indicated the presence of an oxygen ring due to the transformation of C=C olefin double bond into an epoxide form. Furthermore, the test of the antibacterial activity of hyptolide and epoxy hyptolide was carried out by disk diffusion method. The results revealed that hyptolide and epoxy hyptolide have a border antimicrobial spectrum in a dose-dependent manner. The maximum inhibition zone (IZ) of hyptolide was observed in *Bacillus subtilis* and the IZ was found to be 28.00 mm in comparison with amoxicillin as the control had 7.58 mm IZ. Interestingly, the most effective antibacterial activity in *Salmonella typhi* caused by the presence of epoxy hyptolide with the maximum IZ was 21.80 mm, compared to amoxicillin that had 6.320 mm IZ. It can be concluded that Gram-negative bacteria was more susceptible to epoxy hyptolide in comparison to hyptolide. The cell wall structure of the Gram-positive and Gram-negative bacteria could be the main reason for the bacteria's susceptibility.

## INTRODUCTION

*Hyptis pectinata* (L.) Poit is a family Lamiaceae plant that can be found in tropical areas such as Brazil, Mexico, India, and Indonesia. This plant popularly known in northeast Brazil as “sambacaita” or “canudinho” is an aromatic herbaceous plant clustered in axillary inflorescences with small bilabial flowers (Basílio *et al.*, 2006; Franzotti *et al.*, 2001). In Indonesia, *Hyptis*

*pectinata* has not been cultivated, but it grows wild and is underutilized by the community (Suzery *et al.*, 2012). The plant has a lot of chemical compounds and biological activities as reported earlier (Luzuriaga-Quichimbo *et al.*, 2018; Suzery *et al.*, 2020). The phytochemical content of *Hyptis pectinata* generally has a skeleton of  $\alpha$ ,  $\beta$ -unsaturated lactones, such as hyptolide compounds (Achmad *et al.*, 1987), pectinolides A-C, sambacaitaric acid, rosmarinic acid (Falcao *et al.*, 2013), pectinolides D-G (Boalino *et al.*, 2003), and spicigerolide (Almtorp *et al.*, 1991). The discovery of  $\alpha$ ,  $\beta$ -unsaturated lactones is an interesting study because of its potential effect as antinociceptive, anti-inflammatory (Franzotti *et al.*, 2001), antileishmanial (Falcao *et al.*, 2013), antimalarial (Melo *et al.*, 2006), antibacterial (Santos *et al.*, 2008), and anticancer (Asy

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## The new two-dimensional light scattering method for recognition of pharmaceutical enantiomers

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#### Key words:

Distinction of optical antipodes, two-dimensional light scattering, valine, glucose.

### ABSTRACT

The results of applying the developed mathematical model of the folding of two-dimensional light scattering (2D-LS) patterns into a descriptor to identify the enantiomers of optically active pharmaceutical substances are presented in the article. The following pharmaceutical substances were a subject of this research: L-valine, D-valine, racemic mixture L, D-valine, L-glucose, D-glucose, and L-ascorbic acid. A digital microscope with high spectral density was used to obtain instant 2D-LS patterns. The obtained data were mathematically processed using the original computer program "Vidan", which uses a mathematical model for the folding of the 2D-LS pattern into descriptors, which are analogs of topological indices in quantitative structure-activity correlations approaches to drug analysis. The 10 descriptors were used as criteria for the difference in the 2D distribution of the scattered light intensity. The use of mono- and multidescrptor analyses allowed us to determine the authenticity of pharmaceutical substances of different classes and their optical isomers. It was found that the dispersion of crystalline substances of optical antipodes up to submicron size led to the leveling of light scattering patterns. The mathematical model was developed and applied for the folding of 2D-LS diagrams into a descriptor. This allowed us to identify the optical antipodes of pharmaceutical substances.

### INTRODUCTION

About 40% of finished dosage forms contain chiral pharmaceutical substances, and only a quarter of them are individual enantiomers (Calcatera and D'Acquarica, 2018). As a rule, the pharmacological activity of chiral substances is limited by one of the enantiomers – the eutomer. In some cases, the inactive enantiomer (distomer) can cause unwanted side reactions and even toxicity. The ballast nontoxic enantiomer that undergoes biotransformation exerts an additional burden on the body.

The pharmacy domain that has been actively developed during the last decade is associated with the creation of enantioselective drugs from already known racemic substances (Challener, 2016; McConnell *et al.*, 2007). This so-called "chiral switching" allows the eutomer to be registered as a

new drug. Reducing the development time of a chiral drug largely depends on the efficiency of determining the absolute configuration and the enantiomeric purity of a substance (Calcatera and D'Acquarica, 2018). In scientific research and the pharmaceutical industry, the X-ray crystallography, nuclear magnetic resonance, enantioselective chromatography, vibrational circular dichroism, and polarimetry are used for the recognition and separation of enantiomers (Sangamithra *et al.*, 2019). It was proposed to create the tool kit "Chiral Technology" as a set of methods for determining the absolute stereochemistry and enantioseparation of chiral molecules (McConnell *et al.*, 2007). The need for pure enantiomers requires the selection of the most cost-effective method of analysis, as well as the expansion of the bank of chiral instruments (Challener, 2016). The search for new reliable systems for the recognition of optical isomers is expanding. It should be directed toward methods of identification without destruction and preliminary sample preparation of a pharmaceutical substance.

These criteria are met by the method of two-dimensional dynamic light scattering (2D-LS) using the developed device and original software (Lesnikov *et al.*, 2016).

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## Synthesis and cytotoxic evaluation of novel chromenes and chromene(2,3-d)pyrimidines

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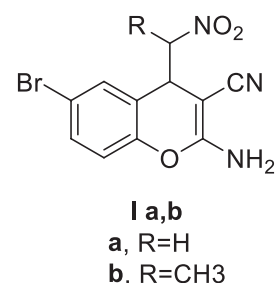
Tetrahydrochromenes, chromene(2,3-d)pyrimidines, chromenotriazolopyrimidine, pyrimidines, triazolopyrimidine, cytotoxic activity.

### ABSTRACT

The synthesis of novel compounds starting from 2-amino-8-(2-chlorobenzylidene)-4-(2-chlorophenyl)-5,6,7,8-tetrahydro-4*H*-chromene-3-carbonitrile **2** has been studied. Diarylidene cyclohexanone reacts with malononitrile to afford compound **2**. Compound **2** reacts with benzoyl chloride to afford compound **3**. *N*-(8-(2-chlorobenzylidene)-4-(2-chlorophenyl)-3-cyano-5,6,7,8-tetrahydro-4*H*-chromen-2-yl)benzamide **3** reacts with acetic anhydride to afford compound **4**. Compound **2** reacts with acetic anhydride to afford 9-(2-chlorobenzylidene)-5-(2-chlorophenyl)-2-methyl-3,5,6,7,8,9-hexahydro-4*H*-chromeno[2,3-*d*]pyrimidin-4-one **5**. Chromene derivative **2** reacts with formic acid to give compound **6**. Compounds **4–6** react with phosphorus oxychloride to give compounds **7a–c**. Chromeno[2,3-*d*]pyrimidine derivatives **7a–c** react with hydrazine hydrate to afford compounds **8a–c**. Chromeno[2,3-*d*]pyrimidine derivatives **8a,b** react with xylose and glucose to give compounds **9a–d**. Chromeno[2,3-*d*]pyrimidine derivatives **9a–d** react with acetic anhydride to give compounds **10a–d**. Screening of most of the synthesized compounds against A-549, CaCo-2, and HT-29 cell lines were done. 2-Amino-8-(2-chlorobenzylidene)-4-(2-chlorophenyl)-5,6,7,8-tetrahydro-4*H*-chromene-3-carbonitrile **2** gives high cytotoxic activity against A-549 and HT-29 cancer cell lines as compared to doxorubicin as the reference drug.

### INTRODUCTION

Chromenes have recently gained the attention of many researchers due to their various applications. Chromene derivatives have shown different remarkable biological activities against various targets. 4-Substituted-4*H*-chromenes have shown significant anticancer activity (Aridoss *et al.*, 2012). Also, 4-substituted-4*H*-chromenes have anticoagulant activity (Bonsignore *et al.*, 1993) and are used as regulators of the potassium cation channel (Jin *et al.*, 2004). 2-Amino-6-bromo-4-(nitromethyl)-4*H*-chromene-3-carbonitrile (**Ia**) and 2-amino-6-bromo-4-(1-nitroethyl)-4*H*-chromene-3-carbonitrile (**Ib**) have afforded good cytotoxic activity with IC<sub>50</sub> < 4 µg/ml and they have activity four times more than the standard drug Etoposide (Zonouzi *et al.*, 2013).



In addition, 4*H*-chromene derivatives have shown spasmolytic, diuretic, anticoagulant, and antianaphylactic activities (Ghorbani-Vaghei *et al.*, 2011). 4*H*-Chromene derivatives bind to the Bcl-2 protein and initiate apoptosis in cancer cells. The Bcl-2 protein improves neoplastic cell proliferation by preventing normal cell turnover. Increasing Bcl-2 gene expressions are present in many types of human cancers and can result in cancer cell resistance to chemotherapy and radiotherapy. Therefore, Bcl-2 protein-binding compounds are promising compounds as anticancer agents (Ghorbani-Vaghei *et al.*, 2011).

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