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Posted Date: 9 May 2025

doi: 10.20944/preprints202505.0693.v1

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## Article

# Functional Beverage Made with the Seaweed *Caulerpa racemosa*: Antioxidant and Pharmacokinetic Properties

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**Abstract:** The potential of seaweed as a source of bioactive compounds including antioxidants made it a versatile form of ingredient that can be incorporated directly or indirectly in the preparation of foods and beverages. Antioxidant constituents are important in managing and regulating oxidative stress and protecting the human body from severe adverse effects due to the excess release of free radicals or reactive oxygen species that promote the onset of chronic diseases. This study aimed to make a functional beverage containing 20 – 30% *Caulerpa racemosa* (seaweed), and identify phytochemicals using GC–MS, determine the antioxidant activity, molecular and drug likeness of the identified compounds. Data showed that the total phenolic content of the juice made with 30% seaweed was  $32.2 \pm 0.5$  µg/GAE, vitamin C  $2.9 \pm 0.1$  µg/mL while the antioxidant activity (DPPH IC<sub>50</sub>) was  $46.8 \pm 3.3$  mg/mL. Twenty compounds were identified of which three met the Lipinski's rule of five. They were then docked with five enzymes involved in oxidative stress and inflammation (cytochrome P450, lipoxygenase, myeloperoxidase, NADPH oxidase, and Xanthin oxidase). Their binding energies ( $\Delta G$ : – 4.1 to – 6.3 Kcal/mol) were comparable to those of known commercial binders ( $\Delta G$ : – 5.0 to – 7.3 Kcal/mol) of each enzyme. Pharmacokinetic analyses showed excellent scores for the three compounds in regard to bioavailability, human intestinal absorption, and blood brain barrier. The sensory test value of the juice showed good odor, taste, and color, with a score between 4.7– 5.9. Overall, the functionalized juice displayed properties that make it potentially useful in the reduction of oxidative stress are related conditions, although in-vivo studies are needed.

**Keywords:** antioxidant; *Caulerpa*; juice; phytochemicals; pharmacokinetic; green algae

## Introduction

Oxidation and reduction reactions are fundamental metabolic processes for all living organisms [Silva et al., 2010]. They produced free radicals which serve as signaling molecules and contribute the immune system. Meanwhile, imbalances between the production of oxidants and the antioxidant defense system lead higher concentrations reactive oxygen/nitrogen species (ROS/RNS) and subsequent damages to tissues and biomolecules, including lipids, DNA, and proteins. Higher ROS/RNS (i.e., oxidative stress) plays an important role in human diseases such as cancer, asthma,

respiratory diseases, cardiovascular dysfunction, atherosclerosis, and diabetes [Silva et al. 2010; White et al., 2014; Yun et al., 2015.].

The use of seaweeds as a food and as complementary medicine is found in archaeological data from about ten thousand years ago (Ganesan et al., 2019). There is a growing interest in the study of bioactive compounds from seaweed as they can play a therapeutic role in disease prevention in humans. Seaweeds contain polysaccharides, carotenoids, C-phycocyanin, fatty acids, and polyphenols (Pramboon et al., 2018, Debbarma et al.) have documented biological properties that could make them useful for the development of functional foods and nutraceuticals. Activities reported for seaweed bioactive compounds include antioxidant, antimicrobial and anticoagulant properties. Seaweeds and their extracts (e.g., phycobiliproteins, alginates) have been used for example, in functionalized foods to increase iron status and maintain higher hemoglobin in human (<https://doi.org/10.1016/j.fshw.2015.03.001>; Sumayaa, S., & Kavitha, K. (2015). Preparation of novel seaweed recipes and standardization for the human consumption. *International Journal of Advanced Research*, 3(10), 159-167). Phycobiliproteins are also used as food colorants (<https://www.mdpi.com/2304-8158/9/2/244#>). A common property of the functionalized seaweed products or their extracts is their capacity to act as antioxidant which prevents damage of biomolecules and improves their functions or prolongs the shelf life of food.

Amongst the seaweeds (family Caulerpaceae), the genus *Caulerpa* is made of green algae including *C. racemosa* that is edible as also known as sea grapes (Maximo et al., 2018). Previous *C. racemosa* exhibits DPPH radical scavenging activities and antioxidant and cytotoxic activities against breast cancer (Sanger et al., 2023).

Juice is a favorable beverage to be functionalized with antioxidants and other bioactive compounds. Drinks made from seaweeds are very rare in the market because of their *fishy* flavor. Innovative processes are required to increase their acceptability. One way to achieve this is include fruits that are common in the marketplace. pineapple (*Ananas comosus*) and citrus lemon (*Citrus arantifolia*) will significantly reduce *fishy* flavor. Pineapple (*Ananas comosus*) and citruslemon (*Citrus arantifolia*) available in tropical regions are well accepted by consumers because of their attractive colors, pleasant flavors, and aroma. Like many fruits, they have nutritional properties and biological properties (e.g., antitumor, antioxidant, antimicrobial) attributed to their phytochemicals (Loizzo et al., 2021; Yapo et al., 2011).

A functionalized seaweed drink or juice with acceptable sensory properties and a biological activity like antioxidant will be novel. The antioxidant activity can be using model systems or biological systems. The molecules can regulate the activity of antioxidant enzymes as well as scavenge free radicals through proton/electron donation, and metal chelating. Some metabolic enzymes, such as cytochrome P450 (CYP450), lipoxygenase (LO), myeloperoxidase (MP), NADPH oxidase (NO), and xanthine oxidase (XO), are known to generate excess ROS under stimuli conditions with ageing leading to redox imbalance and increased risks of chronic diseases [Dharmaraja et al., 2017]. The development of functionalized food or drink that control the activities of these metabolic enzymes will therefore maintain redox balance and health. Computational modeling is useful to study the interaction between enzymes, bioactive compounds or receptors and bioactive compounds before further studies.

Various studies have highlighted the significance of molecular docking studies in identifying novel therapeutic targets for antioxidant compounds, as well as in the prediction of their antioxidant properties (Gupta et al., 2018; Costa et al., 2021). Other works have demonstrated the usefulness of computation to predict absorption, distribution, metabolism and excretion of active compounds as these factors are important to achieve a meaningful biological function.

In this study, *C. racemosa* was used as a functional antioxidant ingredient to formulate and characterize a juice. The pharmacokinetics of the identified compounds and their mechanism to modulate the activity of redox enzymes were investigated using in-silico or computational models.

## Material and Method

### *Collection and Identification of Seaweed*

Fresh *C. racemosa* were collected from Manado district water from May to June 2023. The plant specimen was authenticated by Prof. Dr. Grevo Gerung, M.Sc, Head of Seaweed Anatomy Research Center, Sam Ratulangi University, Manado City. The seaweed was washed under running tap water and rinsed with distilled water. The seaweed was chopped into small pieces and shade-dried for one week for complete dryness. The dried seaweed was ground into a fine powder using a mechanical grinder. The powdered material was stored in airtight containers until further use.

### *Preparation C. racemosa Juice*

**Formulation** The seaweed juice was treated with treatment: mixing of seaweed with pineapple for comparison: A1: 70:30%, A2: 75:25%, and A3: 80:20%. Concentration of Sugar are 65% and lemon citrus 10%. **Preparation raw material:** The Fresh seaweed was washed with running tap water, rinsed in fresh water, then it was poured with juice of citrus lemon 5% to diminish the fishy odor, and that it was rinsed with distilled water. The seaweed was then cut into small pieces and shade-drained for 2 h to achieve complete dryness. In addition, the pineapple was peeled, cleaned with fresh water and distilled water, and then sliced. Seaweed and pineapple materials were stored in a refrigerator to maintain freshness for further use. **The procedure to make 3 formula of Juice (A1, A2, and A3):** First, seaweed and pineapple were mixed with comparison: A1: 70: 30 %, A2: 75:25%, and A3: 80:20 %. Then, each mixture of A1, A2, and A3 was blended, and then each dough of A1, A2, and A3 was poured with sugar 65 %, then and cooked for 15 min, after which, each dough of A1, A2, and A3 was added with citrus lemon 10%, then boiled for 5 min. Finally, juices A1, A2, and A3 were placed in sterile bottles and stored at 5°C. The juice product that will be consumed and also analyzed was a token of 20 ml of juice and dissolved in 100 mL water. Analysis of juice quality consisted of sensory tests (odor and taste value), Total Phenolic Content, fiber content, vitamin C content, DPPH free radical scavenging activity, and pH value.

### *Preparation of C. racemosa Extract*

Approximately 50 g of the dried samples was separately weighed, soaked, and dissolved in 500 ml of ethanol in a 1000-ml conical flask and placed at room temperature for approximately 24 h. The maceration was replaced three times at room temperature. The extract was filtered through Whatman no. 1 filter paper and concentrated using a rotary vacuum evaporator (40°C). The final extracts, in the form of concentrated paste, were used for further studies.

#### 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging activity assay

The DPPH-scavenging capacity of the extracts was determined based on their ability to scavenge stable DPPH radicals using the method described by Sanger et al. (2021). In brief, 2 ml 0.93 M DPPH was mixed with the extract (0.5 ml) at various dilutions. The mixture was then vortexed and incubated at room temperature for 20 min. A spectrophotometer (Shimadzu type 1240, Tokyo, Japan) was used to measure absorbance at 517 nm. The experiment included vitamin C as a positive control. Antioxidant activity was quantified as a percentage of reduction DPPH radicals.

### *Total phenolic content (TPC)*

The TPC of the extracts was measured using the Folin–Ciocalteu reagent, according to Sanger et al. (2019). Briefly, 75% of Folin–Ciocalteu's phenol reagent (1 ml) was added to 0.1 ml of extract (0.1 g dry sample in 10 ml methanol) and vortexed. Then, After adding 1 ml of 7% Na<sub>2</sub> CO<sub>3</sub>, the solution was incubated for 30 min at room temperature. A spectrophotometer (Shimadzu type 1240, Tokyo, Japan) was used to measure absorbance at 750 nm. TPC is expressed as µg gallic acid equivalent (GAE)/g extract.



### *Sensory Analyses*

The hedonic Rating difference test on flavor and odor of formulated juices was performed using the method of Choi (2014) with modifications. Briefly, the hedonic test was performed using 70 randomly examined panelists. The rating test using 7 scale hedonic (1-7) with categorized scale 1 is amat sangat tidak suka and Scale 7 is amat sangat suka.

### *Fiber Content of Formulated Juices*

The fiber content was determined using the standard AOAC method (1995). Fiber content was quantified in 2-g samples previously boiled with diluted H<sub>2</sub>SO<sub>4</sub> (0.3 N). The mixture was filtered and washed with 200 mL boiling water and NaOH (0.5 N). The residue was re-extracted, washed with boiling distilled water and acetone, and finally dried at 105 °C to constant weight. The material was heated at 550 °C for 3 h and its weight was recorded (Praiboon et al., 2018 ).

### *Vitamin C content of Formulated Juices*

Vitamin C content was determined by high-performance liquid chromatography (HPLC) using the Sawant Method with modifications. The vitamin content was determined in triplicate for each seaweed sample and expressed as mg/g of DW seaweed ((Rosemary et al., 2010),

### *Gas Chromatography-Mass Spectrometry (GC-MS) Analysis*

GC-MS analysis of the ethanol extract of *C. racemosa* was performed using GC-MS by the Zong method (Model: GC MS—QP 2010, Shimadzu, Japan) equipped with a VF-5 ms fused silica capillary column of 30 m length, 0.25 mm diameter and 0.25 µm film thickness. For GC-MS analysis, an electron ionization system with an ionization energy of 70 eV was used. The carrier gas used was Helium (99.9%), at a constant flow rate of 1.2 ml/min. injector and mass transfer line temperatures were set at 280 °C and 255 °C, respectively. The oven temperature was set from 50 to 250 °C at 10 °C/min for 5 min and then raised to 300 °C for 10 min. Two microliters of the sample were injected in split mode with a scan range of 50–1000 m/z. The total running time of GC-MS was 49 min. The relative percentage of each component was calculated by comparing with the average peak area normalization value.

### *In Silico Studies*

#### *Ligand and Target Protein Selection*

From the GC-MS analysis of the ethanol extract of *C. racemosa*, 42 compounds were identified. All compounds were analyzed. Compounds were retrieved from the PubChem database (<https://pubchem.ncbi.nlm.nih.gov/>), and used in this study. Five enzymes (receptors) that respond for the production of reactive oxygen species (ROS) during the metabolism, cytochrome P450 (CP450), lipoxygenase (LO), myeloperoxidase (MP), NADPH oxidase (NO) and xanthine oxidase (XO) were selected and obtained from the Protein Data Bank (PDB) <http://www.rcsb.org/pdb/>. the UniProt ID of this target protein was CP40 (ID:1OG5 (ID LO), 1N8Q (ID MP) IDNU (ID NO); 2CDU3NRZ(IDXP)

#### *Pharmacokinetic Properties*

The ADMET properties were tested using SMILE ADMET (Daina et al., 2017). The Profil Pharmacokinetic profile of the ligand was retrieved from <http://www.scfbio-iiitd.res.in/software/drugdesign/lipinski.jsp#anchortag>. Compounds that obey Lipinski's rule were further screened using molecular docking and simulation studies.

#### *Molecular Docking dan Visualisasi*

Docking study performed using Yasara application. and the ligand preparation was optimized using Yasara. The target protein was prepared using the Biovia Discovery Studio 2020. The results were analyzed using BIOVIA Discovery Studio Visualizer 2020 (Systèmes, 2020). Arrangement grid-box for molecular docking with distance <4.5 to know the active site of the receptor and the ΔG dan RMSD dari reseptor dan native ligan

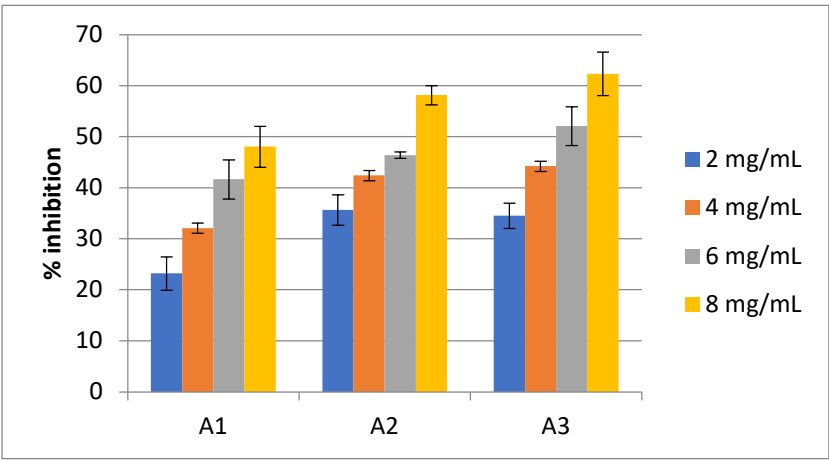
Result and Discussion

Juice of Seaweed

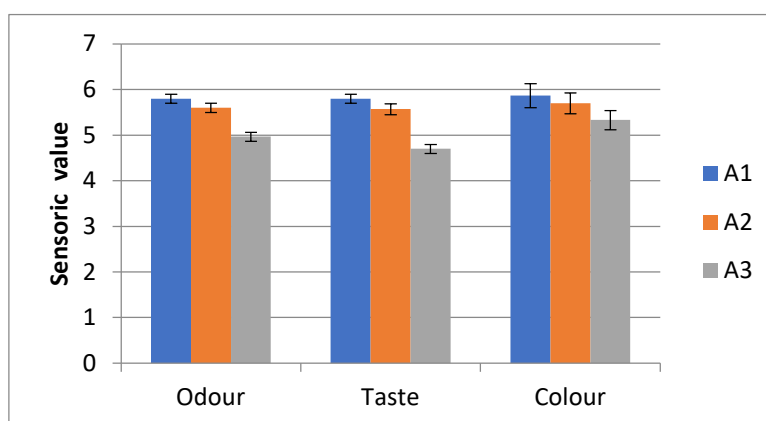
The chemical composition, antioxidant activity, and sonsoric value of juice *C. Racemosa* (A1,A2, and A3) are displayed in **Table 1 and Figure 1and 2**. The range of each quality test consisted of: odour value of 4.97±0.26 - 5,8±0,1; taste value of 4,47-5,58, color value of 5,33±0,21-5,867±0.1; Total Phenolic content of 31.7723±0,141 – 32.1788± 0,509 (µg GAE/g), Fiber content of 0,80±0.04 - 0,94±0.03 %, vitamin C content of 2.7953±0,049 – 2.8923 ±0,076 µg/mL, DPPH free radical scavenger activity of IC<sub>50</sub> 46.75±3,254- 97.55296±8.638 mg/mL dan nilai pH 4.47±0,379 – 4.57±0,115.

**Table 1.** Total phenolic Content (TPC), fiber, Vitamin C, and pH value of juice of *C. racemosa* which is mixed with pineple 70:30 (A1) ,75:25 (A2), and 80:20 % (A3).

Juice	TPC (µg GAE/g)	Fiber (%)	Vitamine C (µg/mL)	pH value
A1	32,1788±0,509	0,80±0,04	2,8923±0,076	4.47±0,379
A2	31,7723±0,141	0,84±0,01	2,7953±0,049	4.57±0,115
A3	31.8646±0,616	0.94±0,03	2.8215±0,048	4.5±0,172



**Figure 1.** DPPH free radical scavenger (2, 4, 6 and 8 mg/mL) of juice of *C. racemosa* which is mixed with pineple 70:30 (A),75:25 (B) and 80:20% (C).



**Figure 2.** Sensoric value (odour, taste and color) of juice of *C. racemosa* which is mixed with pineapple 70:30 (A1), 75:25 (A2) and 80% (A3).

Juice of *C. racemosa* mixed with pineapple (*Ananas comosus*) and Citrus lemon (*Citrus arantifolia*) eliminated the fishy flavor, in addition to increasing the nutritive value and biological activity. *C. arantifolia* is a rich source of ascorbic acid and other bioactive compounds, such as coumarins, carotenoids, limonoids, and flavonoids (in particular, polymethoxylated flavones and flavanones). Citrus flavonoids have been found to possess a wide range of activities that act as free radical scavengers, modulate enzymatic activities, inhibit cellular proliferation, and possess antibiotic, anti-allergenic, anti-diarrheal, anti-ulcer, and anti-inflammatory activities (Lousa et al., 2021). Pineapples are rich in vitamins A, B, and C and minerals (calcium, phosphorus, and potassium), and contain antioxidant compounds such as polyphenols (Hossain and Rahman, 2011). And some phenolic compounds, ferulic acid, and kaempferol (Yapo et al. 2011). Seaweed is beneficial for health because of its nutritive and bioactive compounds, consisting of carbohydrate, protein, mineral, vitamin, little fat, rich vitamin A (beta carotene), B1, B2, B6, B12, C, and niacin, which are also important minerals (calcium and zinc). A large quantity of seaweed is fiber as well known as *dietary fiber* of 5.25-11.83% (Praiboon et al., 2019).

Several studies have shown various remedial effects of algal species against non-communicable diseases, such as inflammation, obesity, diabetes, hypertension, and viral infections. They are low-calorie foods that are rich in vitamins, minerals, essential trace elements, polyunsaturated fatty acids, bioactive metabolites, proteins, polysaccharides, and dietary fibers. Apart from regular consumption, many studies have advocated the health benefits of seaweed supplementation along with a regular diet. Regular consumption of seaweed effectively reduces depressive symptoms in pregnant Japanese women and decreases the risk of suicide in adults (Miyali et al., 2014; Nanri et al. 2013; Miyake et al., 2014). While an oral administration of seaweed extracts (*Fucus vesiculosus*, *Macrocystis pyrifera* and *Laminaria japonica*) with zinc, manganese and vitamin B6, Besides its extensive medicinal properties, seaweeds are recognized for its antioxidant capacities and bioactive polyphenolic compounds (Stephens et al., 2017).

Juice of *C. racemosa* displayed good antioxidant activity of juices A1, A2, and A3 ( $IC_{50}$  46.75 $\pm$ 3.254; - 59.51 $\pm$ 5.894 and 97.55296 $\pm$ 8.638 mg/mL, respectively). Therefore, it could be used as a functional beverage. Its antioxidant capacity is produced by phenol, fiber, and vitamin C from seaweed, pineapple, and citrus lemon. Polysaccharide sulfate in seaweed inhibits obesity and diabetes (Sanger et al., 2018). Frequent consumption of dietary seaweeds decreases the risk of diabetes mellitus in the Korean population (Lee et al., 2010) several studies have shown various remedial effects of algal species against non-communicable diseases, such as inflammation, obesity, diabetes, hypertension, and viral infections (Rajauria et al., 2016).

The sensory test value of the juice showed good odor, taste, and color, with a range of 4.7- 5.9 respectively. Green color of juice *C. racemosa* caused by the chlorophyll. Green Seaweed contains a high

quantity of klorofil and have capacity of antioxidant therefore, chlorofill from seaweed is categorized as a functional *green food* product (Nazir et al., 2015). According to the IFT, food/beverages can be categorized as functional products if they have antioxidant activity. Therefore, this juice can be utilized as a functional ingredient because of the content of fiber, antioxidant, and vitamin produced by seaweed, peanuts, and citrus lemons.

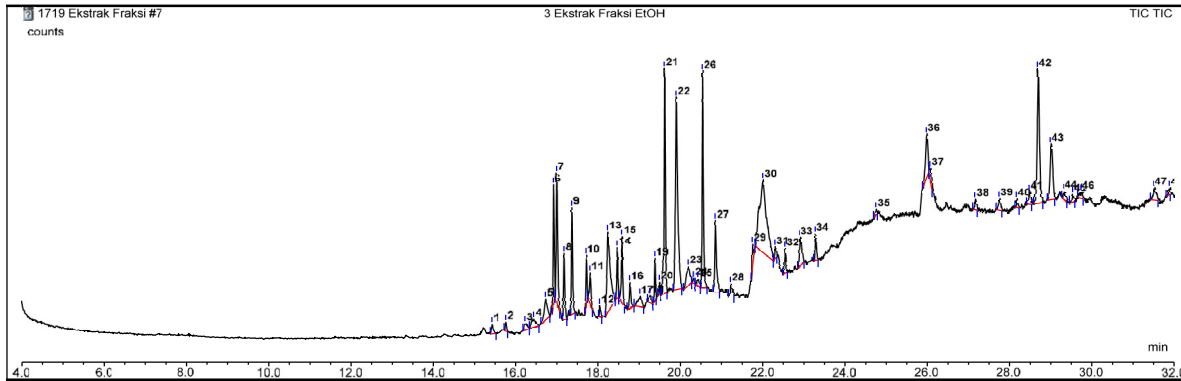
In addition to the benefits of regular consumption of seaweed in the diet, the medicinal properties of seaweed bioactive compounds have been historically recognized. For example, seaweeds are used for the treatment and prevention of goiter, which is caused by the lack of iodine in the diet [Rosenfeld, 2000]. A clinical study indicated that regular consumption of *Undaria* seaweed could effectively minimize the risk of breast cancer in women [Teas et al., 2013]. Studies have also demonstrated potential roles in HIV protection, primarily linked with compounds present in algae, such as phlorotannins, sulfated polysaccharides, certain diterpenes, and lectins [Nagarajan et al., 2015]. Additionally, cancer prevention and metabolic syndrome (METS) associated with obesity, cardiovascular diseases, diabetes, and chronic inflammation are key attributes of algae in relation to human health and wellness (Ganesan et al., 2018)

Anti-oxidant mechanisms play a significant role in protecting the body from various external and internal stresses. A proper balance between oxidant and anti-oxidant plays a key role in protecting against the negative effects of reactive oxygen species (ROS) (Nawzaret al., 2012). antioxidant systems are divided into two categories: endogenous antioxidants & exogenous antioxidants. Endogenous system refers to enzymes include superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase, and non-enzymatic compounds such as bilirubin and albumin. The exogenous system refers to obtaining antioxidants via food and nutritional supplements or pharmaceutical sources that trigger the failure of endogenous antioxidant mechanisms (Nawzar et al. 2013)

GC–MS Analysis

The chemical spectrum profile of the *C. racemosa* extract by GC–MS data was compared with the known compounds stored in the NIST library attached to the GC–MS. The GC–MS

The GC–MS chromatogram of the best phytochemicals is shown in **Figure 3**. The retention time, compound name, molecular formula, molecular weight, percent area, and PubChem ID of the 41 identified phytochemicals are displayed in **Table 2**. The 2D structure of the identified phytochemicals from GC–MS analysis is shown in **Figure 3**. The chemical composition group of *C. racemosa* consisted of alcohols, esters, alcohols, ketones, carboxylic acids, terpenoids, and steroids. Of these, three showed good binding affinity and interacted with the target protein.



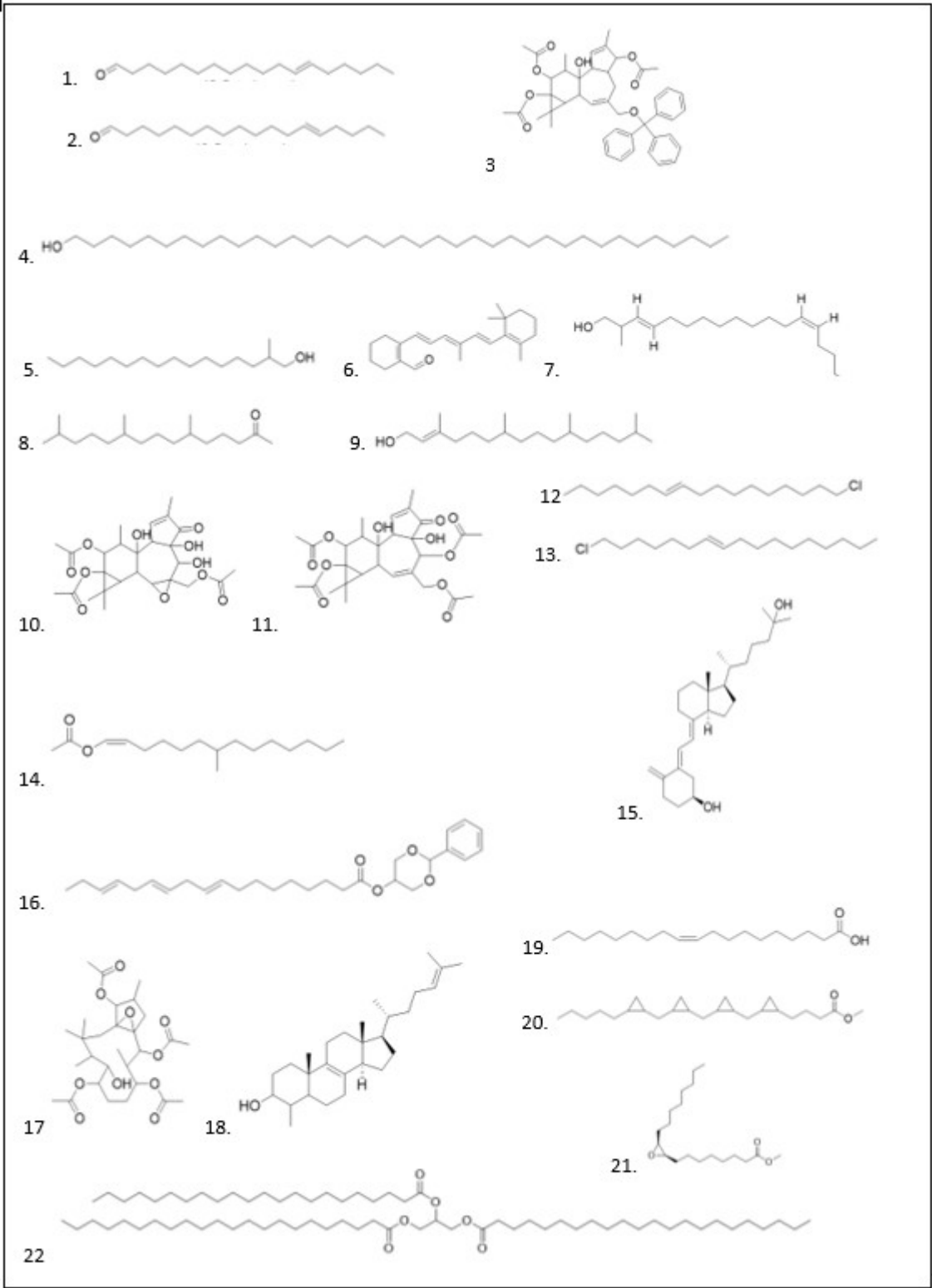
**Figure 3.** GCMS Chromatogram of ethanol extract of *C. racemosa*.

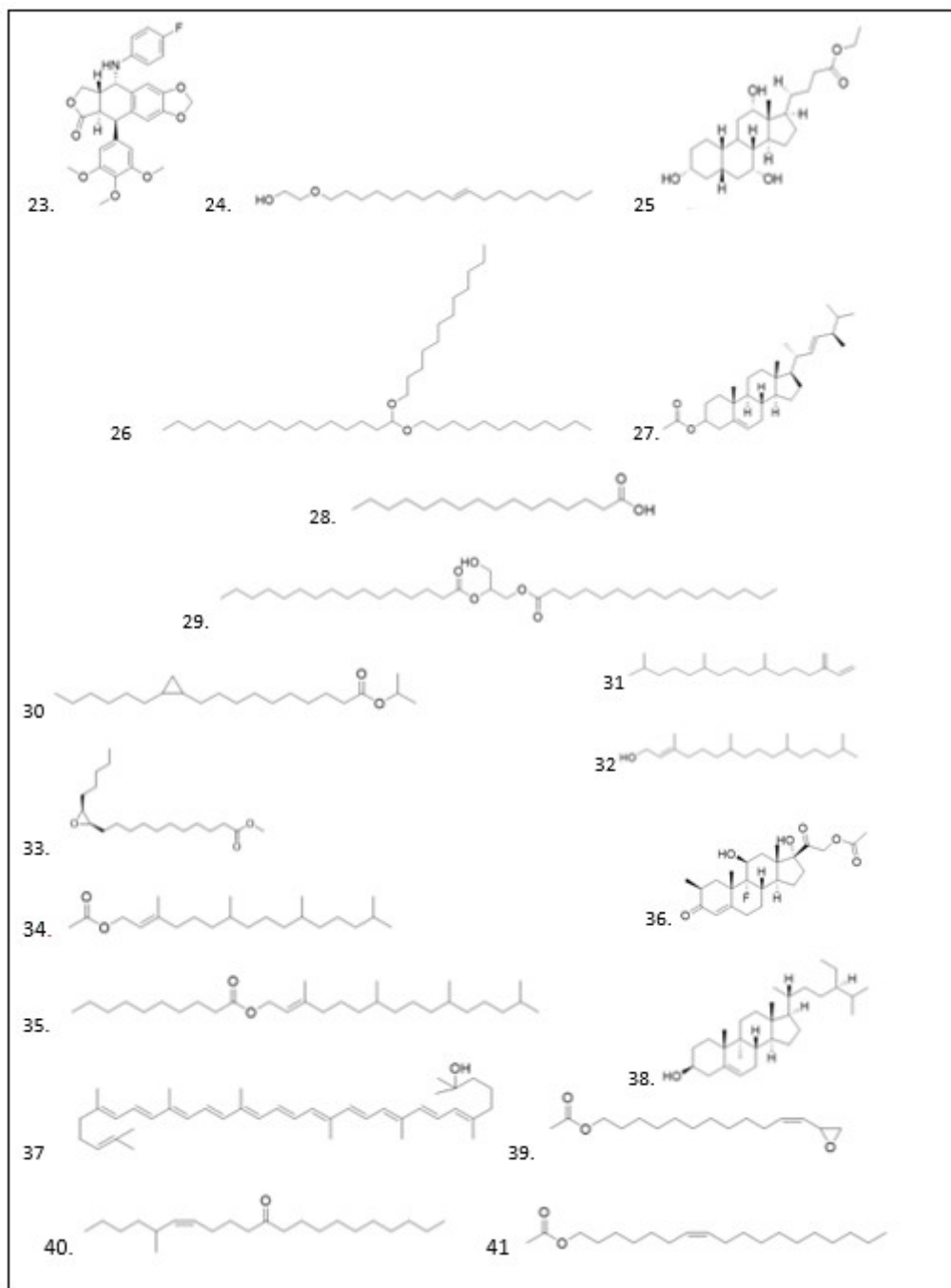
**Table 2.** The phytochemicals, molecule formula, retention time, % are PubChem (CID) from GCMS of ethanol extrat *C. racemosa*.



No	Ligan	Molecule formula	RT	Persen area	PubChem (CID)	Compound Group
1	12-Octadecenal	C <sub>18</sub> H <sub>34</sub> O	17.71	1.31	5367671	Aldehyde
2	13-Octadecenal	C <sub>18</sub> H <sub>34</sub> O	17.71	1.31	5367670	Aldehyde
3	1H-Cyclopropa [3,4]benz [1,2-e]azulene-5,7b,9,9a-tetrol, 1a,1b,4,4a,5,7a,8,9-octahydro-1,1,6,8-tetramethyl-3-[(triphenylmethoxy)methyl]-, 5,9,9a-triacetate	C <sub>28</sub> H <sub>38</sub> O <sub>9</sub>	19.02	1.09	596973	Ester
4	1-Heptatriacotanol	C <sub>37</sub> H <sub>76</sub> O	21.22	0.63	537071	Alcohol
5	2-Methyl-1-hexadecanol	C <sub>17</sub> H <sub>36</sub> O	15.42	0.49	17218	Alcohol
6	2-[4-Methyl-6-(2,6,6-trimethylcyclohex-1-enyl)hexa-1,3,5-trienyl]cyclohex-1-en-1-carboxaldehyde	C <sub>23</sub> H <sub>32</sub> O	16.99	0.96	5363101	Aldehyde
7	2-Methyl-E,E-3,13-octadecadien-1-ol	C <sub>19</sub> H <sub>36</sub> O	16.72	1.65	5364413	Alcohol
8	6,10,14-Trimethylpentadecan-2-one	C <sub>18</sub> H <sub>36</sub> O	16.99	4.48	10408	Keton
9	3,7,11,15-Tetramethyl-2-hexadecen-1-ol	C <sub>20</sub> H <sub>40</sub> O	17.36	3.25	5366244	Alcohol
10	4H-Cyclopropa [5',6']benz [1',2'7,8]azuleno [5,6-b]oxiren-4-one, 8,8a-bis(acetyloxy)-2a-[(acetyloxy)methyl]-1,1a,1b,1c,2a,3,3a,6a,6b,7,8,8a-dodecahydro-3,3a,6b-trihydroxy-1,1,5,7-tetramethyl-5H-Cyclopropa [3,4]benz [1,2-e]azulen-5-one, 4,9,9a-tris(acetyloxy)-3-[(acetyloxy)methyl]-1,1a,1b,4,4a,7a,7b,8,9,9a-decahydro-4a,7b-dihydroxy-1,1,6,8-tetramethyl-	C <sub>26</sub> H <sub>34</sub> O <sub>11</sub>	25,98	2.76	538186	Keton
11	1,1a,1b,4,4a,7a,7b,8,9,9a-decahydro-4a,7b-dihydroxy-1,1,6,8-tetramethyl-	C <sub>28</sub> H <sub>36</sub> O <sub>11</sub>	25,98	2.76	538181	Aldehyde
12	17-Chloro-7-heptadecene	C <sub>17</sub> H <sub>33</sub> Cl	19.61	7.09	5364489	Alkena
13	7-Heptadecene, 1-chloro-	C <sub>17</sub> H <sub>33</sub> Cl	19.61	7.09	5364485	Alkena
14	7-Methyl-Z-tetradecen-1-ol acetate	C <sub>17</sub> H <sub>32</sub> O <sub>2</sub>	16,72	1.65	5363222	Ester
15	9,10-Secocholesta-5,7,10(19)-triene-3beta,25-diol	C <sub>27</sub> H <sub>44</sub> O <sub>2</sub>	28.68	7.48	6506392	Alcohol
16	9,12,15-Octadecatrienoic acid, 2-phenyl-1,3-dioxan-5-yl ester	C <sub>28</sub> H <sub>40</sub> O <sub>4</sub>	16.43	0.96	5367498	Ester
17	9-Desoxo-9-x-acetoxy-3,8,12-tri-O-acetylingol	C <sub>28</sub> H <sub>40</sub> O <sub>10</sub>	24.74	0.27	537583	Alcohol
18	4-Methylcholesta-8,24-dien-3-ol	C <sub>28</sub> H <sub>46</sub> O	22.90	1.69	44150703	Alcohol
19	cis-10-Nonadecenoic acid	C <sub>19</sub> H <sub>36</sub> O <sub>2</sub>	18.46	1.39	5312513	Carboxylic acid

	Cyclopropanebutanoic acid, 2-[[2-[[2-(2-					
20	pentylcyclopropyl)methyl]cyclopropyl)methyl]cyclopropyl)methyl]-, methyl ester	C <sub>25</sub> H <sub>42</sub> O <sub>2</sub>	17.81	1.18	554084	Ester
21	Cyclopropanedodecanoic acid, 2-oktil metil ester	C <sub>15</sub> H <sub>28</sub> O <sub>2</sub>	16.22	0.51	11447830	Carboxilic acid
22	Docosanoic acid, 1,2,3-propanetriyl ester	C <sub>69</sub> H <sub>134</sub> O <sub>6</sub>	22.54	0.81	62726	Ester
23	(22E)-Ergosta-5,22-dien-3-ol acetate	C <sub>30</sub> H <sub>48</sub> O <sub>2</sub>	28,99	3.62	5352877	Ester
24	Ethanol, 2-(9-octadecenyloxy)-, (E)-	C <sub>20</sub> H <sub>40</sub> O <sub>2</sub>	17.17	1.99	5367702	Ester
25	Ethyl iso-allocholate	C <sub>26</sub> H <sub>44</sub> O <sub>5</sub>	16.22	0.51	6452096	Ester
26	Furo(3',4':6,7)naphtho(2,3-d)-1,3-dioxol-6(5aH)-one, 9-((4-fluorophenyl)amino)-5,8,8a,9-tetrahydro-5-(3,4,5-trimethoxyphenyl)-, (5R,5aR,8aS,9S)-	C <sub>28</sub> H <sub>26</sub> FNO <sub>7</sub>	19.25	0.44	468876	Alkaloid
27	1,1-Bis(dodecyloxy)hexadecane	C <sub>40</sub> H <sub>82</sub> O <sub>2</sub>	19.61	7.09	41920	Alkena
28	Hexadecanoic acid	C <sub>16</sub> H <sub>32</sub> O <sub>2</sub>	18,23	6.35	985	Carboxilic acid
29	Hexadecanoic acid, 1-(hydroxymethyl)-1,2-ethanediyl ester	C <sub>35</sub> H <sub>68</sub> O <sub>5</sub>	20.84	3.04	99931	Ester
30	i-Propyl 11,12-methylene-octadecanoate	C <sub>22</sub> H <sub>42</sub> O <sub>2</sub>	18.77	1.02	91692516	Ester
31	Neophytadiene	C <sub>20</sub> H <sub>38</sub>	16,91	3.19	10446	Alkena
32	Oxiraneundecanoic acid,3-pentyl-, methyl ester, cis-	C <sub>13</sub> H <sub>24</sub> O <sub>3</sub>	17.81	1.18	86131368	Carboxilic acid
33	Phytol	C <sub>20</sub> H <sub>40</sub> O	19.89	10.81	5280435	Alcohol
34	Phytol, acetate	C <sub>22</sub> H <sub>42</sub> O <sub>2</sub>	20.53	6.04	6428538	Ester
35	Phytyl decanoate	C <sub>30</sub> H <sub>58</sub> O <sub>2</sub>	20.53	6.04	91711717	Ester
36	Pregn-4-ene-3,20-dione, 21-(acetyloxy)-9-fluoro-11,17-dihydroxy-2-methyl-, (2beta,11beta)-	C <sub>24</sub> H <sub>33</sub> FO <sub>6</sub>	19.02	1.09	31719	Steroid
37	Rhodopin	C <sub>40</sub> H <sub>58</sub> O	29,32	0.45	5365880	Terpenoid
38	β-Sitosterol	C <sub>29</sub> H <sub>50</sub> O	22.01	12,44	175268335	Steroid
39	Z-(13,14-Epoxy)tetradec-11-en-1-ol acetate	C <sub>16</sub> H <sub>28</sub> O <sub>3</sub>	19.89	10.81	5363633	Ester
40	Z-5-Methyl-6-heneicosen-11-one	C <sub>22</sub> H <sub>42</sub> O	17.71	1.31	5363254	Keton
41	Z-7-Octadecen-1-ol acetate	C <sub>20</sub> H <sub>38</sub> O <sub>2</sub>	16.99	4.48	5363553	Ester





**Figure 3.** Molecule structure of Fitochemical compounds of *Caulerpa racemosa* 1. 12-Octadecenal; 2. 13-Octadecenal; 3. 1H-Cyclopropa [3,4]benz [1,2-e]azulene-5,7b,9,9a-tetrol, 1a,1b; 4. 4a,5,7a,8,9-octahydro-1,1,6,8-tetramethyl-3-[(triphenylmethoxy)methyl]-; 5. 9,9a-triacetate 4. 1-Heptatriacotanol 5. 2-Methyl-1-hexadecanol; 6. 1H-Cyclopropa [3,4]benz [1,2-e]azulene-5,7b,9,9a-tetrol, 1a,1b,4,4a,5,7a,8,9-octahydro-1,1,6,8-tetramethyl-3-[(triphenylmethoxy)methyl]-, 5,9,9a-triacetate; 7. 2-[4-Methyl-6-(2,6,6-trimethylcyclohex-1-enyl)hexa-1,3,5-trienyl]cyclohex-1-en-1-carboxaldehyde; 8. 2-Methyl-E,E-3,13-octadecadien-1-ol; 9. 6,10,14-Trimethylpentadecan-2-one; 10. 3,7,11,15-Tetramethyl-2-hexadecen-1-ol; 11. 4H-Cyclopropa [5',6']benz [1',2',7,8]azuleno [5,6-b]oxiren-4-one, 8,8a-bis(acetyloxy)-2a-[(acetyloxy)methyl]-1,1a,1b,1c,2a,3,3a,6a,6b,7,8,8a-dodecahydro-3,3a,6b-trihydroxy-1,1,5,7-tetramethyl-; 12. 5H-Cyclopropa [3,4]benz [1,2-e]azulen-5-one, 4,9,9a-tris(acetyloxy)-3-[(acetyloxy)methyl]-1,1a,1b,4,4a,7a,7b,8,9,9a-decahydro-4a,7b-dihydroxy-1,1,6,8-tetramethyl-; 13. 17-Chloro-7-heptadecene; 14. 7-Heptadecene, 1-chloro- 15. 7-Methyl-Z-tetradecen-1-ol acetate; 15. 9,10-Secocholesta-5,7,10(19)-triene-3beta,25-diol; 16.. 9,12,15-Octadecatrienoic acid, 2-phenyl-1,3-dioxan-5-yl ester; 17. 9-Desoxo-9-x-acetoxy-3,8,12-tri-O-acetylingol; 18. 4-Methylcholesta-8,24-dien-3-ol ;19. cis-10-Nonadecenoic

acid 20. Cyclopropanebutanoic acid, 2-[[2-[(2-pentylcyclopropyl)methyl]cyclopropyl]methyl]cyclopropyl]methyl]-, methyl ester; 21. Cyclopropanedodecanoic acid, 2oktil metil ester; 22. Docosanoic acid, 1,2,3-propanetriyl ester; 23. (22E)-Ergosta-5,22-dien-3-ol acetate; 24. Ethanol, 2-(9-octadecenyl)-, (E)- 25. Ethyl iso-allocholate; 26. Furo(3',4':6,7)naphtho(2,3-d)-1,3-dioxol-6(5aH)-one, 27. 9-((4-fluorophenyl)amino)-5,8,8a,9-tetrahydro-5-(3,4,5-trimethoxyphenyl)-, (5R,5aR,8aS,9S)-; 28. 1,1-Bis(dodecyloxy)hexadecane; 29.. Hexadecanoic acid; 30.. Hexadecanoic acid, 31. 1-(hydroxymethyl)-1,2-ethanediyl ester; 32. i-Propyl 11,12-methylene-octadecanoate; 33. Neophytadiene; 34. Oxiraneundecanoic acid,3-pentyl-, methyl ester, cis- 35. Phytol 36. Phytol, acetate 36. Phytol decanoate 37. Pregn-4-ene-3,20-dione, 21-(acetyloxy)-9-fluoro-11,17-dihydroxy-2-methyl-, (2beta,11beta)- 38. Rhodopin; 39.  $\beta$ -Sitosterol; 39. Z-(13,14-Epoxy)tetradec-11-en-1-ol acetate; 40. Z-5-Methyl-6-heneicosen-11-one; 41. Z-7-Octadecen-1-ol acetate.

3. Evaluation of Molecular Docking

The literature shows that Molecular docking has been an important tool for studies of receptor-ligand interactions in the inhibition of enzymes related to antioxidant activity. This technique has clarified doubts and clarified the possible region of the receptor where the activity occurs, the amino acid residues involved in the interactions, and the atoms that directly interact with the ligand (Gupta, et al. 2018). Phenolic compounds, such as carotenoids, flavonoids, vitamin C, and minerals, such as selenium and zinc, are important exogenous antioxidant compounds. Thus, the antioxidant system is vital for a healthy body. In recent years, various studies have suggested the importance of antioxidant compounds and their defense mechanisms (Menchaca et al., 2020).

Virtual screening involves evaluation of a large number of small compounds based on their molecular properties using computational methods. The pharmacokinetic profiles of the compounds identified by GC-MS were analyzed. Profile of pharmacokinetic targeting of *C. racemosa* using *Lipinski's Rule of Five* ((RO5)parameter (Table 3). Lipinski's rule components are molecular weight < 500, log P not greater than 5, hydrogen bond donors not more than 5, hydrogen bond acceptors not more than 10, number of atoms from 20 to 70, and 10 or fewer rotatable bonds (Shaji et al., 2018). Compounds that obey Lipinski's rule were further screened using molecular docking and simulation studies.

Table 3. Profil Farmakokinetik dari Ligan Target menggunakan parameter *Lipinski's Rule of Five*.

No	Ligan	Berat Molekul <500	H-Donor <5	H-Akseptor <10	LogP <5	Refraksi Molar 40-130	Penyimpan gan
1	12-Octadecenal	266.000000	0	1	6.222801	85.515968	1
2	13-Octadecenal	266.000000	0	1	6.222801	85.515968	1
3	1H-Cyclopropa [3,4]benz [1,2-e]azulene-5,7b,9,9a-tetrol, 1a,1b,4,4a,5,7a,8,9-octahydro-1,1,6,8-tetramethyl-3-[(triphenylmethoxy)methyl]-, 5,9,9a-triacetate	312.000000	5	6	-0.053101	77.145782	1
4	1-Heptatriacotanol	312.000000	5	6	-0.053101	77.145782	1
5	2-Methyl-1-hexadecanol	256.000000	1	1	5.706000	81.944763	1
6	2-[4-Methyl-6-(2,6,6-trimethylcyclohex-1-enyl)hexa-1,3,5-trienyl]cyclohex-1-en-1-carboxaldehyde	81.944763	0	1	6.641202	103.926971	1
7	2-Methyl-E,E-3,13-octadecadien-1-ol	280.000000	1	1	6.038201	90.990761	1
8	6,10,14-Trimethylpentadecan-2-one	268.000000	0	1	6.014501	85.399971	1
9	3,7,11,15-Tetramethyl-2-hexadecen-1-ol	296.000000	1	1	6.364101	95.561760	1
10	4H-Cyclopropa [5',6']benz [1',2',7,8]azuleno [5,6-b]oxiren-4-one, 8,8a-bis(acetyloxy)-2a-[(acetyloxy)methyl]-1,1a,1b,1c,2a,3,3a,6a,6b,7,8,8a-dodecahydro-3,3a,6b-trihydroxy-1,1,5,7-tetramethyl-	522.000000	0	11	4.684239	129.402466	2



11	5H-Cyclopropa [3,4]benz [1,2-e]azulen-5-one, 4,9,9a-tris(acetyloxy)-3-[(acetyloxy)methyl]-1,1a,1b,4,4a,7a,7b,8,9,9a-decahydro-4a,7b-dihydroxy-1,1,6,8-tetramethyl-17-Chloro-7-heptadecene	548.000000	0	11	5.092820	138.002487	2
12	7-Heptadecene, 1-chloro-	272.500000	0	0	6.872602	85.554970	1
13	7-Methyl-Z-tetradecen-1-ol acetate	272.500000	0	0	6.872602	85.554970	1
14	9,10-Secocholesta-5,7,10(19)-triene-3beta,25-diol	268.000000	0	2	5.272600	82.163971	1
15	9,12,15-Octadecatrienoic acid, 2-phenyl-1,3-dioxan-5-yl ester	400.000000	2	2	6.733902	122.648552	1
16	9-Desoxo-9-x-acetoxy-3,8,12-tri-O-acetylingol	440.000000	0	4	6.540953	135.386978	1
17	4-Methylcholesta-8,24-dien-3-ol	536.000000	0	10	5.651121	141.818985	2
18	<b>cis-10-Nonadecenoic acid</b>	398.000000	1	1	7.698903	123.645737	1
19	Cyclopropanebutanoic acid, 2-[[2-[(2-pentylcyclopropyl)methyl]cyclopropyl]methyl]cyclopropyl)methyl]-, methyl ester	<b>296.000000</b>	<b>1</b>	<b>2</b>	<b>5.039920</b>	<b>102.327286</b>	<b>0</b>
20	<b>Cyclopropanedodecanoic acid, 2-oktil metil ester</b>	374.000000	0	2	6.222682	127.046967	1
21	Docosanoic acid, 1,2,3-propanetriyl ester (22E)-Ergosta-5,22-dien-3-yl acetate	<b>240.000000</b>	<b>1</b>	<b>2</b>	<b>4.772099</b>	<b>71.146782</b>	<b>0</b>
22	Ethanol, 2-(9-octadecenyl)-, (E)-Ethyl iso-allocholate	312.000000	5	6	-0.053101	77.145782	0
23	Furo(3',4':6,7)naphtho(2,3-d)-1,3-dioxol-6(5aH)-one, 9-((4-fluorophenyl)amino)-5,8,8a,9-tetrahydro-5-(3,4,5-trimethoxyphenyl)-, (5R,5aR,8aS,9S)-	440.000000	0	2	7.507115	150.931992	1
24	1,1-Bis(dodecyloxy)hexadecane	312.000000	1	2	5.749202	110.685280	1
25	Hexadecanoic acid	436.000000	3	5	3.927198	119.034340	0
26	Hexadecanoic acid, 1-(hydroxymethyl)-1,2-ethanediyl ester	507.000000	1	8	4.435399	130.275681	1
27	i-Propyl 11,12-methylene-octadecanoate	312.000000	5	6	-0.053101	77.145782	1
28	Neophytadiene	312.000000	5	6	-0.053101	77.145782	1
29	<b>Oxiraneundecanoic acid, 3-pentyl-, methyl ester, cis-</b>	256.000000	1	2	5.552299	77.947777	1
30	Phytol	338.000000	0	2	6.129292	118.590973	1
31	Phytol, acetate	278.000000	0	0	7.167703	94.055969	1
32	Phytyl decanoate	<b>228.000000</b>	<b>1</b>	<b>3</b>	<b>3.370800</b>	<b>63.545784</b>	<b>0</b>
33	Pregn-4-ene-3,20-dione, 21-(acetyloxy)-9-fluoro-11,17-dihydroxy-2-methyl-, (2beta,11beta)-	296.000000	1	1	6.364101	95.561760	0
34	Rhodopin	338.000000	0	2	6.934901	105.108963	1
35	β-Sitosterol	450.000000	0	2	8.799607	162.773972	1
36	Z-(13,14-Epoxy)tetradec-11-en-1-ol acetate	436.000000	2	6	2.690500	109.585564	0
37	Z-5-Methyl-6-heneicosen-11-one	554.000000	1	1	9.998867	189.588913	2
38	Z-7-Octadecen-1-ol acetate	368.000000	0	1	1.510640	93.379990	0
39		565.000000	2	10	1.031598	152.134506	1
40		322.000000	0	1	6.447083	118.461472	1
41		310.000000	0	2	5.705202	108.268982	1

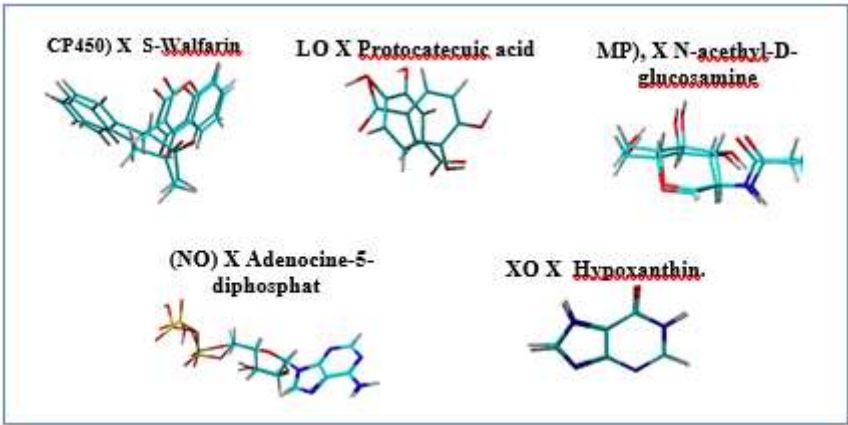
The outcomes of the virtual screening technique are shown (Table 3.) We finalized three bioactive compounds that obey Lipinski’s rule, such as cis-10-Nonadecenoic acid, cyclopropanedodecanoic acid cyclopropanedodecanoic acid, 2-octyl-, methyl ester, and oxiraneundecanoic acid 3-pentyl-, methyl ester, and cis-, which acted as ligands for further investigation in molecular docking studies.

Validation of Protein Target

The five enzymes (receptors) that respond to the production of reactive oxygen species (ROS) during metabolism, cytochrome P450 (CP450), lipoxygenase (LO), myeloperoxidase (MP), NADPH oxidase (NO), and xanthine oxidase (XO), were selected and obtained from the Protein Data Bank (PDB) [Morris et al., 1998]. Based on the standard protocol established by our research group for each analyzed receptor [Silva et al., 2018; Santos et al., 2018; Cruz et al., 2018,]. Table 6 shows the protocols

used for the validation and subsequent docking analyses of each receptor. The calculations were performed with default parameters using the genetic algorithm following the protocol described by Pereira et al. and Padilha et al. [49,50].

Data about validation protocols for molecular docking Validation protokol of Cytochrome P450 (CP450) X S-Walfarin (A); Lipoxxygenase (LO) X Protocatecuic acid (B); Myeloperoxidase (MP), X N-acethyl-D-glucosamine (C); NADPH Oxidase (NO) X Adenocine-5-diphosphat (D); Xanthine oxidase (XO) X Hypoxanthin can be seen in **Figure 4**.



**Figure 4.** Validation protokol Molecular docking of Cytochrome P450 (CP450) X S-Walfarin; Lipoxxygenase (LO) X Protocatecuic acid; Myeloperoxidase (MP), X N-acethyl-D-glucosamine; NADPH Oxidase (NO) X Adenocine-5-diphosphat; Xanthine oxidase (XO) X Hypoxanthin.

According to the literature, RMSD values expressing the relationship between the calculated X crystallographic data of the complexed ligand must be less than 2.0 Å [Costa et al., 2018, Hevener et al., 2009; Gowthana et al., 2008]. The similarity in the overlapping of crystallographic poses (orientation + conformation, cyan) and calculated was obtained via molecular docking and graphically displayed a low RMSD value displayed in. **Table 4**, what characterizes the good results according to the literature. A total of 20 molecules were docked in the five receptors cited, and the binding affinity ( $\Delta G$ ) for the molecules evaluated at each receptor is shown in **Figure 4** These values were used to classify the best poses obtained in the molecular docking analyses. Only the smallest  $\Delta G$  values for the best pose are presented. The larger the peaks, the lower the  $\Delta G$ , and consequently, the more significant the interaction between the receptor and the ligands for antioxidant ability (Costa et al., 2018).

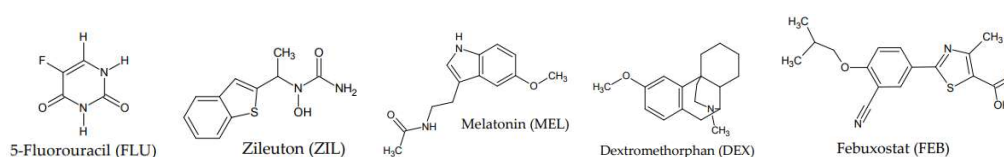
**Table 4.** Data obtained in the validation of the molecular docking protocols for the receptors cytochrome P450 (CP450), lypoxxygenase (LO), myeloperoxidase (MP), NADPH oxidase (NO) and xanthine oxidase (XO).

No	Molecular docking	Resolution	$\Delta G$ (Kkal/mol)	RMSD
1	Cytochrome P450 (CP40) X S walfarin	2.55 Å	-10.4260	0.6311 Å
2	Lipoxxygenase (LO) X Protocatecuic acid	2.10 Å	-6.6490	1.9756 Å
3	Myeloperoxidase (MP) X N-acethyl-D-glucosamine	1.85 Å	-4.2060	0.7344 Å
4	NADPH Oxidase (NO) X Adenocine-5-diphosphat	1.80 Å	:-8.8380	0.9495 Å
5	Xanthine oxidase (XO) X Hypoxanthin.	1.80 Å	- 5.9700	0.1940 Å

### Molecular Docking Studies of Proteins with Bioactive Compound

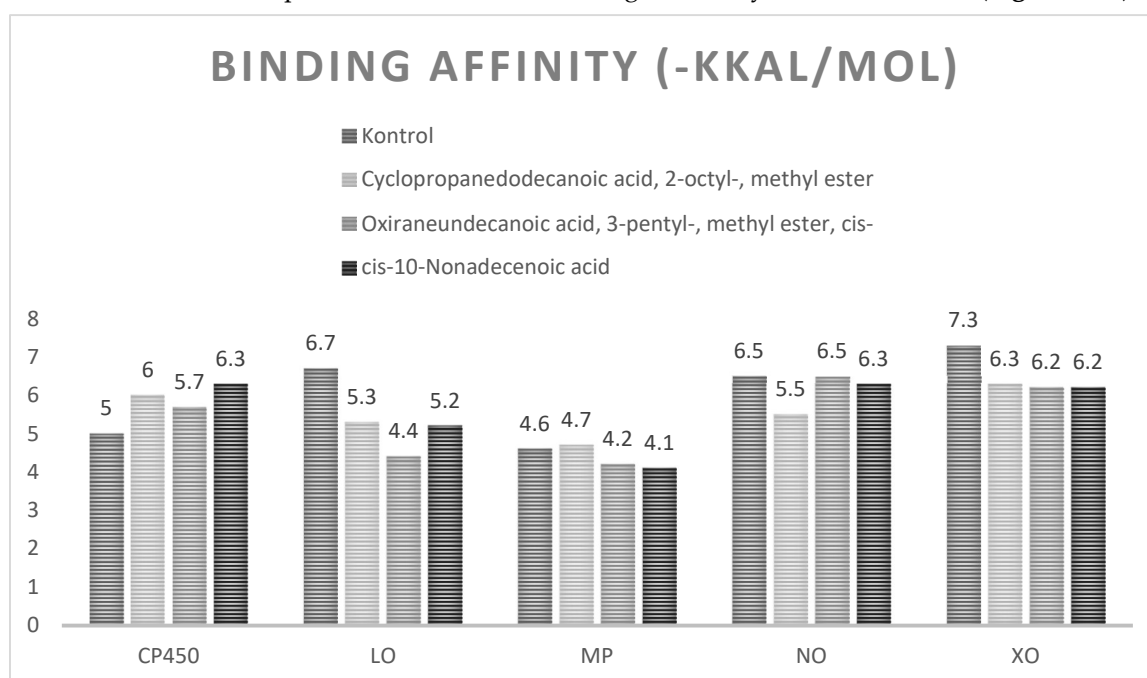
The anticancer effect of *Caulerpa racemosa* was examined against HL60 (the Human promyelocytic leukemia) cell line, which showed remarkable cell growth. Apoptotic body formation and DNA damage in treated HL-60 cancer cells also showed dose-dependent sub-G1 DNA accumulation in HL-60 cells (Lakmal, et al., 2014). *C. racemosa* shows cytotoxic activity against breast cancer cells (Sanger et al., 2013). In silico simulations of new molecules with potential epithelial anticancer activity proposed by *C. racemosa* using virtual screening

Molecular docking using three ligand phytochemicals of *C. racemosa* and ligand control are commercially available drugs (**Figure 5**) with each inhibitory activity, such as 5-fluorouracil (FLU) for CP450 (Gunes et al., 2006); LO for Zileuton (ZIL) (Saul et al., 2017; Allegra et al., 2011; Galijasevic et al., 2008); MP for Melatonin (MEL) (Blair-Johnson et al., 2001; Hevener et al., 2009; and Yalkowsky et al., 1979); NO for Dextromethorphan (DEX) (Liu et al., 2009; Wu et al., 2018) and XO for Febuxostat (FEB) (Teles fujima et al. 2018, Malik et al. 2018).

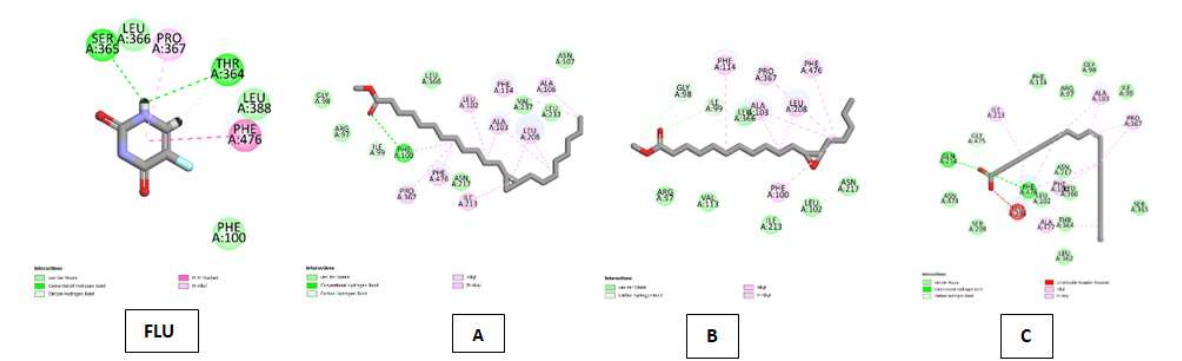


**Figure 5.** Ligand control available as a commercially available drug: FLU, ZIL, MEL, DEX and FEB.

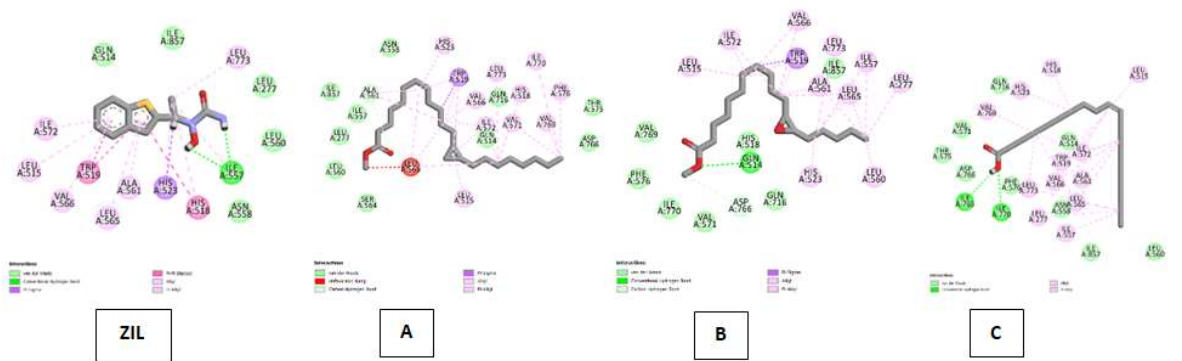
The Protein-ligand interaction binding energies provide a better understanding of how well drugs bind. Each Binding energy of cis-10-Nonadecenoic acid with CP450, LO of, MP, NO of and XO were -6.3, -5.2, -4.1, -6.3, and -6.2 Kcal/mol, Cyclopropanedodecanoic acid, 2-octyl-, methyl ester with CP450, LO of, MP, NO of and XO were -6, -5.3, -4.7, -5.5 and -6.2 (Kcal/mol) and Oxiraneundecanoic acid 3-pentyl-, methyl ester, cis- with CP450, LO of, MP, NO of and XO were -5.7, -4.4, -4.2, -6.5, -6.2 Kcal/mol (**Figure 4**). The binding energy of drug control of each enzyme oxidant are near with the binding of each ligand, such as 5-fluorouracil (FLU) with CP450 was -5 Kcal/mol; LO with Zileuton (ZIL) was 6.7 Kcal/mol; MP with Melatonin (MEL) was 4.6 Kcal/mol; NO with Dextromethorphan (DEX) was -6.5 Kcal/mol and XO with Febuxostat (FEB) was 7.3 Kcal/mol. The three bioactive compounds interacted with the protein and formed a complex, which was visualized using PyMol, and their 2D interaction patterns were identified using Discovery Studio visualizer (**Figure 6-10**).



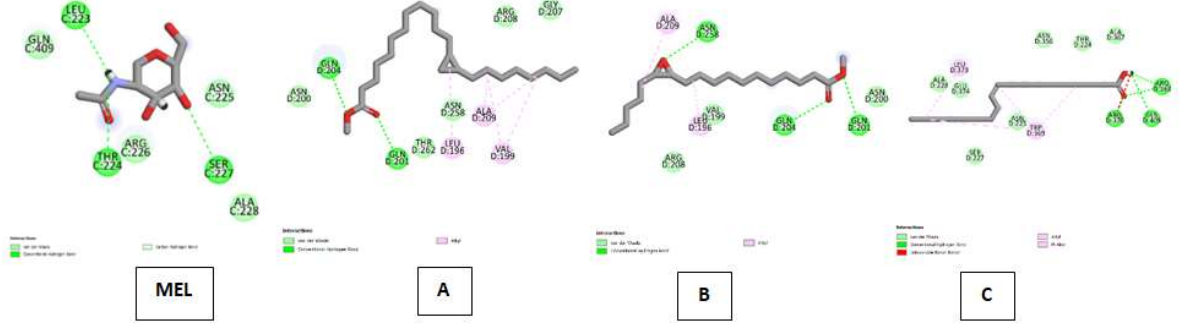
**Figure 5.** Perbandingan *Binding Affinity* antara senyawa aktif Cyclopropanedodecanoic acid, 2-octyl-, methyl ester; Oxiraneundecanoic acid, 3-pentyl-, methyl ester, cis-; cis-10 Nonadecenoic acid dan ligand kontrol CP450, LO, MP, NO dan XO .



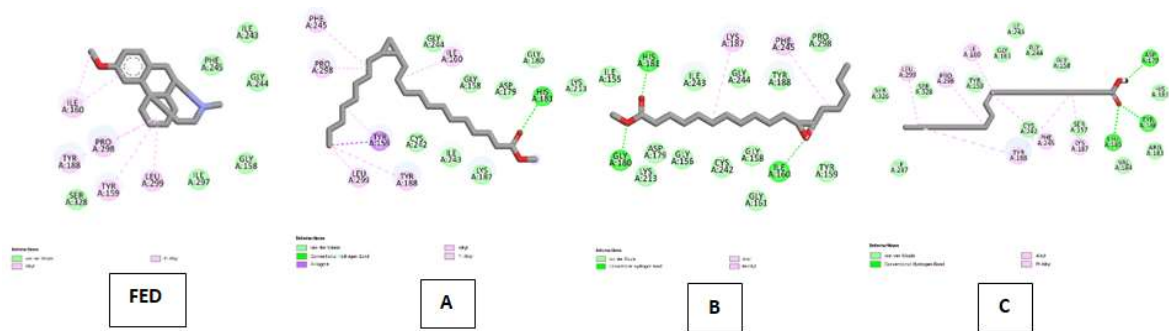
**Figure 6.** Visualisasi Hasil *Molekular Docking* antara Ligan control Flu, Cyclopropanedodecanoic acid, 2-octyl-, methyl ester (A) ; Oxiraneundecanoic acid, 3-pentyl-, methyl ester (B), cis- dan cis-10-Nonadecenoic acid (C) secara terhadap CP450.



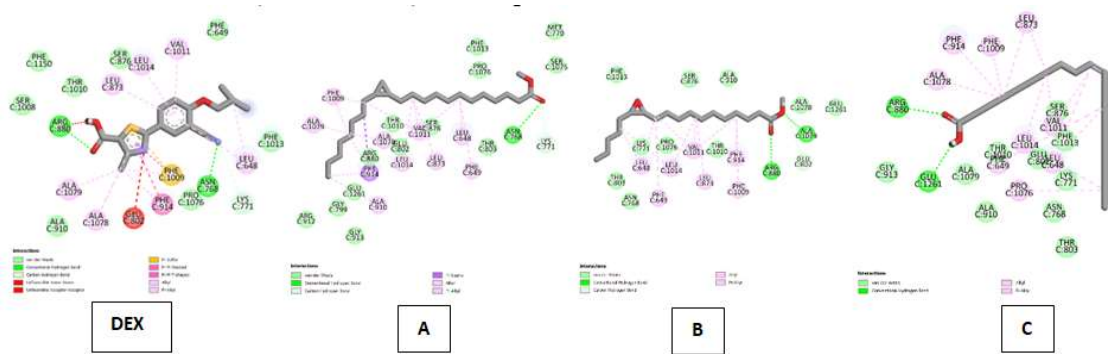
**Figure 7.** Visualisasi Hasil *Molekular Docking* antara Ligan control ZIL, Cyclopropanedodecanoic acid, 2-octyl-, methyl ester (A) ; Oxiraneundecanoic acid, 3-pentyl-, methyl ester, cis- dan cis-10-Nonadecenoic acid (C) terhadap LO.



**Figure 8.** Visualisasi Hasil *Molekular Docking* antara Ligan control MEL, Cyclopropanedodecanoic acid, 2-octyl-, methyl ester ; Oxiraneundecanoic acid, 3-pentyl-, methyl ester, cis- dan cis-10-Nonadecenoic acid (C) secara berturut-turut (kanan ke kiri) terhadap MP.



**Figure 9.** Visualisasi Hasil *Molekular Docking* antara Ligan control FED , Cyclopropanedodecanoic acid, 2-octyl-, methyl ester ; Oxiraneundecanoic acid, 3-pentyl-, methyl ester, cis- dan cis-10-Nonadecenoic acid secara berturut-turut (kanan ke kiri) terhadap XO.



**Figure 10.** Visualisasi Hasil *Molekular Docking* antara Ligan control DEX , Cyclopropanedodecanoic acid, 2-octyl-, methyl ester ; Oxiraneundecanoic acid, 3-pentyl-, methyl ester, cis- dan cis-10-Nonadecenoic acid terhadap NO.

**Figure 6** shows the interaction data of the tested A, B, C, and control (FLU) molecules with the CP450 receptor. Three amino acid residues (Leu 366, Phe 476, and pro 367) were common to A, B, and C and FLU with CP450 (Indicated by Blue in **Table 6** ). This shows the degree of correspondence between the control and the tested molecules, indicating that these may have potential antioxidant ability. A, B, and C molecules with a number of interactions (seventeen, threeteen and 20 interactions, respectively) showed a BA ( $-6 \text{ kcal mol}^{-1}$ ;  $-5,7$  and  $-6.3 \text{ kcal mol}^{-1}$ , respectively) higher than the control (FLU) with BA =  $-5 \text{ kcal mol}^{-1}$  (seven interactions). It was possible to verify the tendency of the BA value to decrease with an increase in the number of interactions.

**Table 6.** Interaksi Ikatan Kimia antara ligan senyawa aktif dan ligan kontrol dengan Reseptor target.

Reseptor	Ligan	Asam amino yang berinteraksi
Cytochrome P450 (CP450) Kode PDB : 1OG5 <b>Gambar 5</b>	5-fluorouracil (FLU)	<b>Van Der Waals</b> : LEU A: 366, LEU A: 388, PHE A:100 ; <b>Conventional Hydrogen Bond</b> : SER A:365, THR A:364 ; <b>Carbon Hydrogen Bond</b> :THR A:364 ; <b>Pi-Pi Stacked</b> : PHE A:476 ; <b>Pi-Alkyl</b> : PRO A:367.
	Cyclopropanedodecanoic acid, 2-octyl-, methyl ester	<b>Van Der Waals</b> : GLY A:98, ARG A:97, ASN A:2017, LEU A:366, VAL A:237, LEU A:233, ASN A:107 ; <b>Conventional Hydrogen Bond</b> : PHE A:100 ; <b>Carbon Hydrogen Bond</b> : ILE A:99, <b>Alkyl &amp; Pi-Alkyl</b> :PHE A:476, PRO A:367, ILE A:213, LEU A:208,



	ALA A:103, LEU A:102, PHE A:114, ALA A:106
Oxiraneundecanoic acid, 3-pentyl-, methyl ester, cis-	<b>Van Der Waals</b> : ARG A:97, VAL A:113, ILE A:213, LEU A:102, ASN A:12017, <a href="#">LEU A:366</a> ; <b>Carbon Hydrogen Bond</b> : GLY A:98, ILE A:99 ; <b>Alkyl &amp; Pi-Alkyl</b> : PHE A:114, ALA A:103, LEU A:208, <a href="#">PRO A:367</a> , <a href="#">PHE A:476</a> .
cis-10-Nonadecenoic acid	<b>Van Der Waals</b> : SER A:209, ASN A:474, GLY A:475, PHE A:114, ARG A:97, GLY A:98, ILE A:99, <a href="#">SER A:365</a> , LEU A:362, THR A:364, <a href="#">LEU A:366</a> , ASN A:217, LEU A :102 ; <b>Conventional Hydrogen Bond</b> : GLN A:214, <a href="#">PHE A:476</a> ; <b>Unfavorable Acceptor-Acceptor</b> : LEU A:208, <b>Alkyl &amp; Pi-Alkyl</b> : ILE A:213, ALA A:103, <a href="#">PRO A:367</a> , PHE A:100, ALA A:477
Zileuton (ZIL)	<b>Van Der Waals</b> : <a href="#">ILE A: 857</a> , <a href="#">GLN A:514</a> , ASN A : 558, LEU A:560, LEU A:277 ; <b>Conventional Hydrogen Bond</b> : ILE A:557 ; <b>Pi-Sigma</b> : HIS A:523 ; <b>Pi-Pi Stacked</b> : <a href="#">HIS A:518</a> , TRP A:519 ; <b>Alkyl &amp; Pi-Alkyl</b> : <a href="#">HIS A:518</a> , <a href="#">LEU A:773</a> , <a href="#">HIS A: 523</a> , ILE A:557, <a href="#">LEU A : 565</a> , <a href="#">ALA A:561</a> , <a href="#">ILE A:572</a> , <a href="#">VAL A:566</a> , LEU A:515
Cyclopropanedodecanoic acid, 2-octyl-, methyl ester	<b>Van Der Waals</b> : SER A:564, <a href="#">LEU A:560</a> , LEU A:557, <a href="#">ILE A:857</a> , ASN A:558, GLN A:716, <a href="#">GLN A:514</a> , THR A:575, ASP A:766 ; <b>Carbon Hydrogen Bond</b> : <a href="#">ALA A:561</a> , <b>Unfavorable Bump</b> : <a href="#">LEU A:565</a> , <b>Pi-Sigma</b> ; TRP A:519 ; <b>Alkyl &amp; Pi-Alkyl</b> : LEU A:515, <a href="#">HIS A:523</a> , <a href="#">VAL; A:566</a> , <a href="#">ILE A:572</a> , VAL A:571, <a href="#">VAL A:566</a> , <a href="#">LEU A:773</a> , <a href="#">HIS A:518</a> , ILE A:770, VAL:769
Lipoxygenase (LO) Kode PDB : 1N8Q <b>Gambar 6</b>	<b>Van Der Waals</b> : VAL A:769, PHE A:576, ILE A:770, VAL A:571, <a href="#">HIS A:518</a> , GLN A:716, <a href="#">ILE A:857</a> ; <b>Carbon Hydrogen Bond</b> : ASP A:766 ; <b>Conventional Hydrogen Bond</b> : <a href="#">GLN A:514</a> ; <b>Alkyl &amp; Pi-Alkyl</b> : <a href="#">LEU A:515</a> , <a href="#">ILE A:572</a> , <a href="#">VAL A:566</a> , <a href="#">LEU A:773</a> , <a href="#">ALA A:561</a> M LEU A:565, <a href="#">HIS A:523</a> , LEU A:560, LEU A:773, <a href="#">ALA A:561</a> , <a href="#">LEU A:565</a> , LRU A:560
cis-10-Nonadecenoic acid	<b>Van Der Waals</b> : LEU A:560, <a href="#">ILE A:857</a> , ASN A:558, <a href="#">GLN A:514</a> , PHE A:576, ASP A:776, THR A:575, VAL A:571, GLN A:716 ; <b>Conventional Hydrogen Bond</b> : ILE A:765, ILE A 770 ; <b>Alkyl &amp; Pi-Alkyl</b> : VAL A:769, <a href="#">HIS A:523</a> , <a href="#">HIS A:518</a> , <a href="#">LEU A:515</a> , <a href="#">ILE A:572</a> , TRP A:519, <a href="#">VAL A:566</a> , <a href="#">ALA :561</a> , <a href="#">LEU A:565</a> , <a href="#">LEU A:773</a> , LEU A:277, ILE A:557.

Myeloperoxidase (MP) Kode PDB : 1DNU <b>Gambar 7</b>	Melatonin (MEL)	<b>Van Der Waals</b> : ALA C:228, ASN C:255, ARG C:226, GLN C:409 ; <b>Conventional Hydrogen Bond</b> : SER C:227, THR C:224, LEU C:223,
	Cyclopropanedodecanoic acid, 2-octyl-, methyl ester	<b>Van Der Waals</b> : ASN D:200, THR D:262, ASN D:258, ARG D:208, GLY D:207 ; <b>Conventional Hydrogen Bond</b> : GLN D:204, GLN D:201 ; <b>Alkyl</b> : ALA D:209, LEU D:196, VAL D:199
	Oxiraneundecanoic acid, 3-pentyl-, methyl ester, cis-	<b>Van Der Waals</b> : VAL D:199, ARG D:208, ASN D:200 ; <b>Conventional Hydrogen Bond</b> :ASN D:258, GLN D:204, GLN D:201 ; <b>Alkyl</b> : ALA D:209, LEU D:196
	cis-10-Nonadecenoic acid	<b>Van Der Waals</b> : ALA D:228, GLU D:374, SER D:227, ASN D:225, ASN D:356, THR D:224, ALA D:367 ; <b>Conventional Hydrogen Bond</b> : ARG D:363, GLN D:409, ARG D:370 ; <b>Alkyl &amp; Pi-Alkyl</b> :LEU D:373, TRP D:369.
NADPH oxidase (NO) Kode PDB : 2CDU <b>Gambar 8</b>	Dextromethorphan (DEX)	<b>Van Der Waals</b> : ILE A:243, <a href="#">PHE A:245</a> , <a href="#">GLY A:244</a> , <a href="#">GLY A:158</a> , ILE A:297, SER A:328 ; <b>Alkyl &amp; Pi-Alkyl</b> : ILE A:160, PRO A:298, <a href="#">TYR A:188</a> , <a href="#">TYR A:159</a> , LEU A:299
	Cyclopropanedodecanoic acid, 2-octyl-, methyl ester	<b>Van Der Waals</b> : CYS A:242, <a href="#">ILE A:243</a> , LYS A:187, LYS A:213, GLY A:180, ASP A:179, <a href="#">GLY A:158</a> , <a href="#">GLY A:244</a> ; <b>Conventional Hydrogen Bond</b> :HIS A:181 ; <b>Pi-Sigma</b> : <a href="#">TYR A:159</a> ; <b>Alkyl &amp; Pi-Alkyl</b> :ILE A:160, <a href="#">PHE A:245</a> , PRO A:298, <a href="#">TYR A:188</a> , LEU A:299
	Oxiraneundecanoic acid, 3-pentyl-, methyl ester, cis-	<b>Van Der Waals</b> : LYS A:213, ASP A:179, GLY A:156, CYS A:242, <a href="#">GLY A:158</a> , GLY A:161, <a href="#">TYR A:159</a> , PRO A:298, <a href="#">TYR A:188</a> , <a href="#">GLY A:244</a> , ILE A:243, ILE A:155 ; <b>Conventional Hydrogen Bond</b> :HIS A:181, GLY A:180 ; <b>Alkyl &amp; Pi-Alkyl</b> :LYS A:187, <a href="#">PHE A:245</a> .
	cis-10-Nonadecenoic acid	<b>Van Der Waals</b> : ILE A: 297, SER A:326, SER A:328, <a href="#">THYR A:159</a> , GLY A:161, <a href="#">ILE A:243</a> , <a href="#">GLY A:244</a> , <a href="#">GLY A:158</a> , CYS 242, SER A:157, VAL A:184, ARG A:183 ; <b>Conventional Hydrogen Bond</b> : TYR A:186, LEU A:185 ; <b>Alkyl &amp; Pi-Alkyl</b> :LEU A:299, PRO A:298, ILE A:160, <a href="#">TYR A:188</a> , <a href="#">PHE 245</a> , LYS 187.
Xanthine oxidase (XO) Kode PDB: 3NRZ <b>Gambar 9</b>	Febuxostat (FEB)	<b>Van Der Waals</b> : <a href="#">ALA C:910</a> , SER C:1008, PHE C:1150, <a href="#">THR C:1010</a> , <a href="#">SER C:876</a> , <a href="#">PHE C:1013</a> , <a href="#">PHE C:649</a> , <a href="#">PRO C:1076</a> ; <b>Conventional Hydrogen Bond</b> : <a href="#">ASN C:768</a> , <a href="#">ARG C:880</a> ; <b>Carbon Hydrogen Bond</b> : <a href="#">LYS C:771</a> ; <b>Unfavorable Donor-Donor</b> : <a href="#">GLU C:802</a> ; <b>Unfavorable Acceptor-</b>

	<b>Acceptor :</b> ARG C:880 ; <b>Pi-Sulfur :</b> PHE C:1009, <b>Pi-Pi Stacked :</b> PHE C:1009; <b>Pi-Pi T-shaped :</b> PHE C:1009 ; <b>Alkyl &amp; Pi-Alkyl :</b> ALA C:1079, ALA C:1078, PHE C:1009, LEU C:648, LEU C:873, LEU C:1014, VAL C:1011
Cyclopropanedodecanoic acid, 2-octyl-, methyl ester	<b>Van Der Waals :</b> ARG C:912, GLY C:913, GLY C:799, GLU C:1261, ARG C:880, GLU C:802, THR C:1010, SER C:876, THR C:803, SER C:1075, MET C:770, PHE C:1013, PRO C:1076 ; <b>Conventional Hydrogen Bond :</b> ASN C:768 ; <b>Carbon Hydrogen Bond :</b> LYS C:771 ; <b>Pi-SigmaI :</b> PHE C:914 ; <b>Alkyl &amp; Pi-Alkyl :</b> ALA C:910, ALA C:1079, PHE C:1009, ALA C:1078, LEU C:1014, VAL C:1011, LEU C:873, PHE C:649, LEU C:648.
Oxiraneundecanoic acid, 3-pentyl-, methyl ester, cis-	<b>Van Der Waals :</b> PHE C:1013, SER C:876, ALA C:910, ALA C:1078, FLU C:1261, THR C:1010, PRO C:1076, LYS C:771, THR C:803, ASN C:768 ; <b>Conventional Hydrogen Bond :</b> ARG C:880 ; <b>Carbon Hydrogen Bond :</b> GLU C:802 ; <b>Alkyl &amp; Pi-Alkyl :</b> LEU C:648, PHE C:649, LEU C:1014, VAL C:1011, PHE C:914, PHE C:1009
cis-10-Nonadecenoic acid	<b>Van Der Waals :</b> GLY C:913, ALA C:1079, THR C:1010, GLU C:802, ALA C:910, ASN 768, THR C:803, LYS C:771, PHE C:1013, SER C:876 ; <b>Conventional Hydrogen Bond :</b> GLU C:1261, ARG C:880 ; <b>Alkyl &amp; Pi-Alkyl :</b> ALA C:1078, PHE C:914, PHE C:1009, LEU C:873, VAL C:1011, LEU 648, LEU C:1014, PHE C:649, PRO C:1076.

Specific interactions occur between some of these residues and the phenyl group of S-warfarin, which bundles against the side chains of PHE476 ( $\pi$ - $\pi$  interaction), PHE100, and ALA103 (hydrogen bond), and interacts with PRO 367 (William et al., 2003). **Table 5** displays a high similarity of interactions with the CP450 receptor between the tested and control molecules and the findings of William et al. (2003). The interactions Phe 476 and Pro 367 With CP450 are FLu, A,B, and C), and the interactions PHE 100 with CP450 are (Flu, A, and C). Interaction of 103 with CP40 (A, B, and C). These results for the tested molecules, together with good BA values in relation to FLU, indicate a good antioxidant ability of these molecules.

A maximum of 78 interactions were observed in the LO receptor (**Figure 7**). In the LO (**Table 6**), the ILE 857, GLN 514, HIS 518, HIS 523; LEU 773, LEU 565, ALA 561, ILE 572, VAL 566, and LEU 511 residues interacted with all molecules, indicating good antioxidant activity. In the LO receptor (**Table 6**) For this receptor an increase in the number of interactions provided an increase in the BA value, when compared to A (22 interactions and BA = -5.3 kcal.mol<sup>-1</sup>), B (21 interactions and BA -4.4; C ( 23 interaction and BA – 5.2) and with ZIL control 16 interactions and BA = -6.7 kcal.mol<sup>-1</sup>). These BA values are relatively close to those of the ZIL control, which indicates good antioxidant ability of the tested molecules in the ZIL receptor (William et al. 2003).

For the MP receptor (**Figure 5**), a maximum of 37 interactions were observed. In the PDB file (1DNU) [Blair-Johnson et al., 2001), the active site of attachment has its location pointed out to the

ASN192, GLN201, and VAL199 amino acid residues, which interact with the N-acetyl-D-glucosamine ligand. This ligand was complexed with the MP receptor available in the PDB. The three previously mentioned residues interact with the control molecule (MEL), GLN 201 interacts with B and C, and VAL 199 interacts with A, indicating a reasonable antioxidant ability of the molecules tested. Other indications of good antioxidant ability are the similarities with the control molecule: A, B, and C interact with amino acid residues (**Table 6**) to the control and BA values ( $-4.7 \text{ kcal mol}^{-1}$  for A,  $-4.2 \text{ kcal mol}^{-1}$  for B,  $4.1 \text{ kcal mol}$  for C and  $-4.6 \text{ kcal mol}^{-1}$  for the MEL control).

In NO (see **Figure 8**), the ILE 243, PHE 245, GLY 244, GLY 158, TYR 188, and TYR 159 residues interacted with all molecules (blue in **Table 6**), indicating a good antioxidant. For the NO receptor (**Table 6**), a maximum of 62 interactions were observed. For this receptor an increase in the number of interactions provided an increase in the BA value, when compared to A (13 interactions and  $\text{BA} = -5.5 \text{ kcal.mol}^{-1}$ ), B (15 interactions and  $\text{BA} -6.5$ ; C (22 interaction and  $\text{BA} - 6,3$ ) and with DEX control (11 interactions and  $\text{BA} = -6.5 \text{ kcal.mol}^{-1}$ ). These BA values are relatively close to those of the DEX control, which indicates the good antioxidant ability of the tested molecules in the NO receptor.

Another evidence of this antioxidant ability is the similarity of the interactions and the active site with results obtained from the literature (Lountos et al., 2006). The active site is surrounded by ILE160, ILE243, ASP179, LYS213, VAL214, and TYR188 residues, which interact with the ligand adenosine-5'-diphosphate in the NO receptor (Costa et al. 2018). From the list of residues, five interacted with A (ILE243, ILE 160, ASP179, LYS213, and THR 188), four with B (ILE 243, ASP179, LYS 213, and TYR188), three with C (ILE 243, ILE 160, THR 188), and three with the DEX control (ILE 243, ILE 160, and TYR 188).

In XO (**Table 6**), the residues that interacted with all molecules are displayed blue in **Table 6**. For this receptor an increase in the number of interactions provided an increase in the BA value, when compared to A (25 interactions and  $\text{BA} = -6.3 \text{ kcal.mol}^{-1}$ ), B (18 interactions and  $\text{BA} = -6.2 \text{ kcal.mol}^{-1}$ ; C (21 interactions and  $\text{BA} = -6.2 \text{ kcal.mol}^{-1}$ ) and Control FEB (23 interactions and  $\text{BA} = -7.3 \text{ kcal.mol}^{-1}$ ). These BA values are relatively close which indicates a good antioxidant ability of the tested molecules in the XO receptor.

The interaction of ligands with receptor Cytochrome P450 (CP450), lipoxygenase (LO), myeloperoxidase (MP), NADPH oxidase (NO), and xanthine oxidase (XO) formed chemical bonds consisting of hydrogen binding, ionic interaction, hydrophobic interaction, hydrogen bonding, interaksi ionik, interaksi hidrofobik,  $\pi$ - $\pi$  interactions, and cation- $\pi$  interactions (**Table 6** dan **Figure 6-10**). Computation method predicts the interaction, binding affinity, and conformation of the ligand-protein complex (Okimoto et al., 2009). Shah dan Misra (2011) The higher the hydrogen binding with amino acid residues, the stronger the binding skor, the lower the energi, and the more stable the structure. *van der Waals interaction* are non-covalent bonds that are involved in electrostatic binding. This interaction is weak and breaks down easily, but the interaction is significant; therefore, it contributes to the stability of the molecule (Vladilo and Hassanali, 2018). The lower the free binding energy, the more stable the binding of the ligand and receptor, and the higher the energy binding, the weaker the strengthening of the protein-ligand complex (Funkhouser, 2007).

The antioxidant abilities of control molecules may be related to the amino acid residues with which the molecules interact. For this reason, the observation of the common residues and BA values close to the tested molecules, controls, and literature suggests that the tested molecules can have good antioxidant ability. This relationship is evident for A, B, and C, which have high similarity in the presented characteristics (among themselves, compared to controls and BA values). The anticancer potency of the mechanism by which algae exert their effects is complex because of their noteworthy structural diversity, which entails multiple interactions (Peng, et al., 201; Maeda et al., 2008)

Since certain seaweeds have long been used in the treatment of cancer, many kinds of crude or partially purified polysaccharides from various brown and red algae have been tested for their properties and have shown antitumor activity against experimental tumors (Ramberg et al., 2010; Harvey, 2004]. Epidemiological data are supported by animal model studies showing the protective effects of dietary algae against skin (De Sousa et al., 2007), intestinal (Watanabe et al., 1978), and

mammary cancers (Funahashi, et al., 2002; Namvar, et al., 2012).. An algal antioxidant-mediated mechanism (Tierney,et al., 2010; Wang et al., 2008) enhances the host’s defense by increasing natural killer cell activity (Myers at al., 2011), activating the nonspecific immune system (Ramberg et al., 2010 9), inhibiting cell growth in the G1 phase, inducing terminal differentiation (Mohamed et al., 2012), and inhibiting the complex process of angiogenesis (Nawzar et al., 2013 ).

Continuous attack of reactive oxygen species on DNA is a significant cause of cancer development. Cells reduce oxidative stress either by repairing damaged nucleotides and lipid peroxidation byproducts or by directly reducing the pro-oxidative state via enzymatic and nonenzymatic antioxidants. Several studies on experimental animals have shown that seaweed can reduce the risk of cancer involving cell proliferation and antioxidant activity (Bayro et al., 2021), and consumption of seaweed has been shown to increase antioxidant enzymes (endogenous antioxidants) such as superoxide dismutase, glutathione peroxidase, and catalase activity in vivo (Corsetto et al., 2020; Korivi et al., 2019).

Pharmacokimetic Properties

In Designing new drugs that are active orally, the drug likeness criteria obey *Lipinski’s Rule of Five profile*, such as: Molecular Weight) ≤500, Hydrogen Bond Donor (HDB) less than 15, hydrogen bond acceptor (HBA) less than 10, octanal-water partition coefficient (Mi Logp) ≤5, and polar surface area (Refraction molar 40-130 Å) (Shaji, et al., 2018). The estimation of drug-likeness properties of *Lipinski’s Rule of Five* phytochemicals of *C. racemosa* followed the criteria of candidates for new drugs (Tabel 2).

Drug candidates must follow *favorable ADMET prediction*. Pharmacokinetic processes of drug targets include adsorption, distribution metabolism, extraction, and toxicity. The identified compounds of *C.racemosa* with lower binding affinity obeyed *Lipinski Rule profile of Five* compounds: cyclopropanedodecanoic acid, 2-octyl-, methyl ester; oxiraneundecanoic acid, 3-pentyl-, methyl ester, cis- and cis-10-Nonadecenoic acid, The Pharmacokinetic analyses are presented in **Table 7**.

**Table 7.** ADME properties cyclopropanedodecanoic acid, 2-octyl-, methyl ester ; oxiraneundecanoic acid, 3-pentyl-, methyl ester, dan cis-10-Nonadecenoic acid.

No.	Compound	HIA	BBB	Plasma protein Binding	CP450	p-Gp	Log Kp	BiA Score
1.	Cyclopropan edodecanoic acid, 2-octyl-, methyl ester	100.000000	17.5431	100.000000	inhibitor	Inhibitor	-1,25	0,55
2	Oxiraneunde canoic acid, 3-pentyl-, methyl ester, cis-	98.555395	6.62728	100.000000	Inhibitor	No	-3,62	0,55
3	cis-10- Nonadecenoi c acid	98.386939	9.69018	100.000000	Inhibitor	Inhibitor	0,525741	0,85

**Note:** HIA (human gastrointestinal absorption); blood-brain barrier (BBB) permeation; P-gp (permeability glycoprotein), cytochrome P450 (CYP), i: inhibition, Log K<sub>p</sub> (skin permeability coefficient), BiA Score (Bioavailability Score).

The pharmacokinetic analysis of compounds A, B, and C consisted of human intestinal absorption (HIA), Bioavailability Score (BiA), Blood Brain barrier (BBB), permiability-glycoprotein



(P-gp), penghambatan isoenzymes cytochrome P450 (CYP), (skin permeability coefficient), and Bioavailability Score (BiA Score). A, B, and C exhibit high HIA values. According to theory, they are good candidates for the design of oral drugs. HIA is an important parameter for the discovery of new drugs. HIA High absorption: 70–100%, medium absorption: 20–70%, and low absorption: 0–20% (Gurung et al., 2016). The HIA of compounds A, B, and C HIA are high (100.00, 98.5555395, and 98.386939, respectively). *Blood–brain barrier* (BBB) criterion is beneficial for observing the effect of a compound on *central nervous system* and is considered dangerous if a drug is only at the peripheral level. A, B, and C exhibit good BBB values. The P-Gp substrate is a drug transporter that is important for determining the absorption and excretion of many drugs. B and C are P-gp inhibitors. P450 enzymes responsible for drug metabolism and the inhibition of these proteins could cause an increase in plasma levels and toxicity. In silico calculations indicated that these compounds (A, B, and C) are inhibitors of cytochrome P450 enzymes. Log  $K_p$  senyawa A,B dan C dengan nilai masing-masing -1.25, -3.62 and 0.525741 (cm/s) showed are not cause skin sensitivity. A BiA score of 1 indicates that the compound is a good candidate therapeutic agent (Fukunishi and Nakamura., 2011). Components A and B present predicted BiA values close to 1, which is good theoretical data for the development of new drugs. The drug-likeness score is a value that theoretically indicates the similarity of a compound to a known therapeutic agent. ADMET profile (**Table 5**) according to all parameters.

Compounds A,B, and C were good drug candidates based on the molecular docking of antioxidant compounds and pharmacokinetic analysis. The biological activity of the test compound showed its potential as a cancer candidate in the future.

## Conclusions

The study of the antioxidant ability of this article was started from the Data Quality of Juice of *C. racemosa*, which is mixed with peanepile and cirus lemone, and can be utilized as a beverage functional as a source of antioxidant and fibers. Validation of the crystallographic data docking protocols of the studied molecules of biological receptors (FLU, ZIL, MEL, DEX, and XIL). The molecular docking protocols for the five receptors (CP450, MP, LO, NO, and XO) showed RMSD values lower than 2.0 Å. This allowed the theoretical data to be in good agreement with the experimental data. The binding affinity (BA) was evaluated for poses with lower  $\Delta G$  values. The CP450, MP, LO, NO, and XO receptors presented positive values of BA, and the interactions of the molecules test in relation to the control molecules, and findings of the literature show good antioxidant ability to the tested molecules.

Analysis of the Pharmacokinetic (Lipinsky profile (Ro5) method and ADMET (Human intestinal absorption (HIA); Bioavailability Score (BiA); Blood Brain barrier (BBB); Permiability-glycoprotein (P-gp), isoenzymes cytochrome P450 (CYP) inhibition, (skin permeability coefficient) and Bioavailability Score (BiA Score), Compound A, B, and C of *C. racemosa* are potential drug candidates.

The results obtained in this study reveal that *C. racemosa* has the potential to be utilized as a functional beverage source of antioxidant that could inhibit oxidative stress diseases, such as cancer. Potential antioxidant ability of the five receptors (CP450, MP, LO, NO, and XO) via ROS generation. Thus, Cyclopropanedodecanoic acid, 2-octyl-, methyl ester, oxiraneundecanoic acid, 3-pentyl-, methyl ester, cis- and cis-10-Nonadecenoic acid may be used for further analyses to evaluate their efficiency in the reduction of oxidative stress as possible anticancer drugs for use in the pharmaceutical industry.

**Data Availability Statement:** The data supporting the findings of this study are available from the corresponding author upon reasonable request.

**Acknowledgement:** This study received financial support from various sources, including a grant from the Ministry of Research and Technology/National Research and Innovation Agency, Republic of Indonesia, through the Basic Research Scheme DRPM 2021 and PNBP Unsrat 2021). The authors wish to thank Sam

Ratulangi University, Agricultural Bogor Institute, Gaja Mada University, and Pajajaran University Bandung for providing the laboratory equipment and analysis for conducting this research.

**Conflicts of Interest:** The authors declare no conflict of interest.

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