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RESEARCH ARTICLES

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MISSION & VISION

The Indonesian Biomedical Journal mission is to assist, enlighten and support all health related policies by delivering information with speed. Its mission is represented by the Logo which is based on two main elements: the Caduceus Staff and naga Antaboga, which are prominent figures in Indonesian "wayang", specifi cally in the famous Mahabharata tale.

AIMS & SCOPE

The Indonesian Biomedical Journal is an open access, peer-reviewed journal that encompasses all fundamental and molecular aspects of basic medical sciences, emphasizing on providing the molecular studies of biomedical problems and molecular mechanisms.

The Indonesian Biomedical Journal is dedicated to publish original research and review articles covering all aspects in biomedical sciences. The editors will carefully select manuscript to present only the most recent findings in basic and clinical sciences. All professionals concerned with biomedical issues will find this journal a most valuable update to keep them abreast of the latest scientific development.

THE LOGO

The 'Indonesian Biomedical Journal' insignia is designed based on two main elements; the Caduceus staff and Naga Antaboga, which are prominent figures in Indonesian 'wayang', specifically in the famous Mahabharata tale. Wayang is the traditional Indonesian puppetry and drama which has its root in Hinduism It is now an ingrained part of Indonesian culture and heritage.

Antaboga's name in his youth is Nagasesa. His father, Antawisesa is a giant snake who weds the goddess Dewi Sayati, daughter of Sang Hyang Wenang, the Principal God. Due to his services to heavenly beings, Nagasesa is honoured with the title 'Bathara' or 'Sang Hyang', which means 'God'. Since then, he is called Sang Hyang Antaboga, in recognition of his new position. His other names are Sang Hyang Nagasesa, Sang Hyang Anantaboga and Sang Hyang Basuki. As a God, Sang Hyang Antaboga is master of the underworld, which in wayang rates as significant as the realm above. His palace is in Saptapratala, the seventh plane below earth.

Sang Hyang Antaboga adopts a human outlook in his customary appearance. In critical situations, he can change his form into a giant snake. He possesses a magical power which enables him to alter his exterior according to his will. As the guardian of the holy water Amerta, he is also endowed with the ability to bring back to life those who die earlier than their natural time.

With the objective of strengthening the tie between them, the Gods reward Sang Hyang Antaboga with a female deity, Dewi Supreti, for a wife. One of the children from this marriage, Dewi Nagagini, will one day marry Bima or Werkudara, the second son of Pandawa family. Bima is one of the central figures in Mahabharata story.

In Indonesian or Javanese mythology, the word 'Naga' means a giant snake. The Indonesian word for snake itself is 'ular'. It is common practice for the Indonesians however to use the two words simultaneously, hence 'ular naga,' to describe a giant snake. Ular naga is widely revered. It is believed to be sacred and bring luck.

The logo of the Indonesian Biomedical Journal, which expresses its mission and vision, is a varied adaptation of the Caduceus staff. The pair of wings on top of the staff represents the speed of information and transformation, thus creation of a new beginning. The staff itself stands for authority. Likewise, in ancient Greek mythology, the pair of snakes or in this logo; the Antabogas, symbolizes the source of life and wisdom. Their intertwining position or 'double helix' incidentally is also the shape of DNA and signifies creation and stability.

In short, the logo of the Indonesian Biomedical Journal represents its mission to assist, enlighten and support all health related policies by delivering information with speed.

The Indonesian Biomedical Journal has been published by The Prodia Education and Research Institute since April 2009. The Indonesian Biomedical Journal, a triannually (April, August and December) published scientific journal, contains original research and review articles covering all aspects in biomedical sciences. All manuscripts submitted to The Indonesian Biomedical Journal will be screened for plagiarism and blind peer-reviewed by 2 or more reviewers to present valuable and authentic findings in basic and clinical sciences. This journal provides immediate open access to its content on the principle that making research freely available to the public supports a greater global exchange of knowledge. This content licensing is in accordance with a CC license: CC-BY-NC.

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Content

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REVIEW ARTICLE

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RESEARCH ARTICLE

The Antioxidant and Cytotoxic Effects of *Cosmos caudatus* Ethanolic Extract on Cervical Cancer

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Abstract

BACKGROUND: Oxidative stress is closely related to all aspects of cancer. *Cosmos caudatus* ethanolic extract (CCEE) has been proved to have antioxidant effect that inhibited cancer cell growth due to its bioactive compounds such as catechin, quercetin and chlorogenic acid. This study aimed to evaluate antioxidant and anticancer activity of CCEE and its compounds.

METHODS: Total phenol was measured according to the Folin-Ciocalteu method. Catechin, quercetin and chlorogenic acid contained in CCEE were identified by high-performance liquid chromatography (HPLC). Antioxidant activity was evaluated by 2,2′-azino-bis-(3-ethylbenzthiazoline-6-sulfonic acid) (ABTS)-reducing activity, 1,1-diphenyl-2-picrylhydrazyl (DPPH) scavenging activity, and ferric reducing antioxidant power (FRAP) activity test. The cytotoxic activity of CCEE was determined by MTS [3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium] assay on HeLa cells.

RESULTS: The result showed that total phenol of CCEE was 181.64±0.93 µg Cathecin/mg extract. ABTS-reducing activity test showed that catechin had the highest activity (2.90±0.04 µg/mL), while CCEE had moderate activity compared to other compounds. FRAP activity test demonstrated that catechin had the highest activity (315.83 µM Fe(II)/µg) compared to other compounds. DPPH scavenging activity of CCEE was 22.82±0.05 µg/mL. Cytotoxicity test on HeLa cell showed that CCEE had lower activity (inhibitory concentration $(IC)_{50}$= 89.90±1.30 µg/mL) compared to quercetin (IC_{50} = 13.30±0.64 µg/mL).

CONCLUSION: CCEE has the lowest antioxidant activity compared to quercetin, catechin, and chlorogenic acid and has the lowest anticancer activity compared to quercetin. However, CCEE and its compounds has potential as antioxidant and anticancer properties.

KEYWORDS: antioxidant, anticancer, catechin, *Cosmos caudatus*, quercetin

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Introduction

Initiation, promotion and progression are the three multistage of cancer.(1,2) Oxidative stress is related to the cancer initiation and progression by increasing DNA mutations or inducing DNA damage, genome instability and cell proliferation.(3) Wide spectrum of diseases, such as most type of cancer, are involving the role of reactive oxygen species (ROS).(4) Imbalance between production of free radicals and reactive metabolites called oxidants or ROS are the sign of oxidative stress, leading to damage of important biomolecules and cells which potentially affected on the whole organism.(5)

Cosmos caudatus locally known as '*Ulam raja*' and widely used as traditional medicine in Southeast Asia, is a herb of the family Compositae. Some studies reported that *C. caudatus* contains some bioactive compounds such as ascorbic acid, quercetin, chlorogenic acid and catechin. These natural compounds have been reported to be excellent antioxidants.(6-8) *C. caudatus* is suggested to have high antioxidant capacity, antidiabetic activity, antihypertensive properties, anti-inflammatory responses, bone protective effect, antimicrobial activity and anticancer properties.(9,10) This research aimed to evaluate the antioxidant potency and cytotoxic effect of *C. caudatus* ethanol extracts. Therefore, we also used high performance liquid chromatography (HPLC) method to observe the compounds in the *C. caudatus* extracts based on standard compound.(11)

Methods

Plant Extract Preparation

Leaves of *C. caudatus* were collected from Cihideung, Lembang, West Java, Indonesia. The plants were identified by herbarium staff, Department of Biology, School of Life Science and Technology, Bandung Institute of Technology, Bandung, West Java, Indonesia. The *C. caudatus* simplicia (300 g) was extracted with ethanol 70% using maceration technique. Ethanol filtrate was filtered, and waste was re-macerated in triplicate. Using RV 10 rotary evaporator (IKA Works, Wilmington, NC, USA) at 50˚C, the filtrate was concentrated to obtain extract. The extract was stored at -20˚C.(12-14)

HPLC Assay

C. caudatus ethanolic extract (CCEE) chemical profiling analysis was performed using HPLC. Quantification of CCEE was done using the standard chlorogenic acid (Chengdu Biopurify Phytochemical, Sichuan, China), catechin (Sigma Aldrich, Darmstadt, Germany) and quercetin (Sigma Aldrich). HPLC analysis used the Hitachi Pump HPLC L-6200, Hitachi L-4000 UV detector and Reverse Phase Column C-18 (Phenosphere ODS-2, Phenomenex, 4.6 mm x 250 mm). Acetonitrile 70% (Merck, Darmstadt, Germany) was used as mobile phase (isocratic) with flow rate of 1.0 mL/min. The samples were then dissolved in methanol 70% (1 mg/mL), filtered through a 0.22 µm syringe, and injected (20 µL) to the column. UV absorbance was measured at 254 nm.(11)

Total Phenolic Content Assay

Total phenolic content was measured according to the Folin-Ciocalteu method. Briefly 15 µL of samples was placed into microplate then added 75 µL of Folin-Ciocalteu's reagent 2.0 M (Merck), followed by 60 µL of sodium carbonate 7.5% (Merck). The mixture was incubated at 45˚C for 15 minutes.(15,16) Subsequently, absorbance value was measured at 760 nm using microplate reader (Multiskan™ GO Microplate Spectrophotometer, Thermo Scientific, Waltham, MA, USA). Total phenolic content expressed as catechin equivalent was calculated by the following formula:

$$C = \frac{c \times v}{m}$$

C: total content of phenolic compounds (µg/mg) of *C. caudatus* in catechin equivalent;
c: the concentration of catechin established from the calibration curve (µg/mL);
V: the volume of extract (mL);
m: the weight of extract (mg).

2,2′-Azino-bis-(3-ethylbenzthiazoline-6-sulfonic acid) (ABTS)-reducing Activity Assay

$ABTS^+$ solution was produced by reacting 14 mM ABTS and 4.9 mM potassium persulfate (Merck) (1:1 volume ratio) for 16 hours in dark condition at room temperature. The mixture was then diluted with 5.5 mM PBS (pH 7.4) until the absorbance of the solution was 0.70±0.02 at wavelength 745 nm. In brief, 2 µL of various concentrations of sample (0.23, 0.47, 0.94, 1.88, 3.75, 7.50, 15.00 µg/mL; µM) was added to each well at 96-well microplate, then the fresh 198 µL $ABTS^+$ solution (Sigma Aldrich) was added. Then, the plate was incubated for 6 minutes at 30˚C and calculated its absorbance at 745 nm. The ratio of reducing $ABTS^+$ absorbance in the presence of the sample relative to the absorbance in the absence of the sample (negative control) was determined as the inhibition percentage of ABTS radical (%). The calculation of the median Inhibitory Concentration $(IC)_{50}$ was also measured.(14,16,17)

Ferric Reducing Antioxidant Power (FRAP) Assay

The FRAP reagent was prepared by mixing acetate buffer (10 mL) 300 mM, ferric chloride hexahydrate (Merck) (1 mL) 20 mM dissolved in distilled water, and 1 mL of 2,4,6-Tris(2-pyridyl)-s-triazine (TPTZ) (Sigma Aldrich) 10 mM dissolved in HCl 40 mM. In 96-well microplate, 7.5 µL of various concentrations of sample (1.17, 2.34, 4.69, 9.38,

18.75, 37.50, 75.00 µg/mL; µM) was mixed with 142.5 µL FRAP reagent, and incubated at 37˚C for 30 minutes. The absorbance value was measured at 593 nm with Multiskan™ GO Microplate Spectrophotometer (Thermo Scientific). The standard curve was created using $FeSO_4$, between 0.019 and 95 µg/mL $FeSO_4$. The measurement results were expressed in µM Fe(II)/µg extract.(14,16,18)

2,2-Diphenyl-1-picrylhydrazil (DPPH) Scavenging Assay

The DPPH scavenging assay was used to measure the radical scavenging activity of the samples.(14) Samples (50 µL) with various concentrations were added to each well in a 96-well microplate. It was followed by addition of 200 µL of DPPH (Sigma Aldrich) solution (0.077 mmol/L in methanol) into the well. The mixture was then incubated in the dark for 30 minutes at room temperature. The absorbance was read using a microplate reader at 517 nm wavelength. The radical scavenging activity was measured using the following formula:

$$\% \text{ Scavenging} = (Ac - As) / Ac \times 100$$

Ac = negative control absorbance (without sample).

As = sample absorbance.

Cytotoxicity Assay

The cervical cancer cells (HeLa$^-$ (American Type Culture Collection (ATCC) CC-Chemokine Ligand 2 (CCL-2)) were obtained from Stem Cell and Cancer Institute, Jakarta, Indonesia. The cells were maintained in Dulbecco modified Eagle's medium containing 10% FBS (Invitrogen, California, USA), 100 U/mL penicillin (Invitrogen) and 100 mg/mL streptomycin (Invitrogen). Then, the cells were incubated at 37˚C, 5% CO_2 .(12) Briefly, $5x10^3$ of cells were seeded in 96 well-plates for 24 hours.(12,13) The medium was discarded, then 180 µL of fresh medium was added into each well. The cells were treated with 20 µL of *C. caudatus* ethanol extract in various concentrations (1000, 500, 250, 125, 62.5, 31.25, 16.125 µg/mL) and quercetin in various concentrations (200, 100, 50, 25, 12.5, 6.25, 3.125 µM). Dimethyl sulfoxide (DMSO) 10% was added in different well as blank. All samples and blank were set in triplicate and incubated for 24 hours. Untreated cells were employed as control. The 3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium (MTS) assay (Promega, Madison,WI, USA) was used to determine cell viability.(12) Twenty µL MTS was added to each well. The plate was incubated in 5% CO_2 at 37˚C for 4 hours. The absorbance was measured at 490 nm with a microplate reader. The data were then presented as percentage of viable cells (%).(12,13)

Results

Total Phenolic Content

Total phenolic content of the sample was measured, this study show that CCEE has total phenolic content is 181.64±0.93 µg Cathecin/mg extract.

HPLC Assay

The compounds content of CCEE was evaluated using HPLC with quercetin, catechin and chlorogenic acid as standard. Figure 1 shows that quercetin, catechin, and chlorogenic acid had retention time at 1.64 minutes, 1.40 minutes and 1.30 minutes, respectively. CCEE has peak at 1.403 minutes, it is close with catechin peak (1.40 minutes) which was assumed as catechin. This HPLC assay indicated that CCEE contained catechin compound.

ABTS-reducing Activity

ABTS-reducing activity of CCEE, catechin, quercetin and chlorogenic acid can be seen in Figure 2A and Table 1. Figure 2A shows ABTS-reducing activity in concentration-dependent manner, where higher concentration of sample increased ABTS-reducing activity. At the highest concentration of sample (15 µg/mL), catechin has the highest percentage of ABTS-reducing activity (73.53%) compared to quercetin (62.10%), CCEE (24.94%) and chlorogenic acid (22.46%). This results indicated that CCEE had low ABTS-reducing activity among other compounds except chlorogenic acid.

Table 1. IC_{50} value of ABTS-reducing activity of CEE, catechin, quercetin and chlorogenic acid.

Sample	ABTS-reducing Activity	
	IC_{50} (µM)	IC_{50} (µg/mL)
CCEE	-	31.97±1.42
Catechin	10.00±0.15	2.90±0.04
Quercetin	12.04±0.16	3.64±0.05
Chlorogenic Acid	35.94±2.14	12.70±0.76

*CCEE = *C. caudatus* ethanolic extract, ABTS = 2,2′-azino-bis-(3-ethylbenzthiazoline-6-sulfonic acid). The data was presented as mean±standard deviation. The ABTS-reducing activity assay was measured in triplicate for each sample.

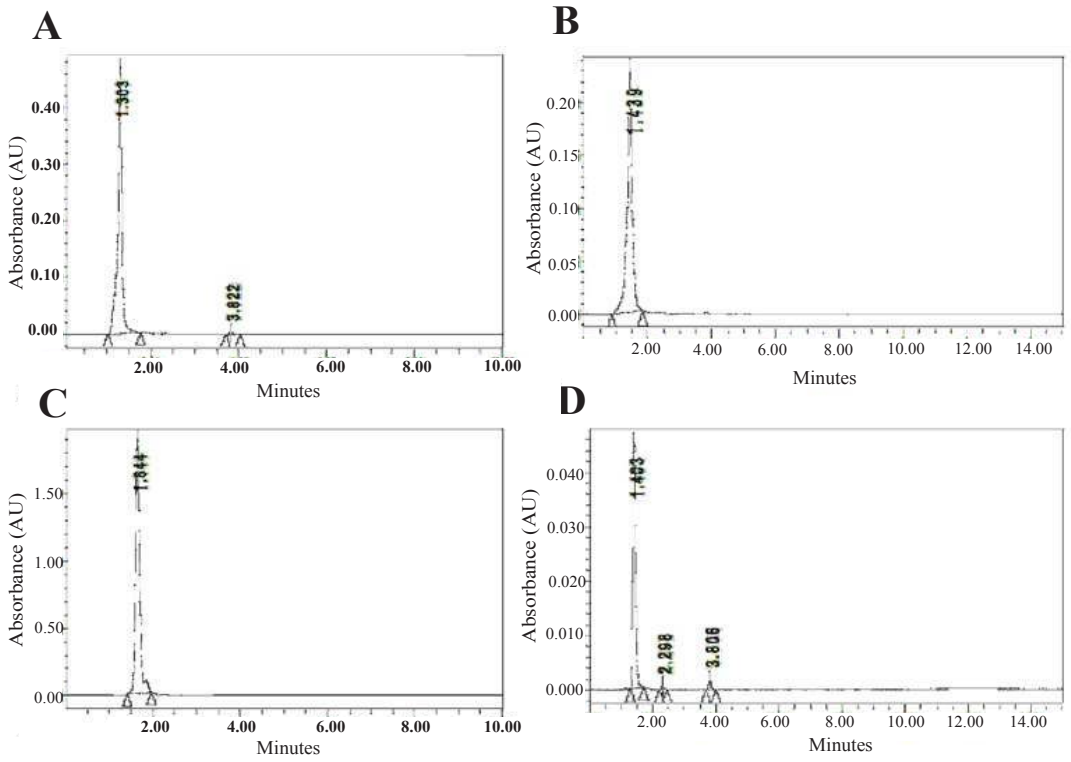

Figure 1. Chromatogram of extract and compounds with HPLC. A: Chlorogenic acid; B: Catechin; C: Quercetin; D: CCEE . *CCEE = *C. caudatus* ethanolic extract, HPLC = High-Performance Liquid Chromatography. This research was conducted in triplicate for each treatment.

Table 1 shows that catechin had the lowest IC_{50} value (2.90±0.04 µg/mL) compared to quercetin (3.64±0.05 µg/mL), chlorogenic acid (12.70±0.76 µg/mL), and CCEE (31.97±1.42 µg/mL). This finding supported the result of ABTS-reducing activity demonstrated the lowest activity of CCEE compared to other samples.

FRAP Activity

FRAP activity of CCEE, catechin, quercetin and chlorogenic acid can be seen in Figure 2B. The antioxidant activity of CCEE, catechin, quercetin and chlorogenic acid were evaluated using FRAP activity assay. Catechin had the highest activity (315.83 µM Fe(II)/µg) compared to

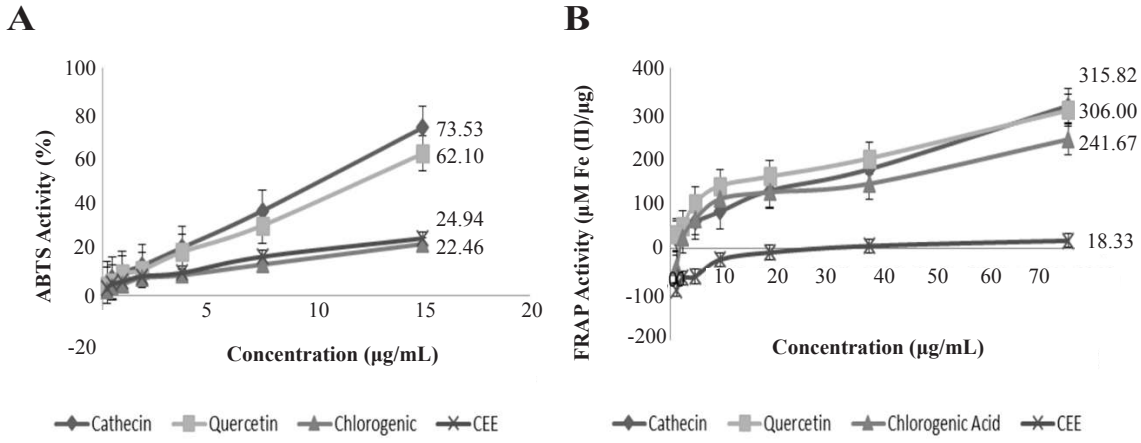

Figure 2. ABTS and FRAP activity of CCEE, catechin, quercetin and chlorogenic acid. *CCEE = *C. caudatus* ethanolic extract, ABTS = 2,2′-azino-bis-(3-ethylbenzthiazoline-6-sulfonic acid), FRAP = Ferric Reducing Antioxidant Power. This research was conducted in triplicate for each treatment. CCEE, catechin, quercetin and chlorogenic acid in ABTS assay were diluted in DMSO to reach the final concentration of 0.23; 0.47; 0.94; 1.88; 3.75; 7.50; 15.00 (µg/mL for CEE and µM for compounds), while in FRAP assay were diluted in DMSO to reach the final concentration of 1.17; 2.34; 4.69; 9.38; 18.75; 37.50; 75.00 (µg/mL for CCEE and µM for compounds).

quercetin (306.00 µM Fe(II)/µg), chlorogenic acid (241.67 µM Fe(II)/µg) and CCEE (18.33 µM Fe(II)/µg). This indicated that CCEE had the lowest antioxidant activity compared to other compounds (Figure 2B).

DPPH Scavenging Activity

The median IC_{50} of DPPH scavenging activity of CCEE, catechin, quercetin and chlorogenic acid can be seen in Table 1. It shows that the IC_{50} value of DPPH scavenging activity of CCEE (22.82±0.05 µg/mL) indicated antioxidant activity through scavenging DPPH free radical.

Cytotoxic Activity

Figure 3 shows the correlation between CCEE and quercetin concentration and its cytotoxicity on HeLa cell. Viability of cells decreased in concentration-dependent manner. The increased concentration was correlated with increased toxicity (<90% viable cells). The highest extract concentration (1000.00 µg/mL and 200.00 µM) demonstrated the lowest of viability of cells by CCEE was 19.23% and quercetin 34.07%, respectively. CCEE and quercetin can inhibit the growth of HeLa cancer cell line with minimum inhibitory concentration (IC_{50}) values 89.90±1.30 µg/mL and 43.99±2.15 µM (13.30±0.64 µg/mL), respectively (Table 2). This indicated that CCEE had lower cytotoxicity compared to quercetin.

Table 2. IC_{50} value cytotoxicity HeLa cells of CCEE and quercetin.

Sample	Cytotoxic Activity	
	IC_{50} (µM)	IC_{50} (µg/mL)
CCEE	-	89.90±1.30
Quercetin	43.99±2.15	13.30±0.64

*CCEE = *C. caudatus* ethanolic extract. IC_{50} of CCEE and quercetin was presented as µg/mL and µM, respectively. The data was presented as mean±standard deviation. This research was conducted in triplicate for each treatment.

Discussion

C. caudatus has been known as a potential herb that has antioxidant and anticancer activity.(19) *C. caudatus* has been reported to have high antioxidant capacity, mainly due to its polyphenol content.(7) The rich-phenolic foods are the sources of natural antioxidants.(19,20) The total phenolic content of CCEE in this study was 181.64 µg Cathecin/mg extract. The result of other study showed that *C. caudatus* has high total phenolic content (1274±98 GAE mg/100 g fresh weight) in the acetone/water system.(7) The aqueous extract of *C. caudatus* has also been known to have the highest phenolic content.(21) Other study showed that the total phenolic content of *C. caudatus* ethanol extract (1144.6 mg/100g) was higher than *C. caudatus* water solvent (844.8 mg/100g).(22) High phytochemical contents, antioxidants, proteins, amino acids, vitamins and minerals are associated with risk reduction of free radical-related degenerative diseases.(23)

In this study, HPLC analysis was evaluated to determine compounds content of *C. caudatus*. Quercetin, catechin and chlorogenic acid were used as standards. Figure 1 shows that CCEE peaked at 1.403 minutes which was assumed as catechin. This indicated CCEE contain catechin compound.

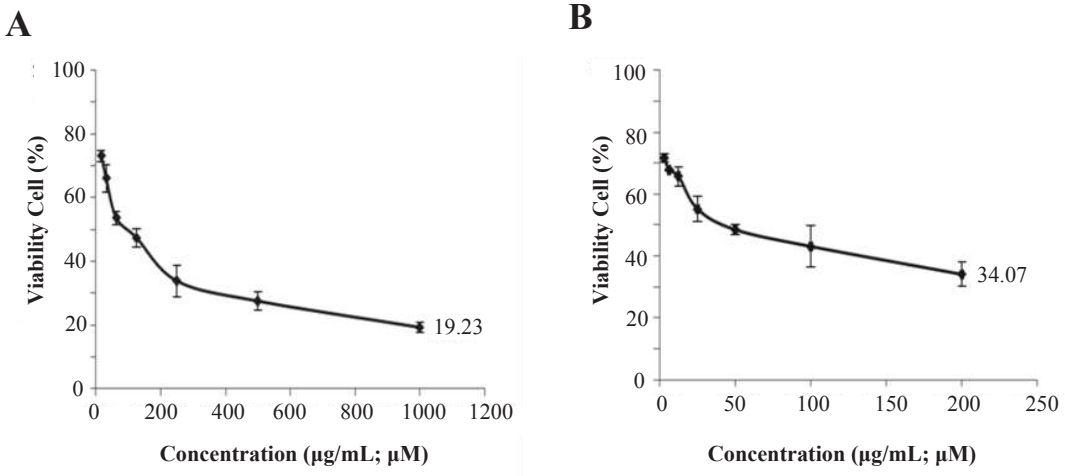

Figure 3. Viability of HeLa cell of CEE and quercetin. A: CEE; B: Quercetin. *CCEE = *C. caudatus* ethanolic extract. This research was conducted in triplicate for each treatment. CCEE was diluted in DMSO to reach the final concentration of 16.125; 31.25; 62.50; 125.00; 250.00; 500.00; 1000.00 (µg/mL); Quercetin was diluted in DMSO to reach the final concentration of 3.125; 6.25; 62.50; 12.50; 25.00; 50.00; 100.00 200.00 (µM).

Based on Noriham, *et al*., study, *C. caudatus* ethanol extract measured by HPLC show presence of catechin.(24)

ABTS-reducing activity of CCEE had moderate activity compared to catechin, quercetin and chlorogenic acid. Based on the result above, CCEE had moderate activity compared to catechin, quercetin and chlorogenic acid, meanwhile in previous study, CCEE had the highest ABTS-reducing activity compared to other plants (4.71 µmol TE/g fw).(25) High antioxidants activity of *C. caudatus* was associated with the ability to reduce oxidative stress.(7) Another study also proved that *C. caudatus* had extremely high antioxidant compared to other plants through total antioxidant capacity (ascorbic acid equivalent antioxidant capacity (AEAC) value).(10)

In this research, DPPH scavenging activity of CCEE (IC_{50}=22.82 µg/mL), indicated that antioxidant activity through DPPH free radical scavenging activity. In our previous studies, the IC_{50} DPPH scavenging activity values of catechin were 7.02 µg/mL (26) and 8.11 µM (27), while DPPH values of quercetin were 4.279 µg/mL (28), 3.244 µg/mL (29) and 19.200 µg/mL (21). The FRAP activity value of CCEE was the lowest among other compounds. Some studies reported that *C. caudatus* had greater antioxidant activity than *Sauropus androgynus* (L) Merr and *Centella asiatica* in DPPH and FRAP assays.(30) Other study showed that *C. caudatus* had the greatest FRAP activity among other plants (25), also CCEE had the highest DPPH scavenging activity which was correlated with flavonoid content in the plants. *C. caudatus* had been reported to possess the highest flavonoid and phenolic content.(25) *C. caudatus* aqueous extract is a good source of antioxidant because it has the highest DPPH and FRAP values.(10) In another study, *C. caudatus* had the highest free radical scavenging potential extract (86.85%).(31) CCEE also showed beneficial activities in reducing number of parameters such as peroxyl value as an antioxidant. Phenolic content in CCEE plays a key role in scavenging free radicals which cause oxidative stress.(19) In addition, phenolic compounds have been shown to possess antioxidant ability which facilitates scavenging electrophiles and active oxygen species, slows down nitrosation and chelates metal ions to limit auto-oxidation, and increases the ability to adjust some enzyme actions.(32,33)

Tumorigenesis occurs due to the increasing free radicals that lead to DNA damage and mutation, apoptosis inhibition, cell cycle/proliferation stimulation, and DNA repair inhibition.(34) The role of ROS in cancer development can be determined in three different stages. Firstly, generating DNA damage including mutations and structural alterations is the ROS first role, followed by the second stage which is the promotion stage where ROS blocks cell-cell communication leading to abnormal gene expression and modification of second messenger, resulting in increased cell proliferation or decreased cell apoptosis. Last stage, furthermore, is the progression of cancer caused by oxidative stress affecting further DNA alterations.(1) Free radicals can react with membrane fatty acids and form lipid peroxides, accumulation of which leads to production of carcinogenic agents.(35) In this study, CCEE had lower cytotoxicity on HeLa cell compared to quercetin. These results were confirmed by Lee and Vairappan that found a weak cytotoxic activity of the ethanolic extract of *C. caudatus* against P388 murine leukemia cells.(9) However, in other study, *C. caudatus* exhibited the highest DPPH free radical scavenging, ABTS-reducing activity, FRAP and inhibition of linoleic acid.(24)

Conclusion

C. caudatus and its compounds showed antioxidant activities as measured through ABTS-reducing activity, DPPH scavenging activity, and FRAP activity. CCEE has the lowest antioxidant activity compared to quercetin, catechin and chlorogenic acid. CCEE also has the lowest cytotoxic activity compared to quercetin. However, CCEE and its compounds has potential as antioxidant and anticancer properties.

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LEMBAR HASIL PENILAIAN
SEJAWAT SEBIDANG atau *PEER REVIEW*

KARYA ILMIAH : JURNAL ILMIAH

Judul Karya Ilmiah (Artikel)	:	The Antioxidant and Cytotoxic Effects of Cosmos caudatus Ethanolic Extract on Cervical Cancer
Jumlah Penulis	:	9 orang
Nama-nama Penulis	:	Betty Nurhayati, Ira Gustira Rahayu, Sonny Feisal Rinaldi, Wawan Sofwan Zaini, Ervi Afifah, Seila Arumwardana, Hanna Sari Widya Kusuma, Rizal, **Wahyu Widowati**
Status Penulis	:	~~Penulis Pertama~~ / Penulis ke 9 / Penulis Korespondensi **)
Identitas Jurnal Ilmiah	: a.	Nama jurnal : Indones Biomed J
	b.	Nomor ISSN : 20853297, 23559179
	c.	Vol., No., Bulan, Tahun : Vol.10, No.3, Dec 2018
	d.	Penerbit : Prodia Education and Research Institute.
	e.	DOI Artikel (jika ada) : 10.18585/inabj.v10i3.441
	f.	Alamat Web Jurnal : https://inabj.org/index.php/ibj/article/view/44
	g.	Terindeks di : Scopus Q4, SJR 0.160

Kategori Publikasi Jurnal Ilmiah: *(beri tanda √ yang dipilih)*

- [√] ~~Jurnal Ilmiah Internasional~~ / Internasional Bereputasi **)
- [ ] Jurnal Ilmiah Nasional Terakreditasi
- [ ] Jurnal Ilmiah Nasional / Nasional terindeks ***)

HASIL PENILAIAN (*Peer Review*) :

No	Komponen Yang Dinilai		Nilai Maksimal JURNAL ILMIAH			Nilai Akhir Yang Diperoleh *)
			Internasional / Bereputasi [√]	Nasional Terakreditasi [ ]	Nasional ***) [ ]	
a.	Kelengkapan unsur isi karya	(10%)	4			3,5
b.	Ruang lingkup dan kedalaman pembahasan	(30%)	12			11,6
c.	Kecukupan dan kemutakhiran data/ informasi dan metodologi	(30%)	12			11,7
d.	Kelengkapan unsur dan kualitas penerbitan	(30%)	12			11,8
	Total	**100%**	**40**			38,6

Catatan Penilaian ARTIKEL oleh Reviewer :

a. Kelengkapan dan kesesuaian unsur.....
Paper ditulis dengan baik, tuntun mengikuti kaidah penulisan karya ilmiah internasional bereputasi

b. Ruang lingkup & kedalaman pembahasan .....
Penelitian antioksidan dan antikanker ekstrak kenkir pada sel kanker serviks

c. Kecukupan & kemutakhiran data serta metodologi... sumber pustaka mutakhir, hasil penelitian membahas hubungan antioksidan dengan antikanker. Uji HPLC dilakukan untuk identifikasi senyawa dan antioksidan menggunakan metode DPPH, FRAP.

d. Kelengkapan unsur dan kualitas penerbit .....
Jurnal InaBJ terindeks Scopus Q4 SJR 0,16. Penerbit Prodia Education and Research Institute.

e. Indikasi plagiasi .....

Tidak terdapat indikasi plagiarism atau self - plagiarism

f. Kesesuaian bidang ilmu .....

Paper bidang biomedik sesuai dengan bidang ilmu penulis

REVIEWER 1

(Prof. Dr. Chrismis Novalinda Ginting, M.Kes)
NIK : 0115127801
UNIVERSITAS PRIMA INDONESIA

LEMBAR HASIL PENILAIAN
SEJAWAT SEBIDANG atau *PEER REVIEW*

KARYA ILMIAH : JURNAL ILMIAH

Judul Karya Ilmiah (Artikel) : The Antioxidant and Cytotoxic Effects of Cosmos caudatus Ethanolic Extract on Cervical Cancer

Jumlah Penulis : 9 orang

Nama-nama Penulis : Betty Nurhayati, Ira Gustira Rahayu, Sonny Feisal Rinaldi, Wawan Sofwan Zaini, Ervi Afifah, Seila Arumwardana, Hanna Sari Widya Kusuma, Rizal, **Wahyu Widowati**

Status Penulis : ~~Penulis Pertama~~ / Penulis ke 9 / Penulis Korespondensi **)

Identitas Jurnal Ilmiah :

a. Nama jurnal : Indones Biomed J
b. Nomor ISSN : 20853297, 23559179
c. Vol., No., Bulan, Tahun : Vol.10, No.3, Dec 2018
d. Penerbit : Prodia Education and Research Institute.
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Kategori Publikasi Jurnal Ilmiah: *(beri tanda √ yang dipilih)*

☑ ~~Jurnal Ilmiah Internasional~~ / Internasional Bereputasi **)

☐ Jurnal Ilmiah Nasional Terakreditasi

☐ Jurnal Ilmiah Nasional / Nasional terindeks ***)

HASIL PENILAIAN (*Peer Review*) :

No	Komponen Yang Dinilai		Nilai Maksimal JURNAL ILMIAH			Nilai Akhir Yang Diperoleh *)
			Internasional / Bereputasi ☑	Nasional Terakreditasi ☐	Nasional ***) ☐	
a.	Kelengkapan unsur isi karya	(10%)	4			3,4
b.	Ruang lingkup dan kedalaman pembahasan	(30%)	12			11,7
c.	Kecukupan dan kemutakhiran data/ informasi dan metodologi	(30%)	12			11,9
d.	Kelengkapan unsur dan kualitas penerbitan	(30%)	12			11,9
	Total	**100%**	**40**			38,8

Catatan Penilaian ARTIKEL oleh Reviewer :

a. Kelengkapan dan kesesuaian unsur.....
Jurnal ini sudah cukup lengkap dan ada kesesuaian antara unsur dan isinya
.....

b. Ruang lingkup & kedalaman pembahasan .....
Ruang lingkup bahasan sudah memadai dan ada kedalaman dalam pembahasannya
.....

c. Kecukupan & kemutakhiran data serta metodologi.....
secara umum metodologi masih terbatas dan belum sepenuhnya.
.....

d. Kelengkapan unsur dan kualitas penerbit .....

Kualitas penerbit sudah memenuhi reputasi yang baik

e. Indikasi plagiasi

secara umum belum terlihat adanya unsur plagiasi

f. Kesesuaian bidang ilmu

Jurnal ini sudah sesuai dengan bidang ilmu yang diteliti

REVIEWER 2

(Prof. Dr. Ermi Girsang, M. Kes)
NIK : 0117057501
UNIVERSITAS PRIMA INDONESIA

LEMBAR HASIL PENILAIAN
SEJAWAT SEBIDANG atau *PEER REVIEW*

KARYA ILMIAH : JURNAL ILMIAH

Judul Karya Ilmiah (Artikel)	:	The Antioxidant and Cytotoxic Effects of Cosmos caudatus Ethanolic Extract on Cervical Cancer
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Status Penulis	:	~~Penulis Pertama~~ / Penulis ke 9 / Penulis Korespondensi **)
Identitas Jurnal Ilmiah	:	
a. Nama jurnal	:	The Indonesian Biomedical Journal,
b. Nomor ISSN	:	20853297, 23559179
c. Vol., No., Bulan, Tahun	:	Vol.10, No.3, Dec 2018
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Kategori Publikasi Jurnal Ilmiah: *(beri tanda √ yang dipilih)*

- [√] ~~Jurnal Ilmiah Internasional~~ / Internasional Bereputasi **)
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- [ ] Jurnal Ilmiah Nasional / Nasional terindeks ***)

HASIL PENILAIAN (*Peer Review*) :

No	Komponen Yang Dinilai		Nilai Maksimal JURNAL ILMIAH			Nilai Akhir Yang Diperoleh *)
			Internasional / Bereputasi [√]	Nasional Terakreditasi [ ]	Nasional ***) [ ]	
a.	Kelengkapan unsur isi karya	(10%)	4			3,45
b.	Ruang lingkup dan kedalaman pembahasan	(30%)	12			11,65
c.	Kecukupan dan kemutakhiran data/ informasi dan metodologi	(30%)	12			4,75
d.	Kelengkapan unsur dan kualitas penerbitan	(30%)	12			11,85
	Total	**100%**	**40**			38,7

Catatan Penilaian ARTIKEL oleh Reviewer :

a. Kelengkapan dan kesesuaian unsur.....
Paper ditulis dengan baik, tuntun mengikuti kaidah penulisan karya ilmiah internasional bereputasi
Jurnal ini sudah cukup lengkap dan ada kesesuaian antara unsur dan isinya

b. Ruang lingkup & kedalaman pembahasan .....

Penelitian antioksidan dan antikanker ekstrak kenikir pada sel kanker serviks.

Ruang lingkup bahasan sudah memadai dan ada kedalaman dalam pembahasannya

c. Kecukupan & kemutakhiran data serta metodologi Sumber pustaka mutakhir, hasil penelitian membahas hubungan antioksidan dengan antikanker. Uji HPLC dilakukan untuk identifikasi senyawa dan antioksidan digunakan metode DPPH, FRAP

Secara umum metodologi ~~sud~~ masih terbatas dan belum sepenuhnya

d. Kelengkapan unsur dan kualitas penerbit
Jurnal INABJ terindeks scopus Q4 SJR 0,16. Penerbit Prodoa Education and Research Institute

Kualitas penerbit sudah memenuhi reputasi yang baik

e. Indikasi plagiasi

Tidak terdapat indikasi plagiarism atau self-plagiarism

Secara umum belum terlihat adanya unsur plagiasi

f. Kesesuaian bidang ilmu

Paper bidang biomedik sesuai dengan bidang ilmu penulis

Jurnal ini sudah sesuai dengan bidang ilmu yang diteliti

Medan,
Reviewer 2

(Prof. Dr. Erni Girsang, M.Kes)
NIK : 0117057501
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Medan,
Reviewer 1

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NIK : 0115127801
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