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# Effectiveness of Plant Bioactive Compounds as Colorectal Cancer Cell Line Inhibitors: A Systematic Review

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**Abstract:** Cancer is a non-communicable disease and one of the highest causes of human death. It has been well documented that active substances have been shown in vitro to have anticancer properties. The purpose of this article is to examine the therapeutic implications of active substances involved in colorectal anticancer activity. We looked through the databases of PubMed, Science Direct, and Google Scholar in our systematic review to find papers released between 2013 and 2023. Ten studies were selected and published between 2013 and 2023. From the results obtained on plant data used as colorectal anticancer, it was reported that plants contain active phenolic compounds, flavonoids, alkaloids, gallic acid, saponins, triterpenoid/steroid, hydroquinones, triterpenoids, phenols, glycosides, quercetin, kaempferol, artemisinin, and tannins that can act as colorectal anticancer agents and are proven to be an inhibitor of cell line growth in colorectal cancer.

**Keywords:** Anti-cancer, cell culture, colorectal.

## Introduction

Colorectal cancer is one of the most common malignant tumors in the world, and in recent years the morbidity and mortality rates have continued to increase due to unbalanced diets such as consuming foods that are high in fat and low in fiber (Cai & Zhigang, 2021). Consuming high-fat foods will lead to increased levels of cholesterol, triglycerides, unsaturated fatty acids, and bile acids. These cholesterol and bile acids will be converted into secondary bile acids, cholesterol metabolites, and toxic substances by bacteria in the colon that can damage the colon mucosa, triggering inflammation (Harahap, 2019). Inflammation in this mucosa, resulting some disorders such as colitis and IBD (inflammatory bowel disease) that can increasing risk of colorectal cancer (Bajpai et al, 2019).

Tertiary hospital-based survey in Indonesia revealed that CRC accounted for 73.7% of all gastrointestinal malignancies in 2002-2011(Makmun, 2014). In Indonesia, colorectal cancer ranks fourth with an incidence rate of 12.1 per 100,000 population and a mortality rate of 6.9 per 100,000 population (Ferlay et al., 2021). Cell culture has marked a major change in research, one of them is research on cancer cells. Cell culture is one of methods to test the cytotoxicity of potential bioactive compounds against cancer cell lines. (Rodríguez-Hernández et al., 2014). In the medical world, cells derived from certain tissues or organs can be used to research or diagnose a disease, for example, in viral or bacterial infections and in vitro studies for cancer (Thorpe, 2007).

Animal cell culture involves the placement of one or more living cells of animal origin in an isolated environment whose physicochemical properties are able to mimic their physiological conditions (Rodríguez-Hernández et al., 2014). Based on the source of cells used, cells can be divided into two categories: primary cells and cell lines. Primary cultures facilitate the growth of

cell populations derived from a specific region or tissue of the mammalian system. These comparatively isolated cell populations can be easily maintained in a conditioned environment that mimics the minimal essential requirements for their growth and survival. These cells can be used to examine the effects of specific drugs, synthetic molecules, or bodily fluids from disease patients (Ghosh & Sathyaprabha, 2018).

A cell line is a group of cells produced from a multicellular organism that, although ordinarily unable to multiply forever, is able to divide owing to a mutation that prevents the cells from going through normal cell demise (Chaudhary & Pamela, 2019). In this article, we have summarized research on the type of cell line used, the source of the plant/extract, and the type of compound. Aim of this articles is to make it easier for other researchers to conduct in-depth invitro studies on the various phytopharmaceutical potentials available.

## Methods and Materials

The basis for the preparation of this review was the review of research articles on the effects of plant bioactive compounds on various colon cancer cell lines. International databases such as Google Scholar, PubMed and Science Direct were used as the data source for this review search. The keywords used for the search using the PICO strategy, such as: "cell lines colon cancer," "active agent for cancer," and "therapeutic effects of medicinal plants on colon cancer," or a combination of keywords searched using Boolean operators. The keywords use Boolean operators such as "therapeutic effects active compound" AND "colon cancer". Inclusion and exclusion criteria are used to analyze and select articles.

The inclusion criteria are adjusted to the purpose of the review article, so the journal inclusion criteria used are research data that produce primary data that discusses the cytotoxic effects of plant bioactive compounds on colon cancer cell lines, original articles, colon cancer cell line research subjects, journal publication years in the last ten years, namely 2013-2030, full-text articles and indexed by Scopus Q1 - Q4.

Exclusion criteria that will be used to select articles are articles that discuss colon cancer. Articles that do not specifically discuss the effects of plant compounds on colon cancer, bioactive compounds other than plants on colon cancer, and research subjects are humans or microorganisms. Then, the literature is a journal review, short report, case report, and clinical trial report. Journals following the criteria of keywords, titles, and abstracts are reviewed in full text to determine the content and adjust to the topic under review. Searched for journals used for review by looking at the inclusion and exclusion criteria. The analysis carried out in this article review was carried out descriptively.

## Results and Discussions

Here are the steps in systematically reviewiHere are the steps in systematically reviewing journals. First, the journal identification process through the international database was selected and 29 journal articles were obtained. With several criteria such as the article must be original, the publication of the article is 10 years and above, and the topic of the article is about cell culture. Furthermore, screening of articles that discuss colorectal cancer cell lines was carried out. And finally the eligibility selection where articles are selected with criteria that discuss the effects of bioactive compounds on colorectal cancer cell lines and articles are full text articles.

The prism diagram in the selection of the results obtained from the review is that of the 11 journals categorized as inclusion journals, 2 of them are compiled by authors who are all foreign nationals. The remaining eight journals are composed mostly of a collection of Indonesian or joint authors. The journal publication year ranges from 2015 to 2021, dominated by journals published in 2021 with six journals. The types of cell lines used in these journals are quite diverse, ranging from HT-29 colon cancer cell line, human colon cancer cell line, WiDr colon cell line, and HCT116 colon cell line.

This review's most widely used cell line is the WiDr colon cell line in as many as five journals. As for the aspect of plant extracts used, each journal uses different extracts. The plant extracts used include Sungkai leaf extract (*Peronema canescens* Jack), Paku Atai leaf

(*Angiopteris ferox* Copel), Baru Cina leaf (*Artemisia cina*), Pirdot leaf (*Saurauia vulcani*), Binahong leaf (*Anredera cordifolia* [Tenore] Steen. ), rhizome of Ganyong (*Canna indica*), Randorung (*Helicteres hirsuta*), water soybean (*Glycine soja* L.), and Salayar (*Ficus deltoidea* Jack). In addition to the diversity in plant aspects, there are differences in the extraction methods used. Most journals use the maceration method (with solvents such as ethanol reagent, methanol reagent, and dichloromethane reagent). However, some journals use fractionation with solvents such as n-hexane and ethyl acetate.

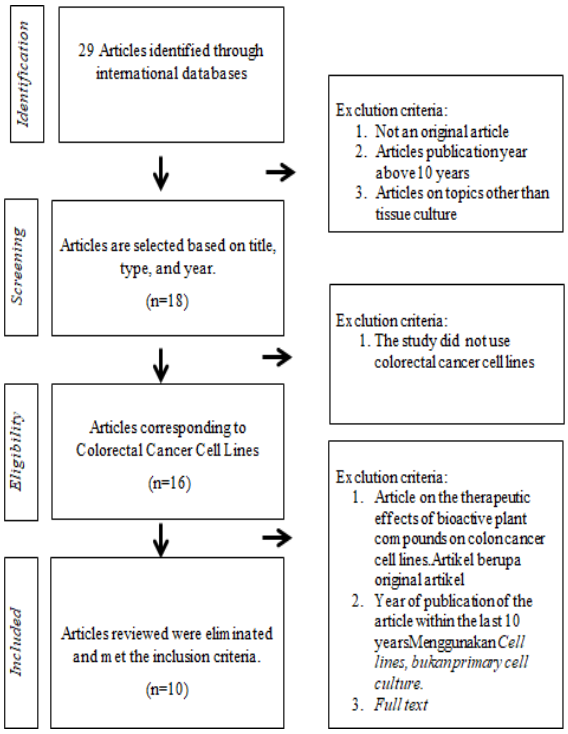


**Figure 1.** Prism diagram in the selection of articles

The compounds highlighted in the journals also vary, including alkaloids, saponins, flavonoids, hydroquinone, tannins, steroids, triterpenoids, phenols, glycosides, quercetin, kaempferol and artemisinin. Another difference of concern is the method of execution of each journal. Methods such as the most commonly used measurement of cytotoxicity are the MTT assays. In addition to cytotoxicity, other aspects that are often measured are the inhibition of the cell cycle, the induction of apoptosis, and the rate of cell necrosis; all three parameters can be measured by flow cytometry. Other methods include LC-MS analysis of chemical profiles, HPLC determination of quercetin, kaempferol, and artemisinin, ICC specific protein assays, and TLC screening of phytochemicals, cytotoxicity assays, in silico molecular binding assays, phytochemical evaluation of functional groups by Fourier transform infrared (FTIR) spectroscopy, liquid chromatography-high resolution mass spectrometry (LC-HRMS), etc.

One form of cancer that is frequently encountered or endured by individuals worldwide is colorectal cancer. This is among the three most prevalent kind of cancer which can affect both men and women. A person's age, genetics, colitis, smoking, unhealthy lifestyle, and inadequate diet can all be factors in the development of colorectal cancer (Yumi et al., 2016; Kuipers et al., 2016). The prevalence of colorectal cancer keeps rising annually. Based on GLOBOCAN statistics from 2018, colorectal cancer ranks fourth globally in terms of cancer incidence. In Indonesia, the incidence rate adjusted for age is 12.8 per 100,000, while the overall case fatality rate is 9.5%. Cancer is often treated with pharmaceuticals like radiation therapy, chemotherapy, or a mix of the two. However, adverse effects from chemotherapy might include discomfort, gastrointestinal distress, and diminished hair growth. Moreover, the chemotherapy medications assault healthy cells while destroying cancerous ones (Luanpitpong, 2012).

### *Peronema canescens*

These sungkai plants, a member of Verbenaceae, grow in tropical areas like Indonesia (Rosdiana, 2014). The Dayak community, which is located in Indonesia, employs the leaves of *Peronema canescens* as a traditional medicine called jamu in the East Kalimantan region. It is used to cure fever, swine flu stomach ache, and as an antimicrobial on the skin and inside the oral cavity. Juvenile *Peronema canescens* leaves serve as an antisplasmodic, antidema, and anti-inflammatory drug in Lampung and South Sumatra (Yani et al., 2013; Ramadenti et al., 2017; Ibrahim et al., 2017). *Peronema canescens* leaves are a kind of medicinal material that is rich in secondary metabolic products, including flavonoids, terpenoids, and phenolic substances, all of which are beneficial to human health. based on the quantity and arrangement among the available OH

groups (Maigoda et al., 2022).

***Angiopteris ferox***

*Angiopteris ferox* Copel, or in Indonesian, "paku atai" is one of the ferns used as medicinal plants in Indonesia. The people of East Kalimantan have long-empowered red atai spikes (*Angiopteris ferox* Copel) as an herb that is thought to have potential as a breast anticancer and antitoxic. Sap, leaves, stems, and bulbs are among the often utilized plant components. Phytochemical examination of ethanol-derived extracts of red atai spike bulbs yielded results that included groupings of chemicals such steroids, flavonoids, alkaloids, tannins, and saponins (Sundu et al., 2018; Nur et al., 2019). Flavonoid compounds in this plant play a role in inhibiting cancer cells through carcinogenesis inactivation, cell cycle inhibition, angiogenesis inhibition, cell proliferation and apoptosis mechanisms (Burhan et al., 2019; Aisyah et al., 2020).

***Artemisia cina***

Artemisinin is the predominant secondary metabolite chemical produced by the herbal plant *Artemisia cina,* which is a member of the Compositae family (Kasmiyati et al., 2020). Numerous bioactive natural products, roughly classified as terpenoids (mono-, sesqui-, and triterpenes) with antiproliferative abilities against malignant cells and polyphenolic secondary metabolites (flavonoids, flavonoid glycosides, and coumarins) with antioxidant activity were discovered during chemical compound exploration of the Artemisia genus. The cytotoxic properties of the n-hexane extract of A. cina in comparison to the methanol extract can be explained by two main chemical classes with distinct polarities: polyphenols (polar) and terpenoids (non-polar) (Al-Sarayah et al., 2020).

From the research of Kasmiyati et al. (2021), Using NIR, anticancer chemicals from A. cina's polyploid (P) and wild (W) plants were found. Using the MTT test and doxorubicin (D) as a control, cytotoxic effect was ascertained. IC50 values are calculated using probit analysis from SPSS16. W contains norutin, whereas P contains the four identified chemicals. TW, P, and D had IC50 values in WiDr of 295.5, 84.1, and 0.5 µg/mL, in HTB 183 of 322.4, 128.6, and 39.9 µg/mL, and in Vero of 104, 315.6, and 295.5 µg/mL, correspondingly. The WiDr W, P, and D selectivity indexes were 34, 4, and 91, whereas the HTB 183 values were 31, 3, and 7, in that order. W contains norutin, whereas P contains rutin, artemisinin, quercetin, and kaemferol. Compared to doxorubicin, both plants had lower cellular toxicity. WiDR and HTB 183 shown selectivity in both plants.

***Saurauia vulcani***

People in North Sumatra have long utilized the plant as an alternative medication. As a result, the leaves as well as other plant components (such as the branches, sticks, bark, and roots) have anti-diabetic and therapeutic properties that may be utilized to treat various digestive system-related illnesses. In general, *Saurauia vulcani,* also known as "pirdot" in the locals tongue, grows unrestrained along the boundaries of woods. From Simalungun, Toba, and North Tapanuli districts to other locations close to the highway, this species can be spotted along the Sumatra roadway (Pasaribu et al., 2020). Studies on the plant *Saurauia vulcani* and related taxa may lead to the discovery of therapeutic compounds with properties like antioxidants, immunomodulators, anticholesterol, and antimicrobials that might treat illnesses.

These species include several chemical components, including glycosides, terpenoids, alkaloids, flavonoids, saponins, and tannins, according to data (Rosidah et al., 2021; Rosidah et al., 2021). Based on the test results utilizing WiDr cancer cells, ethyl acetate-based prickly leaf extract exhibited potent cytotoxic properties towards these cancer cells. In comparison, the cytotoxic activity of the methanol and n-hexane extract of pirdot leaves was moderate to rather slight. In addition, the HCT 116 cells' cytotoxic test revealed that the leaves of Pirdot exhibited no cytotoxic properties in the methanol, ethyl acetate, or n-hexane extracts. (Pasaribu et al., 2021). If an extract's IC50 value is less than 10 µg/ml, it may be considered to have very high cytotoxic property; if it is between 10 and 100 µg/ml, it can be considered to have strong cytotoxic activity; and if it is between 100 and 500 µg/ml, it can be considered to have moderate cytotoxic properties. In this instance, the bare minimum amount of leaf extract required to diminish or completely stop the development of cancer cells is known as the IC50 value. (Medita, 2023).

**Table 1.** Summary of research results (inclusion) data)

| No | Authors | Year | Types Of Cell Lines | Plant Extract Source | Compounds | Result |
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| 1. | Arsyik Ibrahim, Siswandono, Bambang Prajogo Ew | 2021 | HT-29 colon cancer cell line dan primary Adenocarcinoma (AdenoCa pT3N1cM1) colon cancer cells. | *Peronema canescens* Jack/ Sungkai leaf | SF3 | Extraction by maceration method using methanol solvent, fractionation process using vacuum column chromatography (VCC) with polarity gradient eluent. Cytotoxicity of SF3 was measured by MTT assay. Cell cycle inhibition, apoptosis induction, and cell necrosis were evaluated by the flow cytometry method. Results: The cytotoxicity value (IC50) against AdenoCa cells was 1.897 µg/ml. The inhibitory activity of synthesis and mitosis phases of the cell cycle showed that different concentrations of SF3 had inhibitory activity on HT-29 (29.614 µg/ml) by 26.79% and 0.16%, AdenoCa cells (14.807 µg/ml) by 10.27% and 19.29%, respectively. For induced apoptosis activity in HT-29 (29.614 µg/ml) and AdenoCa (14.807 µg/ml) cells were 26.58% and 11.50%, respectively. While the necrosis activity in HT-29 (29.614 µg/ml) and AdenoCa (14.807 µg/ml) cells was 0.02% and 9.56%, respectively. |
| 2. | Syamsu Nur , Andi Nur Aisyah, Endang Lukitaningsih, Rumiyati, Rini Indriani Juhardi, Rezkiawati Andirah, Andi Sitti Hajar | 2021 | Epithelioid carcinoma, human colon cancer, and mammary gland breast cancer. | *Angiopteris ferox* Copel/ Atai spike leaf | Ethyl acetate fraction | The study showed that the ethyl acetate fraction contributed an antioxidant with very strong activity and a cytotoxic with moderate activity against all three types of cancer cells (epitheloid carcinoma, colon cancer, and breast cancer). LC-MS prediction showed that the phenolic and flavonoid groups of the compounds responded to their effects. Therefore, A ferox Copel is potentially developed as an anticancer agent, although the sample still needs further testing. |
| 3. | Elizabeth Betty Elok Kristiani, Sri Kasmiyati, Maria Marina Herawati | 2021 | WiDr colon and HTB-183 lung cancer cell lines | *Artemisia cina* extract /Baru cina leaf | Ethyl acetate fraction | The research method used was quantitative method with experimental design. The determination of quercetin, kaempferol and artemisinin was done by HPLC. The cytotoxic activity of the extracts was determined by the MTT method. The specific proteins associated with apoptosis were determined by ICC assay. The content of the three bioactive compounds in the ethyl acetate extract was higher than that in the |

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| | | | | | | hexane extract, with the extracts of genotypes J and KJT showing higher levels than those of genotypes M and TWN. The IC50 values (µg/mL) of the extracts against the tested cancer cells were about 400-700 for hexane extract and 200-500 for ethyl acetate extract. BCl-2 expression of both cancer cell lines was decreased by the treatment with TWN-EA and M-EA, while P53 expression was increased. TWN-EA induced apoptosis of HTB-183 cell line through caspase-8 and caspase-9 pathways, but M-EA induced only caspase-9 pathway. TWN and M genotypes have the potential to be used as anticancer agents in colon and lung cancer. |
| 4. | G. Pasaribu, S. Hudiyono, E. Budianto, A.H. Cahyana And G. Pari | 2021 | Human Colon WIDR and HCT-116 Cancer Cells | *Saurauia vulcani* leaf extract/ Pirdot leaf | Alkaloids, saponins, flavonoids, triterpenoids / steroids, tannins, and hydroquinone | Colorectal anti-cancer activity was tested in vitro by MTT method against WiDr and HCT 116 cancer cells by using n-hexane, ethyl acetate and liquid methanol fractions as solvents. The results of phytochemical analysis showed that Saurauia vulcani (Pirdot Leaf) leaf extract contained tannins, saponins, flavonoids and terpenoids. Chemical component analysis of the ethyl acetate fraction showed the presence of fatty acid groups. The n-hexane, ethyl acetate and methanol fractions showed cytotoxicity against WiDr cell lines with IC50 values of 456.19, 97.41 and 191.92 ppm, respectively. While the cytotoxic activity of the leaf extract against HCT cell line was achieved with IC50 values of 777.35, 568.53 and 529.39 ppm corresponding to n-hexane, ethyl acetate and methanol fractions, respectively. The leaf extract in ethyl acetate fraction was the most effective in inhibiting WiDr cells. |
| 5. | Rifki Febriansah, Harena Anggun Lakshita | 2021 | WiDr Colon Cancer Cell Line | Binahong (*Anredera cordifolia* [Tenore] Steen)/ Binahong leaf n-hexan fraction | Flavonoid | Samples were prepared by maceration using 70% ethanol and fractionation using n-hexane. Phytochemical screening was carried out by thin layer chromatography method (chromatographic technique useful for separating organic compounds). Antioxidant test was performed using 1,1-diphenyl-2-dipicrylhydrazyl assay while 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide assay |

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| | | | | | | was designed for cytotoxic test on WiDr colon cancer cells to identify its single effect and combination with 5-fluorouracil as chemotherapeutic agent. Furthermore, in silico assay with molecular tethering was used to determine 4',6,7-trihydroxyaurone as an active compound on NFB against protein Kb kinase (IKK) and COX-2 inhibitors. |
| 6. | Sri Kasmiyati, Elizabeth B.E. Kristiani, Maria M. Herawati, Ferdy S. Rondonuwu | 2021 | WiDR colon cancer and HTB183 lung cancer cell lines | *Artemisia cina* extract /Baru cina leaf | Hexsan extract | Anticancer compounds were detected by NIR. Cytotoxic activity was determined using MTT assay with Doxorubicin (D) as control. Calculation of IC50 values using SPSS16 with probit analysis. P contained the four determined compounds, while W did not contain rutin. The IC50 values of W, P, and D were 295.5, 84.1, and 0.5 µg/mL in WiDr, 322.4, 128.6, and 39.9 µg/mL in HTB 183, while the actual values were 104, 315.6, and 295.5 µg/mL, respectively. The selectivity indices of W, P, and D were 34, 4, and 91 in WiDr, while those of HTB 183 were 31, 3, and 7, respectively. P contained artemisinin, quercetin, kaemferol and rutin, while W did not contain rutin. The cytotoxicity of both plants was less than doxorubicin. Both plants were selective against WiDR and HTB 183. |
| 7. | Ifandari,, Sitarina Widyarini, L. Hartanto Nugroho, Rarastoeti Pratiwi | 2020 | WiDr colon cancer cell line | Rhizome Ganyong (*Canna indica*)/ Tasbih flower | Dichloromethane extract | Phytochemical content of two different variants of ganyong (known as ganyong in Indonesia), namely red ganyong and green ganyong. These two discrete samples were extracted using two different solvents, dichloromethane and ethanol, followed by evaluation using Fourier Transform Infra-Red (FTIR) spectroscopy to detect functional groups. To analyze the elemental composition of chemical compounds, the samples were then injected into high-resolution liquid chromatography-high-resolution mass spectrometry (LC-HRMS). Cell viability assay was performed to evaluate the cytotoxic activity of compounds extracted from two edible ganyong cultivars in two different solvents. FTIR results showed that red and green ganyong extracts contained 17 and 18 |

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| | | | | | | functional group compounds, respectively. In addition, the cell viability of WiDr cells treated with red ganyong dichloromethane extract was lower than green ganyong or red ganyong ethanol extract. Notably, LC-HRMS results of the most potent dichloromethane extract of edible red ganyong revealed the presence of fatty acid compounds. These results suggest that both ganyong variants could potentially be used as promising candidates for colon cancer treatment. |
| 8. | Triet Thanh Nguyen, Nadine Kretschmer, Eva-Maria Pferschy-Wenzig, Olaf Kunertb And Rudolf Bauer | 2018 | Leukemia CCRF-CEM, breast MDA-MB-231, colon HCT116 and glioblastoma U251 cancer cells | Aerial part of *Helicteres hirsuta* / Randorung plant | Triterpenoidal Phenol | In this study, two terpenoids: 3β-O-acetylbetulinic acid (1) and simiarenol (2), and three phenolic compounds: 4,4'-sulfinylbis(2-(tert-butyl)-5-methylphenol) (3), 7-O-methylisoscutellarein (4), 7,4'-di-O-methylisoscutellarein (5), and a mixture of stigmasterol and β-sitosterol were isolated and structurally described from the aerial parts of Helicteres hirsuta Lour. Compounds 1-5 were tested for cytotoxicity on four human cancer cell lines: leukemia CCRF-CEM, breast MDA-MB-231, colon HCT116 and glioblastoma U251 cancer cells. Among them, compounds 1 and 3 showed moderate activity on CCRF-CEM and HCT116 cancer cells with IC50 values ranging from 14.6 to 31.5 Mm ($P < 0.05$). This is the first time these compounds have been reported from this plant. To our knowledge, compound 3 is novel, although it has been chemically synthesized before, and compounds 1, 2, and 4 are new to this plant family (Sterculiaceae). |
| 9. | DA Hidayat Dan S Dwira | 2018 | HCT-116 colon carcinoma cell line | *Glycine soja* L. extract)/ Water soybean | Ethanol extract | The thin-layer chromatography (TLC), phytochemical screening tests, and MTT assay were performed. TLC revealed that there were six different compound components in the ethanol extract of the black soybean. The phytochemical screening test identified six classes of chemical compounds, namely alkaloids, tannins, flavonoids, saponins, triterpenoids, and glycosides. MTT assay of black soybean ethanol extract on HCT-116 cells showed a half maximum inhibitory |

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| | | | | | | concentration (IC50) value of 97.56 µg/ml with moderate cytotoxic properties compared to cisplatin, used as positive control, which had an IC50 Value of 55.51 µg/ml with moderate cytotoxic properties. Based on statistics, there was a significant difference in absorbance values between concentration groups (p = 0.001). Ethanol extract of black soybean has cytotoxic effect on the growth of HCT-116 cells. |
| 10. | Kusmardi Kusmardi, Tedjo Aryo, Wuyung Puspita Eka, Fadilah Fadilah, Priosoeryanto Bambang Pontjo, Fachri Wilzar | 2018 | Human colon cell lines. | *Ficus deltoidea* Jack leaf extract / Salayar plant / Tabat Barito | Ethanol extract | The extract also inhibited the growth of human colon cancer (HCT 116) with an IC50 value of 5.41 mg/mL. Phytochemical screening of the extract showed three groups of compounds: alkaloids, flavonoids and tannins. Aqueous fraction was the best fraction. |

***Anredera cordifolia***

One natural substance from Indonesia, Binahong (A. cordifolia), has the potential to be used for the curative purposes of cancer. Binahong was once utilized as a traditional medication for wound healing (Hadian, 2010). Numerous investigations have been carried out to uncover Binahong's biological function. The active ingredients in binahong contain analgesic, antibacterial, antioxidant, and anti-inflammatory properties. Flavonoids, glycosides, terpenoids, alkaloids, and saponins are the active ingredients (Leliqia et al., 2017). Using an MTT assays, the cytotoxic properties of 5-fluorouracil and NFB (n-Hexane Fraction of Binahong) were examined on WiDr cells. The combination was created to look into how much one extract may increase while the other extract's dosage was set. The combination's range of levels was determined by comparing the extract's and the substance's IC50 values from earlier cytotoxic studies (Fathani, 2020).

Human cell line WiDr cells were first time obtained from a 78-year-old woman's colon, WiDr cells come from the HT-29 colon cancer cell line. (Chen et al., 1987). In Fathani's 2020 study, using quercetin as a positive control molecule, the reactive oxygen species scavenging property of NFB at various doses was assessed using the DPPH technique. With an IC50 concentration of 2851 µg/mL, NFB was shown to have less activity than quercetin, the positive control, which had an IC50 score of 6.87 µg/mL. This is because NFB's ability to lower DPPH free radicals is inadequate and its flavonoid content is insufficient. In order to ascertain if NFB has the ability to prevent WiDr tumor cells from proliferating, this study examined cytotoxic activities. The MTT test was utilized to assess cytotoxic activity. The findings demonstrated that NFB had an IC50 level of 191 µg/mL, which was sufficient to limit the proliferation of WiDr cells, but 5-fluorouracil had an IC50 level of 311 µg/mL (Fathani, 2020).

***Rhizome Ganyong***

There are two cultivar categories of edible ganyong in Indonesia: red and green cultivars. According to Sari et al. (2016), the primary criteria used to categorize ganyong cultivars are the color of the fruit, rachis, and spatha; the coloration of the edge of the leaf and undersurface of the midsection; and the coloration of the buds of the foliage and midribs. The peak bands showed the differences in spectrum patterns among the two cultivars of edible ganyong. While there were changes in the spectrum patterns of both kinds for the solvent dichloromethane, there were none for the ethanol. Compared to the ethanol extract, the peak bands in the red and green ganyong

dichloromethane solvent were easier to see. .

This indicates that the molecules that incline to vary from semi-polar to nonpolar are where the two types diverge from one another. Canna indica rhizome extracts were subjected to phytochemical screening, which revealed the presence of alkaloids, flavonoids, tannins, polyphenols, terpenoids, and saponins. All varieties of extracts included alkaloids; these bonds were identified as the O-H band, N-H band, C = O bond, and C-H bending group. The alkaloid class is known to have the four chemical linkages (Sharmi, 2016). Every one of the four extracts contains terpenoids. Coughendjioua & Djeddi, 2017; Mohandas & Kumaraswamy, 2018) state that the existence of the C-H extend bond, O-H bond, C=O bond, and C-O stretch ester indicates this. C-H stretch vibrations bound in areas 3000 to 2800 cm-1 are known to include lipid groups (Starlin et al., 2012).

***Black Soybean Extract***

Numerous investigations have been carried out about the impact of black soybean on the proliferation of different cancer cells. The proliferation of HT-29 cells has been significantly inhibited by black soybean extract. Six kinds of chemical substances were found by phytochemical screening tests: alkaloids, tannins, flavonoids, saponins, triterpenoids, and glycosides. Research (Triandita, 2019) mentioned that Black soybeans' anthocyanins may reduce reactive oxygen species and responses to inflammation by mutating the APC tumor suppressive gene, which would restrict cell development. A corresponding study (Zou, 2011) also examined the impact of black soybean extract on HT-29 proliferation, demonstrating that delphinidin, the anthocyanin with most inhibitory potential, could inhibit 30%–66% of HT-29 cell growth at a dose of 50 μM. Another study found that black soybean extract possesses an IC50 score of 3.69 mg/ml towards gastric cell carcinomas (Kim, 2008).

***Aerial part of Helicteres hirsuta***

Helicteres species are utilized in traditional Vietnamese medicine as vermifuges, tonic agents, and anti-inflammatory drugs (Pham, 1999). According to earlier research, the primary constituents of the Helicteres species include lignans, flavonoids, and triterpenoids (Li K, 2016). Helicteres angustifolia compounds that have been identified exhibit cytotoxicity towards many cancer cells (Chen, 2006).

***Ficus deltoidea* Jack (FD)**

According to research by Kusmardi et al. (2018), FD ethanol extracts block the production of β-catenin in mice colorectal crypt epithelium cells treated by AOM/DSS. The extract can also stop the development of human colon carcinoma (HCT 116) with an IC50 level of 5.41 mg/mL. Three types of chemicals were identified by phytochemical screening of the extract: tannins, flavonoids, and alkaloids. The best fraction was the water one. Vitexin and isovitexin are the primary potential chemicals to alter protein expression, while FD extract is assumed to affect β-catenin expression based on the outcomes of in silico research using molecular docking (Shafaei A et al., 2014), extend oscillations confined in areas 3000–2800 cm-1 from C–H (Starlin et al., 2012).

## Conclusions

In vitro studies on different colon cancer cell lines have been performed on more than ten plants. Active compounds in these plants, including phenolics, flavonoids, alkaloids, hydroquinone, saponins, steroids, tannins, phenolics, glycosides, triterpenoids, quercetin, kaempferol, artemisinin, and hydroquinone have potential anticancer activities and have been implicated in the inhibition of growth of colorectal cancer cell lines.

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