INTRODUCTION

Reactive oxygen species (ROS) are highly reactive species, due to the presence of unpaired valence shell electrons. Free radicals or ROS are regularly and continuously produced as byproducts of normal cellular metabolism in aubrooms. Free radical chain reactions are usually produced in the mitochondrial respiratory chain, liver mixed functions, and by drugs or xenobiotic such as synthetic pesticides. In addition, chemical mobilization of fat stores under various conditions such as lactation, exercise, fever, and even infection can cause an increase in radical activity that leads to oxidative stress [1,2].

Oxidative injury now appears the fundamental mechanism underlying a number of human neurologic and other disorders [3] such as neurodegenerative disorders, for example, Alzheimer's disease, Parkinson's disease, multiple sclerosis, Down's syndrome, inflammation, viral infection, autoimmune disorder, gastrointestinal inflammation, ulcer, mutagenesis, and carcinogenesis [4-6]. Moreover, the ROS also initiate the multistage carcinogenesis process starting with the DNA damage and accumulation of genetic events in one or a few lines, which leads to the progressive dysplastic cellular appearance, deregulated cell growth, and finally carcinoma [7].

Cancer is the leading cause of mortality worldwide. According to the cancer reports published by the World Health Organization and the World Cancer Research Fund, the incidence of cancer is still increasing, especially due to diet, environment, and carcinogenic virus infections [8,9].

Cancer is a multistep disease, incorporating physical, environmental, metabolic, chemical, and genetic factors, which play a direct and/or indirect role in the induction and deterioration of cancers. In Indonesia, colon and rectal cancer are ranked fourth of cancer deaths after lung, liver, and stomach cancer every year [10]. Therefore, proper prevention and treatment efforts are needed to reduce the incidence of death from colon cancer. Diet with high consumption of antioxidant-rich fruits and vegetables significantly reduces the risk of many cancer diseases suggesting that confident antioxidants could be effective agents for the inhibition of cancer spread [11].

Doxorubicin is one of the chemotherapeutic agents included in the main class of cytotoxic agents that are anthracyclines that have broad-spectrum antitumor activity. However, the use of doxorubicin is restricted because it can cause toxicity in normal cells, cardiotoxicity leading to heart failure [12] so that treatment becomes less effective. In other side, plants have many phytochemicals with various bioactivities including antioxidant, anti-inflammatory, and anticancer activities which are safe [13-15]. One of the useful plants is male papaya (Carica papaya L.) flower. Male papaya flowers have long been known to be a very important source in maintaining public health. Flower papaya males have been studied where the plant part of flower papaya males has high antioxidants. For ages, papaya has been used as a medicinal plant traditionally, due to its antibacterial, antioxidant, anticancer, and antitumor activities [16-18] and is well known for a wide variety of medicinal uses.

By keeping in view all the properties of antioxidants, their use in the treatment of different degenerative and neurological disorders; present research work was designed for the isolation of bioactive components of male flower extracts and assessment of anticancer activity on different cancer cell lines, using different extracts of the male flower of C. papaya L. Therefore, the aim of the present study was to investigate the in vitro antioxidant and cytotoxic activity of papaya male flower extracts on human colon cancer cell (WiDr).
Medanense (MEDA) University of Sumatera Utara. Voucher specimen was collected and deposited in the Pharmacognosy Laboratory, Faculty of Pharmacy, University of Sumatera Utara.

**Preparation of extract and fractions**

Extraction was done by percolation method using ethanol solvent. 200 g of powdered papaya male flower is percolated in 1 L ethanol solvent 24 h, then filtered, do it continuously until the filtrate obtained is clear and colorless. 10 g concentrated ethanolic extract, then fractioned using hexane solvent to get the hexane fraction [19,20].

**Preliminary phytochemical screening**

Phytochemical screening carried out on various papaya male flower hexane fraction included examining the chemical metabolites constituent of alkaloids, flavonoids, glycosides, tannins, triterpenoids, and steroids [21-23].

**Measurement of the antioxidant activity using α,α-diphenyl-β-picrylhydrazyl (DPPH)**

Analysis of DPPH radical scavenging activity was carried out according to Blois method. 0.5 mM DPPH was added to each sample. A dilution series was prepared for ascorbic acid and hexane fraction. After incubation for 30 min in the dark condition, and absorbance was taken at 515 nm and calculated the % inhibition of DPPH radical [24,25]. Test was carried out in triplicate.

Statistical analysis

All the data were expressed as mean ± standard deviation. The significant difference of data between different groups was compared by ANOVA followed by Duncan’s test.

### RESULTS

**Phytochemical screening**

Phytochemical screening results of the hexane fraction of papaya male flowers showed different chemical compound in different extract.

**DPPH scavenging activity of free radical**

The result of the radical scavenging capacities determined by DPPH assay is shown in Table 1.

**Cytotoxicity on WiDr cell**

The anticancer activity of papaya male flower hexane fraction was investigated using a MTT assay on colon cancer cell (WiDr cell). Fig. 1 shows that the effect of fraction on WiDr cell and normal human cell (Vero cell).

**DISCUSSION**

Although papaya has been reported for its benefits and biological activities, little is known scientifically about its male flower antioxidant and anticancer activity. The present study was aimed to reveal the effect of hexane fraction from papaya male flowers on the antioxidant and anticancer potential on WiDr cell (colon cancer cell). Preliminary phytochemical screening was the first step to do. The phytochemical screening (Table 2) results show that the hexane fraction of papaya male flower revealed the strong presence of triterpenoids and steroids phytochemical constituents.

Free radicals are one of the major factors necessary to cause DNA mutation, which in turn triggers the initiation stage of carcinogenesis [27]. To protect human beings against free radicals problem, it is important to identify the new sources of safe and inexpensive antioxidants of natural origin. Antiradical power of natural sources was measured using the DPPH method which is stable, quick, reliable, and reproducible. The hexane fraction of papaya male flower shows a good potential antioxidant activity (IC50=100.81±1.180). It is very important to point out that a low IC50 value reflects a high antioxidant of the fraction [28,29].

An investigation was done on anticancer properties of papaya leaves significant growth inhibitory activity of the papaya extract on tumor cell lines was observed [16]. Another study shows that the hexane fraction of papaya male flower had a good anticancer effect on breast cancer. In the current study, the effect of hexane fraction of papaya male flower was tested on WiDr cell and Vero cell (normal human cell) using MTT to see the cytotoxic effect. MTT assay study shows that hexane fraction had a good IC50 value on cell viability (IC50: 64.105 µg/mL). This result indicated that hexane fraction could suppress the growth of WiDr cell. It can happen due to the triterpenoids and steroids compound in the hexane fraction. Another possibility is due to the antioxidant activity from the hexane fraction of papaya male flower [30,31].

**CONCLUSIONS**

From overall, the study of antioxidant and anticancer potential of hexane fraction from papaya (C. papaya L.) male flower could be concluded that papaya male flower is an excellent source of antioxidant
and is a promising source of potential anticancer source. These findings indicate the medicinal value of papaya in terms of cancer chemotherapy and chemoprevention.

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AUTHORS CONTRIBUTION
All the authors have contributed equally.

CONFLICTS OF INTERESTS
Declared none

REFERENCES