INTRODUCTION

Figs (Ficus carica L.) containing active compounds such as phenols, terpenoids, flavonoids and alkaloids in vitro have shown to have effect in inhibiting the proliferation of various cancer cells and antioxidant properties (Joseph and Justin Raj, 2011). Research was conducted by Ghanbari et al., (2012) show that olive oil has the main class content of phenol compounds namely phenolic acids, flavonoids, lignans and biophenol which have potential as antioxidants and anticancer.

Cancer is one of the life-threatening diseases in the world. In Indonesia, the prevalence of cancer is the number seven cause of death (Wahyuni et al.,...
The prevalence of cervical cancer in Indonesia is in the first rank, followed by breast cancer (Dasar, 2013). Cervical cancer is a malignant disease caused by infection from Human Papilloma Virus (HPV) that occurs around the cervical tissue (Fitriana and Ambarini, 2012). The prevalence of HPV infection as many as 75% occurs in women who have had free sex before marriage (Cancer Foundation of Indonesia, 2017).

Patients infected with HPV are treated with chemotherapy, radiation therapy, or even to undergo surgery (Lui and Grandis, 2012). Chemotherapy can produce very strong toxic effects to cancer cells and can attack normal cells so that they cause adverse side effects (Baqtayyan, 2012). Therefore, there is a need for alternative treatments for cervical cancer, one of which uses medicinal plants mentioned in the Qur’an, in the first and second verse of At-Tin which means “For the sake of figs and olives”, these figs and olive plants are mentioned together (Ministry of Religion of the Republic of Indonesia, 2014).

In the results of a study by Kichaoui et al., (2016) it was shown that fig fruit (Ficus carica L.) extract contains the compound of Quercetin-3-O-glucoside which has been proven to have an intrinsic mechanism that is capable of reducing HeLa cell proliferation. Likewise, in the study of Yao et al., (2014), it was stated that olive oil extract (Olea europaea L.) contains Oleuropein compounds and intrinsically has a cytotoxic effect on HeLa cells. Because both can potentially inhibit the proliferation of HeLa cervical cancer cells, a research related to the combination of figs and olive oil as anticancer agents is needed, so that they can be used as effective and maximum treatment and expected to have a synergistic and mutual reinforcing mechanism to inhibit proliferation of HeLa cervix cancer cell (Yao et al., 2014). Therefore, aim of the study to evaluate antioxidant and cytotoxic activity of combined Ficus carica L. and Olea europeae L. against HeLa cervical cancer cells

**METHODS**

**Figs Extraction**

Extraction was carried out through maceration method using 70% ethanol with a ratio of 1:4 for 5 days, stirred every day. Extracts were separated from the solution by evaporation with temperatures below 50°C until thick extracts were formed and stored at 4°C (Jasmine et al., 2015).

**Flavonoid Identification**

As many as 1 ml of ethanol extract samples of figs and olive oil were put into the test tube, then added sulfuric acid (H2SO4) 2N as many as 2 drops and strongly shaken. Samples positively contain flavonoids when the solution undergoes a very striking color change to yellow, red or brown (Lisi, Runtuwene and Wewengkang, 2017).

**Cytotoxic Test**

Cells were planted on 96-well plates with 5x10^3 cells/wells incubated for 24 hours. Cells were treated through samples with a ratio of 1:0; 1:3; 1:1; 3:1; 0:1 for 24 hours. The media were removed and washed with 100μl PBS (Sigma), adding MTT reagent 5 mg / mL to each well and incubated at 37°C for 4 hours. Alive cells can convert MTT reagent to purple formazan after incubation by adding SDS 10% HCL 0.01 N reagent stopper and incubating it for 24 hours. To read absorbance with an ELISA reader is at λ 595 nm (Cancer Chemoprevention Research Center, 2015).

**Test of antioxidant activity using the DPPH method**

To make a DPPH (1.1 diphenyl-2-picrylhydrazyl) solution of 1000 ppm is done by weighing DPPH 10
mg diluted with ethanol in a 10 mL volumetric flask. Measuring flasks are coated with aluminum foil and stored in a closed cupboard to avoid light. Fig extract, olive oil and a combination of both with comparisons of 3:1 are dissolved using ethanol in a 10 mL volumetric flask, then made in concentration series of 5, 10, 15, 20, 25 mg/L. It was taken 2 mL from each concentration and added with 2 mL DPPH solution which was placed in a test tube and vortexed for 2 minutes then incubated for 30 minutes. Absorbance was measured at a wavelength of 516 nm with UV-Vis spectrophotometry. Then it is calculated as the percentage of DPPH color reduction by using the equation:

\[
\text{Antidote to free radical activity (\%) = } \frac{1 - \text{Sample Absorbance}}{\text{Control Absorbance}} \times 100% \quad (\text{Munte, Runtuwene and Citraningtyas, 2015})
\]

Data analysis of cytotoxic test was using probit analysis to obtain IC₅₀ values of samples that showed a percentage of culture death cell as much as 50%. Then, Data analysis of antioxidant test was using linear regression.

**RESULTS**

The results of the determination showed that the fig was a family of Moraceae and a species of Ficus

**Table 1. Phytochemical Screening Test of Fig Fruit Extract (Ficus carica L.) and Olive Oil (Olea europeae L.)**

<table>
<thead>
<tr>
<th>No</th>
<th>Parameter Test</th>
<th>Reagent</th>
<th>Color</th>
<th>Method</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Flavonoid of Fig Fruit</td>
<td>H₂SO₄₂N</td>
<td>Dark Brown</td>
<td>Tube Test</td>
<td>Positive</td>
</tr>
<tr>
<td></td>
<td>Extract</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Flavonoid of Olive Oil</td>
<td>H₂SO₄₂N</td>
<td>Dark Brown</td>
<td>Tube Test</td>
<td>Positive</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

**Table 2. Total Flavonoid Content of Fig Fruit Extract and Olive Oil**

<table>
<thead>
<tr>
<th>Sample</th>
<th>Replication</th>
<th>Absorbance</th>
<th>Flavonoid Substance (mg/g QE)</th>
<th>Mean (mg/g QE)</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fig Fruit</td>
<td>1</td>
<td>0.3911</td>
<td>177.9661</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>0.3921</td>
<td>179.6610</td>
<td>179.3220</td>
<td>1.2222</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>0.3925</td>
<td>180.3390</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>0.4204</td>
<td>227.6271</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Olive Oil</td>
<td>2</td>
<td>0.4169</td>
<td>221.6949</td>
<td>231.1864</td>
<td>11.6851</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>0.4302</td>
<td>244.2373</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Tabel 3. IC₅₀ value of figs extract, olive oil and a combination of both by comparison (1:3, 1:1, 3:1) to HeLa cervical cancer cells.**

<table>
<thead>
<tr>
<th>Concentration Comparison</th>
<th>IC₅₀ Cytotoxic (µg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Fig Fruit Extract : Olive Oil)</td>
<td>Doxorubicin Positive Control</td>
</tr>
<tr>
<td>1 : 0</td>
<td>13063.915</td>
</tr>
<tr>
<td>0 : 1</td>
<td>679.593</td>
</tr>
<tr>
<td>1 : 3</td>
<td>1562.356</td>
</tr>
<tr>
<td>1 : 1</td>
<td>746.923</td>
</tr>
<tr>
<td>3 : 1</td>
<td>563.626</td>
</tr>
<tr>
<td>Doxorubicin Positive Control</td>
<td>13.707</td>
</tr>
</tbody>
</table>
carica L. and olive oil was a family of Oleaceae and a species of Olea europaea L.

The results of figs extraction were obtained as many as 318.70 grams with extract water content values of 6.08%. The results of phytochemical test analysis of figs and olive oil extracts have flavonoids. The phytochemical test results are presented in the Table 1. Test results for total flavonoids levels are presented in Table 2.

Cytotoxic activity tests of figs and olive oil extracts and a combination of both were carried out to determine the inhibitory activity of HeLa cervical cancer cells using the MTT assay method. The cytotoxic test results are presented in table 3.

Determination of antioxidant activity of figs, olive oil and combination of both extracts with a ratio of 3:1 was carried out by measuring IC50 values using the DPPH method. The IC50 test results of antioxidant activity are presented in Table 4.

DISCUSSIONS

The results of the determination showed that the samples of figs from the species of Ficus carica L. and olive oil from the type of Olea europaea L contribute thick extract as many as 318.70 grams, so that the percentage of yield was 58.34%. The fig extract was obtained with a moisture content of 6.08% with a requirement of 5-30% thick extract of water content (Voigt, 1994).

The qualitative test of flavonoids was carried out using a tube method which aims to ensure the presence of flavonoids contained in figs and olive oil extract. Figs and olive oil extracts showed positive flavonoids with striking color changes from orange to brown (Puspa et al., 2017).

The average of total flavonoid content of olive oil is 231.19 mg/g QE and the results of the total flavonoid content of fig extract is 179.32 mg/g QE. From the results of the two samples, the results of the total flavonoid levels above can be seen that the highest total flavonoid levels are found in olive oil.

According to (Tiwary et al., 2015), the potential of an extract is said to have cytotoxic activity if the IC50 value <1000 μg / mL and no cytotoxic activity if the IC50 value is > 1000 μg/mL. Cytotoxic tests on HeLa cervical cancer cells obtained IC50 values in figs, olive oil and combination of both had significantly different results. In the cytotoxic test results, it was obtained from a combination of fig and olive oil in a ratio of 3:1 and it had cytotoxic activity when compared to extracts of figs which did not have cytotoxic activity. This is believed to be related to antioxidant activity from a combination of figs extract and olive oil.

Antioxidant activity showed that the combination of figs and olive oil with a ratio of 3:1 had the highest antioxidant activity because the IC50 values obtained belonging to a very strong antioxidant and if the IC50 value is <50 ppm (Garcia-Davis et al., 2019). Antioxidant activity in fig extract belongs to moderate antioxidants because the IC50 value is in the range of 101-150 ppm, and the IC50 value of olive oil has antioxidant activity which is classified as very strong because it has an IC50 value of <50 ppm (Garcia-Davis et al., 2019). This is in line with the research conducted by Ouchemouck et al., (2017) which stated that the flavonoid compounds contained in Ficus carica have no effect on cytotoxic tests in concentrations tested but have antioxidant activity. This is supported by the results of the test for total flavonoid content of olive oil of 231.18 mg/g QE and fig extract of 179.32 mg/g QE.

The combined index value of a combination
sample of fig extract and olive oil in a ratio of 1:3 has an antagonistic effect because it enters into a combination index range of 1.45-3.3. At a ratio of 1:1, it has a mild to moderate antagonistic effect because it enters the combination index range from 1.1 to 1.45. At a ratio of 3:1, it has a mild to moderate synergistic effect because it enters into a combination index range of 0.7-0.9 (Suttirak and Manurakchinakorn, 2014), so it can be interpreted that the combination of fig and olive oil extract in a ratio of 3:1 has synergistic effects and increase cytotoxic activity against HeLa cervical cancer cells when combined.

CONCLUSIONS
This study showed the presence of antioxidant activity and cytotoxic power on a combination of fig extract (Ficus carica L.) and olive oil (Olea europaea L.) on HeLa cervical cancer cells (21,0689 ppm and 563,626 μg / mL). The combination of fig extract (Ficus carica L.) and olive oil (Olea europaea L.) in a ratio of 3:1 has a synergistic effect, cytotoxic and a very strong antioxidant activity in inhibiting the proliferation of HeLa cervical cancer cell.

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REFERENCES


