Mario Melchiori, Stefano Frondosi - Triterpenoids of L. sufraginus, holothurin A, holothurin B, and scabraiside that might play a role in cancer cell apoptosis, proliferation, and metastasis.

MATERIAL AND METHOD

Bohadschia argus sample in this study was obtained from Kamal Village, West Seram, Mollucas Indonesia. The sample was washed with water to remove dirt and sand. Then the sample was stored on a cold state.

Bohadschia argus Extraction

Extraction of B. argus carried out by maceration method. B. argus was weighed 25 g and crushed. The sample was macerated into the hot water 80°C ± 500 mL for ± 2 hours. Maceration results were filtered using filter paper. After filtered, the extraction is then separated from water contain using freezdry.

Analysis Using LC-MS

The analysis of compound extract B. argus was performed by the LC-MS (Shimadzu LCMS - 8040 LC/MS), 1 μL sample was injected into the column 2 mm D x 150 mm 3 μm, Capillary voltage 3.0 kV, with column temperature 35°C and Flow rate 0.5 mL.min⁻¹. Desolvation gas flow 6 L.hr⁻¹, run time 120 minutes.

Network Construction

Network analysis was used to understanding the effect of the active compound in sea cucumber B. argus. The network analyzing active compound with protein was constructed using App Cytoscape 3.6.0.8 [20]. Six proteins related cancer cell was obtained by STRING network diseases then active compounds and protein interaction was established with STITCH proteins/compound network. In the network graphic, proteins and active compounds were presented as nodes, while compounds-proteins and proteins-proteins interaction were presented as edges.

RESULT AND DISCUSSION

Based on the results of LC-MS, the active compound of B. argus extract are shown in Table 1. Chondroitin sulfate is an active compound of B. argus extract that may act as anti-metastasis [5]. Another compound like Holothurin B and Holothurin A that included in the Triterpene glycoside [6]. Triterpene glycoside is the most abundant compound in sea cucumber [7]. It was...
secondary metabolite on sea cucumber which plays a role in cancer cells with inducing apoptosis by activating caspase, anti-proliferation and arrest cell cycle on S or G2/M [8].

Table 1. Sea cucumber *B. argus* active compound induce apoptosis and cell cycle arrest in breast cancer cell

<table>
<thead>
<tr>
<th>Compound</th>
<th>Activity</th>
<th>Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frondoside A</td>
<td>Induce Apoptosis</td>
<td>[9]</td>
</tr>
<tr>
<td>Holohurin A</td>
<td>Induce apoptosis, Anti-metastasis</td>
<td>[10]</td>
</tr>
<tr>
<td>Holohurin B</td>
<td>Induce Apoptosis</td>
<td>[13]</td>
</tr>
<tr>
<td>Echinoside A</td>
<td>Induce Apoptosis</td>
<td>[11][12]</td>
</tr>
<tr>
<td>Cucumarioside</td>
<td>S phase Arrest</td>
<td>[13]</td>
</tr>
<tr>
<td>Chondroitin</td>
<td>Inhibit proliferation, Anti-Metastasis</td>
<td>[5]</td>
</tr>
<tr>
<td>sulfate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scabraside</td>
<td>Activated Caspase 3</td>
<td>[4]</td>
</tr>
</tbody>
</table>

Induction apoptosis is one of the most prominent markers of cytotoxic antitumor agents. Some of the natural compounds from sea cucumber induce apoptotic pathways to inhibit cancer progression. Frondoside A induces apoptotic cell through increased expression of P53, and induction CASP9, CASP3, CASP7 cell death in breast cancer cells [4]. Cucumarioside demonstrated anticancer effects through its ability to cause the arrest of the cell cycle during the S phase and was shown to induce apoptosis [13].

Analysis of *B. argus* Active Compound Target Network

Sea cucumber contains several active compounds that potentially for anti-cancer [8]. The interaction among active compound and its protein target have been constructed (Fig. 1). The active compounds interacted with proteins that involve in the apoptosis, metastasis, and proliferation.

The network constructed is shown that several compounds from sea cucumber targets are proteins which play a role in breast cancer like MMP9, CASP9, TP53, CASP3, CHSY1. Some of the active compounds have direct interaction with a protein related to breast cancer and other compounds have indirect interaction. Frondoside A has direct interaction with Matrix metallopeptidase 9 (MMP9), and inhibit the growth of cancer cell [4,9,15]. MMP9 have interaction with several proteins such as TP53, BCL2, NFKB1, and BAX. The compound is capable of inducing apoptosis through various mechanisms, including the intracellular caspase, decreasing BCL2 and increasing CASP3 [16].

Chondroitin sulfate is one of the active compounds found in *B. argus* interact directly with several proteins like CHSY1, ARSB, and CSPG4. The compound is able to inhibit Chondroitin synthase-1 (CHSY1) expression that links to cell apoptosis and proliferation [17]. CHSY1 interact with CSPG4 responsible for regulating apoptosis and suppressing cell proliferation and metastasis [18]. Several compounds like Echinoside A whereas indirect interact with a protein that has a function for controlling cell cycle and apoptosis [12]. The active compounds in *B. argus* interacted with many proteins that involved in the cell cycle, metastasis, and apoptosis [19]. The ability of the active compounds in sea cucumber compounds to inhibit cancer cell can be modified to fit the genetic profile of cancer cells for the purpose of treatment.

CONCLUSION

The *B. argus* contains active compound such as Frondoside A, chondroitin sulfate, echinoside A, holothurin A, holothurin B, and scabraside. The compound has interaction with some of the proteins like MMP9, CASP9, TP53, CASP3, BCL2, BAX, NFKB1, and CHSY1 that play a role on cancer cell apoptosis, cell cycle and metastasis. The mechanism for killing cancer cells using the active compounds contained in sea cucumber *B. argus* has been investigated. Future researchers may conduct a study that develops treatment using the active compounds in *B. argus*.

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REFERENCES


