

## I. INTRODUCTION

### 1.1 Background

*Anguilla marmorata* is the most widespread anguillid species in the world (Arai and Chino, 2018). *A. marmorata* is also known as one of the fish that contain high nutrient and has delicious taste. In Japan, it is known as “unagi”. *A. marmorata* contains higher Omega-3 PUFAs, especially *eicosapentaenoic acid* (EPA) and *docosahexaenoic acid* (DHA) than other anguillid species. Polyunsaturated fatty acids (PUFA) in *A. marmorata* is 19.96% (DHA 9.14% and EPA 2.93%). While, *A. japonica* only contains 13.32% PUFA (DHA 6.93% and EPA 2.0%) (Ahn *et al.*, 2015) and *A. bicolor* contains 11.44% PUFA (DHA 5.16% and EPA 1.15%) (Widyasari *et al.*, 2014). Omega-3 PUFAs are produced by *A. marmorata* because the food source of this fish is microalgae, krill, and small fishes which contain high EPA and DHA (Cholewski, Tomczykowa and Tomczyk, 2018).

Omega-3 is an essential nutrient for the human body. It is usually used as dietary supplements in the form of fish oil (Oti-Boakye *et al.*, 2017). Omega-3 fatty acids have a beneficial effect in cardiovascular diseases, inflammatory diseases, asthma, allergy, and diabetes (Khan *et al.*, 2015). Omega-3 PUFAs also have the ability in prevention of cancers such as gastric cancer (Abedi *et al.*, 2020), pancreatic cancer (Fukui *et al.*, 2013), prostate cancer (Shin *et al.*, 2013), and breast cancer (Pizzato *et al.*, 2018). Omega-3 can affect tumor growth by alteration of cell cycle, change of membrane organization, inhibit angiogenesis, and alteration of gene expression (Ma *et al.*, 2019). Furthermore, as anti-cancer drugs, omega-3 has particular activity that

can be cytotoxic to tumor cells but little or no cytotoxicity to normal cells (D'Eliseo and Velotti, 2016). In addition, giving  $\omega$ -3 to cancer patients aims to provide nutritional support for cancer patients who suffer from weight loss, fatigue, inflammation, or post surgery complications (Wei, Wu and Chen, 2022).

One of the most commonly diagnosed cancer is breast cancer. Breast cancer is heterogeneous disease and various factors contributes to its incidence, such as population structure, lifestyle, genetic factors, and environment (Momenimovahed and Salehiniya, 2019). According to data from GLOBOCAN (Global Burden of Cancer) 2020, for both sexes combined, female breast cancer is the most commonly diagnosed cancer (2.3 million new cases, representing 11.7% of total cases) and it is the fifth leading cause of cancer mortality worldwide, with 685,000 deaths (6.9 % of all cancer cases) (Sung *et al.*, 2021). Currently, many efforts have been developed to reduce breast cancer incidence such as surgery, radiation therapy and systemic therapy (Harbeck *et al.*, 2019). However, radiation therapy and systemic therapy developed adverse events (Saini *et al.*, 2015) and surgery does not demonstrate any benefit in patient with metastatic breast cancer (Fitzal *et al.*, 2018). Therefore, the research to find the safety alternative treatments of breast cancer has been carried out by many researchers, one of which is fish oil as traditional medicine.

*A. marmorata* as one of the source of high omega-3 has threatening hazard because of the current conditions of water. Lately, various types of pollutants such as heavy metals, plastics, detergent waste and other chemicals that cause health problems are abundant and accumulate in the waters. Fish as bioaccumulate organism, accumulate toxic materials through their food chain in their fats and lipids

(Rawn *et al.*, 2006), and it is dangerous for consumers because it can counteract the positive effect of omega-3 fatty acids and pose risks (Briones and Lazaro-Lianos, 2015). In addition, the heavy metals contained in fish oil which is used as anti-cancer drugs are able to reduce the sensitivity of cancer cells during treatment by affecting the structure of cell membranes (Romaniuk *et al.*, 2017), inhibiting the repair of damaged DNA and increasing the invasion and metastasis of cancer cells (Yuan, Yang and Li, 2016).

Research on the use of fish oil (source of omega-3) as an anti-cancer has been carried out by several researchers. Schley, Brindley and Field (2007) found that treatment of fish oil (60  $\mu\text{mol/L}$  EPA + 40  $\mu\text{mol/L}$  DHA) to MDA-MB-231 cells decreased the number of live cells by 62%. Research on the effect of fish oil as anti-cancer drugs has been carried out by Ghosh-Choudhury *et al.* (2009), in which the results showed that giving 10% fish oil (Harlan Bioproducts) for 2 weeks to mice that had been inoculated with MDA MB-231 breast cancer cells in the mammary fat pads could inhibit breast tumor growth in 3 weeks. Furthermore, Davison *et al.* (2018), stated that addition of fish oil capsule (63% Omega-3; 51% EPA and 21.4% DHA) reduced the number of TamR and MCF-7 cells migrating after 48h by decreasing phospho-Src (p-Src) and COX-2 expression in both cell lines.

Research on *A. marmorata* fish oil as an anti breast cancer is still rarely done. Therefore, it is necessary to conduct further studies regarding to the test of heavy metal contents and it's potential as an anti breast cancer.

## 1.2 Problem Formulation

Based on the description of the background above, the researcher limits the problems to be discussed, namely:

1. How is the oil safety of giant mottled eel (*A. marmorata*) used in this study based on the heavy metal contents?
2. Does giant mottled eel oil (*A. marmorata*) have potential as an anti breast cancer?

## 1.3 Research Objectives

The aims of this research are:

1. To knowing the oil safety of giant mottled eel (*A. marmorata*) used in this study based on the heavy metal contents.
2. To get information about the potential of giant mottled eel oil (*A. marmorata*) as an anti breast cancer.

## 1.4 Significance of The Research

This research is useful to provide information for academics and the public about the oil quality of giant mottled eel (*A. marmorata*) and its potential as an anti breast cancer.

