Estrogen deficiency causes various health problems in postmenopausal women, including osteoporosis [1, 2]. Phytoestrogen emerged as a potential alternative of estrogen with minimum side effects. Phytoestrogens are a group of compounds derived from plants that have a structure similar to estrogen or can replace the function of estrogen in maintaining homeostasis in the brain, both in conjunction with estrogen receptors (ER-dependent) or not (ER-independent) [3], thus it is an alternative treatment for osteoporosis-induced estrogen deficiency [4].

C. cainito is one type of plant that is widely grown in East Java, Indonesia, and suspected contains phytoestrogen compounds [5]. This study aimed to analyze the metabolite profiling result of fractions of C. cainito through in silico study against 3OLS protein, an X-ray protein of ERβ. So, it can predict the types of the phytoestrogens contents which have antiosteoporosis property.

**MATERIALS AND METHODS**

- Download protein ERβ (ID: 3OLS) from PDB file and compounds from various extracts of C. cainito leaves.
- Preparation of internal ligand used Biovia Discovery Studio Visualizer 2016.
- Preparation structure compound from C. cainito extracts used Avogadro 1.0.1.
- Molecular docking internal ligand and compound from C. cainito extract with 3OLS protein used PyRx 0.8 (Autodock Vina).
- Visualize result of molecular docking with Biovia Discovery Studio Visualizer 2016.
- Analysis of the physicochemical properties of compounds predicted by ERβ agonists used the SwissADME webtool.

**RESULT**

![Figure 1. Internal ligand position after docking with 3OLS](image)

**DISCUSSION**

Extraction with various types of solvents was carried out on the dry powder of C. cainito leaves to separate the compounds based on their polarity, so that organic solvents with different polarity were selected. Separation aims to obtain data on the content of secondary metabolites in C. cainito leaves as a whole, to predict phytoestrogen compounds that are ERβ agonists.

A compound is classified as an ERβ agonist if it has a pharmacophore distance of about 10.862 Å, and has one pharmacophore group that binds to the amino acid His 475, and another pharmacophore group that binds to the amino acids Glu 305 or Arg 346. The binding affinity value was also calculated to show the stability of the compound in binding to the receptor [6]. From the results of this in silico study, it was shown that 11 compounds in C. cainito were an ERβ agonist.

Determination of physicochemical parameters of the 11 compounds was also carried out using the SwissADME web tool, to estimate the potential of the 11 compounds as oral antiosteoporosis drugs from the C. cainito leaves.

Phytoestrogens have a high potential to overcome estrogen deficiency-induced osteoporosis and maintaining the homeostasis of bone density. Phytoestrogens can bind to ERβ and causes the production of pro-osteoblastogenesis cytokines such as TGF-β, IGF-1, and IGF-2 in high amounts. Production of these cytokines will induce differentiation of preosteoblast into mature osteoblasts, and a massive bone formation process will occur. Besides, the increase in cytokines will also inhibit the differentiation of preosteoclast into mature osteoclasts, which causes inhibition of the bone resorption process [7,8,9].

**REFERENCES**