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COMPUTATIONAL STUDY OF GINGER (*ZINGIBER OFFICINALE*) AS E6 INHIBITOR IN HUMAN PAPILLOMAVIRUS TYPE 16 (HPV-16) INFECTION

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ABSTRACT : Cervical cancer caused by a high-risk type of HPV-16 infection, causing death for a woman due to not being treated early. However, some problems such as the high cost of chemotherapy trigger a new perspective on alternative treatments through natural ingredients. The chemical compound of *Zingiber officinale* has potential as an antiviral agent, but its specific molecular mechanism is unknown. This study will predict the molecular mechanism of chemical compounds from *Zingiber officinale* as an antiviral candidate for HPV-16 infection, through the *in silico* approach. Chemical compounds from *Zingiber officinale* in this study were obtained from the database, then molecular docking simulations, protein-ligand interaction analysis, and 3D molecular visualization were performed. We demonstrated that 6-gingerol in *Zingiber officinale* was predicted as a drug candidate because it has the lowest binding energy. The antiviral activity of HPV-16 from *Zingiber officinale* is very possible, through inhibiting the mechanism of E6 protein by 6-gingerol. We recommend these results of computational simulations in this study, can be used as a reference for drug design through *in vitro* and *in vivo* analysis.

Key words : Antiviral candidate, E6 inhibitor, HPV, *in silico*, *Zingiber officinale*.

INTRODUCTION

The death of women in the world is triggered by cervical cancer that occurs due to HPV infection (King *et al*, 2015). HPV has DNA as genetic material, these virus form including non-enveloped viruses, and is generally divided into two types based on pathogenicity when replicating in host cells (Liu *et al*, 2017). HPV is composed of two types of genes, such as early gene (E) and late (L) (Mirabello *et al*, 2016). It has different roles when replicating viruses, such as regulation of the replication process, growth of a tumor or cancerous lesions, and virus assembly (Bansal *et al*, 2016). The most vulnerable type triggers cervical cancer in women, one of which is HPV-16, which is considered high risk, while the low-risk type only produces warts when infecting someone (Ramakrishnan *et al*, 2015).

This viral infection disrupts the regulation of activation for tumor suppressor proteins such as p53 (Travé and Zanier, 2016). Specific oncoproteins in HPV-16 such as E6 work through binding with p53, thus triggering degradation via proteasomes (Tomaiæ *et al*, 2016). Study related to handling HPV-16 infections consists of prevention strategies through vaccination and therapy by administering antiviral drugs (Dadar *et al*, 2018).

Zingiber officinale or ginger is a plant that grows with rhizome and is often used in everyday life, such as drinks and cooking spices (Mao *et al*, 2019). Previous research revealed the chemical compound *Zingiber officinale* has antiviral activity against the human respiratory syncytial virus (HRSV) (Chang *et al*, 2013), hepatitis C virus (HCV) (Abdel-Moneim *et al*, 2013) and influenza (Raal *et al*, 2013). However, previous studies did not explain the molecular mechanism of the chemical compound of *Zingiber officinale* to act as an antiviral and to predict potential antiviral candidates for HPV.

The study of drug design requires a very long time, but in conducting prefix research on the potential of a plant as a drug candidate can be done through the *in silico* approach (March-Vila *et al*, 2017). Drug design simulation with *in silico* study is able to predict the mechanism of candidate drug compounds contained in a natural material, namely through several analyzes such